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Centro de Ciências Biológicas e da Saúde
Programa de Pós-graduação em Ciências da Saúde
Mestrado

ALTERAÇÕES GENÔMICAS GLOBAIS E EXPRESSÃO DIFERENCIAL DE MICRORNAS EM CARCINOMA PENIANO: VIAS MOLECULARES AFETADAS E POTENCIAIS ALVOS TERAPÊUTICOS

JENILSON MOTA DA SILVA

São Luís
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Dissertação apresentado ao Programa de Pós-graduação em Ciências da Saúde da Universidade Federal do Maranhão como requisito parcial para obtenção do título de Mestre em Ciências da Saúde.

Orientadora: Profa. Dra. Silma Regina Ferreira Pereira

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BANCA EXAMINADORA

_____

Profa. Dra. Silma Regina Ferreira Pereira
Universidade Federal do Maranhão

_____

Profa. Dra. Ana Paula Silva de Azevedo dos Santos
Universidade Federal do Maranhão

_____

Profa. Dra. Luciane Regina Cavalli
Instituto de Pesquisa Pelé Pequeno Príncipe

_____

Prof. Dr. Alexander Birbrair
Universidade Federal de Minas Gerais

“A ciência trabalha na fronteira entre conhecimento e ignorância.
Não temos medo de admitir o que não sabemos. Não há vergonha nisso.
A única vergonha é fingir que temos todas as respostas”
- Neil deGrasse Tyson -

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RESUMO

Em países desenvolvidos, o câncer de pênis (CaPe) é uma neoplasia rara. No entanto, em países em desenvolvimento a incidência é maior, como no Brasil, principalmente na região Nordeste, que se caracteriza por baixos níveis socioeconômicos e alta prevalência de infecção pelo papilomavírus humano (HPV). Alterações genéticas e epigenéticas têm sido estudadas em diversos tumores, porém o papel dos microRNAs (miRNAs) no estabelecimento e progressão do CaPe ainda não está claro, principalmente para aqueles associados ao HPV. Neste estudo, focamos em duas abordagens: 1) usamos array-CGH para identificar miRNAs localizados em citobandas com alterações no número de cópias (CNAs). Em seguida, análise de bioinformática foi usada para identificar potenciais vias celulares e alvos terapêuticos; 2) identificamos miRNAs diferencialmente expressos (miRDE) nos tumores usando a plataforma nCounter® Human v.3 miRNA Expression (Nanostring Technologies™, Seattle, WA, EUA). Em seguida, avaliamos o efeito do miRNAs nas redes de interações gênicas e alvos drogáveis usando as plataformas DIANA-tools, *STarMir*, KEGG (*Kyoto Encyclopedia of Genes and Genomes*), Pharmaco-miR e DGIdb (*Drug Gene Interaction Database*). A análise de aCGH identificou 269 miRNAs e 2,395 genes que foram mapeados em regiões contendo CNAs, 92,6% e 96,7% dos quais estavam em sítios de integração de HPV (HPVis), respectivamente. O enriquecimento de vias revelou cinco principais vias de sinalização (sinalização *hippo*, degradação de lisinas, biossíntese de mucinas tipo *O*-glicano, príons e proteoglicanos em câncer), bem como a via de carcinogênese associada à infecção por HPV. O painel de expressão global revelou 507 miRDE em comparação com tecidos penianos não-tumorais. Entre os miRNAs mais superexpressos e subexpressos (n=25), 92% são encontrados em HPVis. A análise de predição farmacogenômica pelo Pharmaco-miR e DGIdb com esses miRNAs identificou *EGFR*, *COX2*, *MDM2* e *MDM4* como potenciais alvos terapêuticos. Também realizamos a análise de previsão de alvos pelo *STarMir*, através do qual observamos que todos os 13 miRNAs superexpressos regulam negativamente os genes *TP53* e *RB1*, principalmente por meio de interações em regiões “seedless” não-canônicas. Observamos que *miR-1206*, *miR-376b-3p* e *miR-495-3p* são todos associados à invasão perineural, e destacamos o *miR-376a-2-5p* como possível marcador de prognóstico. Em conclusão, nossos achados indicam que o HPV está associado à desregulação de CNAs e miRNAs, perturbando vias de sinalização envolvidas no estabelecimento e progressão do tumor peniano mediado pelo HPV, o que abre perspectivas para novos potenciais alvos para o tratamento dos pacientes.

Palavras-chaves: câncer de pênis; vias celulares; marcadores moleculares; Papilomavírus humano

ABSTRACT

Penile cancer (PeCa) is a rare neoplasm in developed countries. However, its incidence is higher in developing ones, such as Brazil, particularly in the Northeast region, which is characterized by low socioeconomic levels and a high prevalence of human papillomavirus infection (HPV). Genetic and epigenetic alterations have been studied in several tumors, however the role of microRNAs (miRNAs) on the establishment and progression of PeCa is still unclear, especially for those associated with HPV. In this study we focused on two approaches: 1) we used array-CGH to identify miRNAs located at cytobands with copy number alterations (CNAs). Further, bioinformatics analysis were used to identify potential cellular pathways and therapeutic targets; 2) we identified differentially expressed miRNAs (miRDE) in the tumors using *nCounter® Human* v.3 *miRNA Expression* platform (*Nanostring Technologies™*, Seattle, WA, USA). After that, we assessed the effect of miRNAs on gene interaction networks and druggable targets using the DIANA-tools, *STarMir*, KEGG (*Kyoto Encyclopedia of Genes and Genomes*), Pharmaco-miR, and DGIdb (*Drug Gene Interaction Database*) platforms. The aCGH analysis identified 269 miRNAs and 2,395 genes that were mapped to regions containing CNAs, 92.6% and 96.7% of which were at HPV integration sites (HPVis), respectively. Pathway's enrichment revealed five major signaling pathways (*hippo* signaling, lysine degradation, *O*-glycan mucin biosynthesis, prions and proteoglycans in cancer), as well as the carcinogenesis pathway associated with HPV infection. The global expression panel revealed 507 miRDE compared to non-tumor penile tissues, of which 92% of the most overexpressed and underexpressed (n=25) are found in HPVis. Pharmaco-miR and DGIdb pharmacogenomic prediction analysis of those miRNAs identified *EGFR*, *COX2*, *MDM2* and *MDM4* as potential therapeutic targets. We also performed the *STarMir* target prediction analysis, whereby we found that all 13 overexpressed miRNAs downregulate *TP53* and *RB1*, primarily through non-canonical "seedless" regions. Furthermore, we describe miR-1206, miR-376b-3p and miR-495-3p associated with perineural invasion, and we highlight miR-376a-2-5p as possible prognostic marker. In conclusion, our findings indicate that HPV is associated with deregulation of CNAs and miRNAs, disrupting signaling pathways involved in the establishment and progression of HPV-mediated penile tumors, opening perspectives for new potential targets for the treatment of patients.

Keywords: Penile Cancer; Cellular Pathways; Molecular Markers; Human papillomavirus

LISTA DE SIGLAS E ABREVIATURAS

AGO	Argonauta
CaPe	Câncer de Pênis
CDS	Sequência Codificante
CEC	Carcinoma de Células Escamosas
CNA	Alteração de Número de Cópias
DGCR8	*DiGeorge syndrome critical region gene 8*
DNMT1	DNA-metiltransferase 1
EGFR	Receptor do Fator de Crescimento Epidermal
HPV	Papiloma Vírus Humano
KEGG	*Kyoto Encyclopedia of Genes and Genomes*
miRISC	Complexo de Silenciamento Induzido por miRNA
mRNA	RNA mensageiro
NGS	*Next-generation Sequencing*
OMS	Organização Mundial da Saúde
PAMPs	Padrões Moleculares Associados à Patógenos
pb	Pares de Base
Pré-miRNA	miRNA precursor
PRR	Receptor de Reconhecimento de Padrões
Ran-GTP	Proteína Nuclear Relacionada-Ras
shRNA	*Short Hairpin RNA*
TSmiR	miRNA Supressor de Tumor
UTR	Região não-traduzida
VEGF	Fator de Crescimento Endotelial Vascular
VEGFA	Fator de Crescimento Endotelial Vascular A

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1. INTRODUÇÃO

O câncer de pênis (CaPe) é uma doença com alta incidência em países com baixas condições socioeconômicas, como por exemplo, o Brasil, que registrou 5,7 casos por 100.000 pessoas-ano entre 1996 e 2006, sendo a terceira maior incidência mundial de câncer de pênis (MONTES CARDONA, GARCÍA-PERDOMO, 2017). Embora considerado raro em países desenvolvidos, a incidência de casos vem aumentando nas últimas décadas, principalmente em homens mais jovens (D'HAUWERS et al., 2012; HANSEN et al., 2018; KIDD et al., 2017).

A baixa incidência de casos de CaPe em países desenvolvidos tem como consequência o baixo número de trabalhos científicos se comparado, por exemplo, a outros cânceres (COELHO et al., 2018). Dessa forma, questões importantes a respeito da etiologia ainda são pouco conhecidas. Apesar disso, alguns fatores de risco têm sido associados a doença. Dentre eles, destaca-se a idade avançada, má higiene, presença de fimose, infecção pelo Papilomavírus Humano (HPV) e múltiplos parceiros sexuais (COELHO et al., 2018; SOARES et al., 2020).

O diagnóstico é geralmente feito por exames físicos, mas exames de imagem também podem ser realizados. O tratamento é baseado na remoção do tumor primário por excisão simples, penectomias parciais ou totais e, além do uso de quimioterápicos e radioterapia de acordo com a clínica do paciente (HAKENBERG et al., 2018a). Os métodos de diagnóstico de imagem são os menos invasivos, entretanto, possuem baixa especificidade e sensibilidade para detectar tumores primários e metástases linfonodais (HEYNS et al., 2010). Desta forma, identificar marcadores moleculares de baixo custo e pouco invasivos que possam auxiliar no diagnóstico preciso e prognóstico desse tipo de câncer é de suma importância.

Alterações genéticas em carcinoma peniano foram descritas anteriormente e tem sido associadas a gênese e progressão da doença (LA-TOUCHE et al., 2016). Nosso grupo de pesquisa demonstrou recentemente que os genes *TP53* e *RB1* são regulados negativamente em tumores penianos HPV-positivos, sugerindo que este vírus pode controlar a expressão das proteínas supressoras de tumor P53 e RB por outros mecanismos, além da via de sinalização canônica do HPV/*TP53*/*RB1*. Além disso, nosso estudo revelou que a amplificação dos genes *EGFR* e *ERBB3* é um dos mecanismos genéticos que podem estar envolvidos no estabelecimento e/ou progressão do câncer peniano associado à infecção por HPV de alto risco (MACEDO et al., 2020).

Além dos mecanismos citados, existem outros de regulação da expressão gênica que não afetam a sequência do DNA, porém, uma vez desregulados, podem desencadear processos

tumorigênicos. Nesse contexto, incluem-se as alterações epigenéticas, que são modificações potencialmente reversíveis, onde temos como exemplo a metilação do DNA, condensação do DNA por proteínas histonas e atividade de microRNAs (GRIFFITHS et al., 2016).

Os microRNAs (miRNAs) constituem uma classe de pequenos RNAs, não codificadores, expressos endogenamente capazes de regular a expressão de genes a nível pós-transcricional (O'BRIEN et al., 2018). Nesse contexto, a compreensão dos mecanismos moleculares envolvidos em algumas doenças, como por exemplo, no câncer, tornou-se mais complexa, uma vez que o envolvimento de miRNAs tornou-se mais visível. Além disso, os miRNAs vem sendo apontados como marcadores moleculares que podem apresentar perfis de expressão relacionados ao estabelecimento e progressão tumoral, podendo agir tanto como oncogenes quanto como supressores tumorais (MARCHI et al., 2017).

Vários miRNAs possuem sua expressão alterada em tecidos neoplásicos podendo estar regulados negativamente ou superexpressos. Dependendo de sua expressão, os miRNAs podem ser divididos em dois grupos gerais: os oncomiRs que possuem expressão aumentada em células neoplásicas e inibem a expressão de genes supressores de tumor, e os TSmiRs ou miRNAs supressores de tumor que possuem expressão reduzida ou basal (BANNO et al., 2014). Os poucos estudos realizados sobre miRNAs em CaPe demonstraram alterações semelhantes a outros cânceres (AYOUBIAN et al., 2021; FURUYA et al., 2021; HARTZ et al., 2016; KUASNE et al., 2017; PETA et al., 2017; PINHO et al., 2020; ZHANG et al., 2015), no entanto, os alvos desses miRNAs, bem como as vias moleculares afetadas e a relação com HPV não são totalmente conhecidas.

Portanto, levando em consideração a escassez de trabalhos sobre miRNAs em câncer de pênis, principalmente sobre os alvos e as vias moleculares envolvidas, nos propusemos a investigar o papel de miRNAs em vias moleculares possivelmente envolvidas no estabelecimento e progressão do carcinoma peniano.

2. REFERENCIAL TEÓRICO

2.1. Epidemiologia do Câncer de Pênis

Raro em países desenvolvidos e com uma alta incidência em países em desenvolvimento, o CaPe é uma neoplasia agressiva frequente em homens a partir de 40 anos, embora, recentemente, vem se observando um aumento de casos em homens mais jovens (ADASHEK, NECCHI, SPIESS, 2019; MACEDO et al., 2020). A frequência de CaPe em

países da Ásia, África e América do Sul é superior em comparação aos países do Nordeste Europeu e América do Norte (MONTES CARDONA, GARCÍA-PERDOMO, 2017). Apesar disso, estudos vêm demonstrando que países não impactados por grandes limitações socioeconômicas vem observando um aumento nas taxas de incidência e mortalidade de CaPe, principalmente em pacientes mais jovens (D'HAUWERS et al., 2012; HANSEN et al., 2018; KIDD et al., 2017). Mudanças no comportamento sexual que levam a uma maior exposição à infecção pelo HPV e o não uso de preservativos são explicações mais plausíveis para o aumento da incidência (HANSEN et al., 2018)

Na América do Sul a maior incidência é relatada no Brasil, com média de 5,7 casos a cada 100.000 homens-ano (1996-2006), sendo as regiões Norte e Nordeste do país aquelas que apresentam as maiores incidências (MONTES CARDONA, GARCÍA-PERDOMO, 2017). Para efeito de comparação, nos Estados Unidos (EUA) o número de casos da doença varia de 0,2-1,2 casos a cada 100.000 homens, correspondendo a 0,5% dos canceres que afetam os homens (CHRISTODOULIDOU et al., 2015).

No estado do Maranhão é relatado uma incidência de 6,15 casos por 100.000 homens e uma taxa anual bruta de 1,18 por 100.000 homens, caracterizando a região com a maior incidência no país e provavelmente no mundo. Acredita-se que a incidência no Maranhão seja ainda maior, fato que pode ser justificado pelos poucos serviços de referência disponíveis, impossibilitando a triagem efetiva dos pacientes, que em sua maioria são residentes de municípios do interior do Estado (COELHO et al., 2018).

2.2. Etiologia

Apesar do recente aumento de trabalhos sobre o CaPe, ainda não se conhece por completo os mecanismos relacionados ao surgimento e progressão da doença. Entretanto, alguns fatores de risco têm sido associados à doença. Dentre eles, destacam-se a idade avançada, má higiene, a presença de fimose, a infecção pelo HPV, inflamação crônica e o histórico de múltiplos parceiros sexuais (CHRISTODOULIDOU et al., 2015; COELHO et al., 2018). A maior parte dos homens com neoplasias de pênis está na faixa etária acima dos 40 anos, embora venha sendo observado o aumento da incidência em homens com idade abaixo dos 40 anos (ADASHEK, NECCHI, SPIESS, 2019; MACEDO et al., 2020).

A fimose é uma condição anatômica do pênis presente em homens não-circuncidados que impossibilita a retração do prepúcio para expor completamente a glande, sendo bastante

frequente entre os recém-nascidos. A presença da fimose intensifica a presença de esmegma e retém as células epidérmicas deixando a região propícia para a proliferação de microrganismos (SOARES et al., 2020). Um estudo populacional realizado em Porto Rico mostrou que a idade precoce de iniciação sexual somado a uma alta prevalência de múltiplos parceiros podem contribuir para o aumento das infecções de HPV e desenvolvimento de CaPe (COLÓN-LÓPEZ et al., 2012). Em CaPe o potencial carcinogênico do HPV se deve, principalmente, à atividade de suas oncoproteínas E1, E2, E5, e em especial a E6 e E7. As duas últimas interagem com importantes proteínas supressoras de tumor, a E6 interfere diretamente na P53, enquanto a E7 se liga a proteína do Retinoblastoma (pRB) mediando a ubiquitinação e sua degradação . Essas alterações levam a perda de controle do ciclo celular, indução da proliferação, inibição da apoptose e instabilidade genética (ALEMANY et al., 2016; MCBRIDE, WARBURTON, 2017; SAKAMOTO et al., 2019).

A inflamação crônica é um fator de risco que pode iniciar ou promover o câncer por meio da geração de espécies reativas de oxigênio e citocinas pró-inflamatórias e, inversamente, a inflamação pode ocorrer de forma secundária ao câncer afetando a progressão da doença (HAKENBERG et al., 2018b; HANAHAN, WEINBERG, 2011). O processo de inflamação pode estar associado a infecção pelo HPV ou pode ser um fator independente deste. O HPV é detectado por receptores de reconhecimento de padrões (PRR's) antes que as respostas imunes inatas possam ser desencadeadas (YONEYAMA, FUJITA, 2010). Os PRR's reconhecem especificamente padrões moleculares associados à patógenos (PAMP's) (KAWAI, AKIRA, 2006; KUMAR, KAWAI, AKIRA, 2011; THOMPSON et al., 2011) e, ativam cascatas de sinalização específicas para induzir a expressão gênica de alvos, incluindo a ativação de interferons tipo I e citocinas pró-inflamatórias (KAWAI, AKIRA, 2006; KUMAR, KAWAI, AKIRA, 2011).

Além da infecção pelo HPV a inflamação pode ser causada por outros microrganismos e lesões. A inflamação granulomatosa necrosante, por exemplo, tem sido associada à infecção não-sexualmente transmissível por micobactéria após instalação do Bacillus *Calmette-Guérin* (KURESHI et al., 2006; LESTRE et al., 2011; VENYO, 2015). Várias outras espécies bacterianas e leveduras sobre o prepúcio tem o potencial de causar condições inflamatórias (ARIDOGAN, IZOL, ILKIT, 2011). A balanite, uma lesão inflamatória da glande é comumente ocasionada pela falta de higiene, mas pode resultar também da exposição a medicamentos

comuns, como antibióticos e alérgenos, à preservativos de látex, ao propilenoglicol em lubrificantes, alguns espermicidas e corticosteroides (MORRIS, KRIEGER, 2017).

2.3. Aspectos Clínicos

O tipo histológico mais comum de CaPe é o Carcinoma de Células Escamosas (CEC), presente em 95% dos casos, e que se caracteriza por células queratinizadas com vários graus de atividades mitóticas (REIS et al., 2010). Entre os subtipos histológicos o mais frequente é o usual (48-65%) seguido pelo condilomatoso (~17%), verrucoso (~8%), papilar (~7%) e basalóide (~5%) (CHAUX et al., 2010).

Histologicamente, o CaPe apresenta padrões teciduais semelhantes aos demais carcinomas epidermóides, apresentando graus histológicos bem, moderadamente e pouco diferenciados (CUBILLA et al., 2012). Embora o algoritmo de diagnóstico primário não tenha mudado significativamente nos últimos anos, o sistema de estadiamento foi revisado de forma significativa. O sistema TNM, sigla em inglês para *Tumor-Node-Metastasis* é usado para o estadiamento do câncer de pênis (Tabela 1), proposto e revisado pela *American Joint Comittee on Cancer* (AJCC) e a *International Union Against Cancer* (IUAC) (MARCHIONI et al., 2018).

Tabela 1. Sistema de classificação TNM para Câncer de Pênis de acordo com o *American Joint Comitee on Cancer* (AJCC) e a *International Union Against Cancer* (IUAC), 2017.

	Estadiamento para o Aspecto do Tumor Primário (T)
pTx	Tumor primário não pode ser avaliado
pT0	Sem evidência de tumor primário
pTis	Carcinoma *In Situ*
pTa	Carcinoma verrucoso não invasivo, não associado com invasão destrutiva
pT1	Tumor invade tecido conectivo subepitelial
pT1a	Tumor invade tecido conectivo subepitelial sem invasão linfovascular, não é pobremente diferenciado ou indiferenciado
pT1b	Tumor invade tecido conectivo subepitelial com invasão linfovascular ou é pobremente diferenciado ou indiferenciado
pT2	Tumor invade corpo esponjoso ou corpo cavernoso
pT3	Tumor invade uretra
pT4	Tumor invade estruturas adjacentes

Estadiamento para Invasão de Linfonodos (N)	
pNx	Linfonodos não podem ser avaliados
pN0	Sem metástases em linfonodos regionais
pN1	Metástases intranodal em um único linfonodo inguinal
pN2	Metástases em múltiplos linfonodos ou linfonodos inguinais bilaterais
pN3	Metástases em linfonodo(s) pélvico(s), unilateral ou bilateral ou extensão extranodal das metástases linfonodais regionais.
Estadiamento para Invasão de outros Tecidos/Órgãos (M)	
M0	Sem metástases a distância
Mx	Não pode ser avaliado
M1	Metástases à distância
Estadiamento para Grau Histológico	
Gx	Grau ou diferenciação não pode ser avaliado
G1	Bem diferenciado
G2	Moderadamente diferenciado
G3 – G4	Pobremente indiferenciado ou indiferenciado

Fonte: Adaptado de EDGE et al., (2017)

Além da classificação anterior que é exclusivamente baseada na morfologia da célula, a Sociedade Internacional de Patologia Urológica apresentou à Organização Mundial da Saúde (OMS) em 2016, uma nova classificação baseada na distinção clinicopatológica em relação a infecção pelo HPV. Com isso, a nova divisão classifica os tumores em tipos não relacionados ao HPV e tipos relacionados ao HPV. O tipo de CEC não relacionado ao HPV mais comum é o usual, seguido pelos papilares, adenoescamoso e sarcomatóide, este último com o pior prognóstico dentre todos os carcinomas penianos. O principal fator de risco associado a esses subtipos é a inflamação crônica discutida no tópico anterior (HAKENBERG et al., 2018b). Por outro lado, os tipos de CEC relacionados ao HPV são os basalóides, verrucosos ou condilomatosos, verrucosos basalóides e os raros tipos basalóides papilares (MOCH et al., 2016).

2.4. Sintomas, Diagnóstico e Tratamento

Os principais sintomas clínicos do CaPe são alterações na cor e espessura da pele, formação de nódulos, feridas ou úlceras persistentes com ou sem sangramento, odor fétido e

prurido intenso. Os sintomas podem surgir isoladamente ou acompanhados de outros, mas que ao longo do tempo vão se acumulando (AMERICAN SOCIETY OF CLINICAL ONCOLOGY, 2017a).

O diagnóstico é geralmente feito por exames físicos e biópsias. Enquanto que os exames de imagem, como os raios-x, tomografia computadorizada e ressonância magnética são geralmente utilizados para indicar o estadiamento, mas também podem ser usados para acompanhar o diagnóstico (HAKENBERG et al., 2018a). Apesar de o diagnóstico por imagem ser um método menos invasivo ele possui baixa especificidade e sensibilidade para detectar tumores primários e metástases linfonodais (HEYNS et al., 2010).

As opções atuais de tratamento para malignidades e pré-malignidades urogenitais está relacionada ao estadiamento da doença, morbidade e toxicidade do tratamento (RAFAEL et al., 2022). Em CaPe o tratamento é baseado principalmente na remoção do tumor primário por excisão simples, penectomias parciais ou totais (AMERICAN SOCIETY OF CLINICAL ONCOLOGY, 2017b). Por outro lado, as cirurgias são frequentemente associadas à altas taxas de morbidade devido à complicações pós-operatórias, como linfedema, infecções, problemas psicossociais e psicossexuais (GAARENSTROOM et al., 2013; HAKENBERG et al., 2018a; HEYNS, MENDOZA-VALDÉS, POMPEO, 2010; THOMAS et al., 2021). Em estágios mais avançados o tratamento cirúrgico é acompanhado com imunoterapia tópica, quimioterapia (imiquimode, 5-fluorouracil, cisplatina, doxorrubicina, ifosfamida, metotrexato e paclitaxel) e radioterapia. (HAKENBERG et al., 2018a; MANJUNATH et al., 2017; NECCHI et al., 2017; O'BRIEN et al., 2017; PROTZEL, HAKENBERG, 2009). Em casos de comprometimento linfonodal é realizado a linfadenectomia unilateral ou bilateral (ZHANG et al., 2017). As linfadenectomias podem ainda ser realizadas como medidas profiláticas, uma vez que 20% dos linfonodos clinicamente negativos podem possuir metástases ocultas (CHIPOLLINI et al., 2017).

Os CEC são geralmente tumores radiossensíveis. Assim, os carcinomas de células escamosas de pênis podem, em princípio, ser tratados por radioterapia percutânea ou braquiterapia focal. No entanto, devido à falta de dados sobre a radiossensibilidade e a resistência de CEC de pênis, nenhum tratamento diferenciado com radioterapia pode ser indicado e os casos devem ser avaliados individualmente (HAKENBERG et al., 2018a). A resistência à quimio e radioterapia em CaPe está relacionada dentre vários fatores a aspectos genéticos e moleculares (DENIS et al., 2021; IBILIBOR et al., 2022). Desta forma, a

identificação de marcadores moleculares que possam auxiliar no diagnóstico preciso, prognóstico e tratamento desse tipo de câncer é de grande importância para garantir um tratamento adequado e uma sobrevida livre de doença para os pacientes. Em nosso estudo (MACEDO et al., 2020), mostramos que *EGFR* (Receptor do Fator de Crescimento Epidermal) é afetado por ganho no número de cópias gênicas, além de estar superexpresso em CEC de pênis. Por isso, sugerimos o uso de inibidores de EGFR como tratamento para pacientes com CaPe com superexpressão de EGFR. Interessantemente, um estudo recente (KUASNE et al., 2021), mostrou que o crescimento de células derivadas de CaPe com superexpressão de EGFR foi inibido por inibidores de EGFR (cetuximabe, gefitinibe e erlotinibe).

Nos últimos anos, a busca por biomarcadores de diagnóstico, prognóstico e tratamento se voltou em parte para o epigenôma e, em especial, para os microRNAs. Os microRNAs são pequenas moléculas endógenas que desempenham uma série de funções biológicas, que podem apresentar perfis de expressão diferenciados em algumas doenças e que podem ser identificados e quantificados em tecidos e fluídos corporais (HAMMOND, 2016).

2.5. MicroRNAs: Biogênese e Função

Os microRNAs (miRNAs ou miRs) são pequenas moléculas endógenas de RNA fita simples formadas por aproximadamente de 18 a 25 nucleotídeos, não-codificadoras de proteínas, mas que possuem a capacidade de regular a expressão de genes a nível pós-transcricional, ou seja, a nível do RNA mensageiro (mRNA) além de possuir diversas funções biológicas (O'BRIEN et al., 2018).

Genes de miRNAs são genes não-codificadores, cujo único produto transcricional é o miRNA. Em alguns casos, o miRNA está localizado dentro de um íntron ou região não-traduzida (UTR) de um gene codificador de proteína (HAMMOND, 2016). A via canônica de biogênese é a via dominante pela qual os miRNAs são processados, nesse aspecto os miRNAs são transcritos no núcleo celular pela RNA polimerase II ao longo de todo o genoma como longas cadeias lineares, denominadas priRNAs ou microRNAs primários. Os priRNAs sofrem processos de clivagem pela RNAse III (enzima Drosha) e seu cofator DGCR8 (*DiGeorge Syndrome Critical Region 8 Gene*), adquirindo um tamanho médio de 70 nucleotídeos. Os agora chamados miRNAs precursores (pré-miRNAs) adquirem um formato de grampo (*hairpin*), ocasionado pela complementariedade parcial de bases. Nessa etapa, os pré-miRNAs são transportados para o citoplasma celular com o auxílio das proteínas Exportina-5 e Ran-GTP

(Proteína Nuclear Relacionada-Ras). No citoplasma os pré-miRNAs são clivados pela enzima RNAse III (Dicer), adquirindo um tamanho médio de 20 pares de bases (pb). Esse processamento envolve a remoção do *loop* terminal, resultando em um duplex miRNA maduro. Cada uma das sequências desse duplex podem ser reconhecidas e incorporadas ao complexo proteico RISC (Complexo de Silenciamento Induzido por RNA) e então se ligar ao seu mRNA alvo (HAMMOND, 2016; O'BRIEN et al., 2018) (Figura 1).

Embora a maioria dos miRNAs identificados seja produzida pela via canônica descrita acima, existem outros exemplos de biogênese alternativa. Essas vias fazem uso de diferentes combinações de proteínas envolvidas na via canônica, principalmente Drosha, Dicer, Exportinas, Ran-GTP e AGO1-4 (Argonautas 1-4). Em geral, a biogênese de miRNAs por vias não-canônicas pode ser agrupadas em vias independentes de Drosha/DGCR8 e independentes de Dicer (O'BRIEN et al., 2018). Um exemplo de miRNAs produzidos pela via independente de Drosha/DGCR8 são os miRtrons, nesse caso os pré-miRNAs são gerados a partir de íntrons do mRNA durante o *splicing* (RUBY et al., 2007). Outro exemplo deste modelo são os pré-miRNAs com 7-metilguanosina [(m^7G)-capa], que são exportados diretamente para o citoplasma através da Exportina-1 sem a necessidade de clivagem por Drosha (XIE et al., 2013).

Na via não-canônica independente de Dicer, os miRNAs são processados por Drosha/DGCR8 a partir de transcritos endógenos de RNA conhecidos como shRNA (*short hairpin RNA*) (YANG et al., 2010). Após a clivagem por Drosha/DGCR8 o pré-miRNA por ter um tamanho insuficiente para ser substrato de Dicer acaba por se ligar diretamente a proteína Argonauta-2 (AGO2) para completar sua maturação. O conhecimento dessas vias não-canônicas é de particular relevância em estudos que envolvem o nocaute de Drosha/DGCR8 ou Dicer (O'BRIEN et al., 2018). Todos os mecanismos de biogênese canônica e não-canônica são mostrados na Figura 1.

A maioria dos estudos sobre miRNAs estão focados na sua capacidade de inibir a expressão gênica. Essa regulação pós-transcricional é decorrente da interação entre o complexo de silenciamento induzido por miRNA (miRISC) e o mRNA alvo (O'BRIEN et al., 2018). Essa interação é determinada por regiões conhecidas como "seeds" presentes nos miRNAs maduros, sendo compostas por 2 a 9 nucleotídeos, e que se iniciam a partir do 2º nucleotídeo da extremidade 5' do miRNA (FLAMAND et al., 2017; LAL et al., 2009; SHIN et al., 2010). Quando o pareamento da sequência seed do miRNA com os sítios do mRNA é total, o complexo miRISC é induzido a clivar o mRNA entre o 10º e 11º pb pareado. Contudo, se o pareamento

das sequências for parcial, ocorrerá somente a repressão da região e impedimento da tradução do mRNA (HAMMOND, 2016). Além das regiões seed os miRNAs podem se ligar ao mRNA alvo por meio de regiões não-canônicas conhecidas como seedless (FLAMAND et al., 2017; LAL et al., 2009; SHIN et al., 2010).

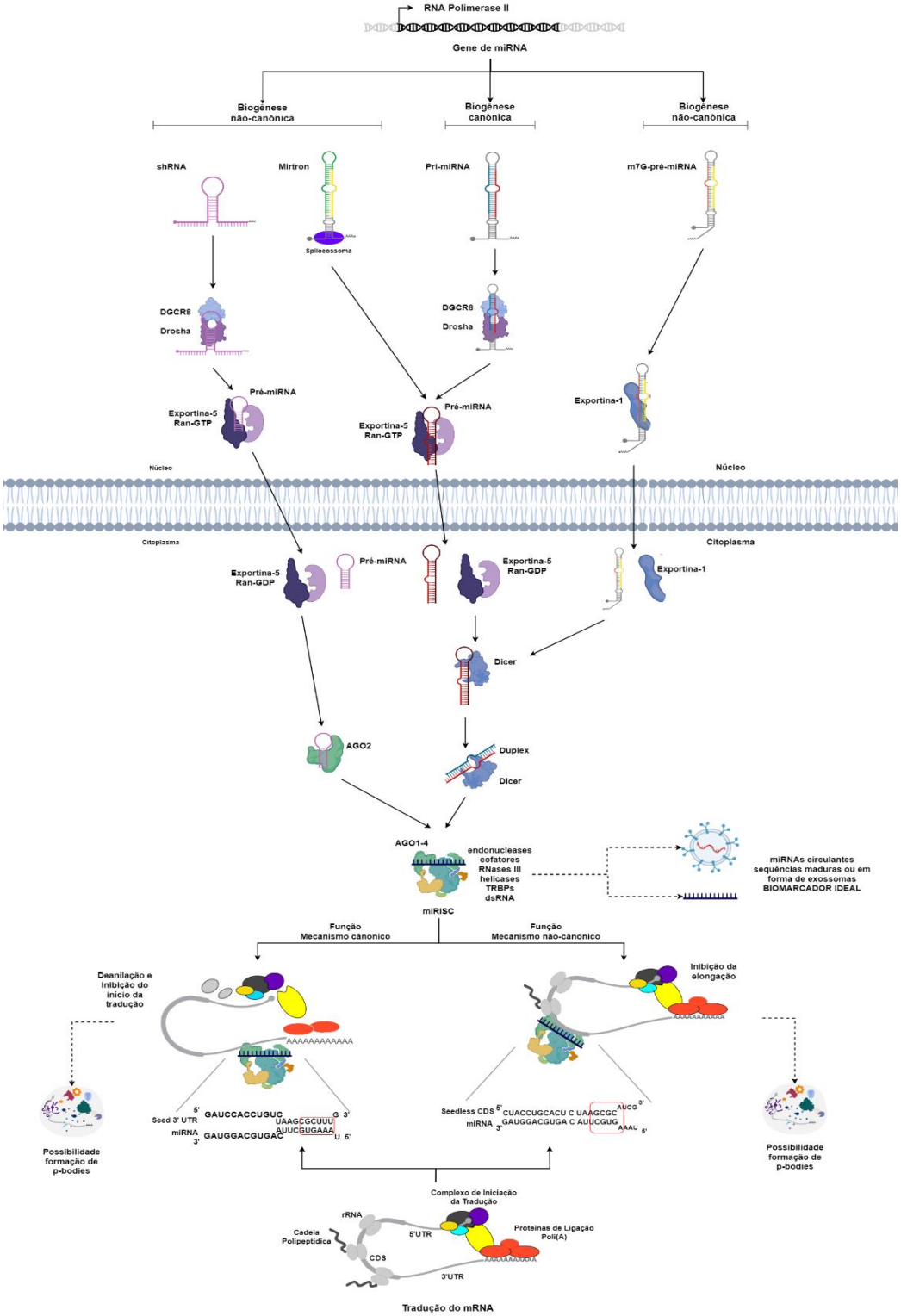

Figura 1. Biogênese e mecanismo de ação dos microRNAs. A biogênese canônica do miRNA começa com a geração do transcrito do pri-miRNA. O complexo Drosha/DGCR8, cliva o pri-miRNA para produzir o pré-miRNA. O pré-miRNA é exportado para o citoplasma de forma dependente de Exportin5-RanGTP e processado para produzir o duplex de miRNA maduro. As fitas 5p (5') ou 3p (3') do duplex são carregadas por proteínas Argonautas (AGO) para formar um complexo de silenciamento induzido por miRNA (miRISC). Em vias não-canônicas, shRNAs são processados através de clivagem dependente de AGO2, mas independente de Dicer. Mirtrons são exportados via Exportina 5-RanGTP, enquanto, m^7G-pré-miRNA são exportados via Exportina 1. Todas as vias levam a um complexo miRISC funcional. MiRNAs podem ser expelidos pela célula se tornando elementos circulantes em tecidos e fluídos corporais. O mecanismo de ação canônico dos miRNAs ocorre quando o miRISC se liga aos mRNAs alvos para induzir a inibição da tradução. O processo de ligação ocorre geralmente por meio de sequências altamente conservadas "seed" que compreendem os nucleotídeos 2-8 da extremidade 5' do miRNA maduro (sequência 5p ou 3p). Dependendo do tipo de ligação o miRISC recluta proteínas que induzem a desadenilação do mRNA. O mecanismo de ação não-canônico ocorre por meio de qualquer ligação que não seja por meio das regiões seed. Nesse caso, o miRNA pode se hibridizar nas três regiões do mRNA alvo (3'UTR/5'UTR/CDS). Como efeito, ligações seedless impedem que a elongação da cadeia polipeptídica seja concluída, formando em alguns casos proteínas deformadas. Em ambos mecanismos, miRISC-mRNA pode ser levado para regiões de armazenamento e processamento conhecido como *p*-bodies. Fonte: criado pelo autor.

Estudos iniciais haviam demonstrado que as regiões UTRs do mRNA eram os únicos sítios de pareamento dos miRNAs. No entanto, HAUSSER et al. (2013) propuseram que além dos sítios das regiões UTRs, as regiões CDS (Sequências Codificantes) também possuem sítios que funcionam através de mecanismos semelhantes e têm um impacto comparável na expressão gênica. Suas evidências mostraram que as regiões CDS desencadeiam processos mais potentes para a inibição da tradução, enquanto os sítios localizados em UTRs são mais eficientes no desencadeamento da degradação do mRNA. Os dois processos celulares seriam combinados para deixar a regulação pós-transcricional mais flexível quanto ao tempo e magnitude. Todos os mecanismos são mostrados na Figura 1.

O miRISC e seus mRNAs cognatos não degradados podem ainda se aglomerar e formar sítios citoplasmáticos conhecidos como *P-bodies*, os quais podem variar quanto ao tamanho e ao número dentro da célula, além de serem altamente móveis (LUO et al., 2018). Além disso, os *P-bodies* são formações reversíveis, funcionando somente como regiões de estocagem de

miRISCs e mRNAs reprimidos, que podem ser recuperados para tradução ou degradados (KROSCHWALD et al., 2015).

Os miRNAs podem ainda ser liberados em fluídos extracelulares o que reforça ainda mais o seu potencial uso como biomarcadores não-invasivos em uma variedade de doenças (HAMMOND, 2016). Os miRNAs extracelulares são altamente estáveis, resistindo a degradação à temperatura ambiente por até 4 dias e a condições deletérias, como ebulição, congelamento, descongelamentos múltiplos e alterações bruscas no pH. Além disso, os miRNAs podem ser encontrados em vesículas como exossomas, microvesículas e corpos apoptóticos, podendo estar associados ou não a proteínas (O'BRIEN et al., 2018). Nas células-alvo esses miRNAs circulantes podem atuar como reguladores parácrinos modulando as atividades celulares. Nesse sentido, os miRNAs podem também desempenhar atividades semelhantes a hormônios (IFTIKHAR e CARNEY, 2016).

2.5.1. MicroRNAs em Câncer

Desde a descoberta do primeiro microRNA, *lin-4*, por LEE et al. (1993) em *Caenorhabditis elegans*, os miRNAs vêm sendo amplamente estudados devido ao seu potencial de silenciamento de mRNAs, evidenciando-os como potenciais biomarcadores de diagnóstico e prognóstico no câncer (HAMMOND, 2016). A primeira evidência relacionando miRNAs com câncer foi feita por CALIN et al. (2002), os quais descreveram uma deleção na região 13q14, frequente em pacientes com Leucemia Linfocítica Crônica (LLC), que envolve os genes de miRNAs *MIR-15* e *MIR-16-1*.

Os miRNAs envolvidos em processos neoplásicos são divididos em dois grupos principais, os oncomiRs (miRNAs oncogênicos) e os TSmiRs (miRNAs supressores de tumor) (ENIAFE, JIANG, 2021). Enquanto os oncomiRs possuem expressão aumentada em células neoplásicas, os TSmiRs possuem expressão reduzida. Os oncomiRs inibem a expressão de genes supressores de tumor, controlando a diferenciação celular e apoptose, enquanto os TSmiRs regulam negativamente a expressão de oncogenes.

Alterações na expressão e no número de cópias de miRNAs foram relatadas em diversas neoplasias. LUPICKI et al. (2018), por exemplo, relataram em câncer de mama o potencial impacto de 93 miRNAs alterados em pelo menos 15 vias moleculares. Ainda em câncer de mama, por meio de uma análise integrada foi possível identificar um painel de 17 miRNAs, com alto poder discriminatório entre tipos tumorais triplo negativos e não triplo negativos,

sendo alguns desses miRNAs significativamente associados ao grau tumoral (SUGITA et al., 2019).

Em CaPe o primeiro estudo em larga escala sobre miRNAs demonstrou padrões de expressão semelhantes a outros cânceres do sistema geniturinário (ZHANG et al., 2015). A análise evidenciou um grande número de miRNAs desregulados em tumores penianos, sendo alguns desses miRNAs diferencialmente expressos, quando comparados com a expressão em tecidos normais e adjacentes. Usando um painel de miRNAs em CaPe, Barzon et al. (2014) identificaram a subexpressão dos *miR-23b*, *miR-145*, *miR-146a* e *miR-218* e a superexpressão do *miR-196a*, com esse último sendo significativamente associado a um grau mais avançado da doença.

Análises integradas entre miRNAs e mRNAs também foram capazes de identificar algumas vias moleculares relacionadas ao desenvolvimento e progressão do CaPe (KUASNE et al., 2017). Nessas análises, o *miR-424-5p* além de afetar os processos de angiogênese é um regulador de *FGFR1*, um dos principais genes envolvidos na via de sinalização VEGF (Fator de Crescimento Endotelial Vascular). Embora o papel de *VEGF* e da angiogênese permaneça inexplorado no CaPe, o envolvimento das vias dos fatores de crescimento epidermais foi relatado, como por exemplo, a do *EGFR* (Receptor do Fator de Crescimento Epidermal) (MACEDO et al., 2020) e do *VEGFA* (Fator de Crescimento Endotelial Vascular A) (FURUYA et al., 2021).

Redes de interações entre miRNAs e genes diferencialmente expressos foram descritos com a capacidade de discriminar com alta acurácia tecidos tumorais e não-tumorais de pênis (FURUYA et al., 2021). Baseado nas diferenças em que os miRNAs podem ter entre subtipos teciduais, AYOUBIAN et al (2021) investigaram o perfil de expressão de miRNAs no contexto dos tipos histológicos de tumores de pênis HPV-positivo. Os autores não identificaram diferenças nos níveis de expressão de miRNAs entre tecidos tumorais e normais e, apesar disso, sugeriram que 95 miRNAs são diferencialmente expressos no tipo usual HPV-negativo enquanto 247 miRNAs, nos subtipos basalóides/verrucosos HPV-positivo. Um painel de 118 miRNAs desregulados entre tumores metastáticos e não-metastáticos de pênis também foi sugerido pelos autores (AYOUBIAN et al., 2021). Apesar desses estudos terem apresentado resultados que relacionam miRNAs a HPV, todos os trabalhos possuem coortes majoritariamente HPV-negativos, com métodos de detecção viral limitados à alguns subtipos. Além disso, as análises de enriquecimento de vias direcionam a vias sem relação direta com a

infecção por HPV. Dessa forma, ainda há escassez de trabalhos sobre o papel de miRNAs na carcinogênese peniana associada à HPV.

2.5.2. Relação microRNAs-HPV

Aproximadamente 15-20% dos 12,7 milhões de casos de câncer por ano são atribuídos à infecções e, 9.9% têm uma etiologia viral (PLUMMER et al., 2016; ZAPATKA et al., 2020). Mais recentemente, estudos sobre o epigenoma do câncer vem destacando o papel dos vírus tumorais, em particular o HPV, no desenvolvimento e progressão da doença. As proteínas virais E6 e E7 do HPV são consistentemente expressas em lesões e cânceres associados ao HPV e são os principais impulsionadores da transformação celular (ANNA SZYMONOWICZ, CHEN, 2020; DE MARTEL et al., 2017; MESRI, FEITELSON, MUNGER, 2014). As proteínas E6 e E7 não possuem atividades enzimáticas e, em vez disso, funcionam associando-se às proteínas celulares do hospedeiro (ANNA SZYMONOWICZ, CHEN, 2020; MESRI, FEITELSON, MUNGER, 2014). As oncoproteínas E6 e E7 do HPV de alto risco também interagem com diversas outras proteínas, tais como fatores de transcrição, alterando assim a expressão gênica celular e, além disso, conseguem controlar os mecanismos epigenéticos (ANNA SZYMONOWICZ, CHEN, 2020; DE MARTEL et al., 2017).

Um dos mecanismos epigenéticos mais importantes regulado pelas oncoproteínas virais é a metilação do DNA. A oncoproteína E7 se liga a DNMT1 (DNA metiltransferase 1) e estimula sua atividade (BURGERS et al., 2007), e pode também ativar a transcrição de *DNMT1* através da via pRB/E2F (ANNA SZYMONOWICZ, CHEN, 2020). Além disso, E6 regula positivamente *DNMT1* pela supressão de P53 (YEUNG et al., 2017). Como consequência do controle desse mecanismo, a expressão da *E*-caderina é suprimida e a adesão entre células epiteliais escamosas é reduzida (D'COSTA et al., 2012).

Além da metilação do DNA, o HPV consegue regular globalmente a expressão dos miRNAs, seja por regulação direta, por metilação ou por controle de redes de interações gênicas. Uma das primeiras evidências dessa relação miRNAs-HPV foi identificada por WANG et al. (2008), que observaram uma baixa expressão do *miR-34a* em linhagens celulares de câncer de cérvix infectadas com HPV de alto risco. A redução na expressão ocorre exatamente na fase inicial de reprodução do vírus, quando é verificada a redução da proteína supressora de tumor P53 pela atividade da oncoproteína E6. WANG et al. (2008) também observaram que a oncoproteína E7 do HPV16 regula positivamente a expressão do *miR-21*.

O HPV também interfere em vias extremamente complexas como a do eixo *KDM5C* / *LNC_000231* / *miR-497-5p* / *CCNE1* descrito por ZHANG et al. (2020), no qual a oncoproteína E6 desestabiliza KDM5C, desencadeando a modificação H3K4me3 (trimetilação no 4º resíduo de lisina da proteína histona H3) na região promotora de *LNC_000231*, ativando sua expressão. A ativação de *LNC_000231* suprime a expressão do *miR-497-5p* e mantem a expressão da ciclina E1 (*CCNE1*). Esse eixo, uma vez alterado por E6, promove a proliferação celular, formação de colônias de células cancerosas cervicais e a formação de tumor.

Em CEC de pênis *miR-146a* apresentou níveis menores de expressão quando associado a HPV16 e a superexpressão de *EGFR*, sugerindo que esse miRNA exerce uma atividade supressora de tumor, tendo como alvo *EGFR* (PETA et al., 2016). Adicionalmente, Barzon et al. (2014) mostraram que *miR-218*, em CEC de pênis, tem sua expressão diminuída, relacionada com a capacidade de E6 hipermetilar a região promotora do gene *SLIT2*. Em câncer colorretal esse miRNA regula negativamente a angiogênese e a transição epitélio-mesênquima, através da inibição da expressão do Fator de Crescimento do Tecido Conjuntivo (*CTGF*) (LUN et al., 2018) e, além disso, consegue promover a apoptose tendo como alvo a proteína anti-apoptótica c-FLIP (MENG et al., 2018). Recentemente, AYOUBIAN et al. (2021) identificaram um painel de miRNAs diferencialmente expressos entre tumores de pênis HPV-positivo e HPV-negativo. Curiosamente, 99.1% dos miRNAs foram regulados negativamente. Apesar disso, o estudo não conseguiu identificar diferenças entre os níveis de expressão entre tecidos tumorais e normais, e não apresentou explicações plausíveis para essa limitação.

A via PI3K/Akt desempenha um papel essencial em vários cânceres associados ao HPV. A atividade dessa via é significativamente aumentada pela ação das oncoproteínas E6 e E7, causando a ativação de *EGFR* e, consequentemente, a ativação da cascata MAPK/ERK. Ambas, PI3K/Akt e MAPK/ERK, acabam por regular grande parte dos processos de crescimento, invasão e metástase de células cancerosas. O *miR-125b* é um dos que regulam o crescimento celular, atuando sob a via PI3K/Akt, no entanto, ele é um alvo crítico de E6 (ZHU et al., 2018). Os genes MAPK1 e MAPK4 são elementos-chave da via MAPK/ERK e são regulados negativamente pelos *miR-329-3p* e *miR-200c*, respectivamente (LI et al., 2017; MEI et al., 2018), no entanto, são frequentemente desregulados pela atividade de E5 (BARBU et al., 2020).

2.6. A Pesquisa Prospectiva *Pan-Cancer*

Desde a identificação do primeiro miRNA em *C. elegans*, pesquisadores estudaram os mecanismos regulatórios entre os miRNAs e os seus genes alvos de forma abrangente. Por exemplo, metodologias baseadas em sequências canônicas de miRNAs foram propostas para prever suas relações regulatórias (AGARWAL et al., 2015; TONG, RU, ZHANG, 2018). No entanto, essas metodologias não permitiram identificar com precisão a relação reguladora do gene-miRNA. Mas, com o desenvolvimento da tecnologia de sequenciamento, um grande número de dados de expressão de miRNAs de inúmeras espécies foi acumulado (por exemplo, aqueles disponíveis no repositório de banco de dados *Gene Expression Omnibus*) (BARRETT et al., 2012).

A partir do momento em que miRNAs foram associados ao câncer e foram identificados alterados em diversos deles, pesquisas prospectivas do tipo "*pan-cancer*" foram iniciadas com o objetivo de identificar semelhanças e/ou diferenças moleculares entre cânceres que compartilham entre si semelhanças histológicas e causais (CHEN et al., 2018; MA et al., 2018; MIN et al., 2021; TAN et al., 2019). O *The Cancer Genome Atlas* (TCGA) (HOADLEY et al., 2018) e NCI-60 (MARSHALL et al., 2017) possuem dados inestimáveis e fornecem novos paradigmas para explorar o relacionamento regulatório do gene-miRNA em diferentes tipos de cânceres.

Desde 2012 comparações entre carcinomas de células escamosas (DOTTO, RUSTGI, 2016; HOADLEY et al., 2014) sugeriram que tumores de diferentes tipos locais compartilham algumas assinaturas moleculares comuns e diferentes, o que também foi corroborado posteriormente (CANCER GENOME ATLAS NETWORK, 2015; CANCER GENOME ATLAS RESEARCH NETWORK, 2012; THE CANCER GENOME ATLAS RESEARCH NETWORK, 2014, 2017a, 2017b). Esses estudos destacaram alterações genômicas de potencial interesse biológico ou terapêutico que são comuns e diferentes entre tumores de células escamosas.

A tradução e interpretação dos resultados da pesquisa molecular na terapia do câncer provou ser bem-sucedida, mas continua sendo um desafio (THE CANCER GENOME ATLAS RESEARCH NETWORK, 2017a, 2017b). Isso é particularmente ambicioso para cânceres raros e mortais, como o CEC de pênis. Novas evidências moleculares podem ser valiosas para melhorar o prognóstico, identificar alvos de terapia e avaliar semelhanças entre o CaPe e outros tumores de células escamosas. Até o momento apenas um estudo original (CHAHOUD et al.,

2021) comparou o perfil molecular geral e 13 genes diferencialmente mutados em CaPe com outros carcinomas de células escamosas. CHAHOUD et al. (2021) observaram que o CEC de pênis compartilha considerável semelhança molecular e histológica com o câncer de células escamosas de cabeça e pescoço (HNSC), especificamente variantes somáticas em genes participantes da via Notch. Essas semelhanças podem fornecer novas estratégias molecularmente direcionadas para CEC de pênis por meio de ensaios moleculares de coortes de pacientes com HNSC.

2.7. Análise Integrada de Dados

Definir o conjunto de alvos dos miRNAs é importante por vários motivos, seja para conhecer o papel biológico de um determinando miRNA ou conjunto de miRNAs, ou para o desenvolvimento de alvos prognósticos e terapêuticos. De qualquer forma, a identificação dos alvos e dos miRNAs segue três abordagens gerais: a previsão por bioinformática, o isolamento bioquímico do miRNA/complexo e análise da expressão de miRNAs ou genes (HAMMOND, 2016). A previsão por bioinformática e a análise da expressão de miRNAs serão utilizadas neste estudo.

Algumas técnicas de biologia molecular são projetadas para traçar um perfil de muitos miRNAs de uma única vez e, geralmente, com alto rendimento. Nesse caso, temos como exemplo as plataformas de *Next-Generation Sequencing* (NGS) e as de hibridização por microarranjos e *barcode* (HAMMOND, 2016). O primeiro método é especialmente poderoso, pois é possível caracterizar novos miRNAs, enquanto a maioria dos outros métodos está limitada à detecção de sequências conhecidas.

As plataformas de microarranjos e *barcode* também permitem identificar vários miRNAs por vez. O *array Comparative Genomic Hybridization* (aCGH), por exemplo, é uma técnica de citogenética molecular capaz de identificar, em um genoma mapeado por sondas, alterações no número de cópias (CNAs) (CALIN, CROCE, 2006; MACEDO et al., 2020; SILVA et al., 2021) e variação no número de cópias (CNV) (ZHANG et al., 2021). Em comparação com outras técnicas de citogenética e biologia molecular, o aCGH para CNAs é mais específico e sensível às alterações, permitindo identificar essas alterações a nível de ganhos genômicos (aumento de 3 a 4 cópias gênicas), amplificações (≥5 cópias), perdas (ausência de 1 cópia) e deleções (ausência das 2 cópias) (CHEUNG; BI, 2018). O aCGH vem

sendo muito utilizado na identificação de alterações genéticas de diversos cânceres, como por exemplo o de mama e pênis (LUPICKI et al., 2018; MACEDO et al., 2020), respectivamente.

Outro método de identificação de alto rendimento é a plataforma *nCounter*® (*NanoString Technologies*, Inc.), capaz de identificar a expressão alterada de aproximadamente 827 miRNAs simultaneamente. A técnica se baseia na captura de cada miRNA, por meio de sondas fluorescentes que posteriormente serão quantificadas como um código de barras para a identificação dos transcritos (TSANG et al., 2017).

A identificação *in sílico* dos alvos de miRNAs é outro método de análise integrada de dados e permite descrever vias envolvidas em diversos processos moleculares. O servidor web DIANA Tools foi lançado em 2006 com essa premissa (VLACHOS et al., 2015), e tem por objetivo catalogar as interações dos miRNAs experimentalmente validados e publicados, e de fornecer algoritmos para interpretar as redes de interações miRNA/gene. O servidor DIANA apresenta o mais um dos mais completos sistemas de análise de miRNAs e de seus alvos curados manualmente (RECZKO et al., 2012). Possui o sistema microT v.5.0, que hospeda o algoritmo de previsão microT-CDS, um dos poucos algoritmos disponíveis online que consegue identificar interações entre miRNAs e mRNAs alvos por meio das regiões UTRs e CDS (regiões não-traduzidas e sequências codificantes, respectivamente). O servidor DIANA apresenta ainda o miRPath v.3.0, um software dedicado à avaliação de funções de miRNAs e identificação de suas vias celulares. A análise é baseada nos algoritmos de interação do Tarbase e microT-CDS. Apresenta ainda suporte funcional a todas as vias moleculares da KEGG (*Kyoto Encyclopedia of Genes and Genomes*) e múltiplas vias do GO (*Gene Ontology*) (VLACHOS et al., 2015).

À medida que conhecemos mais sobre os miRNAs e suas interações com os genes, as ferramentas de análise *in sílico* se tornam mais indispensáveis, e ao longo do tempo elas são aperfeiçoadas, a fim de suportar cenários de pesquisas mais exigentes (VLACHOS et al., 2015).

Até o momento, poucos trabalhos sobre miRNAs em CaPe foram realizados e a maioria possuem coortes majoritariamente HPV-negativos, com métodos de detecção viral limitados à alguns subtipos. Considerando, portanto, a escassez de trabalhos sobre miRNAs e a alta prevalência de HPV em câncer peniano no estado do Maranhão, e todos os demais aspectos abordados até o momento é de grande valia investigar o papel dos miRNAs na tumorigênese peniana associada ao HPV.

Nesse estudo, avaliamos a infecção pelo HPV por dois métodos de detecção sensíveis (Nested-PCR, capaz de identificar até 40 subtipos virais e o sequenciamento direto) o que nos

permitiu identificar a maior taxa de infecção por HPV descrita em CaPe (MACEDO et al., 2020; RIBERA-CORTADA et al., 2021). Avaliamos o papel dos miRNAs em vias moleculares e identificamos potenciais alvos terapêuticos a partir de ensaios moleculares e uma abordagem *in sílico*.

3. OBJETIVOS

3.1. Geral

Identificar, a partir de uma abordagem genômica e de expressão diferencial de miRNAs, as principais vias moleculares envolvidas no carcinoma peniano e os seus potenciais alvos terapêuticos.

3.2. Específicos

Capítulo I: 1º Artigo

- Identificar alterações no número de cópias (CNAs) genômicas em tumores penianos;
- Identificar genes e miRNAs presentes em regiões cromossômicas com CNAs;
- Determinar por ferramentas *in sílico* os genes alvos a partir de miRNAs presentes em CNAs;
- Determinar por ferramentas *in sílico* os miRNAs que regulam os genes afetados por CNAs;
- Identificar por ferramentas *in sílico* as vias moleculares a partir dos genes e miRNAs afetados por CNAs;
- Correlacionar os achados moleculares com os parâmetros clínico-histopatológicos dos tumores;
- Apontar possíveis alvos prognósticos e terapêuticos para o câncer de pênis por meio de análise integrada entre alterações de número de cópias gênicas e de miRNAs.

Capítulo II: 2º Artigo

- Determinar um painel de miRNAs diferencialmente expressos em carcinoma peniano comparado com tecido não tumoral adjacente ao tumor;
- Identificar miRNAs potencialmente reguladores dos genes *TP53* e *RB1*;
- Identificar as regiões seed e seedless de hibridização em *TP53* e *RB1*.

Capítulo III: 3º Artigo

- Identificar miRNAs diferencialmente expressos em tecidos tumorais de pênis em relação a tecidos não tumorais adjacentes aos tumores primários;
- Determinar um painel de miRNAs diferencialmente expressos entre doença avançada e inicial;
- Correlacionar os dados de expressão de miRNAs em câncer de pênis em relação a outros tipos de câncer;
- Correlacionar a expressão dos miRNAs com os parâmetros clínico-histopatológicos dos tumores de pênis;
- Determinar por ferramentas *in sílico* os genes alvos e vias moleculares a partir de miRNAs diferencialmente expressos;
- Descrever possíveis interações entre as oncoproteínas do HPV e os genes alvos dos miRNAs diferencialmente expressos;
- Revelar possíveis alvos prognósticos e terapêuticos para o câncer de pênis a partir dos genes regulados pelos miRNAs diferencialmente expressos.

4. RESULTADOS

4.1. Capítulo 1

HPV-associated penile cancer: impact of copy number alterations in miRNA/mRNA interactions and potential druggable targets

Jenilson da Silva, Leudivan Nogueira, Ronald Coelho, Amanda de Deus, André Khayat, Rafael Marchi, Edivaldo de Oliveira, Ana Paula dos Santos, Luciane Cavalli and Silma Pereira

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HPV-associated penile cancer: Impact of copy number alterations in miRNA/mRNA interactions and potential druggable targets

Jenilson da Silva[a], Leudivan Nogueira[a,b], Ronald Coelho[b], Amanda Deus[a,b], André Khayat[c], Rafael Marchi[d], Edivaldo de Oliveira[e], Ana Paula dos Santos[f], Luciane Cavalli[d] and Silma Pereira[g,*]
[a]*Postgraduate Program in Health Science, Federal University of Maranhão, São Luís, MA, Brazil*
[b]*Aldenora Bello Cancer Hospital, São Luís, MA, Brazil*
[c]*Oncology Research Center, Federal University of Pará, Belém, PA, Brazil*
[d]*Research Institute Pelé Pequeno Príncipe, Faculdades Pequeno Príncipe, Curitiba, PR, Brazil*
[e]*Tissue Culture and Cytogenetics Laboratory, Institute of Evandro Chagas, Belém, PA, Brazil*
[f]*Department of Physiological Sciences, Federal University of Maranhão, São Luís, MA, Brazil*
[g]*Laboratory of Genetics and Molecular Biology, Department of Biology, Federal University of Maranhão, São Luís, MA, Brazil*

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Abstract.
BACKGROUND: Penile cancer (PeCa) is a rare disease, but its incidence has increased worldwide, mostly in HPV$^+$ patients. Nevertheless, there is still no targeted treatment for this carcinoma.
OBJECTIVE: To predict the main signaling pathways involved in penile tumorigenesis and its potential drug targets.
METHODS: Genome-wide copy number profiling was performed in 28 PeCa. Integration analysis of CNAs and miRNAs and mRNA targets was performed by DIANA-TarBase v.8. The potential impact of the miRNAs/target genes on biological pathways was assessed by DIANA-miRPath v.3.0. For each miRNA, KEGG pathways were generated based on the tarbase and microT-CDS algorithms. Pharmaco-miR was used to identify associations between miRNAs and their target genes to predict druggable targets.
RESULTS: 269 miRNAs and 2,395 genes were mapped in cytobands with CNAs. The comparison of the miRNAs mapped at these cytobands and the miRNAs that were predicted to regulate the genes also mapped in these regions, resulted in a set of common 35 miRNAs and 292 genes. Enrichment pathway revealed their involvement in five top signaling pathways. EGFR and COX2 were identified as potential druggable targets.
CONCLUSION: Our data indicate the potential use of EGFR and COX2 inhibitors as a target treatment for PeCa patients.

Keywords: Genomic profiling, molecular target, biomarkers, human papillomavirus, penile tumor

1. Introduction

Penile cancer (PeCa) is a rare malignancy; however, it is a public health concern in developing countries. In Brazil, it represents 2% of all male cancers, occurring more frequently in the North and Northeast regions. Maranhão state (Northeast region), where the patients of this study were obtained, presents with the highest

*Corresponding author: Silma Regina Ferreira Pereira, Laboratory of Genetics and Molecular Biology, Department of Biology, Federal University of Maranhão, 1966, Avenida dos Portugueses, São Luís, MA, Brazil. Tel.: +55 98 32729576; E-mail: silma.pereira@ufma.br.

PeCa rates in Latin America and worldwide [1]. The patients in this region are usually diagnosed with advanced tumour stages, and lymph node involvement, which invariably confers poor prognosis. Human papillomavirus (HPV) has been linked to nearly 50% of PeCa cases worldwide [2,3]. In our region however, our previous study, revealed a higher frequency of HPV-related PeCa, in nearly 97% of the cases [4].

The available surgical treatment for advanced PeCa involves partial or total amputations of the penis and lymphadenectomy, which are associated with post-surgical complications and high morbidities [5,6]. The combined use of chemotherapy was observed to marginally increase the survival rate of the patients [7–10], with however the inherent toxicity of the chemo-agents. In addition, the rarity of this tumour makes it difficult to conduct large-scale clinical trials, so there are still no effective treatment strategies for advanced PeCa patients. Therefore, effective and less toxic treatments, such as the ones based on targeted therapy, are critically needed to treat PeCa.

MicroRNAs (miRNAs), non-coding RNA molecules, have emerged as one of the promising molecular markers for therapeutic use in several types of cancers [11–13]. These molecules are preferentially mapped in genomic regions with copy number gains and/or losses, as well as in regions of fragile sites [14,15]. Further studies have confirmed that miRNAs play important roles in oncogenesis by regulating the expression of genes located within the regions affected by CNA, and/or miRNAs expression changes can be driven by CNAs within their own genomic regions [16–18].

A large number of integration strategies for distinct "omics" platforms have been described and have significantly contributed to the characterization of tumour molecular landscapes, such as the ones performed by the International Cancer Genome Consortium (ICGC) and The Cancer Genome Atlas (TCGA). Most of these strategies are based on computational pipelines, where the data is gathered from independent and public available resources. In PeCa there is relatively limited information of the somatic alterations that occur at the distinct molecular levels and consequently of the integrated molecular signatures.

Therefore, and considering the prevalence of PeCa in developing countries, as well as the increasing number of cases worldwide, our main objective was to determine the predictive impact of copy number alterations in the miRNA/mRNA interactions, and to identify the potentially affected functional pathways in penile tumorigenesis. In addition, we aimed to determine whether the observed alterations and/or the signaling pathways involved, could be potentially targeted by the current clinically approved drugs.

2. Materials and methods

2.1. Experimental subjects

2.1.1. Patient accrual, social and clinical-histopathological variables

Tumour tissues of 28 PeCa patients, collected at the Hospital Aldenora Bello (São Luís, Maranhão, Brazil) were included in this study. The fresh tumour tissue samples were obtained at the diagnosis and before any cancer treatment. The clinical and histopathological variables were obtained from patients' medical records. All patients signed consent form, which was approved by the Ethics Committee on Human Beings at the Federal University of Maranhão and by the National Research Ethics Commission (CONEP), Brazil (CAAE protocol number: 46371515.5.0000.5087).

The mean age at diagnosis of the patients was 64.6 $\pm$ 15.2, ranging from 32 to 85 years old. Most of the patients were married (75%) and presented low level of education (only 17.9% presented high school degree); 50% self-declared current smoker or declared to have been a smoker in the past 5 years, and 63.3% declared to regularly drink alcohol.

The tumours were classified as Squamous Cell Carcinoma (SCC), presenting an average size of 3.6 $\pm$ 2.2 cm, ranging from 0.5 to 10 cm. In most of the patients (39.3%), the tumours were restricted to the glans. The most frequent histological subtypes were condylomatous and usual, present in 42.9% and 39.3% of the cases, respectively. Tumour grades II and III were the most frequent, present in 59.6% and 25.9% of the patients, respectively. Lymph node and perineural invasion were observed at diagnosis in 16% and 20% of the patients, respectively. Phimosis was observed in 54.5% of the patients, most of which (91.7%) with over 40 years old. Most of the patients (75%) were submitted to partial penectomy. This clinical-histopathological information from the patients is presented in Table 1.

2.1.2. HPV genotyping

HPV genotyping was performed for all the patients by nested-PCR (according to BioGenetics Molecular Technologies (Uberlândia, Minas Gerais, Brazil) (patent number BR102017004615.0), and DNA sequencing, according to our previous protocol [4]. All the

Table 1
Clinical-histopathological characterization of the PeCa patients evaluated in this study ($n = 28$)

Case	Age	Phymosis ocurrence	HPV subtype	Histological subtype	Predominant lesion	Tu. size[b]	Tu. grade	Tu. stage	Lymphatic invasion	Perineural invasion
01	62	No	16	Usual	Ulcerated	2.5	II	pT3	Yes	Yes
02	80	N/A	16	Condilomatous	Ulcerated	10	II	pT2	No	No
03	81	Yes	18,53	Condilomatous	Ulcerated	2.1	II	pT1	No	No
04	76	Yes	30	Condilomatous	Ulcerated	3	I	pT1b	Yes	No
05	74	Yes	73,74	Usual and basaloid	Verrucous	0.8	I	pT2	No	No
06	78	N/A	16,06	Usual and basaloid	Vegetative	4	III	pT1b	No	No
07	57	No	58	Usual and condilomatous	Nodular ulcerated	3	III	pT2	No	No
08	85	No	16	Condilomatous	Nodular ulcerated	4	III	pT3	No	Yes
09	83	No	16	Usual	Ulcerated	4.5	III	pT3	No	Yes
10	40	No	59,66	Condilomatous	Ulcer-vegetative	3	II	pT2	No	No
11	68	N/A	16,66	Condilomatous	Verrucous	5.5	I	pT3	No	No
12	41	Yes	56	Condilomatous	Vegetative	3.5	II	pT2	No	No
13	74	No	11,35,59	Condilomatous	Vegetative	9	II	pT3	No	No
14	65	N/A	16,74	Condilomatous	Vegetative	3.5	II	pT2	No	No
15	51	N/A	16,35,59	Usual	Ulcer-vegetative	3	II	pT2	Yes	No
16	32	No	16,44,74	Usual and condilomatous	Ulcer-vegetative	3.7	II	pT2	No	No
17	69	No	16,30	Condilomatous	Vegetative	3.5	I	pT2	No	No
18	37	Yes	Positive[a]	Usual	Nodular ulcerated	5.0	III	pT3	No	Yes
19	54	Yes	Positive[a]	Usual	Vegetative	0.8	II	pT2	Yes	No
20	44	Yes	16	Usual	Ulcerated	1.7	II	pT1	No	No
21	51	Yes	16	Basaloid	Vegetative	N/A	II	pT2	N/A	N/A
22	71	Yes	Positive[a]	Usual	Ulcerated	2	III	Tis	No	No
23	74	No	Positive[a]	Condilomatous	Ulcerated	1.8	II	pT1a	No	No
24	83	Yes	35,59	Usual	Ulcer-vegetative	N/A	II	pT2	N/A	N/A
25	77	N/A	Positive[a]	Usual	Ulcerated	0.5	ni	N/A	No	No
26	73	Yes	16	Usual	Ulcerated	N/A	II	pT1	N/A	N/A
27	71	No	16	Usual	Ulcerated	3.2	III	pT3	No	No
28	59	Yes	Positive[a]	Condilomatous	Verrucous	5.5	II	pT3	No	Yes

[a]No information on HPV genotype; [b]Tu = tumor (mm); N/A = not available.

patients were HPV positive, of which 95.5% presented high-risk subtypes. HPV16 was the most common subtype, present in 63.6% of cases, followed by subtypes 35, 59, 74 (13.6%, each); 30, 44, 66 (9%, each); 06, 18, 53, 58 and 73 (4.5%, each). Multiple infections were detected in 50% of the cases (Table 1).

2.1.3. Copy number data of the PeCa tumours

All the patients were profiled for genome-wide copy number alterations (CNAs) by array-Comparative Genomic Hybridization (aCGH) analysis, as reported by Macedo et al. [4]. The aCGH analysis showed a total number of 2,314 CNAs, with a mean of 82.6 ± 53.5 CNAs per case (ranged from 23 to 224). Most of the CNAs observed were gains (56.9%/1,316), followed by losses (37.3%/864), amplifications (4.0%/92), and deletions (1.8%/42).

2.2. Integration analysis of CNA and miRNAs and mRNA targets

This analysis was performed by two different approaches: i. By the mapping of the genes and miRNAs at the main regions with CNA, called here CNA-genes and CNA-miRNAs, respectively, and ii. By the identification of common gene targets of the selected miRNAs above, that may be affected by both CNAs and miRNA expression alterations. The workflow of the study design and corresponding results are presented in the results section (Fig. 1).

2.2.1. Mapping of miRNAs in genomic regions with CNAs

Initially, the complete aCGH data for all the 28 patients were analyzed to identify the most affected cytobands with CNAs. Only the CNAs present in at least 25% of the cases were considered. Next, the annotation of genes and miRNAs located in the cytobands with CNAs were obtained from the *Agilent Cytogenomics v.7.0* interval base reports (*Agilent Technologies, Inc.*). The location of each miRNA was further confirmed using miRBase v.22 (http://www.mirbase.org) [19]. The genomic regions that were sites of HPV integration were accessed by the HPVbase platform (http://crdd.osdd.net/servers/hpvbase/index.html), according to Kumar Guptar and Kumar [20].

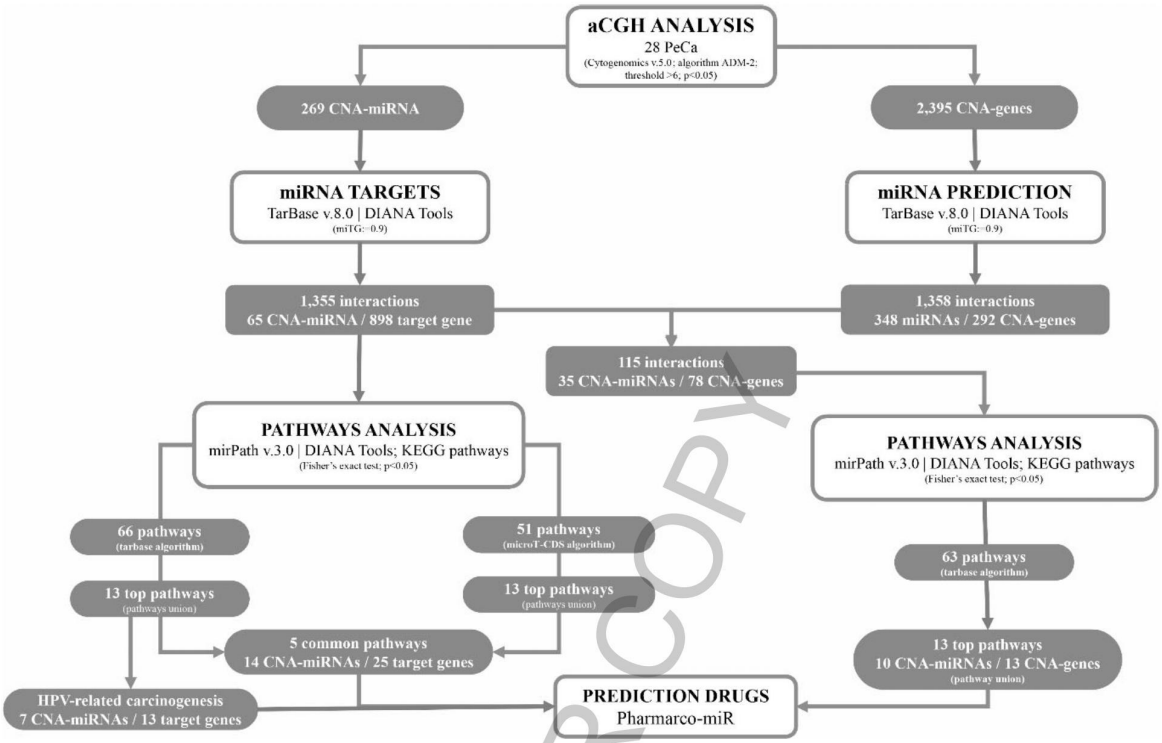

Fig. 1. Study design and corresponding results of the aCGH and miRNA data integration approaches, followed by the functional enrichment pathway and druggable targets predicted analysis. In one approach (269 CNA-miRNAs), 1,355 interactions were identified involving 65 CNA-miRNAs and 898 target genes (TarBase v.8.0). MiRPath v.3.0 was used for the enrichment of pathways considering two prediction algorithms, tarbase and microT-CDS. Five common pathways (14 CNA-miRNAs and 25 target genes) were identified comparing the two pathway methods. In addition, tarbase enrichment revealed an HPV-related carcinogenesis pathway (7 CNA-miRNAs and 13 target genes). In a second approach (2,395 CNA-genes), 1,358 interactions were identified involving 348 miRNAs and 292 CNA-genes. Comparing the interactions with the first approach, 115 common interactions were revealed, that is, between 35 CNA-miRNAs and 78 CNA-genes. Pathways enrichment was conducted with these interactions where it revealed 13 top pathways (10 CNA-miRNA and 13 CNA-genes). The Pharmarco-miR program was used to identify drugs targeting miRNA targets in both approaches.

2.2.2. *Association of genomic regions with CNAs and miRNAs with clinical and histopathological parameters from the patients*

The association analysis of each clinical-histopathological variable and copy number alterations was performed using bivariate tests and X^2 Pearson or *Fisher's Exact* test, when applicable. The significance level was $P < 0.05$. The statistical tests were performed using the *Graphpad Prism* v.8.4.3 software.

2.2.3. *Identification of mRNA targets*

The targets of the miRNAs mapped in the regions with CNA (CNA-miRNAs) were identified by the DIANA-TarBase v.8 (carolina.imis.athena-innovation.gr/diana_tools/web/index.php?r=tarbasev8/index) [21]. Only target genes presenting *miRNA Target Gene* (miTG) score $\geqslant 0.9$ were included in this analysis. In addition, we identified the miRNAs that potentially regulate the CNA-genes and selected the common miRNAs/target genes of both integration analysis.

2.2.4. *Enrichment pathways analysis*

To assess the potential impact of the miRNAs/target genes (that were mapped in the main cytobands selected above) on biological pathways associated with cancer, we used DIANA-miRPath v.3.0 tools (http://snf-515788.vm.okeanos.grnet.gr/) based on p-values (FDR correction), according to Vlachos et al. [22]. The KEGG (*Kyoto Encyclopedia of Genes and Genomes*) was used for pathways enrichment analysis ($p < 0.05$). For each miRNA, KEGG pathways were generated based on the tarbase and microT-CDS algorithms of the DIANA tools. Top pathways were identified using the "pathway union" function.

Table 2
Cytobands with CNAs in PeCa ($n = 28$) analyzed by aCGH in association with clinical-histopathological parameters

Cytoband	CNA event	HPV integration site (genotype)[a]	Variables	P-value
2p16.3	Gain	Yes (16, 18)	Tumor pT1	0.0130
			Ulcerated	0.0338
			Tumor size $>$ 5.1 cm	0.0238
2p12-p11.2	Gain	Yes (16)	Subtype usual	0.0472
			Vegetative	0.0461
			Tumor size $>$ 5.1 cm	0.0204
3q26.1	Gain	Yes (45)	Ulcer-vegetative	0.0126
			Verrucous	0.0343
4p14-p13	Loss	Yes (16)	Tumor size $>$ 5.1 cm	0.0198
4q13.2	Loss/deletion	Yes (16)	Ulcer-vegetative	0.0017
7p22.3-p11	Gain	Yes (16, 45)	Perineural invasion	0.0075
7q21.11	Gain	Yes (16, 35)	Tumor pT3	0.0381
			Tumor size $>$ 5.1 cm	0.0409
8p23.1	loss/deletion	Yes (16)	Vegetative	0.0233
9p21	Gain	Yes (16,18)	Tumor pT1	0.0078
11q24-q25	Gain	Yes (16)	Tumor pT1	0.0243
14q11.2	Loss	Yes (16, 18)	Perineural invasion	0.0038
14q12	Gain	Yes (16)	HPV16 and multiple infections	0.0044
15q11.2-q13.3	Gain	Yes (18)	Vegetative	0.0490
			Tumor pT1	0.0297
15q26.2-q26.3	Gain	Yes (16)	Age $>$ 40 years	0.0330
			Grade I	0.0022
22q11.21	Gain	Yes (33)	Perineural invasion	0.0412
			Tumor pT2	0.0404

[a]genotypes identified in previous studies according to HPVbase. aCGH performed by Cytogenomics v.5.0 software; Agilent Technologies Inc, CA, algorithm ADM-2; threshold > 6.

2.3. Analysis of druggable targets

Pharmaco-miR (www.pharmaco-mir.org) was used to identify associations between miRNAs and their target genes to predict druggable targets, as described in the literature [23]. This analysis was performed for: i. mRNA targets identified by both algorithms (tarbase and microT-CDS); ii. mRNA targets related to HPV infection, and iii. miRNAs/mRNA target genes involved in the the top KEGG pathways identified. PathVisio v.3.3 [24] and Biorender (https://biorender.com/) were used to rebuild KEGG pathways including the miRNAs, their respective gene targets and corresponding predicted drugs.

3. Results

The overall results of this study with the corresponding study design are presented in Fig. 1.

3.1. Copy number alterations and their association with clinical and histopathological parameters

Genome-wide copy number analysis in the 28 PeCa patients analyzed by aCGH revealed 38 altered cytobands with copy number alterations (CNAs), from which 89.5% were HPV integration sites in the host genome. The association analysis of the main affected cytobands with CNAs and the clinical-histopathological parameters from the patients revealed 15 cytobands (Table 2). All these altered cytobands were already described as HPV integration sites according to HPVbase. Gains on 14q12 presented association with HPV16 and multiple infections, while gains on 15q26.2-q26.3 were associated with age $>$ 40 years. Gains on 2p16.3, 9p21, 11q24-q25 and 15q11.2-q13.3 showed association with early stages of the primary tumour (pT1). On the other hand, gains on 7q21.11, 7p22.3-p11 and 22q11.21, and loss on 14q11.2 and 4p14-13 were associated with intermediate stages of the tumour (perineural invasion, pT2, pT3 and tumour size $>$ 5.1 cm).

3.2. Mapping of genes and miRNAs in genomic regions with CNA

According to the annotations of the *CytoGenomics* base interval report, 30 of the 38 affected cytobands harbored miRNAs (Fig. 1, Supplementary Table 1). Interestingly, 28 of these 30 cytobands (93.3%) are HPV integrated sites according to HPVbase. A total of

269 miRNAs were mapped in these cytobands (CNA-miRNAs), 211 in regions affected by copy number gains (78.4%), 27 by losses (10%), 13 by amplification (4.8%), and 18 by losses and deletions (6.7%).

A second integration approach was based on the identification of miRNAs that potentially regulated the genes mapped at the main affected cytobands: 2,395 genes were identified to be mapped at the 38 cytobands with CNAs (CNA-genes). Based on the TarBase/Diana Tools, considering miTG $\geqslant$ 0.9, 292 of these genes were predicted to be regulated by 348 miRNAs. The comparison of the miRNAs mapped at the main cytobands and the miRNAs that were predicted to regulate the genes also mapped in these regions, resulted in 35 miRNAs (Fig. 1, Supplementary Table 2A).

3.3. Prediction of mRNA targets in regions with CNA

Target prediction analysis (considering miTG $\geqslant$ 0.9) revealed that 65 out of 269 miRNAs mapped in the affected cytobands, potentially regulate 898 gene targets (Fig. 1, Supplementary Table 2B). *MiR-30d*, mapped at 8q24.22 presented the highest number of targets (229 genes), followed by *miR-30b* (mapped at 8q24.22), and *miR-548d* (mapped at 8q24.13) with 224 and 134 target genes, respectively. *MiR-151a-3p* (8q24.22), *miR-649* (22q11.21), *miR-1269a* (22q11.21), *miR-3150b-3p* (8q22.1), *miR-4286* (8p23.1), *miR-4435* (2p11.2), *miR-4473* (9p21), and *miR-4802-5p* (4p14) presented the lowest number of targets (1 gene, each).

In addition, the identification of the genes mapped at the affected cytobands and that were predicted to be regulated by the 35 miRNAs mapped at the same cytobands, resulted in 78 mRNA targets *(Fig. 1)*. From these miRNAs, *miR-30b-3p*, *miR-30d-5p* and *miR-548d-3p* were the ones to present the highest number of target genes, 19, 19 and 10, respectively.

3.4. Pathway enrichment analysis

The main biological functions related to the 65 miRNAs mapped at the 30 cytobands (CNA-miRNAs) were evaluated by KEGG pathway enrichment analysis using two distinct algorithms. The tarbase algorithm revealed 66 pathways, among the top 13: adherens junction (hsa04520), cell cycle (hsa04110), ECM-receptor interaction (hsa04512), fatty acid biosynthesis (hsa00061), fatty acid metabolism (hsa01212), glioma (hsa05214), *hippo* signaling pathway (hsa04390), lysine degradation (hsa00310), mucin type O-Glycan biosynthesis (hsa00512), prion diseases (hsa05020), proteoglycans in cancer (hsa05205), steroid biosynthesis (hsa00100), and viral carcinogenesis (hsa05203). The microT-CDS prediction algorithm revealed 51 main KEGG pathways, among the top 13: axon guidance (hsa04360), foxO signaling pathway (hsa04068), GABAergic synapse (hsa04727), *hippo* signaling pathway (hsa04390), long-term depression (hsa04730), lysine degradation (hsa00310), morphine addiction (hsa05032), mucin type O-Glycan biosynthesis (hsa00512), prion diseases (hsa05020), proteoglycans in cancer (hsa05205), signaling pathways regulating pluripotency of stem cells (hsa04550), steroid hormone biosynthesis (hsa00140), and TGF-beta signaling pathway (hsa04350). The significant pathways revealed by both of the miRNA prediction algorithms used are shown in Fig. 2 and Supplementary Table 3A and B.

Notably, five common pathways were identified by both algorithms: *hippo* signaling pathway (*miR-548d-5p*, *miR-548k*, *miR-548n* and *miR-4517*), lysine degradation (*miR-339-5p*, *miR-548d-3p* and *miR-624-3p*), mucin type O-Glycan biosynthesis (*miR-30b-5p*, *miR-30d-5p* and *miR-5680*), prion diseases (*miR-30d-3p* and *miR-148a-3p*) and proteoglycans in cancer (*miR-100-5p*, *miR-148a-3p* and *miR-217*). Furthermore, considering that all the tumours were HPV positive, we also investigated the HPV-associated carcinogenesis pathway, in which 13 genes were identified as potentially regulated by miRNAs mapped in regions with gains or amplifications (tarbase algorithm). Interestingly, these genes have also been described as negatively controlled by HPV oncoproteins (KEGG- hsa05203) (Supplementary Fig. 1, Table 3).

Pathway enrichment analysis using the two algorithms (tarbase and microT-CDS) was also conducted considering the common genes ($n = 78$) mapped at the main cytobands and that were also target of the miRNAs ($n = 35$) mapped at the same affected cytobands. In this analysis however, no common pathways were identified between these two prediction algorithms. Therefore, the pathways enrichment analysis results of the tarbase algorithm were chosen, considering that they were based on experimental validations of miRNA/mRNA target interactions. This analysis revealed 63 pathways, which top 13 involved 13 genes (*CCNE2*, *E2F5*, *EPAS1*, *INHBA*, *LYN*, *PDE7A*, *PPP1CB*, *PPP3R1*, *RAC1*, *SEMA3D*, *SOS1*, *YWHAQ*, and *YWHAZ*) (Table 4). Of note, these genes are also involved in molecular pathways directly related to cancer, such as the P53 (hsa04115) and TGF-β (hsa04350) signaling pathways, proteoglycans in cancer (hsa05205), and viral carcinogenesis (hsa05203).

Fig. 2. Targeted KEGG pathway clusters/heatmap regulated by the miRNAs mapped at the cytobands mostly affected by CNAs in the cases studied. A: Top pathways identified by the tarbase algorithm; B: Top pathways identified by the microT-CDS algorithm ($P < 0.05$; DIANA/miRPath v.3). Red colors indicate a stronger role of the miRNAs on a given pathways as compared to the lighter colors. Blue arrows indicate the miRNAs and corresponding signaling pathways that were identified by both algorithms (tarbase and microT-CDS).

Table 3
Target genes identified as potentially regulated by miRNAs mapped in regions with gains or amplifications and also described as negatively controlled by HPV oncoproteins (DIANA-miRPath v.3.0; KEGG: hsa05203)

Gene	HPV oncoprotein	CNA-miRNA	*P*-value	Biological consequence
ATP6V0D1	E5	miR-148a-3p	0.0001	Inhibition of V-ATPase-dependent endosomal acidification and increased recycling of EGFR-receptor to the cell surface
CCNA2	E7	miR-148a-3p	0.0001	Deregulation of the cell cycle by inactivating cyclin A2 (*CCNA2*)
		miR-4429	0.0048	
		miR-548a-3p	0.0152	
		miR-548d-5p	0.0262	
CDK2	E7	miR-548a-3p	0.0152	Alteration of cell cycle
CDKN1B	E7	miR-30d-3p	0.0007	Disruption of the cell cycle checkpoint by inactivating P27 (*CDKN1B*)
		miR-148a-3p	0.0001	
		miR-548a-3p	0.0152	
		miR-550a-3-5p	0.0499	
CHD4	E7	miR-148a-3p	0.0001	Increased cell growth
		miR-185-5p	0.023	
EP300	E6	miR-30d-3p	0.0007	Inhibition of P53 activation through the E6-P300 complex (*EP300*)
		miR-148a-3p	0.0001	
IRF3	E6	miR-148a-3p	0.0001	Inactivation of apoptotic activity promoted by P53 by the association E6-IRF3 (*IRF3*)
JUN	E7	miR-4429	0.0048	Disturbance of the transcription factor c-JUN (*JUN*)
PKM	E7	miR-148a-3p	0.0001	Increased cell growth
		miR-4429	0.0048	
RB1	E7	miR-30d-3p	0.0007	Inactivation of tumor suppressor protein pRB
		miR-148a-3p	0.0001	
RBL2	E7	miR-550a-3-5p	0.0499	Increased cell proliferation by inactivating P130 (*RBL2*)
TBP	E7	miR-148a-3p	0.0001	Inhibition of transcription factors
		miR-548a-3p	0.0152	
UBR4	E7	miR-148a-3p	0.0001	Alteration of cell membrane morphogenesis and cell migration by the interaction of E7 with P600 (*UBR4*)
		miR-4429	0.0048	

DIANA-miRPath v.3.0; KEGG: HPV-mediated viral carcinogenesis pathway – hsa05203.

Table 4
Top 13 signaling pathways with the involvement of 13 genes observed with gains of copy number and also targeted by miRNAs mapped at the main affected cytobands (Tarbase algorithm)

CNA-gene	Cytoband	CNA-miRNA	Top pathways
CCNE2	8q11.1-24.3	miR-30b-5p	Oocyte meiosis, pathways in cancer, P53 signaling pathway
		miR-30d-5p	
E2F5	8q11.1-24.3	miR-1-3p	Cell cycle
EPAS1	2p25.3-p11.1	miR-148a-3p	Pathways in cancer
INHBA	7p22.3-p11	miR-548d-3p	Signaling pathways regulating pluripotency of stem cells and TGF-beta signaling pathway
LYN	8q11.1-24.3	miR-185-5p	Viral carcinogenesis
PDE7A	8q11.1-24.3	miR-30b-5p	Fatty acid biosynthesis and metabolism and pathways in cancer
		miR-30d-5p	
PPP1CB	2p25.3-p11.1	miR-148a-3p	Hippo signaling pathway, oocyte meiosis and proteoglycans in cancer
PPP3R1	2p25.3-p11.1	miR-298	Axon guidance and oocyte meiosis
		miR-30b-5p	
		miR-30d-5p	
RAC1	7p22.3-p11	miR-589-3p	Adherens junction, axon guidance, pathways in cancer, proteoglycans in cancer and viral carcinogenesis
SEMA3D	7q21.11	miR-548a-3p	Viral carcinogenesis
SOS1	2p25.3-p11.1	miR-148a-3p	FoxO signaling pathway, gap junction, glioma, pathways in cancer and proteoglycans in cancer
		miR-548d-5p	
YWHAQ	2p25.3-p11.1	miR-1-3p	Cell cycle, hippo signaling pathway, oocyte meiosis and viral carcinogenesis
YWHAZ	8q11.1-24.3	miR-1-3p	Cell cycle, hippo signaling pathway, oocyte meiosis and viral carcinogenesis

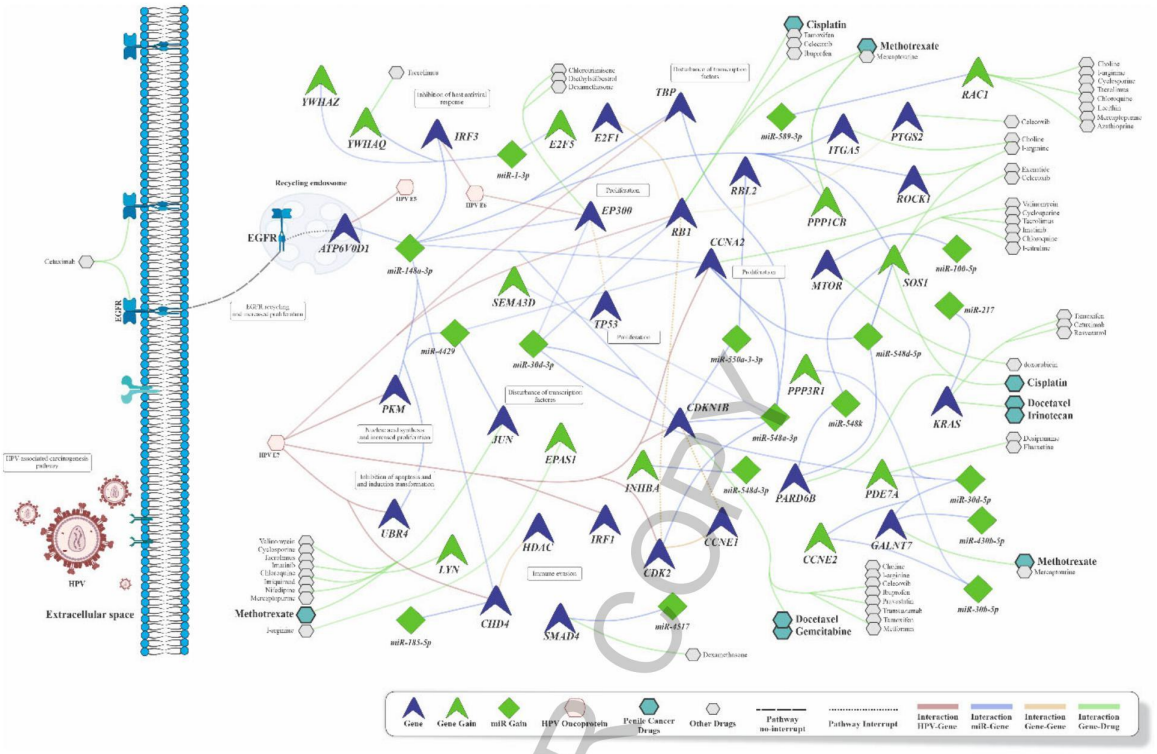

Fig. 3. Integrative network analysis showing the main pathways and the druggable targets predicted by Pharmaco-miR analysis. The network was generated by PathVisio v3.3 and Biorender softwares using the data generated through the Diana-Tools, KEGG and Pharmaco-miR.

3.5. Drug targets prediction

Finally, drug prediction analysis was performed using the five common pathways identified from CNA-miRNA (hippo signaling, lysine degradation, O-glycan mucin biosynthesis, prion, and proteoglycan diseases in cancer), as well as using the 13 main common pathways identified from the CNA-genes, and CNA-miRNAs analysis. Moreover, considering the high prevalence of HPV infection in the PeCa patients of this study, the HPV-mediated carcinogenesis pathway was also used for drug prediction. This analysis revealed drugs currently used to treat PeCa, such as Cisplatin, which acts on the *PARD6B* (regulated by *miR-548k/548d-5p*), and *RB1* (regulated by *miR-30d-3p* and *miR-148a-3p*) genes. In addition, the *MTOR* (regulated by *miR-100-5p*) and *SOS1* (regulated by *miR-148a-3* and *miR548k/548d-5p*) pathways were found to be susceptible candidates to pharmacological inhibition by Doxorubicin and Imatinib, respectively. Interestingly, Cetuximab (an EGFR inhibitor) and Celecoxib (selective cyclooxygenase-2 inhibitor (COX2) were detected as alternative therapies for PeCa (Fig. 3 and Supplementary Table 4).

4. Discussion

PeCa is a rare disease in developed countries and, despite the recent increase in the number of molecular studies performed in these tumours [25–29], their molecular basis is still not well understood. In this study we evaluated the role of miRNAs in the molecular pathways associated with HPV-positive tumours, considering the high frequency (63.3%) of high-risk HPV genotypes (HPV16) in the PeCa patients. This is an unusual high frequency compared to the literature, which have described the HPV16 genotype as the most prevalent in PeCa, although in frequencies less than 50% [3,27].

The aCGH analysis revealed 89.5% of the altered cytobands are mapped in HPV integration sites in the host genome. These findings support that HPV integration sites are generally located on or nearby regions of fragile sites, and that CNAs in these regions can be potentially triggered by the virus insertion [30]. It is

also relevant to point out, that all the 15 cytobands that showed an association with clinical and histopathological parameters are regions of HPV integration sites. For example, the 14q12 region showed an association with the HPV16 genotype and multiple infections. CNAs on chromosomes 2p, 9p, 11q and 15q were associated to early stages of the tumour, while CNAs on 4p, 7p, 7q, 14q and 22q to intermediate tumour stages. These findings, together with our previous study [4], reinforce that CNAs play an important role in HPV-related PeCa, and can indicate candidate genes within these affected regions, that can be used as molecular markers for these patients.

Herein, we identified potential molecular markers affected by CNAs using prediction analysis to determine the interaction of genes and miRNAs mapped at these regions with CNAs and their corresponding gene targets. To our knowledge this is the first study conducted in PeCa patients, where this integration approach was performed. This integrative analysis, followed by functional enrichment pathways analysis, using both tarbase and microT-CDs algorithms, revealed five common pathways: Hippo signaling, lysine degradation, mucin type O-Glycan biosynthesis, prion diseases, and proteoglycans in cancer. Hippo signaling, which is a pathway associated with cell proliferation and survival [31]. The miRNAs that were mapped in the CNAs, *miR-548d-5p*, *miR-548k*, *miR-548n*, and *miR-4517*, were previously demonstrated to regulate several genes involved in these cellular process [32–35]. Interestingly, this pathway presents a feedback relationship with the TGF-B signaling pathway [36], in which the downstream genes *BMPR2* and *SMAD4* are involved. These genes are also targets of *miR-548d-5p* (*BMPR2*) and *miR-4517* (*BMPR2* and *SMAD4*), which loss was previously associated with aggressive tumour phenotypes, such as tumours with larger sizes, metastasis development, and chemotherapy resistance [37,38]. Therefore, we suggest that the negative regulation of these genes by *miR-548d-5p*, and *miR-4517* can be one of the molecular mechanisms relevant to the penile tumorigenesis.

The role of miRNAs in the lysine's degradation pathway is not completely understood. *MiR-548d-3p*, mapped at 8q24.13 and affected in our cases by gain of copy number, is predicted to regulate several gene targets involved in this pathway, such as *KMT2 A*, *KMT2D*, *SUV420H1*, *WHSC1L1*, and *SETD7*. The altered expression of these genes has been described in several cancers [39–43], however the mechanisms that lead to their expression alterations is not clear.

The third pathway affected by the miRNAs located in regions with CNAs of this study, is the biosynthesis of mucin's type O-glycan. O-glycans-type mucins are constituents of the main compounds of mucous, forming physical-chemical barriers [44]. The O-glycosylation process involve several genes from the *GALNT* or GalNac-T (N-acetyl-galactosaminyltransferases) family, which abnormal expression have been associated with cancer progression [44,45]. In our study, the *GALNT1*, *GALNT2*, *GALNT3* and *GANLT7* genes were identified as potential targets for *miR-30b-5p* and *miR-30d-5p*, mapped at 8q24.22 region, affected by gain of copy number. Interestingly, Gaziel-Sovran et al. [46] observed an increase in the metastatic potential in melanoma by the repression of *GALNT1* and *GALNT7* due to the high expression of *miR-30b/30d*. In gastric carcinoma, negative regulation of *GALNT2* is associated with more advanced stages of the tumour, lymph node metastasis and reduced disease-free survival [45]. It was also observed that the downregulation of *GALNT2* modifies the O-glycosylation of EGFR and affects the EGFR-AKT signaling [44]. Additionally, the lower expression of *GALNT3* in pancreatic cancer has been associated with altered glycosylation of the ErbB family receptors, and with increased aggressiveness [47]. Altogether, these findings support the role of *miR-30b/30d* in the O-glycan mucin pathway via regulation of the *GALNT* gene family, and their association with aggressive tumour types.

Our analysis also revealed that *miR-20d-3d* and *miR-148a-3p* target the *PRNP* gene. This gene is involved in Prion diseases, where it regulates pathways of oxidative stress, proliferation, adhesion, and cell survival. Although most of the studies on *PRNP* are focused on the nervous system, recent evidence indicates that this gene also regulates these process in cancer cells [48]. The role of miRNAs in the regulation of *PRNP* is still uncertain, since the physiological functions of the PrP^c protein, encoded by the *PRNP* gene, remain ambiguous [49]. However, it is suggested that changes in PrP^c expression affect NF-κB activation, TNFα production [49], and EGFR signaling [50], pathways and mechanisms closely related to cancer development. Moreover, our integrated analysis showed that *miR-100-5p*, *miR-148a-3p*, and *miR-217* negatively regulate genes involved in the Proteoglycans pathway. Proteoglycans are important constituents of the extracellular matrix and regulate the bioavailability of hormones, growth factors, receptors, cytokines, and gene expression [51].

Considering that in this study all the tumours were HPV positive, we also investigated the HPV-associated

carcinogenesis pathway. The tarbase algorithm revealed that both miRNAs and HPV oncoproteins can negatively regulate genes related to proliferation, cell cycle and apoptosis. For example, although endosomal acidification is required for the initial stages of HPV infection [52], inhibition of acidification by the HPV oncoprotein E5 has already been reported [53–55]. Moreover, the *ATP6V0D1* gene has been identified as a target for *miR-148a-3p*. This gene encodes one of the subunits of the vacuolar-ATPase enzyme and is responsible for endosomal acidification and consequent degradation of some cellular components, such as the EGFR [56]. Thus, *miR-148a-3p* and HPV-E5 may both inhibit the endosomal acidification and, consequently, increase the availability of EGFR. The involvement of EGFR in PeCa was previously reported in other studies, including our own [4], where *EGFR* was observed with gain of copy number and gene overexpression.

Other genes that are usually targeted by HPV oncoproteins have also been identified as targeted by miRNAs in the HPV-mediated carcinogenesis pathway. In the cases of this study, *miR-148a-3p* and *miR-30d-3p* are mapped at regions with gains (at 7p15.2 and 8q24.22, respectively), which were among the miRNAs predicted to regulate *RB1* and *CDKN1B*, both genes involved in cell cycle and apoptosis [57]. Previously, we demonstrated the reduced expression of *RB1* in PeCa and suggested the occurrence of other mechanisms for RB repression than the canonical HPV/*TP53*/*RB1* signaling pathway [4]. Therefore, based on this present study, upregulation of these miRNAs' expression, could be another mechanism that leads to the negative regulation of *RB1* in HPV^+ PeCa.

Additional integrated analysis considering the 78 genes affected by CNAs and regulated by CNA-miRNAs highlighted the involvement of other genes (*CCNE2*, *E2F5*, *EPAS1*, *INHBA*, *LYN*, *PDE7A*, *PPP-1CB*, *PPP3R1*, *RAC1*, *SEMA3D*, *SOS1*, *YWHAQ*, and *YWHAZ*) in the previously discussed pathways, such as P53 signaling, hippo and TGF-β signaling, proteoglycans in cancer and viral carcinogenesis. Thus, we emphasize the critical role of these pathways in penile tumorigenesis, however, functional assays are essential to confirm their biological role in PeCa.

The conventional treatment for PeCa patients is usually based on 5-Fluorouracil, Doxorubicin, Cisplatin, Ifosfamide, Methotrexate, and Paclitaxel, mostly in combination with radiotherapy. This treatment regimen is effective, however, patients' tumours eventually become resistant, which can lead to disease recurrence and death [6,9].

The drug prediction analysis conducted in our study, based on the main pathways described above indicated several molecular markers which inhibitory drugs could be repurposed for the treatment of HPV-related PeCa. The *EGFR* gene emerged as one of these known druggable targets, which we consider one of the most promising markers that can be used for PeCa treatment. This is based on our findings showing its gain of copy number and higher expression in most of the PeCa cases analyzed [4], and its involvement in the HPV-mediated carcinogenesis pathway, where its expression is affected by the endosomal acidification triggered by *miR-148a-3p* and the HPV-E5 oncoprotein. Thus, Cetuximab, a recombinant monoclonal antibody directed to EGFR, could be considered an alternative therapy for patients with PeCa that express this receptor. Interestingly, a recent study [58] has demonstrated that the growth of one PeCa-derived cell line overexpressing EGFR, was inhibited by EGFR inhibitors, corroborating with our findings. In addition, combined with chemotherapy, Cetuximab is the first line therapy for metastatic colorectal and squamous cell carcinomas [59–61], where it has been shown satisfactory responses [62,63].

In addition to EGFR inhibitors, the drug prediction analysis performed revealed the Celecoxib, a selective inhibitor of *COX2*. Interestingly, we previously reported in the PeCa cases of this study, the association of the overexpression of EGFR and COX2 [4], suggesting that their inhibitors could be used for PeCa treatment. Furthermore, *in vitro* studies have demonstrated the efficacy of the combination of COX2 inhibitors with other drugs in cancer cells. For example, Mishra et al. [64] demonstrated that N-acetyl-cysteine and Celecoxib inhibit the initiation of cutaneous tumours. Velmurugan et al. [65] showed that the combined treatment of Celecoxib and Calyculin-A inhibited the epithelial-mesenchymal transition in oral cancer cells. Other studies showed that treatment with Celecoxib prevents Doxorubicin-induced drug resistance in canine and mouse lymphoma cell lines [66]. These findings reinforce that COX2 and EGFR are promising druggable targets and could be considered as alternative therapeutic strategies to treat PeCa patients.

5. Conclusion

In conclusion, our analysis showed that CNAs present a significant impact on the regulation of miRNAs and their corresponding gene targets. The genes, miRNAs, and mRNA targets mapped in chromosome

regions with CNAs, can affect signaling pathways with relevance to the HPV-mediated carcinogenesis, and point out to druggable targets that could be potentially "repurposed" to treat PeCa patients with HPV infection.

Conflict of interest

The authors declare that they have no competing interest.

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Author contributions

Conception: J.S. and S.P.
Interpretation or analysis of data: J.S., L.C. and S.P.
Preparation of the manuscript: J.M., L.C. and S.P.
Revision for important intellectual content: J.M., L.N., R.C. A.D., A.K., R.M., A.P.S., L.C. and S.P.

Supplementary data

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4.2. Capítulo 2

Upregulated miRNAs on the *TP53* and *RB1* binding seedless regions in high-risk HPV-associated penile cancer

Jenilson da Silva, Carla Cutrim da Costa, Ingryd de Farias Ramos, Ana Carolina Laus, Luciane Sussuchi, Rui Manuel Reis, André Salim Khayat, Luciane Regina Cavalli and Silma Regina Pereira

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Upregulated miRNAs on the *TP53* and *RB1* Binding Seedless Regions in High-Risk HPV-Associated Penile Cancer

*Jenilson da Silva[1], Carla Cutrim da Costa[2], Ingryd de Farias Ramos[3], Ana Carolina Laus[4], Luciane Sussuchi[4], Rui Manuel Reis[4], André Salim Khayat[5,6], Luciane Regina Cavalli[7] and Silma Regina Pereira[8]**

[1]Postgraduate Program in Health Science, Federal University of Maranhão, São Luís, Brazil, [2]Degree in Biological Sciences, Department of Biology, Federal University of Maranhão, São Luís, Brazil, [3]Postgraduate Program in Oncology and Medical Sciences, Federal University of Pará, Belém, Brazil, [4]Molecular Oncology Research Center, Barretos Cancer Hospital, Barretos, Brazil, [5]Oncology Research Center, Federal University of Pará, Belém, Brazil, [6]Institute of Biological Sciences, Federal University of Pará, Belém, Brazil, [7]Research Institute Pelé Pequeno Príncipe, Faculdades Pequeno Príncipe, Curitiba, Brazil, [8]Laboratory of Genetics and Molecular Biology, Department of Biology, Federal University of Maranhão, São Luís, Brazil

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Rio de Janeiro State University, Brazil

***Correspondence:**
Silma Regina Pereira
silma.pereira@ufma.br

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Cancer development by the human papillomavirus (HPV) infection can occur through the canonical HPV/p53/RB1 pathway mediated by the E2/E6/E7 viral oncoproteins. During the transformation process, HPV inserts its genetic material into host Integration Sites (IS), affecting coding genes and miRNAs. In penile cancer (PeCa) there is limited data on the miRNAs that regulate mRNA targets associated with HPV, such as the *TP53* and *RB1* genes. Considering the high frequency of HPV infection in PeCa patients in Northeast Brazil, global miRNA expression profiling was performed in high-risk HPV-associated PeCa that presented with *TP53* and *RB1* mRNA downregulated expression. The miRNA expression profile of 22 PeCa tissue samples and five non-tumor penile tissues showed 507 differentially expressed miRNAs: 494 downregulated and 13 upregulated (let-7a-5p, miR-130a-3p, miR-142-3p, miR-15b-5p miR-16-5p, miR-200c-3p, miR-205-5p, miR-21-5p, miR-223-3p, miR-22-3p, miR-25-3p, miR-31-5p and miR-93-5p), of which 11 were identified to be in HPV16-IS and targeting *TP53* and *RB1* genes. One hundred and thirty-one and 490 miRNA binding sites were observed for *TP53* and *RB1*, respectively, most of which were in seedless regions. These findings suggest that up-regulation of miRNA expression can directly repress *TP53* and *RB1* expression by their binding sites in the non-canonical seedless regions.

Keywords: penile cancer, tumor suppressor repression, miRNA, HPV, *TP53*, *Rb1*

INTRODUCTION

The *TP53* gene is known as the "sentinel gene" due to its ability to identify cell damage and to coordinate complex mechanisms to mediate cell repair, protecting genome stability and, consequently, cell homeostasis. Therefore, it is not surprising that *TP53* tumor suppressor is the most frequently mutated gene in human tumors. Most of the alterations described are missense mutations, whereby the protein loses its primary function, or it acquires oncogenetic functions (Datta et al., 2017; Wang and Sun, 2017; Sammons et al., 2020). In addition, the p53 mutant protein

may also facilitate the adaptation of tumor cells to the disadvantageous environment that arises as the tumor grows (Mantovani et al., 2019).

The association between human papillomavirus (HPV) and some cancers, including cervical, head and neck, vulvar, anorectal, and penile squamous cell carcinomas (SCC), is well characterized by the canonical mechanism involving the HPV oncogenes E6 and E7 and p53 and RB1 proteins (de Martel et al., 2017). During the transformation process, HPV inserts its genetic material into host human integration sites (IS), which have been identified in regions harboring cancer-related genes, as well as in regions presenting copy number alterations (CNAs) (Busso-Lopes et al., 2015; Macedo et al., 2020; Pinatti et al., 2021). Indeed, integration of DNA-copy number alterations and other omics data have shown that DNA methylation, mRNA, and miRNA expressions alterations affect coding-genes and miRNAs located within or near the HPV common integration sites (Barzon et al., 2014; Groves and Coleman, 2018; Rosa et al., 2019; Pinatti et al., 2021).

In the last decade, it has been also demonstrated that the wild-type p53 protein plays primarily its role as a transcription factor by regulating a large network of protein-coding genes and non-coding RNAs, including miRNAs, both inducing or repressing their targets (Hermeking, 2012; Fischer, 2017). In addition, the p53 protein regulates miRNA processing, primarily through its central DNA-binding domain, a target site of most cancer-specific mutations. Interestingly, miRNAs can also regulate p53 expression by matching in the seed region into the 3′UTR of *TP53* mRNA, directly inducing the repression of *TP53* or its regulators (Hermeking, 2012; Hermeking et al., 2014). Although several tumor-specific alterations in the p53-miRNA network have been described in different cancers (Hermeking, 2012; Datta et al., 2019), there is no data on miRNAs targeting of *TP53* gene in HPV-associated penile cancer.

PeCa is a rare carcinoma in developed countries, but it presents higher incidence rates in South America, Asia, and Africa, where limited economic and social conditions play a large impact leading to delay in diagnosis, and treatment initiation. In Brazil, specifically in the Northeast region that is particularly affected by low socio-economic conditions and educational levels and high frequency of HPV infection, presents a high incidence of PeCa, with patients presenting additional comorbidities, which contributes to a high incidence of mortality rates (Macedo et al., 2020; Silva et al., 2021) However, even in countries that are not impacted by major economic limitations, the incidence and mortality rates of PeCa has increased, mainly among younger patients (Hansen et al., 2018). Hence, the increased occurrence of PeCa, irrespectively of the countries' socioeconomic conditions, has suggested that HPV infection is possibly the main triggering mechanism for tumor development, in addition to poor hygiene of the genital region, phimosis, uncircumcision, and chronic inflammation (Christodoulidou et al., 2015; Kidd et al., 2017; Adashek et al., 2019).

PeCa treatment options are limited. No effective target therapy is available, mainly due to the scarcity of knowledge on the molecular pathways involved in the development and progression of these tumors. Limited data is available on the role and mechanisms of miRNA deregulation in PeCa, including those that disrupt miRNAs targets that regulate critical genes associated with the action of HPV, such as the *TP53* and *RB1* genes. Considering the high frequency of HPV infection in patients with advanced PeCa in Maranhão State, in Northeast of Brazil, in the present study miRNAs expression analysis was performed in high-risk HPV-associated PeCa with *TP53* and *RB1* mRNA downregulated expression, as previously reported by our group in >80 and 60% of the patients, respectively (Macedo et al., 2020).

This study opens the opportunity to better understand the role of *TP53* and *RB1* transcriptional regulators in HPV-associated penile carcinomas and brings much needed knowledge on the molecular tumorigenesis of this still-neglected tumor.

MATERIALS AND METHODS

Sample Cohort

Fresh PeCa chemotherapy-naive surgical resection tissue specimens were obtained from 22 patients from the Aldenora Hospital, São Luís, Maranhão, Brazil. These patients are a subset of a larger cohort of 37 patients previously investigated for HPV *status*, gene, and protein expression for *TP53* and *RB1* (Macedo et al., 2020). All the samples were collected under patients' written informed consent, approved by the Research Ethics Committee on Humans from the Federal University of Maranhão and by the National Research Ethics Commission (CONEP-Brazil, CAAE: 46371515.5.0000.5087). Tumor and adjacent non-tumor tissues, sampled from 2 cm distant from the tumor site after histopathological assessment, were obtained before any cancer treatment. At the time of the sample collection, the patients had no history of other cancers or sexually transmitted diseases.

The clinical and histopathological variables were obtained from patients' medical records. The mean age of the patients at diagnosis was 64.22 ± 15.63 years, ranging from 32 to 85 years old. The patients declared themselves smokers (41%) and alcoholics (45.5%). All tumors were classified as squamous cell carcinoma (SCC), and the condylomatous and keratinized histological subtypes localized mostly in the glans, corpus cavernosum, and corpus spongiosum were the most frequent, 45.4 and 36.4%, respectively. Tumor grades II and III were the most frequent, present in 54.5 and 27.3% of the patients, respectively. Lymphatic and perineural invasion were positive in 18.2 and 22.8% of the patients, who presented mostly ulcerated lesions (68.2% of the cases), followed by vegetative (18.2%) and verrucous (13.6%). Penectomy (partial and total) was performed in 95.4% of the patients. The primary tumor of each patient was positive for HPV by Nested-PCR and DNA sequencing, as described in Macedo *et al.* In this subset, the multiple infections were detected in 50.0% of the cases. The HPV16 genotype was the most frequent (72.2%), followed by the 74 (16.6%), 30, 59 and 66 (11%, each) genotypes. Genotypes found in lower frequencies were 6, 18, 30, 35, 44, 53, 58, and 73 (**Supplementary Table S1**). Four cases were positive for HPV, but not genotyped since the samples did not have sufficient DNA for Nested-PCR and/or DNA sequencing analysis. **Table 1** and

TABLE 1 | Clinical-histopathological profile of patients diagnosed with HPV positive penile carcinoma (n = 22).

Variable	Number (%)	Variable	Number (%)
1. Histological subtype		5. Lesion	
Condylomatous	10 (45.4%)	Ulcerated	15 (68.2%)
Keratinized PeCa	8 (36.4%)	Vegetative	4 (18.2%)
Mixed	4 (18.2%)	Verrucous	3 (13.6%)
2. Tumor size		6. Tumor site	
0.6–2.0	4 (18.2%)	Glans	9 (40.9%)
2.1–5.0	15 (68.2%)	Glans and foreskin	7 (31.8%)
5.1—10.0	3 (13.6%)	Foreskin	2 (9.1%)
3. Tumor stage		Glans, foreskin and other areas	4 (18.2%)
pT1	6 (27.3%)	7. Surgery type	
pT2	9 (40.9%)	Preserved penis	1 (4.5)
pT3	7 (31.8%)	Partial penectomy	16 (72.7%)
4. Tumor grade		Radical penectomy	5 (22.7%)
I	4 (18.2%)	8. Phimosis occurrence	
II	12 (54.5%)	Yes	8 (36.3%)
III	6 (27.3%)	No	9 (41.0%)
—	—	No information	5 (22.7%)

Supplementary Table S1 present the detailed patients' clinical-histopathological information.

Considering our previous study (Macedo et al., 2020) in which we have demonstrated *TP53* and *RB1* down-regulated expression at both mRNA (by real-time PCR) and protein (by immunohistochemistry) levels (86 and 65% of the cases, respectively), in this study, we investigated the possible mechanisms by which these genes might be repressed in HPV-associated PeCa. For that, a subset of 22 tumors was evaluated for differential miRNA expression in relation to adjacent non-tumor tissues (n = 5). Fifteen of the 22 tumors have data on the expression of *TP53* and *RB1* (73 and 69% of the tumors are underexpressed, respectively) (**Supplementary Table S1**). Subsequently, prediction miRNAs binding sites analysis were performed in the *TP53* and *RB1* gene, followed by a search for molecular pathways potentially involved in penile carcinogenesis in HPV-positive patients.

Global miRNA Expression Analysis

Total RNA from 22 PeCa tumors and five adjacent non-tumor tissues was isolated using the TRIzol protocol (Invitrogen Carlsbad, CA, United States). RNA concentration and quality were tested by measuring the 260/280 and 260/230 ratios using the Nanodrop 2001 spectrophotometer (Willington, DE, United States). Expression of miRNAs was determined using the *nCounter® Human v.3 miRNA expression* platform (*Nanostring Technologies™*, Seattle, Wa, United States), which contains human probes from miRBase v.22 (http://www.mirbase.org) targeting 827 human miRNAs, six positive controls, eight negative controls, three positive binding controls, three negative binding controls, five internal reference genes (*ACTB*, *B2M*, *GAPDH*, *RPL19,* and *RPL0*) and five miRNA controls (ath-miR- 159a, cel-miR-248, cel-miR-254, osa-miR-414, and osa-miR-442) as previously reported at the Molecular Oncology Research Center (Pessôa-Pereira et al., 2020; Causin et al., 2021). The raw data were pre-processed and exported as RCC files. The raw data of the study, as well as the clinical information of the patients are available for access from the *Gene Expression Omnibus* (GEO), under registration GSE197121.

Differential miRNA Expression Analysis

The raw data were normalized and analyzed using the ROSALIND® Nanostring platform (https://rosalind.onramp.bio/). Adjacent non-tumor tissues distant 2 cm for the primary tumor were used as control. Read distribution percentages, identity heatmaps, and sample MDS plots were generated as part of the QC step. The normalization was conducted following the background subtraction based on POS_A probes correction factors (positive control normalization and codeset normalization). For both steps, the geometric mean of each probeset was used to create a normalization factor. The fold changes, p-values for comparisons were calculated using the t-test method ($p \leq 0.05$). p-value adjustment was performed using the Benjamini–Hochberg ($p \leq 0.01$) method to estimate false discovery rates (FDR). The clustering of miRNAs for the final heatmap was constructed using the PAM (Partitioning Around Medoids) through a method using the FPC R library (Hennig, 2020) that takes into account the direction and type of all signals in a pathway, the position, function, and type of each miRNA identified. Fold change (≥2 for miRNAs upregulated and ≤-2 for miRNAs downregulated), p-value and adjusted p-value were used as selection criteria for miRDE.

Prediction of miRNA Binding Sites in the *TP53* and *RB1* Gene Sequences

The *STarMir* software (Kanoria et al., 2016) was used to identify the miRNAs binding regions in *TP53* and *RB1* genes (CLIP-data). The construction design and nucleic acid fold of *STarMir* are obtained from the *Mfold* package (Zuker, 2003) and *Sfold* which contains the *Srna* module (Ding et al., 2004). *Sfold* applies a two-step model for hybridization between mRNA and miRNA. In this model, hybridization of the miRNA-target occurs at an accessible target site and then the hybrid elongates to form the complete

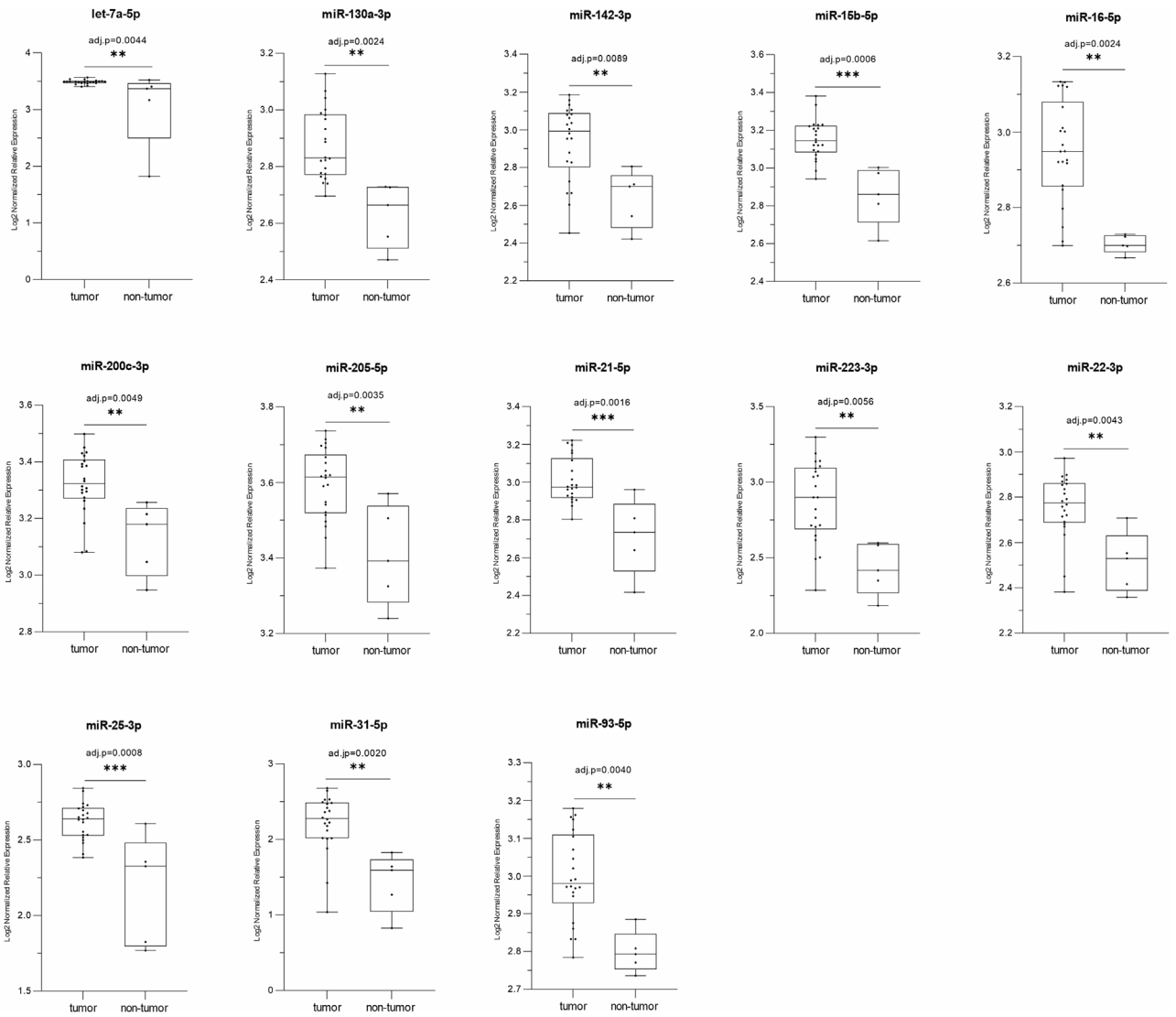

FIGURE 1 | The box-plots represent a comparison of the relative expression levels of the 13 miRDE upregulated in tumors ($n = 22$) versus normal tissue ($n = 5$); $p \leq 0.05$ by *t*-test and adj.-p ≤ 0.01 by Benjamini–Hochberg; $^{*}p \leq 0.05$, $^{**}p \leq 0.01$ and $^{***}p \leq 0.001$.

miRNA-target duplex. The minimum free energy of hybridization was obtained from the RNA*hybrid* tool (Rehmsmeier et al., 2004; Long et al., 2007). Only interactions in "seed" and "seedless" regions with LogitProb values ≥0.5; $\Delta G_{hybrid} \leq -10.00$ and site-access ≥ 0.4 were considered.

Pathway's Enrichment Analysis

Pathway's enrichment analysis was performed by miRPath v.3 - DIANA TOOLS software (Vlachos et al., 2015) using the Tarbase prediction algorithm and considering the *p*-value threshold ≤0.05. The generated pathways are part of the *Kyoto Encyclopedia of Genes and Genomes* (KEGG). The *TP53* and *RB1* genes were used as filters to generate KEGG pathways. The *'pathways union'* function was used to generate the related top pathways, considering the *p*-value threshold ≤0.05 and enrichment analysis method by Fisher's Exact Test.

RESULTS

Overexpressed miRNAs Targeting TP53 and RB1 in Penile Cancer Patients

Differential miRNA expression analysis was performed in the 22 PeCa tissues. The global miRNA expression profile of these tumors showed 507 differentially expressed miRNAs (miRDE) compared to a group of five adjacent non-tumor penile tissues. Among these miRDE, 494 (97.4%) miRNAs were downregulated and 13 (2.6%) upregulated (**Figure 1**; **Table 2**). Considering the previously detected lower *TP53* mRNA expression (85.7% (12/14) and lower protein expression in 87.5% (14/16) of these cases (Macedo et al., 2020), we further investigated the up-regulated miRNAs in the subset of 22 tumors, of which 73% were downregulated. The miRDEs let-7a-5p, miR-130a-3p, miR-15b-5p, miR-21-5p, and miR-25-3p were overexpressed in

TABLE 2 | Thirteen differentially expressed miRNAs observed upregulated in the PeCa patients, and their respective chromosomal location and HPV integration sites (presented by miRNA number).

miRNAs	Cytoband	Start—Stop (bp)	Integration site HPV (genotype)[a]	miRNA expression	Frequency (%)	Log2FC	*p*-Value	Adj.-*p*
let-7a-5p	9q22.32	96,938,234–96,938,325	yes, (16.18)	upregulated	100.0	2.2266	0.0019	0.0044
miR-130a-3p	11q12.1	57,641,198–57,641,286	yes, (16)	upregulated	100.0	1.1603	0.0008	0.0024
miR-142-3p	17q22	58,331,222–58,331,327	yes, (16)	upregulated	86.4	1.4576	0.0054	0.0089
miR-15b-5p	3q25.33	160,404,588–160,404,685	yes, (16)	upregulated	100.0	1.6509	0.0000	0.0006
miR-16-5p	13q14.2	50,623,109–50,623,197	yes, (16)	upregulated	95.5	1.2512	0.0008	0.0024
miR-200c-3p	12p13.31	6,963,694–6,963,771	no	upregulated	95.5	1.2541	0.0023	0.0049
miR-205-5p	1q32.2	209,428,820–209,432,384	yes, (16.18)	upregulated	95.5	1.4610	0.0013	0.0035
miR-21-5p	17q23.1	59,841,262–59,841,342	yes, (16.18)	upregulated	100.0	1.4629	0.0004	0.0016
miR-223-3p	Xq12	66,018,870–66,018,979	no	upregulated	95.5	2.0222	0.0028	0.0056
miR-22-3p	17p13.3	1,617,197–1,617,281	yes, (16)	upregulated	91.0	1.0605	0.0018	0.0043
miR-25-3p	7q22.1	100,093,560–100,093,643	yes, (16)	upregulated	100.0	1.5448	0.0001	0.0008
miR-31-5p	9p21.3	21,512,114–21,512,184	yes, (16)	upregulated	91.0	2.0012	0.0006	0.0020
miR-93-5p	7q22.1	99,691,391–99,691,470	yes, (16)	upregulated	95.5	1.0525	0.0016	0.0040

[a]*Data obtained from HPVBase (Kumar Gupta and Kumar, 2015) and VISDB (Tang et al., 2020).*

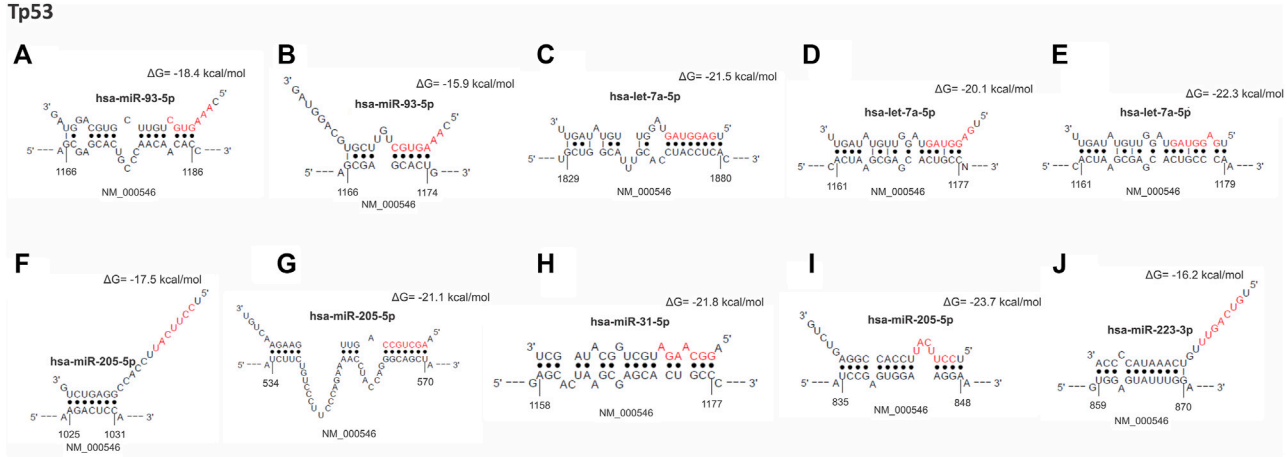

FIGURE 2 | From **(A–J)**, hybrid mRNA (*TP53*)—miRNA upregulated. The upper and lower sequences represent the miRNA in the 3′-5′ sense and 5′-3′ sense hybridization sites in the mRNA, repectively. The numbers at the ends of the mRNA show the starting and ending position of the hybridization sites. Dots between the sequences indicate the paired nucleotides. Nucleotides in red mark the "seed" sequence in miRNA. The energy resulting from the hybridization was calculated by the RNA*hybrid* algorithm.

100% of cases. Interestingly, 84.6% (n = 11) of miRDEs were found to be located at HPV integration sites. The HPV integration sites were identified as target regions of the oncogenic HPV16 genotype, the most frequently detected genotype in our study cohort (**Supplementary Table S1**).

Figure 1 Relative expression of thirteen miRNAs upregulated (tumor vs. non-tumor) in the PeCa studied.

Prediction of miRNA binding sites revealed that all 13 up-regulated miRNAs targeted the *TP53* gene, acting as negative regulators of this tumor suppressor gene expression. We found 131 target sites for these miRNAs: 98.5% in the non-canonical seedless regions and two in the seed regions (**Supplementary Table S2**). Interestingly, *TP53* presents 129 seedless sites, in which all 13 differentially expressed miRNAs could bind. The coding region presented the highest number of target seedless regions with 81/129 sites (62.8%), followed by 3′UTR with 32/129 sites (24.8%) and 5′UTR with 16/129 sites (12.4%). Bindings in the gene seed regions were observed to occur with miR-22-3p and let-7a-5p and both interactions were of 8mer-type. The binding between let-7a-5p and *TP53* occurred in a canonical 3′UTR region, while the binding of miR-22-3p occurred in a non-canonical coding region (site position: 534–570 (bp); seed position: 564–570 (bp). This region is highly conserved (site conservation = 0.963 and seed conservation = 0.933). Our

TABLE 3 | Top 10 miRNA binding regions identified in TP53 and RB1 genes.

miRNA	Site position[a]	LogitProb[b]	Region	ΔG_{hybrid}[c]	ΔG_{total}[d]	Site access[e]	Site consv[f]	Site location[g]
Binding regions in TP53								
miR-93-5p	1,166–1,174	0.864	CDS	−15.900	−15.316	0.714	0.959	0.820
miR-93-5p	1,166–1,186	0.848	CDS	−18.400	−18.018	0.805	0.981	0.820
let-7a-5p	1829–1850	0.835	3′UTR[h]	−21.500	−12.736	0.631	0.001	0.357
let-7a-5p	1,161–1,177	0.831	CDS	−20.100	−19.630	0.767	0.900	0.816
let-7a-5p	1,161–1,179	0.808	CDS	−22.300	−21.904	0.783	0.910	0.816
miR-205-5p	1,025–1,031	0.787	CDS	−17.500	−10.665	0.602	0.997	0.701
miR-22-3p	534–570	0.762	CDS[i]	−21.100	2.9490	0.448	0.963	0.285
miR-31-5p	1,158–1,177	0.755	CDS	−21.800	-16.974	0.667	0.912	0.813
miR-205-5p	835–848	0.755	CDS	−23.700	-13.153	0.442	0.907	0.540
miR-223-3p	859–870	0.727	CDS	−16.200	-6.7460	0.421	0.803	0.560
Binding regions in RB1								
let-7a-5p	2,506–2,517	0.953	CDS[i]	−18.100	−16.708	0.823	0.999	0.840
miR-130a-3p	2,529–2,537	0.917	CDS	−17.100	−11.446	0.708	1.000	0.848
miR-31-5p	4,704–4,721	0.912	3′UTR	−20.100	−17.244	0.651	1.000	0.963
let-7a-5p	4,686–4,712	0.911	3′UTR	−22.100	−17.127	0.608	0.999	0.953
miR-31-5p	4,704–4,719	0.899	3′UTR	−18.700	−16.076	0.627	1.000	0.963
miR-31-5p	4,704–4,717	0.898	3′UTR	−17.200	−14.545	0.672	1.000	0.963
let-7a-5p	4,686–4,719	0.896	3′UTR	−20.700	−14.420	0.573	1.000	0.953
miR-130a-3p	2,529–2,534	0.892	CDS	−15.900	−10.778	0.646	1.000	0.848
miR-142-3p	2002–2026	0.883	CDS	−18.500	−12.601	0.692	0.847	0.659
let-7a-5p	562–571	0.878	CDS	−15.500	−14.118	0.846	0.957	0.142

[a]*Start and end position of the target region (site) predicted to be bound by miRNA.*
[b]*Probability of the site being an miRNA binding site as predicted by our nonlinear logistic model.*
[c]*A measure of stability for miRNA:target hybrid as computed by RNAhybrid.*
[d]*A measure of the total energy change of the hybridization.*
[e]*A measure of structural accessibility as computed by the average probability of a nucleotide being single-stranded (i.e., unpaired) for the nucleotides in the predicted binding site.*
[f]*Conservation score by the PhastCons program for the binding site.*
[g]*Relative starting location of the predicted binding site along the length of the sequence (e.g., for 3′′ UTR, 0 indicates the 5′′ end of the UTR, and one corresponds to the 3′′ end).*
[h]*"seed" region in 3′UTR ("seed" position: 1843–1849, binding: 8mer).*
[i]*"seed" region in CDS ("seed" position: 564–570, binding: 8mer).*

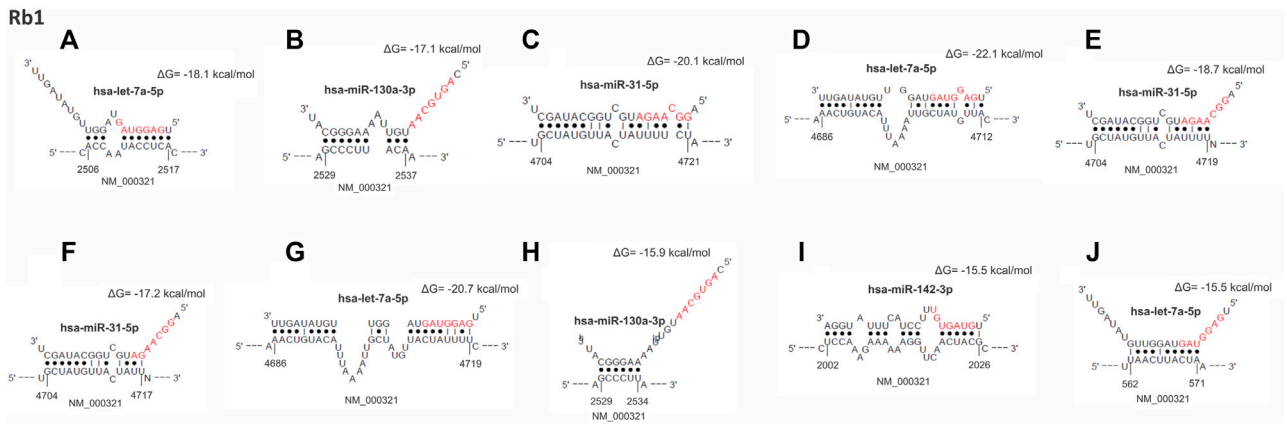

FIGURE 3 | From **(A–J)**, hybrid mRNA (RB1)—miRNA upregulated. The upper and lower sequences represent the miRNA in the 3′-5′ sense and 5′-3′ sense hybridization sites in the mRNA, respectively. The numbers at the ends of the mRNA show the starting and ending position of the hybridization sites. Dots between the sequences indicate the paired nucleotides. Nucleotides in red mark the "seed" sequence in miRNA. The energy resulting from the hybridization was calculated by the RNA*hybrid* algorithm.

analysis also revealed that miR-93-5p and let-7a-5p can bind to a higher number of seedless regions, 21 and 20 predicted binding sites, respectively, while miR-15b-5p, miR-16-5p, miR-223-5p, miR-22-5p, and miR-31-5p bind to a lower number of regions, i.e., five predicted sites for each. Considering the size of the *TP53* mRNA (2,591 bp; transcript variant 1, NCBI Reference Sequence:

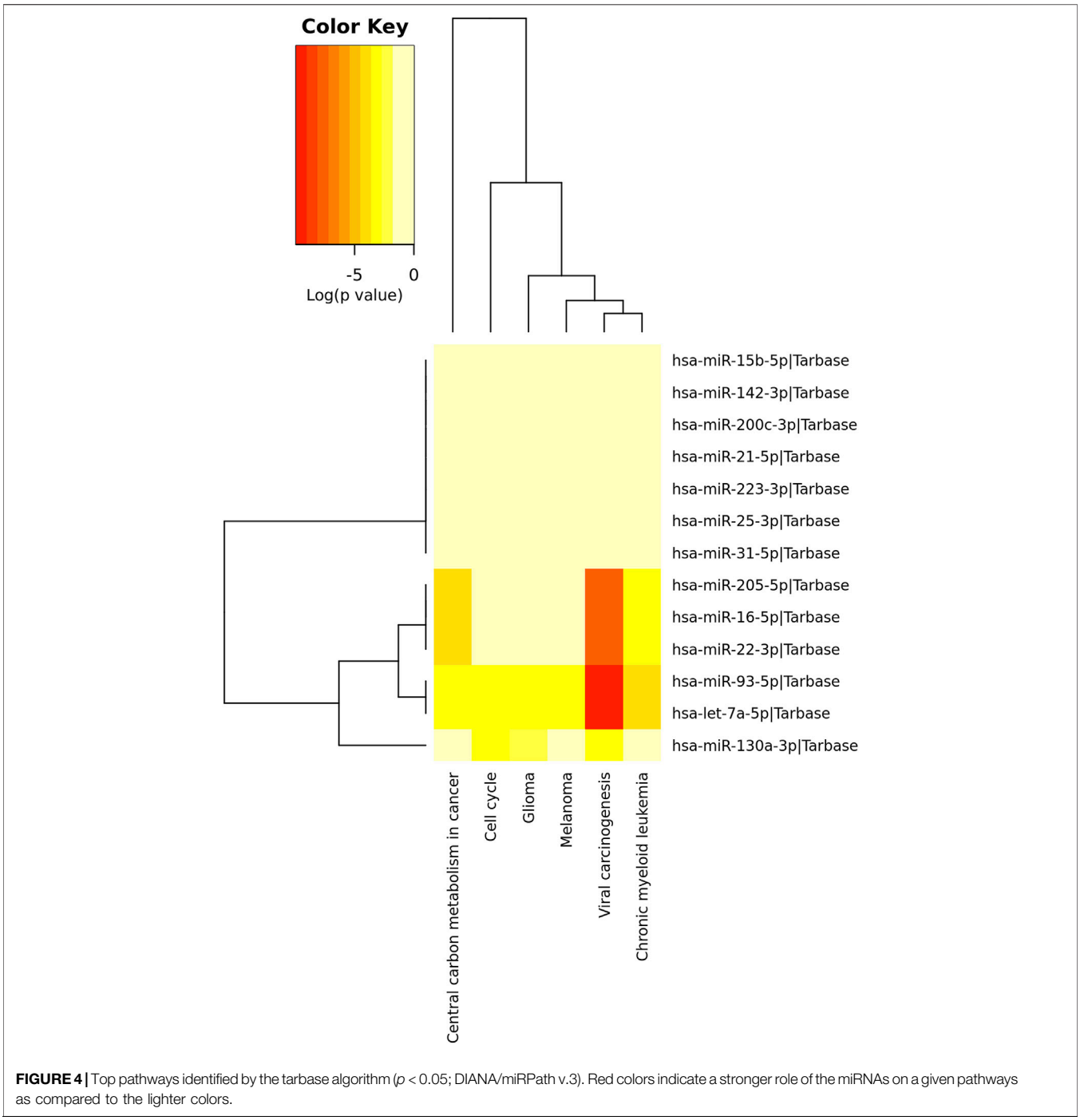

FIGURE 4 | Top pathways identified by the tarbase algorithm ($p < 0.05$; DIANA/miRPath v.3). Red colors indicate a stronger role of the miRNAs on a given pathways as compared to the lighter colors.

NM_000546.5) we observed that the 1,000–1073bp, 2,500–2580bp, and 835–899bp intervals are miRNA binding hotspots regions, harboring a total of 22, 16 and 14 sites, respectively. **Figure 2**; **Table 3** show the ten main binding sites observed in the *TP53* gene.

Figure 2 Top 10 miRNAs binding site regions identified in the *TP53* gene.

The lower expression of *RB1* gene was also found in 69% of the tumors. Interestingly, we observed that the thirteen overexpressed miRNAs that down-regulated *TP53* also regulated *RB1* expression (**Figure 3**). A total of 490 miRNA binding sites were identified for *RB1* (**Supplementary Table S3**), of which 477 (97.3%) were located in the non-canonical seedless regions, while 13 (2.7%) were in the seed regions. Bindings in the seed regions occurred with seven overexpressed miRNAs (miR-93-5p, let-7a-5p, miR-25-3p, miR-130a-3p, miR-200c-3p, miR-205-5p, and miR-142-3p), most of which were 7mer-A1 (46.2%). Other binding sites identified in the seed regions were offset-6mer

TABLE 4 | Top six molecular pathways involving overexpressed miRNAs targeting *TP53* and *RB1* genes.

KEGG Pathway	*p*-Value pathway	miRNAs name	Target gene	*p*-Value interaction
Viral carcinogenesis (hsa05203)	$<1.00 \times 10^{-325}$	let-7a-5p	*TP53* and *RB1*	1.16×10^{-10}
		miR-130a-3p	*RB1*	0.0039733
		miR-16-5p	*TP53*	6.44×10^{-08}
		miR-205-5p	*TP53*	6.44×10^{-08}
		miR-22-3p	*TP53*	6.44×10^{-08}
		miR-93-5p	*TP53* and *RB1*	1.16×10^{-10}
Central carbon metabolism in cancer (hsa05230)	3.39×10^{-06}	let-7a-5p	*TP53*	0.0011443
		miR-16-5p	*TP53*	0.0005629
		miR-205-5p	*TP53*	0.0005629
		miR-22-3p	*TP53*	0.0005629
		miR-93-5p	*TP53*	0.0011443
Chronic myeloid leukemia (hsa05220)	1.33×10^{-05}	let-7a-5p	*TP53* and *RB1*	0.0005998
		miR-16-5p	*TP53*	0.0041602
		miR-205-5p	*TP53*	0.0041602
		miR-22-3p	*TP53*	0.0041602
		miR-93-5p	*TP53* and *RB1*	0.0005998
Glioma (hsa05214)	0.0064303	let-7a-5p	*TP53* and *RB1*	0.0017756
		miR-130a-3	*RB1*	0.0105785
		miR-93-5p	*TP53* and *RB1*	0.0017756
Melanoma (hsa05218)	0.0120334	let-7a-5p	*TP53* and *RB1*	0.0041201
		miR-93-5p	*TP53* and *RB1*	0.0041201
Cell cycle (hsa04110)	0.0224147	let-7a-5p	*TP53* and *RB1*	0.0038093
		miR-130a-3	*RB1*	0.0014269
		miR-93-5p	*TP53* and *RB1*	0.0038093

(23.0%), 6mer, and 7mer-m8 (15.4%, each) (**Supplementary Table S2A**). The *RB1* gene also presented the highest number of miRNA target sites in seedless regions (490 in total), in which all 13 differentially expressed miRNAs can bind. The *RB1* coding region also had the highest number of seedless regions (57.0%), followed by 3′UTR (42.4%) and 5′UTR (0.6%). The miRNA let-7a-5p showed the highest number of seedless bindings (77 predicted sites), followed by miR-93-5p (74 predicted sites). The miRNAs presenting a smaller number of regions were miR-16-5p, miR-205-5p, miR-223-3p (22 predicted sites, each) and miR-22-3p (19 predicted sites). The *RB1* gene also presented hotspots regions where several miRNAs can bind. The intervals between 2,202–2297pb and 1906–1997 pb house a total of 21, and 19 sites, respectively (NCBI Reference Sequence: NM_000321.3). **Table 3** shows the top 10 binding sites in *RB1*.

Figure 3 Top 10 miRNAs binding site regions identified in the *RB1* gene.

Molecular Pathways

KEGG pathway analysis was performed to identify the involvement of the 13 upregulated miRNAs above in disease and signaling pathways. This analysis revealed a total of 13 KEGG pathways (**Supplementary Table S3**), of which the top was: viral carcinogenesis (hsa05203) (p=$<1.00 \times 10^{-325}$), central carbon metabolism in cancer (hsa05230) ($p = 3.39 \times 10^{-06}$), chronic myeloid leukemia (hsa05220) ($p = 1.33 \times 10^{-05}$), glioma (hsa05214) ($p = 0.0064$), melanoma (hsa05218) ($p = 0.0120$) and cell cycle (hsa04110) ($p = 0.0224$) (**Figure 4**; **Table 4**).

Figure 4 Unsupervised hierarchical grouping of the 13 miRNAs differentially expressed and top related pathways.

DISCUSSION

It is well known that the integration of the human papillomavirus (HPV) can occur at or near cancer-related genes (Durst et al., 1987). However, it is not completely understood the mechanisms by which the HPV virus controls its integration into the host cell genome and the molecular consequences that ultimately lead to the development and progression of the HPV infected tumors. Studies have used high-performance technologies to identify virus integration sites in the host genome to better understand the molecular alterations that occur in the host cell, leading to the loss of its genomic stability (Akagi et al., 2014; Bodelon et al., 2016; Liu et al., 2016; Gao et al., 2017; Rosa et al., 2019). The most well-known example is the canonical HPV/*TP53*/*RB1* signaling pathway initiated by the viral E2 disruption. This leads to the loss of the negative feedback control of the viral oncoproteins E6 and E7, mediating ubiquitination and degradation of the p53 and pRb proteins, respectively (Squarzanti et al., 2018). Other authors proposed that HPV integration also directly causes activation of oncogenes or inactivation of tumor suppressors, as reported in HPV-related squamous cell carcinomas (Parfenov et al., 2014; Hu et al., 2015).

In our previous study, we showed downregulated mRNA expression of the *TP53* and *RB1* genes in 86 and 65% of high-

risk HPV-associated PeCa, respectively. In the present subset of cases, we evaluated miRNAs' expression, and observed that 73 and 69% were downregulated for both genes, respectively, suggesting the existence of other regulatory mechanisms in addition to the canonical HPV/*TP53*/*RB1* pathway (Macedo et al., 2020). Although not all the cases presented with expression alterations in these genes, these results were recently corroborated by Furuya *et al.*, who also described *TP53* reduced expression levels in penile tumors.

Compared to other cancers (Santos et al., 2018; Datta et al., 2019; Hussen et al., 2021; Liu et al., 2021), few studies have described epigenetic events in penile tumors, whether evaluating miRNAs (Zhang et al., 2015; Hartz et al., 2016; Kuasne et al., 2017; Peta et al., 2017; Ayoubian et al., 2021; Furuya et al., 2021) or by evaluating methylation patterns (Feber et al., 2015; Kuasne et al., 2015; Marchi et al., 2017). Changes by both mechanisms could justify the downregulation of *TP53* and *RB1*, however only *RB1* has been reported to be hypermethylated (Marchi et al., 2017). Additionally, as most pathogenic variants of these genes have been described in coding regions, the mRNA downregulation of *TP53* and *RB1* does not appear to be due to mutations (Feber et al., 2016; Wang et al., 2019; Chahoud et al., 2021). Furthermore, few studies have evaluated patients' cohorts with a high incidence of HPV infection, remaining poorly known the impact of HPV infection in disrupting mRNA/miRNA networks in penile tumors (Zhang et al., 2015; Hartz et al., 2016; Kuasne et al., 2017; Ayoubian et al., 2021; Furuya et al., 2021). In the present study, our main goal was to determine whether altered miRNAs expression could be associated with the down-regulation of the *TP53* and *RB1* expression in the etiopathogenesis of HPV-associated PeCa. This goal is of critical relevance to these particular virus associated with infected tumors, considering that the patient cohort investigated, from the State of Maranhão in Northeastern Brazil, is characterized by advanced PeCa and a high rate of HPV infection (>90%), as we reported previously (Coelho et al., 2018; Macedo et al., 2020). In addition, this study can provide useful information to target HPV-specific molecular pathways in human cancers.

In the present study, all patients were tested for HPV by nested-PCR followed by DNA sequencing. Using two highly sensitive methods we successfully detected HPV infection in 100% of men with PeCa, all of them with high-risk subtypes. Despite the high HPV prevalence in all human populations, occurring as hundreds of types, subtypes, and variants, many of them are not associated with cancer. On the other hand, it is well established the correlation between high-risk HPV and severe dysplasia, *in situ* and invasive cancer, usually as monoclonal lesions due to clonal selection from less advanced precursors (Pontén and Guo, 1998). This may explain why we were able to detect HPV in 100% of the primary tumor since all of them presented high-risk genotypes.

It is well established that p53 regulates the expression of both protein-coding genes and non-coding RNAs (Hermeking, 2012; Fischer, 2017). *TP53*-regulated miRNAs can mediate tumor suppression in response to cellular stress; similarly, the expression and activity of p53 can also be under the control of miRNAs (Hermeking, 2012). More than 20 miRNAs have been described to directly regulate p53 via canonical bindings (seed) in 3′UTR (reviewed by Liu et al., 2017). Down regulation of *TP53* through seed sequences induce phenotypes that are consistent with loss of p53 function, such as reduced apoptosis, cellular senescence, increased invasion, and growth of tumor cells (Hermeking, 2012; Deng and Sui, 2013; Hermeking et al., 2014). Despite the increasing number of miRNAs that form the TP53 mRNA/miRNAs interaction network, there is no information on *TP53*-repressor miRNAs in HPV-associated PeCa. Our data revealed a total of 507 differentially expressed miRNA (miRDE) between the tumor and non-tumor tissue of HPV-infected PeCa patients, of which 494 were downregulated and 13 were upregulated. Among the 13 miRDE upregulated, five (let-7a-5p, miR-130a-3p, miR-15b-5p, miR-21-5p and miR-25-3p) were found overexpressed in 100% of the tumors analyzed. Moreover, miR-130a-3p, miR-15b-5p and miR-31-5p were predicted as novel regulator for *TP53* gene; while miR-142-3p, miR-200c-3p, miR-205-5p, miR-223-3p, miR-22-3p, miR-25-3p and miR-31-5p for *RB1*.

Several studies have shown up-regulated expression of these miRNAs in several types of tumors. Overexpression of let-7a-5p has been observed in HCV-related cirrhosis (Petkevich et al., 2021) and liver cancer and ovarian cancer, where it presents a non-invasive diagnostic potential (Liu et al., 2021). Corroborating our data, some studies have also suggested that *TP53* is a target of let-7a-5p (Balakrishnan et al., 2014; Pillai et al., 2014; Nunez Lopez et al., 2019; Zhou et al., 2019). MiR-130a-3p is recognized as a miRNA with tumor suppressor action (Kong et al., 2018; Song et al., 2021), that may act directly (Causin et al., 2021) or indirectly (Hu et al., 2021) in cancer progression. On the other hand, miR-15b-5p has generally been described to act on cell proliferation mechanisms, such as the ones involving the *LATS2* (Liu et al., 2020), *BCL-2* (Zhang et al., 2015), and *PTPN4*/*STAT3* pathways (Liu et al., 2020).

Interestingly, down-regulation of *TP53* by miR-25 resulted in a decrease in apoptosis in HCT116 colon cancer cells, A549 cells, NSCLC, and multiple myeloma cells (Kumar et al., 2011). In lung cancer, miR-25 was observed to promote cell proliferation and also inhibit apoptosis by down-regulating the expression of the *MOAP1*/*TP53* axis genes (Wu et al., 2015). Moreover, recent evidence shows that miR-25-3p may also act with LncRNAs on a *LINC00858*/miR-25/*SMAD7* axis modulating *TP53*-wild expression in colorectal carcinoma (Zhan et al., 2020). (Wang et al., 2021) also observed that exosomal miR-25-3p induced cell proliferation and resistance to temozolomide in glioblastoma through down-regulation of *FBXW7*, promoting c-Myc and cyclin E expression. MiR-21-5p, also observed up-regulated in this study, was shown by (Huang et al., 2021) to negatively regulate the tumor suppressor *PDCD4* and cause resistance to by Osimertinib by interfering with MEK/ERK signaling.

These results are in concordance with the suppressive effect of these miRNAs in the HPV-related genes observed in PeCa in the present study. Our computational analysis revealed that *TP53* and *RB1* have 131 and 490 target sites for the 13 upregulated miRNAs, respectively. The highest number of miRNA binding sites were identified in coding regions, and not in UTR regions, as reported by

(Hafner et al., 2010) Furthermore, 98.5 and 97.3% of the sites in *TP53* and *RB1*, respectively, are in non-canonical seedless regions, presenting high levels of complementarity and conservation. Although most miRNA targets have sites that are perfectly complementary to the seed region, it has been shown that miRNAs can directly interact with seedless binding sequences, even improving their function (Shin et al., 2010). (Lal et al., 2009) for example, presented evidence of cell proliferation control by miR-24 in the *E2F2*/*MYC* axis through seedless binding in the 3′UTR region. (Park et al., 2017). also showed that destabilization of miRNAs targets is dramatically increased when binding occurs in non-canonical seedless regions. Therefore, we propose that the 13 miRNAs overexpressed in PeCa directly repress *TP53* and *RB1* by silencing their messenger RNA at different binding sites, especially in non-canonical seedless regions.

Although a unique miRNA may have a pivotal role in a particular pathway, most miRNAs act targeting multiple mRNAs, affecting the same or several gene pathways. Considering the 13 upregulated miRNAs, we predicted six main pathways by the enrichment analysis. Viral carcinogenesis (hsa05203), in which *TP53* and *RB1* act, was the main pathway affected ($p < 1.00 \times 10\text{-}325$). MiR-205-5p, miR-16-5p, miR-22-3p, miR-93-5p, let-7a-5p, and miR-130a-3p were involved in most of the pathways affected. Glioma and cell cycle pathways, in addition to viral carcinogenesis, were previously shown to be regulated by other miRNAs identified in cytobands affected by CNVs in the same population from Maranhão State (Silva et al., 2021). Thus, these current findings reinforce the involvement of these pathways in HPV-associated penile tumorigenesis.

It is worth highlighting that 84.6% of miRDE were observed to be located in HPV integration sites (HPV-IS), including the five miRDE overexpressed in 100% of cases (sites at 3q25.33, 7q22.1, 9q22.32, 11q12.1, and 17q23.1). Several viruses mediate tumorigenesis by expressing viral oncogenes or activating host oncogenes through the integration of viral DNA into the human genome (Lee and Dutta, 2009; Tuna and Amos, 2017). We have recently shown that chromosomal regions with gene copy number alterations (CNA) are present in HPV-IS, such as 2p12-p11.2 and 14q32.33 (observed in 100% of PeCa patients), which can also affect the expression of miRNAs located in these regions (Macedo et al., 2020; Silva et al., 2021). These regions were also described in other HPV-associated tumors (Wentzensen et al., 2004; Kumar Gupta and Kumar, 2015; Holmes et al., 2016; Liu et al., 2016). This data shows the close connection of CNAs and miRNA deregulation located in HPV-IS. Altogether, our present data, support that miRNAs located in HPV-IS can directly repress genes related to HPV infection, such as *TP53* and *RB1*, highlighting HPV insertion as one of the factors that trigger epigenetic mechanisms.

CONCLUSION

In this study, we suggest that the HPV-related genes, *TP53* and *RB1*, are directly down-regulated by 13 miRNAs located in high-risk HPV integration sites, notably for the HPV16 subtype, present in 72% of the PeCa patients studied. Considering that the expression and activity of *TP53* and *RB1* can be under the control of miRNAs, our findings provide a new understanding of the role of high-risk HPV infection in penile tumorigenesis through an epigenetic mechanism.

DATA AVAILABILITY STATEMENT

The datasets presented in this study can be found in online repositories. The names of the repository/repositories and accession number(s) can be found below: https://www.ncbi.nlm.nih.gov/geo/, GSE197121.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by Research Ethics Committee on Humans from the Federal University of Maranhão and by the National Research Ethics Commission (CONEP-Brazil, CAAE: 46371515.5.0000.5087). The patients/participants provided their written informed consent to participate in this study.

AUTHOR CONTRIBUTIONS

Conceptualization, SP and JS; Methodology, SP, JS, RR, AL, LS, and CC; Formal Analysis, SP, AK, IF, and JS; Investigation, JS and SP; Resources, SP and AK; Writing—Original Draft Preparation, SP and JS; Writing—Review and Editing, SP and LC; Visualization, LC and AK; Supervision, SP; Project Administration, SP; Funding Acquisition, SP and AK.

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SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fgene.2022.875939/full#supplementary-material

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4.3. Capítulo 3

MiRNAs profiling for advanced high-risk human papillomavirus-associated penile squamous cell carcinomas

Jenilson da Silva, Amanda de Deus, André Alvares Marques Vale, Ana Paula Azevedo da Silva, Leudivan Nogueira, Ana Carolina Laus, Luciane Sussuchi, Rui Manuel Reis and Silma Regina Pereira

Artigo em publicação

MiRNAs profiling for advanced high-risk human papillomavirus-associated penile squamous cell carcinomas

Jenilson da Silva[1,2], Amanda de Deus[1,2], André Alvares Marques Vale[2,3], Ana Paula Azevedo da Silva[3]; Leudivan Nogueira[3], Ana Carolina Laus[4], Luciane Sussuchi[4], Rui Manoel Reis[4,5,6] and Silma Regina Pereira[2,*]

[1] Postgraduate Program in Health Science, Federal University of Maranhão, São Luís, MA, Brazil, 65080-805

[2] Laboratory of Genetics and Molecular Biology, Department of Biology, Federal University of Maranhão, São Luís, MA, Brazil, 65080-805

[3] Laboratory of Applied Cancer Immunology, Department of Physiological Sciences, Federal University of Maranhão, São Luís, MA, Brazil, 65080-805

[3] Aldenora Bello Cancer Hospital, São Luís, MA, Brazil, 65031-630

[4] Research Center in Molecular Oncology, Hospital do Câncer de Barretos, Barretos, SP, Brazil, 14784-400

[5] Institute for Research in Health and Life Sciences (ICVS), School of Medicine, University of Minho, Braga, Portugal, 4710-057

[6] ICVS/3B's – PT Government Associate Laboratory, Braga/Guimarães, Portugal, 4710-057

Correspondent: silma.pereira@ufma.br; Tel.: +55-98-32728543

Key-words: HPV-Integration Sites, penile cancer, prognostic markers, perineural invasion.

Abstract:

Penile cancer (PeCa) is a rare tumor, normally associated with socioeconomic conditions in low-income countries, so that the delay in diagnosis and treatment results in more advanced tumors, higher comorbidity and mortality. Studies have shown that human papillomavirus (HPV) infection is one of PeCa main risk factors, so that viral integration sites have been related to copy number alterations (CNAs) global and genes, impacting miRNAs/mRNA interactions and, consequently, in the molecular pathways related to them. However, studies on differentially expressed microRNAs (miRDEs) in PeCa are still too scarce, especially in PeCa with high-risk HPV (hrHPV), to investigate the role of these gene regulators in tumor progression. In this study, we evaluated 827 miRNAs (Nanostring Technologies™, Seattle, WA, USA) in 22 penile squamous cell tumors from hrHPV patients and 5 non-tumor tissues. Among the 507 miRDEs identified, 25 of the most differentially expressed (Log2FC $\geq$1 and $\leq$-2.9) are related to 43 top molecular pathways, in which the most statistically significant being fatty acid biosynthesis pathway, prions, microRNAs (miRNAs) in cancer and hippo signaling ($p < 1.0^{-325}$, each). Of these, 92% (n=23/25) are within HPV integration sites (HPVis). Furthermore, miR-1206, miR-376b-3p and miR-495-3p were downregulated and are related to perineural invasion of tumors. Comparison of clinical groups (advanced disease *vs.* early disease) revealed 143 miRDEs. ROC analysis of one (miR-376a-2-5p), two (miR-376a-2-5p and miR-551b-3p) and five (miR-99a-5p, miR-150-5p, miR-155-5p, let-7c-5p and miR-342-3p) miRDEs showed robust discriminatory power

between the two clinical groups, AUC=0.9 and p= 0.0114 each. The highest sensitivity and specificity value were observed for miR-376a-2-5p, with 100% and 83.3%, respectively. The results of this study confirm that specific miRNAs can serve as potential diagnostic and prognostic markers in PeCa and are associated with HPV-dependent pathways.

1 Introduction

Penile cancer (PeCa) is a rare neoplasm with a high incidence in low- and middle-income countries (Thomas et al., 2021). Brazil stands out among the countries with the highest global incidence rates, with the Northeast region of the country having the greatest number of cases (Christodoulidou et al., 2015; Macedo et al., 2020). However, even in high-income countries, incidence and mortality rates have increased in recent decades, especially in young men (Hansen et al., 2018). Increased incidence of PeCa, regardless of socioeconomic conditions has reinforced that Human Papillomavirus (HPV) infection is possibly the main factor for the development of penile tumor, in addition to known risk factors, such as poor genital hygiene, phimosis, chronic inflammation, tobacco use and immunosuppression (Adashek et al., 2019; Christodoulidou et al., 2015; Kidd et al., 2017; Thomas et al., 2021).

Although pathological factors that predict lymph node metastasis (LNM) and the prognosis of PeCa, such as tumor grade, stage, lymphovascular, lymph node and extranodal invasion, have been accepted and included in the cancer staging, the analysis of their results is not very accurate (Djajadiningrat et al., 2013; Hakenberg et al., 2015; Lont et al., 2007; Protzel et al., 2009). On the other hand, perineural invasion (PNI), a risk factor that has a high predictive value for advanced PeCa, gained attention only in the updates of the 8th TNM (tumor, lymph node and metastasis) staging guideline (Paner et al., 2018), inspite of demonstrating a predictive role in LNM, mortality, and cancer-specific survival (reviewed by Zhou et al., 2018). Thus, this pathological factor has been limited in clinical practice, there is a lack of studies on PNI in hrHPV-positive penile squamous cell carcinomas (PSCC) and there are no biomarkers for PNI in advanced PeCa.

Our previous studies support the role of hrHPV infection in PSCC. In these studies, we describe a high frequency of cytobands with copy number alterations (CNAs) that are also HPV-integration sites (HPVis), as well as the impact of microRNA (miRNAs) and corresponding target genes affected by CNAs on HPV-associated molecular pathways (da Silva et al., 2022; Macedo et al., 2020; Silva et al., 2021). Data on changes in miRNA expression have been associated with penile carcinogenesis (Ayoubian et al., 2021; Furuya et al., 2021; Hartz et al., 2016; Kuasne et al., 2017; Murta et al., 2022; Zhang et al., 2015), however, few have evaluated differentially expressed miRNA (miRDEs), and even few biomarkers for disease have been proposed. Furthermore, all studies of miRDEs in PSCC have mostly HPV-negative patients cohorts. Thus, there is a need to unravel the role of miRDEs in advanced PSCC associated with hrHPV.

Considering the role of HPV infection in the classification of PeCa (Moch et al., 2016), the high frequency of hrHPV infection in patients with advanced PSCC in Northeast Brazil, and the absence of biomarkers for advanced PeCa, our study was designed. For the understanding of these interactions networks, we investigated the profile of miRDEs (available in GSE197121; da Silva et al., 2022) and conducted a prospective analysis with the aim of identifying a molecular signature for miRNA-based penile carcinogenesis. We described potential molecular markers and dysregulated pathways that may help to clarify the mechanisms underlying the development of PSCC, which may serve as a basis for future therapeutic strategies.

2 Materials and Methods

2.1 Study Population

The samples in this study are a subset of the patient samples obtained at the Aldenora Bello Cancer Hospital, São Luís, Maranhão, Brazil (Macedo et al., 2020). All patients admitted in the study signed written informed consent, which was approved by the Research Ethics Committee on Humans from the Federal University of Maranhão and by the National Research Ethics Commission (CONEP, Brazil; CAAE: 46371515.5.0000.5087). Fresh tumor tissues from 22 patients with clinical and histopathological diagnosis of penile cancer and 5 non-tumor adjacent tissues (2 cm distant from the tumor), were obtained at the time of surgery and before any cancer treatment. Clinical and histopathological data were obtained from the patients' charts in coded form.

The mean age at diagnosis was 64.2 ± 15.6, ranging from 32 to 85 years. Most patients were married (77.3%) and had a low level of education, being 18.1% had completed high school. Most patients (47.4%) reported being smokers or reported having smoked in the last 5 years and 55.5% reported consuming alcohol regularly. Most patients (77.3%) were submitted to partial penectomy. All tumors were classified as Squamous Cell Carcinoma (SCC), with a mean size of 4.4 ± 2.4 cm, ranging from 0.8 to 10 cm. In most patients (40.9%) the tumors were restricted to the glans, and the most frequent histological types were condylomatous (45.4%) and usual (36.4%). Most tumors were classified as Grade 2 (54.5%) and 3 (27.3%), while lymphatic and perineural invasion were observed in 19% and 23.8% of patients, respectively. Phimosis was observed in 44.4% of patients, the majority being (87.5%) over 40 years old. The clinical and histopathological data of the patients are presented in **Table 1** and **Supplementary Table S1**.

Table 1. Geral clinical-histopathological profile of patients with PSCC in this study (n=22).

Characteristic	Number (%)	Characteristic	Number (%)
Stage (pT)		**Lesion characteristic**	
pT1	6 (27.3%)	Ulcerated	9 (41%)
pT2	9 (40.9%)	Vegetative	4 (18.2%)
pT3	7 (31.8%)	Verrucous	3 (13.6%)
Grade (Gx)		Nodular ulcerated	3 (13.6%)
G1	4 (18.2%)	Ulcer-vegetative	3 (13.6%)
G2	12 (54.5%)	**Anatomical site of the tumor**	
G3	6 (27.3%)	Glans only	9 (40.9%)
Lymphatic invasion		Glans and foreskin	7 (31.8%)
Positive	4 (18.2%)	Foreskin	2 (9.1%)
Negative	17 (77.3%)	Glans, foreskin and others areas	4 (18.2%)
No information	1 (4.5%)	**Type of surgery**	
Perineural invasion		Postectomy	1 (4.5)
Positive	5 (22.8%)	Partial penectomy	16 (72.7%)
Negative	16 (72.7%)	Total penectomy	5 (22.7%)

No information	1 (4.5%)	**Phymosis**	
Tumor size		Yes	8 (36.3%)
0,6 - 2,0	4 (18.2%)	No	9 (41.0%)
2,1 - 5,0	15 (68.2%)	No information	5 (22.7%)
5,1 – 10,0	3 (13.6%)	**Smoking**	
Histological type		Yes	9 (41.0%)
Usual	8 (36.4%)	No	10 (45.4%)
Condylomatous	10 (45.4%)	No information	3 (13.6%)
Usual and basaloid	2 (9.1%)	**Alcoholism**	
Usual and condylomatous	2 (9.1%)	Yes	10 (45.4%)
		No	7 (31.9%)
---		No information	5 (22.7%)

2.2 HPV genotyping

All patients with CaPe were positive for HPV, as described by Macedo *et al*. (2020). HPV genotyping was performed in all patients by nested-PCR [according to BioGenetics Molecular Technologies (Uberlândia, Minas Gerais, Brazil) (patent number BR102017004615.0)] and by DNA sequencing. Most patients (94.4%) had hrHPV subtypes. HPV16 was the most frequent subtype, present in 72.2% of cases, followed by HPV74 (16.6%), HPV30, HPV59 and HPV66 (11% each). Other less frequent genotypes were 6, 18, 30, 35, 44, 53, 58 and 73. Multiple infections were detected in 50% of the cases and HPV16 was present in 75% of them (**Supplementary Table S1**).

2.3 miRNA Expression Analysis

A total of 22 tumors were evaluated for differential expression of miRNAs relative to five adjacent non-tumor tissues, as described in our previous study (da Silva et al., 2022) (data available for access from the *Gene Expression Omnibus* (GEO), under registration GSE197121). Briefly, total RNA from 22 PeCa tumors and 5 adjacent non-tumor tissues was isolated using the TRIzol protocol (Invitrogen, Walthan, Ma, USA). RNA concentration and quality were tested by measuring the 260/280 and 260/230 ratios using the Nanodrop 2001 spectrophotometer (Willington, DE, USA). MiRNA expression was evaluated using the nCounter® Human v.3 miRNA Expression platform (Nanostring Technologies™, Seattle, Wa, USA), according to the manufacturer protocol. We performed two differential expression analysis between tumors and adjacent non-tumor tissues with objective of compare the expression pattern between paired samples of the expression global: (i) expression between 22 tumors and 5 non-tumor tissues; and (ii) expression between 5 tumors paired with their respective non-tumor tissues (**Supplementary Figure S1**). Raw data were normalized using the ROSALIND® Nanostring platform (https://rosalind.onramp.bio/). Distribution percentages, heatmaps and other graphs were generated as part of the QC step. Normalization was performed following background subtraction based on the correction factors of the POS_A probes (positive control normalization and codeset normalization). For both steps, the geometric mean of each set of probes was used to create a normalization factor. Fold Change (≥ 2 and ≤ -2) and p-values for comparisons were calculated using the t-test ($p \leq 0.05$). The p-value adjustment (adj.-*p*) was performed using the Benjamini-Hochberg method ($p \leq 0.01$) to estimate false discovery rates (FDR). The clustering of miRNAs for the heatmap was constructed using PAM (*Partitioning Around Medoids*) through a

method using the FPC-R library (Hennig, 2020) that takes into account the pathways, functions and types of each identified miRNA.

As the aim of identify a panel of miRNAs that differentiate advanced disease from early disease, tumor samples were stratified based on two clinical groups: (i) advanced disease, comprising tumors with positive perineural invasion, pT3 staging, tumor grade 2 and 3 (5 samples) and; (ii) early disease, comprising tumors with negative perineural invasion, pT1 and pT2 staging, tumor grade 1 and 2 (12 samples). Data were analyzed under the same parameters as above.

2.4 Cross-study between TCGA data

In objective of compare PSCC miRNA expression data with other squamous carcinomas and identify CaPe-specific miRDEs, we accessed RNA-seq data from miRNAs available in The Cancer Genome Atlas (TCGA). We used data from head and neck squamous cell carcinoma (HNSC) studies (TCGA, Firehose Legacy) in which analyzes of 497 tumors and 44 non-tumors are deposited; and Pan-cancer Analysis of Whole Genome (The ICGC/TCGA Pan-Cancer Analysis of Whole Genomes Consortium, 2020), which has a total of 749 samples of 18 types of cancers (breast, endometrial, ovarian, gastroesophagus, head and neck, melanoma, hepatobiliary, non-small cell lung, bladder, lung, colorectal, uterine endometrium, cervix, renal, sarcoma, prostate, thyroid cancer, and glioma). The HNSC-TCGA data were accessed through the ENCORI platforms (J.-H. Li et al., 2014) (https://starbase.sysu.edu.cn/index.php; accessed 28 Jan 2022) and UALCAN (Chandrashekar et al., 2017) (http://ualcan.path.uab.edu/index.html; accessed 28 Jan 2022). Pan-Cancer data were accessed through cBioPortal (Cerami et al., 2012; J. Gao et al., 2013) (https://www.cbioportal.org/; accessed on 25 Apr 2022). Tumor and normal samples were statistically compared by t-test ($p \leq 0.05$) with Log2(RPM+1).

2.5 Association between miRDEs with clinical and histopathological parameters of patients

Relative expression of each miRNA was verified as to normality using the Shapiro-Wilk test. To compare two groups, the t-test was used when the data presented normally distributed, otherwise the Mann-Whitney test was used. To compare three or more clinical parameters, one-way ANOVA analysis with Tukey's post-hoc was used for data with normal distribution, otherwise the Kruskal-Wallis test with Dunn's correction was performed. The significance level was $p \leq 0.05$ and adj.-$p \leq 0.01$. Statistical tests were performed using GraphPad Prism v.9 software.

2.6 Receiver Operator Characteristic (ROC) curve analysis

The discriminatory power of miRDEs between clinical groups was tested constructing the ROC curve and calculating the Area Under the Curve (AUC). Sensitivity (%) was plotted against specificity (%) for normalized expression values. An AUC of 100% denotes perfect discrimination by miRDE, while an AUC of 50% denotes low discrimination by miRDE. AUCs and confidence intervals (CI) corresponding of 95% were calculated for each miRDE. Correction by Wilson/Brown method was used with a significance level of $p \leq 0.05$. MiRDEs with higher AUC were combined to determine a more robust panel between clinical groups. Panels that presented the ROC curves with the highest AUC values were selected to calculate the Youden Index (J), with objective of identify the point with larger sensitivity and specificity. Statistical tests were performed using GraphPad Prism v.9 software.

2.7 Target genes and pathway enrichment analysis

The DIANA-Tarbase v.8 (Karagkouni et al., 2018) and miRTarBase (Huang et al., 2019) databases were used to determine interactions between miRDEs and validated target genes, based on miTG (miRNA Target Gene) ≥ 0.8; strong experimental assays (luciferase reporter assay, western blot and qPCR) and less strong (microarray, NGS and pSilac). Diana-miRPath v.3.0 (Vlachos et al., 2015) was used to identify the signaling pathways that are affected by miRDEs, using the Kyoto Encyclopedia of Genes and Genomes (KEGG) platform. The prediction of target genes was made by micro-TCDS algorithms (v.5) with $p<0.05$, microT of 0.8 and miTG ≥ 0.8. The top pathways were identified using the "pathways union" function.

2.8 Protein-protein interactions and construction of networks

Protein-protein interactions (PPI) between target genes were obtained through I2D (Kotlyar et al., 2016), STRING v.11 (Szklarczyk et al., 2019) and BioGRID v.4.4 (Oughtred et al., 2021). We apply a minimum interaction score of 0.9 (high confidence). Interactions between HPV oncoproteins and human genes (integration sites) were accessed through the HPVbase databases (Kumar Gupta & Kumar, 2015) (http://crdd.osdd.net/servers/hpvbase/index.html) (accessed 12 Apr 2022) and VISDB (Tang et al., 2020) (https://bioinfo.uth.edu/VISDB/index.php/homepage) (accessed 12 Apr 2022).

InterSPPI-HVPPI (http://zzdlab.com/hvppi/) (Yang et al., 2020) (accessed 24 Dec 2021) was used to verify protein-virus and protein-human interactions through a sequence embedding-based encoding method. The amino acid sequences of human and viral proteins were obtained from the genes of the KEGG platform. Proteins of the HPV16 genotype (E5 id: P06927; E6 id: P03126 and E7 id: P03129) were used. The Drug Gene Interaction Database v.4.2 (DGIdb) (Freshour et al., 2021) was used to identify associations between miRNAs, genes and drugs. Cytoscape v.3.8.2 (Shannon, 2003) and PathVisio 3 v.3.3 (Kutmon et al., 2015) were used to reconstruct pathways including HPV oncoproteins, miRNAs and their respective predicted targets and drugs.

3 Results

3.1 Profile of miRDEs in hrHPV-positive penile tumors

In this study we used the data of 507 miRDEs of penile tumors in relation to adjacent non-tumor tissues, deposited in the Gene Expression Omnibus (GSE197121) described previously (da Silva et al., 2022) (**Supplementary Table S2**). The expression pattern of miRDEs was similar in both the group of 22 tumors *vs*. 5 adjacent non-tumor tissues and also in the paired group (5 tumors *vs*. 5 adjacent non-tumor tissues) (**Supplementary Figure S1**). In addition to the 13 upregulated miRDEs described by da Silva et al (2022): (let-7a-5p, miR-130a-3p, miR-142-3p, miR-15b-5p, miR-16-5p, miR-200c-3p, miR-205-5p, miR-21-5p, miR-223-3p, miR-22-3p, miR-25-3p, miR-31-5p and miR-93-5p), we describe 12 miRDEs that showed the lowest expression levels (Log2FC ≤ -2.9): miR-1206, miR-144-3p, miR-190b, miR-376b-3p, miR-381-5p, miR-433-3p, miR-495-3p, miR-508-3p, miR-509-3-5p, miR-509-3p, miR-544a and miR-661, totaling 25 miRDEs, from which comparison analyzes were performed with TCGA miRNA expression data, target prediction and pathway enrichment. Interestingly, 92% (n=23/25) of these miRDEs are within HPVis, in which the HPV16 subtype is the most frequent. **Figure 1A** and **Table 2** show all of the top 25 miRDEs in penile cancer associated with hrHPV.

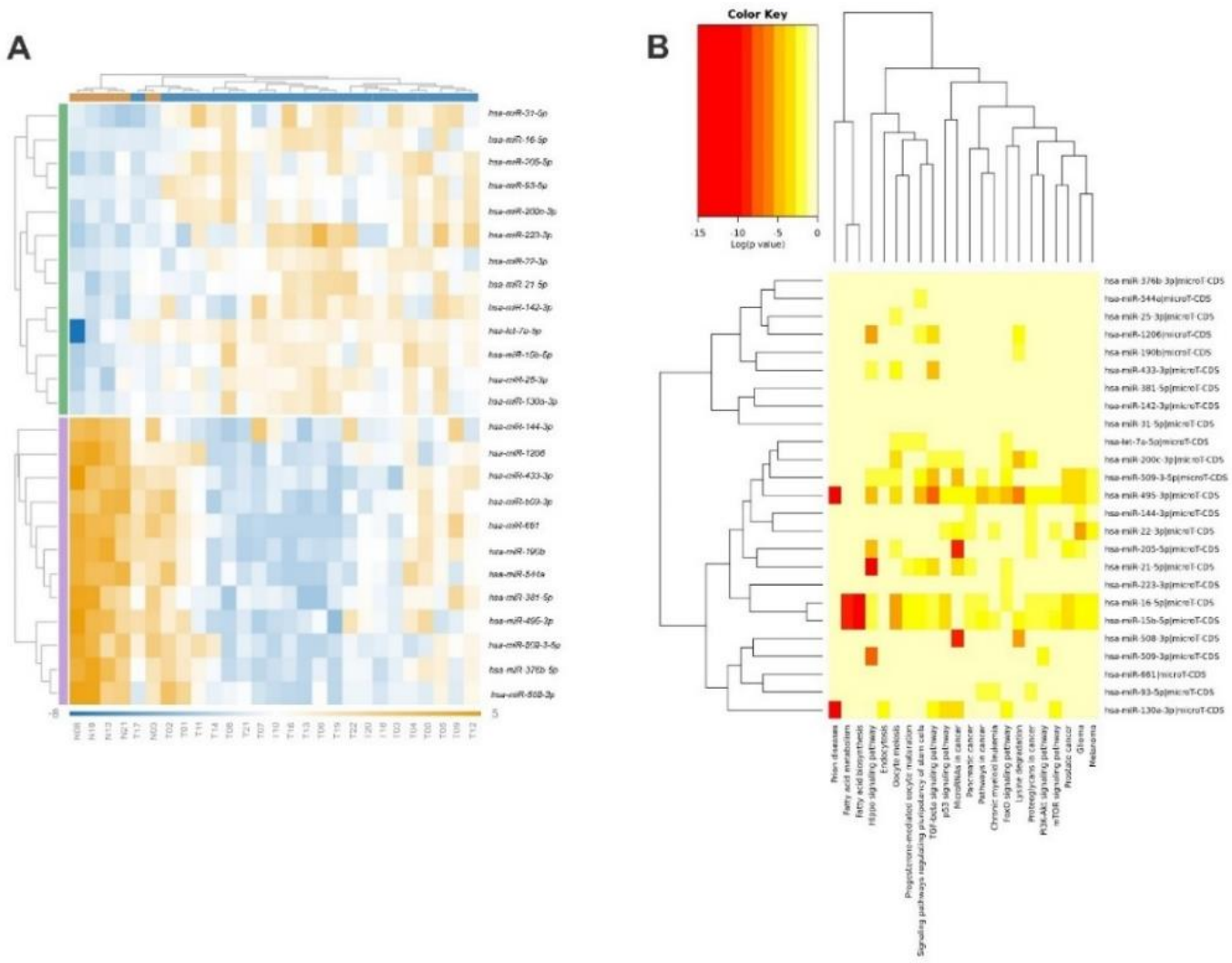

Figure 1. Unsupervised hierarchical clustering of the 25 miRDE more upregulated and downregulated and related top pathways. In (**A**), the heatmap generated by miRNA expression patterns showed two distinct groups (upper cluster) formed by tumor samples (blue bar) and normal samples (orange bar). The hierarchical group on the left is formed by miRNAs upregulated (green bar) and downregulated (pink bar). On the heatmap, orange colors indicate upregulated miRNAs and blue colors indicate downregulated miRNAs. In (**B**), the heatmap shows a compilation of the top pathways identified by the prediction method. On the right, the 25 miRDE and the target prediction algorithm used. Below is a compilation of the top pathways identified. Yellow colors indicate low impact of miRNAs on pathways, orange and red colors indicate medium and high impact, respectively.

Table 2. Top 25 miRDEs in hrHPV penile tumors and miRDEs described for HNSC-TCGA.

			PSCC (this study) (22 tumors and 5 non-tumors)					HNSC (TCGA) (497 tumors and 44 non-tumors)			
miRNAs	**Cytoband**	**Start – End (pb)**	**HPV Integration Site (genotype)***	**Expression Differential**	**Log2FC**	***p-value***	**Adj.-*p***	**Expression Differential**	**Log2FC**	***p-value***	**Adj.-*p***
let-7a-5p	9q22.32	96,938,234 - 96,938,325	yes, (16,18)	upregulated	2.2266	0.0019	0.0044	downregulated	0.79	<0.0001	0.0003
miR-130a-3p	11q12.1	57,641,198 - 57,641,286	yes, (16)	upregulated	1.1603	0.0008	0.0024	upregulated	1.86	<0.0001	<0.0001
miR-142-3p	17q22	58,331,222 - 58,331,327	yes, (16)	upregulated	1.4576	0.0054	0.0089	upregulated	2.30	<0.0001	<0.0001
miR-15b-5p	3q25.33	160,404,588 - 160,404,685	yes, (16)	upregulated	1.6509	<0.0001	0.0006	upregulated	1.96	<0.0001	<0.0001
miR-16-5p	13q14.2	50,623,109 - 50,623,197	yes, (16)	upregulated	1.2512	0.0008	0.0024	upregulated	1.60	<0.0001	<0.0001
miR-200c-3p	12p13.31	6,963,694 - 6,963,771	no	upregulated	1.2541	0.0023	0.0049	upregulated	1.51	<0.0001	0.0013
miR-205-5p	1q32.2	209,428,820 - 209,432,384	yes, (16,18)	upregulated	1.4610	0.0013	0.0035	upregulated	2.35	<0.0001	<0.0001
miR-21-5p	17q23.1	59,841,262 - 59,841,342	yes, (16,18)	upregulated	1.4629	0.0004	0.0016	upregulated	2.67	<0.0001	<0.0001
miR-223-3p	Xq12	66,018,870 - 66,018,979	no	upregulated	2.0222	0.0028	0.0056	upregulated	1.26	0.059	0.17
miR-22-3p	17p13.3	1,617,197 - 1,617,281	yes, (16,18)	upregulated	1.0605	0.0018	0.0043	upregulated	0.93	0.047	0.83
miR-25-3p	7q22.1	100,093,560 - 100,093,643	yes, (16)	upregulated	1.5448	0.0001	0.0008	upregulated	1.79	<0.0001	<0.0001
miR-31-5p	9p21.3	21,512,113 - 21,512,191	yes, (18)	upregulated	2.0012	0.0006	0.0020	upregulated	6.15	<0.0001	<0.0001
miR-93-5p	7q22.1	99,691,391 - 99,691,470	yes, (16)	upregulated	1.0525	0.0016	0.0040	upregulated	2.79	<0.0001	<0.0001
miR-1206	8q24.21	129,021,144 - 129,021,202	yes, (16,18,45)	downregulated	-3.0310	<0.0001	0.0005	IE	1.07	0.77	0.82
miR-144-3p	17q11.2	27,188,551 - 27,188,636	yes, (16)	downregulated	-2.9494	<0.0001	0.0006	downregulated	0.37	<0.0001	<0.0001
miR-190b	1q21.3	154,193,662 - 154,193,747	yes, (16,18)	downregulated	-3.0044	<0.0001	0.0006	downregulated	0.49	0.015	0.0550
miR-376b-3p	14q32.31	101,040,436 - 101,040,535	yes, (16)	downregulated	-2.9871	<0.0001	0.0005	downregulated	0.74	0.0081	0.033
miR-381-5p	14q32.31	101,045,918 - 101,045,996	yes, (16)	downregulated	-2.9859	<0.0001	0.0006	downregulated	0.18	<0.0001	0.0002
miR-433-3p	14q32.2	100,881,886 - 100,881,978	yes, (16)	downregulated	-2.9974	<0.0001	0.0006	downregulated	0.45	<0.0001	<0.0001
miR-495-3p	14q32.31	101,033,755 - 101,033,836	yes, (16)	downregulated	-3.1037	<0.0001	0.0007	downregulated	0.36	<0.0001	<0.0001
miR-508-3p	Xq27.3	146,318,431 - 146,318,545	yes, (16)	downregulated	-2.9449	<0.0001	0.0006	downregulated	1.80	<0.0001	0.0045
miR-509-3-5p	Xq27.3	146,341,170 - 146,341,244	yes, (16)	downregulated	-2.9414	<0.0001	0.0006	downregulated	0.34	<0.0001	0.0025
miR-509-3p	Xq27.3	147,260,532 - 147,260,625	yes, (16)	downregulated	-3.0481	<0.0001	0.0006	upregulated	4.15	0.097	0.26
miR-544a	14q32.31	101,048,658 - 101,048,748	yes, (16)	downregulated	-3.0781	<0.0001	0.0006	IE	1.01	0.58	0.82
miR-661	8q24.3	145,019,359 - 145,019,447	yes, (16,18)	downregulated	-3.1792	<0.0001	0.0006	IE	1.26	0.55	0.82

*data obtained from HPVBase (Kumar Gupta & Kumar, 2015) (accessed on 12 Apr 2022) and VISDB (Tang et al., 2020) (https://bioinfo.uth.edu/VISDB/index.php/homepage) (accessed on 12 Apr 2022); IE = Insignificant expression.

3.2 Cross-study with TCGA-data

We compared the top 25 miRDEs in PSCC with differential expression data described in head and neck squamous cell carcinoma available in TCGA (497 tumors and 44 non-tumors) (**Table 2**). Most of the miRDEs in PSCC (80%, n=20) showed the same expression levels in HNSC. We emphasize that miR-1206, miR-544a and miR-661, downregulated in PSCC, didn't showed changes in their expression in HNSC. In objective of investigate the expression of these miRNAs in other cancers, we performed a comparative analysis with expression data from 749 samples of 18 types of cancers from the "Pan-cancer Analysis of Whole Genomes" project (The ICGC/TCGA Pan-Cancer Analysis of Whole Genomes Consortium, 2020) [acessed cBioPortal (Cerami et al., 2012; J. Gao et al., 2013) (https://www.cbioportal.org/; on 25 Apr 2022)]. Interestingly, miR-661 and miR-1206 are not differentially expressed in any of the 18 cancers evaluated, although 18% (n=132) and 21% (n=157) of the samples had the amplified genes, respectively. On the other hand, miR-544 was differentially expressed only in glioblastoma.

3.3 MiRDEs and their association with clinical and histopathological parameters

Analysis from differential expression of the 25 miRDEs with the clinical and histopathological parameters of the tumors revealed an association between the negative expression of miR-1206 (p= 0.0044), miR-376b-3p (p= 0.0392) and miR-495-3p (p= 0.0341) with perineural invasion. In addition, overexpression of let-7a-5p (p= 0.0504), miR-200c-3p (p= 0.0524) and miR-205-5p (p= 0.01) was associated with tumor grade, having a difference between intermediate and advanced grade tumors (adj.-*p*= 0.0597, 0.0459 and 0.0073, respectively). Additionally, miR-142-3p was associated with tumor staging (p= 0.0126), being differentially expressed between early and intermediate staging tumors (pT1 *vs*. pT2, adj.-*p*= 0.0257) and between intermediate and advanced tumors (pT2 *vs*. pT3, adj.-*p*= 0.0329). The data association between miRDEs and clinical-histopathological parameters are presented in **Table 3**.

Table 3. miRDE in association with clinical and histopathological parameters.

miRDE	Expression Differential	Variables	*p-value*	Group (*p-value*)
let-7a-5p	upregulated	Grade	0.0504	G2 *vs.* G3 (0.0597)
miR-200c-3p	upregulated	Grade	0.0524	G2 *vs.* G3 (0.0459)
miR-205-5p	upregulated	Grade	0.0100	G2 *vs.* G3 (0.0073)
miR-142-3p	upregulated	Staging	0.0126	pT1 *vs.* pT2 (0.0257) pT2 *vs.* pT3 (0.0329)
miR-144-3p	downregulated	Staging	0.0197	pT1 *vs.* pT2 (0.0199)
miR-15b-5p	upregulated	Size	0.0192	2.1-5 *vs.* 5.1-10 (0.0190)
		Lesion	0.0191	ulcerated *vs.* vegetative (0.0371) vegetative *vs.* verrucous (0.0353)
miR-16-5p	upregulated	Lesion	0.0202	ulcerated *vs.* vegetative (0.0395)
miR-25-3p	upregulated	Lesion	0.0386	ulcerated *vs.* vegetative (0.0304)
		Size	0.0007	0.6-2 *vs.* 2.1-5 (0.0005) 0.6 - 2 *vs.* 5.1-10 (0.0160)
miR-93-5p	upregulated	Size	0.0286	0.6-2 *vs.* 2.1-5 (0.0221)
miR-130a-3p	upregulated	Lesion	0.0154	ulcerated *vs.* vegetative (0.0111)

3.4 *In silico* functional analysis and miRNA/mRNA interaction networks

The potential biological impact of miRDEs was predicted from experimentally validated interactions between miRNAs and their target genes. Thus, of the top 25 miRDEs, only miR-1206 had no validated targets. The 24 miRDEs regulate a total of 2,284 genes in 3,419 interactions (**Supplementary Table S4A**). Between them miR-661, miR-16-5p and miR-15b-5p had the highest number of targets (459, 438 and 395 target genes, respectively). On the other hand, miR-376b-3p, miR-495-3p and miR-509-5p were those with lowest number of targets (2, 2 and 3 target genes, respectively). We identified 43 KEGG pathways (**Supplementary Table S4A**), 15 of which are top ($p \leq 0.00017$): fatty acid biosynthesis (hsa00061), prion diseases (hsa05020), cancer microRNAs (hsa05206), hippo signaling pathway (hsa04390), TGF-beta signaling pathway (hsa04350), oocyte meiosis (hsa04114), lysine degradation (hsa00310), glioma (hsa05214), foxO signaling pathway (hsa04068), signaling pathways that regulate stem cell pluripotency (hsa04550), prostate cancer (hsa05215), cancer proteoglycans (hsa05205), p53 signaling pathway (hsa04115), mTOR signaling pathway (hsa04150) and fatty acid metabolism (hsa01212). All top pathways identified are shown in **Figure 1B** and **Supplemental Table S4B**.

Through the analysis of enrichment pathways, it was possible identify two large distinct clusters (**Figure 1B**). The largest cluster comprises 16 miRDEs, most of which are upregulated. This cluster had the greatest impact on the top identified pathways. The smallest cluster is composed of six downregulated and three upregulated miRDEs, and had a low impact on the top identified pathways. Furthermore, miR-200c-3p and let-7a-5p related to tumor grade, and miR-16-5p and miR-15-5p related to tumor lesion were identified forming highly related clusters. In addition to the top pathways, we identified twelve genes regulated by miRDEs that had not yet been described in penile cancer. **Table 4** shows the twelve target genes regulated by miRDEs in PSCC associated with hrHPV.

Table 4. New target genes identified as potentially regulated by miRDEs in PSCC-hrHPV.

Gene	miRDE	Expression Differential	miTG	*p-value*	Biological consequence
MDM2	*miR-661*	downregulated	0.800	0.001	Ubiquitination and degradation of p53
MDM4	miR-433-3p	downregulated	0.800	0.001	Ubiquitination and degradation of p53
	miR-661	downregulated	0.800	0.001	
LDLR	miR-130a-3p	upregulated	0.960	0.001	Deregulation of cholesterol metabolism
HSPA1B	miR-142-3p	upregulated	0.802	0.001	Protein instability
VPS37C	miR-15b-5p	upregulated	0.850	0.001	ESCRT-I (endosomal sorting complex required for transport I) dysregulation
	miR-16-5p	upregulated	0.859	0.001	
CHMP2B	miR-200c-3p	upregulated	0.812	0.001	ESCRT-III (endosomal sorting complex required for transport III) dysregulation
DDX3X	miR-15b-5p	upregulated	0.992	0.002	Loss of expression induces resistance to chemotherapy, while its expression is related to viral replication
	miR-16-5p	upregulated	0.993		
	miR-25-3p	upregulated	0.869		
	miR-495-3p	downregulated	1.000		
PTEN	miR-22-3p	upregulated	0.911	0.002	Inhibition of apoptosis and induction of cell proliferation and growth
	miR-205-5p	upregulated	0.937		
	miR-130a-3p	upregulated	0.861		
IKBKB	miR-15b-5p	upregulated	0.861	0.008	Inhibition of apoptosis and increased cell survival
	miR-16-5p	upregulated	0.892		
PRDM4	miR-15b-5p	upregulated	1.000	0.008	Cell cycle progression, activation of PI3K/AKT signaling and *PTEN* inhibition
	miR-16-5p	upregulated	1.000		
WASL	mir-130a-3p	upregulated	0.919	0.007	Destabilization of the cytoskeleton
MET	miR-144-3p	downregulated	0.800	0.007	Increased cell survival and induction of cell migration and invasion.
	miR-433-3p	downregulated	0.800	0.007	

3.5 Human-protein *vs*. HPV-oncoprotein interactions and druggable targets

Docking by sequence incorporation between human-protein and HPV-oncoprotein was performed with twelve predicted genes shown in **Table 4**. In this analysis, E7 oncoprotein interacts strongly with the DDX3X (score= 0.758) and HSPA1B (score= 0.6) and moderately interacts with CHMP2B (score= 0.506), PTEN (score= 0.470), IKBKB (score= 0.455), WASL (score= 0.433) and PRDMD4 (score= 0.429) proteins. E5 and E6 interact with HSPA1A (E5 score= 0.461, E6 score= 0.415) and DDX3X (E5 score= 0.408, E6 score= 0.566) proteins.

From the twelve predicted genes (**Table 4**) and miRDEs that regulate them, we performed an analysis to identify drug interactions. We identified five MDM2 inhibitors (nutlin-3; diplamine B; lissoclinidine B, RG-7112 and serdemetan), two drugs (epirubicin and docetaxel) targeting the MDM4 pathway, and nineteen drugs targeting the PTEN-PI3K/AKT and MET signaling pathway. All interactions between HPV oncoproteins, genes and drugs are shown in **Figure 2**.

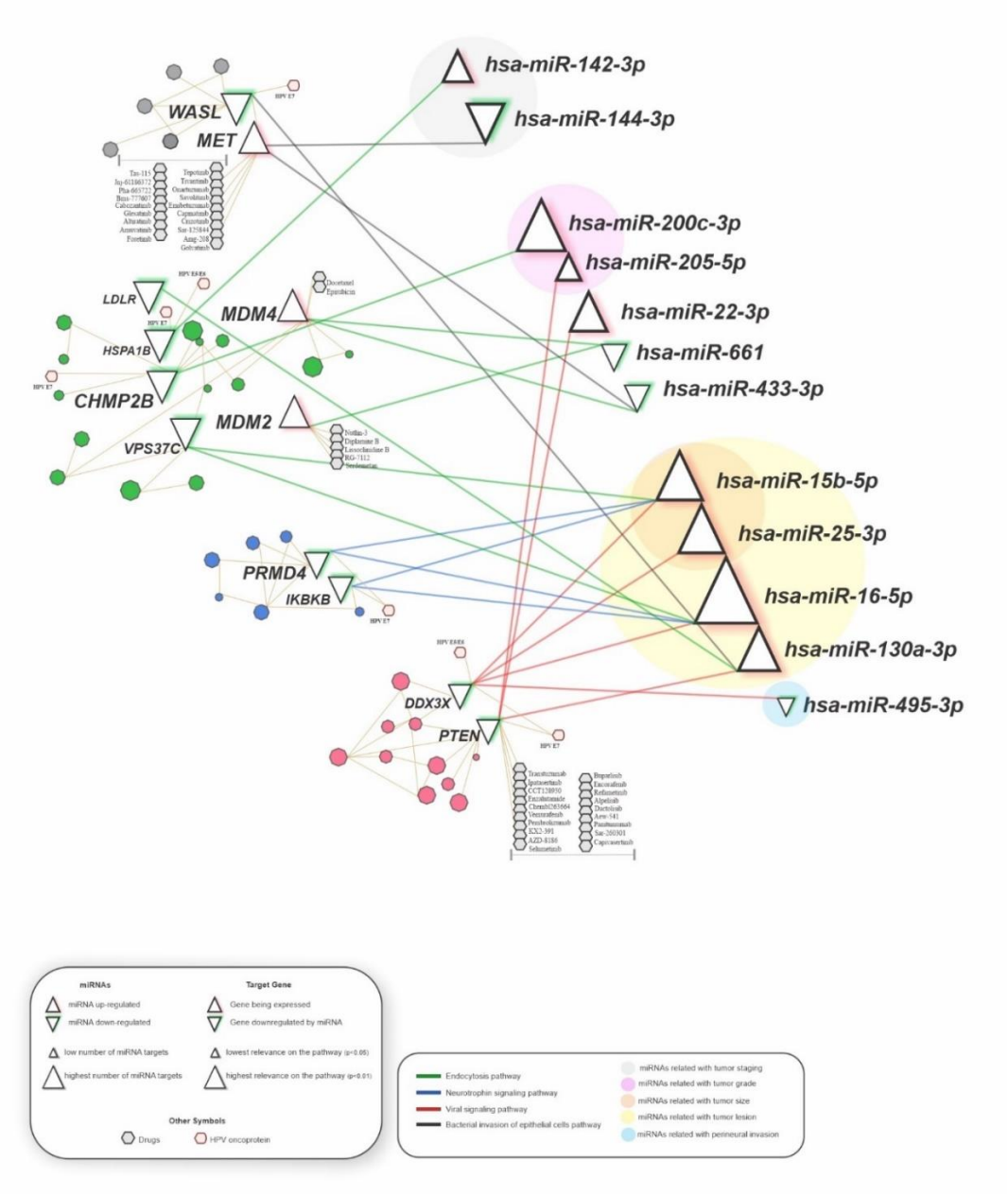

Figure 2. Integrative network between miRDEs and targets, HPV oncoproteins and predicted drugs. Significance of symbols and colors are shown in the tables below the integrative network. The network was generated by Cytoscape v.3.8.2 and PathVisio v3.3 software.

3.6 Panel of miRDEs as potential prognostic marker in PSCC

Stratification of patients with PSCC in two clinical groups, (i) advanced disease and (ii) early disease, revealed a panel of 143 miRDEs, of which 5 (3.5%) are upregulated and 138 (96.5%) are downregulated (**Supplementary Table S3**). Interestingly, the 5 upregulated miRNAs (miR-99a-5p, miR-150-5p, miR-155-5p, let-7c-5p, miR-342-3p) and the 5 most downregulated (miR-891a-5p, miR -376a-2-5p, miR-551b-3p, miR-1285-5p and miR-362-3p; FC≤-1.8 and *p*-value≤0.05), are within HPVis. Comparison of the 10 miRDEs between clinical groups (advanced disease *vs.* early disease) this study with miRDEs in HNSC-TCGA showed that 50% (n=5) have the same expression levels (p≤0.05) (**Table 5**). Comparative analysis between the 10 miRDEs with *Pan-cancer* data (ICGC/TCGA) revealed that these miRNAs were described expressing variably in the 18 types of cancers evaluated. **Figure 3A** and **Table 5** show the top 10 miRDEs that differentiate patients with advanced disease from those with early disease.

Table 5. Top 10 miRDEs between advanced and early clinical groups in PSCC associated with hrHPV and miRDEs described for HNSC-TCGA.

	PSCC (this study) (5 advancing tumors and 12 early tumors)						HNSC (TCGA) (497 tumors and 44 non-tumors)		
miRNAs	**Cytoband**	**Start– End (pb)**	**HPV Integration Site (genotype)***	**Expression Differential**	**Log2FC**	***p-value***	**Expression Differential**	**Log2FC**	***p-value***
miR-99a-5p	21q21.1	16,539,089 - 16,539,169	yes, (16,18)	upregulated	1.7381	0.0351	downregulated	0.3	<0.0001
miR-150-5p	19q13.33	50,004,042 - 50,004,125	yes, (16)	upregulated	1.4423	0.0324	upregulated	1.08	0.21
miR-155-5p	21q21.3	26,946,292 - 26,946,356	yes, (16,18)	upregulated	1.3684	0.0264	upregulated	1.56	0.0026
let-7c-5p	21q21.1	16,539,828 - 16,539,911	yes, (16,18)	upregulated	1.1359	0.0280	downregulated	0.33	<0.0001
miR-342-3p	14q32.2	100,575,992 - 100,576,090	yes, (16,18)	upregulated	1.1259	0.0077	upregulated	1.87	<0.0001
miR-891a-5p	Xq27.3	145,109,312 - 145,109,390	yes, (16)	downregulated	-1.8318	0.0077	downregulated	0.75	<0.0001
miR-376a-2-5p	14q32.31	101,040,069 - 101,040,148	yes, (16)	downregulated	-1.8661	0.0054	downregulated	0.61	0.044
miR-551b-3p	3q26.2	168,269,642 - 168,269,737	yes, (16)	downregulated	-1.9444	0.0020	upregulated	1.66	0.47
miR-1285-5p	7q21.2	91,833,329 - 91,833,412	yes, (16,28,31,45)	downregulated	-1.9779	0.0121	N/A	-	-
miR-362-3p	Xp11.23	49,773,572 - 49,773,636	yes, (16)	downregulated	-2.6208	0.0091	downregulated	0.65	<0.0001

* data obtained from HPVBase (Kumar Gupta & Kumar, 2015) (accessed on 12 Apr 2022) and VISDB (Tang et al., 2020) (https://bioinfo.uth.edu/VISDB/index.php/homepage) (accessed on 12 Apr 2022); N/A= not available.

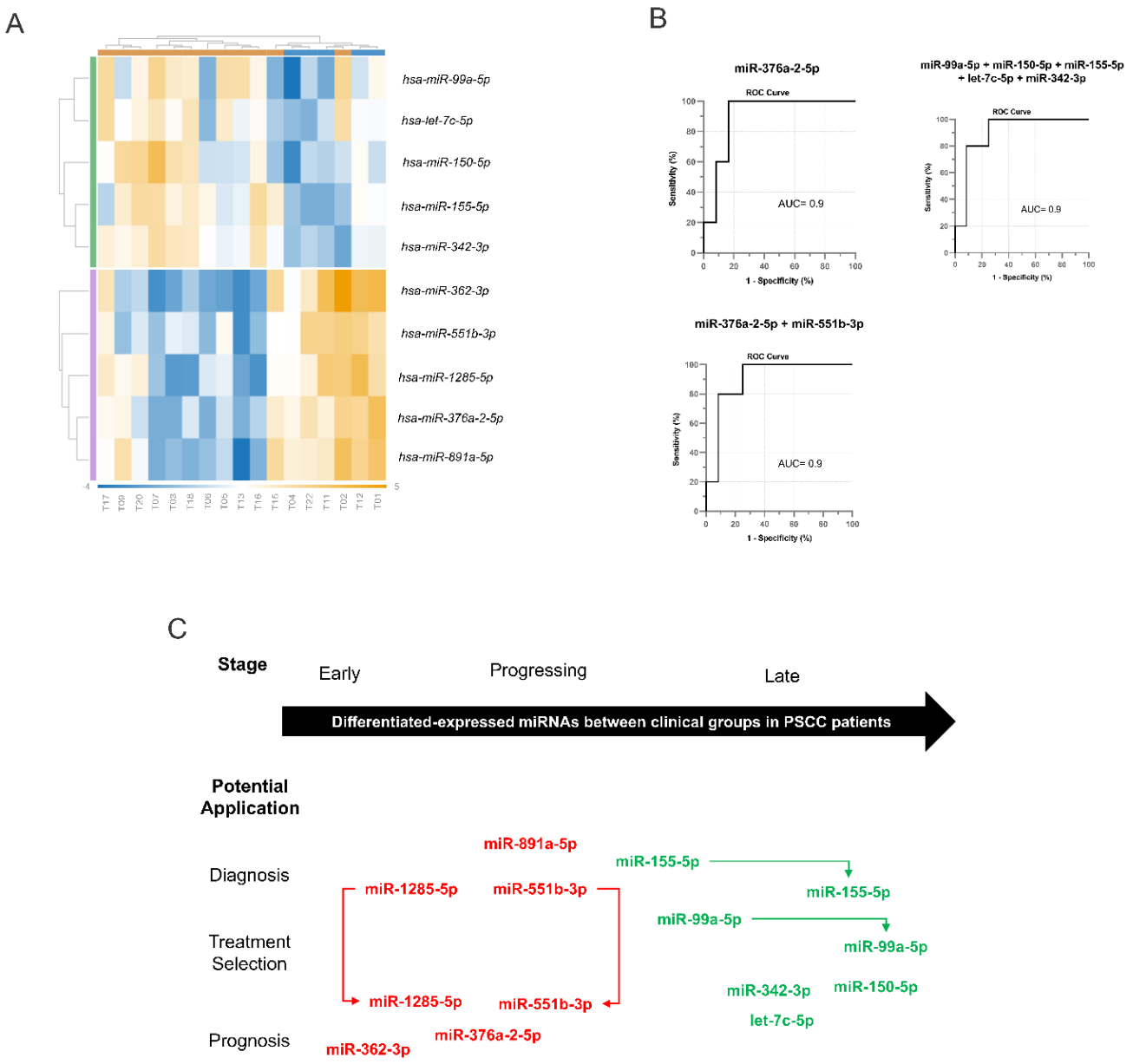

Figure 3. Unsupervised hierarchical clustering of the 10 miRDEs with ROC curve analysis and progression line in PSCC-hrHPV. In (**A**), heatmap generated by miRNA expression patterns showed two distinct groups (upper cluster) formed by advancing tumors samples (blue bar) and early tumors samples (orange bar). The hierarchical group on the left is formed by the upregulated (green bar) and downregulated (pink bar) miRNAs. On the heatmap, orange colors indicate upregulated miRNAs and blue colors indicate downregulated miRNAs. In (**B**), ROC curve analysis showing AUC equal to 0.9. In each of the three graphs the *p-value* was equal to 0.0114. In (**C**), PSCC progression line and potential application of the top 10 miRDE as disease biomarkers. miRDEs in red and green colors indicate downregulated and upregulated miRNAs, respectively. Arrows indicate that the same miRDE can be used in different stages and/or applications.

3.7 Analysis ROC

ROC curve analysis was performed for top 10 miRDEs between clinical groups. Analysis on top 10 miRDEs according to PSCC staging resulted in AUC values superiors than 0.8 (**Supplementary Figure S2**). The upregulated miR-376a-2-5p was the individual miRDE that achieved an accuracy of AUC= 0.9 (p= 0.0114; 95% CI= 0.7483 to 1,000). In addition, we performed an analysis combining different miRDEs with objective to determine the most robust panel. As result, a panel with all five

upregulated miRNAs (miR-99a-5p + miR-150-5p + miR-155-5p + let-7c-5p + miR-342-3p) and another with two downregulated miRNAs (miR-376a-2-5p + miR-551b-3p) showed the highest discriminatory power with an AUC value of 0.9 (p= 0.0114; 95% CI= 0.7475 to 1,000), each (**Figure 3B**). The ROC curve that presented the highest sensitivity and specificity value was miR-376a-2-5p with 100% and 83.3%, respectively. The panel with all five upregulated and two downregulated miRDE (AUC= 0.9, each) had sensitivity and specificity of 100% and 75%, respectively, each. Combined analysis of ROC curve, PAM (by FPC-R library) and predicted targets (by MirPath v.3) was used to create a PSCC progression line using the top 10 miRDE as disease biomarkers (**Figure 3C**).

4 Discussion

In this study, miRDEs between hrHPV-positive penile tumors and adjacent non-tumors tissues were investigated by expression matrix analysis. Our panel showed that 507 miRNAs are differentially expressed at statistically significant levels in hrHPV-positive tumors in relation to non-tumors tissue. The majority of miRDEs (97.4%) identified were downregulated. Our findings corroborate Ayoubian et al. (2021) who identified a panel of miRNAs in HPV-positive penile tumors where 99.1% were downregulated. The large number of downregulated miRNAs may be mainly related to the activity of HPV E6 and E7 oncoproteins in regulating networks of gene interactions and the ability of the virus to integrate into the human genome (D. Gao et al., 2016; Santos et al., 2016; Santos et al., 2018; Wald et al., 2011). In addition, we observed that 92% of the 25 miRDE most altered (tumor *vs.* normal) are within HPVis, which supports that viral genome integration is one of the main mechanisms that lead to oncogene and miRNA dysregulation (reviewed by Lee & Dutta, 2009; Soto et al., 2017; Tuna & Amos, 2017). Addition, we have also described genes and miRNAs present in genomic regions with CNAs that are also in HPVis (Macedo et al., 2020; Silva et al., 2021).

When performing a comparative analysis between miRDEs in hrHPV-PSCC and those differentially expressed in HNSC, we found that most miRDEs (80%, n=20/25) had the same expression levels in both tumors. This similarity of molecular profiles between HPV-associated squamous cell tumors grants the possibility of expanding the potential drugs to be tested in clinical trials in view of the rarity of penile tumors (Ghafouri-Fard et al., 2020; Guo et al., 2021; Pavlíková et al., 2022; Shaw et al., 2021). Furthermore, miR-1206 and miR-661, both downregulated in our study, showed no changes in HNSC and also in other non-HPV-associated cancers. The miR-1206 is one of six annotated miRNAs found at the non-coding locus PVT1, located at 8q24 (Conte et al., 2017). The role of miR-1206 is still unclear, although some evidence has shown that the PVT1 locus is linked to innate and adaptive immunity and p53 signaling functions (Bisio et al., 2013). Some polymorphisms and variants have been described in miR-1206 in patients with acute lymphoblastic leukemia (ALL) and chronic myeloid leukemia (CML) being associated with methotrexate-induced oral mucositis and increased risk in CML (Gutierrez-Camino et al., 2017; Hassan, 2019). Ayoubian et al. (2021) also identified this downregulated miRNA in HPV-positive penile tumors. Two other diseases in which changes in miR-1206 expression were identified were pancreatic cancer (Yu et al., 2021) and ischemic heart disease (Abd el-Aziz et al., 2021). These data provide evidence that miR-1206 is expressed in few tissues, especially in penile tumors, and may have significant clinical value. However, more studies should be carried out to support this hypothesis.

Recent studies on miR-661 have yielded apparently conflicting conclusions, demonstrating that this miRNA has antagonistic functions depending on the type of cancer (Li et al., 2015; Liu et al., 2017; Liu et al., 2022). In glioma, miR-661 is often reported to be downregulated, inhibiting proliferation, migration and invasion of tumor cells by regulating hTERT and participating in the regulation of competing endogenous RNAs (ceRNAs) (Li et al., 2015; Liu et al., 2022). Furthermore, in breast cancer

miR-661 down-regulates *MDM2* and *MDM4* to activate p53 (Hoffman et al., 2014). On the other hand, in small cell lung cancer, miR-661 promotes tumor invasion and metastasis by directly inhibiting *RB1* (Liu et al., 2017). The antagonistic role can be explained by the amplification of the miR-661 locus in tumors harboring p53 mutations, as demonstrated by Hoffman et al. (2014), in contrast to tumors that show p53-wild type.

We detected 13 miRDEs related to clinical and histopathological parameters. Between them, miR-1206, miR-376b-3p and miR-495-3p are downregulated miRNAs related to perineural invasion. In particular, miR-376b-3p is a tumor suppressor that controls proliferation, metastasis and apoptosis via inhibition of *RGS1* and *KLF15* (X.-W. Liu et al., 2020; Zhang et al., 2021). Ayoubian et al. (2021) identified the sequence -5p of the miR-376b downregulated in HPV-positive penile tumors. To our knowledge, our study is the first to show that antagomir (3p) is also downregulated in HPV-positive penile tumors. The miR-495-3p is also a tumor suppressor that inhibits cell proliferation, invasion, migration through the control of the axis C1q/TNF-protein-related 3 (Zhao et al., 2019) and regulates multiple epigenetic modifiers, among them DNA-methyltransferase-1 (*DNMT1*) (Eun et al., 2018). Interestingly, the HPV E7 oncoprotein binds to DNMT1 and stimulates its DNA-methyltransferase activity (Burgers et al., 2007), and can also activate *DNMT1* transcription via the pRB/E2F pathway (McCabe et al., 2005). These evidences support the hypothesis that HPV can control the expression of genes and mainly of miRNAs via DNA methylation. Corroborating this, Barzon et al. (2014) showed that the tumor suppressor miR-218-1 is downregulated in hrHPV-positive penile tumors due to hypermethylation of the promoter of the *SLIT2* gene that contains *MIR218-1* in its intronic region.

Our prediction of mRNA/miRNA interactions showed genes regulated by miRDE that had not yet been described in penile cancer. The *MDM2* (regulated by miR-661, downregulated) and *MDM4* (regulated by miR-433-3p and miR-661, both downregulated) genes are responsible for controlling p53 protein levels via ubiquitination and degradation. Furthermore, the tumor suppressor *PTEN* was identified as targets of three upregulated miRNAs (miR-22-3p, miR-205-5p and miR-130a-3p). In our previous study, we showed that this same cohort had reduced levels of p53 protein expression (87.5%, n=14/16 evaluated cases) and *TP53* mRNA (85.7%, n=12/14 evaluated cases) (Macedo et al., 2020). One of the possible mechanisms for this regulation would be via miRNAs activity, which was addressed by us in another study (da Silva et al., 2022). We also previously showed that *PTEN* presented losses and deletions in the number of gene copies in (88.8%, n=8/9 evaluated cases) (Macedo et al., 2020). We now provide evidence that *PTEN* can be regulated by epigenetic mechanisms in addition to copy number alterations.

Our *in silico* analysis of human-protein *vs.* virus-protein interactions showed important genes that can be regulated by HPV oncoproteins and also by miRDEs. Although functional studies are needed to validate this data, interactions between HPV-proteins and human-proteins are known through canonical mechanisms, such as the HPV/*TP53*/*RB1* axis (Flaherty et al., 2014; Kidd et al., 2017). These proteins reprogram cellular signal transduction pathways (reviewed by McLaughlin-Drubin et al., 2012), causing alterations in expression and number of copies in tumor genetic markers (Mesri et al., 2014). In addition, our prediction of pharmacological targets showed inhibitors targeting *MDM2*, a gene regulated by downregulated miRNAs. As the expression of these p53 inactivators is increased in several cancers, targeting drugs to reactivate p53 has emerged as a promising therapeutic strategy for cancer (Ribeiro et al., 2014). Nutlin-3 is a cis-imidazoline known to inhibit the interaction between MDM2 and p53, therefore inducing apoptosis. The nutlin-3 structure is also used as a model for the development of several other compounds with the same function, some of which have an inhibitory effect superior to that of nutlin-3 (Ribeiro et al., 2014; Yu et al., 2009).

Differential expression of miRNAs between clinical groups revealed 143 miRDEs. Interestingly, the top 10 most altered miRDEs are within HPVis, with the HPV16 subtype being able to deregulate all these regions. In addition, all upregulated miRNAs (let-7c-5p, miR-150-5p, miR-155-5p, miR-342-3p and miR-99a-5p) from this panel (advanced disease *vs.* early disease) were associated with resistance to drugs used in cancer treatment (doxorubicin, cisplatin, paclitaxel, gefitinib and taxanes) (Chen et al., 2020; Kazmierczak et al., 2022; B. Liu et al., 2022; Saberinia et al., 2020; Zheng et al., 2019). ROC analysis revealed that all top 10 miRDEs have high discriminating accuracy (AUC= 0.8) between these clinical groups. The downregulated miR-376a-2-5p was the only individual miRDE that reached AUC score= 0.9 (p= 0.0114), two other panels of miRDEs also reached AUC= 0.9 (miR-99a-5p + miR-150-5p + miR-155-5p + let-7c-5p + miR-342-3p, all upregulated; and miR-376a-2-5p + miR-551b-3p, both downregulated). To date, there are no studies on miR-376a-2-5p in literature, and the only experimentally described target is the *SRPK1* gene (Serine/Arginine-Rich Splicing Factor Kinase 1), which hybridizes by ligation of the type 7mer-m8 at position 1542-1563, 3'UTR (Untranslated region) [predicted by miRTarBase (Huang et al., 2019) by PAR-CLIP/AGO2 data (Lipchina et al., 2011)]. More studies with larger cohorts are needed to explore the therapeutic and prognostic potential of these 10 miRDEs, in particular miR-376a-2-5p in patients with hrHPV-PSCC.

In conclusion, the interaction networks involving HPV and miRNAs are highly complex and involve several micro and macro pathways. In this study we provided molecular signatures based on miRNAs. We showed that some miRDEs in hrHPV-PSCC and HNSC present the same expression levels, opening the possibility of amplification of potential drugs to be tested in PeCa. We also described some miRDEs regulating pathways involved in tumor development and that these miRNAs are also related to important clinical parameters such as perineural invasion, tumor grade and staging, and therefore those miRDEs can be used to indicate druggable targets. Finally, we highlight miR-376a-2-5p as a potential prognostic marker for patients with hrHPV-positive PSCC.

5 Conflict of Interest

The authors declare that the research was conducted in the absence of any commercial or financial relationship that could be interpreted as a potential conflict of interest.

6 Author contributions

"Contextualization, SRP and JS; Methodology, SRP, JS, LN, AD, RC, ACL, LS, RMR; Formal Analysis, SRP and JS; Research, JS and SRP; Resources, SRP; Writing - Preparation of the Original Manuscript, SRP , AV and JS; Writing – Review and Editing, SRP and APSA; Supervision, SRP; Project Management, SRP; Resource Acquisition, SRP".

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9 Data availability

The raw expression data is available for access from GEO under registry GSE197121. Other data are available from the corresponding author upon reasonable request.

5. CONSIDERAÇÕES FINAIS

O câncer de pênis é um problema de saúde pública em países em desenvolvimento. O diagnóstico nesses países é tardio e o tratamento na maioria dos casos é mutilante, o que causa sérios problemas psicológicos e reduz a sobrevida global dos pacientes. Há situações em que se verifica casos de pacientes com linfonodos clinicamente negativos que, após um tempo, apresentam metástase. Apesar da gravidade dessa doença, ainda são poucos os trabalhos sobre a gênese e progressão tumoral, principalmente no que diz respeito aos aspectos genéticos e epigenéticos. Atualmente, os miRNAs têm sido destacados como importantes biomarcadores que podem ser usados para diagnóstico e prognóstico em diferentes tipos de cânceres, uma vez que essas moléculas podem possuir perfis de alteração relacionados às características dos tumores. Os miRNAs desempenham um papel fundamental no controle da expressão gênica e conhecer as redes de interações às quais fazem parte é de vital importância para a compreensão da tumorigênese.

No capítulo 1 deste estudo, avaliamos o impacto das alterações no número de cópias em miRNAs e genes. A partir da análise do aCGH identificamos 38 citobandas afetadas por CNAs, das quais 89.5% são sítios de integração do HPV. Análise estatística revelou 15 citobandas relacionadas a importantes parâmetros clínicos, como estadiamento do tumor, grau tumoral e infecção por HPV. Das 38 citobandas alteradas, 30 abrigam miRNAs. Interessantemente, 28 dessas 30 citobandas (93.3%) são sítios de integração do HPV. Um total de 269 miRNAs foram mapeados nessas regiões, sendo a maioria (78.4%, n=211 miRNAs) em regiões com ganho no número de cópias.

Por meio de diversas ferramentas de análise *in sílico* conduzimos uma investigação com o objetivo de identificar as interações miRNAs/mRNA em tumores de pênis HPV-positivo. Por meio dessa abordagem, observamos cinco principais vias (sinalização *hippo*, degradação de lisinas, biossíntese de mucinas tipo *O*-glicano, príons e proteoglicanos em câncer) nas quais os genes que participam são regulados pelos miRNAs. Essas vias estão relacionadas diretamente com a instabilidade genômica, proliferação, sobrevivência celular, manutenção do microambiente tumoral, invasão e metástase. Além dessas cinco principais vias, identificamos ainda a via de carcinogênese viral (HPV), onde as oncoproteínas do HPV e miRNAs regulam os mesmos genes. Nessa via observamos que o *miR-148a-3p* e a oncoproteína E5 regulam negativamente o gene *ATP6V0D1* levando a consequente redução da acidificação endossômica e reciclagem do receptor-EGFR para a superfície celular. Além disso, por meio das redes de

interações genes-miRNAs, identificamos drogas inibidoras de *COX2* e *EGFR* (celecoxibe e cetuximabe, respectivamente) dois genes que estão relacionados as vias de inflamação e proliferação celular.

Em nosso estudo anterior (MACEDO et al., 2020), mostramos a subexpressão do mRNA de *TP53* e *RB1* e sugerimos a existência de outros mecanismos regulatórios além da via canônica HPV/*TP53*/*RB1*. Um dos possíveis mecanismos propostos são os miRNAs. Dessa forma, no capítulo 2 deste estudo, avaliamos a expressão diferencial de miRNAs em um subconjunto de amostras da coorte de MACEDO et al. (2020), com o objetivo de identificar miRNAs que regulam negativamente *TP53* e *RB1*. Nosso painel de miRNAs diferencialmente expressos revelou 507 miRNAs alterados (tumor *vs.* normal). A maioria dos miRNAs (97.4%, n=494) estiveram subexpressos e 13 (2.6%) superexpressos. Interessantemente, 11 dos 13 miRNAs superexpressos (84.6%) estão localizados em sítios de integração de HPV.

Nossa predição de alvos mostrou que todos os 13 miRNAs superexpressos regulam negativamente *TP53* e *RB1*, principalmente por se ligarem em regiões seedless não-canônicas. Embora a maioria dos miRNAs tenham sítios que são perfeitamente complementares às regiões seed (canônicas), vários estudos mostraram que miRNAs podem interagir diretamente por meio de suas regiões seedless e aumentar a capacidade de regulação.

No capítulo 3, nós aprofundamos o estudo do painel de 507 miRNAs diferencialmente expressos (tumor *vs.* normal) apresentado no capítulo 2. Selecionamos os 13 miRNAs superexpressos e os 12 miRNAs mais subexpressos com base no *fold change* e nível de significância, formando assim um subgrupo/painel de 25 miRNAs. Interessantemente, 23 (92%) dos 25 miRNAs estão dentro de sítios de integração de HPV. Em adição, 13 dos 25 miRNAs (tumor *vs*. normal) foram significativamente associados a parâmetros clínicos e histopatológicos dos pacientes. Destaca-se os miR-1206, miR-376b-3p e o miR-495-3p, todos subexpressos, por serem associados à invasão perineural.

Ainda no capítulo 3, construímos um segundo painel de miRNAs diferencialmente expressos, além do painel tumoral *vs.* normal. No segundo painel, agrupamos os pacientes em dois grupos clínicos, (i) doença avançada *vs.* (ii) doença inicial, com o objetivo de identificar miRNAs que diferenciasse pacientes entre esses grupos clínicos. Nós identificamos 143 miRNAs diferencialmente expressos, dos quais 5 (3.5%) miRNAs estiveram superexpressos e 138 (96.5%) estiveram subexpressos. Nesse painel (doença avançada *vs.* doença inicial) os 5 miRNAs superexpressos e os 5 miRNAs mais subexpressos (com base no *fold change* e nível

de significância) estão localizados em sítios de integração de HPV. Análise de curva ROC evidenciou que todos os top 10 miRDE possuem alto poder discriminatório entre grupos clínicos (AUC≥ 0.8 e p≤ 0.05). Um miRDE (miR-376a-2-5p) e dois painéis (i. miR-99a-5p + miR-150-5p + miR-155-5p + let-7c-5p + miR-342-3p; e ii. miR-376a-2-5p + miR-551b-3p) apresentaram valores AUC= 0.9 (p= 0.0114, cada) demonstrando alto valor preditivo entre pacientes com doença avançada e inicial de CaPe. O miR-376a-2-5p foi aquele que apresentou o maior valor de sensibilidade e especificidade com 100% e 75%, respectivamente.

Com base em nossos resultados, concluímos que as alterações no número de cópias apresentam um impacto significativo na regulação dos miRNAs e seus genes alvos. As citobandas afetadas por CNAs apresentam relevância, uma vez que estão relacionadas a importantes parâmetros clínicos. Além disso, o conhecimento de alterações nessas citobandas impulsionam a busca por marcadores nessas regiões. Identificamos miRNAs e genes afetadas por CNAs que atuam em vias de sinalização com relevância para a carcinogênese peniana. Mostramos um painel de miRNAs diferencialmente expressos entre tumores penianos HPV-positivo e tecido normal, fornecendo evidências do papel do HPV na regulação dos miRNAs. Identificamos três miRNAs diferencialmente expressos (miR-1206, miR-376b-3p e o miR-495-3p) relacionados a invasão perineural. E um painel de miRNAs diferencialmente expressos entre grupos clínicos (doença avançada *vs.* doença inicial). Evidenciamos como biomarcador para doença avançado o miR-376a-2-5p, por apresentar alto sensibilidade e especificidade entre grupos clínicos. Por fim, destacamos as drogas inibidoras de COX2 e EGFR (celecoxibe e cetuximabe), como opções de tratamento para pacientes que superexpressam esses marcadores. Esses resultados fornecem novas informações sobre os mecanismos epigenéticos em câncer de pênis e possibilitam novos estudos futuros.

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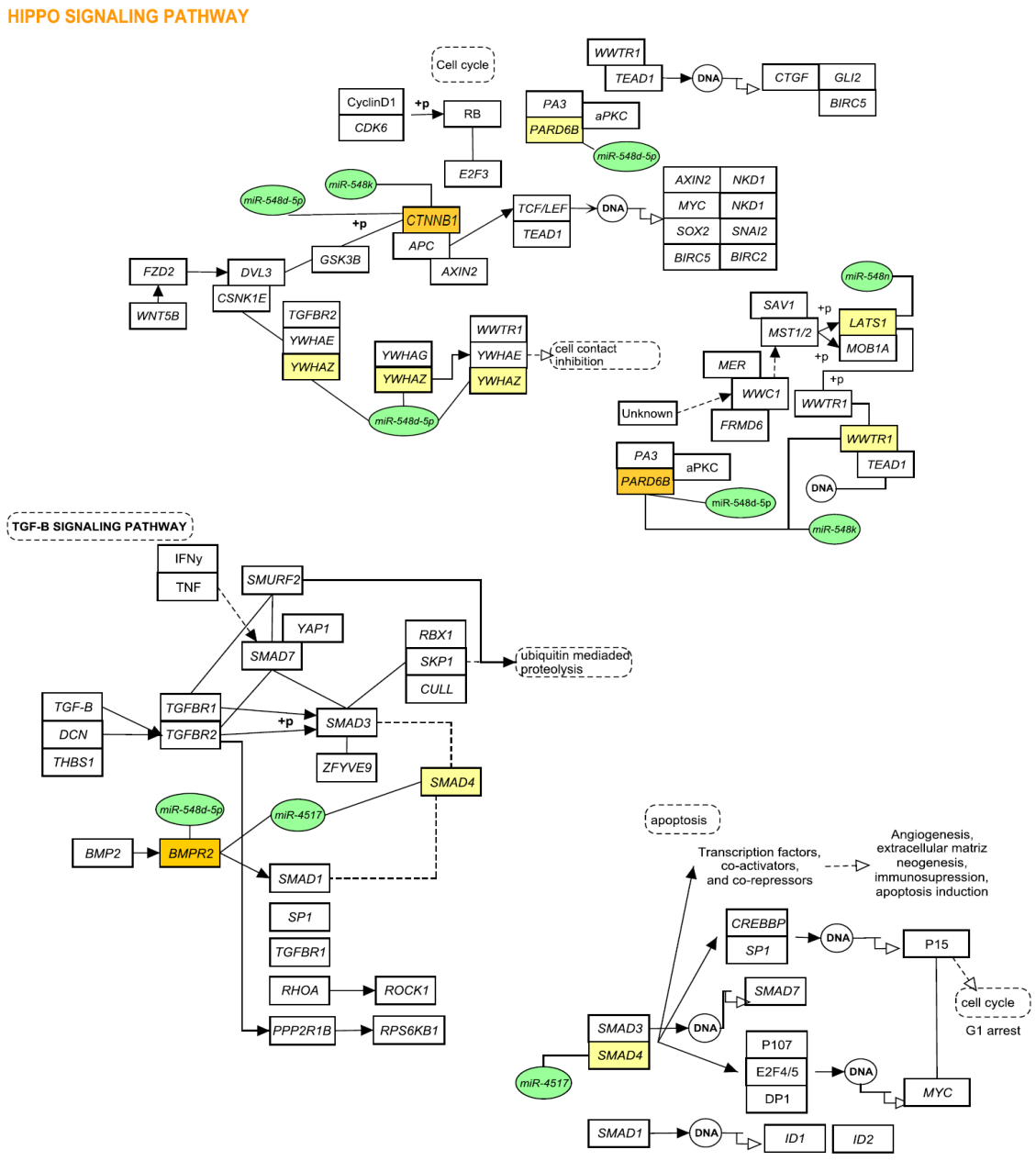
ANEXOS

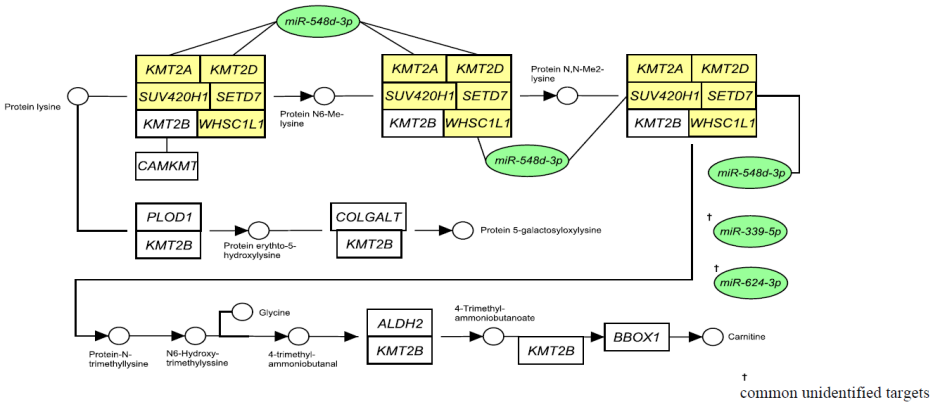
Anexo A – Material Suplementar Artigo 1

Supplementary Fig. 1. Top 5 KEGG pathways identified by both algorithms (tarbase and microT-CDS) and pathway HPV-mediated viral carcinogenesis potentially affected by miRNAs identified in altered cytobands.

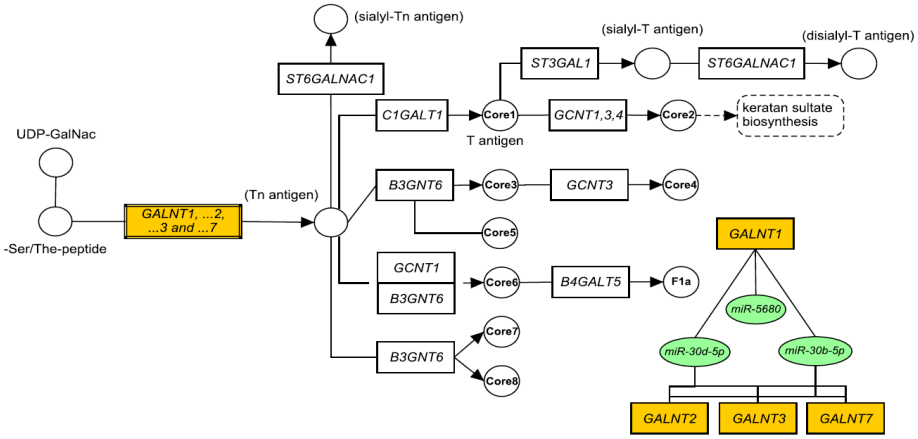


In yellow: genes targeted by one miRNA; in orange: genes targeted by more than one miRNA; in green: miRNAs with gain and/or amplification (PathVision v.3.3).

LYSINE DEGRADATION

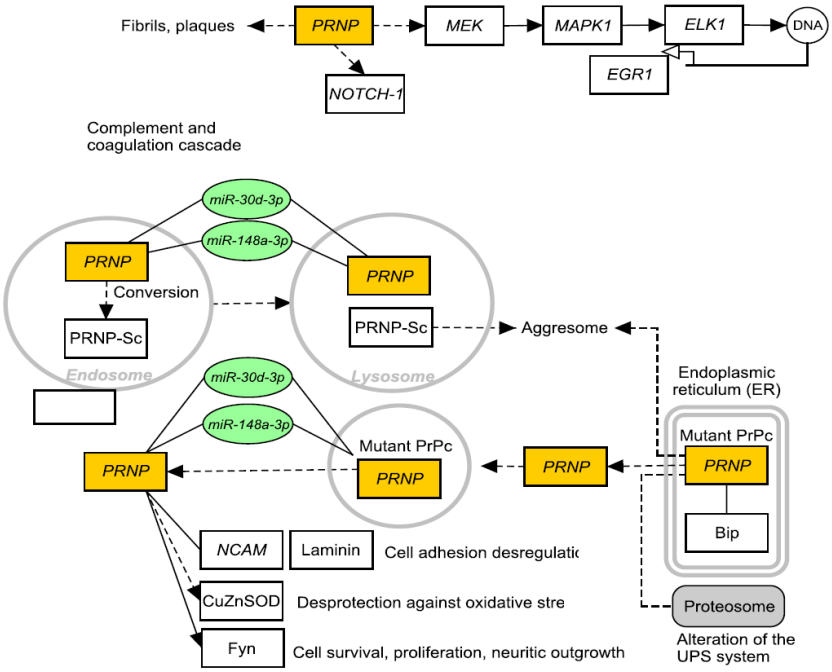


MUCIN TYPE O-GLYCAN BIOSYNTHESIS

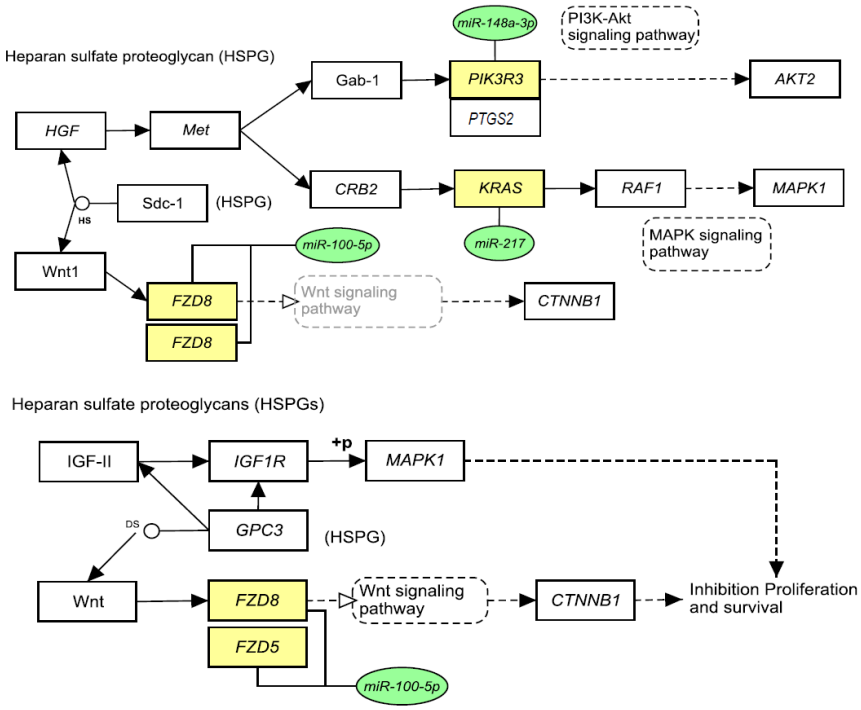


In yellow: genes targeted by one miRNA; in orange: genes targeted by more than one miRNA; in green: miRNAs with gain and/or amplification (PathVision v.3.3).

PRION DISEASE

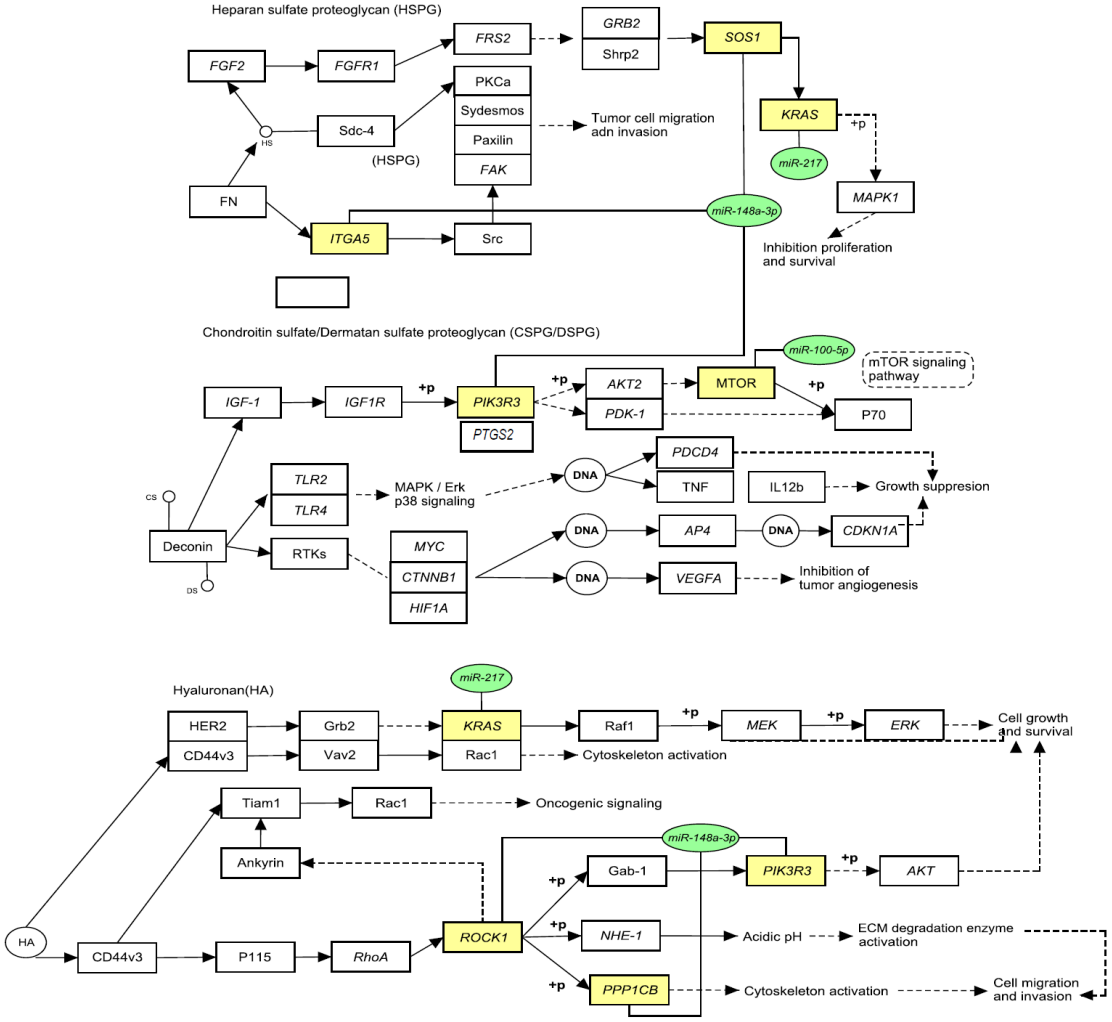


PROTEOGLICANS IN CANCER



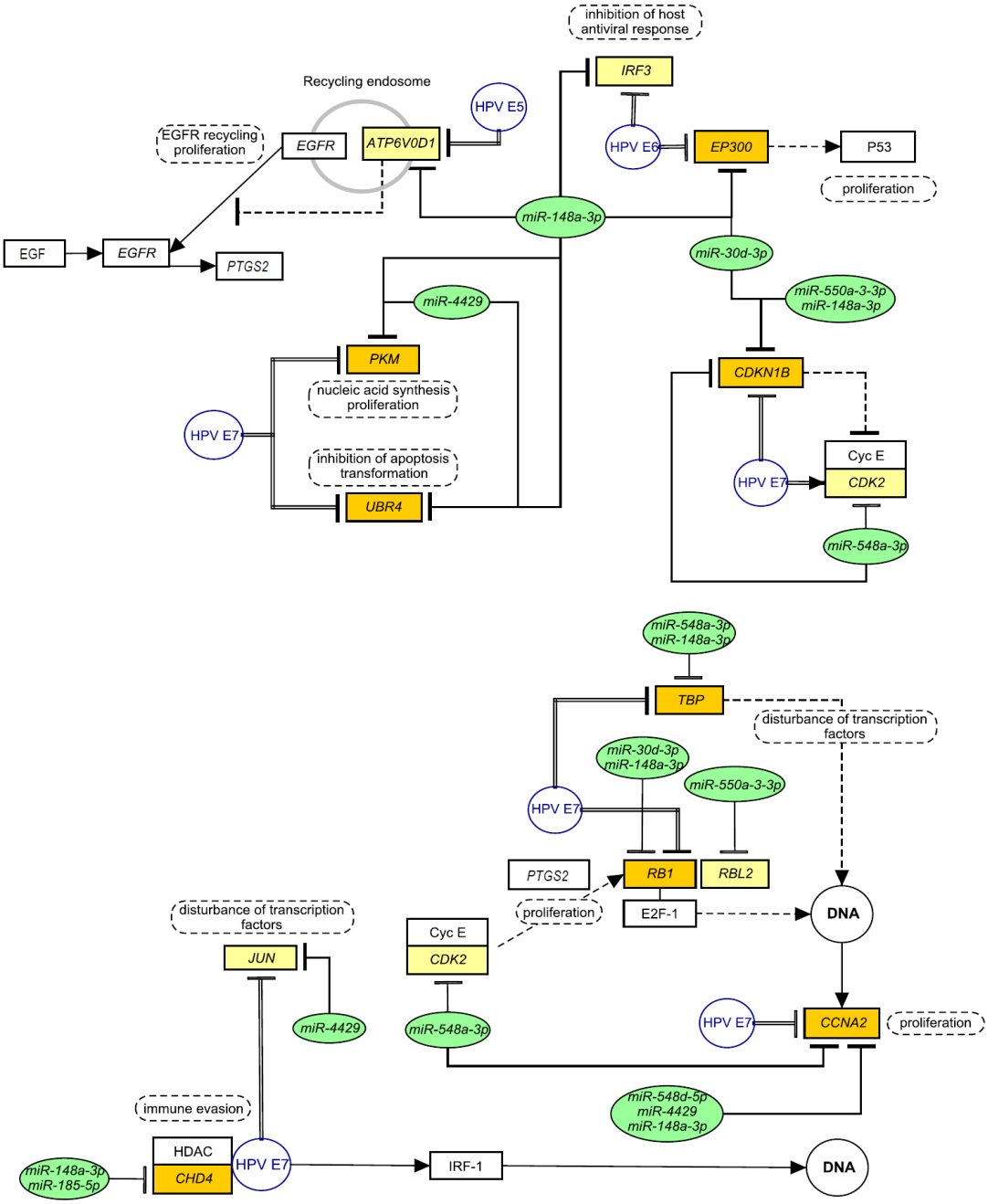
In yellow: genes targeted by one miRNA; in orange: genes targeted by more than one miRNA; in green: miRNAs with gain and/or amplification (PathVision v.3.3).

PROTEOGLICANS IN CANCER



In yellow: genes targeted by one miRNA; in orange: genes targeted by more than one miRNA; in green: miRNAs with gain and/or amplification (PathVision v.3.3).

HPV-MEDIATED VIRAL CARCINOGENESIS



In yellow: genes targeted by one miRNA; in orange: genes targeted by more than one miRNA; in green: miRNAs with gain and/or amplification (PathVision v.3.3).

Supplementary Table 1. Cytobands with CNA (n=30) and corresponding miRNAs and genes mapped in these affected regions (gene annotation based on Interval Probe Reports/Cytogenomics v.5.0; Agilent Technologies Inc, CA, algorithm ADM-2; threshold > 6).

Cytoband	Start - Stop (bp)	Size (Mb)	CNA event	Frequency of cases	HPV integration site (genotype [a])	Number of CNA-genes [b]	Number of CNA-miRNAs	CNA-miRNAs
1p36.3	564424 - 5932567	3.36	gain	82.1%	yes (16)	30	4	*MIR-551A, MIR-1302-2, MIR-6859, MIR-6859-2*
2p25.3-p11.1	10702 - 91906643	91.8	gain	42.9%	yes (16,18,45)	631	23	*MIR-217, MIR-3125, MIR-3126, MIR-3682, MIR-4261, MIR-4262, MIR-4263, MIR-4429, MIR-4430, MIR-4431, MIR-4432, MIR-4433A, MIR-4433B, MIR-4434, MIR-4757, MIR-4765, MIR-4778, MIR-5192, MIR-548AD, MIR-548S, MIR-558, MIR-7158, MIR-7515*
2p16.3	49454482 - 52545479	3.09	gain	53.6%	yes (16,18)	3	2	*MIR-559, MIR-8485*
2p12-p11.2	76510135 - 90248715	13.7	gain	82.1%	yes (16)	18	6	*MIR-4435, MIR-4436A, MIR-4779, MIR-4780, MIR-5000, MIR-6071*
3q26.1	162639153 - 166955811	4.31	gain	42.9%	yes (45)	7	1	*MIR-1263*
4p14-p13	37028964 - 41618637	4.58	loss	28.6%	yes (16)	24	2	*MIR-5592, MIR-4802*
4q13.2	67166142 - 70283558	3.11	loss/deletion	32.1%	yes (16)	1	1	*MIR-1269A*

5q13.2	69426248 - 70369959	0.94	loss/deletion	42.9%	yes (18)	17	2	*MIR-4803, MIR-4804*
7p22.3-p11	58764 - 57955498	57.8	gain	39.3%	yes (16,45)	415	25	*MIR-1183, MIR-1200, MIR-1302-6, MIR-148A, MIR-196B, MIR-3146, MIR-339, MIR-3683, MIR-3943, MIR-4648, MIR-4649, MIR-4655, MIR-4656, MIR-4657, MIR-548N, MIR-550A, MIR-550A-2, MIR-550A-3, MIR-550B, MIR-550B-2, MIR-589, MIR-6836, MIR-6837, MIR-6838, MIR-6874*
7p12.1-11.2	50656155 - 57955498	7.29	gain	67.9%	yes (16)	10	2	*MIR-3147, MIR-4283*
7q21.11	77522944 - 86346517	8.82	gain	53.6%	yes (16,35)	17	1	*MIR-548M*
8p23.1	6942281 - 8079920	1.13	loss/deletion	75.0%	yes (16)	24	15	*MIR-124, MIR-1322, MIR-3674, MIR-3926, MIR-3926-2, MIR-4286, MIR-4659A, MIR-4659B, MIR-4660, MIR-548I-3, MIR-5692A-2, MIR-596, MIR-597, MIR-598, MIR-8055*
8q11.1-q24.3	46924418 - 146293435	99.3	gain	53.6%	yes (16,18)	592	57	*MIR-12123, MIR-124-2, MIR-2052, MIR-2053, MIR-3149, MIR-3150A, MIR-3150B, MIR-3151, MIR-378D-2, MIR-4470, MIR-4471, MIR-4661, MIR-548A, MIR-5680, MIR-5681A,*

								MIR-5681B, MIR-5708, MIR-599, MIR-7705, MIR-8084, MIR-875, MIR-9903, MIR-10400, MIR-1204, MIR-1205, MIR-1206, MIR-1207, MIR-1208, MIR-1234, HSA-MIR-1302-7, MIR-151A, MIR-30B, MIR-30D, MIR-3610, MIR-3686, MIR-4472, MIR-4662A, MIR-4662B, MIR-4663, MIR-4664, MIR-5194, MIR-548AA, MIR-548AZ, MIR-548D, MIR-661, MIR-6844, MIR-6845, MIR-6846, MIR-6847, MIR-6848, MIR-6849, MIR-6850, MIR-6893, MIR-7112, MIR-7848, MIR-937, MIR-939
9p21	20260828 - 33183586	12.9	gain	35.7%	yes (16,18)	3	6	*MIR-31, MIR-4473, MIR-4474, MIR-491, MIR-873, MIR-876*
9q34.3	139393352 - 139440753	0.47	gain	50.0%	yes (16,18)	2	1	*MIR-4673*
10q26.13	123274734 - 127081469	3.8	gain	82.1%	yes (16)	1	1	*MIR-3941*
11q13.4	70494567 - 71752079	1.25	gain	42.9%	yes (16)	18	2	*MIR-3664, MIR-548K*

11q24-q25	130002757 - 134720344	4.71	gain	28.6%	yes (16)	23	12	*MIR-4492, MIR-6716, MIR-6756, LET-7A-2, MIR-100, MIR-10526, MIR-125B, MIR-4493, MIR-3167, MIR-6090, MIR-8052, MIR-4697*
14q11.2	19100682 - 20497737	1.39	loss	71.4%	yes (16,18)	2	4	*MIR-208A, MIR-208B, MIR-4707, MIR-6717*
14q12	25609148 - 30840211	5.23	gain	35.7%	yes (16)	5	4	*MIR-3171, MIR-4307, MIR-624, MIR-7703*
14q32.33	106331956 - 107216227	0.84	amplification	100.0%	yes (16)	5	13	*MIR-12121, MIR-203A, MIR-203B, MIR-4507, MIR-4537, MIR-4538, MIR-4539, MIR-4710, MIR-5195, MIR-6765, MIR-7641-2, MIR-8071, MIR-8071-2*
15q11.2-q13.3	23981875 - 28195618	4.21	gain	46.4%	yes (18)	132	13	*MIR-1268A, MIR-3118-2, MIR-3118-3, MIR-3118-4, MIR-4508, MIR-4509, MIR-5701, MIR-5701-2, MIR-5701-3, MIR-4715, MIR-4509-2, MIR-4509-3, MIR-211*
15q26.2-q26.3	95208833 - 102465355	7.25	gain	32.1%	yes (16)	10	4	*MIR-1469, MIR-4714, MIR-1302-10, MIR-6859-3*
16p11.2-p11.1	28184110 - 35177478	6.99	gain	35.7%	no	6	8	*MIR-3680-2, MIR-4517, MIR-4518, MIR-4519, MIR-4721, MIR-6862-2, MIR-762, MIR-9901*

18p11.31-p11.21	3323849 - 15325187	12	gain	35.7%	yes (16)	15	8	*MIR-3156-2, MIR-4526, MIR-5190, MIR-7153, MIR-6788, MIR-3976, MIR-4317, MIR-6718*
19p13.2	7188845 - 12847613	5.65	loss	28.6%	yes (16,18)	192	16	*MIR-199-A1, MIR-5598, MIR-4322, MIR-1181, MIR-1238, MIR-638, MIR-4748, MIR-6793, MIR-6886, MIR-7974, MIR-6885, MIR-6790, MIR-3940, MIR-6791, MIR-6792, MIR-4999*
19p13.11-p12	18893101 - 24100639	5.2	loss	25.0%	yes (16)	51	2	*MIR-640, MIR-1270*
20q13.32-q13.33	57353677 - 62849271	5.49	gain	42.9%	yes (16)	31	21	*MIR-296, MIR-298, MIR-1, MIR-124-3, MIR-1257, MIR-133A-2, MIR-1914, MIR-3195, MIR-3196, MIR-4326, MIR-4533, -MIR-4758, MIR-548AG-2, MIR-646, MIR-647, MIR-6813, MIR-941, MIR-941-2, MIR-941-3, MIR-941-4, MIR-941-5*
22q11.21	19584758 - 20311762	0.73	gain	60.7%	yes (33)	5	10	*MIR-1286, MIR-1306, -MIR-185, MIR-301B, MIR-3198, MIR-3618, MIR-4761, MIR-648, MIR-649, MIR-6816*
Yp11.3-p11.2	13303 - 10063619	10	loss	28.6%	no	39	3	*MIR-3690-2, MIR-6089-2, MIR-9985*

In bold, the cytobands that presented association with clinical and histopathological parameters (P<0.05) (n=15).[a] genotypes identified in previous studies according to HPVbase. [b] The number of genes does not reflect the total number of genes present in each of the chromosomal cytobands, but only those genes with changes in the number of copies identified by the aCGH analysis.

Supplementary Table 2A. All interactions among the 292 CNA-gene and 348 miRNAs in PeCa (DIANA-TarBase v.8 | miTG ≥ 0.9). In bold, the common 35 miRNAs and 78 mRNA targets.

CNA-gene	miRNA	miTG score	CNA-gene	miRNA	miTG score
ARHGAP28	*hsa-let-7a-5p*	1	*ZNF91*	*hsa-miR-130a-5p*	0.963
ARHGAP28	*hsa-let-7b-5p*	1	*ARL4A*	*hsa-miR-17-5p*	0.962
ARHGAP28	*hsa-let-7f-5p*	1	*GLCCI1*	*hsa-miR-501-3p*	0.962
ARHGAP28	*hsa-let-7g-5p*	1	*HNRNPA2B1*	*hsa-miR-548h-5p*	0.962
ARHGAP28	*hsa-let-7i-5p*	1	*LAPTM4B*	*hsa-miR-128-3p*	0.962
ARHGAP28	*hsa-let-7c-5p*	1	*PLAG1*	*hsa-miR-21-5p*	0.962
ARHGAP28	*hsa-let-7e-5p*	1	*RMND5A*	*hsa-miR-548i*	0.962
ARHGAP28	*hsa-miR-98-5p*	1	*ZNF208*	*hsa-miR-146b-5p*	0.962
ATAD2B	*hsa-miR-29a-3p*	1	*AHR*	*hsa-miR-374a-5p*	0.961
ATAD2B	*hsa-miR-29b-3p*	1	*ANTXR1*	*hsa-miR-155-5p*	0.961
ATAD2B	*hsa-miR-29c-3p*	1	*ATAD2B*	*hsa-miR-29b-2-5p*	0.961
ATAD2B	*hsa-miR-26a-5p*	1	*CRISPLD1*	*hsa-miR-23b-3p*	0.961
ATAD2B	*hsa-miR-26b-5p*	1	*ELAVL2*	*hsa-miR-30e-5p*	0.961

AVL9	*hsa-miR-24-3p*	1	*FAM98A*	*hsa-miR-1976*	0.961
AVL9	*hsa-miR-484*	1	*FAM98A*	*hsa-miR-27a-3p*	0.961
CCNE2	*hsa-miR-30a-5p*	1	*FAM98A*	*hsa-miR-27b-3p*	0.961
CCNE2	***hsa-miR-30b-5p***	**1**	*HAS2*	*hsa-miR-424-5p*	0.961
CCNE2	*hsa-miR-30c-5p*	1	*HAS2*	*hsa-miR-497-5p*	0.961
CCNE2	***hsa-miR-30d-5p***	**1**	*HNRNPA2B1*	*hsa-miR-500a-5p*	0.961
CCNE2	*hsa-miR-30e-5p*	1	*ITSN2*	*hsa-miR-200b-3p*	0.961
CCNE2	*hsa-miR-34a-5p*	1	*MAFK*	*hsa-miR-15b-5p*	0.961
COL5A3	*hsa-miR-29c-3p*	1	*MRPL4*	*hsa-miR-3179*	0.961
COL5A3	*hsa-miR-29a-3p*	1	*NCOA1*	*hsa-miR-3613-3p*	0.961
CYP1B1	*hsa-miR-27b-3p*	1	*PURB*	*hsa-miR-373-5p*	0.961
ETV1	*hsa-miR-20a-5p*	1	*RHOB*	*hsa-miR-19b-3p*	0.961
FAM98A	*hsa-miR-26b-5p*	1	*SQLE*	*hsa-miR-579-3p*	0.961
FBXO32	*hsa-miR-19a-3p*	1	*TRPS1*	*hsa-miR-186-5p*	0.961
FBXO32	*hsa-miR-19b-3p*	1	*ZFP36L2*	*hsa-miR-221-3p*	0.961
FMN2	*hsa-miR-32-5p*	1	*ZNRF2*	*hsa-miR-15a-5p*	0.961

FMN2	*hsa-miR-92a-3p*	1	*BIRC6*	*hsa-miR-30e-5p*	0.96
GLCCI1	*hsa-miR-30a-5p*	1	*ELAVL2*	*hsa-miR-30a-5p*	0.96
GLCCI1	***hsa-miR-30b-5p***	**1**	***ELAVL2***	***hsa-miR-30d-5p***	**0.96**
GLCCI1	*hsa-miR-30c-5p*	1	*GLI3*	*hsa-miR-200c-3p*	0.96
GLCCI1	***hsa-miR-30d-5p***	**1**	*JAZF1*	*hsa-miR-182-5p*	0.96
GLCCI1	*hsa-miR-30e-5p*	1	*LDLR*	*hsa-miR-130a-3p*	0.96
GLI3	*hsa-miR-7-5p*	1	*LDLR*	*hsa-miR-106a-5p*	0.96
HGF	*hsa-miR-26b-5p*	1	*OSBPL3*	*hsa-miR-590-3p*	0.96
HOXA7	***hsa-miR-196b-5p***	**1**	*PTCD3*	*hsa-miR-16-5p*	0.96
HOXA7	*hsa-miR-196a-5p*	1	*ZFP36L2*	*hsa-miR-371a-5p*	0.96
HOXA9	***hsa-miR-196b-5p***	**1**	*ZNF709*	*hsa-miR-181b-5p*	0.96
ITGB8	*hsa-miR-20a-5p*	1	*AVL9*	*hsa-miR-103a-3p*	0.959
ITGB8	*hsa-miR-106b-5p*	1	*AVL9*	*hsa-miR-107*	0.959
LBH	*hsa-miR-128-3p*	1	*EHBP1*	*hsa-miR-3613-3p*	0.959
LCLAT1	*hsa-miR-30c-5p*	1	*LDLR*	*hsa-miR-493-5p*	0.959
LCLAT1	***hsa-miR-30d-5p***	**1**	*MYCN*	*hsa-miR-29a-3p*	0.959

MAP4K3	*hsa-let-7a-5p*	1	*NCOA1*	*hsa-miR-219a-5p*	0.959
MAP4K3	*hsa-let-7b-5p*	1	***PDS5A***	***hsa-miR-624-3p***	**0.959**
MAP4K3	*hsa-let-7c-5p*	1	***PURB***	***hsa-miR-548a-3p***	**0.959**
MAP4K3	*hsa-let-7e-5p*	1	*RMND5A*	*hsa-miR-5582-3p*	0.959
MAP4K3	*hsa-let-7f-5p*	1	*SOX11*	*hsa-miR-1226-3p*	0.959
MAP4K3	*hsa-let-7g-5p*	1	*TEX261*	*hsa-miR-766-5p*	0.959
MAP4K3	*hsa-let-7i-5p*	1	*ZNF100*	*hsa-miR-27a-3p*	0.959
MAP4K3	*hsa-miR-98-5p*	1	*ZNF100*	*hsa-miR-27b-3p*	0.959
MMP16	*hsa-miR-29a-3p*	1	***ARRDC4***	***hsa-miR-548d-3p***	**0.958**
MMP16	*hsa-miR-29b-3p*	1	*CALB1*	*hsa-miR-186-5p*	0.958
MMP16	*hsa-miR-29c-3p*	1	*CDC42EP3*	*hsa-miR-27a-3p*	0.958
MTDH	***hsa-miR-30b-5p***	**1**	*FOXN2*	*hsa-miR-363-3p*	0.958
MTDH	*hsa-miR-30c-5p*	1	*HNRNPA2B1*	*hsa-miR-513b-5p*	0.958
MTDH	***hsa-miR-30d-5p***	**1**	*MTDH*	*hsa-miR-548am-5p*	0.958
MTDH	*hsa-miR-30e-5p*	1	*MTDH*	*hsa-miR-548c-5p*	0.958
MTDH	*hsa-miR-30a-5p*	1	*MTDH*	*hsa-miR-548o-5p*	0.958

MYBL1	*hsa-miR-454-3p*	1	*PPP1CB*	*hsa-miR-23b-3p*	0.958
NDUFA4	*hsa-miR-147b*	1	*RHOB*	*hsa-miR-548e-3p*	0.958
PDE7A	***hsa-miR-30b-5p***	**1**	*RMND5A*	*hsa-miR-548j-5p*	0.958
PDE7A	*hsa-miR-30c-5p*	1	*TMEM65*	*hsa-miR-3653-3p*	0.958
PDE7A	***hsa-miR-30d-5p***	**1**	*TNRC18*	*hsa-miR-34a-5p*	0.958
PDE7A	*hsa-miR-30e-5p*	1	*TOX*	*hsa-miR-23b-3p*	0.958
PDE7A	*hsa-miR-30a-5p*	1	*ZNF208*	*hsa-miR-23a-3p*	0.958
PLAG1	*hsa-miR-16-5p*	1	*ZNF91*	*hsa-miR-23c*	0.958
PLAG1	*hsa-miR-15a-5p*	1	*CCT4*	*hsa-miR-141-5p*	0.957
PLAG1	*hsa-miR-15b-5p*	1	*CCT6A*	*hsa-miR-148b-3p*	0.957
PLAG1	*hsa-miR-424-5p*	1	*EML4*	*hsa-miR-30c-5p*	0.957
PLAG1	*hsa-miR-195-5p*	1	*LAPTM4A*	*hsa-miR-141-5p*	0.957
PLAG1	*hsa-miR-141-3p*	1	*MBOAT2*	*hsa-miR-181b-5p*	0.957
POLE4	*hsa-miR-7-5p*	1	***PREPL***	***hsa-miR-185-5p***	**0.957**
PPP3R1	*hsa-miR-106b-5p*	1	*PURB*	*hsa-miR-133a-3p*	0.957
PPP3R1	*hsa-miR-20a-5p*	1	*PURB*	*hsa-miR-23b-3p*	0.957

PRKCE	*hsa-miR-96-5p*	1	*RMND5A*	*hsa-miR-548am-5p*	0.957
PXDN	*hsa-miR-29b-3p*	1	*RMND5A*	*hsa-miR-548c-5p*	0.957
PXDN	*hsa-miR-29a-3p*	1	*RMND5A*	*hsa-miR-548o-5p*	0.957
PXDN	*hsa-miR-29c-3p*	1	*TNRC18*	*hsa-miR-449a*	0.957
RAD21	*hsa-miR-32-5p*	1	*UBE2W*	*hsa-miR-32-3p*	0.957
RMND5A	*hsa-miR-138-5p*	1	*ZNF704*	*hsa-miR-548at-5p*	0.957
RNF19A	*hsa-miR-29a-3p*	1	*ZNF91*	*hsa-miR-23b-3p*	0.957
RNF19A	*hsa-miR-29c-3p*	1	*ARL4A*	*hsa-miR-20b-5p*	0.956
SAMD12	*hsa-miR-106b-5p*	1	*ASXL2*	*hsa-miR-92b-3p*	0.956
SAMD12	*hsa-miR-20a-5p*	1	*ATAD2B*	*hsa-miR-4698*	0.956
SEMA3A	*hsa-miR-30a-5p*	1	*DPYSL5*	*hsa-miR-128-3p*	0.956
SEMA3A	***hsa-miR-30d-5p***	**1**	*FAM110C*	*hsa-miR-25-3p*	0.956
SEMA3A	*hsa-miR-30e-5p*	1	*PI15*	*hsa-miR-590-3p*	0.956
SOX11	*hsa-miR-1305*	1	*PPP1CB*	*hsa-miR-23a-3p*	0.956
SOX11	*hsa-miR-590-3p*	1	*PURB*	*hsa-miR-23a-3p*	0.956
UBE2W	*hsa-miR-92a-3p*	1	*TRIB1*	*hsa-miR-23c*	0.956

UBE2W	*hsa-miR-20a-5p*	1	*UBE2W*	*hsa-miR-222-5p*	0.956
UBE2W	*hsa-miR-92b-3p*	1	*ZFP36L2*	*hsa-miR-222-3p*	0.956
UBE2W	*hsa-miR-106a-5p*	1	*ZNF253*	*hsa-miR-130a-5p*	0.956
UBE2W	*hsa-miR-429*	1	*E2F5*	*hsa-miR-3065-5p*	0.955
WIPI2	*hsa-miR-15a-5p*	1	***EML4***	***hsa-miR-30b-5p***	**0.955**
ZBTB10	*hsa-miR-19a-3p*	1	*GNA12*	*hsa-miR-450b-5p*	0.955
ZBTB10	*hsa-miR-19b-3p*	1	*H2AFV*	*hsa-miR-494-3p*	0.955
ZFHX4	*hsa-miR-548at-5p*	1	*HAS2*	*hsa-miR-106a-5p*	0.955
ZFP36L2	*hsa-miR-101-3p*	1	*MTHFD2*	*hsa-miR-205-3p*	0.955
ZFP36L2	*hsa-miR-144-3p*	1	*PTCD3*	*hsa-miR-29b-2-5p*	0.955
ZNF513	*hsa-miR-340-5p*	1	*RAB10*	*hsa-miR-1301-3p*	0.955
ZNF788	*hsa-miR-181b-5p*	1	*TCF24*	*hsa-miR-200a-3p*	0.955
ZNF788	*hsa-miR-181d-5p*	1	*TMEM106B*	*hsa-miR-26b-5p*	0.955
CACNA2D1	*hsa-miR-103a-3p*	0.999	*TRIB1*	*hsa-miR-23a-3p*	0.955
CACNA2D1	*hsa-miR-107*	0.999	*ZNF208*	*hsa-miR-23b-3p*	0.955
CDK13	*hsa-miR-141-3p*	0.999	*BIRC6*	*hsa-miR-30a-5p*	0.954

DPYSL5	*hsa-miR-29a-3p*	0.999	*CACNA2D1*	*hsa-miR-450b-5p*	0.954
DPYSL5	*hsa-miR-29b-3p*	0.999	*CCNE2*	*hsa-miR-5582-3p*	0.954
DPYSL5	*hsa-miR-29c-3p*	0.999	*CRIM1*	*hsa-miR-374a-5p*	0.954
E2F5	*hsa-miR-34a-5p*	0.999	*E2F5*	*hsa-miR-34c-5p*	0.954
E2F5	*hsa-miR-449a*	0.999	*KBTBD2*	*hsa-miR-101-3p*	0.954
ETV1	*hsa-miR-106b-5p*	0.999	*LDLR*	*hsa-miR-140-5p*	0.954
FMN2	*hsa-miR-144-3p*	0.999	*PAPOLG*	*hsa-miR-590-3p*	0.954
FOXN2	***hsa-miR-548d-3p***	**0.999**	*PXDN*	*hsa-miR-19a-3p*	0.954
HGF	*hsa-miR-26a-5p*	0.999	*RAB10*	*hsa-miR-374a-5p*	0.954
HOXA13	*hsa-miR-126-5p*	0.999	***RMND5A***	***hsa-miR-548d-5p***	**0.954**
HOXA9	*hsa-miR-196a-5p*	0.999	*ROCK2*	*hsa-miR-520a-3p*	0.954
ITGB8	*hsa-miR-106a-5p*	0.999	*SERTAD2*	*hsa-miR-25-3p*	0.954
LAPTM4A	*hsa-miR-495-3p*	0.999	*TRIB1*	*hsa-miR-23b-3p*	0.954
LCLAT1	***hsa-miR-30b-5p***	**0.999**	*ZNF208*	*hsa-miR-766-3p*	0.954
MACC1	*hsa-miR-362-3p*	0.999	*ZNF704*	*hsa-miR-21-3p*	0.954
MACC1	*hsa-miR-3679-5p*	0.999	*CDK13*	*hsa-miR-142-5p*	0.953

MTDH	*hsa-miR-26a-5p*	0.999	*EFR3A*	*hsa-miR-3065-5p*	0.953
MTDH	*hsa-miR-26b-5p*	0.999	*FAM110C*	*hsa-miR-15b-5p*	0.953
MTSS1	*hsa-miR-182-5p*	0.999	*FLRT2*	*hsa-miR-126-5p*	0.953
PDE7A	*hsa-miR-582-5p*	0.999	*GFPT1*	*hsa-miR-27b-3p*	0.953
PDS5A	*hsa-miR-3944-5p*	0.999	*GFPT1*	*hsa-miR-548j-5p*	0.953
PELI1	*hsa-miR-21-5p*	0.999	*GLCCI1*	*hsa-miR-7-1-3p*	0.953
PPFIA1	*hsa-miR-34a-5p*	0.999	***LBH***	***hsa-miR-548d-3p***	**0.953**
PPP3R1	*hsa-miR-106a-5p*	0.999	*MTDH*	*hsa-miR-548i*	0.953
PURB	*hsa-miR-101-3p*	0.999	*NOTCH1*	*hsa-miR-200b-3p*	0.953
RAB10	***hsa-miR-124-3p***	**0.999**	*PELI1*	*hsa-miR-374b-5p*	0.953
RAD21	*hsa-miR-92a-3p*	0.999	*SMC6*	*hsa-miR-579-3p*	0.953
RAD21	*hsa-miR-92b-3p*	0.999	*ZNF12*	*hsa-miR-181a-5p*	0.953
RBAK	*hsa-miR-135b-5p*	0.999	*ZNF91*	*hsa-miR-23a-3p*	0.953
RHOB	***hsa-miR-30b-5p***	**0.999**	*ZNRF2*	*hsa-miR-374a-5p*	0.953
RHOB	*hsa-miR-30c-5p*	0.999	*ARMC1*	*hsa-miR-32-5p*	0.952
RNF19A	*hsa-miR-29b-3p*	0.999	*CCT6A*	*hsa-miR-1305*	0.952

ROCK2	*hsa-miR-142-3p*	0.999	***CCT6A***	***hsa-miR-148a-3p***	**0.952**
SEMA3A	***hsa-miR-30b-5p***	**0.999**	***FAM98A***	***hsa-miR-548d-3p***	**0.952**
SEMA3A	*hsa-miR-30c-5p*	0.999	*HOXA13*	*hsa-miR-27b-3p*	0.952
STMN2	*hsa-miR-29a-3p*	0.999	***PLEKHF2***	***hsa-miR-124-3p***	**0.952**
UBE2W	*hsa-miR-106b-5p*	0.999	*RNF139*	*hsa-miR-583*	0.952
UBE2W	*hsa-miR-20b-5p*	0.999	*TSPAN13*	*hsa-miR-1277-5p*	0.952
WIPI2	*hsa-miR-16-5p*	0.999	*ZNF561*	*hsa-miR-155-5p*	0.952
WIPI2	*hsa-miR-15b-5p*	0.999	*ZNF704*	*hsa-miR-548h-5p*	0.952
WIPI2	*hsa-miR-195-5p*	0.999	*AVL9*	*hsa-miR-1303*	0.951
WIPI2	*hsa-miR-182-5p*	0.999	***BIRC6***	***hsa-miR-30d-5p***	**0.951**
ZBTB44	*hsa-miR-1277-5p*	0.999	*MTDH*	*hsa-miR-548j-5p*	0.951
CCDC126	*hsa-miR-454-3p*	0.998	*RAD21*	*hsa-miR-363-3p*	0.951
EFR3A	*hsa-miR-32-5p*	0.998	*TRPS1*	*hsa-miR-26a-5p*	0.951
EPAS1	*hsa-miR-182-5p*	0.998	*ZBTB10*	*hsa-miR-27a-3p*	0.951
FAM110C	*hsa-miR-92a-3p*	0.998	*ZBTB10*	*hsa-miR-140-5p*	0.951
FAM20C	*hsa-miR-92a-3p*	0.998	*ZNF709*	*hsa-miR-4476*	0.951

FAM20C	*hsa-miR-32-5p*	0.998	*CCND1*	*hsa-miR-20a-5p*	0.95
HOXA5	*hsa-miR-196a-5p*	0.998	*CREB5*	*hsa-miR-590-5p*	0.95
HOXA5	***hsa-miR-196b-5p***	**0.998**	*EPAS1*	*hsa-miR-30a-3p*	0.95
HOXA9	*hsa-miR-182-5p*	0.998	***GFPT1***	***hsa-miR-548d-5p***	**0.95**
KCMF1	*hsa-miR-664a-3p*	0.998	*HNRNPA2B1*	*hsa-miR-130a-5p*	0.95
MAP4K3	*hsa-let-7g-3p*	0.998	*MTDH*	*hsa-miR-142-5p*	0.95
MAT2A	*hsa-miR-30a-5p*	0.998	*PELI1*	*hsa-miR-590-5p*	0.95
MTURN	*hsa-miR-182-5p*	0.998	*PNPT1*	*hsa-miR-155-5p*	0.95
PDE7A	*hsa-miR-23a-3p*	0.998	*PPP3R1*	*hsa-miR-4516*	0.95
PDE7A	*hsa-miR-23b-3p*	0.998	*RNF139*	*hsa-miR-27a-3p*	0.95
PELI1	*hsa-miR-374a-5p*	0.998	*ROCK2*	*hsa-miR-590-3p*	0.95
PRKCE	*hsa-miR-101-3p*	0.998	*ZNF100*	*hsa-miR-23a-3p*	0.95
RAB11FIP5	*hsa-miR-106a-5p*	0.998	*ANTXR1*	*hsa-miR-576-5p*	0.949
RBAK	*hsa-miR-135a-5p*	0.998	*APBA2*	*hsa-miR-182-5p*	0.949
RNF19A	*hsa-miR-20a-3p*	0.998	*CREB5*	*hsa-miR-20a-5p*	0.949
ROCK2	*hsa-miR-20a-5p*	0.998	*DPYSL5*	*hsa-miR-5682*	0.949

SAMD12	*hsa-miR-17-5p*	0.998	*EPAS1*	*hsa-miR-127-5p*	0.949
SOS1	*hsa-miR-148b-3p*	0.998	*GFPT1*	*hsa-miR-548h-5p*	0.949
STK17A	*hsa-miR-96-5p*	0.998	*HNRNPA2B1*	*hsa-miR-148b-3p*	0.949
STMN2	*hsa-miR-29b-3p*	0.998	*LDLR*	*hsa-miR-19b-3p*	0.949
STMN2	*hsa-miR-29c-3p*	0.998	*OSGIN2*	*hsa-miR-141-3p*	0.949
TRPS1	*hsa-miR-126-5p*	0.998	*PXDN*	*hsa-miR-19b-3p*	0.949
UBE2K	*hsa-miR-3065-5p*	0.998	*RTN4*	*hsa-miR-21-5p*	0.949
UBE2W	*hsa-miR-200c-3p*	0.998	*SEMA3C*	*hsa-miR-502-3p*	0.949
UBE2W	*hsa-miR-200b-3p*	0.998	*SERTAD2*	*hsa-miR-548l*	0.949
ASXL2	*hsa-miR-3662*	0.997	*TCF24*	*hsa-miR-141-3p*	0.949
AVL9	*hsa-miR-149-5p*	0.997	*TRIQK*	*hsa-miR-450b-5p*	0.949
C2orf42	*hsa-miR-19b-3p*	0.997	*TRPS1*	*hsa-miR-30e-5p*	0.949
CDK13	*hsa-miR-200a-3p*	0.997	*ZFHX4*	*hsa-miR-23b-3p*	0.949
FAM20C	*hsa-miR-92b-3p*	0.997	*ZNF704*	*hsa-miR-548a-5p*	0.949
LCLAT1	*hsa-miR-30e-5p*	0.997	*ZNF704*	*hsa-miR-548j-5p*	0.949
MYCN	*hsa-let-7i-5p*	0.997	*AZIN1*	*hsa-miR-590-3p*	0.948

PDE7A	*hsa-miR-23c*	0.997	*BIRC6*	*hsa-miR-196a-5p*	0.948
RBAK	*hsa-miR-155-5p*	0.997	*CACNA2D1*	*hsa-miR-15a-5p*	0.948
RHOB	***hsa-miR-30d-5p***	**0.997**	*CCT6A*	*hsa-miR-301a-3p*	0.948
RHOB	*hsa-miR-30e-5p*	0.997	*DUSP11*	*hsa-miR-374a-5p*	0.948
RMND5A	*hsa-miR-548h-3p*	0.997	*KDELR2*	*hsa-miR-142-3p*	0.948
RMND5A	*hsa-miR-548z*	0.997	*PDS5A*	*hsa-miR-1305*	0.948
ROCK2	*hsa-miR-106a-5p*	0.997	*PPM1G*	*hsa-miR-132-3p*	0.948
SOX11	*hsa-miR-27a-3p*	0.997	*PPP3R1*	*hsa-miR-7-1-3p*	0.948
SOX11	*hsa-miR-27b-3p*	0.997	*SEMA3C*	*hsa-miR-501-3p*	0.948
TPD52	*hsa-miR-34a-5p*	0.997	*SOX11*	*hsa-miR-4793-3p*	0.948
UBE2V2	***hsa-miR-4803***	**0.997**	*TRPS1*	*hsa-miR-155-5p*	0.948
UBE2W	*hsa-miR-17-5p*	0.997	*ZNF440*	*hsa-miR-181a-5p*	0.948
UBE2W	*hsa-miR-93-5p*	0.997	*AVL9*	*hsa-miR-15a-5p*	0.947
ZNF704	*hsa-miR-181a-5p*	0.997	*CCT6A*	*hsa-miR-130a-3p*	0.947
C2orf42	*hsa-miR-19a-3p*	0.996	*CREB5*	*hsa-miR-106b-5p*	0.947
CHAC2	*hsa-miR-3174*	0.996	*CRIM1*	*hsa-miR-9-5p*	0.947

CRIM1	*hsa-miR-7-1-3p*	0.996	*DNAJC27*	*hsa-miR-32-5p*	0.947
EFR3A	*hsa-miR-92b-3p*	0.996	*LDLR*	*hsa-miR-19a-3p*	0.947
FBXO48	*hsa-miR-106b-5p*	0.996	*PPP1CB*	*hsa-miR-23c*	0.947
FBXO48	*hsa-miR-20a-5p*	0.996	*SERTAD2*	*hsa-miR-501-3p*	0.947
GLCCI1	*hsa-miR-141-3p*	0.996	***TRPS1***	***hsa-miR-30d-5p***	**0.947**
HNRNPA2B1	*hsa-let-7f-2-3p*	0.996	*ZFHX4*	*hsa-miR-96-5p*	0.947
HOXA5	*hsa-miR-27a-3p*	0.996	*CCT6A*	*hsa-miR-130b-3p*	0.946
HOXA5	*hsa-miR-27b-3p*	0.996	*DNAJC27*	*hsa-miR-27a-3p*	0.946
HOXA5	*hsa-miR-26a-5p*	0.996	*GFPT1*	*hsa-miR-548am-5p*	0.946
MYBL1	***hsa-miR-301b-3p***	**0.996**	*GFPT1*	*hsa-miR-548au-5p*	0.946
MYCN	*hsa-let-7b-5p*	0.996	*GFPT1*	*hsa-miR-548c-5p*	0.946
MYCN	*hsa-let-7c-5p*	0.996	*GFPT1*	*hsa-miR-548o-5p*	0.946
PCMTD1	*hsa-miR-92a-3p*	0.996	*LDLR*	*hsa-miR-106b-5p*	0.946
ROCK2	*hsa-miR-17-5p*	0.996	*RAB10*	*hsa-miR-548ar-3p*	0.946
SAMD12	*hsa-miR-20b-5p*	0.996	*SERTAD2*	*hsa-miR-502-3p*	0.946
UBE2W	*hsa-miR-128-3p*	0.996	*SOX11*	*hsa-miR-629-3p*	0.946

UBR5	*hsa-miR-27b-3p*	0.996	*TRIB1*	*hsa-miR-224-5p*	0.946
ZNF704	*hsa-miR-181b-5p*	0.996	*ZNF253*	*hsa-miR-23b-3p*	0.946
ZNF788	*hsa-miR-181a-5p*	0.996	*ZNF440*	*hsa-miR-181c-5p*	0.946
ZNF788	*hsa-miR-181c-5p*	0.996	*CAD*	*hsa-miR-18a-5p*	0.945
ARMC1	*hsa-miR-92a-3p*	0.995	*CHN2*	*hsa-miR-429*	0.945
ATAD2B	*hsa-miR-5682*	0.995	*FKBP14*	*hsa-miR-340-5p*	0.945
DPY19L1	***hsa-miR-30d-5p***	**0.995**	***GLCCI1***	***hsa-miR-203a-3p***	**0.945**
DPY19L1	*hsa-miR-30e-5p*	0.995	*HOXA13*	*hsa-miR-27a-3p*	0.945
EIF2AK2	*hsa-miR-141-3p*	0.995	*HOXA5*	*hsa-miR-484*	0.945
FAM110C	*hsa-miR-32-5p*	0.995	***MBOAT2***	***hsa-miR-548d-3p***	**0.945**
HNRNPA2B1	*hsa-miR-548an*	0.995	*OSGIN2*	*hsa-miR-92b-3p*	0.945
HNRNPA2B1	*hsa-miR-330-5p*	0.995	*PLAG1*	*hsa-miR-10a-3p*	0.945
HOXA5	*hsa-miR-26b-5p*	0.995	***POLR1A***	***hsa-miR-1207-5p***	**0.945**
ID2	*hsa-miR-340-5p*	0.995	*PURB*	*hsa-miR-1301-3p*	0.945
JAZF1	*hsa-miR-200c-3p*	0.995	*PURB*	*hsa-miR-548j-5p*	0.945
KLHL5	*hsa-miR-181a-5p*	0.995	*RAC1*	*hsa-miR-650*	0.945

MYT1L	*hsa-miR-497-5p*	0.995	*RAD21*	*hsa-miR-25-3p*	0.945
PURB	*hsa-miR-20a-5p*	0.995	*ZBTB10*	*hsa-miR-27b-3p*	0.945
PURB	*hsa-miR-590-3p*	0.995	*ZNF100*	*hsa-miR-23b-3p*	0.945
SAMD12	*hsa-miR-93-5p*	0.995	*ZNF250*	*hsa-miR-130b-3p*	0.945
SNTB1	*hsa-miR-24-3p*	0.995	*ZNF253*	*hsa-miR-23a-3p*	0.945
STRN	*hsa-miR-21-5p*	0.995	*CACNA2D1*	*hsa-miR-424-5p*	0.944
SYBU	*hsa-miR-130a-3p*	0.995	*CACNA2D1*	*hsa-miR-195-5p*	0.944
TMSB10	*hsa-miR-27a-3p*	0.995	*GFPT1*	*hsa-miR-27a-3p*	0.944
TMSB10	*hsa-miR-27b-3p*	0.995	*HGF*	*hsa-miR-16-1-3p*	0.944
ZFPM2	*hsa-miR-103a-3p*	0.995	*OSGIN2*	*hsa-miR-200a-3p*	0.944
EFR3A	*hsa-miR-92a-3p*	0.994	*PAPOLG*	*hsa-miR-1305*	0.944
GLCCI1	*hsa-miR-153-3p*	0.994	*RAB10*	*hsa-miR-16-5p*	0.944
ILF3	*hsa-miR-4422*	0.994	*SOX11*	*hsa-miR-129-5p*	0.944
KLF10	*hsa-miR-30a-5p*	0.994	*ZBTB44*	*hsa-miR-27a-3p*	0.944
KLHL5	*hsa-miR-181c-5p*	0.994	*ZFP36L2*	*hsa-miR-590-3p*	0.944
MYCN	*hsa-let-7e-5p*	0.994	***BIRC6***	***hsa-miR-30b-5p***	**0.943**

MYCN	*hsa-let-7a-5p*	0.994	*CCDC126*	*hsa-miR-19a-3p*	0.943
MYCN	*hsa-let-7f-5p*	0.994	*CCDC126*	*hsa-miR-19b-3p*	0.943
MYCN	*hsa-let-7g-5p*	0.994	*CCND1*	*hsa-miR-19b-3p*	0.943
SYBU	*hsa-miR-19a-3p*	0.994	***CCT6A***	***hsa-miR-301b-3p***	**0.943**
TIA1	*hsa-miR-19b-3p*	0.994	*FAM110C*	*hsa-miR-15a-5p*	0.943
ZFHX4	***hsa-miR-148a-5p***	**0.994**	*IMPAD1*	*hsa-miR-590-3p*	0.943
ZFPM2	*hsa-miR-107*	0.994	*LDLR*	*hsa-miR-20a-5p*	0.943
APBB2	*hsa-miR-20a-5p*	0.993	*NCOA1*	*hsa-miR-23a-3p*	0.943
BIRC6	*hsa-miR-545-5p*	0.993	*PLAG1*	*hsa-miR-29b-3p*	0.943
CCNE2	*hsa-miR-577*	0.993	*TRPS1*	*hsa-miR-30c-5p*	0.943
CCT4	*hsa-miR-335-3p*	0.993	*CACNA2D1*	*hsa-miR-7-1-3p*	0.942
E2F5	*hsa-let-7d-5p*	0.993	*CARD11*	*hsa-miR-155-5p*	0.942
E2F5	***hsa-miR-1-3p***	**0.993**	*GLCCI1*	*hsa-miR-33b-5p*	0.942
EML4	*hsa-miR-125b-2-3p*	0.993	*GNAI1*	*hsa-miR-32-3p*	0.942
GLCCI1	*hsa-miR-200a-3p*	0.993	*RAB10*	*hsa-miR-522-3p*	0.942
HOXA9	*hsa-let-7f-2-3p*	0.993	*RDH14*	*hsa-miR-545-5p*	0.942

MYT1L	*hsa-miR-424-5p*	0.993	*ROCK2*	*hsa-miR-335-3p*	0.942
OTUD6B	*hsa-miR-182-5p*	0.993	*TMEM65*	*hsa-miR-590-3p*	0.942
RAB2A	*hsa-miR-186-5p*	0.993	*TRIB1*	*hsa-miR-616-5p*	0.942
ROCK2	*hsa-miR-106b-5p*	0.993	*BIRC6*	*hsa-miR-30c-5p*	0.941
SAMD12	*hsa-miR-381-3p*	0.993	*ETV1*	*hsa-miR-582-5p*	0.941
SERTAD2	***hsa-miR-548k***	**0.993**	*NDUFA4*	*hsa-miR-205-5p*	0.941
SPAST	*hsa-miR-132-3p*	0.993	*RAB10*	*hsa-miR-15b-5p*	0.941
SYBU	*hsa-miR-301a-3p*	0.993	*RNF139*	*hsa-miR-136-5p*	0.941
SYBU	***hsa-miR-301b-3p***	**0.993**	*SDC1*	*hsa-miR-10b-5p*	0.941
TIA1	*hsa-miR-19a-3p*	0.993	*TTYH3*	*hsa-miR-96-5p*	0.941
TMEM106B	*hsa-miR-32-3p*	0.993	*AZIN1*	*hsa-miR-212-3p*	0.94
TMEM200C	*hsa-miR-106b-5p*	0.993	*CRIM1*	*hsa-miR-101-5p*	0.94
TMEM200C	*hsa-miR-20a-5p*	0.993	*KCNK3*	*hsa-miR-23a-3p*	0.94
TNRC18	*hsa-miR-27b-3p*	0.993	*MTHFD2*	*hsa-miR-450b-5p*	0.94
TRIB1	*hsa-miR-130a-5p*	0.993	*RAB10*	*hsa-miR-195-5p*	0.94
UBE2K	*hsa-miR-548l*	0.993	*RB1CC1*	*hsa-miR-375*	0.94

ZNF704	*hsa-miR-106a-5p*	0.993	*TMEM106B*	*hsa-miR-320a*	0.94
CRIM1	*hsa-miR-520a-3p*	0.992	*TMEM106B*	*hsa-miR-320b*	0.94
DOCK6	*hsa-miR-148b-3p*	0.992	***TRPS1***	***hsa-miR-30b-5p***	**0.94**
FBXO32	*hsa-miR-23b-3p*	0.992	*ZFP36L2*	*hsa-miR-4496*	0.94
GLCCI1	*hsa-miR-33a-5p*	0.992	*AVL9*	*hsa-miR-424-5p*	0.939
HNRNPA2B1	*hsa-miR-326*	0.992	*DNAJC27*	*hsa-miR-27b-3p*	0.939
KLF10	***hsa-miR-30d-5p***	**0.992**	*EPAS1*	*hsa-miR-30e-3p*	0.939
KLF10	*hsa-miR-30e-5p*	0.992	*PELI1*	*hsa-miR-122-5p*	0.939
LCLAT1	***hsa-miR-124-3p***	**0.992**	*PLAG1*	*hsa-miR-29c-3p*	0.939
PI15	*hsa-miR-29b-3p*	0.992	*FAM20C*	*hsa-miR-363-3p*	0.938
RTKN	*hsa-miR-145-5p*	0.992	*FEZ2*	*hsa-miR-200c-3p*	0.938
SOS1	***hsa-miR-148a-3p***	**0.992**	*HNRNPA2B1*	*hsa-miR-103a-2-5p*	0.938
SOX11	*hsa-miR-141-3p*	0.992	*KCNK3*	*hsa-miR-23b-3p*	0.938
ST3GAL5	*hsa-miR-19a-3p*	0.992	*PLAG1*	*hsa-miR-29a-3p*	0.938
ST3GAL5	*hsa-miR-19b-3p*	0.992	*PURB*	*hsa-miR-3607-3p*	0.938
TNRC18	*hsa-miR-27a-3p*	0.992	*ROCK2*	*hsa-miR-497-5p*	0.938

UBE2W	*hsa-miR-363-3p*	0.992	*SOS1*	*hsa-miR-548ak*	0.938
UBR5	*hsa-miR-361-5p*	0.992	*SOS1*	*hsa-miR-548w*	0.938
C2orf42	*hsa-miR-424-5p*	0.991	*TMEM106B*	*hsa-miR-320d*	0.938
C2orf68	*hsa-miR-506-3p*	0.991	*TRPS1*	*hsa-miR-20a-5p*	0.938
CEBPZ	***hsa-miR-1-3p***	**0.991**	*AHR*	*hsa-miR-302a-3p*	0.937
CRIM1	*hsa-miR-520c-3p*	0.991	*HERPUD2*	*hsa-miR-340-5p*	0.937
DDX1	*hsa-miR-499a-5p*	0.991	*MIOS*	*hsa-miR-103a-3p*	0.937
FAM98A	*hsa-miR-660-3p*	0.991	*PURB*	*hsa-miR-548am-5p*	0.937
KLF10	*hsa-miR-30c-5p*	0.991	*PURB*	*hsa-miR-548c-5p*	0.937
MAP4K3	*hsa-let-7d-5p*	0.991	*PURB*	*hsa-miR-548o-5p*	0.937
POMC	*hsa-miR-488-3p*	0.991	*SDC2*	*hsa-miR-7-1-3p*	0.937
PPP3R1	*hsa-miR-182-5p*	0.991	*TMEM106B*	*hsa-miR-320c*	0.937
UBE2W	*hsa-miR-25-3p*	0.991	*DPY19L4*	*hsa-miR-128-3p*	0.936
UBR5	*hsa-miR-106a-5p*	0.991	***FOXK1***	***hsa-miR-185-3p***	**0.936**
ZFPM2	*hsa-miR-429*	0.991	*HNRNPA2B1*	*hsa-miR-521*	0.936
AZIN1	*hsa-miR-3065-5p*	0.99	*LAPTM4A*	*hsa-miR-320e*	0.936

CCDC126	*hsa-miR-1277-5p*	0.99	*RNF19A*	*hsa-miR-200c-3p*	0.936
CDK13	*hsa-miR-320a*	0.99	*SWSAP1*	*hsa-miR-125a-5p*	0.936
FAM110C	*hsa-miR-367-3p*	0.99	***TTYH3***	***hsa-miR-1914-3p***	**0.936**
FAM136A	*hsa-miR-29a-3p*	0.99	*FAM98A*	*hsa-miR-3157-5p*	0.935
HNRNPA2B1	*hsa-miR-4738-3p*	0.99	*ITSN2*	*hsa-miR-200c-3p*	0.935
HOXA9	*hsa-miR-1277-5p*	0.99	*PXDN*	*hsa-miR-488-3p*	0.935
KCNK3	*hsa-miR-130a-5p*	0.99	*RAB10*	*hsa-miR-15a-5p*	0.935
MYBL1	*hsa-miR-130b-3p*	0.99	*RMND5A*	*hsa-miR-374a-5p*	0.935
PLAG1	*hsa-miR-497-5p*	0.99	*RRM2B*	*hsa-miR-548h-3p*	0.935
RNF139	*hsa-miR-202-3p*	0.99	*RRM2B*	*hsa-miR-548z*	0.935
SOX11	*hsa-miR-200a-3p*	0.99	***SWSAP1***	***hsa-miR-125b-5p***	**0.935**
TAF4	*hsa-miR-548f-3p*	0.99	*TWISTNB*	*hsa-miR-590-3p*	0.935
TIA1	*hsa-miR-338-3p*	0.99	***UBE2K***	***hsa-miR-548n***	**0.935**
UTP23	*hsa-miR-1277-5p*	0.99	*ZNF704*	*hsa-miR-129-5p*	0.935
ZBTB44	*hsa-miR-513b-5p*	0.99	*ATAD2B*	*hsa-miR-374a-5p*	0.934
ZNF208	*hsa-miR-16-1-3p*	0.99	*DNAJC27*	*hsa-miR-20a-5p*	0.934

AHR	*hsa-miR-340-5p*	0.989	*EGFR*	*hsa-miR-579-3p*	0.934
ARHGAP28	***hsa-miR-196b-5p***	**0.989**	*PURB*	*hsa-miR-548i*	0.934
ATL2	*hsa-miR-16-5p*	0.989	*AHR*	*hsa-miR-302b-3p*	0.933
GLCCI1	*hsa-miR-93-3p*	0.989	*EPAS1*	*hsa-miR-142-5p*	0.933
HOXA5	*hsa-miR-128-3p*	0.989	*EXT1*	*hsa-miR-665*	0.933
MACC1	*hsa-miR-141-3p*	0.989	*FAM126A*	*hsa-miR-128-3p*	0.933
MYBL1	*hsa-miR-301a-3p*	0.989	*LAPTM4A*	*hsa-miR-107*	0.933
PDE7A	*hsa-miR-212-3p*	0.989	*MAF1*	*hsa-miR-148b-3p*	0.933
PI15	*hsa-miR-29c-3p*	0.989	*MYBL1*	*hsa-miR-7-1-3p*	0.933
PLAG1	*hsa-miR-4726-3p*	0.989	*SERTAD2*	*hsa-miR-93-5p*	0.933
PPP3R1	*hsa-miR-96-5p*	0.989	***UBE2W***	***hsa-miR-1269a***	**0.933**
RNF19A	*hsa-miR-140-5p*	0.989	*ZFP36L2*	*hsa-miR-335-3p*	0.933
SOS1	*hsa-miR-128-3p*	0.989	***ZNF91***	***hsa-miR-296-3p***	**0.933**
SOX11	*hsa-miR-497-3p*	0.989	*AZIN1*	*hsa-miR-323a-3p*	0.932
TET3	*hsa-miR-3689a-5p*	0.989	*CCND1*	*hsa-miR-106b-5p*	0.932
TET3	*hsa-miR-3689b-5p*	0.989	*EIF2AK2*	*hsa-miR-590-3p*	0.932

TET3	*hsa-miR-3689e*	0.989	*FAM126A*	*hsa-miR-30c-2-3p*	0.932
TMSB10	*hsa-miR-128-3p*	0.989	*FOXN2*	*hsa-miR-367-3p*	0.932
YWHAZ	***hsa-miR-1-3p***	**0.989**	*PELI1*	*hsa-miR-29b-2-5p*	0.932
C8orf76	*hsa-miR-101-3p*	0.988	*RAB10*	*hsa-miR-5582-3p*	0.932
FAM84B	*hsa-miR-641*	0.988	*RNF19A*	*hsa-miR-200b-3p*	0.932
GLCCI1	*hsa-miR-495-3p*	0.988	*SOS1*	*hsa-miR-548y*	0.932
HNRNPA2B1	***hsa-miR-548n***	**0.988**	*STRN*	*hsa-miR-513a-3p*	0.932
INHBA	*hsa-miR-153-3p*	0.988	*ZNF490*	*hsa-miR-766-3p*	0.932
PLEKHF2	*hsa-miR-1305*	0.988	*ZNF716*	*hsa-miR-130a-5p*	0.932
PPP3R1	*hsa-miR-372-3p*	0.988	*ADCY1*	*hsa-miR-149-5p*	0.931
SOX11	*hsa-miR-32-5p*	0.988	*DNAJC27*	*hsa-miR-106a-5p*	0.931
ZFP36L2	*hsa-miR-582-5p*	0.988	*FOXN2*	*hsa-miR-548ar-3p*	0.931
ZNF704	*hsa-miR-125a-5p*	0.988	*LAPTM4A*	*hsa-miR-103a-3p*	0.931
ZNF704	***hsa-miR-125b-5p***	**0.988**	*PLAG1*	*hsa-miR-103a-3p*	0.931
ATL2	*hsa-miR-218-5p*	0.987	*PPM1G*	*hsa-miR-212-3p*	0.931
CRISPLD1	*hsa-miR-29c-3p*	0.987	*PURB*	*hsa-miR-107*	0.931

DPY19L1	*hsa-miR-30c-5p*	0.987	*RBM12B*	*hsa-miR-499a-5p*	0.931
FOXN2	*hsa-miR-32-5p*	0.987	*SEMA3A*	*hsa-miR-15b-5p*	0.931
GLCCI1	*hsa-miR-101-3p*	0.987	***TAF4***	***hsa-miR-548d-5p***	**0.931**
INHBA	*hsa-miR-26a-5p*	0.987	*YIPF4*	*hsa-miR-424-5p*	0.931
MYBL1	*hsa-miR-15a-5p*	0.987	*CACNA2D1*	*hsa-miR-26a-1-3p*	0.93
NRBP1	*hsa-miR-497-5p*	0.987	*CCDC126*	*hsa-miR-944*	0.93
PDE7A	*hsa-miR-132-3p*	0.987	*DPY19L4*	*hsa-miR-27b-3p*	0.93
PPP1CB	*hsa-miR-7-1-3p*	0.987	*EML4*	*hsa-miR-132-3p*	0.93
PPP1CB	*hsa-miR-340-5p*	0.987	*POLR1A*	*hsa-miR-15b-5p*	0.93
PRKD3	*hsa-miR-130b-3p*	0.987	*PURB*	*hsa-miR-548y*	0.93
REEP1	*hsa-miR-30e-5p*	0.987	*SAMD12*	*hsa-miR-1271-3p*	0.93
RMND5A	*hsa-miR-21-5p*	0.987	*TMEM200C*	*hsa-miR-106a-5p*	0.93
ROCK2	*hsa-miR-302a-3p*	0.987	*BIRC6*	*hsa-miR-653-5p*	0.929
SERTAD2	*hsa-miR-548am-5p*	0.987	*GNAI1*	*hsa-miR-33a-3p*	0.929
SERTAD2	*hsa-miR-548c-5p*	0.987	*IMPAD1*	*hsa-miR-500a-5p*	0.929
SERTAD2	***hsa-miR-548d-5p***	**0.987**	*PURB*	*hsa-miR-584-5p*	0.929

SERTAD2	*hsa-miR-548o-5p*	0.987	*SOS1*	*hsa-miR-548j-5p*	0.929
SERTAD2	***hsa-miR-124-3p***	**0.987**	*VCPIP1*	*hsa-miR-577*	0.929
UBR5	*hsa-miR-27a-3p*	0.987	*AVL9*	*hsa-miR-16-5p*	0.928
UBXN2A	*hsa-miR-27b-3p*	0.987	*BCL11A*	*hsa-miR-182-5p*	0.928
WWP1	*hsa-miR-182-5p*	0.987	*CCDC126*	*hsa-miR-374a-5p*	0.928
ZNF704	*hsa-miR-93-5p*	0.987	*EFR3A*	*hsa-let-7f-2-3p*	0.928
ARHGAP28	*hsa-let-7d-5p*	0.986	*FOXN2*	*hsa-miR-92a-3p*	0.928
ARHGAP28	*hsa-miR-196a-5p*	0.986	*MAP4K3*	*hsa-miR-338-5p*	0.928
ARMC1	*hsa-miR-25-3p*	0.986	*MBOAT2*	*hsa-miR-125a-5p*	0.928
CYP26B1	*hsa-miR-141-3p*	0.986	*PLAG1*	*hsa-miR-107*	0.928
DPY19L1	***hsa-miR-30b-5p***	***0.986***	*TOX*	*hsa-miR-643*	0.928
DPY19L1	*hsa-miR-193a-3p*	0.986	*WIPI2*	*hsa-miR-424-5p*	0.928
FAM110C	*hsa-miR-195-5p*	0.986	*ARL4A*	*hsa-miR-106b-5p*	0.927
HERPUD2	*hsa-miR-92a-3p*	0.986	*EMC2*	*hsa-miR-3689a-5p*	0.927
HOXA9	*hsa-miR-26a-5p*	0.986	*EMC2*	*hsa-miR-3689b-5p*	0.927
MYBL1	*hsa-miR-15b-5p*	0.986	*EMC2*	*hsa-miR-3689e*	0.927

NRBP1	*hsa-miR-200b-3p*	0.986	*HNRNPA2B1*	*hsa-miR-618*	0.927
NRBP1	*hsa-miR-429*	0.986	*KBTBD2*	*hsa-miR-497-5p*	0.927
PI15	*hsa-miR-29a-3p*	0.986	*LAPTM4A*	*hsa-miR-494-3p*	0.927
PRKD3	*hsa-miR-130a-3p*	0.986	***PURB***	***hsa-miR-548d-5p***	**0.927**
UBXN2A	*hsa-miR-27a-3p*	0.986	*RAD21*	*hsa-miR-338-5p*	0.927
WWP1	*hsa-miR-142-5p*	0.986	*SOS1*	*hsa-miR-548am-5p*	0.927
ZNRF2	*hsa-miR-107*	0.986	*SOS1*	*hsa-miR-548c-5p*	0.927
FAM20C	*hsa-miR-367-3p*	0.985	*SOS1*	*hsa-miR-548o-5p*	0.927
GLCCI1	*hsa-miR-27b-5p*	0.985	*SOS1*	*hsa-miR-548au-5p*	0.927
HOXA9	*hsa-miR-26b-5p*	0.985	*TMEM65*	*hsa-miR-605-5p*	0.927
ITSN2	*hsa-miR-19a-3p*	0.985	*TWIST1*	*hsa-miR-361-5p*	0.927
NOTCH1	*hsa-miR-34a-5p*	0.985	*UBR5*	*hsa-miR-140-5p*	0.927
NRBP1	*hsa-miR-19a-3p*	0.985	*CA2*	*hsa-miR-338-5p*	0.926
NRBP1	*hsa-miR-19b-3p*	0.985	*CAD*	*hsa-miR-18b-5p*	0.926
NRBP1	*hsa-miR-200c-3p*	0.985	***EPAS1***	***hsa-miR-148a-3p***	**0.926**
PPP3R1	*hsa-miR-30c-5p*	0.985	*PELI1*	*hsa-miR-378a-5p*	0.926

PPP3R1	***hsa-miR-30b-5p***	**0.985**	*PREPL*	*hsa-miR-141-3p*	0.926
REEP1	*hsa-miR-30c-5p*	0.985	*RBM12B*	*hsa-miR-381-3p*	0.926
SDC2	*hsa-miR-590-3p*	0.985	*SOS1*	*hsa-miR-548i*	0.926
UBE2W	*hsa-miR-367-3p*	0.985	***UTP23***	***hsa-miR-1270***	**0.926**
ZFHX4	*hsa-miR-26a-5p*	0.985	*ZNRF2*	*hsa-miR-153-3p*	0.926
ATAD2B	*hsa-miR-421*	0.984	*CEP104*	*hsa-miR-1277-5p*	0.925
CACNA2D1	*hsa-miR-182-5p*	0.984	*FOXN2*	*hsa-miR-92b-3p*	0.925
EIF2AK2	*hsa-miR-200a-3p*	0.984	*GFPT1*	*hsa-miR-19a-3p*	0.925
ELAVL1	*hsa-miR-224-3p*	0.984	*GFPT1*	*hsa-miR-19b-3p*	0.925
ETV1	*hsa-miR-106a-5p*	0.984	*HNRNPA2B1*	*hsa-miR-548o-3p*	0.925
FAM110C	*hsa-miR-16-5p*	0.984	*KCNK3*	*hsa-miR-23c*	0.925
FOXN2	*hsa-miR-186-5p*	0.984	***LYN***	***hsa-miR-185-5p***	**0.925**
FOXN2	*hsa-miR-34a-5p*	0.984	*MPP6*	*hsa-miR-27a-3p*	0.925
GLCCI1	*hsa-miR-502-3p*	0.984	*RAC1*	*hsa-miR-548z*	0.925
HERPUD2	*hsa-miR-92b-3p*	0.984	*RMND5A*	*hsa-miR-182-5p*	0.925
LAPTM4A	*hsa-miR-3613-3p*	0.984	*ROCK2*	*hsa-miR-33a-5p*	0.925

MYBL1	*hsa-miR-340-5p*	0.984	***SOS1***	***hsa-miR-548d-5p***	**0.925**
REEP1	***hsa-miR-30b-5p***	**0.984**	*TWISTNB*	*hsa-miR-181d-5p*	0.925
REEP1	***hsa-miR-30d-5p***	**0.984**	*ARL4A*	*hsa-miR-106a-5p*	0.924
RMND5A	***hsa-miR-548d-3p***	**0.984**	*CACNA2D1*	*hsa-miR-497-5p*	0.924
RPIA	***hsa-miR-124-3p***	**0.984**	*CCNE2*	*hsa-miR-548b-3p*	0.924
SERTAD2	*hsa-miR-625-5p*	0.984	*EIF2AK2*	*hsa-miR-143-3p*	0.924
ZFP36L2	*hsa-miR-513b-5p*	0.984	*GNAI1*	*hsa-miR-320a*	0.924
ZNF844	*hsa-miR-181b-5p*	0.984	*HNRNPA2B1*	*hsa-miR-502-5p*	0.924
AHR	*hsa-miR-96-5p*	0.983	***INHBA***	***hsa-miR-548d-3p***	**0.924**
BIRC6	*hsa-miR-181b-5p*	0.983	*RBAK*	*hsa-miR-942-5p*	0.924
BIRC6	*hsa-miR-181c-5p*	0.983	*RNF19A*	*hsa-miR-429*	0.924
DNAJC27	*hsa-miR-92b-3p*	0.983	*SEMA3A*	*hsa-miR-16-5p*	0.924
FAM126A	***hsa-miR-548k***	**0.983**	*SERTAD2*	*hsa-miR-17-5p*	0.924
FAM20C	*hsa-miR-25-3p*	0.983	*SOCS5*	*hsa-miR-367-3p*	0.924
FOXN2	*hsa-miR-183-5p*	0.983	*YIPF4*	*hsa-miR-26b-5p*	0.924
KANK2	*hsa-miR-429*	0.983	*ZFP36L2*	*hsa-miR-142-3p*	0.924

MAFK	*hsa-miR-16-5p*	0.983	*ARL4A*	*hsa-miR-20a-5p*	0.923
MAFK	*hsa-miR-195-5p*	0.983	*DPY19L4*	*hsa-miR-27a-3p*	0.923
PELI1	*hsa-miR-548l*	0.983	*GFPT1*	*hsa-miR-513b-5p*	0.923
PURB	*hsa-miR-450b-5p*	0.983	*KBTBD2*	*hsa-miR-424-5p*	0.923
RB1CC1	*hsa-miR-133b*	0.983	*MYCN*	*hsa-miR-200c-3p*	0.923
BIRC6	*hsa-miR-181d-5p*	0.982	*PURB*	*hsa-miR-582-5p*	0.923
CREB5	*hsa-miR-212-3p*	0.982	*PXDN*	*hsa-miR-335-3p*	0.923
CRIM1	***hsa-miR-873-5p***	**0.982**	*UBR5*	*hsa-miR-590-3p*	0.923
EVI5L	*hsa-miR-34a-5p*	0.982	*ZBTB10*	*hsa-miR-5010-3p*	0.923
EVI5L	*hsa-miR-19a-3p*	0.982	*MMP16*	*hsa-miR-507*	0.922
EVI5L	*hsa-miR-19b-3p*	0.982	*MYBL1*	*hsa-miR-103a-3p*	0.922
FAM84B	*hsa-miR-27b-3p*	0.982	*PDE7A*	*hsa-miR-570-3p*	0.922
INHBA	*hsa-miR-26b-5p*	0.982	*PREPL*	*hsa-miR-200a-3p*	0.922
LDLR	*hsa-miR-150-5p*	0.982	*RMND5A*	*hsa-miR-590-3p*	0.922
MAT2A	*hsa-miR-26a-5p*	0.982	***AZIN1***	***hsa-miR-30b-5p***	**0.921**
MAT2A	*hsa-miR-26b-5p*	0.982	*GREB1*	*hsa-miR-26a-5p*	0.921

MYBL1	*hsa-miR-16-5p*	0.982	***MAP4K3***	***hsa-miR-548n***	**0.921**
PPP3R1	*hsa-miR-30e-5p*	0.982	*MYBL1*	*hsa-miR-107*	0.921
PRKCE	*hsa-miR-141-3p*	0.982	*NCOA2*	*hsa-miR-374b-5p*	0.921
PRKCE	*hsa-miR-182-5p*	0.982	*RB1CC1*	*hsa-miR-522-3p*	0.921
SERTAD2	*hsa-miR-1275*	0.982	*SOS1*	*hsa-miR-106b-5p*	0.921
UBE2V2	*hsa-miR-30e-5p*	0.982	*ZFP36L2*	*hsa-miR-138-1-3p*	0.921
ZBTB10	*hsa-miR-1305*	0.982	*NCOA2*	*hsa-miR-200a-3p*	0.92
ZFHX4	*hsa-miR-26b-5p*	0.982	*PAG1*	*hsa-miR-497-5p*	0.92
ZNF704	*hsa-miR-20b-5p*	0.982	*POLR1A*	*hsa-miR-424-5p*	0.92
BHLHE22	*hsa-miR-24-3p*	0.981	*STAMBP*	*hsa-miR-130b-5p*	0.92
CRIM1	*hsa-miR-106b-5p*	0.981	*STARD3NL*	*hsa-miR-548e-3p*	0.92
CRISPLD1	*hsa-miR-29a-3p*	0.981	*TAF2*	*hsa-miR-26a-5p*	0.92
CRISPLD1	*hsa-miR-29b-3p*	0.981	*ATP6V1C1*	*hsa-miR-340-5p*	0.919
EFR3A	*hsa-miR-128-3p*	0.981	***AZIN1***	***hsa-miR-30d-5p***	**0.919**
HEATR5B	*hsa-miR-24-3p*	0.981	*AZIN1*	*hsa-miR-30a-5p*	0.919
KANK2	*hsa-miR-200b-3p*	0.981	*BHLHE22*	*hsa-miR-27b-3p*	0.919

KLHL5	*hsa-miR-181b-5p*	0.981	*CRIM1*	*hsa-miR-548ab*	0.919
KLHL5	*hsa-miR-181d-5p*	0.981	*CRIM1*	*hsa-miR-548b-5p*	0.919
MAFK	*hsa-miR-15a-5p*	0.981	*CYP26B1*	*hsa-miR-15a-5p*	0.919
MAPRE3	*hsa-miR-106b-5p*	0.981	*EFR3A*	*hsa-miR-25-3p*	0.919
OSGIN2	*hsa-miR-92a-3p*	0.981	*EMC2*	*hsa-miR-3689f*	0.919
RHOB	*hsa-miR-548f-3p*	0.981	*MAT2A*	*hsa-miR-29b-2-5p*	0.919
ROCK2	*hsa-miR-20b-5p*	0.981	*MAT2A*	*hsa-miR-340-5p*	0.919
STK17A	*hsa-miR-1290*	0.981	*MBOAT2*	*hsa-miR-181a-5p*	0.919
ZNF704	*hsa-miR-106b-5p*	0.981	*NUDCD1*	*hsa-miR-181a-2-3p*	0.919
ZNF704	*hsa-miR-17-5p*	0.981	*PRR15*	*hsa-miR-20a-5p*	0.919
B3GNT2	*hsa-miR-141-3p*	0.98	*UBE2K*	*hsa-miR-548a-5p*	0.919
BIRC6	*hsa-miR-181a-5p*	0.98	*UBXN2A*	*hsa-miR-20a-5p*	0.919
CHN2	*hsa-miR-200b-3p*	0.98	*ZBTB10*	*hsa-miR-361-5p*	0.919
ELAVL1	*hsa-miR-1305*	0.98	*ZBTB10*	*hsa-miR-142-5p*	0.919
KANK2	*hsa-miR-200c-3p*	0.98	*ZFHX4*	*hsa-miR-130b-5p*	0.919
NOTCH1	*hsa-miR-340-5p*	0.98	*AZIN1*	*hsa-miR-30c-5p*	0.918

PDE7A	*hsa-miR-150-5p*	0.98	*COX7A2L*	*hsa-miR-20a-5p*	0.918
PURB	*hsa-miR-34a-5p*	0.98	*CRIM1*	*hsa-miR-548j-5p*	0.918
RAC1	*hsa-miR-182-5p*	0.98	*FLRT2*	*hsa-miR-877-3p*	0.918
ROCK2	*hsa-miR-93-5p*	0.98	*PLAG1*	*hsa-miR-302c-3p*	0.918
TAF4	*hsa-miR-548e-3p*	0.98	*POLR1A*	*hsa-miR-15a-5p*	0.918
TNFRSF11B	*hsa-miR-765*	0.98	*RB1CC1*	*hsa-miR-664a-3p*	0.918
WIPI2	*hsa-miR-497-5p*	0.98	*SEMA3A*	*hsa-miR-15a-5p*	0.918
APBB2	*hsa-miR-106a-5p*	0.979	*SERTAD2*	*hsa-miR-340-5p*	0.918
ARMC1	*hsa-miR-107*	0.979	*TRPS1*	*hsa-miR-106b-5p*	0.918
CCT6A	*hsa-miR-92a-3p*	0.979	*ZNF100*	*hsa-miR-580-3p*	0.918
DPYSL5	*hsa-miR-19a-3p*	0.979	*EFR3A*	*hsa-miR-590-3p*	0.917
ETV1	*hsa-miR-17-5p*	0.979	*FAM84B*	*hsa-miR-320a*	0.917
FAM98A	***hsa-miR-1306-5p***	**0.979**	*KBTBD2*	*hsa-miR-7-5p*	0.917
FBXO11	*hsa-miR-155-5p*	0.979	*NCOA2*	*hsa-miR-141-3p*	0.917
GLI3	*hsa-miR-629-3p*	0.979	*NECAB1*	*hsa-miR-101-3p*	0.917
PPP3R1	***hsa-miR-30d-5p***	**0.979**	*PURB*	*hsa-miR-1304-3p*	0.917

PRKCE	*hsa-miR-143-3p*	0.979	*RB1CC1*	*hsa-miR-135b-5p*	0.917
RB1CC1	*hsa-miR-340-5p*	0.979	*SKAP2*	*hsa-miR-548f-3p*	0.917
UBE2K	***hsa-miR-548k***	**0.979**	*SQLE*	*hsa-miR-664a-3p*	0.917
ZFHX4	*hsa-miR-17-3p*	0.979	*UBE2W*	*hsa-miR-126-5p*	0.917
ZFP36L2	*hsa-miR-506-3p*	0.979	*ZBTB10*	*hsa-miR-107*	0.917
ZNF704	*hsa-miR-20a-5p*	0.979	*BHLHE22*	*hsa-miR-27a-3p*	0.916
ARMC1	*hsa-miR-103a-3p*	0.978	*GLCCI1*	*hsa-miR-590-5p*	0.916
CACNA2D1	*hsa-miR-1305*	0.978	***LDLR***	***hsa-miR-185-5p***	**0.916**
CHN2	*hsa-miR-200c-3p*	0.978	*SERTAD2*	*hsa-miR-590-3p*	0.916
FMN2	*hsa-miR-25-3p*	0.978	*UBE2K*	*hsa-miR-548h-5p*	0.916
FOXN2	*hsa-miR-182-5p*	0.978	*ZBTB10*	*hsa-miR-103a-3p*	0.916
HAS2	*hsa-miR-130a-5p*	0.978	*ZFHX4*	*hsa-miR-499a-3p*	0.916
LBH	*hsa-miR-27a-3p*	0.978	*AZIN1*	*hsa-miR-183-5p*	0.915
LBH	*hsa-miR-27b-3p*	0.978	*KBTBD2*	*hsa-miR-143-5p*	0.915
MAPRE3	*hsa-miR-20a-5p*	0.978	*LAPTM4A*	*hsa-miR-548an*	0.915
NRBP1	*hsa-miR-424-5p*	0.978	*MRPL19*	*hsa-miR-218-5p*	0.915

PDS5A	*hsa-miR-10a-3p*	0.978	*NCOA2*	*hsa-miR-23a-3p*	0.915
RMND5A	*hsa-miR-548ar-3p*	0.978	*SOS1*	*hsa-miR-183-3p*	0.915
RNF19A	*hsa-miR-155-5p*	0.978	*CYP26B1*	*hsa-miR-15b-5p*	0.914
UBE2V2	***hsa-miR-30d-5p***	**0.978**	*MBOAT2*	*hsa-miR-545-3p*	0.914
YWHAZ	*hsa-miR-497-3p*	0.978	*MYCN*	*hsa-miR-200b-3p*	0.914
ZNF440	*hsa-miR-181d-5p*	0.978	*NCOA2*	*hsa-miR-23b-3p*	0.914
ZNF704	*hsa-miR-130b-5p*	0.978	*RAB10*	*hsa-miR-140-5p*	0.914
CRIM1	*hsa-miR-20a-5p*	0.977	***SEMA3D***	***hsa-miR-548a-3p***	**0.914**
DPY19L4	*hsa-miR-23a-3p*	0.977	*SOS1*	*hsa-miR-20a-5p*	0.914
DPY19L4	*hsa-miR-23b-3p*	0.977	*STAMBP*	*hsa-miR-101-3p*	0.914
EPDR1	*hsa-miR-577*	0.977	*HOXA5*	*hsa-miR-96-5p*	0.913
ETV1	*hsa-miR-93-5p*	0.977	*PCLO*	*hsa-miR-34a-5p*	0.913
GFPT1	*hsa-miR-141-5p*	0.977	*PURB*	*hsa-miR-103a-3p*	0.913
KLF11	*hsa-miR-10a-5p*	0.977	*SOX11*	*hsa-miR-101-3p*	0.913
MAFK	*hsa-miR-497-5p*	0.977	*ZNF704*	*hsa-miR-1202*	0.913
MTHFD2	*hsa-miR-9-5p*	0.977	*ZNRF2*	*hsa-miR-424-5p*	0.913

PPP1CB	***hsa-miR-148a-3p***	**0.977**	*ATAD2B*	*hsa-miR-452-3p*	0.912
PRKD3	***hsa-miR-301b-3p***	**0.977**	*FAM92A1*	*hsa-miR-26a-5p*	0.912
RB1CC1	*hsa-miR-10b-5p*	0.977	*FOXN2*	*hsa-miR-222-3p*	0.912
RB1CC1	*hsa-miR-10a-5p*	0.977	*LOXL3*	*hsa-miR-34a-5p*	0.912
TET3	*hsa-miR-3689f*	0.977	*MTHFD2*	*hsa-miR-92a-3p*	0.912
UBE2W	*hsa-miR-20a-3p*	0.977	*PLAG1*	*hsa-miR-30c-5p*	0.912
ZNF440	*hsa-miR-181b-5p*	0.977	*PLEKHF2*	*hsa-miR-454-3p*	0.912
DPY19L1	*hsa-miR-155-5p*	0.976	*RMND5A*	*hsa-miR-27a-3p*	0.912
ETV1	*hsa-miR-20b-5p*	0.976	*RMND5A*	*hsa-miR-625-3p*	0.912
LDLR	***hsa-miR-301b-3p***	**0.976**	*SOCS5*	*hsa-miR-32-5p*	0.912
OSGIN2	*hsa-miR-25-3p*	0.976	*ZBTB44*	*hsa-miR-27b-3p*	0.912
PLAG1	*hsa-miR-590-5p*	0.976	*C2orf68*	*hsa-miR-29a-3p*	0.911
UBE2V2	*hsa-miR-30a-5p*	0.976	*CA2*	*hsa-miR-23b-3p*	0.911
YIPF4	*hsa-miR-590-3p*	0.976	*CA2*	*hsa-miR-23a-3p*	0.911
CRIM1	*hsa-miR-330-5p*	0.975	*CCND1*	*hsa-miR-548f-3p*	0.911
CRIM1	*hsa-miR-526b-3p*	0.975	*CDC42EP3*	*hsa-miR-499a-3p*	0.911

MAF1	***hsa-miR-148a-3p***	**0.975**	***EFR3A***	***hsa-miR-548d-3p***	**0.911**
NCOA1	*hsa-miR-493-5p*	0.975	*ETV1*	*hsa-miR-660-5p*	0.911
PURB	*hsa-miR-106a-5p*	0.975	*HNRNPA2B1*	*hsa-miR-20a-3p*	0.911
SERTAD2	*hsa-miR-106b-5p*	0.975	*OCLN*	*hsa-miR-106a-5p*	0.911
SOS1	*hsa-miR-548l*	0.975	*PRR15*	*hsa-miR-106b-5p*	0.911
ITGB8	*hsa-miR-542-3p*	0.974	*RHOB*	*hsa-miR-499a-3p*	0.911
LDLR	*hsa-miR-301a-3p*	0.974	***TRIQK***	***hsa-miR-30b-5p***	**0.911**
SERTAD2	*hsa-miR-20a-5p*	0.974	*TRIQK*	*hsa-miR-30c-5p*	0.911
SPRED2	*hsa-miR-218-5p*	0.974	*UBE2K*	*hsa-miR-548j-5p*	0.911
YWHAQ	***hsa-miR-1-3p***	**0.974**	*UBXN2A*	*hsa-miR-106b-5p*	0.911
ZNF704	***hsa-miR-548n***	**0.974**	*YWHAZ*	*hsa-miR-4328*	0.911
AVL9	*hsa-miR-30a-5p*	0.973	*ZNF250*	*hsa-miR-301a-3p*	0.911
EPAS1	*hsa-miR-20a-5p*	0.973	*AZIN1*	*hsa-miR-32-3p*	0.91
HOXA13	*hsa-miR-34a-5p*	0.973	*CYP26B1*	*hsa-miR-16-5p*	0.91
RAD21	*hsa-miR-16-2-3p*	0.973	*NCOA2*	*hsa-miR-629-3p*	0.91
SEMA3D	*hsa-miR-548o-3p*	0.973	*PURB*	*hsa-miR-186-5p*	0.91

SOX11	*hsa-miR-20a-3p*	0.973	*RAB10*	*hsa-miR-378a-3p*	0.91
CCT6A	*hsa-miR-92b-3p*	0.972	*UBE2W*	*hsa-miR-148b-3p*	0.91
DPYSL5	*hsa-miR-19b-3p*	0.972	*YWHAZ*	*hsa-miR-1303*	0.91
ELAVL2	***hsa-miR-30b-5p***	**0.972**	*APBB2*	*hsa-miR-330-3p*	0.909
HNRNPA2B1	*hsa-miR-186-5p*	0.972	*FAM92A1*	*hsa-miR-26b-5p*	0.909
PDGFA	*hsa-miR-186-5p*	0.972	*FOXK1*	*hsa-miR-23a-3p*	0.909
PLAG1	*hsa-miR-503-5p*	0.972	***IQCE***	***hsa-miR-124-3p***	**0.909**
PLAG1	*hsa-miR-199a-3p*	0.972	*PURB*	*hsa-miR-1246*	0.909
PPP3R1	*hsa-miR-340-5p*	0.972	***IMPAD1***	***hsa-miR-548n***	**0.908**
SOCS5	*hsa-miR-9-5p*	0.972	*LDLR*	*hsa-miR-152-3p*	0.908
TMEM65	*hsa-miR-101-3p*	0.972	*LDLR*	*hsa-miR-454-3p*	0.908
YIPF4	*hsa-miR-361-5p*	0.972	*MATN3*	*hsa-miR-19a-3p*	0.908
ANTXR1	*hsa-let-7g-3p*	0.971	*SOCS5*	*hsa-miR-363-3p*	0.908
AVL9	***hsa-miR-30d-5p***	**0.971**	*SRSF7*	*hsa-miR-122-5p*	0.908
AVL9	***hsa-miR-30b-3p***	**0.971**	*TRPS1*	*hsa-miR-374a-5p*	0.908
AVL9	*hsa-miR-3689a-3p*	0.971	*TRPS1*	*hsa-miR-588*	0.908

B3GNT2	*hsa-miR-200a-3p*	0.971	*TRPS1*	*hsa-miR-96-5p*	0.908
EIF2AK2	*hsa-miR-664a-3p*	0.971	*CCDC126*	*hsa-miR-130b-3p*	0.907
MRPL19	*hsa-miR-590-3p*	0.971	*EFEMP1*	*hsa-miR-9-5p*	0.907
PRKD3	*hsa-miR-301a-3p*	0.971	*EFR3A*	*hsa-miR-628-5p*	0.907
RAD21	*hsa-miR-590-3p*	0.971	***FSCN1***	***hsa-miR-185-3p***	**0.907**
RB1CC1	*hsa-miR-141-3p*	0.971	*PCMTD1*	*hsa-miR-182-5p*	0.907
RBAK	*hsa-miR-664a-3p*	0.971	*POLR1A*	*hsa-miR-16-5p*	0.907
SAMD12	***hsa-miR-550a-3-5p***	**0.971**	***POLR1A***	***hsa-miR-589-5p***	**0.907**
SAMD12	***hsa-miR-550a-5p***	**0.971**	*RAB10*	*hsa-miR-450b-5p*	0.907
SERTAD2	*hsa-miR-32-5p*	0.971	*RMND5A*	*hsa-miR-33b-5p*	0.907
TRPS1	*hsa-miR-106a-5p*	0.971	*SLA*	*hsa-miR-155-5p*	0.907
ZNRF2	*hsa-miR-101-3p*	0.971	***SLC5A6***	***hsa-miR-4802-5p***	**0.907**
ARRDC4	*hsa-miR-590-3p*	0.97	***STAU2***	***hsa-miR-148a-5p***	**0.907**
AVL9	*hsa-miR-30e-5p*	0.97	*TPRKB*	*hsa-miR-155-5p*	0.907
CCT6A	*hsa-miR-32-5p*	0.97	*ZBTB10*	*hsa-miR-590-3p*	0.907
EFR3A	*hsa-miR-363-3p*	0.97	*AHR*	*hsa-miR-302d-3p*	0.906

HNRNPA2B1	*hsa-miR-548a-5p*	0.97	*ARL4A*	*hsa-miR-340-5p*	0.906
INHBA	*hsa-miR-452-5p*	0.97	*CRIM1*	*hsa-miR-424-5p*	0.906
MYCN	*hsa-miR-29b-3p*	0.97	*FAM110C*	*hsa-miR-107*	0.906
PPP3R1	***hsa-miR-298***	**0.97**	*MAT2A*	*hsa-miR-122-3p*	0.906
RB1CC1	*hsa-miR-200a-3p*	0.97	*MATN3*	*hsa-miR-19b-3p*	0.906
RMND5A	*hsa-miR-374b-5p*	0.97	*MTDH*	*hsa-miR-129-5p*	0.906
SOS1	*hsa-miR-106a-5p*	0.97	*MYBL1*	*hsa-miR-424-5p*	0.906
UBE2V2	***hsa-miR-30b-5p***	**0.97**	*RMND5A*	*hsa-miR-27b-3p*	0.906
ZNRF2	*hsa-miR-16-5p*	0.97	*SOX11*	*hsa-miR-33a-3p*	0.906
BIRC6	***hsa-miR-196b-5p***	**0.969**	*TRPS1*	*hsa-miR-361-5p*	0.906
CDC42EP3	*hsa-miR-27b-3p*	0.969	*NCOA2*	*hsa-miR-374a-5p*	0.905
EPAS1	*hsa-miR-106b-5p*	0.969	*PKIA*	*hsa-miR-200c-3p*	0.905
H2AFV	*hsa-miR-7-5p*	0.969	*PLAG1*	*hsa-miR-302a-3p*	0.905
HNRNPA2B1	*hsa-miR-548j-5p*	0.969	*TMEM65*	*hsa-miR-758-3p*	0.905
HNRNPA2B1	*hsa-miR-152-3p*	0.969	*AHR*	*hsa-miR-548l*	0.904
LRPPRC	*hsa-miR-335-3p*	0.969	*AZIN1*	*hsa-miR-224-5p*	0.904

PAG1	*hsa-miR-103a-3p*	0.969	*CCDC126*	*hsa-miR-301a-3p*	0.904
RMND5A	*hsa-miR-548y*	0.969	*EIF2AK2*	*hsa-miR-944*	0.904
TMEM106B	*hsa-miR-26a-5p*	0.969	*FAM98A*	*hsa-miR-766-3p*	0.904
YWHAZ	*hsa-miR-1302*	0.969	*H2AFV*	*hsa-miR-378g*	0.904
AHR	*hsa-miR-32-3p*	0.968	*HOXA13*	*hsa-miR-128-3p*	0.904
CACNA2D1	*hsa-miR-15b-5p*	0.968	*MMP16*	*hsa-miR-26b-5p*	0.904
FMN2	*hsa-miR-101-3p*	0.968	***PLAG1***	***hsa-miR-30d-5p***	**0.904**
GLCCI1	*hsa-miR-144-3p*	0.968	*RAB10*	*hsa-miR-374b-5p*	0.904
PREPL	*hsa-miR-1277-5p*	0.968	***RAC1***	***hsa-miR-589-3p***	**0.904**
RBAK	*hsa-miR-103a-2-5p*	0.968	*ROCK2*	*hsa-miR-424-5p*	0.904
UBE2W	*hsa-miR-579-3p*	0.968	*SKAP2*	*hsa-miR-548e-3p*	0.904
ZNF100	*hsa-miR-130a-5p*	0.968	*STRN*	*hsa-miR-5690*	0.904
HNRNPA2B1	***hsa-miR-491-3p***	**0.967**	*TCF7L1*	*hsa-miR-20a-5p*	0.904
HOXA9	*hsa-let-7a-3p*	0.967	*TMEM65*	*hsa-miR-126-5p*	0.904
SNRNP27	*hsa-miR-27a-3p*	0.967	*TTYH3*	*hsa-miR-92a-2-5p*	0.904
SNRNP27	*hsa-miR-27b-3p*	0.967	*CRIM1*	*hsa-miR-106a-5p*	0.903

SPTBN1	*hsa-miR-26a-5p*	0.967	*PLAG1*	*hsa-miR-302b-3p*	0.903
UBE2V2	*hsa-miR-30c-5p*	0.967	*PLAG1*	*hsa-miR-30a-5p*	0.903
ARMC1	*hsa-miR-197-3p*	0.966	*TAF2*	*hsa-miR-26b-5p*	0.903
AZIN1	*hsa-miR-330-3p*	0.966	*TCF7L1*	*hsa-miR-106b-5p*	0.903
CCND1	*hsa-miR-19a-3p*	0.966	*TRIQK*	*hsa-miR-30e-5p*	0.903
EIF2AK3	*hsa-miR-125b-2-3p*	0.966	*TRPS1*	*hsa-miR-302d-3p*	0.903
PAG1	*hsa-miR-107*	0.966	*VCPIP1*	*hsa-miR-130b-3p*	0.903
UBR5	*hsa-miR-548l*	0.966	*YIPF4*	*hsa-miR-16-5p*	0.903
ZFP36L2	*hsa-miR-1277-5p*	0.966	*ZHX2*	*hsa-miR-5680*	0.903
ZNF208	*hsa-miR-770-5p*	0.966	*BHLHE22*	*hsa-miR-26a-5p*	0.902
ZNF91	*hsa-miR-135b-3p*	0.966	*BIRC6*	*hsa-miR-183-3p*	0.902
ELAVL2	*hsa-miR-30c-5p*	0.965	*FAM126A*	*hsa-miR-27a-3p*	0.902
FAM84B	*hsa-miR-27a-3p*	0.965	*FAM126A*	*hsa-miR-27b-3p*	0.902
LDLR	*hsa-miR-130b-3p*	0.965	*FOXK1*	*hsa-miR-23b-3p*	0.902
PI15	*hsa-miR-3065-3p*	0.965	*HAS2*	*hsa-miR-106b-5p*	0.902
PPP3R1	*hsa-miR-342-3p*	0.965	*ILF3*	*hsa-miR-513b-5p*	0.902

SPTBN1	*hsa-miR-26b-5p*	0.965	*NBN*	*hsa-miR-182-5p*	0.902
ZFHX4	*hsa-miR-500a-3p*	0.965	***PLAG1***	***hsa-miR-30b-5p***	**0.902**
AHR	*hsa-let-7b-3p*	0.964	*PPM1G*	*hsa-miR-106b-5p*	0.902
ARL4A	*hsa-miR-93-5p*	0.964	*PPM1G*	*hsa-miR-20a-5p*	0.902
ASXL2	*hsa-miR-92a-3p*	0.964	*RBM12B*	*hsa-miR-7-1-3p*	0.902
ATAD2B	*hsa-miR-27a-3p*	0.964	*TRPS1*	*hsa-miR-302b-3p*	0.902
CCND1	*hsa-miR-511-5p*	0.964	*UBE2W*	*hsa-miR-27b-3p*	0.902
EML4	***hsa-miR-30d-5p***	**0.964**	*COX7A2L*	*hsa-miR-106b-5p*	0.901
FOXK1	*hsa-miR-186-5p*	0.964	*DPY19L4*	*hsa-miR-548d-5p*	0.901
MIOS	*hsa-miR-107*	0.964	*FLRT2*	*hsa-miR-7-5p*	0.901
PURB	*hsa-miR-23c*	0.964	*HAS2*	*hsa-miR-202-3p*	0.901
ZNRF2	*hsa-miR-15b-5p*	0.964	*HOXA9*	*hsa-miR-140-3p*	0.901
ATAD2B	*hsa-miR-27b-3p*	0.963	*SKAP2*	*hsa-miR-205-3p*	0.901
AVL9	***hsa-miR-30b-5p***	**0.963**	*TRPS1*	*hsa-miR-302c-3p*	0.901
AVL9	*hsa-miR-30c-5p*	0.963	*VCPIP1*	*hsa-miR-301a-3p*	0.901
BIRC6	*hsa-miR-1277-5p*	0.963	*AZIN1*	*hsa-miR-548l*	0.9

C2orf68	*hsa-miR-186-5p*	0.963	*CCDC126*	*hsa-miR-130a-3p*	0.9
DNAJC27	*hsa-miR-92a-3p*	0.963	*EPAS1*	*hsa-miR-374a-5p*	0.9
EML4	*hsa-miR-30a-5p*	0.963	***HERPUD2***	***hsa-miR-31-5p***	**0.9**
EML4	*hsa-miR-30e-5p*	0.963	*NCOA1*	*hsa-miR-22-3p*	0.9
FOXN2	*hsa-miR-5582-3p*	0.963	*PDE4A*	*hsa-miR-19a-3p*	0.9
HERPUD2	*hsa-miR-25-3p*	0.963	*PPM1B*	*hsa-miR-499a-3p*	0.9
RHOB	*hsa-miR-19a-3p*	0.963	*PPP1CB*	*hsa-miR-29b-2-5p*	0.9
TRPS1	*hsa-miR-3613-3p*	0.963	*RNF139*	*hsa-miR-101-3p*	0.9
ZFHX4	*hsa-miR-9-5p*	0.963	*UBE2W*	*hsa-miR-27a-3p*	0.9
ZNF91	*hsa-miR-183-3p*	0.963	*ZNF250*	*hsa-miR-130a-3p*	0.9

Supplementary Table 2B. All interactions among the 65 CNA-miRNAs and 898 target genes in PeCa (DIANA-TarBase v.8 | miTG ≥ 0.9)

Target Gene	CNA-miRNA	miTG score	Target Gene	CNA-miRNA	miTG score
AFF4	*hsa-miR-203a-3p*	1	*FBXO28*	*hsa-miR-548n*	0.962
ATF7	*hsa-miR-124-3p*	1	*GATA6*	*hsa-miR-124-3p*	0.962
BRWD3	*hsa-miR-30b-5p*	1	*IRAK3*	*hsa-miR-124-3p*	0.962
BRWD3	*hsa-miR-30d-5p*	1	*LPPR2*	*hsa-miR-1207-5p*	0.962
CBX5	*hsa-miR-1207-5p*	1	*PHACTR2*	*hsa-miR-30d-5p*	0.962
CCNE2	*hsa-miR-30b-5p*	1	*SEC22C*	*hsa-miR-30d-5p*	0.962
CCNE2	*hsa-miR-30d-5p*	1	*TSPAN3*	*hsa-miR-548d-3p*	0.962
CTBP1	*hsa-miR-1306-5p*	1	*UTRN*	*hsa-miR-1-3p*	0.962
DCUN1D3	*hsa-miR-30b-5p*	1	*ZNF148*	*hsa-miR-548n*	0.962
DESI2	*hsa-miR-30b-5p*	1	*ZNF460*	*hsa-miR-125b-5p*	0.962
DESI2	*hsa-miR-30d-5p*	1	*ATXN1*	*hsa-miR-301b-3p*	0.961
ERLIN1	*hsa-miR-30b-5p*	1	*CHD9*	*hsa-miR-30b-5p*	0.961
ERLIN1	*hsa-miR-30d-5p*	1	*CUX1*	*hsa-miR-548d-3p*	0.961
GALNT7	*hsa-miR-30b-5p*	1	*DDIT4*	*hsa-miR-30b-5p*	0.961

GALNT7	*hsa-miR-30d-5p*	1	*HMGB2*	*hsa-miR-548d-3p*	0.961
GLCCI1	*hsa-miR-30b-5p*	1	*PANK3*	*hsa-miR-548n*	0.961
GLCCI1	*hsa-miR-30d-5p*	1	*RBMS2*	*hsa-miR-4429*	0.961
HAND1	*hsa-miR-196b-5p*	1	*AKAP10*	*hsa-miR-30b-5p*	0.96
HOXA7	*hsa-miR-196b-5p*	1	*C7orf60*	*hsa-miR-301b-3p*	0.96
HOXA9	*hsa-miR-196b-5p*	1	*ELAVL2*	*hsa-miR-30d-5p*	0.96
KLHL20	*hsa-miR-30b-5p*	1	*FAM118A*	*hsa-miR-125b-5p*	0.96
KLHL20	*hsa-miR-30d-5p*	1	*G3BP1*	*hsa-miR-548d-3p*	0.96
LCLAT1	*hsa-miR-30d-5p*	1	*HNRNPU*	*hsa-miR-589-3p*	0.96
MAGT1	*hsa-miR-124-3p*	1	*PANK3*	*hsa-miR-548d-3p*	0.96
MAML1	*hsa-miR-30b-5p*	1	*TMEM87B*	*hsa-miR-30b-5p*	0.96
MAML1	*hsa-miR-30d-5p*	1	*UBE4A*	*hsa-miR-548d-5p*	0.96
MEX3B	*hsa-miR-30b-5p*	1	*ACAP2*	*hsa-miR-30d-5p*	0.959
MEX3B	*hsa-miR-30d-5p*	1	*ACTR1A*	*hsa-miR-30b-5p*	0.959
MFHAS1	*hsa-miR-125b-5p*	1	*DDIT4*	*hsa-miR-548d-5p*	0.959
MIER1	*hsa-miR-301b-3p*	1	*DR1*	*hsa-miR-4517*	0.959

MTDH	*hsa-miR-30b-5p*	1	*EFNB2*	*hsa-miR-301b-3p*	0.959
MTDH	*hsa-miR-30d-5p*	1	*HIPK1*	*hsa-miR-589-3p*	0.959
OSBPL11	*hsa-miR-148a-3p*	1	*MARCH7*	*hsa-miR-548d-5p*	0.959
PCDH10	*hsa-miR-185-5p*	1	*PDS5A*	*hsa-miR-624-3p*	0.959
PCTP	*hsa-miR-125b-5p*	1	*PURB*	*hsa-miR-548a-3p*	0.959
PDE7A	*hsa-miR-30b-5p*	1	*SSH2*	*hsa-miR-548n*	0.959
PDE7A	*hsa-miR-30d-5p*	1	*ZBTB18*	*hsa-miR-548d-3p*	0.959
PFN2	*hsa-miR-30b-5p*	1	*ACAP2*	*hsa-miR-30b-5p*	0.958
PFN2	*hsa-miR-30d-5p*	1	*ARRDC4*	*hsa-miR-548d-3p*	0.958
PIP4K2A	*hsa-miR-30b-5p*	1	*ARSK*	*hsa-miR-589-3p*	0.958
PIP4K2A	*hsa-miR-30d-5p*	1	*CNTN1*	*hsa-miR-124-3p*	0.958
PLAGL2	*hsa-miR-30b-5p*	1	*HIF1AN*	*hsa-miR-31-5p*	0.958
PLAGL2	*hsa-miR-30d-5p*	1	*HIPK2*	*hsa-miR-30b-5p*	0.958
PPARGC1B	*hsa-miR-30b-5p*	1	*RAI14*	*hsa-miR-30b-5p*	0.958
PPARGC1B	*hsa-miR-30d-5p*	1	*RAP2C*	*hsa-miR-217*	0.958
PTPN9	*hsa-miR-124-3p*	1	*SLC30A7*	*hsa-miR-4517*	0.958

R3HDM1	*hsa-miR-30b-5p*	1	*STT3B*	*hsa-miR-30b-5p*	0.958
R3HDM1	*hsa-miR-30d-5p*	1	*USP15*	*hsa-miR-30d-5p*	0.958
RC3H2	*hsa-miR-148a-3p*	1	*XIAP*	*hsa-miR-548d-3p*	0.958
ROCK1	*hsa-miR-124-3p*	1	*AIDA*	*hsa-miR-548n*	0.957
SEMA3A	*hsa-miR-30d-5p*	1	*ALPK3*	*hsa-miR-125b-5p*	0.957
SETD7	*hsa-miR-30d-5p*	1	*ANKRD50*	*hsa-miR-125b-5p*	0.957
SFRP1	*hsa-miR-1-3p*	1	*AVEN*	*hsa-miR-30b-5p*	0.957
SLC9A6	*hsa-miR-196b-5p*	1	*CELF1*	*hsa-miR-589-3p*	0.957
SNAI1	*hsa-miR-30d-5p*	1	*DCDC2*	*hsa-miR-196b-5p*	0.957
SOCS1	*hsa-miR-30d-5p*	1	*DIRAS1*	*hsa-miR-491-5p*	0.957
SRSF11	*hsa-miR-148a-3p*	1	*LNPEP*	*hsa-miR-548k*	0.957
SYNGR3	*hsa-miR-30b-5p*	1	*MAP3K2*	*hsa-miR-148a-5p*	0.957
TBC1D10B	*hsa-miR-30d-5p*	1	*MARCH6*	*hsa-miR-30d-5p*	0.957
TLE1	*hsa-miR-30b-5p*	1	*NUFIP2*	*hsa-miR-873-5p*	0.957
TNKS2	*hsa-miR-1-3p*	1	*OXSR1*	*hsa-miR-31-5p*	0.957
UST	*hsa-miR-1-3p*	1	*PAFAH1B2*	*hsa-miR-30b-5p*	0.957

ZCCHC24	*hsa-miR-124-3p*	1	*PREPL*	*hsa-miR-185-5p*	0.957
ZNF543	*hsa-miR-125b-5p*	1	*PUM1*	*hsa-miR-548d-3p*	0.957
ZNRF1	*hsa-miR-30b-5p*	1	*RAD23B*	*hsa-miR-30d-5p*	0.957
ZSWIM6	*hsa-miR-125b-5p*	1	*REST*	*hsa-miR-548a-3p*	0.957
AMOTL1	*hsa-miR-124-3p*	0.999	*SH3PXD2A*	*hsa-miR-217*	0.957
ANKRA2	*hsa-miR-30b-5p*	0.999	*SLC7A1*	*hsa-miR-125b-5p*	0.957
B4GALT5	*hsa-miR-148a-3p*	0.999	*G3BP1*	*hsa-miR-548k*	0.956
BNIP3L	*hsa-miR-30b-5p*	0.999	*HMGCS1*	*hsa-miR-589-3p*	0.956
BNIP3L	*hsa-miR-30d-5p*	0.999	*ITGA8*	*hsa-miR-30d-3p*	0.956
BRWD1	*hsa-miR-30b-5p*	0.999	*NFIA*	*hsa-miR-548a-3p*	0.956
BRWD1	*hsa-miR-30d-5p*	0.999	*ONECUT2*	*hsa-miR-548n*	0.956
CAMK2N1	*hsa-miR-30b-5p*	0.999	*SLC41A2*	*hsa-miR-30d-5p*	0.956
CAND1	*hsa-miR-148a-3p*	0.999	*SOGA1*	*hsa-miR-30b-3p*	0.956
CCDC117	*hsa-miR-30d-5p*	0.999	*TMED7*	*hsa-miR-148a-5p*	0.956
CD99	*hsa-miR-30d-5p*	0.999	*CSNK1A1*	*hsa-miR-148a-5p*	0.955
CDC37L1	*hsa-miR-30b-5p*	0.999	*EML4*	*hsa-miR-30b-5p*	0.955

CDC37L1	*hsa-miR-30d-5p*	0.999	*FAM133A*	*hsa-miR-30d-5p*	0.955
CEP350	*hsa-miR-30b-5p*	0.999	*MIB1*	*hsa-miR-30b-5p*	0.955
CPNE8	*hsa-miR-30b-5p*	0.999	*PTBP1*	*hsa-miR-124-3p*	0.955
CPNE8	*hsa-miR-30d-5p*	0.999	*SLC30A1*	*hsa-miR-548d-3p*	0.955
CPSF6	*hsa-miR-30b-5p*	0.999	*TBL1XR1*	*hsa-miR-301b-3p*	0.955
CPSF6	*hsa-miR-30d-5p*	0.999	*B4GALT5*	*hsa-miR-301b-3p*	0.954
CUL5	*hsa-miR-148a-3p*	0.999	*DUSP5*	*hsa-miR-624-5p*	0.954
DCUN1D3	*hsa-miR-30d-5p*	0.999	*FIGN*	*hsa-miR-30b-5p*	0.954
FAM160B1	*hsa-miR-30b-5p*	0.999	*GGA2*	*hsa-miR-124-3p*	0.954
FAM160B1	*hsa-miR-30d-5p*	0.999	*GRSF1*	*hsa-miR-548d-3p*	0.954
FOXN2	*hsa-miR-548d-3p*	0.999	*HBP1*	*hsa-miR-301b-3p*	0.954
FRMD8	*hsa-miR-124-3p*	0.999	*IBA57*	*hsa-miR-125b-5p*	0.954
GFPT2	*hsa-miR-30d-5p*	0.999	*MECP2*	*hsa-miR-185-5p*	0.954
IL11	*hsa-miR-124-3p*	0.999	*PVRL3*	*hsa-miR-30b-5p*	0.954
LCLAT1	*hsa-miR-30b-5p*	0.999	*RMND5A*	*hsa-miR-548d-5p*	0.954
MAP3K9	*hsa-miR-148a-3p*	0.999	*RNF2*	*hsa-miR-148a-5p*	0.954

MLK4	*hsa-miR-30b-5p*	0.999	*SKIL*	*hsa-miR-548d-3p*	0.954
MLLT10	*hsa-miR-148a-3p*	0.999	*USP37*	*hsa-miR-30b-5p*	0.954
NEK9	*hsa-miR-124-3p*	0.999	*ARL8B*	*hsa-miR-148a-3p*	0.953
NRP1	*hsa-miR-1-3p*	0.999	*C4orf3*	*hsa-miR-30d-5p*	0.953
NUP210	*hsa-miR-125b-5p*	0.999	*CD2AP*	*hsa-miR-30d-5p*	0.953
PHTF2	*hsa-miR-30d-5p*	0.999	*CLOCK*	*hsa-miR-30d-5p*	0.953
PPP6R1	*hsa-miR-148a-3p*	0.999	*ERO1LB*	*hsa-miR-548n*	0.953
PSMD11	*hsa-miR-196b-5p*	0.999	*KPNA6*	*hsa-miR-125b-5p*	0.953
RAB10	*hsa-miR-124-3p*	0.999	*LBH*	*hsa-miR-548d-3p*	0.953
RAB38	*hsa-miR-30d-5p*	0.999	*PPARG*	*hsa-miR-548d-5p*	0.953
RARG	*hsa-miR-30b-5p*	0.999	*SLC35F5*	*hsa-miR-124-3p*	0.953
RARG	*hsa-miR-30d-5p*	0.999	*TMED8*	*hsa-miR-548d-3p*	0.953
RASA2	*hsa-miR-30b-5p*	0.999	*UGCG*	*hsa-miR-548d-3p*	0.953
RBM20	*hsa-miR-125b-5p*	0.999	*ZFAND5*	*hsa-miR-30d-5p*	0.953
RBM26	*hsa-miR-30b-5p*	0.999	*ADAMTS5*	*hsa-miR-148a-3p*	0.952
RBM26	*hsa-miR-30d-5p*	0.999	*CNOT6*	*hsa-miR-301b-3p*	0.952

RHOB	*hsa-miR-30b-5p*	0.999	*ENTPD4*	*hsa-miR-196b-5p*	0.952
RNF219	*hsa-miR-148a-3p*	0.999	*FAM98A*	*hsa-miR-548d-3p*	0.952
RORA	*hsa-miR-30b-5p*	0.999	*IRAK1*	*hsa-miR-589-5p*	0.952
RORA	*hsa-miR-30d-5p*	0.999	*KIAA1958*	*hsa-miR-4429*	0.952
SEMA3A	*hsa-miR-30b-5p*	0.999	*OTUD3*	*hsa-miR-548a-3p*	0.952
SIX4	*hsa-miR-124-3p*	0.999	*PLEKHF2*	*hsa-miR-124-3p*	0.952
SKIDA1	*hsa-miR-301b-3p*	0.999	*SLC6A9*	*hsa-miR-30d-5p*	0.952
SPEN	*hsa-miR-30b-5p*	0.999	*TBP*	*hsa-miR-148a-3p*	0.952
SPEN	*hsa-miR-30d-5p*	0.999	*UBR4*	*hsa-miR-148a-3p*	0.952
SSR1	*hsa-miR-548d-3p*	0.999	*USP37*	*hsa-miR-30d-5p*	0.952
STC2	*hsa-miR-1-3p*	0.999	*ZNF207*	*hsa-miR-548k*	0.952
STK39	*hsa-miR-30d-5p*	0.999	*BIRC6*	*hsa-miR-30d-5p*	0.951
SYNGR3	*hsa-miR-30d-5p*	0.999	*BRWD1*	*hsa-miR-125b-5p*	0.951
TBC1D10B	*hsa-miR-30b-5p*	0.999	*JMY*	*hsa-miR-1270*	0.951
TLE1	*hsa-miR-30d-5p*	0.999	*MLLT10*	*hsa-miR-548a-3p*	0.951
TMEM181	*hsa-miR-30d-5p*	0.999	*SLC6A9*	*hsa-miR-30b-5p*	0.951

ZNRF1	*hsa-miR-30d-5p*	0.999	*TOP2A*	*hsa-miR-548k*	0.951
ZSCAN29	*hsa-miR-125b-5p*	0.999	*VGF*	*hsa-miR-1914-3p*	0.951
CCDC117	*hsa-miR-30b-5p*	0.998	*ANKRD17*	*hsa-miR-203a-3p*	0.95
CD99	*hsa-miR-30b-5p*	0.998	*FAM178A*	*hsa-miR-148a-3p*	0.95
CDK5R1	*hsa-miR-148a-3p*	0.998	*GFPT1*	*hsa-miR-548d-5p*	0.95
CUL2	*hsa-miR-30b-5p*	0.998	*IFT52*	*hsa-miR-1-3p*	0.95
CUL2	*hsa-miR-30d-5p*	0.998	*IKZF2*	*hsa-miR-30d-5p*	0.95
DCAF12	*hsa-miR-597-5p*	0.998	*RHOU*	*hsa-miR-124-3p*	0.95
EFNB2	*hsa-miR-1-3p*	0.998	*RUNX3*	*hsa-miR-301b-3p*	0.95
GALNT1	*hsa-miR-30b-5p*	0.998	*TMED7*	*hsa-miR-548d-5p*	0.95
HNRNPUL2	*hsa-miR-30b-5p*	0.998	*ZNF148*	*hsa-miR-30d-5p*	0.95
HOXA5	*hsa-miR-196b-5p*	0.998	*AKT1*	*hsa-miR-548d-3p*	0.949
ITGA5	*hsa-miR-148a-3p*	0.998	*EDC3*	*hsa-miR-30b-5p*	0.949
JOSD1	*hsa-miR-30b-5p*	0.998	*FAM127A*	*hsa-miR-124-3p*	0.949
JOSD1	*hsa-miR-30d-5p*	0.998	*FAM133A*	*hsa-miR-30b-5p*	0.949
KLF13	*hsa-miR-125b-5p*	0.998	*FZD5*	*hsa-miR-100-5p*	0.949

LRCH2	*hsa-miR-30b-5p*	0.998	*GSK3B*	*hsa-miR-624-5p*	0.949
LRCH2	*hsa-miR-30d-5p*	0.998	*LRRC47*	*hsa-miR-589-3p*	0.949
MCL1	*hsa-miR-125b-5p*	0.998	*AGO1*	*hsa-miR-301b-3p*	0.948
MLK4	*hsa-miR-30d-5p*	0.998	*ANXA7*	*hsa-miR-124-3p*	0.948
PHTF2	*hsa-miR-30b-5p*	0.998	*CBX6*	*hsa-miR-589-3p*	0.948
PLAGL2	*hsa-miR-548d-3p*	0.998	*FBXL20*	*hsa-miR-30b-5p*	0.948
PPP1R18	*hsa-miR-30d-5p*	0.998	*FBXL20*	*hsa-miR-30d-5p*	0.948
S100PBP	*hsa-miR-30b-5p*	0.998	*G6PD*	*hsa-miR-1-3p*	0.948
SEC24A	*hsa-miR-30b-5p*	0.998	*HSPD1*	*hsa-miR-1-3p*	0.948
STT3A	*hsa-miR-124-3p*	0.998	*NOTCH2*	*hsa-miR-4326*	0.948
THAP2	*hsa-miR-124-3p*	0.998	*PRTG*	*hsa-miR-196b-5p*	0.948
TMEM181	*hsa-miR-30b-5p*	0.998	*SCAMP2*	*hsa-miR-124-3p*	0.948
ZNF148	*hsa-miR-548d-5p*	0.998	*TAOK1*	*hsa-miR-548k*	0.948
CAMK2N1	*hsa-miR-30d-5p*	0.997	*ULK2*	*hsa-miR-301b-3p*	0.948
CBFB	*hsa-miR-30b-5p*	0.997	*USP15*	*hsa-miR-30b-5p*	0.948
CBFB	*hsa-miR-30d-5p*	0.997	*ZNF148*	*hsa-miR-30b-5p*	0.948

CCDC47	*hsa-miR-196b-5p*	0.997	*AMMECR1*	*hsa-miR-548d-5p*	0.947
CEP350	*hsa-miR-30d-5p*	0.997	*CAMSAP2*	*hsa-miR-4803*	0.947
DDX6	*hsa-miR-124-3p*	0.997	*CBFB*	*hsa-miR-301b-3p*	0.947
DUS1L	*hsa-miR-125b-5p*	0.997	*CD2AP*	*hsa-miR-30b-5p*	0.947
ELOVL5	*hsa-miR-30b-5p*	0.997	*DHX36*	*hsa-miR-30d-5p*	0.947
ELOVL5	*hsa-miR-30d-5p*	0.997	*FIGN*	*hsa-miR-30d-5p*	0.947
GALNT2	*hsa-miR-30d-5p*	0.997	*HIPK2*	*hsa-miR-30d-5p*	0.947
GFPT2	*hsa-miR-30b-5p*	0.997	*IGF1R*	*hsa-miR-1207-5p*	0.947
HNRNPUL2	*hsa-miR-30d-5p*	0.997	*JAG1*	*hsa-miR-124-3p*	0.947
INO80D	*hsa-miR-30b-5p*	0.997	*KIAA0226*	*hsa-miR-148a-3p*	0.947
KLHL15	*hsa-miR-548a-3p*	0.997	*MLXIP*	*hsa-miR-30d-5p*	0.947
LRRC1	*hsa-miR-124-3p*	0.997	*NACC1*	*hsa-miR-939-5p*	0.947
PTGFRN	*hsa-miR-30b-5p*	0.997	*NPTN*	*hsa-miR-301b-3p*	0.947
PTGFRN	*hsa-miR-30d-5p*	0.997	*THOC2*	*hsa-miR-203a-3p*	0.947
RHOB	*hsa-miR-30d-5p*	0.997	*TNPO1*	*hsa-miR-4517*	0.947
SOCS3	*hsa-miR-30d-5p*	0.997	*TRPS1*	*hsa-miR-30d-5p*	0.947

SRSF3	*hsa-miR-597-5p*	0.997	*GNA13*	*hsa-miR-124-3p*	0.946
UBE2V2	*hsa-miR-4803*	0.997	*HNRNPA1*	*hsa-miR-548d-3p*	0.946
WDR82	*hsa-miR-30b-5p*	0.997	*NEK7*	*hsa-miR-4517*	0.946
WDR82	*hsa-miR-30d-5p*	0.997	*PALLD*	*hsa-miR-876-5p*	0.946
WIPF1	*hsa-miR-124-3p*	0.997	*QSER1*	*hsa-miR-4473*	0.946
ADAM10	*hsa-miR-148a-3p*	0.996	*SPCS3*	*hsa-miR-548d-3p*	0.946
ANKRA2	*hsa-miR-30d-5p*	0.996	*TNRC6C*	*hsa-miR-30b-5p*	0.946
ATP13A3	*hsa-miR-548d-3p*	0.996	*TRA2B*	*hsa-miR-548k*	0.946
C5orf30	*hsa-miR-148a-3p*	0.996	*UBE4A*	*hsa-miR-1-3p*	0.946
CCDC170	*hsa-miR-1-3p*	0.996	*UBR4*	*hsa-miR-4429*	0.946
CCNJ	*hsa-miR-196b-5p*	0.996	*ANKRD52*	*hsa-miR-4664-5p*	0.945
CCNT2	*hsa-miR-30b-5p*	0.996	*AP1S1*	*hsa-miR-1207-5p*	0.945
CCNT2	*hsa-miR-30d-5p*	0.996	*CAND1*	*hsa-miR-649*	0.945
COL1A2	*hsa-miR-196b-5p*	0.996	*DROSHA*	*hsa-miR-30b-3p*	0.945
FIGN	*hsa-miR-548d-5p*	0.996	*GJC1*	*hsa-miR-589-3p*	0.945
FMNL3	*hsa-miR-3150b-3p*	0.996	*GLCCI1*	*hsa-miR-203a-3p*	0.945

GALNT2	*hsa-miR-30b-5p*	0.996	*MBOAT2*	*hsa-miR-548d-3p*	0.945
GALNT3	*hsa-miR-30d-5p*	0.996	*ORC2*	*hsa-miR-30b-5p*	0.945
HOXB7	*hsa-miR-196b-5p*	0.996	*PFN2*	*hsa-miR-151a-3p*	0.945
INHBB	*hsa-miR-148a-3p*	0.996	*POLR1A*	*hsa-miR-1207-5p*	0.945
INO80D	*hsa-miR-30d-5p*	0.996	*RB1*	*hsa-miR-148a-3p*	0.945
KLF9	*hsa-miR-30d-5p*	0.996	*SMARCD2*	*hsa-miR-301b-3p*	0.945
LCOR	*hsa-miR-30b-5p*	0.996	*SSR1*	*hsa-miR-196b-5p*	0.945
LCOR	*hsa-miR-30d-5p*	0.996	*ZMYM3*	*hsa-miR-589-3p*	0.945
MAN1A2	*hsa-miR-30b-5p*	0.996	*BAG1*	*hsa-miR-589-5p*	0.944
MAN1A2	*hsa-miR-30d-5p*	0.996	*BRPF1*	*hsa-miR-125b-5p*	0.944
MAPK14	*hsa-miR-124-3p*	0.996	*C5orf24*	*hsa-miR-4517*	0.944
MYBL1	*hsa-miR-301b-3p*	0.996	*FKBP1A*	*hsa-miR-548d-3p*	0.944
NR6A1	*hsa-miR-196b-5p*	0.996	*KCNJ2*	*hsa-miR-196b-5p*	0.944
RASA2	*hsa-miR-30d-5p*	0.996	*LIN7C*	*hsa-miR-548d-5p*	0.944
RNF111	*hsa-miR-5680*	0.996	*LRRC8B*	*hsa-miR-30b-5p*	0.944
S100PBP	*hsa-miR-30d-5p*	0.996	*PDIK1L*	*hsa-miR-548d-3p*	0.944

SESTD1	*hsa-miR-148a-3p*	0.996	*PKM*	*hsa-miR-148a-3p*	0.944
STK39	*hsa-miR-30b-5p*	0.996	*PKM*	*hsa-miR-4429*	0.944
STX6	*hsa-miR-185-5p*	0.996	*POGK*	*hsa-miR-185-5p*	0.944
SYT4	*hsa-miR-550a-3p*	0.996	*RAP2C*	*hsa-miR-30d-5p*	0.944
TAOK1	*hsa-miR-30b-5p*	0.996	*TMEM87A*	*hsa-miR-597-5p*	0.944
TAOK1	*hsa-miR-30d-5p*	0.996	*ZNF280C*	*hsa-miR-1-3p*	0.944
TRIM2	*hsa-miR-1-3p*	0.996	*BIRC6*	*hsa-miR-30b-5p*	0.943
TSC1	*hsa-miR-301b-3p*	0.996	*CCT6A*	*hsa-miR-301b-3p*	0.943
UBE3C	*hsa-miR-30b-5p*	0.996	*CDS1*	*hsa-miR-301b-3p*	0.943
ZBTB26	*hsa-miR-196b-5p*	0.996	*CERS2*	*hsa-miR-124-3p*	0.943
ZNF521	*hsa-miR-30b-5p*	0.996	*CHD9*	*hsa-miR-30d-5p*	0.943
ARID5B	*hsa-miR-30b-5p*	0.995	*GIGYF1*	*hsa-miR-548d-3p*	0.943
CDK6	*hsa-miR-548d-5p*	0.995	*LRRC8B*	*hsa-miR-30d-5p*	0.943
DPY19L1	*hsa-miR-30d-5p*	0.995	*PALM2-AKAP2*	*hsa-miR-548d-3p*	0.943
ELL2	*hsa-miR-30d-5p*	0.995	*PI4K2B*	*hsa-miR-124-3p*	0.943
GALNT1	*hsa-miR-30d-5p*	0.995	*PTP4A1*	*hsa-miR-217*	0.943

GTF3C3	*hsa-miR-125b-5p*	0.995	*SETD7*	*hsa-miR-548d-3p*	0.943
HELZ	*hsa-miR-4429*	0.995	*SMARCD1*	*hsa-miR-1207-5p*	0.943
HNRNPA3	*hsa-miR-1-3p*	0.995	*STT3B*	*hsa-miR-30d-5p*	0.943
LRRC8D	*hsa-miR-30b-5p*	0.995	*TNRC6C*	*hsa-miR-30d-5p*	0.943
LRRC8D	*hsa-miR-30d-5p*	0.995	*ZNF292*	*hsa-miR-4659a-3p*	0.943
MFSD6	*hsa-miR-30b-5p*	0.995	*ZNF614*	*hsa-miR-301b-3p*	0.943
MFSD6	*hsa-miR-30d-5p*	0.995	*ARID3A*	*hsa-miR-125b-5p*	0.942
NPTN	*hsa-miR-148a-3p*	0.995	*ARRDC3*	*hsa-miR-148a-3p*	0.942
PAWR	*hsa-miR-30d-5p*	0.995	*BTF3L4*	*hsa-miR-548n*	0.942
RAB32	*hsa-miR-30d-5p*	0.995	*CNN3*	*hsa-miR-1-3p*	0.942
SLC16A1	*hsa-miR-124-3p*	0.995	*EPB41L4A*	*hsa-miR-30b-3p*	0.942
SOCS3	*hsa-miR-30b-5p*	0.995	*HIPK1*	*hsa-miR-1207-5p*	0.942
TAOK1	*hsa-miR-548d-3p*	0.995	*HIPK1*	*hsa-miR-548a-3p*	0.942
TMEM87A	*hsa-miR-30b-5p*	0.995	*OVOL1*	*hsa-miR-30b-5p*	0.942
TRIM45	*hsa-miR-124-3p*	0.995	*PPP2R2A*	*hsa-miR-31-5p*	0.942
VKORC1L1	*hsa-miR-30b-5p*	0.995	*RFX1*	*hsa-miR-124-3p*	0.942

VKORC1L1	*hsa-miR-30d-5p*	0.995	*SCARB2*	*hsa-miR-125b-5p*	0.942
YWHAB	*hsa-miR-148a-3p*	0.995	*UTRN*	*hsa-miR-4517*	0.942
BRWD1	*hsa-miR-548d-5p*	0.994	*ACTR3B*	*hsa-miR-589-3p*	0.941
CCKBR	*hsa-miR-148a-3p*	0.994	*BRWD1*	*hsa-miR-548d-3p*	0.941
DDX3X	*hsa-miR-4999-5p*	0.994	*DHX36*	*hsa-miR-30b-5p*	0.941
FAM134A	*hsa-miR-125b-5p*	0.994	*EDC3*	*hsa-miR-30d-5p*	0.941
MET	*hsa-miR-301b-3p*	0.994	*IGF2BP1*	*hsa-miR-939-5p*	0.941
MET	*hsa-miR-589-3p*	0.994	*LHX2*	*hsa-miR-124-3p*	0.941
SAMD4A	*hsa-miR-30b-5p*	0.994	*SENP5*	*hsa-miR-1270*	0.941
SECISBP2L	*hsa-miR-301b-3p*	0.994	*ZSCAN29*	*hsa-miR-30d-5p*	0.941
TRIAP1	*hsa-miR-125b-5p*	0.994	*C4orf3*	*hsa-miR-30b-5p*	0.94
UBE3C	*hsa-miR-30d-5p*	0.994	*MLLT10*	*hsa-miR-301b-3p*	0.94
UBN1	*hsa-miR-125b-5p*	0.994	*MLXIP*	*hsa-miR-30b-5p*	0.94
ZFHX4	*hsa-miR-148a-5p*	0.994	*NRAS*	*hsa-miR-196b-5p*	0.94
ZNF521	*hsa-miR-30d-5p*	0.994	*PRNP*	*hsa-miR-30d-3p*	0.94
CELF1	*hsa-miR-548d-3p*	0.993	*SON*	*hsa-miR-100-3p*	0.94

CPSF6	*hsa-miR-125b-5p*	0.993	*TCF4*	*hsa-miR-301b-3p*	0.94
DIP2B	*hsa-miR-548d-5p*	0.993	*TRPS1*	*hsa-miR-30b-5p*	0.94
E2F5	*hsa-miR-1-3p*	0.993	*TSPYL1*	*hsa-miR-589-3p*	0.94
ELL2	*hsa-miR-30b-5p*	0.993	*ZDHHC21*	*hsa-miR-30b-5p*	0.94
G3BP1	*hsa-miR-548d-5p*	0.993	*ACAA2*	*hsa-miR-124-3p*	0.939
JARID2	*hsa-miR-548d-3p*	0.993	*ARGLU1*	*hsa-miR-873-5p*	0.939
LIN7C	*hsa-miR-30d-5p*	0.993	*CNOT3*	*hsa-miR-939-5p*	0.939
MAGT1	*hsa-miR-548n*	0.993	*FAM175B*	*hsa-miR-301b-3p*	0.939
NDRG3	*hsa-miR-1-3p*	0.993	*GNA13*	*hsa-miR-30d-5p*	0.939
NFIA	*hsa-miR-548d-3p*	0.993	*NAA25*	*hsa-miR-30b-5p*	0.939
PDS5B	*hsa-miR-4659a-3p*	0.993	*PBX1*	*hsa-miR-4429*	0.939
SEC24A	*hsa-miR-30d-5p*	0.993	*PTPN4*	*hsa-miR-301b-3p*	0.939
SECISBP2L	*hsa-miR-647*	0.993	*RC3H2*	*hsa-miR-301b-3p*	0.939
SERTAD2	*hsa-miR-548k*	0.993	*RC3H2*	*hsa-miR-30d-3p*	0.939
SMARCC1	*hsa-miR-548d-3p*	0.993	*SH3PXD2B*	*hsa-miR-1-3p*	0.939
SYBU	*hsa-miR-301b-3p*	0.993	*WDR26*	*hsa-miR-30b-5p*	0.939

YOD1	*hsa-miR-30d-5p*	0.993	*CDKN1B*	*hsa-miR-148a-3p*	0.938
ZNF711	*hsa-miR-30d-5p*	0.993	*E2F3*	*hsa-miR-4429*	0.938
ACVR1	*hsa-miR-301b-3p*	0.992	*MED13*	*hsa-miR-296-3p*	0.938
ADRA2A	*hsa-miR-30b-5p*	0.992	*PABPN1*	*hsa-miR-1207-5p*	0.938
CDK16	*hsa-miR-185-3p*	0.992	*QSER1*	*hsa-miR-124-3p*	0.938
CDK6	*hsa-miR-5680*	0.992	*RSF1*	*hsa-miR-148a-5p*	0.938
DAAM1	*hsa-miR-125b-5p*	0.992	*SAMD10*	*hsa-miR-1207-5p*	0.938
DNAJB4	*hsa-miR-548d-5p*	0.992	*STK35*	*hsa-miR-550a-5p*	0.938
GPR137C	*hsa-miR-148a-3p*	0.992	*TARDBP*	*hsa-miR-624-3p*	0.938
IGF2BP1	*hsa-miR-196b-5p*	0.992	*ZBTB8OS*	*hsa-miR-548d-3p*	0.938
ITPR3	*hsa-miR-124-3p*	0.992	*ZDHHC5*	*hsa-miR-876-5p*	0.938
KLF10	*hsa-miR-30d-5p*	0.992	*ZNF367*	*hsa-miR-548d-3p*	0.938
LCLAT1	*hsa-miR-124-3p*	0.992	*CEBPA*	*hsa-miR-124-3p*	0.937
MMGT1	*hsa-miR-548d-3p*	0.992	*HELZ*	*hsa-miR-548a-3p*	0.937
PAWR	*hsa-miR-30b-5p*	0.992	*LRP6*	*hsa-miR-30b-5p*	0.937
SEC23A	*hsa-miR-30b-5p*	0.992	*NAA25*	*hsa-miR-30d-5p*	0.937

SIK1	*hsa-miR-148a-3p*	0.992	*PHACTR2*	*hsa-miR-30b-5p*	0.937
SLC7A11	*hsa-miR-4517*	0.992	*SFXN1*	*hsa-miR-4429*	0.937
SOS1	*hsa-miR-148a-3p*	0.992	*SPOPL*	*hsa-miR-124-3p*	0.937
UBN1	*hsa-miR-30d-5p*	0.992	*UBE2D2*	*hsa-miR-30d-5p*	0.937
BBX	*hsa-miR-589-5p*	0.991	*EGR2*	*hsa-miR-124-3p*	0.936
CEBPZ	*hsa-miR-1-3p*	0.991	*FOXK1*	*hsa-miR-185-3p*	0.936
DNAJB4	*hsa-miR-548k*	0.991	*HECA*	*hsa-miR-550a-3p*	0.936
FOXJ3	*hsa-miR-1207-5p*	0.991	*NFYA*	*hsa-miR-203a-3p*	0.936
GPD2	*hsa-miR-548d-5p*	0.991	*OAS2*	*hsa-miR-589-5p*	0.936
MATR3	*hsa-miR-1-3p*	0.991	*PAK2*	*hsa-miR-148a-5p*	0.936
RORA	*hsa-miR-548d-5p*	0.991	*SIM1*	*hsa-miR-125b-5p*	0.936
S1PR1	*hsa-miR-148a-3p*	0.991	*SLC30A1*	*hsa-miR-148a-5p*	0.936
SEC23A	*hsa-miR-30d-5p*	0.991	*TMEM56*	*hsa-miR-30d-5p*	0.936
SPRED1	*hsa-miR-1-3p*	0.991	*TTYH3*	*hsa-miR-1914-3p*	0.936
TAGLN2	*hsa-miR-1-3p*	0.991	*BCL11B*	*hsa-miR-30d-5p*	0.935
TANC1	*hsa-miR-148a-3p*	0.991	*FAM13A*	*hsa-miR-30d-5p*	0.935

TMEM87A	*hsa-miR-30d-5p*	0.991	*IFNAR2*	*hsa-miR-30d-5p*	0.935
YOD1	*hsa-miR-30b-5p*	0.991	*KDM6B*	*hsa-miR-589-5p*	0.935
ALG9	*hsa-miR-30d-5p*	0.99	*MYLIP*	*hsa-miR-548k*	0.935
CAPZA1	*hsa-miR-30d-5p*	0.99	*NUFIP2*	*hsa-miR-30d-5p*	0.935
CD47	*hsa-miR-548k*	0.99	*RAP2C*	*hsa-miR-30b-5p*	0.935
CDK6	*hsa-miR-4429*	0.99	*RNASEH2C*	*hsa-miR-185-3p*	0.935
FAM43A	*hsa-miR-30d-5p*	0.99	*SNX3*	*hsa-miR-548a-3p*	0.935
FNDC3B	*hsa-miR-548k*	0.99	*SWSAP1*	*hsa-miR-125b-5p*	0.935
G3BP1	*hsa-miR-1-3p*	0.99	*TGFBR2*	*hsa-miR-301b-3p*	0.935
GALNT3	*hsa-miR-30b-5p*	0.99	*UBE2K*	*hsa-miR-548n*	0.935
IRF1	*hsa-miR-301b-3p*	0.99	*ZDHHC21*	*hsa-miR-548aa*	0.935
LPP	*hsa-miR-124-3p*	0.99	*DSG2*	*hsa-miR-30d-5p*	0.934
PAWR	*hsa-miR-548n*	0.99	*NACC1*	*hsa-miR-1914-3p*	0.934
RTN4R	*hsa-miR-30b-5p*	0.99	*NUCKS1*	*hsa-miR-30b-5p*	0.934
RYBP	*hsa-miR-548n*	0.99	*PLEKHG2*	*hsa-miR-876-5p*	0.934
SBNO1	*hsa-miR-125b-5p*	0.99	*PPP1R3B*	*hsa-miR-124-3p*	0.934

SH2B3	*hsa-miR-30d-5p*	0.99	*RSF1*	*hsa-miR-4429*	0.934
TPM3	*hsa-miR-1-3p*	0.99	*SBF2*	*hsa-miR-301b-3p*	0.934
ZDHHC18	*hsa-miR-939-5p*	0.99	*STK35*	*hsa-miR-550a-3-5p*	0.934
ARHGAP28	*hsa-miR-196b-5p*	0.989	*WDR26*	*hsa-miR-30d-5p*	0.934
ARID5B	*hsa-miR-30d-5p*	0.989	*ANKRD52*	*hsa-miR-939-5p*	0.933
DYRK2	*hsa-miR-125b-5p*	0.989	*BCL11B*	*hsa-miR-30b-5p*	0.933
EDEM3	*hsa-miR-30b-5p*	0.989	*CAB39*	*hsa-miR-550a-3-5p*	0.933
EDEM3	*hsa-miR-30d-5p*	0.989	*CDK16*	*hsa-miR-873-5p*	0.933
HELZ	*hsa-miR-548d-3p*	0.989	*CPE*	*hsa-miR-30b-5p*	0.933
KLC2	*hsa-miR-125b-5p*	0.989	*CUX1*	*hsa-miR-5680*	0.933
LIN7C	*hsa-miR-30b-5p*	0.989	*EEA1*	*hsa-miR-124-3p*	0.933
MYO5A	*hsa-miR-30d-5p*	0.989	*GATAD2B*	*hsa-miR-1207-5p*	0.933
PHF6	*hsa-miR-124-3p*	0.989	*ORC2*	*hsa-miR-30d-5p*	0.933
PJA2	*hsa-miR-5680*	0.989	*UBE2W*	*hsa-miR-1269a*	0.933
PKN2	*hsa-miR-589-5p*	0.989	*VLDLR*	*hsa-miR-548d-5p*	0.933
ROCK1	*hsa-miR-148a-3p*	0.989	*ZDHHC21*	*hsa-miR-30d-5p*	0.933

RRP15	*hsa-miR-548d-3p*	0.989	*ZNF493*	*hsa-miR-876-5p*	0.933
SERBP1	*hsa-miR-548d-5p*	0.989	*ZNF91*	*hsa-miR-296-3p*	0.933
STRIP1	*hsa-miR-30b-5p*	0.989	*ELL*	*hsa-miR-30d-5p*	0.932
TCF12	*hsa-miR-5680*	0.989	*KHNYN*	*hsa-miR-125b-5p*	0.932
YWHAZ	*hsa-miR-1-3p*	0.989	*PRX*	*hsa-miR-1306-5p*	0.932
ZBTB6	*hsa-miR-30b-5p*	0.989	*RAPH1*	*hsa-miR-589-3p*	0.932
ADAR	*hsa-miR-1-3p*	0.988	*TMEM101*	*hsa-miR-125b-5p*	0.932
ALG9	*hsa-miR-30b-5p*	0.988	*TRIM33*	*hsa-miR-203a-3p*	0.932
BTBD3	*hsa-miR-148a-3p*	0.988	*ZNF800*	*hsa-miR-301b-3p*	0.932
C7orf60	*hsa-miR-30b-5p*	0.988	*C7orf60*	*hsa-miR-148a-3p*	0.931
CCDC97	*hsa-miR-30d-5p*	0.988	*CREG1*	*hsa-miR-31-5p*	0.931
CLTC	*hsa-miR-1-3p*	0.988	*EFNA3*	*hsa-miR-491-5p*	0.931
EPG5	*hsa-miR-30b-5p*	0.988	*PNISR*	*hsa-miR-548aa*	0.931
GALNT1	*hsa-miR-5680*	0.988	*SLC30A7*	*hsa-miR-548d-3p*	0.931
GPR137C	*hsa-miR-1-3p*	0.988	*TAF4*	*hsa-miR-548d-5p*	0.931
HNRNPA2B1	*hsa-miR-548n*	0.988	*BHLHE41*	*hsa-miR-148a-3p*	0.93

JDP2	*hsa-miR-30b-5p*	0.988	*CNOT4*	*hsa-miR-548d-3p*	0.93
JDP2	*hsa-miR-30d-5p*	0.988	*EIF4EBP2*	*hsa-miR-185-5p*	0.93
NDEL1	*hsa-miR-30b-5p*	0.988	*FAM13A*	*hsa-miR-30b-5p*	0.93
NR6A1	*hsa-miR-30b-5p*	0.988	*HRK*	*hsa-miR-301b-3p*	0.93
NR6A1	*hsa-miR-30d-5p*	0.988	*INSIG1*	*hsa-miR-873-5p*	0.93
RTN4R	*hsa-miR-30d-5p*	0.988	*IRF4*	*hsa-miR-30d-5p*	0.93
TBX22	*hsa-miR-124-3p*	0.988	*KATNAL1*	*hsa-miR-30b-3p*	0.93
UBE2Z	*hsa-miR-1207-5p*	0.988	*PLAGL2*	*hsa-miR-185-5p*	0.93
ZNF704	*hsa-miR-125b-5p*	0.988	*SBF2*	*hsa-miR-148a-3p*	0.93
ARPC3	*hsa-miR-1-3p*	0.987	*SEMA6A*	*hsa-miR-876-5p*	0.93
C7orf60	*hsa-miR-30d-5p*	0.987	*ABHD13*	*hsa-miR-548d-3p*	0.929
CDK6	*hsa-miR-548k*	0.987	*BRWD1*	*hsa-miR-548k*	0.929
DDI2	*hsa-miR-30b-5p*	0.987	*ENPP4*	*hsa-miR-4517*	0.929
ELOVL5	*hsa-miR-124-3p*	0.987	*HIAT1*	*hsa-miR-548k*	0.929
IER3	*hsa-miR-124-5p*	0.987	*LIFR*	*hsa-miR-125b-5p*	0.929
IKZF2	*hsa-miR-5680*	0.987	*MARCH6*	*hsa-miR-30b-5p*	0.929

KIAA0355	*hsa-miR-30b-5p*	0.987	*PANK3*	*hsa-miR-4517*	0.929
NETO2	*hsa-miR-1-3p*	0.987	*PURG*	*hsa-miR-301b-3p*	0.929
PTPLAD1	*hsa-miR-1-3p*	0.987	*SOCS3*	*hsa-miR-203a-3p*	0.929
RRAGD	*hsa-miR-124-3p*	0.987	*TM9SF3*	*hsa-miR-548d-5p*	0.929
SAMD4A	*hsa-miR-30d-5p*	0.987	*C5orf24*	*hsa-miR-548d-3p*	0.928
SERTAD2	*hsa-miR-124-3p*	0.987	*DOC2A*	*hsa-miR-196b-5p*	0.928
SERTAD2	*hsa-miR-548d-5p*	0.987	*FAM210B*	*hsa-miR-30d-5p*	0.928
SMARCD2	*hsa-miR-30b-5p*	0.987	*KATNA1*	*hsa-miR-124-3p*	0.928
SMARCD2	*hsa-miR-30d-5p*	0.987	*KIF5B*	*hsa-miR-548d-3p*	0.928
XRN2	*hsa-miR-203a-3p*	0.987	*LRRC8C*	*hsa-miR-30d-5p*	0.928
YWHAE	*hsa-miR-876-3p*	0.987	*MED13*	*hsa-miR-548k*	0.928
ZBTB18	*hsa-miR-4803*	0.987	*NR6A1*	*hsa-miR-125b-5p*	0.928
ARPP19	*hsa-miR-548a-3p*	0.986	*NUCKS1*	*hsa-miR-624-5p*	0.928
CAMK2D	*hsa-miR-30d-5p*	0.986	*PABPN1*	*hsa-miR-548d-3p*	0.928
CAPRIN1	*hsa-miR-1-3p*	0.986	*PARD6B*	*hsa-miR-548d-5p*	0.928
DDI2	*hsa-miR-30d-5p*	0.986	*SEH1L*	*hsa-miR-548n*	0.928

DEDD	*hsa-miR-148a-3p*	0.986	*TMED8*	*hsa-miR-1306-5p*	0.928
DPY19L1	*hsa-miR-30b-5p*	0.986	*TMEM56*	*hsa-miR-30b-5p*	0.928
EPG5	*hsa-miR-30d-5p*	0.986	*USP25*	*hsa-miR-339-3p*	0.928
FBXO3	*hsa-miR-4517*	0.986	*ZBTB18*	*hsa-miR-30b-5p*	0.928
GOLGA1	*hsa-miR-30b-5p*	0.986	*AFF4*	*hsa-miR-4517*	0.927
LY75	*hsa-miR-548n*	0.986	*CDK12*	*hsa-miR-30d-5p*	0.927
MZT1	*hsa-miR-30b-5p*	0.986	*CDR2L*	*hsa-miR-125b-5p*	0.927
NDEL1	*hsa-miR-30d-5p*	0.986	*IGFBP5*	*hsa-miR-185-5p*	0.927
PEX3	*hsa-miR-548d-5p*	0.986	*PCGF3*	*hsa-miR-30b-5p*	0.927
PHAX	*hsa-miR-148a-3p*	0.986	*PURB*	*hsa-miR-548d-5p*	0.927
RAB32	*hsa-miR-30b-5p*	0.986	*RPS16*	*hsa-miR-876-5p*	0.927
RQCD1	*hsa-miR-30d-5p*	0.986	*YWHAB*	*hsa-miR-217*	0.927
SH2B3	*hsa-miR-30b-5p*	0.986	*ZDHHC17*	*hsa-miR-148a-3p*	0.927
GNA13	*hsa-miR-185-5p*	0.985	*ZNF516*	*hsa-miR-548d-3p*	0.927
KIF2A	*hsa-miR-1-3p*	0.985	*CELSR2*	*hsa-miR-548d-3p*	0.926
PPP3R1	*hsa-miR-30b-5p*	0.985	*DIP2C*	*hsa-miR-4429*	0.926

SCML1	*hsa-miR-30d-5p*	0.985	*ELL*	*hsa-miR-30b-5p*	0.926
SHCBP1	*hsa-miR-4517*	0.985	*EPAS1*	*hsa-miR-148a-3p*	0.926
TBL1XR1	*hsa-miR-548d-3p*	0.985	*IREB2*	*hsa-miR-4803*	0.926
ZNF711	*hsa-miR-30b-5p*	0.985	*MED28*	*hsa-miR-548k*	0.926
DNAJC13	*hsa-miR-30d-5p*	0.984	*PANK3*	*hsa-miR-548k*	0.926
FAM43A	*hsa-miR-30b-5p*	0.984	*PRKAA1*	*hsa-miR-301b-3p*	0.926
FOXO1	*hsa-miR-4803*	0.984	*PSMD11*	*hsa-miR-548d-3p*	0.926
KLF9	*hsa-miR-30b-5p*	0.984	*SLC30A7*	*hsa-miR-124-3p*	0.926
LY75	*hsa-miR-548d-5p*	0.984	*UTP23*	*hsa-miR-1270*	0.926
MTMR9	*hsa-miR-301b-3p*	0.984	*WEE1*	*hsa-miR-548a-3p*	0.926
PTPRG	*hsa-miR-196b-5p*	0.984	*ZNF106*	*hsa-miR-548n*	0.926
REEP1	*hsa-miR-30b-5p*	0.984	*ARPP19*	*hsa-miR-203a-3p*	0.925
REEP1	*hsa-miR-30d-5p*	0.984	*BBC3*	*hsa-miR-296-5p*	0.925
RMND5A	*hsa-miR-548d-3p*	0.984	*C16orf52*	*hsa-miR-491-5p*	0.925
RPIA	*hsa-miR-124-3p*	0.984	*CEP85L*	*hsa-miR-30b-5p*	0.925
RTCA	*hsa-miR-301b-3p*	0.984	*GNA13*	*hsa-miR-30b-5p*	0.925

SOGA1	*hsa-miR-1207-5p*	0.984	*IGF2BP1*	*hsa-miR-185-5p*	0.925
SRP54	*hsa-miR-548d-3p*	0.984	*IRF4*	*hsa-miR-30b-5p*	0.925
TMED7	*hsa-miR-148a-3p*	0.984	*LYN*	*hsa-miR-185-5p*	0.925
UBAC1	*hsa-miR-30b-5p*	0.984	*MAP3K2*	*hsa-miR-4429*	0.925
ADAMTS1	*hsa-miR-548k*	0.983	*NEUROD1*	*hsa-miR-1-3p*	0.925
C9orf41	*hsa-miR-30b-5p*	0.983	*PVRL4*	*hsa-miR-939-5p*	0.925
FAM126A	*hsa-miR-548k*	0.983	*SKIL*	*hsa-miR-30d-5p*	0.925
MYO5A	*hsa-miR-30b-5p*	0.983	*SOS1*	*hsa-miR-548d-5p*	0.925
PCDH19	*hsa-miR-4803*	0.983	*ZNF148*	*hsa-miR-548k*	0.925
PGM3	*hsa-miR-30d-5p*	0.983	*ZSCAN29*	*hsa-miR-30b-5p*	0.925
PRTG	*hsa-miR-4803*	0.983	*AFF4*	*hsa-miR-30d-5p*	0.924
SEMA4C	*hsa-miR-125b-5p*	0.983	*ANKRD52*	*hsa-miR-491-5p*	0.924
TMEM109	*hsa-miR-589-3p*	0.983	*ARF3*	*hsa-miR-185-5p*	0.924
TPM4	*hsa-miR-1-3p*	0.983	*INHBA*	*hsa-miR-548d-3p*	0.924
VAT1	*hsa-miR-124-3p*	0.983	*KMT2D*	*hsa-miR-548d-3p*	0.924
ZBTB11	*hsa-miR-30d-5p*	0.983	*LRRC8C*	*hsa-miR-30b-5p*	0.924

ZNF689	*hsa-miR-339-5p*	0.983	*MIB1*	*hsa-miR-548d-3p*	0.924
CRIM1	*hsa-miR-873-5p*	0.982	*NRXN3*	*hsa-miR-548d-3p*	0.924
FUBP1	*hsa-miR-1-3p*	0.982	*NUCKS1*	*hsa-miR-30d-5p*	0.924
GATAD2B	*hsa-miR-491-5p*	0.982	*NUFIP2*	*hsa-miR-30b-5p*	0.924
MRPL34	*hsa-miR-185-5p*	0.982	*RNF11*	*hsa-miR-548k*	0.924
OSBP	*hsa-miR-124-3p*	0.982	*STEAP4*	*hsa-miR-301b-3p*	0.924
PGM3	*hsa-miR-30b-5p*	0.982	*ZBTB33*	*hsa-miR-589-3p*	0.924
PTPN13	*hsa-miR-30d-5p*	0.982	*AP1G1*	*hsa-miR-550a-3-5p*	0.923
SLC50A1	*hsa-miR-124-3p*	0.982	*APPL1*	*hsa-miR-148a-5p*	0.923
SOS	*hsa-miR-548k*	0.982	*BLZF1*	*hsa-miR-125b-5p*	0.923
UBN1	*hsa-miR-30b-5p*	0.982	*C1orf174*	*hsa-miR-30b-5p*	0.923
WHSC1L1	*hsa-miR-301b-3p*	0.982	*MAK16*	*hsa-miR-548d-5p*	0.923
ZBTB11	*hsa-miR-30b-5p*	0.982	*MAX*	*hsa-miR-873-5p*	0.923
ZFP62	*hsa-miR-125b-5p*	0.982	*NEUROD1*	*hsa-miR-30d-5p*	0.923
ATL3	*hsa-miR-5680*	0.981	*SLC35C1*	*hsa-miR-30b-5p*	0.923
CAPZA1	*hsa-miR-30b-5p*	0.981	*TMEM56*	*hsa-miR-548d-5p*	0.923

CCDC6	*hsa-miR-148a-3p*	0.981	*ZNF264*	*hsa-miR-548a-3p*	0.923
CCND2	*hsa-miR-548d-3p*	0.981	*CDK12*	*hsa-miR-30b-5p*	0.922
CDKN1B	*hsa-miR-30d-3p*	0.981	*HIPK3*	*hsa-miR-548d-3p*	0.922
EIF1AX	*hsa-miR-548d-3p*	0.981	*IRF3*	*hsa-miR-148a-3p*	0.922
GTF2A1	*hsa-miR-4429*	0.981	*KPNA4*	*hsa-miR-491-3p*	0.922
GTF2H1	*hsa-miR-548k*	0.981	*MYO9A*	*hsa-miR-1207-5p*	0.922
KAT6A	*hsa-miR-185-5p*	0.981	*NRXN3*	*hsa-miR-30b-5p*	0.922
LIFR	*hsa-miR-30b-5p*	0.981	*ACKR3*	*hsa-miR-548a-3p*	0.921
MTX3	*hsa-miR-589-3p*	0.981	*ARHGAP1*	*hsa-miR-185-3p*	0.921
NUFIP2	*hsa-miR-548aa*	0.981	*ARL6IP1*	*hsa-miR-548d-5p*	0.921
PKN2	*hsa-miR-548k*	0.981	*AZIN1*	*hsa-miR-30b-5p*	0.921
PNN	*hsa-miR-548d-3p*	0.981	*DLL1*	*hsa-miR-548d-3p*	0.921
SBNO1	*hsa-miR-30d-3p*	0.981	*ITPKB*	*hsa-miR-550a-3p*	0.921
SNX18	*hsa-miR-30d-5p*	0.981	*MAP4K3*	*hsa-miR-548n*	0.921
TSPAN12	*hsa-miR-196b-5p*	0.981	*MMD*	*hsa-miR-548d-5p*	0.921
UBC	*hsa-miR-301b-3p*	0.981	*NRAS*	*hsa-miR-548d-3p*	0.921

ZAK	*hsa-miR-548d-5p*	0.981	*PPM1A*	*hsa-miR-4659a-3p*	0.921
ZNF792	*hsa-miR-125b-5p*	0.981	*SEL1L*	*hsa-miR-30b-3p*	0.921
DCP2	*hsa-miR-148a-3p*	0.98	*SPTSSA*	*hsa-miR-548d-3p*	0.921
FICD	*hsa-miR-301b-3p*	0.98	*VIM*	*hsa-miR-30d-5p*	0.921
GJC1	*hsa-miR-550a-5p*	0.98	*ZC3H7B*	*hsa-miR-125b-5p*	0.921
KIAA0355	*hsa-miR-30d-5p*	0.98	*ZCCHC14*	*hsa-miR-301b-3p*	0.921
LIFR	*hsa-miR-30d-5p*	0.98	*CACHD1*	*hsa-miR-589-3p*	0.92
NUPL1	*hsa-miR-148a-3p*	0.98	*CCNA2*	*hsa-miR-548d-5p*	0.92
PLXNC1	*hsa-miR-30d-5p*	0.98	*DMXL2*	*hsa-miR-30b-5p*	0.92
POLR3D	*hsa-miR-196b-5p*	0.98	*EFCAB14*	*hsa-miR-124-3p*	0.92
PRTG	*hsa-miR-124-3p*	0.98	*MTOR*	*hsa-miR-100-5p*	0.92
RAPGEF2	*hsa-miR-30d-5p*	0.98	*NEUROD1*	*hsa-miR-30b-5p*	0.92
RQCD1	*hsa-miR-30b-5p*	0.98	*PIK3R3*	*hsa-miR-148a-3p*	0.92
SNX18	*hsa-miR-30b-5p*	0.98	*ZNF264*	*hsa-miR-548d-3p*	0.92
SUV420H1	*hsa-miR-30d-3p*	0.98	*AZIN1*	*hsa-miR-30d-5p*	0.919
TOMM70A	*hsa-miR-148a-3p*	0.98	*HIPK3*	*hsa-miR-301b-3p*	0.919

ZNF721	*hsa-miR-217*	0.98	*PCGF3*	*hsa-miR-30d-5p*	0.919
ALCAM	*hsa-miR-148a-3p*	0.979	*REEP3*	*hsa-miR-548k*	0.919
FAM98A	*hsa-miR-1306-5p*	0.979	*SERTAD3*	*hsa-miR-125b-5p*	0.919
MAP3K9	*hsa-miR-301b-3p*	0.979	*SLC33A1*	*hsa-miR-548k*	0.919
PPARGC1A	*hsa-miR-30d-5p*	0.979	*ZSWIM6*	*hsa-miR-31-5p*	0.919
PPP3R1	*hsa-miR-30d-5p*	0.979	*CHD9*	*hsa-miR-4517*	0.918
PTPN13	*hsa-miR-30b-5p*	0.979	*CKAP2*	*hsa-miR-185-5p*	0.918
RAPGEF2	*hsa-miR-30b-5p*	0.979	*DESI1*	*hsa-miR-5680*	0.918
RYBP	*hsa-miR-548k*	0.979	*KRAS*	*hsa-miR-217*	0.918
UBE2K	*hsa-miR-548k*	0.979	*LPGAT1*	*hsa-miR-589-5p*	0.918
ZBTB6	*hsa-miR-30d-5p*	0.979	*RGS4*	*hsa-miR-31-5p*	0.918
ADRA2A	*hsa-miR-30d-5p*	0.978	*SRSF1*	*hsa-miR-1-3p*	0.918
APPBP2	*hsa-miR-873-5p*	0.978	*TRAF6*	*hsa-miR-548k*	0.918
CPEB4	*hsa-miR-548d-5p*	0.978	*CPE*	*hsa-miR-30d-5p*	0.917
ELL2	*hsa-miR-548d-5p*	0.978	*ETV3*	*hsa-miR-125b-5p*	0.917
HIPK2	*hsa-miR-148a-5p*	0.978	*HOMEZ*	*hsa-miR-125b-5p*	0.917

MARCKSL1	*hsa-miR-548aa*	0.978	*MEGF9*	*hsa-miR-125b-5p*	0.917
PTP4A1	*hsa-miR-30d-5p*	0.978	*MIER1*	*hsa-miR-4517*	0.917
SEC23IP	*hsa-miR-203a-3p*	0.978	*NUFIP2*	*hsa-miR-4326*	0.917
SLC35G1	*hsa-miR-125b-5p*	0.978	*SESTD1*	*hsa-miR-589-5p*	0.917
UBE2V2	*hsa-miR-30d-5p*	0.978	*STK35*	*hsa-miR-124-3p*	0.917
CREBL2	*hsa-miR-196b-5p*	0.977	*WDR82*	*hsa-miR-548d-5p*	0.917
IER3IP1	*hsa-miR-125b-5p*	0.977	*BTAF1*	*hsa-miR-4326*	0.916
JARID2	*hsa-miR-301b-3p*	0.977	*CCDC71L*	*hsa-miR-30b-5p*	0.916
PAFAH1B2	*hsa-miR-30d-5p*	0.977	*LDLR*	*hsa-miR-185-5p*	0.916
PARD6B	*hsa-miR-548k*	0.977	*PPP1R27*	*hsa-miR-548d-5p*	0.916
PLXNC1	*hsa-miR-30b-5p*	0.977	*SOGA1*	*hsa-miR-296-5p*	0.916
PPP1CB	*hsa-miR-148a-3p*	0.977	*CDV3*	*hsa-miR-647*	0.915
PRKD3	*hsa-miR-301b-3p*	0.977	*CHD4*	*hsa-miR-148a-3p*	0.915
SHISA2	*hsa-miR-550a-5p*	0.977	*GINM1*	*hsa-miR-124-3p*	0.915
WWTR1	*hsa-miR-548k*	0.977	*MTPN*	*hsa-miR-4517*	0.915
CDC37L1	*hsa-miR-589-3p*	0.976	*RAB4A*	*hsa-miR-217*	0.915

CPS1	*hsa-miR-548d-5p*	0.976	*USP12*	*hsa-miR-548n*	0.915
DAP	*hsa-miR-185-5p*	0.976	*VIM*	*hsa-miR-30b-5p*	0.915
DUSP3	*hsa-miR-491-5p*	0.976	*WASL*	*hsa-miR-301b-3p*	0.915
FZD8	*hsa-miR-100-5p*	0.976	*DLGAP4*	*hsa-miR-30b-5p*	0.914
GOLGA1	*hsa-miR-30d-5p*	0.976	*GCH1*	*hsa-miR-873-5p*	0.914
KLHL28	*hsa-miR-548k*	0.976	*JADE1*	*hsa-miR-301b-3p*	0.914
LDLR	*hsa-miR-301b-3p*	0.976	*KLHL18*	*hsa-miR-30b-3p*	0.914
LEMD3	*hsa-miR-124-3p*	0.976	*NUP155*	*hsa-miR-548k*	0.914
PRRG4	*hsa-miR-4517*	0.976	*PDCD4*	*hsa-miR-1-3p*	0.914
PTP4A1	*hsa-miR-30b-5p*	0.976	*SEMA3D*	*hsa-miR-548a-3p*	0.914
RANBP10	*hsa-miR-124-3p*	0.976	*TWSG1*	*hsa-miR-217*	0.914
RORA	*hsa-miR-125b-5p*	0.976	*ZNF548*	*hsa-miR-1270*	0.914
TMEM87B	*hsa-miR-30d-5p*	0.976	*ANKIB1*	*hsa-miR-301b-3p*	0.913
AP1AR	*hsa-miR-548d-3p*	0.975	*CGN*	*hsa-miR-124-3p*	0.913
C6orf62	*hsa-miR-148a-5p*	0.975	*CREB3L2*	*hsa-miR-124-3p*	0.913
CNBP	*hsa-miR-4435*	0.975	*IFNAR2*	*hsa-miR-30b-5p*	0.913

FNDC3B	*hsa-miR-548d-3p*	0.975	*RRN3*	*hsa-miR-4286*	0.913
LATS1	*hsa-miR-548n*	0.975	*SHOC2*	*hsa-miR-491-5p*	0.913
MAF1	*hsa-miR-148a-3p*	0.975	*SKIL*	*hsa-miR-30b-5p*	0.913
NCOA5	*hsa-miR-589-3p*	0.975	*ABCA12*	*hsa-miR-30d-5p*	0.912
NCR3LG1	*hsa-miR-30b-5p*	0.975	*CBX5*	*hsa-miR-624-3p*	0.912
NHLRC2	*hsa-miR-548k*	0.975	*CDK2*	*hsa-miR-548a-3p*	0.912
PRELID2	*hsa-miR-196b-5p*	0.975	*ELK3*	*hsa-miR-124-3p*	0.912
PSAP	*hsa-miR-301b-3p*	0.975	*HDAC5*	*hsa-miR-185-5p*	0.912
TNKS2	*hsa-miR-4429*	0.975	*IRS2*	*hsa-miR-30d-5p*	0.912
WAPAL	*hsa-miR-548n*	0.975	*PAPPA*	*hsa-miR-589-5p*	0.912
ZBTB7A	*hsa-miR-4664-5p*	0.975	*PSKH1*	*hsa-miR-124-3p*	0.912
ATXN1	*hsa-miR-148a-3p*	0.974	*RAB21*	*hsa-miR-548k*	0.912
AVEN	*hsa-miR-30d-5p*	0.974	*ZBTB18*	*hsa-miR-30d-5p*	0.912
CCND2	*hsa-miR-124-3p*	0.974	*ZNF451*	*hsa-miR-4517*	0.912
CDK16	*hsa-miR-296-5p*	0.974	*CCNA2*	*hsa-miR-148a-3p*	0.911
DPYSL2	*hsa-miR-30b-5p*	0.974	*EFR3A*	*hsa-miR-548d-3p*	0.911

EXOC8	*hsa-miR-196b-5p*	0.974	*EOGT*	*hsa-miR-301b-3p*	0.911
GAREM	*hsa-miR-301b-3p*	0.974	*KIAA1147*	*hsa-miR-30d-5p*	0.911
KMT2A	*hsa-miR-548d-3p*	0.974	*LRP6*	*hsa-miR-30d-5p*	0.911
LY75	*hsa-miR-548k*	0.974	*PARP9*	*hsa-miR-185-5p*	0.911
OTUD4	*hsa-miR-148a-3p*	0.974	*RIT1*	*hsa-miR-125b-5p*	0.911
RBM12	*hsa-miR-30b-5p*	0.974	*SESTD1*	*hsa-miR-301b-3p*	0.911
RBM12	*hsa-miR-30d-5p*	0.974	*TRIQK*	*hsa-miR-30b-5p*	0.911
YWHAQ	*hsa-miR-1-3p*	0.974	*UBAC1*	*hsa-miR-30d-5p*	0.911
ZNF281	*hsa-miR-125b-5p*	0.974	*UBE2D2*	*hsa-miR-30b-5p*	0.911
ZNF704	*hsa-miR-548n*	0.974	*ZNF689*	*hsa-miR-550a-5p*	0.911
CCL28	*hsa-miR-548d-3p*	0.973	*CELSR2*	*hsa-miR-939-5p*	0.91
CTNNB1	*hsa-miR-148a-5p*	0.973	*DDX3X*	*hsa-miR-124-3p*	0.91
DNAJC13	*hsa-miR-30b-5p*	0.973	*GOLPH3*	*hsa-miR-1-3p*	0.91
PFN2	*hsa-miR-1-3p*	0.973	*IRS2*	*hsa-miR-30b-5p*	0.91
TRAK2	*hsa-miR-148a-3p*	0.973	*MLK4*	*hsa-miR-196b-5p*	0.91
ZBTB34	*hsa-miR-548d-3p*	0.973	*NFIC*	*hsa-miR-4664-5p*	0.91

CPEB4	*hsa-miR-548a-3p*	0.972	*NUFIP2*	*hsa-miR-548k*	0.91
ELAVL2	*hsa-miR-30b-5p*	0.972	*PLEKHA3*	*hsa-miR-548d-3p*	0.91
MAP1B	*hsa-miR-589-3p*	0.972	*AKAP11*	*hsa-miR-548aa*	0.909
MBNL2	*hsa-miR-548d-5p*	0.972	*CBX5*	*hsa-miR-185-5p*	0.909
OLA1	*hsa-miR-589-3p*	0.972	*CSTF2T*	*hsa-miR-548d-5p*	0.909
STK17B	*hsa-miR-30b-5p*	0.972	*DCBLD2*	*hsa-miR-31-5p*	0.909
WDR26	*hsa-miR-548d-5p*	0.972	*DLGAP4*	*hsa-miR-30d-5p*	0.909
ZFAND5	*hsa-miR-30b-5p*	0.972	*ENAH*	*hsa-miR-185-5p*	0.909
AVL9	*hsa-miR-30b-3p*	0.971	*FRMD6*	*hsa-miR-301b-3p*	0.909
AVL9	*hsa-miR-30d-5p*	0.971	*IGF2BP1*	*hsa-miR-185-3p*	0.909
BRPF1	*hsa-miR-148a-3p*	0.971	*IQCE*	*hsa-miR-124-3p*	0.909
C9orf41	*hsa-miR-30d-5p*	0.971	*MLLT3*	*hsa-miR-124-3p*	0.909
CDK19	*hsa-miR-148a-3p*	0.971	*NECAP2*	*hsa-miR-124-3p*	0.909
CDKN1B	*hsa-miR-550a-3-5p*	0.971	*PARP9*	*hsa-miR-589-3p*	0.909
FSTL5	*hsa-miR-301b-3p*	0.971	*PNISR*	*hsa-miR-548d-5p*	0.909
HIPK1	*hsa-miR-124-3p*	0.971	*PTBP1*	*hsa-miR-1-3p*	0.909

KLF5	*hsa-miR-148a-3p*	0.971	*RAB3B*	*hsa-miR-589-5p*	0.909
MECP2	*hsa-miR-301b-3p*	0.971	*RAP1B*	*hsa-miR-298*	0.909
PCSK7	*hsa-miR-125b-5p*	0.971	*RYBP*	*hsa-miR-873-5p*	0.909
RNF2	*hsa-miR-876-3p*	0.971	*SRSF1*	*hsa-miR-548d-3p*	0.909
SAMD12	*hsa-miR-550a-5p*	0.971	*AFF4*	*hsa-miR-30b-5p*	0.908
SH3BGRL	*hsa-miR-548d-5p*	0.971	*ATP6V0D1*	*hsa-miR-148a-3p*	0.908
SLC30A7	*hsa-miR-548n*	0.971	*CBFB*	*hsa-miR-1270*	0.908
TBL1XR1	*hsa-miR-30b-5p*	0.971	*IMPAD1*	*hsa-miR-548n*	0.908
TBL1XR1	*hsa-miR-30d-5p*	0.971	*PGM2L1*	*hsa-miR-301b-3p*	0.908
TUSC3	*hsa-miR-30b-5p*	0.971	*RAB7A*	*hsa-miR-30d-5p*	0.908
ATP11A	*hsa-miR-148a-3p*	0.97	*RASSF3*	*hsa-miR-196b-5p*	0.908
CAMK2D	*hsa-miR-30b-5p*	0.97	*RNF41*	*hsa-miR-301b-3p*	0.908
DSEL	*hsa-miR-301b-3p*	0.97	*TFPI2*	*hsa-miR-30b-5p*	0.908
EP300	*hsa-miR-148a-3p*	0.97	*ZNF292*	*hsa-miR-148a-5p*	0.908
KAT6A	*hsa-miR-548aa*	0.97	*ZNF493*	*hsa-miR-296-3p*	0.908
NEUROD1	*hsa-miR-873-5p*	0.97	*ATXN1*	*hsa-miR-148a-5p*	0.907

PPP3R1	*hsa-miR-298*	0.97	*BCL9*	*hsa-miR-30d-5p*	0.907
RAD23B	*hsa-miR-30b-5p*	0.97	*C1orf174*	*hsa-miR-30d-5p*	0.907
ROBO1	*hsa-miR-548d-3p*	0.97	*CDK6*	*hsa-miR-589-3p*	0.907
SNRPD3	*hsa-miR-589-3p*	0.97	*FSCN1*	*hsa-miR-185-3p*	0.907
STAG2	*hsa-miR-30d-5p*	0.97	*KLF6*	*hsa-miR-124-3p*	0.907
TBPL1	*hsa-miR-30b-5p*	0.97	*LARP4*	*hsa-miR-196b-5p*	0.907
UBE2V2	*hsa-miR-30b-5p*	0.97	*LDOC1L*	*hsa-miR-31-5p*	0.907
ZNF711	*hsa-miR-301b-3p*	0.97	*MAPK14*	*hsa-miR-185-5p*	0.907
AFF4	*hsa-miR-124-3p*	0.969	*NOTCH2*	*hsa-miR-548d-5p*	0.907
AKAP10	*hsa-miR-30d-5p*	0.969	*POLR1A*	*hsa-miR-589-5p*	0.907
ATXN1	*hsa-miR-30d-5p*	0.969	*PSIP1*	*hsa-miR-548d-3p*	0.907
BIRC6	*hsa-miR-196b-5p*	0.969	*SH3PXD2A*	*hsa-miR-185-3p*	0.907
CDS1	*hsa-miR-548n*	0.969	*SLC5A6*	*hsa-miR-4802-5p*	0.907
DDIT4	*hsa-miR-30d-5p*	0.969	*STAU2*	*hsa-miR-148a-5p*	0.907
NCR3LG1	*hsa-miR-30d-5p*	0.969	*UBXN7*	*hsa-miR-548d-3p*	0.907
NPTX1	*hsa-miR-148a-3p*	0.969	*ZNRF1*	*hsa-miR-148a-3p*	0.907

SH2B3	*hsa-miR-124-3p*	0.969	*ETNK1*	*hsa-miR-876-5p*	0.906
STAG2	*hsa-miR-30b-5p*	0.969	*KAT2B*	*hsa-miR-548d-3p*	0.906
CSNK1A1	*hsa-miR-30d-5p*	0.968	*SASH1*	*hsa-miR-301b-3p*	0.906
EOGT	*hsa-miR-148a-3p*	0.968	*SLC25A22*	*hsa-miR-1-3p*	0.906
GSK3B	*hsa-miR-624-3p*	0.968	*SNAPIN*	*hsa-miR-30d-5p*	0.906
MYLIP	*hsa-miR-548d-5p*	0.968	*TRIM3*	*hsa-miR-939-5p*	0.906
PPIG	*hsa-miR-4999-5p*	0.968	*YTHDF1*	*hsa-miR-548k*	0.906
RAP2C	*hsa-miR-148a-5p*	0.968	*AKIRIN1*	*hsa-miR-548d-5p*	0.905
SEC22C	*hsa-miR-30b-5p*	0.968	*CDK16*	*hsa-miR-125b-5p*	0.905
TMEM135	*hsa-miR-1-3p*	0.968	*COLGALT1*	*hsa-miR-873-5p*	0.905
CCDC47	*hsa-miR-548d-5p*	0.967	*EGR1*	*hsa-miR-548d-3p*	0.905
CENPB	*hsa-miR-939-5p*	0.967	*FAM63B*	*hsa-miR-4517*	0.905
HNRNPA2B1	*hsa-miR-491-3p*	0.967	*SEL1L*	*hsa-miR-125b-5p*	0.905
NRXN3	*hsa-miR-30d-5p*	0.967	*STK38*	*hsa-miR-873-5p*	0.905
PPP6R1	*hsa-miR-301b-3p*	0.967	*AGO1*	*hsa-miR-124-3p*	0.904
PTPN4	*hsa-miR-4803*	0.967	*CBX8*	*hsa-miR-30d-5p*	0.904

RAB8B	*hsa-miR-148a-5p*	0.967	*ELK4*	*hsa-miR-124-3p*	0.904
REEP3	*hsa-miR-30d-5p*	0.967	*HCFC1*	*hsa-miR-876-3p*	0.904
RNF157	*hsa-miR-30b-5p*	0.967	*KCNC4*	*hsa-miR-4664-5p*	0.904
RORA	*hsa-miR-148a-5p*	0.967	*KLF12*	*hsa-miR-148a-5p*	0.904
SOX4	*hsa-miR-185-3p*	0.967	*PLAG1*	*hsa-miR-30d-5p*	0.904
TM4SF1	*hsa-miR-30d-5p*	0.967	*PPP2R2A*	*hsa-miR-4999-5p*	0.904
WIPF2	*hsa-miR-124-3p*	0.967	*RAC1*	*hsa-miR-589-3p*	0.904
AP1G1	*hsa-miR-550a-5p*	0.966	*TMPO*	*hsa-miR-548k*	0.904
ATXN1	*hsa-miR-30b-5p*	0.966	*TOR1AIP2*	*hsa-miR-548d-3p*	0.904
BTBD3	*hsa-miR-301b-3p*	0.966	*ABCA12*	*hsa-miR-30b-5p*	0.903
COL3A1	*hsa-miR-196b-5p*	0.966	*API5*	*hsa-miR-548k*	0.903
CSNK1A1	*hsa-miR-30b-5p*	0.966	*FAM204A*	*hsa-miR-589-3p*	0.903
DENND4B	*hsa-miR-939-5p*	0.966	*FOXK2*	*hsa-miR-597-5p*	0.903
NABP1	*hsa-miR-301b-3p*	0.966	*PTGFRN*	*hsa-miR-548d-5p*	0.903
PM20D2	*hsa-miR-548d-3p*	0.966	*XRN2*	*hsa-miR-548k*	0.903
RNPEPL1	*hsa-miR-124-3p*	0.966	*ZBTB39*	*hsa-miR-30b-5p*	0.903

SHISA2	*hsa-miR-550a-3-5p*	0.966	*ZBTB39*	*hsa-miR-30d-5p*	0.903
SLC7A11	*hsa-miR-30b-5p*	0.966	*C3orf38*	*hsa-miR-548n*	0.902
TBPL1	*hsa-miR-30d-5p*	0.966	*FAM210B*	*hsa-miR-30b-5p*	0.902
TM4SF1	*hsa-miR-30b-5p*	0.966	*GPR158*	*hsa-miR-1-3p*	0.902
TUSC3	*hsa-miR-30d-5p*	0.966	*IGF2BP1*	*hsa-miR-491-5p*	0.902
PTEN	*hsa-miR-30d-3p*	0.965	*JUN*	*hsa-miR-4429*	0.902
PTPN1	*hsa-miR-1-3p*	0.965	*PLAG1*	*hsa-miR-30b-5p*	0.902
PTRF	*hsa-miR-589-5p*	0.965	*PRNP*	*hsa-miR-148a-3p*	0.902
REEP3	*hsa-miR-30b-5p*	0.965	*RBL2*	*hsa-miR-550a-3-5p*	0.902
RNF157	*hsa-miR-30d-5p*	0.965	*RNF10*	*hsa-miR-196b-5p*	0.902
SCML1	*hsa-miR-30b-5p*	0.965	*RNF44*	*hsa-miR-296-5p*	0.902
SLC41A2	*hsa-miR-30b-5p*	0.965	*SBK1*	*hsa-miR-30b-5p*	0.902
SLC7A11	*hsa-miR-30d-5p*	0.965	*SRI*	*hsa-miR-1-3p*	0.902
SYPL1	*hsa-miR-30b-5p*	0.965	*TPM4*	*hsa-miR-30b-5p*	0.902
TSHZ1	*hsa-miR-301b-3p*	0.965	*UGT8*	*hsa-miR-548n*	0.902
ZAK	*hsa-miR-548k*	0.965	*CTNNB1*	*hsa-miR-548d-5p*	0.901

ZDHHC23	*hsa-miR-301b-3p*	0.965	*G3BP1*	*hsa-miR-30b-5p*	0.901
ZNF274	*hsa-miR-148a-3p*	0.965	*SYNJ2*	*hsa-miR-31-5p*	0.901
BTG1	*hsa-miR-876-3p*	0.964	*ARL5B*	*hsa-miR-148a-5p*	0.9
DHX33	*hsa-miR-125b-5p*	0.964	*C6orf62*	*hsa-miR-548d-3p*	0.9
DPYSL2	*hsa-miR-30d-5p*	0.964	*CCNA2*	*hsa-miR-4429*	0.9
EML4	*hsa-miR-30d-5p*	0.964	*CCNA2*	*hsa-miR-548a-3p*	0.9
IKZF2	*hsa-miR-30b-5p*	0.964	*CHD4*	*hsa-miR-185-5p*	0.9
SYPL1	*hsa-miR-30d-5p*	0.964	*EP300*	*hsa-miR-30d-3p*	0.9
TRA2B	*hsa-miR-548d-5p*	0.964	*GALNT1*	*hsa-miR-30d-5p*	0.9
AVL9	*hsa-miR-30b-5p*	0.963	*GALNT1*	*hsa-miR-5680*	0.9
C11orf58	*hsa-miR-4517*	0.963	*GALNT2*	*hsa-miR-30d-5p*	0.9
C16orf70	*hsa-miR-301b-3p*	0.963	*GALNT3*	*hsa-miR-30d-5p*	0.9
CANX	*hsa-miR-148a-3p*	0.963	*GALNT7*	*hsa-miR-30d-5p*	0.9
FAM160B1	*hsa-miR-4429*	0.963	*HERPUD2*	*hsa-miR-31-5p*	0.9
LARP4	*hsa-miR-548d-5p*	0.963	*LATS1*	*hsa-miR-548n*	0.9
OTUD3	*hsa-miR-301b-3p*	0.963	*NUCKS1*	*hsa-miR-548d-3p*	0.9

S1PR1	*hsa-miR-301b-3p*	0.963	*RB1*	*hsa-miR-30d-3p*	0.9
SENP5	*hsa-miR-548d-3p*	0.963	*SETD7*	*hsa-miR-30d-5p*	0.9
SMARCD2	*hsa-miR-550a-3p*	0.963	*SMAD4*	*hsa-miR-4517*	0.9
SNTB2	*hsa-miR-30d-5p*	0.963	*SPOPL*	*hsa-miR-301b-3p*	0.9
STK17B	*hsa-miR-30d-5p*	0.963	*TBP*	*hsa-miR-548a-3p*	0.9
STRIP1	*hsa-miR-30d-5p*	0.963	*WHSC1L1*	*hsa-miR-548d-3p*	0.9
ACTR1A	*hsa-miR-30d-5p*	0.962	*YWHAZ*	*hsa-miR-548d-5p*	0.9
EIF4G2	*hsa-miR-548d-3p*	0.962			

Supplementary Table 3A. Top 13 KEGG pathways identified by the Tarbase algorithm (DIANA-miRPath v.3) involving miRNAs mapped in the main cytobands affected by CNAs (Cytogenomics v.5.0 software; Agilent Technologies Inc, CA, algorithm ADM-2; threshold > 6).

KEGG[a] Pathways	P-value	Number of Genes	Number of miRNAs	miRNAs
Adherens junction (hsa04520)	$5.60x10^{-10}$	42	12	hsa-miR-589-5p, hsa-miR-876-3p, hsa-miR-647, hsa-miR-624-3p, hsa-miR-339-3p, hsa-miR-217, hsa-miR-196b-5p, hsa-miR-185-5p, hsa-miR-125b-5p, hsa-miR-124-5p, hsa-miR-124-3p, hsa-miR-1207-5p
Cell cycle (hsa04110)	$9.33x10^{-03}$	66	7	hsa-miR-30d-5p, hsa-miR-30d-3p, hsa-miR-296-3p, hsa-miR-196b-5p, hsa-miR-185-5p, hsa-miR-148a-3p, hsa-miR-124-3p
ECM-receptor interaction (hsa04512)	$2.40x10^{-10}$	28	9	hsa-miR-550a-3-5p, hsa-miR-339-3p, hsa-miR-30d-3p, hsa-miR-196b-5p, hsa-miR-185-5p, hsa-miR-185-3p, hsa-miR-124-5p, hsa-miR-124-3p, hsa-miR-100-3p
Fatty acid biosynthesis (hsa00061)	$<1.00x10^{-325}$	5	11	hsa-miR-4286, hsa-miR-548d-3p, hsa-miR-4664-5p, hsa-miR-30d-5p, hsa-miR-30b-5p, hsa-miR-30b-3p, hsa-miR-185-3p, hsa-miR-148a-3p, hsa-miR-1306-5p, hsa-miR-125b-5p, hsa-miR-100-5p

Fatty acid metabolism (hsa01212)	$<1.00x10^{-325}$	26	12	hsa-miR-4286, hsa-miR-548d-3p, hsa-miR-4664-5p, hsa-miR-30d-5p, hsa-miR-30b-5p, hsa-miR-30b-3p, hsa-miR-185-3p, hsa-miR-151a-3p, hsa-miR-1306-5p, hsa-miR-125b-5p, hsa-miR-124-3p, hsa-miR-100-5p
Glioma (hsa05214)	$1.02x10^{-02}$	35	10	hsa-miR-4286, hsa-miR-550a-5p, hsa-miR-550a-3-5p, hsa-miR-548d-5p, hsa-miR-4429, hsa-miR-296-5p, hsa-miR-196b-5p, hsa-miR-148a-3p, hsa-miR-124-3p, hsa-miR-100-5p
Hippo signaling pathway (hsa04390)	$8.69x10^{-13}$	62	15	hsa-miR-548k, hsa-miR-876-3p, hsa-miR-647, hsa-miR-550a-5p, hsa-miR-548n, hsa-miR-548d-5p, hsa-miR-4517, hsa-miR-339-3p, hsa-miR-30d-5p, hsa-miR-217, hsa-miR-196b-5p, hsa-miR-185-5p, hsa-miR-151a-3p, hsa-miR-1269a, hsa-miR-125b-5p
Lysine degradation (hsa00310)	$<1.00x10^{-325}$	32	24	hsa-miR-1270, hsa-miR-873-5p, hsa-miR-624-3p, hsa-miR-550a-5p, hsa-miR-550a-3-5p, hsa-miR-548d-3p, hsa-miR-491-5p, hsa-miR-491-3p, hsa-miR-4664-5p, hsa-miR-4473, hsa-miR-339-5p, hsa-miR-339-3p, hsa-miR-31-5p, hsa-miR-30d-5p, hsa-miR-30b-5p, hsa-miR-30b-3p, hsa-miR-296-5p,

				hsa-miR-296-3p, hsa-miR-196b-5p, hsa-miR-1914-3p, hsa-miR-185-3p, hsa-miR-148a-3p, hsa-miR-1306-5p, hsa-miR-125b-5p
Mucin type O-Glycan biosynthesis (hsa00512)	$7.59x10^{-03}$	9	6	hsa-miR-5680, hsa-miR-4659a-3p, hsa-miR-4517, hsa-miR-30d-5p, hsa-miR-30b-5p, hsa-miR-100-3p
Prion diseases (hsa05020)	$<1.00x10^{-325}$	3	4	hsa-miR-876-5p, hsa-miR-649, hsa-miR-30d-3p, hsa-miR-148a-3p
Proteoglycans in cancer (hsa05205)	$2.84x10^{-05}$	94	10	hsa-miR-876-3p, hsa-miR-873-5p, hsa-miR-548d-5p, hsa-miR-4659a-3p, hsa-miR-217, hsa-miR-196b-5p, hsa-miR-148a-3p, hsa-miR-125b-5p, hsa-miR-124-3p, hsa-miR-100-5p
Steroid biosynthesis (hsa00100)	$4.06x10^{-07}$	10	11	hsa-miR-876-5p, hsa-miR-873-5p, hsa-miR-647, hsa-miR-550a-5p, hsa-miR-548n, hsa-miR-491-5p, hsa-miR-31-5p, hsa-miR-30d-3p, hsa-miR-148a-3p, hsa-miR-124-3p, hsa-miR-100-3p
Viral carcinogenesis (hsa05203)	$2.85x10^{-04}$	67	7	hsa-miR-550a-3-5p, hsa-miR-548d-5p, hsa-miR-548a-3p, hsa-miR-4429, hsa-miR-30d-3p, hsa-miR-185-5p, hsa-miR-148a-3p

[a] KEGG = Kyoto Encyclopedia of Genes and Genomes; (DIANA-miRPath v.3, p-value threshold <0.05, Fisher's exact test)

Supplementary Table 3B. Top 13 KEGG pathways identified by the microT-CDS algorithm (DIANA-miRPath v.3) involving miRNAs mapped in the main cytobands affected by CNAs.

KEGG[a] Pathways	P-value	Number of Genes	Number of miRNAs	miRNAs Names
Axon guidance (hsa04360)	$2.52x10^{-03}$	70	10	hsa-miR-185-3p, hsa-miR-185-5p, hsa-miR-30b-3p, hsa-miR-30b-5p, hsa-miR-30d-5p, hsa-miR-339-5p, hsa-miR-548a-3p, hsa-miR-548aa, hsa-miR-548d-3p, hsa-miR-548n
FoxO signaling pathway (hsa04068)	$1.80x10^{-04}$	78	13	hsa-miR-148a-3p, hsa-miR-217, hsa-miR-301b-3p, hsa-miR-30b-5p, hsa-miR-30d-5p, hsa-miR-4517, hsa-miR-4803, hsa-miR-548aa, hsa-miR-548d-3p, hsa-miR-548d-5p, hsa-miR-548n, hsa-miR-5680, hsa-miR-548k
GABAergic synapse (hsa04727)	$3.61x10^{-03}$	33	8	hsa-miR-301b-3p, hsa-miR-4517, hsa-miR-491-5p, hsa-miR-550a-3-5p, hsa-miR-550a-5p, hsa-miR-5680, hsa-miR-597-5p, hsa-miR-624-3p
Hippo signaling pathway (hsa04390)	$5.01x10^{-09}$	67	9	hsa-miR-4429, hsa-miR-4517, hsa-miR-548aa, hsa-miR-548d-3p, hsa-miR-548d-5p, hsa-miR-548n, hsa-miR-624-5p, hsa-miR-873-5p, hsa-miR-548k

Long-term depression (hsa04730)	$2.86x10^{-02}$	35	9	hsa-miR-124-3p, hsa-miR-1914-3p, hsa-miR-30b-5p, hsa-miR-30d-5p, hsa-miR-4517, hsa-miR-548aa, hsa-miR-548d-3p, hsa-miR-548n, hsa-miR-647
Lysine degradation (hsa00310)	$4.80x10^{-02}$	20	10	hsa-miR-1207-5p, hsa-miR-1-3p, hsa-miR-339-5p, hsa-miR-548aa, hsa-miR-548d-3p, hsa-miR-624-3p, hsa-miR-624-5p, hsa-miR-649, hsa-miR-876-5p, hsa-miR-1270
Morphine addiction (hsa05032)	$2.78x10^{-11}$	53	15	hsa-miR-1-3p, hsa-miR-148a-5p, hsa-miR-185-3p, hsa-miR-301b-3p, hsa-miR-30b-5p, hsa-miR-30d-5p, hsa-miR-4517, hsa-miR-491-5p, hsa-miR-548a-3p, hsa-miR-550a-3-5p, hsa-miR-550a-5p, hsa-miR-5680, hsa-miR-597-5p, hsa-miR-647, hsa-miR-876-3p
Mucin type O-Glycan biosynthesis (hsa00512)	$<1.00x10^{-325}$	16	14	hsa-miR-124-3p, hsa-miR-296-5p, hsa-miR-30b-5p, hsa-miR-30d-5p, hsa-miR-4286, hsa-miR-491-5p, hsa-miR-548aa, hsa-miR-548n, hsa-miR-550a-3p, hsa-miR-5680, hsa-miR-649, hsa-miR-873-5p, hsa-miR-876-5p, hsa-miR-548k
Prion diseases (hsa05020)	$<1.00x10^{-325}$	8	07	hsa-miR-148a-3p, hsa-miR-301b-3p, hsa-miR-30d-3p, hsa-miR-548d-5p, hsa-miR-548n, hsa-miR-5680, hsa-miR-548k

Proteoglycans in cancer (hsa05205)	$1.03x10^{-06}$	101	12	hsa-miR-100-5p, hsa-miR-1269a, hsa-miR-148a-3p, hsa-miR-185-3p, hsa-miR-217, hsa-miR-298, hsa-miR-339-5p, hsa-miR-4429, hsa-miR-548a-3p, hsa-miR-548aa, hsa-miR-548d-3p, hsa-miR-5680
Signaling pathways regulating pluripotency of stem cells (hsa04550)	$8.36x10^{-08}$	74	14	hsa-miR-100-5p, hsa-miR-1269a, hsa-miR-148a-5p, hsa-miR-217, hsa-miR-4429, hsa-miR-4517, hsa-miR-548a-3p, hsa-miR-548aa, hsa-miR-548d-3p, hsa-miR-548d-5p, hsa-miR-548n, hsa-miR-5680, hsa-miR-876-5p, hsa-miR-548k
Steroid hormone biosynthesis (hsa00140)	$3.00x10^{-06}$	7	02	hsa-miR-491-3p, hsa-miR-548n
TGF-beta signaling pathway (hsa04350)	$2.08x10^{-10}$	45	16	hsa-miR-1306-5p, hsa-miR-148a-5p, hsa-miR-217, hsa-miR-301b-3p, hsa-miR-4326, hsa-miR-4803, hsa-miR-548a-3p, hsa-miR-548aa, hsa-miR-548d-3p, hsa-miR-548d-5p, hsa-miR-548n, hsa-miR-5680, hsa-miR-597-5p, hsa-miR-624-3p, hsa-miR-876-5p, hsa-miR-548k

[a] KEGG = Kyoto Encyclopedia of Genes and Genomes; (DIANA-miRPath v.3, p-value threshold <0.05, Fisher's exact test, microT Threshold 0.8)

Supplementary Table 4. Drugs targeting the genes involved in the top pathways and in the HPV-mediated carcinogenesis pathway.

Gene	Predicted drugs
CCNA2	Exenatide, celecoxib.
CDKN1B	Choline, l-arginine, Celecoxib, Ibuprofen, Pravastatin, Transtuzumab, Tamoxifen, Metformin, Docetaxel, Gemcitabine.
EGFR	Cetuximab
EP300	Chlorotrianisene, Diethstilbestrol, Dexamethasone.
EPAS1	l-arginine.
GALNT7	Methotrexate, Mercaptopurine.
ITGA5	Choline, l-arginine.
JUN	Valinomycin, Cyclosporine, Tacrolimus, Imatinib, Chroloqune, Imiquimod, Nifedipine, Mercaptopurine, Methotrexate.
KRAS	Tamoxifen, Cetuximab, Resveratrol, Docetaxel, Irinotecan.
LYN	Imatinib
MTOR	Doxorubicin.
PARD6B	Cisplatin.
PDE7A	Desipramine, Fluoxetine.
PPP1CB	Methotrexate, Mercaptopurine.
PTGS2	Celecoxib
RAC1	Choline, l-arginine, Cyclosporine, Tacrolinus, Chloroquine, Lecitin Mercaptopurine, Azathioprine.
RB1	Cisplatin, Tamoxifen, Celecoxib, Ibuprofen, Methotrexate, Mercaptopurine.
ROCK1	l-arginine.
SMAD4	Dexamethasone.

SOS1	l-arginine, Valinomycin, Cyclosporine, Tacrolimus, Imatinib, Chloroquine, l-citruline. Cisplatin.
YWHAQ	Tacrolimus

Anexo B – Material Suplementar Artigo 2

Supplementary Material

1 Supplementary Tables

Supplementary Table S1. Detailed clinical-histopathological profile and social habits of patients diagnosed with penile carcinoma enrolled in this study (n =22).

Case	Age	Phymosis	Smoking	Alcoholism	HPV	Tumor site	Histological subtype	Predominant lesion	Penectomy	Tu. Size	Tu. Grade	Tu. Stage	Lymphatic invasion	Perineural invasion	*TP53* expression	*RB1* expression
T01	62	no	N/A	N/A	16	glans	keratinized penile carcinoma	ulcerated	total	2.5	II	pT3	yes	yes	downregulated	downregulated
T02	80	N/A	smoker former	N/A	16	glans, foreskin and other areas	condilomatous	ulcerated	total	10	II	pT2	no	no	downregulated	downregulated
T03	81	yes	yes	N/A	18,53	glans and foreskin	condilomatous	ulcerated	total	2.1	II	pT1	no	no	downregulated	downregulated
T04	37	yes	no	yes	positive	glans and foreskin	keratinized penile carcinoma	nodular ulcerated	total	5	III	pT3	no	yes	N/A	N/A
T05	76	yes	no	yes	30	glans and foreskin	condilomatous	ulcerated	partial	3	I	pT1b	yes	no	downregulated	downregulated
T06	54	yes	yes	yes	positive	foreskin	keratinized penile carcinoma	vegetative	partial	0.8	II	pT2	yes	no	N/A	N/A
T07	74	yes	no	no	73,74	glans, foreskin and other areas	keratinized and basaloid	verrucosa	partial	0.8	I	pT2	no	no	downregulated	downregulated
T08	78	N/A	yes	yes	16,06	glans	keratinized and basaloid	vegetative	partial	4	III	pT1b	no	no	N/A	downregulated
T09	44	yes	no	yes	16	glans, foreskin and other areas	keratinized penile carcinoma	ulcerated	partial	1.7	II	pT1	no	no	downregulated	N/A
T10	57	no	no	yes	58	glans	keratinized and condilomatous	nodular ulcerated	total	3	III	pT2	no	no	N/A	N/A
T11	85	no	N/A	N/A	16	glans and foreskin	condilomatous	nodular ulcerated	partial	4	III	pT3	no	yes	N/A	upregulated

T12	83	no	smoker former	alcoholic former	16	glans and foreskin	keratinized penile carcinoma	ulcerated	partial	4.5	III	pT3	no	yes	Normal	upregulated
T13	40	no	no	no	59,66	glans	condilomatous	ulcer-vegetative	partial	3	II	pT2	no	no	downregulated	upregulated
T14	68	N/A	no	no	16,66	glans and foreskin	condilomatous	verrucosa	partial	5.5	I	pT3	no	no	upregulated	upregulated
T15	65	N/A	N/A	N/A	16,74	glans and foreskin	condilomatous	vegetative	partial	3.5	II	pT2	no	no	downregulated	downregulated
T16	51	N/A	yes	yes	16,35,59	glans, foreskin and other areas	keratinized penile carcinoma	ulcero-vegetante	partial	3	II	pT2	yes	no	downregulated	N/A
T17	74	no	yes	no	positive	glans	condilomatous	ulcerated	partial	1.8	II	pT1a	no	no	downregulated	N/A
T18	32	no	yes	yes	16,44,74	glans	keratinized and condilomatous	ulcer-vegetative	partial	3.7	II	pT2	no	no	N/A	downregulated
T19	71	no	no	no	16	glans	keratinized penile carcinoma	ulcerated	partial	3.2	III	pT3	no	no	downregulated	N/A
T20	69	no	no	no	16,30	glans	condilomatous	vegetative	partial	3.5	I	pT2	no	no	N/A	downregulated
T21	73	yes	smoker former	no	16	foreskin	keratinized penile carcinoma	ulcerated	postectomy	N/A	II	pT1	N/A	N/A	downregulated	N/A
T22	59	yes	no	yes	positive	glans	condilomatous	verrucous	partial	5.5	II	pT3	no	yes	N/A	N/A

N/A = not available; a = No information on HPV genotype; Tu = tumor (mm); Genotyping was performed by nested-PCR and DNA sequencing, except for T04, T06, T17 and T22 because did not have enough DNA for both assays.

Supplementary Table S2A. miRNA binding *'seed'* regions identified in *TP53* and *RB1* genes.

miRNA	Gene	Site Position*	LogitProb[a]	Region	Seed Position[b]	Seed Type[c]	ΔG_{hybrid}[d]	ΔG_{total}[e]	Site Access[f]	Seed Access[g]	Site Consv[h]	Seed Consv[i]	Site Location[j]
hsa-miR-22-3p	*TP53*	534-570	0.762	CDS	564-570	8mer	-21.100	2.949	0.448	0.273	0.963	0.993	0.285
hsa-let-7a-5p	*TP53*	1829-1850	0.835	3'UTR	1843-1849	8mer	-21.500	-12.736	0.631	0.627	0.001	0	0.357
hsa-let-7a-5p	*RB1*	2506-2517	0.953	CDS	2511-2516	7mer-A1	-18.100	-16.708	0.823	0.886	0.999	1	0.840
hsa-let-7a-5p	*RB1*	2085-2103	0.827	CDS	2097-2103	7mer-m8	-19.900	-12.574	0.619	0.968	0.817	1	0.689
hsa-let-7a-5p	*RB1*	2915-2935	0.805	CDS	2929-2934	7mer-A1	-19.700	-12.982	0.524	0.431	0.965	1.000	0.986
hsa-miR-130a-3p	*RB1*	633-648	0.799	CDS	642-648	7mer-m8	-15.900	-12.886	0.566	0.296	0.994	1.000	0.168
hsa-miR-200c-3p	*RB1*	760-784	0.787	CDS	778-783	7mer-A1	-18.200	-6.342	0.474	0.411	0.999	1	0.213
hsa-miR-205-5p	*RB1*	2793-2809	0.787	CDS	2803-2808	7mer-A1	-19.200	-9.408	0.478	0.476	0.980	0.994	0.943
hsa-miR-205-5p	*RB1*	1402-1428	0.768	CDS	1422-1427	7mer-A1	-21.200	-1.732	0.491	0.335	0.975	0.960	0.443
hsa-miR-93-5p	*RB1*	4333-4353	0.765	3'UTR	4347-4352	6mer	-19.100	-12.903	0.532	0.625	0.990	0.998	0.759
hsa-let-7a-5p	*RB1*	3612-3645	0.703	3'UTR	3639-3644	7mer-A1	-20.200	-0.817	0.428	0.178	0.969	1	0.362
hsa-miR-142-3p	*RB1*	1285-1311	0.667	CDS	1305-1310	offset-6mer	-21.400	-7.625	0.479	0.488	0.999	1.000	0.402
hsa-let-7a-5p	*RB1*	2477-2502	0.662	CDS	2496-2501	offset-6mer	-20.000	-4.112	0.472	0.743	0.968	0.996	0.829
hsa-miR-25-3p	*RB1*	4167-4185	0.604	3'UTR	4180-4185	offset-6mer	-17.000	-7.796	0.415	0.291	0.429	0.812	0.667
hsa-miR-25-3p	*RB1*	3381-3416	0.559	3'UTR	3411-3416	6mer	-13.600	-0.088	0.574	0.646	0.719	0.999	0.235

* Start and end position of the target region (site) predicted to be bound by miRNA; [a] Probability of the site being an miRNA binding site as predicted by our nonlinear logistic model; [b] start and end position of the target sub-region complementary to the miRNA seed (i.e. positions 2-7/8 of the miRNA); [c] 6mer, offset 6mer, 7mer-A1, 7mer-m8, and 8mer seed sites; [d] A measure of stability for miRNA:target hybrid as computed by RNAhybrid; [e] A measure of the total energy change of the hybridization; [f] A measure of structural accessibility as computed by the average probability of a nucleotide being single-stranded (i.e., unpaired) for the nucleotides in the predicted binding site; [g] A measure of structural accessibility as computed by the average of single-stranded probabilities of the nucleotides in the target sub-region complementary to the miRNA seed; [h] Conservation score by the PhastCons program for the binding site; [i] Conservation score by the PhastCons program for the target sub-region complementary to the miRNA seed and [j] Relative starting location of the predicted binding site along the length of the sequence (e.g., for 3″ UTR, 0 indicates the 5″ end of the UTR, and 1 corresponds to the 3″ end).

Supplementary Table S2B. miRNA binding *'seedless'* regions identified in *TP53* gene.

miRNA	Gene	Site Position*	LogitProb[a]	Region	ΔG_{hybrid}[b]	ΔG_{total}[c]	Site Access[d]	Site Consv[e]	Site Location[f]
hsa-miR-205-5p	*TP53*	835-845	0.666	CDS	-20.700	-10.990	0.502	0.899	0.540
hsa-miR-130a-3p	*TP53*	1147-1175	0.546	CDS	-22.600	-3.107	0.511	0.788	0.804
hsa-miR-142-3p	*TP53*	835-851	0.576	CDS	-17	-6.646	0.515	0.923	0.540
hsa-miR-223-3p	*TP53*	920-935	0.538	CDS	-19.300	-5.720	0.521	0.938	0.612
hsa-miR-130a-3p	*TP53*	635-645	0.508	CDS	-17.500	-9.863	0.525	0.250	0.371
hsa-let-7a-5p	*TP53*	1340-1359	0.506	CDS	-15.600	-1.373	0.526	0.479	0.967
hsa-miR-16-5p	*TP53*	1057-1073	0.533	CDS	-17.800	-6.503	0.533	0.931	0.728
hsa-let-7a-5p	*TP53*	1026-1046	0.514	CDS	-15.300	3.662	0.534	0.820	0.701
hsa-miR-205-5p	*TP53*	1025-1040	0.688	CDS	-24.500	-12.477	0.537	0.997	0.701
hsa-miR-22-3p	*TP53*	1012-1026	0.530	CDS	-16	-4.737	0.537	0.742	0.690
hsa-miR-142-3p	*TP53*	1009-1032	0.519	CDS	-15.100	-1.908	0.538	0.838	0.687
hsa-miR-21-5p	*TP53*	1010-1023	0.635	CDS	-15.200	-3.538	0.542	0.723	0.688
hsa-let-7a-5p	*TP53*	312-330	0.628	CDS	-19.200	-10.285	0.548	0.002	0.097
hsa-miR-15b-5p	*TP53*	1138-1149	0.501	CDS	-18.100	-11.028	0.558	0.524	0.796
hsa-miR-200c-3p	*TP53*	1009-1023	0.707	CDS	-21.800	-10.288	0.559	0.742	0.687
hsa-miR-142-3p	*TP53*	1152-1176	0.629	CDS	-21.200	-6.168	0.562	0.927	0.808
hsa-miR-22-3p	*TP53*	1012-1029	0.520	CDS	-16.800	-5.746	0.564	0.785	0.690
hsa-miR-21-5p	*TP53*	1010-1026	0.635	CDS	-15.900	-4.153	0.575	0.772	0.688
hsa-miR-25-3p	*TP53*	309-315	0.664	CDS	-16.200	-9.594	0.581	0.000	0.095
hsa-miR-200c-3p	*TP53*	1009-1026	0.716	CDS	-23.100	-11.503	0.587	0.785	0.687
hsa-miR-21-5p	*TP53*	1010-1029	0.637	CDS	-16.600	-5.061	0.593	0.806	0.688
hsa-miR-205-5p	*TP53*	1025-1031	0.787	CDS	-17.500	-10.665	0.602	0.997	0.701
hsa-let-7a-5p	*TP53*	312-328	0.681	CDS	-15.700	-10.053	0.610	0.002	0.097
hsa-let-7a-5p	*TP53*	1180-1195	0.611	CDS	-18.800	-9.278	0.611	0.884	0.832
hsa-miR-200c-3p	*TP53*	1009-1021	0.593	CDS	-16.100	-5.376	0.642	0.702	0.687
hsa-miR-21-5p	*TP53*	1255-1260	0.501	CDS	-11.200	-5.966	0.663	0.457	0.895
hsa-miR-31-5p	*TP53*	1158-1177	0.755	CDS	-21.800	-16.974	0.667	0.912	0.813

hsa-miR-93-5p	*TP53*	1166-1174	0.864	CDS	-15.900	-15.316	0.714	0.959	0.820
hsa-let-7a-5p	*TP53*	1161-1177	0.831	CDS	-20.100	-19.630	0.767	0.900	0.816
hsa-miR-200c-3p	*TP53*	1009-1018	0.715	CDS	-15.900	-11.206	0.777	0.618	0.687
hsa-let-7a-5p	*TP53*	1161-1179	0.808	CDS	-22.300	-21.904	0.783	0.910	0.816
hsa-miR-93-5p	*TP53*	1166-1186	0.848	CDS	-18.400	-18.018	0.805	0.981	0.820
hsa-miR-200c-3p	*TP53*	1177-1190	0.566	CDS	-15	-8.087	0.823	0.998	0.829
hsa-miR-200c-3p	*TP53*	384-396	0.617	CDS	-17.500	-6.698	0.402	0.000	0.158
hsa-miR-205-5p	*TP53*	1025-1036	0.690	CDS	-24.200	-11.901	0.403	0.996	0.701
hsa-miR-130a-3p	*TP53*	672-682	0.535	CDS	-19.800	-10.837	0.404	0.998	0.402
hsa-miR-205-5p	*TP53*	390-404	0.501	CDS	-15.600	-4.991	0.404	0	0.163
hsa-let-7a-5p	*TP53*	617-642	0.581	CDS	-22.100	-6.195	0.407	0.593	0.355
hsa-miR-93-5p	*TP53*	850-866	0.695	CDS	-17.100	-7.102	0.410	0.864	0.552
hsa-miR-93-5p	*TP53*	1039-1055	0.519	CDS	-20.800	-4.274	0.411	0.608	0.712
hsa-miR-16-5p	*TP53*	840-864	0.642	CDS	-18.700	-0.741	0.413	0.931	0.544
hsa-miR-15b-5p	*TP53*	840-864	0.592	CDS	-16.900	1.059	0.413	0.931	0.544
hsa-let-7a-5p	*TP53*	903-922	0.504	CDS	-16.900	3.803	0.417	1.000	0.597
hsa-miR-31-5p	*TP53*	606-616	0.535	CDS	-15.400	-6.172	0.418	0.990	0.346
hsa-miR-200c-3p	*TP53*	384-400	0.532	CDS	-17.600	-3.543	0.419	0.000	0.158
hsa-miR-223-3p	*TP53*	859-870	0.727	CDS	-16.200	-6.746	0.421	0.803	0.560
hsa-miR-205-5p	*TP53*	1025-1034	0.634	CDS	-18.400	-5.023	0.422	0.996	0.701
hsa-miR-200c-3p	*TP53*	548-568	0.540	CDS	-20.800	-2.929	0.423	0.994	0.297
hsa-miR-205-5p	*TP53*	835-863	0.632	CDS	-22.800	-2.410	0.424	0.911	0.540
hsa-miR-93-5p	*TP53*	707-727	0.511	CDS	-21.100	-2.739	0.430	0.880	0.431
hsa-miR-93-5p	*TP53*	1133-1149	0.627	CDS	-22.600	-15.369	0.433	0.530	0.792
hsa-miR-16-5p	*TP53*	1133-1149	0.511	CDS	-21.100	-13.869	0.433	0.530	0.792
hsa-miR-223-3p	*TP53*	1409-1424	0.642	CDS	-16.500	-9.699	0.436	0.049	1.025
hsa-miR-93-5p	*TP53*	557-572	0.548	CDS	-21.600	-7.769	0.436	0.993	0.305
hsa-miR-93-5p	*TP53*	850-868	0.674	CDS	-19.300	-8.099	0.437	0.878	0.552
hsa-miR-200c-3p	*TP53*	384-402	0.548	CDS	-20	-4.954	0.437	0.000	0.158
hsa-miR-25-3p	*TP53*	1015-1038	0.551	CDS	-20	-6.818	0.438	0.904	0.692
hsa-miR-16-5p	*TP53*	840-859	0.631	CDS	-18.100	-2.110	0.439	0.969	0.544
hsa-miR-205-5p	*TP53*	835-848	0.755	CDS	-23.700	-13.153	0.442	0.907	0.540

hsa-miR-142-3p	*TP53*	835-848	0.617	CDS	-15.400	-4.853	0.442	0.907	0.540
hsa-miR-93-5p	*TP53*	1133-1146	0.568	CDS	-19.300	-12.494	0.446	0.637	0.792
hsa-miR-93-5p	*TP53*	1354-1379	0.542	CDS	-15.800	-0.012	0.449	0.693	0.979
hsa-miR-21-5p	*TP53*	887-899	0.548	CDS	-15.100	-2.312	0.450	1	0.584
hsa-miR-93-5p	*TP53*	956-971	0.532	CDS	-16.200	-6.461	0.455	0.952	0.642
hsa-miR-93-5p	*TP53*	1039-1062	0.572	CDS	-26.200	-9.048	0.462	0.702	0.712
hsa-miR-142-3p	*TP53*	835-856	0.577	CDS	-19.500	-2.881	0.463	0.938	0.540
hsa-let-7a-5p	*TP53*	626-640	0.564	CDS	-16.400	-6.098	0.466	0.527	0.363
hsa-let-7a-5p	*TP53*	1409-1427	0.627	CDS	-17.100	-9.534	0.474	0.042	1.025
hsa-let-7a-5p	*TP53*	626-638	0.555	CDS	-15	-4.709	0.477	0.608	0.363
hsa-miR-200c-3p	*TP53*	1009-1035	0.632	CDS	-24.400	-10.523	0.479	0.855	0.687
hsa-miR-25-3p	*TP53*	309-321	0.625	CDS	-17.200	-9.396	0.479	0.000	0.095
hsa-miR-205-5p	*TP53*	835-843	0.642	CDS	-16.400	-8.957	0.482	0.888	0.540
hsa-miR-205-5p	*TP53*	310-322	0.579	CDS	-17.100	-8.965	0.482	0.000	0.096
hsa-miR-130a-3p	*TP53*	1401-1422	0.516	CDS	-16.900	-8.458	0.482	0.036	1.019
hsa-miR-93-5p	*TP53*	1354-1377	0.506	CDS	-15.200	3.774	0.484	0.676	0.979
hsa-miR-15b-5p	*TP53*	553-571	0.500	CDS	-17.500	-3.685	0.484	0.994	0.301
hsa-miR-22-3p	*TP53*	1012-1023	0.543	CDS	-15	-3.822	0.489	0.677	0.690
hsa-miR-205-5p	*TP53*	1025-1049	0.515	CDS	-28.600	-2.910	0.489	0.732	0.701
hsa-miR-205-5p	*TP53*	1397-1418	0.534	CDS	-17.600	-10.818	0.490	0.029	1.015
hsa-miR-93-5p	*TP53*	353-368	0.528	CDS	-17.800	-7.914	0.492	0.027	0.132
hsa-miR-200c-3p	*TP53*	384-393	0.613	CDS	-16.900	-6.214	0.498	4,00E-04	0.158
hsa-miR-200c-3p	*TP53*	1900-1917	0.564	3'UTR	-16.600	-7.381	0.808	0.002	0.413
hsa-let-7a-5p	*TP53*	1787-1807	0.644	3'UTR	-15.300	-11.395	0.749	0.438	0.324
hsa-miR-93-5p	*TP53*	1902-1929	0.508	3'UTR	-15.700	-1.373	0.732	0.001	0.415
hsa-let-7a-5p	*TP53*	1829-1844	0.639	3'UTR	-16.400	-12.640	0.696	0.001	0.357
hsa-let-7a-5p	*TP53*	1786-1809	0.648	3'UTR	-21.200	-14.881	0.670	0.384	0.323
hsa-let-7a-5p	*TP53*	1723-1739	0.569	3'UTR	-15.200	-10.208	0.665	0.006	0.273
hsa-miR-130a-3p	*TP53*	2563-2580	0.559	3'UTR	-16	-5.022	0.657	0.019	0.939
hsa-miR-93-5p	*TP53*	1902-1922	0.510	3'UTR	-15.200	-0.872	0.647	0.001	0.415
hsa-miR-21-5p	*TP53*	2502-2521	0.559	3'UTR	-16.200	-6.312	0.622	0.578	0.891

hsa-miR-31-5p	*TP53*	1822-1838	0.535	3'UTR	-20.400	-8.857	0.598	0.001	0.351
hsa-miR-31-5p	*TP53*	1822-1844	0.643	3'UTR	-24.500	-12.954	0.597	0.001	0.351
hsa-miR-31-5p	*TP53*	2524-2545	0.641	3'UTR	-15.600	-6.032	0.596	0.683	0.908
hsa-miR-21-5p	*TP53*	2502-2526	0.566	3'UTR	-20.700	-10.433	0.582	0.643	0.891
hsa-miR-16-5p	*TP53*	2501-2522	0.575	3'UTR	-17.700	-10.176	0.572	0.566	0.890
hsa-miR-22-3p	*TP53*	2505-2526	0.547	3'UTR	-15.300	-5.430	0.564	0.731	0.893
hsa-let-7a-5p	*TP53*	2525-2541	0.559	3'UTR	-15.300	-7.543	0.563	0.603	0.909
hsa-miR-200c-3p	*TP53*	2506-2523	0.611	3'UTR	-15	-8.168	0.562	0.737	0.894
hsa-miR-31-5p	*TP53*	1822-1836	0.513	3'UTR	-18.600	-7.052	0.546	0.001	0.351
hsa-miR-31-5p	*TP53*	1822-1840	0.588	3'UTR	-23.500	-11.956	0.543	0.001	0.351
hsa-miR-130a-3p	*TP53*	2508-2528	0.612	3'UTR	-16.400	-5.907	0.537	0.860	0.895
hsa-miR-130a-3p	*TP53*	2508-2523	0.652	3'UTR	-16.100	-9.215	0.530	0.828	0.895
hsa-miR-130a-3p	*TP53*	2508-2537	0.515	3'UTR	-16.100	-4.489	0.527	0.764	0.895
hsa-miR-93-5p	*TP53*	1843-1851	0.550	3'UTR	-16.200	-6.998	0.488	0	0.368
hsa-miR-93-5p	*TP53*	2519-2539	0.606	3'UTR	-22.300	-10.560	0.474	0.675	0.904
hsa-miR-31-5p	*TP53*	2525-2534	0.615	3'UTR	-15.200	-7.426	0.459	0.869	0.909
hsa-miR-93-5p	*TP53*	2519-2537	0.600	3'UTR	-20.400	-8.907	0.449	0.719	0.904
hsa-miR-31-5p	*TP53*	2140-2161	0.561	3'UTR	-14.100	-7.042	0.443	0.011	0.603
hsa-miR-31-5p	*TP53*	2491-2511	0.507	3'UTR	-21.200	-11.095	0.436	0.127	0.882
hsa-miR-93-5p	*TP53*	2518-2528	0.644	3'UTR	-19.700	-9.443	0.424	0.879	0.903
hsa-miR-223-3p	*TP53*	1675-1690	0.575	3'UTR	-19.900	-4.840	0.418	0.000	0.235
hsa-miR-142-3p	*TP53*	1632-1645	0.522	3'UTR	-20.200	-4.869	0.413	0.004	0.201
hsa-miR-223-3p	*TP53*	1675-1687	0.598	3'UTR	-16.600	-5.940	0.404	0.000	0.235
hsa-miR-205-5p	*TP53*	206-223	0.523	5'UTR	-16.700	4.951	0.557	0.029	1.046
hsa-miR-130a-3p	*TP53*	16-30	0.542	5'UTR	-17.200	-4.262	0.500	0.943	0.081
hsa-let-7a-5p	*TP53*	13-25	0.583	5'UTR	-15.400	-8.307	0.497	1.000	0.066
hsa-let-7a-5p	*TP53*	13-29	0.582	5'UTR	-19.200	-8.139	0.495	0.969	0.066
hsa-miR-25-3p	*TP53*	13-30	0.540	5'UTR	-17.300	-3.805	0.481	0.953	0.066
hsa-miR-31-5p	*TP53*	209-228	0.557	5'UTR	-18.300	-1.262	0.467	0.039	1.061
hsa-let-7a-5p	*TP53*	13-31	0.605	5'UTR	-26.700	-12.729	0.465	0.944	0.066
hsa-miR-15b-5p	*TP53*	07-30	0.537	5'UTR	-16.100	-0.484	0.458	0.957	0.046
hsa-miR-31-5p	*TP53*	12-28	0.612	5'UTR	-21	-8.837	0.458	0.995	0.051

hsa-miR-22-3p	*TP53*	199-218	0.534	5'UTR	-18.100	2.474	0.451	0.281	1.010
hsa-miR-93-5p	*TP53*	127-142	0.634	5'UTR	-17.300	-5.357	0.437	0.466	0.645
hsa-miR-200c-3p	*TP53*	125-139	0.519	5'UTR	-15.800	3.417	0.433	0.310	0.635
hsa-miR-31-5p	*TP53*	10-30	0.615	5'UTR	-26.100	-9.685	0.427	0.951	0.051
hsa-miR-200c-3p	*TP53*	128-146	0.579	5'UTR	-18.000	-1.580	0.409	0.581	0.650
hsa-miR-25-3p	*TP53*	84-100	0.577	5'UTR	-15.900	-3.798	0.406	0.228	0.426
hsa-miR-15b-5p	*TP53*	221-235	0.672	5'UTR	-17.300	-6.940	0.403	0.234	1.122

* Start and end position of the target region (site) predicted to be bound by miRNA; [a] Probability of the site being an miRNA binding site as predicted by our nonlinear logistic model; [b] A measure of stability for miRNA:target hybrid as computed by RNAhybrid; [c] A measure of the total energy change of the hybridization; [d] A measure of structural accessibility as computed by the average probability of a nucleotide being single-stranded (i.e., unpaired) for the nucleotides in the predicted binding site; [e] Conservation score by the PhastCons program for the binding site; [j] Relative starting location of the predicted binding site along the length of the sequence (e.g., for 3″ UTR, 0 indicates the 5″ end of the UTR, and 1 corresponds to the 3″ end).

Supplementary Table S2C. miRNA binding *'seedless'* regions identified in *RB1* gene.

miRNA	Gene	Site Position	LogitProb†	Region	ΔG_{hybrid}	ΔG_{total}*	Site_Access*	Site Consv*	Site Location*
hsa-miR-130a-3p	*RB1*	2529-2537	0.917	CDS	-17.100	-11.446	0.708	1.000	0.848
hsa-miR-31-5p	*RB1*	4704-4721	0.912	3'UTR	-20.100	-17.244	0.651	1.000	0.963
hsa-let-7a-5p	*RB1*	4686-4712	0.911	3'UTR	-22.100	-17.127	0.608	0.999	0.953
hsa-miR-31-5p	*RB1*	4704-4719	0.899	3'UTR	-18.700	-16.076	0.627	1000	0.963
hsa-miR-31-5p	*RB1*	4704-4717	0.898	3'UTR	-17.200	-14.545	0.672	1.000	0.963
hsa-let-7a-5p	*RB1*	4686-4719	0.896	3'UTR	-20.700	-14.420	0.573	1.000	0.953
hsa-miR-130a-3p	*RB1*	2529-2534	0.892	CDS	-15.900	-10.778	0.646	1.000	0.848
hsa-miR-142-3p	*RB1*	2002-2026	0.883	CDS	-18.500	-12.601	0.692	0.847	0.659
hsa-let-7a-5p	*RB1*	562-571	0.878	CDS	-15.500	-14.118	0.813	0.957	0.142
hsa-miR-200c-3p	*RB1*	3398-3414	0.878	3'UTR	-16.300	-14.615	0.846	0.809	0.245
hsa-miR-93-5p	*RB1*	2496-2518	0.863	CDS	-18.900	-14.159	0.741	0.998	0.836
hsa-miR-205-5p	*RB1*	1997-2016	0.861	CDS	-16.900	-10.178	0.715	0.997	0.657
hsa-miR-93-5p	*RB1*	4502-4513	0.860	3'UTR	-21.200	-17.937	0.510	0.891	0.852
hsa-miR-21-5p	*RB1*	579-608	0.859	CDS	-19.800	-13.221	0.582	0.999	0.148
hsa-miR-31-5p	*RB1*	4704-4739	0.857	3'UTR	-17.100	-11.413	0.501	0.997	0.963
hsa-miR-142-3p	*RB1*	1953-1972	0.854	CDS	-18.500	-10.406	0.665	0.987	0.641
hsa-miR-31-5p	*RB1*	4659-4676	0.854	3'UTR	-17.400	-11.832	0.614	0.993	0.938
hsa-miR-130a-3p	*RB1*	2767-2782	0.852	CDS	-16.400	-8.072	0.653	0.961	0.933
hsa-miR-223-3p	*RB1*	3583-3589	0.852	3'UTR	-11.700	-8.863	0.438	0.964	0.346
hsa-miR-223-3p	*RB1*	1784-1795	0.850	CDS	-17.400	-11.874	0.550	1000	0.581
hsa-miR-93-5p	*RB1*	4502-4517	0.850	3'UTR	-23.900	-20.873	0.555	0.771	0.852
hsa-miR-93-5p	*RB1*	725-738	0.849	CDS	-19.800	-16.717	0.628	0.733	0.201
hsa-miR-93-5p	*RB1*	4502-4511	0.848	3'UTR	-18.300	-14.488	0.471	0.939	0.852
hsa-miR-15b-5p	*RB1*	588-608	0.846	CDS	-17.500	-9.238	0.611	1000	0.151
hsa-miR-93-5p	*RB1*	4702-4719	0.846	3'UTR	-10.900	-8.169	0.658	1000	0.962
hsa-miR-93-5p	*RB1*	1232-1247	0.843	CDS	-15.600	-12.313	0.719	0.923	0.382
hsa-miR-130a-3p	*RB1*	4658-4680	0.842	3'UTR	-18.700	-10.840	0.599	0.991	0.937
hsa-miR-223-3p	*RB1*	4675-4694	0.842	3'UTR	-16.100	-8.561	0.470	0.999	0.947
hsa-let-7a-5p	*RB1*	2763-2773	0.841	CDS	-16.400	-9.961	0.485	0.999	0.932

hsa-miR-223-3p	*RB1*	773-792	0.840	CDS	-18.900	-12.323	0.472	0.999	0.218
hsa-miR-31-5p	*RB1*	4680-4706	0.838	3'UTR	-15.800	-8.671	0.538	1.000	0.949
hsa-let-7a-5p	*RB1*	4653-4671	0.836	3'UTR	-14.900	-9.896	0.683	0.882	0.935
hsa-let-7a-5p	*RB1*	2763-2778	0.835	CDS	-16.600	-9.837	0.601	0.999	0.932
hsa-let-7a-5p	*RB1*	4400-4414	0.832	3'UTR	-10.900	-9.056	0.412	0.899	0.795
hsa-miR-142-3p	*RB1*	4672-4694	0.831	3'UTR	-16.900	-9.585	0.501	0.999	0.945
hsa-miR-142-3p	*RB1*	585-609	0.829	CDS	-17.500	-10.442	0.545	1.000	0.150
hsa-miR-130a-3p	*RB1*	4658-4678	0.826	3'UTR	-14.600	-9.145	0.622	0.990	0.937
hsa-miR-200c-3p	*RB1*	4652-4678	0.826	3'UTR	-16.200	-10.719	0.629	0.906	0.934
hsa-miR-200c-3p	*RB1*	4652-4680	0.825	3'UTR	-18.600	-10.703	0.611	0.912	0.934
hsa-miR-130a-3p	*RB1*	2209-2224	0.824	CDS	-18.600	-10.320	0.577	1000	0.733
hsa-miR-21-5p	*RB1*	1348-1368	0.824	CDS	-18.800	-11.239	0.480	0.999	0.424
hsa-miR-142-3p	*RB1*	4074-4090	0.821	3'UTR	-17.500	-10.351	0.506	0.787	0.616
hsa-miR-142-3p	*RB1*	1953-1970	0.820	CDS	-12.300	-3.732	0.733	0.986	0.641
hsa-miR-200c-3p	*RB1*	1953-1973	0.820	CDS	-15.300	-6.921	0.635	0.987	0.641
hsa-miR-31-5p	*RB1*	4322-4356	0.818	3'UTR	-22.900	-7.727	0.444	0.950	0.753
hsa-let-7a-5p	*RB1*	4724-4745	0.817	3'UTR	-14.500	-6.891	0.464	0.996	0.974
hsa-miR-16-5p	*RB1*	4270-4295	0.817	3'UTR	-16.400	-8.430	0.460	0.998	0.724
hsa-miR-16-5p	*RB1*	3317-3339	0.817	3'UTR	-16.100	-7.382	0.404	0.905	0.200
hsa-miR-205-5p	*RB1*	1685-1692	0.817	CDS	-16.400	-8.626	0.703	0.997	0.545
hsa-miR-93-5p	*RB1*	1232-1253	0.817	CDS	-16.300	-10.122	0.643	0.829	0.382
hsa-miR-205-5p	*RB1*	3850-3864	0.816	3'UTR	-17.200	-6.314	0.436	0.912	0.493
hsa-miR-130a-3p	*RB1*	4329-4350	0.815	3'UTR	-15.300	-6.192	0.430	0.938	0.756
hsa-miR-205-5p	*RB1*	2136-2149	0.815	CDS	-15.100	-7.402	0.513	0.926	0.707
hsa-miR-25-3p	*RB1*	966-981	0.815	CDS	-15.900	-7.580	0.592	0.999	0.287
hsa-miR-93-5p	*RB1*	2496-2512	0.813	CDS	-16.300	-11.509	0.705	0.997	0.836
hsa-miR-223-3p	*RB1*	773-789	0.812	CDS	-17.600	-9.791	0.498	0.999	0.218
hsa-miR-93-5p	*RB1*	1223-1238	0.812	CDS	-15.200	-10.852	0.725	0.824	0.379
hsa-miR-93-5p	*RB1*	2097-2117	0.811	CDS	-10.800	-4.291	0.619	1000	0.693
hsa-miR-142-3p	*RB1*	4300-4315	0.808	3'UTR	-16.900	-7.407	0.591	0.997	0.741
hsa-miR-200c-3p	*RB1*	4078-4093	0.808	3'UTR	-17.900	-7.169	0.522	0.979	0.618

hsa-let-7a-5p	*RB1*	3410-3431	0.807	3'UTR	-20.400	-15.626	0.616	0.454	0.251
hsa-miR-25-3p	*RB1*	1783-1797	0.807	CDS	-17.300	-8.636	0.527	1000	0.580
hsa-miR-22-3p	*RB1*	4073-4093	0.804	3'UTR	-19.900	-9.273	0.459	0.770	0.616
hsa-miR-31-5p	*RB1*	725-738	0.804	CDS	-17.100	-14.017	0.628	0.733	0.201
hsa-miR-31-5p	*RB1*	2133-2151	0.804	CDS	-22.600	-14.890	0.533	0.899	0.706
hsa-miR-142-3p	*RB1*	4325-4350	0.803	3'UTR	-16.700	-8.095	0.497	0.934	0.754
hsa-miR-16-5p	*RB1*	585-608	0.803	CDS	-16.300	-9.267	0.560	1000	0.150
hsa-miR-93-5p	*RB1*	2913-2925	0.803	CDS	-15.900	-11.693	0.522	0.949	0.986
hsa-let-7a-5p	*RB1*	1122-1145	0.802	CDS	-16.900	-11.110	0.531	0.993	0.343
hsa-miR-200c-3p	*RB1*	2521-2532	0.802	CDS	-15.800	-9.390	0.569	1000	0.845
hsa-miR-142-3p	*RB1*	4074-4093	0.800	3'UTR	-17.900	-7.394	0.481	0.807	0.616
hsa-miR-200c-3p	*RB1*	3613-3625	0.800	3'UTR	-15.300	-8.792	0.518	0.970	0.363
hsa-miR-15b-5p	*RB1*	1245-1256	0.799	CDS	-16.200	-11.129	0.558	0.764	0.387
hsa-miR-93-5p	*RB1*	3370-3382	0.799	3'UTR	-15.800	-11.245	0.573	0.283	0.229
hsa-miR-93-5p	*RB1*	3858-3875	0.799	3'UTR	-16.100	-12.674	0.546	0.761	0.498
hsa-miR-200c-3p	*RB1*	1953-1976	0.798	CDS	-16.600	-3.940	0.622	0.989	0.641
hsa-let-7a-5p	*RB1*	3410-3429	0.797	3'UTR	-18.400	-13.675	0.623	0.500	0.251
hsa-let-7a-5p	*RB1*	4724-4743	0.796	3'UTR	-11.800	-4.428	0.460	0.996	0.974
hsa-miR-142-3p	*RB1*	3603-3624	0.795	3'UTR	-16.600	-10.934	0.514	0.690	0.357
hsa-miR-22-3p	*RB1*	474-486	0.794	CDS	-19.100	-11.241	0.615	0.999	0.111
hsa-miR-93-5p	*RB1*	4666-4693	0.793	3'UTR	-15.500	-5.368	0.510	0.995	0.942
hsa-miR-15b-5p	*RB1*	720-739	0.792	CDS	-16.300	-12.693	0.654	0.813	0.199
hsa-miR-15b-5p	*RB1*	3409-3428	0.791	3'UTR	-16.900	-12.241	0.618	0.550	0.251
hsa-miR-31-5p	*RB1*	3128-3142	0.790	3'UTR	-17.400	-12.125	0.542	0.004	0.096
hsa-miR-130a-3p	*RB1*	722-733	0.789	CDS	-14.300	-11.270	0.763	0.689	0.199
hsa-miR-200c-3p	*RB1*	585-597	0.789	CDS	-15.400	-9.279	0.557	1.000	0.150
hsa-miR-16-5p	*RB1*	4736-4762	0.788	3'UTR	-12.900	-4.291	0.477	0.998	0.980
hsa-miR-16-5p	*RB1*	4310-4325	0.788	3'UTR	-15.600	-6.496	0.426	0.995	0.746
hsa-miR-130a-3p	*RB1*	3118-3140	0.787	3'UTR	-18.400	-12.682	0.519	0.041	0.091
hsa-let-7a-5p	*RB1*	4542-4554	0.786	3'UTR	-16.200	-10.299	0.530	0.977	0.874
hsa-miR-16-5p	*RB1*	4310-4332	0.786	3'UTR	-17.800	-6.907	0.432	0.931	0.746
hsa-let-7a-5p	*RB1*	3899-3921	0.785	3'UTR	-16.600	-5.382	0.452	0.961	0.520

hsa-miR-15b-5p	*RB1*	326-342	0.785	CDS	-18.900	-7.844	0.520	0.999	0.057
hsa-let-7a-5p	*RB1*	582-613	0.784	CDS	-17.500	-10.650	0.522	0.999	0.149
hsa-miR-200c-3p	*RB1*	4360-4395	0.784	3'UTR	-17.800	-6.654	0.403	0.938	0.774
hsa-miR-200c-3p	*RB1*	891-901	0.784	CDS	-16.200	-5.948	0.501	0.997	0.260
hsa-let-7a-5p	*RB1*	2528-2551	0.783	CDS	-16.100	-7.441	0.560	0.999	0.848
hsa-miR-31-5p	*RB1*	3584-3604	0.783	3'UTR	-17.600	-4.768	0.404	0.675	0.347
hsa-let-7a-5p	*RB1*	2528-2557	0.782	CDS	-16.800	-8.133	0.598	0.999	0.848
hsa-let-7a-5p	*RB1*	1883-1901	0.782	CDS	-15.100	-8.688	0.479	0.995	0.616
hsa-miR-16-5p	*RB1*	704-729	0.782	CDS	-15.300	-8.586	0.564	0.904	0.193
hsa-let-7a-5p	*RB1*	4644-4664	0.780	3'UTR	-17.500	-8.263	0.630	0.774	0.930
hsa-miR-22-3p	*RB1*	2014-2031	0.779	CDS	-15.400	-5.093	0.471	0.788	0.663
hsa-miR-16-5p	*RB1*	3411-3428	0.778	3'UTR	-15.900	-10.661	0.596	0.500	0.252
hsa-miR-200c-3p	*RB1*	4360-4393	0.778	3'UTR	-15.100	-5.847	0.421	0.934	0.774
hsa-let-7a-5p	*RB1*	3584-3604	0.776	3'UTR	-16.900	-4.068	0.404	0.675	0.347
hsa-miR-200c-3p	*RB1*	4490-4507	0.776	3'UTR	-18.400	-13.994	0.590	0.420	0.845
hsa-miR-25-3p	*RB1*	2371-2391	0.776	CDS	-17.800	-9.103	0.463	0.998	0.791
hsa-miR-200c-3p	*RB1*	2521-2540	0.775	CDS	-16.400	-8.935	0.603	1000	0.845
hsa-miR-22-3p	*RB1*	4304-4326	0.774	3'UTR	-19.700	-5.308	0.434	0.995	0.743
hsa-miR-25-3p	*RB1*	2371-2395	0.774	CDS	-19.600	-8.294	0.412	0.999	0.791
hsa-miR-130a-3p	*RB1*	2491-2507	0.773	CDS	-17.800	-10.470	0.664	0.998	0.834
hsa-miR-93-5p	*RB1*	1847-1872	0.773	CDS	-19.500	-4.158	0.408	0.998	0.603
hsa-miR-130a-3p	*RB1*	4077-4094	0.772	3'UTR	-16.200	-5.492	0.570	0.891	0.618
hsa-miR-223-3p	*RB1*	1784-1807	0.772	CDS	-18.300	-7.358	0.445	0.999	0.581
hsa-miR-93-5p	*RB1*	3456-3473	0.772	3'UTR	-17.400	-11.863	0.572	0.119	0.277
hsa-let-7a-5p	*RB1*	1294-1314	0.771	CDS	-16.800	-4.784	0.414	0.985	0.405
hsa-miR-142-3p	*RB1*	1205-1226	0.771	CDS	-20.700	-10.878	0.482	0.850	0.373
hsa-miR-21-5p	*RB1*	1348-1366	0.771	CDS	-15.100	-5.350	0.471	0.998	0.424
hsa-miR-25-3p	*RB1*	491-502	0.771	CDS	-18.600	-13.270	0.462	0.999	0.117
hsa-miR-31-5p	*RB1*	4644-4662	0.771	3'UTR	-17.300	-7.854	0.598	0.750	0.930
hsa-miR-93-5p	*RB1*	1847-1868	0.771	CDS	-19.100	-4.499	0.450	0.998	0.603
hsa-miR-16-5p	*RB1*	1617-1633	0.770	CDS	-21.500	-11.348	0.460	0.939	0.521

hsa-miR-22-3p	*RB1*	4073-4097	0.770	3'UTR	-21.600	-6.282	0.431	0.720	0.616
hsa-let-7a-5p	*RB1*	4075-4093	0.769	3'UTR	-15.400	-4.868	0.503	0.848	0.617
hsa-miR-130a-3p	*RB1*	3968-3980	0.769	3'UTR	-16.500	-13.304	0.714	0.356	0.558
hsa-miR-223-3p	*RB1*	4307-4316	0.768	3'UTR	-15.400	-3.560	0.478	0.995	0.744
hsa-let-7a-5p	*RB1*	4542-4556	0.767	3'UTR	-20.100	-10.247	0.465	0.949	0.874
hsa-miR-130a-3p	*RB1*	3968-3973	0.767	3'UTR	-15.300	-11.859	0.644	0.473	0.558
hsa-miR-15b-5p	*RB1*	3115-3143	0.766	3'UTR	-18.100	-10.621	0.529	0.100	0.089
hsa-miR-200c-3p	*RB1*	2140-2150	0.766	CDS	-19.500	-9.771	0.641	0.908	0.708
hsa-miR-15b-5p	*RB1*	3115-3133	0.765	3'UTR	-16.900	-12.705	0.587	0.151	0.089
hsa-miR-25-3p	*RB1*	2371-2385	0.765	CDS	-16.300	-8.312	0.474	0.998	0.791
hsa-let-7a-5p	*RB1*	1122-1143	0.764	CDS	-12.400	-6.512	0.513	0.993	0.343
hsa-let-7a-5p	*RB1*	1049-1061	0.763	CDS	-12.900	-8.545	0.588	1000	0.317
hsa-miR-205-5p	*RB1*	2558-2565	0.763	CDS	-15.600	-8.224	0.444	0.999	0.858
hsa-miR-223-3p	*RB1*	576-584	0.761	CDS	-12.300	-7.623	0.576	0.999	0.147
hsa-miR-22-3p	*RB1*	508-525	0.761	CDS	-16.900	-8.978	0.449	0.997	0.123
hsa-miR-31-5p	*RB1*	339-350	0.761	CDS	-16.300	-7.200	0.405	1	0.062
hsa-miR-93-5p	*RB1*	1056-1069	0.761	CDS	-15.100	-8.541	0.420	1000	0.319
hsa-miR-223-3p	*RB1*	4443-4461	0.760	3'UTR	-17.100	-6.904	0.402	0.777	0.819
hsa-miR-22-3p	*RB1*	1955-1974	0.760	CDS	-18.800	-9.964	0.616	0.997	0.642
hsa-miR-25-3p	*RB1*	491-506	0.760	CDS	-20.300	-13.842	0.432	0.999	0.117
hsa-miR-15b-5p	*RB1*	3115-3131	0.759	3'UTR	-15.300	-11.698	0.586	0.168	0.089
hsa-miR-16-5p	*RB1*	704-739	0.759	CDS	-16.300	-8.274	0.569	0.892	0.193
hsa-miR-21-5p	*RB1*	3127-3143	0.759	3'UTR	-15.800	-9.819	0.544	0.004	0.096
hsa-miR-31-5p	*RB1*	1778-1794	0.759	CDS	-17.700	-6.670	0.515	1000	0.578
hsa-miR-93-5p	*RB1*	2386-2413	0.759	CDS	-15.400	-3.874	0.433	0.956	0.797
hsa-miR-205-5p	*RB1*	1280-1295	0.758	CDS	-17.100	-9.382	0.433	1000	0.400
hsa-miR-93-5p	*RB1*	4261-4280	0.758	3'UTR	-15.600	-7.220	0.430	1	0.719
hsa-let-7a-5p	*RB1*	3410-3426	0.757	3'UTR	-15.600	-10.896	0.582	0.588	0.251
hsa-miR-223-3p	*RB1*	4075-4093	0.757	3'UTR	-15.200	-4.668	0.503	0.848	0.617
hsa-let-7a-5p	*RB1*	2344-2364	0.755	CDS	-18.700	-4.799	0.409	0.956	0.781
hsa-miR-130a-3p	*RB1*	2209-2232	0.755	CDS	-19.100	-1.589	0.515	0.984	0.733
hsa-miR-223-3p	*RB1*	3415-3429	0.755	3'UTR	-16.600	-12.111	0.599	0.333	0.254

hsa-miR-31-5p	*RB1*	3383-3407	0.755	3'UTR	-17.200	-5.644	0.541	0.621	0.236
hsa-miR-93-5p	*RB1*	1771-1791	0.755	CDS	-16.800	-7.883	0.425	1000	0.576
hsa-miR-31-5p	*RB1*	2086-2102	0.754	CDS	-15.400	-9.036	0.637	0.796	0.689
hsa-miR-93-5p	*RB1*	2883-2898	0.754	CDS	-16.800	-4.456	0.453	0.994	0.975
hsa-miR-16-5p	*RB1*	3118-3143	0.753	3'UTR	-15.200	-8.595	0.546	0.036	0.091
hsa-miR-21-5p	*RB1*	692-709	0.753	CDS	-17.500	-2.897	0.445	0.993	0.189
hsa-miR-21-5p	*RB1*	704-739	0.752	CDS	-18.500	-10.474	0.569	0.892	0.193
hsa-miR-15b-5p	*RB1*	488-526	0.751	CDS	-17.400	-6.698	0.434	0.980	0.116
hsa-miR-205-5p	*RB1*	4297-4320	0.749	3'UTR	-15.700	-3.248	0.591	0.998	0.739
hsa-miR-25-3p	*RB1*	2445-2456	0.749	CDS	-15.400	-5.139	0.509	1	0.818
hsa-miR-31-5p	*RB1*	605-613	0.749	CDS	-18.200	-10.253	0.472	0.997	0.158
hsa-miR-16-5p	*RB1*	4643-4669	0.748	3'UTR	-15.700	-4.893	0.604	0.783	0.929
hsa-miR-93-5p	*RB1*	583-607	0.748	CDS	-16.700	-9.956	0.575	1000	0.150
hsa-miR-142-3p	*RB1*	769-784	0.747	CDS	-16.100	-8.685	0.429	0.999	0.216
hsa-miR-200c-3p	*RB1*	4078-4097	0.747	3'UTR	-18.100	-2.677	0.473	0.874	0.618
hsa-miR-21-5p	*RB1*	1790-1808	0.747	CDS	-15.500	-6.582	0.432	0.999	0.583
hsa-miR-21-5p	*RB1*	692-713	0.747	CDS	-18.100	-2.166	0.430	0.993	0.189
hsa-miR-21-5p	*RB1*	482-502	0.747	CDS	-17.400	-5.651	0.411	0.999	0.113
hsa-let-7a-5p	*RB1*	3960-3978	0.746	3'UTR	-16.200	-13.257	0.666	0.342	0.554
hsa-miR-130a-3p	*RB1*	4415-4432	0.746	3'UTR	-16.400	-6.311	0.439	0.458	0.804
hsa-miR-200c-3p	*RB1*	4490-4505	0.746	3'UTR	-16.200	-12.685	0.593	0.347	0.845
hsa-miR-205-5p	*RB1*	1685-1715	0.746	CDS	-16.600	-5.737	0.455	0.999	0.545
hsa-miR-223-3p	*RB1*	3854-3874	0.746	3'UTR	-15.600	-5.290	0.451	0.842	0.495
hsa-miR-93-5p	*RB1*	1248-1261	0.746	CDS	-16.700	-9.155	0.488	0.746	0.388
hsa-let-7a-5p	*RB1*	325-343	0.745	CDS	-15.500	-3.901	0.512	1000	0.057
hsa-miR-130a-3p	*RB1*	546-570	0.745	CDS	-15.700	-2.087	0.441	0.982	0.136
hsa-miR-130a-3p	*RB1*	3176-3194	0.744	3'UTR	-19.100	-5.499	0.501	0.611	0.123
hsa-miR-31-5p	*RB1*	1778-1792	0.744	CDS	-15.900	-6.260	0.503	0.999	0.578
hsa-miR-31-5p	*RB1*	1689-1705	0.744	CDS	-15.200	-10.309	0.452	1000	0.546
hsa-miR-130a-3p	*RB1*	3390-3414	0.743	3'UTR	-15.100	-1.810	0.632	0.705	0.240
hsa-miR-15b-5p	*RB1*	2265-2291	0.743	CDS	-23.600	-10.426	0.476	1000	0.753

hsa-miR-15b-5p	*RB1*	2265-2285	0.743	CDS	-22.500	-8.239	0.450	1000	0.753
hsa-miR-31-5p	*RB1*	1931-1951	0.742	CDS	-17.600	-3.629	0.466	0.983	0.633
hsa-let-7a-5p	*RB1*	3597-3617	0.741	3'UTR	-19.800	-12.237	0.538	0.495	0.354
hsa-miR-142-3p	*RB1*	4594-4613	0.741	3'UTR	-15.500	-5.291	0.404	0.937	0.902
hsa-miR-15b-5p	*RB1*	2265-2283	0.741	CDS	-19.300	-7.928	0.473	1	0.753
hsa-let-7a-5p	*RB1*	2020-2043	0.740	CDS	-19.300	-7.459	0.509	0.825	0.665
hsa-miR-223-3p	*RB1*	3415-3427	0.740	3'UTR	-15.900	-11.398	0.553	0.384	0.254
hsa-miR-93-5p	*RB1*	583-610	0.740	CDS	-16.700	-9.911	0.557	1000	0.150
hsa-let-7a-5p	*RB1*	1906-1924	0.739	CDS	-17.600	-7.454	0.521	0.996	0.624
hsa-miR-205-5p	*RB1*	2376-2409	0.738	CDS	-16.800	-4.715	0.491	0.984	0.793
hsa-miR-223-3p	*RB1*	4249-4262	0.738	3'UTR	-15.200	-4.431	0.444	1000	0.712
hsa-miR-200c-3p	*RB1*	2542-2560	0.737	CDS	-16.500	-7.127	0.596	0.998	0.853
hsa-miR-25-3p	*RB1*	1195-1211	0.737	CDS	-18.400	-9.316	0.414	0.984	0.369
hsa-miR-16-5p	*RB1*	504-526	0.735	CDS	-15.800	-6.110	0.421	0.966	0.121
hsa-miR-200c-3p	*RB1*	3760-3773	0.735	3'UTR	-18.300	-10.193	0.498	0.663	0.444
hsa-miR-142-3p	*RB1*	3603-3616	0.734	3'UTR	-15.900	-10.034	0.519	0.519	0.357
hsa-miR-31-5p	*RB1*	4071-4083	0.734	3'UTR	-19.600	-9.022	0.482	0.494	0.615
hsa-miR-93-5p	*RB1*	4072-4094	0.734	3'UTR	-15.100	-4.439	0.463	0.704	0.615
hsa-miR-93-5p	*RB1*	1771-1787	0.734	CDS	-15.400	-5.827	0.417	1000	0.576
hsa-let-7a-5p	*RB1*	3495-3523	0.731	3'UTR	-11.400	-1.521	0.419	0.791	0.298
hsa-miR-22-3p	*RB1*	699-738	0.731	CDS	-20.900	-8.015	0.509	0.903	0.191
hsa-miR-130a-3p	*RB1*	4642-4667	0.730	3'UTR	-15.500	-3.954	0.592	0.755	0.929
hsa-miR-130a-3p	*RB1*	4071-4090	0.730	3'UTR	-16.100	-5.234	0.434	0.671	0.615
hsa-miR-93-5p	*RB1*	1157-1175	0.730	CDS	-13.200	-2.917	0.403	0.947	0.356
hsa-miR-200c-3p	*RB1*	1953-1980	0.729	CDS	-16.800	0.195	0.563	0.991	0.641
hsa-miR-21-5p	*RB1*	2131-2152	0.729	CDS	-15.100	-6.424	0.514	0.907	0.705
hsa-miR-31-5p	*RB1*	3128-3139	0.729	3'UTR	-15.400	-10.354	0.436	0.005	0.096
hsa-miR-93-5p	*RB1*	1965-1976	0.728	CDS	-17.200	-4.059	0.419	0.999	0.645
hsa-miR-22-3p	*RB1*	2110-2136	0.727	CDS	-15.100	-4.077	0.435	0.963	0.698
hsa-miR-25-3p	*RB1*	1527-1541	0.727	CDS	-16.100	-2.878	0.410	1	0.488
hsa-miR-93-5p	*RB1*	2621-2635	0.726	CDS	-16.700	-5.039	0.466	0.907	0.881
hsa-miR-15b-5p	*RB1*	1245-1264	0.725	CDS	-16.300	-8.302	0.486	0.659	0.387

hsa-miR-93-5p	*RB1*	3174-3193	0.725	3'UTR	-16.700	-4.975	0.520	0.595	0.121
hsa-let-7a-5p	*RB1*	3597-3614	0.723	3'UTR	-17.300	-9.745	0.598	0.418	0.354
hsa-miR-130a-3p	*RB1*	1616-1636	0.723	CDS	-23.900	-13.349	0.413	0.951	0.520
hsa-miR-15b-5p	*RB1*	488-506	0.723	CDS	-15.900	-8.912	0.408	0.999	0.116
hsa-miR-31-5p	*RB1*	481-495	0.723	CDS	-18.600	-10.070	0.450	1.000	0.113
hsa-miR-31-5p	*RB1*	2125-2147	0.722	CDS	-20.400	-1.937	0.489	0.913	0.703
hsa-miR-93-5p	*RB1*	3757-3772	0.722	3'UTR	-17.600	-9.883	0.448	0.529	0.442
hsa-let-7a-5p	*RB1*	3389-3405	0.721	3'UTR	-17.300	-4.982	0.523	0.543	0.240
hsa-let-7a-5p	*RB1*	1912-1940	0.721	CDS	-23.500	-5.665	0.472	0.977	0.626
hsa-miR-223-3p	*RB1*	4450-4470	0.721	3'UTR	-17.400	-7.869	0.504	0.538	0.823
hsa-miR-25-3p	*RB1*	2445-2465	0.719	CDS	-16.100	-7.374	0.573	1	0.818
hsa-miR-31-5p	*RB1*	3062-3075	0.718	3'UTR	-16.700	-13.797	0.597	0.077	0.060
hsa-let-7a-5p	*RB1*	691-715	0.717	CDS	-15.100	1.725	0.461	0.994	0.188
hsa-miR-130a-3p	*RB1*	3390-3419	0.717	3'UTR	-15.100	1.004	0.600	0.753	0.240
hsa-miR-31-5p	*RB1*	2473-2505	0.717	CDS	-19.800	1.294	0.450	0.975	0.828
hsa-miR-93-5p	*RB1*	1682-1697	0.716	CDS	-17.700	-8.893	0.479	0.994	0.544
hsa-miR-15b-5p	*RB1*	2265-2281	0.715	CDS	-15.300	-6.150	0.497	1	0.753
hsa-miR-200c-3p	*RB1*	914-930	0.715	CDS	-19.900	-7.796	0.545	1.000	0.268
hsa-miR-223-3p	*RB1*	3411-3425	0.715	3'UTR	-12.500	-7.230	0.557	0.600	0.252
hsa-miR-93-5p	*RB1*	328-348	0.714	CDS	-20.300	-6.365	0.441	1000	0.058
hsa-let-7a-5p	*RB1*	887-902	0.713	CDS	-17.800	-5.822	0.468	0.997	0.259
hsa-miR-142-3p	*RB1*	323-343	0.713	CDS	-14.200	-1.006	0.512	0.999	0.056
hsa-miR-130a-3p	*RB1*	4485-4505	0.712	3'UTR	-15.300	-12.104	0.620	0.278	0.842
hsa-miR-25-3p	*RB1*	2018-2033	0.712	CDS	-15.200	-9.630	0.622	0.766	0.665
hsa-miR-93-5p	*RB1*	1682-1702	0.712	CDS	-20.100	-11.296	0.565	0.995	0.544
hsa-let-7a-5p	*RB1*	2126-2146	0.711	CDS	-19.100	-1.328	0.485	0.905	0.703
hsa-miR-21-5p	*RB1*	3127-3136	0.711	3'UTR	-15.300	-7.819	0.540	0.006	0.096
hsa-miR-93-5p	*RB1*	412-427	0.711	CDS	-15.100	-7.548	0.404	0.991	0.088
hsa-miR-142-3p	*RB1*	549-571	0.709	CDS	-15.700	-1.508	0.507	0.980	0.137
hsa-miR-142-3p	*RB1*	2073-2100	0.709	CDS	-15.100	-4.927	0.454	0.831	0.684
hsa-miR-205-5p	*RB1*	767-792	0.709	CDS	-16.400	-5.492	0.435	0.999	0.216

hsa-let-7a-5p	*RB1*	481-495	0.708	CDS	-17.200	-8.670	0.450	1000	0.113
hsa-miR-15b-5p	*RB1*	1245-1269	0.708	CDS	-17.400	-10.267	0.538	0.548	0.387
hsa-miR-200c-3p	*RB1*	2285-2297	0.708	CDS	-15.900	-1.198	0.436	1000	0.760
hsa-miR-93-5p	*RB1*	1056-1072	0.707	CDS	-15.300	-2.558	0.405	1000	0.319
hsa-miR-15b-5p	*RB1*	625-636	0.705	CDS	-16.600	-10.520	0.484	0.995	0.165
hsa-miR-15b-5p	*RB1*	625-640	0.704	CDS	-16.800	-10.715	0.588	0.990	0.165
hsa-miR-93-5p	*RB1*	2204-2224	0.704	CDS	-21.400	-10.918	0.509	1.000	0.731
hsa-miR-93-5p	*RB1*	1518-1534	0.703	CDS	-16.400	-9.759	0.527	0.998	0.485
hsa-let-7a-5p	*RB1*	3015-3032	0.700	3'UTR	-21.400	-13.943	0.509	0	0.034
hsa-miR-22-3p	*RB1*	2283-2297	0.700	CDS	-15.400	0.354	0.423	0.999	0.760
hsa-miR-93-5p	*RB1*	1652-1664	0.700	CDS	-16.400	-11.807	0.452	0.959	0.533
hsa-miR-130a-3p	*RB1*	4642-4660	0.699	3'UTR	-15.400	-4.185	0.511	0.666	0.929
hsa-miR-200c-3p	*RB1*	3760-3781	0.699	3'UTR	-21.400	-12.192	0.487	0.575	0.444
hsa-miR-200c-3p	*RB1*	2849-2873	0.699	CDS	-22.900	-5.899	0.400	0.996	0.963
hsa-miR-93-5p	*RB1*	328-343	0.699	CDS	-16.100	-2.657	0.498	0.999	0.058
hsa-miR-93-5p	*RB1*	1989-2023	0.698	CDS	-15.700	-7.639	0.648	0.930	0.654
hsa-let-7a-5p	*RB1*	3834-3852	0.697	3'UTR	-12.600	-0.684	0.495	0.900	0.484
hsa-let-7a-5p	*RB1*	3375-3400	0.697	3'UTR	-13.200	-1.045	0.451	0.478	0.232
hsa-miR-93-5p	*RB1*	628-648	0.697	CDS	-16.600	-13.582	0.537	0.992	0.166
hsa-miR-93-5p	*RB1*	328-345	0.697	CDS	-18.900	-3.359	0.455	1000	0.058
hsa-miR-93-5p	*RB1*	1619-1640	0.697	CDS	-16.700	-5.464	0.429	0.953	0.521
hsa-miR-93-5p	*RB1*	2319-2348	0.697	CDS	-19.100	-4.287	0.403	0.963	0.773
hsa-let-7a-5p	*RB1*	2020-2050	0.695	CDS	-19.600	-7.748	0.523	0.815	0.665
hsa-miR-16-5p	*RB1*	4071-4097	0.695	3'UTR	-16.500	-1.095	0.400	0.667	0.615
hsa-miR-21-5p	*RB1*	4401-4429	0.695	3'UTR	-10.900	-3.008	0.400	0.639	0.796
hsa-miR-223-3p	*RB1*	683-701	0.694	CDS	-16.600	-2.385	0.499	0.999	0.186
hsa-miR-93-5p	*RB1*	711-732	0.693	CDS	-15.500	-8.784	0.589	0.830	0.196
hsa-let-7a-5p	*RB1*	3756-3772	0.692	3'UTR	-16.200	-8.167	0.426	0.503	0.441
hsa-miR-21-5p	*RB1*	4071-4084	0.692	3'UTR	-15.500	-4.978	0.517	0.530	0.615
hsa-miR-25-3p	*RB1*	2208-2233	0.692	CDS	-16.900	-3.659	0.484	0.986	0.733
hsa-miR-21-5p	*RB1*	2274-2296	0.691	CDS	-16.500	-1.124	0.461	1.000	0.756
hsa-miR-21-5p	*RB1*	502-526	0.691	CDS	-16.200	-4.253	0.427	0.969	0.121

hsa-miR-25-3p	*RB1*	586-610	0.690	CDS	-18.100	-6.217	0.538	1.000	0.151
hsa-miR-31-5p	*RB1*	2022-2043	0.690	CDS	-18.200	-6.301	0.471	0.819	0.666
hsa-miR-142-3p	*RB1*	1251-1282	0.688	CDS	-15.300	-6.634	0.594	0.694	0.389
hsa-miR-31-5p	*RB1*	2440-2474	0.687	CDS	-15.400	3.127	0.400	0.975	0.816
hsa-miR-93-5p	*RB1*	4437-4458	0.687	3'UTR	-16.700	-6.903	0.414	0.592	0.816
hsa-miR-31-5p	*RB1*	4250-4269	0.684	3'UTR	-15.900	-2.345	0.413	1.000	0.713
hsa-miR-142-3p	*RB1*	710-733	0.681	CDS	-10.700	-6.789	0.574	0.843	0.195
hsa-miR-25-3p	*RB1*	586-606	0.680	CDS	-16.600	-4.770	0.536	1000	0.151
hsa-miR-142-3p	*RB1*	1251-1288	0.679	CDS	-17.100	-7.087	0.594	0.742	0.389
hsa-miR-93-5p	*RB1*	683-701	0.679	CDS	-18.100	-3.885	0.499	0.999	0.186
hsa-miR-31-5p	*RB1*	605-636	0.678	CDS	-21.600	-4.605	0.419	0.982	0.158
hsa-let-7a-5p	*RB1*	3015-3030	0.677	3'UTR	-19.200	-13.083	0.545	0	0.034
hsa-miR-22-3p	*RB1*	2860-2871	0.677	CDS	-17.700	-2.417	0.414	1000	0.967
hsa-miR-200c-3p	*RB1*	4490-4502	0.675	3'UTR	-15.300	-12.258	0.592	0.200	0.845
hsa-miR-200c-3p	*RB1*	2849-2863	0.675	CDS	-15.600	-6.395	0.432	0.994	0.963
hsa-let-7a-5p	*RB1*	1912-1934	0.674	CDS	-18.200	-4.841	0.553	0.976	0.626
hsa-miR-31-5p	*RB1*	2125-2145	0.674	CDS	-18.300	0.163	0.441	0.905	0.703
hsa-miR-93-5p	*RB1*	4643-4663	0.674	3'UTR	-12.800	-2.504	0.590	0.727	0.929
hsa-miR-130a-3p	*RB1*	4450-4472	0.673	3'UTR	-16.200	-5.614	0.469	0.525	0.823
hsa-miR-142-3p	*RB1*	3748-3774	0.672	3'UTR	-16.400	-5.891	0.408	0.428	0.437
hsa-miR-21-5p	*RB1*	2573-2599	0.672	CDS	-16.100	-2.854	0.487	0.990	0.864
hsa-miR-200c-3p	*RB1*	690-701	0.671	CDS	-16.400	-1.064	0.431	0.999	0.188
hsa-miR-22-3p	*RB1*	1381-1392	0.671	CDS	-16.500	-1.720	0.460	1000	0.436
hsa-miR-25-3p	*RB1*	1248-1268	0.670	CDS	-16.100	-8.522	0.510	0.498	0.388
hsa-miR-93-5p	*RB1*	412-423	0.669	CDS	-15.100	-7.620	0.516	1000	0.088
hsa-miR-93-5p	*RB1*	1899-1925	0.669	CDS	-15.100	-3.195	0.504	0.994	0.622
hsa-let-7a-5p	*RB1*	4470-4493	0.668	3'UTR	-17.200	-8.168	0.412	0.347	0.834
hsa-miR-130a-3p	*RB1*	3566-3588	0.668	3'UTR	-16.800	-4.144	0.478	0.401	0.337
hsa-miR-22-3p	*RB1*	2125-2151	0.668	CDS	-18.100	0.363	0.419	0.925	0.703
hsa-miR-25-3p	*RB1*	2940-2954	0.667	CDS	-15.200	-3.888	0.421	0.985	0.995
hsa-miR-130a-3p	*RB1*	1616-1633	0.665	CDS	-19.200	-8.950	0.456	0.943	0.520

hsa-miR-142-3p	*RB1*	4092-4111	0.665	3'UTR	-11.200	-0.869	0.595	0.631	0.626
hsa-miR-93-5p	*RB1*	2769-2798	0.665	CDS	-16.900	-3.497	0.619	0.958	0.934
hsa-miR-93-5p	*RB1*	683-704	0.665	CDS	-19.800	-0.447	0.436	0.998	0.186
hsa-miR-200c-3p	*RB1*	474-489	0.662	CDS	-18.300	-6.268	0.565	0.999	0.111
hsa-miR-22-3p	*RB1*	3059-3077	0.662	3'UTR	-17.400	-8.706	0.491	0.066	0.058
hsa-let-7a-5p	*RB1*	849-872	0.661	CDS	-15.500	1.903	0.441	0.990	0.245
hsa-miR-130a-3p	*RB1*	3118-3138	0.661	3'UTR	-15.400	-5.500	0.509	0.045	0.091
hsa-let-7a-5p	*RB1*	1912-1936	0.659	CDS	-19.400	-5.974	0.511	0.977	0.626
hsa-miR-15b-5p	*RB1*	3167-3193	0.659	3'UTR	-16.400	2.472	0.401	0.611	0.118
hsa-miR-205-5p	*RB1*	3063-3078	0.659	3'UTR	-17.900	-9.230	0.491	0.086	0.060
hsa-miR-25-3p	*RB1*	1253-1272	0.659	CDS	-15.100	-6.687	0.597	0.558	0.390
hsa-miR-25-3p	*RB1*	700-733	0.659	CDS	-15.700	-0.958	0.520	0.886	0.192
hsa-let-7a-5p	*RB1*	4087-4114	0.658	3'UTR	-14.700	-0.586	0.535	0.633	0.623
hsa-miR-142-3p	*RB1*	3112-3133	0.658	3'UTR	-10.900	-4.289	0.581	0.223	0.087
hsa-miR-142-3p	*RB1*	900-930	0.658	CDS	-16.300	-0.721	0.578	1000	0.263
hsa-miR-93-5p	*RB1*	412-429	0.658	CDS	-17.900	-5.551	0.415	0.987	0.088
hsa-miR-130a-3p	*RB1*	3390-3427	0.656	3'UTR	-15.500	1.660	0.605	0.595	0.240
hsa-miR-21-5p	*RB1*	1911-1933	0.656	CDS	-15.300	-1.841	0.556	0.976	0.626
hsa-miR-142-3p	*RB1*	460-468	0.655	CDS	-15.200	-2.439	0.447	0.988	0.105
hsa-miR-22-3p	*RB1*	3059-3067	0.655	3'UTR	-16.600	-7.933	0.408	0.028	0.058
hsa-miR-93-5p	*RB1*	467-487	0.655	CDS	-21.600	-11.060	0.524	0.999	0.108
hsa-let-7a-5p	*RB1*	2020-2041	0.654	CDS	-16.400	-1.868	0.554	0.830	0.665
hsa-miR-16-5p	*RB1*	2025-2049	0.654	CDS	-16.600	-4.600	0.458	0.850	0.667
hsa-miR-31-5p	*RB1*	1449-1459	0.654	CDS	-11.700	-7.117	0.499	0.998	0.460
hsa-miR-25-3p	*RB1*	2906-2924	0.653	CDS	-15.300	-1.973	0.469	0.960	0.983
hsa-miR-130a-3p	*RB1*	3065-3079	0.651	3'UTR	-16.500	-6.666	0.520	0.093	0.062
hsa-miR-31-5p	*RB1*	3025-3048	0.651	3'UTR	-21.200	-7.159	0.417	0.015	0.040
hsa-miR-93-5p	*RB1*	467-490	0.651	CDS	-22.900	-10.497	0.494	0.999	0.108
hsa-miR-25-3p	*RB1*	1963-1983	0.649	CDS	-15.700	0.280	0.430	0.998	0.645
hsa-miR-31-5p	*RB1*	2218-2229	0.648	CDS	-15.200	-2.728	0.483	0.969	0.736
hsa-miR-142-3p	*RB1*	1251-1285	0.647	CDS	-15.600	-4.576	0.583	0.720	0.389
hsa-miR-25-3p	*RB1*	2264-2290	0.647	CDS	-16.600	-3.493	0.477	1000	0.753

hsa-miR-205-5p	*RB1*	3683-3703	0.646	3'UTR	-15.400	-6.537	0.479	0.139	0.401
hsa-miR-142-3p	*RB1*	2073-2114	0.645	CDS	-10.800	1.261	0.494	0.887	0.684
hsa-miR-15b-5p	*RB1*	1617-1636	0.645	CDS	-16.200	-5.748	0.414	0.948	0.521
hsa-miR-205-5p	*RB1*	2906-2928	0.645	CDS	-15.500	-0.960	0.476	0.960	0.983
hsa-let-7a-5p	*RB1*	1906-1920	0.643	CDS	-15.500	-5.329	0.426	0.997	0.624
hsa-miR-16-5p	*RB1*	2267-2287	0.643	CDS	-15.400	-1.382	0.446	1000	0.754
hsa-miR-130a-3p	*RB1*	3968-3988	0.642	3'UTR	-18.200	-4.887	0.465	0.519	0.558
hsa-miR-130a-3p	*RB1*	1616-1631	0.642	CDS	-16.100	-6.238	0.437	0.939	0.520
hsa-miR-93-5p	*RB1*	3174-3202	0.642	3'UTR	-17.200	-1.315	0.444	0.411	0.121
hsa-let-7a-5p	*RB1*	634-653	0.641	CDS	-16.500	-3.575	0.441	0.994	0.168
hsa-miR-223-3p	*RB1*	1474-1491	0.639	CDS	-17.200	-7.779	0.449	0.840	0.469
hsa-miR-25-3p	*RB1*	2264-2284	0.639	CDS	-16.100	-4.100	0.485	1000	0.753
hsa-let-7a-5p	*RB1*	2060-2071	0.638	CDS	-17.600	-6.107	0.418	0.921	0.680
hsa-let-7a-5p	*RB1*	1854-1876	0.638	CDS	-11.900	4.859	0.404	0.999	0.606
hsa-miR-130a-3p	*RB1*	1514-1526	0.638	CDS	-12.700	-7.242	0.485	0.942	0.484
hsa-miR-142-3p	*RB1*	3456-3475	0.638	3'UTR	-11.400	-3.809	0.520	0.136	0.277
hsa-miR-21-5p	*RB1*	1603-1629	0.638	CDS	-18.200	-6.484	0.411	1000	0.516
hsa-miR-93-5p	*RB1*	1617-1636	0.638	CDS	-15.900	-5.448	0.414	0.948	0.521
hsa-miR-31-5p	*RB1*	1615-1633	0.635	CDS	-17.100	-6.873	0.456	0.946	0.520
hsa-miR-31-5p	*RB1*	1615-1636	0.635	CDS	-17.100	-6.574	0.415	0.953	0.520
hsa-let-7a-5p	*RB1*	2574-2587	0.633	CDS	-13.900	-7.311	0.494	0.997	0.864
hsa-miR-15b-5p	*RB1*	1907-1933	0.633	CDS	-17.700	-0.618	0.493	0.979	0.625
hsa-miR-142-3p	*RB1*	4419-4442	0.632	3'UTR	-12.900	-2.613	0.447	0.393	0.806
hsa-miR-223-3p	*RB1*	1474-1486	0.632	CDS	-15.100	-8.156	0.466	0.779	0.469
hsa-let-7a-5p	*RB1*	4413-4443	0.630	3'UTR	-16.900	-3.973	0.400	0.358	0.803
hsa-miR-31-5p	*RB1*	3937-3971	0.630	3'UTR	-21.800	-4.536	0.435	0.372	0.541
hsa-miR-93-5p	*RB1*	726-761	0.630	CDS	-13.400	0.322	0.492	0.887	0.201
hsa-miR-16-5p	*RB1*	2018-2043	0.629	CDS	-15.400	-2.556	0.506	0.832	0.665
hsa-miR-22-3p	*RB1*	1471-1491	0.628	CDS	-15.600	-4.717	0.422	0.863	0.468
hsa-miR-205-5p	*RB1*	4482-4487	0.626	3'UTR	-15.600	-10.472	0.409	0.010	0.841
hsa-miR-142-3p	*RB1*	4633-4657	0.625	3'UTR	-10.700	1.878	0.457	0.730	0.924

hsa-let-7a-5p	*RB1*	1497-1529	0.624	CDS	-17.700	2.218	0.419	0.977	0.478
hsa-miR-142-3p	*RB1*	3973-3988	0.624	3'UTR	-16.600	-5.175	0.409	0.534	0.561
hsa-miR-223-3p	*RB1*	1617-1630	0.623	CDS	-12.200	-2.811	0.452	0.930	0.521
hsa-miR-31-5p	*RB1*	4544-4569	0.623	3'UTR	-18.300	-1.786	0.438	0.731	0.875
hsa-let-7a-5p	*RB1*	1685-1706	0.622	CDS	-10.400	-5.238	0.521	0.999	0.545
hsa-miR-200c-3p	*RB1*	2202-2223	0.622	CDS	-18.100	-3.304	0.442	1000	0.731
hsa-miR-31-5p	*RB1*	2213-2231	0.620	CDS	-16.900	-0.534	0.508	0.980	0.734
hsa-miR-31-5p	*RB1*	3786-3800	0.618	3'UTR	-21.700	-12.335	0.408	0.136	0.458
hsa-miR-31-5p	*RB1*	2818-2841	0.618	CDS	-15.500	-2.010	0.520	0.998	0.952
hsa-miR-130a-3p	*RB1*	608-640	0.617	CDS	-14.600	2.362	0.428	0.979	0.159
hsa-miR-142-3p	*RB1*	3679-3716	0.617	3'UTR	-16.800	-6.172	0.482	0.143	0.399
hsa-miR-93-5p	*RB1*	4168-4191	0.617	3'UTR	-17.500	-2.711	0.423	0.537	0.668
hsa-miR-142-3p	*RB1*	329-347	0.615	CDS	-12.500	1.314	0.433	1000	0.058
hsa-miR-142-3p	*RB1*	460-484	0.614	CDS	-18.400	0.030	0.453	0.995	0.105
hsa-miR-200c-3p	*RB1*	3178-3198	0.614	3'UTR	-16.300	-0.528	0.475	0.468	0.124
hsa-miR-205-5p	*RB1*	3972-3989	0.614	3'UTR	-16.100	-3.415	0.416	0.520	0.560
hsa-miR-205-5p	*RB1*	2962-2974	0.614	3'UTR	-22.500	-8.945	0.401	0.355	0.005
hsa-miR-25-3p	*RB1*	2962-2983	0.613	3'UTR	-21.900	-9.669	0.482	0.313	0.005
hsa-miR-15b-5p	*RB1*	2962-2980	0.610	3'UTR	-20.500	-8.462	0.502	0.363	0.005
hsa-miR-200c-3p	*RB1*	3956-3997	0.610	3'UTR	-17.800	-4.113	0.508	0.430	0.551
hsa-miR-22-3p	*RB1*	2202-2222	0.610	CDS	-16.700	-1.873	0.426	1.000	0.731
hsa-miR-93-5p	*RB1*	3425-3461	0.610	3'UTR	-15.700	1.115	0.519	0.198	0.259
hsa-miR-15b-5p	*RB1*	3217-3232	0.609	3'UTR	-18.800	-8.093	0.418	0.220	0.145
hsa-miR-200c-3p	*RB1*	3760-3788	0.609	3'UTR	-20.500	-6.738	0.457	0.440	0.444
hsa-miR-200c-3p	*RB1*	3178-3202	0.608	3'UTR	-16.900	-1.870	0.468	0.394	0.124
hsa-let-7a-5p	*RB1*	4035-4058	0.606	3'UTR	-16.600	-4.535	0.611	0.176	0.595
hsa-let-7a-5p	*RB1*	615-649	0.605	CDS	-15.800	-0.430	0.439	0.981	0.161
hsa-miR-200c-3p	*RB1*	3436-3447	0.604	3'UTR	-16.500	-5.723	0.513	0.003	0.266
hsa-miR-31-5p	*RB1*	1339-1373	0.603	CDS	-15.300	4.459	0.407	0.999	0.421
hsa-miR-130a-3p	*RB1*	3211-3230	0.601	3'UTR	-17.400	-5.972	0.472	0.123	0.142
hsa-miR-205-5p	*RB1*	2595-2619	0.599	CDS	-16.200	1.261	0.473	0.999	0.872
hsa-miR-93-5p	*RB1*	913-930	0.597	CDS	-17.200	-7.983	0.518	1000	0.268

hsa-miR-130a-3p	*RB1*	3968-3997	0.596	3'UTR	-15.800	-2.439	0.476	0.424	0.558
hsa-miR-205-5p	*RB1*	2861-2875	0.595	CDS	-15.200	-1.904	0.422	1000	0.967
hsa-miR-93-5p	*RB1*	2964-2981	0.594	3'UTR	-16.800	-7.050	0.523	0.272	0.006
hsa-miR-142-3p	*RB1*	617-641	0.593	CDS	-12.600	3.021	0.455	0.974	0.162
hsa-miR-205-5p	*RB1*	2257-2279	0.593	CDS	-16.300	1.362	0.458	1	0.750
hsa-miR-205-5p	*RB1*	406-423	0.593	CDS	-15.200	-1.979	0.419	1000	0.086
hsa-miR-223-3p	*RB1*	461-484	0.592	CDS	-16.900	-1.212	0.472	0.999	0.106
hsa-let-7a-5p	*RB1*	4035-4053	0.590	3'UTR	-15.700	-3.625	0.521	0.217	0.595
hsa-miR-130a-3p	*RB1*	1934-1970	0.589	CDS	-16.100	1.834	0.632	0.987	0.634
hsa-miR-130a-3p	*RB1*	2848-2869	0.589	CDS	-17.300	-1.530	0.450	0.994	0.962
hsa-miR-200c-3p	*RB1*	2849-2871	0.589	CDS	-15.900	2.852	0.426	0.996	0.963
hsa-miR-93-5p	*RB1*	2964-2984	0.589	3'UTR	-17.900	-8.308	0.498	0.233	0.006
hsa-let-7a-5p	*RB1*	2336-2359	0.588	CDS	-16.400	0.462	0.434	0.955	0.779
hsa-miR-142-3p	*RB1*	2599-2624	0.587	CDS	-17.100	4.340	0.441	0.988	0.873
hsa-let-7a-5p	*RB1*	2054-2068	0.586	CDS	-17.300	-7.499	0.496	0.996	0.677
hsa-miR-93-5p	*RB1*	3683-3717	0.586	3'UTR	-15.800	-5.123	0.466	0.123	0.401
hsa-miR-93-5p	*RB1*	2964-2978	0.585	3'UTR	-16.800	-7.390	0.520	0.326	0.006
hsa-let-7a-5p	*RB1*	2447-2472	0.584	CDS	-12.900	0.673	0.485	1	0.818
hsa-miR-16-5p	*RB1*	4545-4570	0.583	3'UTR	-16.200	2.176	0.422	0.698	0.875
hsa-miR-93-5p	*RB1*	458-478	0.583	CDS	-17.300	5.085	0.429	0.993	0.105
hsa-miR-130a-3p	*RB1*	2965-2980	0.581	3'UTR	-15.700	-6.376	0.541	0.266	0.007
hsa-miR-16-5p	*RB1*	3212-3232	0.581	3'UTR	-16.100	-4.783	0.478	0.170	0.142
hsa-miR-200c-3p	*RB1*	3956-3995	0.581	3'UTR	-15.500	-1.578	0.492	0.449	0.551
hsa-miR-93-5p	*RB1*	3683-3721	0.580	3'UTR	-16.800	-2.799	0.485	0.113	0.401
hsa-miR-200c-3p	*RB1*	3211-3231	0.579	3'UTR	-15.400	-3.979	0.457	0.145	0.142
hsa-miR-93-5p	*RB1*	2448-2473	0.579	CDS	-13.500	3.954	0.452	1	0.819
hsa-let-7a-5p	*RB1*	4470-4503	0.578	3'UTR	-11.700	-1.219	0.465	0.338	0.834
hsa-miR-31-5p	*RB1*	458-481	0.575	CDS	-16.400	6.118	0.461	0.994	0.105
hsa-miR-31-5p	*RB1*	458-477	0.573	CDS	-15.700	6.671	0.401	0.993	0.105
hsa-miR-25-3p	*RB1*	3008-3021	0.568	3'UTR	-15.700	-9.726	0.522	0.001	0.030
hsa-miR-93-5p	*RB1*	3223-3238	0.568	3'UTR	-15.900	-5.506	0.420	0.258	0.148

hsa-miR-130a-3p	*RB1*	3265-3284	0.566	3'UTR	-20.300	-9.043	0.483	0.003	0.172
hsa-miR-22-3p	*RB1*	2015-2051	0.566	CDS	-16.800	1.018	0.467	0.838	0.663
hsa-miR-223-3p	*RB1*	461-493	0.565	CDS	-17.300	-0.046	0.483	0.999	0.106
hsa-let-7a-5p	*RB1*	615-646	0.564	CDS	-13.300	2.064	0.475	0.980	0.161
hsa-miR-142-3p	*RB1*	3930-3953	0.561	3'UTR	-16.700	-2.680	0.424	0.156	0.537
hsa-miR-16-5p	*RB1*	3212-3229	0.560	3'UTR	-15.800	-4.010	0.464	0.110	0.142
hsa-miR-200c-3p	*RB1*	3211-3244	0.558	3'UTR	-17.800	-5.614	0.448	0.127	0.142
hsa-miR-130a-3p	*RB1*	2447-2475	0.555	CDS	-15.200	1.492	0.450	1	0.818
hsa-miR-142-3p	*RB1*	3792-3821	0.555	3'UTR	-18.400	0.193	0.430	0.363	0.461
hsa-miR-130a-3p	*RB1*	2447-2477	0.554	CDS	-16.400	1.886	0.442	1	0.818
hsa-miR-31-5p	*RB1*	3225-3253	0.553	3'UTR	-22.600	-8.754	0.406	0.154	0.150
hsa-miR-31-5p	*RB1*	3225-3240	0.551	3'UTR	-17.900	-6.138	0.408	0.246	0.150
hsa-miR-142-3p	*RB1*	2840-2872	0.549	CDS	-16.400	7.221	0.408	0.995	0.959
hsa-miR-142-3p	*RB1*	1510-1528	0.546	CDS	-11.400	1.477	0.447	0.960	0.482
hsa-let-7a-5p	*RB1*	3015-3042	0.545	3'UTR	-17.500	-3.691	0.408	0.012	0.034
hsa-let-7a-5p	*RB1*	615-643	0.543	CDS	-13.200	2.165	0.473	0.978	0.161
hsa-let-7a-5p	*RB1*	46-62	0.542	5'UTR	-10.500	-5.158	0.650	0.993	0.277
hsa-miR-142-3p	*RB1*	4568-4586	0.542	3'UTR	-12.600	-4.662	0.441	0.343	0.888
hsa-miR-200c-3p	*RB1*	3211-3236	0.539	3'UTR	-16.400	-4.634	0.524	0.161	0.142
hsa-miR-93-5p	*RB1*	2448-2479	0.539	CDS	-15.900	4.024	0.404	1	0.819
hsa-let-7a-5p	*RB1*	3271-3296	0.538	3'UTR	-18.200	-3.875	0.451	0.371	0.175
hsa-miR-142-3p	*RB1*	3211-3229	0.536	3'UTR	-13.200	-1.321	0.456	0.107	0.142
hsa-miR-205-5p	*RB1*	2811-2845	0.536	CDS	-16.400	6.842	0.417	0.977	0.949
hsa-miR-205-5p	*RB1*	2654-2687	0.533	CDS	-15.400	6.137	0.424	0.995	0.893
hsa-miR-21-5p	*RB1*	3022-3047	0.532	3'UTR	-15.100	-1.893	0.453	0.013	0.038
hsa-miR-93-5p	*RB1*	3209-3234	0.528	3'UTR	-15.500	-3.013	0.492	0.165	0.141
hsa-let-7a-5p	*RB1*	2976-2989	0.525	3'UTR	-17.100	-7.808	0.434	0.109	0.013
hsa-let-7a-5p	*RB1*	3268-3283	0.523	3'UTR	-17.200	-8.679	0.500	0.002	0.173
hsa-miR-16-5p	*RB1*	2267-2302	0.523	CDS	-16.100	12.116	0.407	1.000	0.754
hsa-miR-22-3p	*RB1*	906-930	0.523	CDS	-16.600	-0.726	0.489	1000	0.266
hsa-miR-142-3p	*RB1*	4568-4584	0.520	3'UTR	-11.600	-4.031	0.490	0.266	0.888
hsa-let-7a-5p	*RB1*	3114-3146	0.519	3'UTR	-10.100	2.533	0.484	0.106	0.089

hsa-let-7a-5p	*RB1*	2223-2249	0.516	CDS	-15.300	-2.673	0.426	0.986	0.738
hsa-miR-16-5p	*RB1*	93-106	0.511	5'UTR	-21.300	-16.200	0.564	0.999	0.560
hsa-miR-200c-3p	*RB1*	3266-3281	0.509	3'UTR	-18.900	-10.201	0.492	0.002	0.172
hsa-miR-200c-3p	*RB1*	163-175	0.508	5'UTR	-18.400	-9.111	0.518	0.986	0.982
hsa-let-7a-5p	*RB1*	3217-3235	0.506	3'UTR	-12.400	-1.748	0.482	0.216	0.145
hsa-miR-15b-5p	*RB1*	2999-3020	0.504	3'UTR	-19.400	-8.500	0.454	0.001	0.025
hsa-miR-130a-3p	*RB1*	3211-3232	0.501	3'UTR	-11.300	0.290	0.470	0.164	0.142

* Start and end position of the target region (site) predicted to be bound by miRNA; [a] Probability of the site being an miRNA binding site as predicted by our nonlinear logistic model; [b] A measure of stability for miRNA:target hybrid as computed by RNAhybrid; [c] A measure of the total energy change of the hybridization; [d] A measure of structural accessibility as computed by the average probability of a nucleotide being single-stranded (i.e., unpaired) for the nucleotides in the predicted binding site; [e] Conservation score by the PhastCons program for the binding site; [j] Relative starting location of the predicted binding site along the length of the sequence (e.g., for 3″ UTR, 0 indicates the 5″ end of the UTR, and 1 corresponds to the 3″ end).

Supplementary Table S3. All pathways involving *TP53* and *RB1* genes and the upregulated miRNAs that regulate them.

KEGG Pathway	p-Value pathway	miRNAs Name	Gene Name
Viral carcinogenesis (hsa05203)	$1.16x10^{-10}$	let-7a-5p	*TP53* and *RB1*
		miR-16-5p	*TP53*
		miR-205-5p	*TP53*
		miR-22-3p	*TP53*
		miR-93-5p	*TP53* and *RB1*
		miR-130a-3p	*RB1*
Chronic myeloid leukemia (hsa05220)	0.0005998	let-7a-5p	*TP53* and *RB1*
		miR-16-5p	*TP53*
		miR-205-5p	*TP53*
		miR-22-3p	*TP53*
		miR-93-5p	*TP53* and *RB1*
		miR-130a-3p	*RB1*
Central carbon metabolism in cancer (hsa05230)	0.0011443	let-7a-5p	*TP53* and *RB1*
		miR-16-5p	*TP53*
		miR-205-5p	*TP53*
		miR-22-3p	*TP53*
		miR-93-5p	*TP53* and *RB1*
Glioma (hsa05214)	0.0017756	let-7a-5p	*TP53* and *RB1*
		miR-16-5p	*TP53*
		miR-205-5p	*TP53*
		miR-22-3p	*TP53*
		miR-93-5p	*TP53* and *RB1*
		miR-130a-3	*RB1*
Cell cycle (hsa04110)	0.0038093	let-7a-5p	*TP53* and *RB1*
		miR-16-5p	*TP53*
		miR-205-5p	*TP53*
		miR-22-3p	*TP53*
		miR-93-5p	*TP53* and *RB1*
		miR-130a-3	*RB1*
Melanoma (hsa05218)	0.0041201	let-7a-5p	*TP53* and *RB1*
		miR-16-5p	*TP53*

		miR-205-5p	*TP53*
		miR-22-3p	*TP53*
		miR-93-5p	*TP53* and *RB1*
		miR-130a-3	*RB1*
Bladder cancer (hsa05219)	0.0183585	let-7a-5p	*TP53* and *RB1*
		miR-16-5p	*TP53*
		miR-205-5p	*TP53*
		miR-22-3p	*TP53*
		miR-93-5p	*TP53* and *RB1*
		miR-130a-3	*RB1*
Endometrial cancer (hsa05213)	0.0309891	let-7a-5p	*TP53* and *RB1*
		miR-16-5p	*TP53*
		miR-205-5p	*TP53*
		miR-22-3p	*TP53*
		miR-93-5p	*TP53* and *RB1*
		miR-130a-3	*RB1*
Hepatitis B (hsa05161)	0.0313645	let-7a-5p	*TP53* and *RB1*
		miR-16-5p	*TP53*
		miR-205-5p	*TP53*
		miR-22-3p	*TP53*
		miR-93-5p	*TP53* and *RB1*
		miR-130a-3	*RB1*
Non-small cell lung cancer (hsa05223)	0.0380989	let-7a-5p	*TP53* and *RB1*
		miR-16-5p	*TP53*
		miR-205-5p	*TP53*
		miR-22-3p	*TP53*
		miR-93-5p	*TP53* and *RB1*
		miR-130a-3	*RB1*
Pancreatic cancer (hsa05212)	0.0478991	let-7a-5p	*TP53* and *RB1*
		miR-16-5p	*TP53*
		miR-205-5p	*TP53*
		miR-22-3p	*TP53*
		miR-93-5p	*TP53* and *RB1*
		miR-130a-3	*RB1*

Small cell lung cancer (hsa05222)	0.0479915	let-7a-5p	*TP53* and *RB1*
		miR-16-5p	*TP53*
		miR-205-5p	*TP53*
		miR-22-3p	*TP53*
		miR-93-5p	*TP53* and *RB1*
		miR-130a-3	*RB1*
Prostate cancer (hsa05215)	0.0492142	let-7a-5p	*TP53* and *RB1*
		miR-16-5p	*TP53*
		miR-205-5p	*TP53*
		miR-22-3p	*TP53*
		miR-93-5p	*TP53* and *RB1*
		miR-130a-3	*RB1*

Anexo C – Material Suplementar Artigo 3

Supplementary Material

1 Supplementary Figures

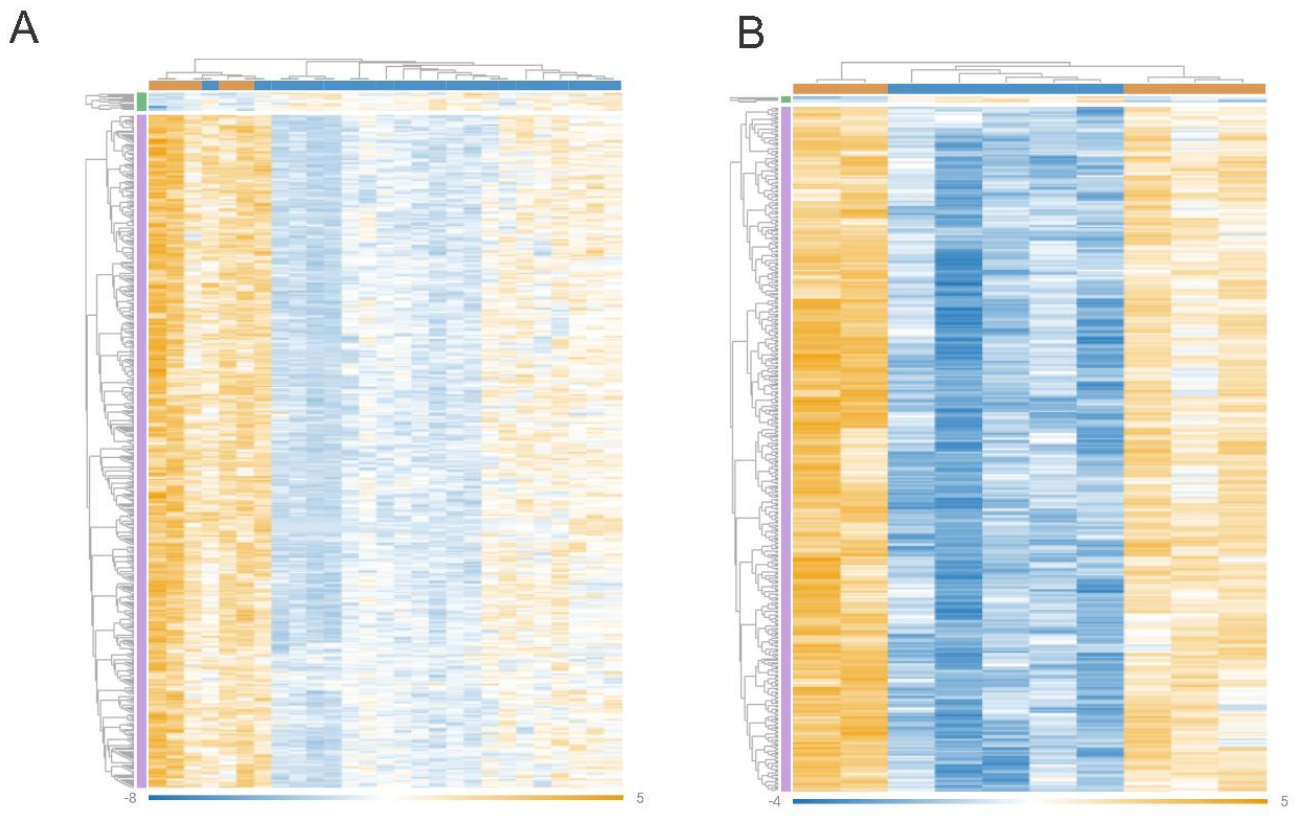


Figure S1. Comparison of the profile of differentially expressed miRNAs in all samples **(A)** and paired samples **(B)** of this study. In **(A)**, heatmap generated by miRNA expression patterns in all samples (22 tumors *vs.* 5 non-tumors). In **(B)**, heatmap generated by miRNA expression patterns in paired samples (5 tumors *vs.* 5 non-tumors). Both heatmaps showed two distinct groups (upper group) formed by tumor samples (blue bar) and non-tumor samples (orange bar). The hierarchical group on the left is formed by the upregulated (green bar) and downregulated (pink bar) miRNAs. Yellow-orange colors indicate upregulated miRNAs and blue colors indicate downregulated miRNAs.

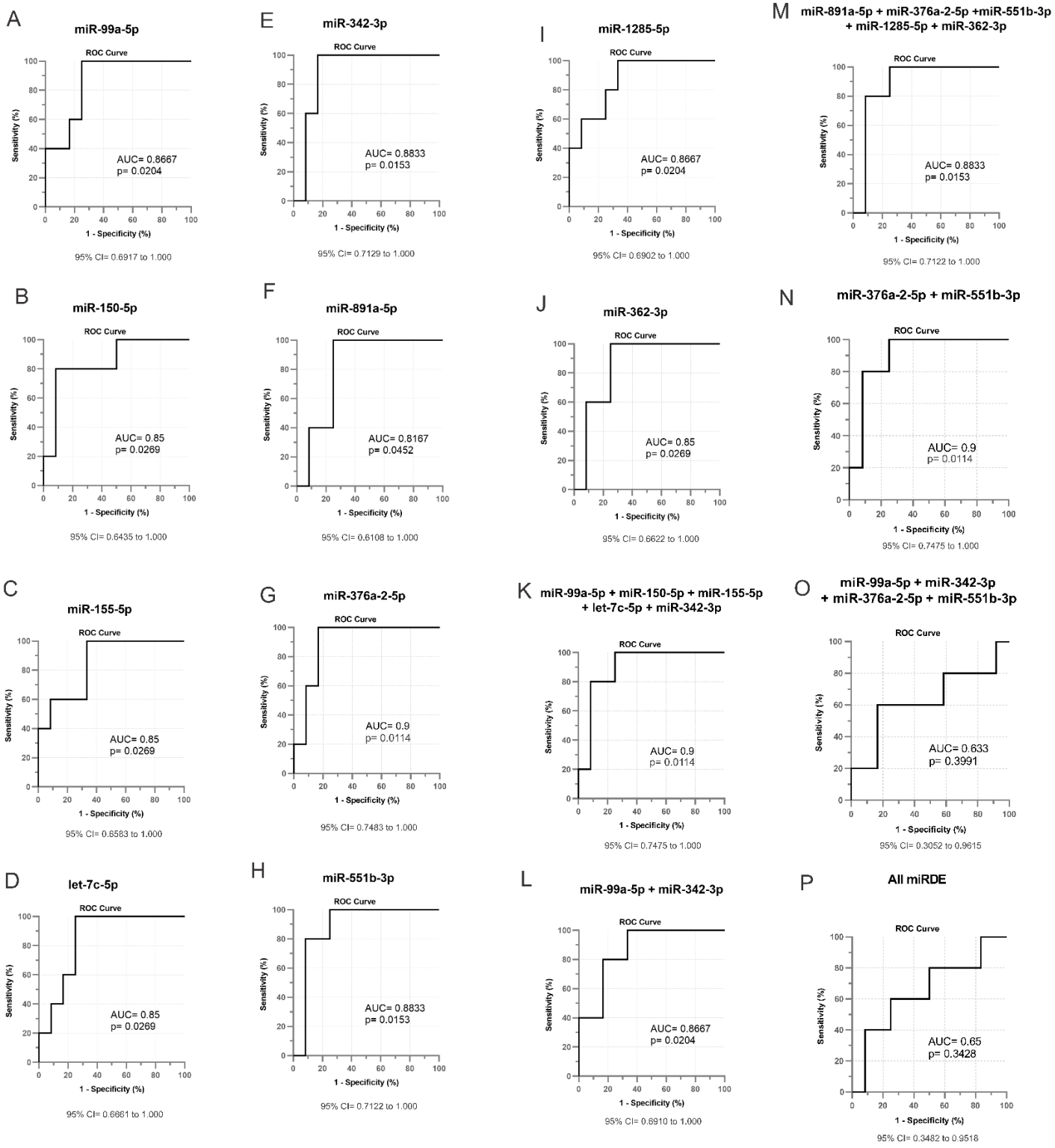


Figure S2. ROC and AUC curve analysis of the top 10 miRDEs between clinical groups (advanced disease *vs.* early disease). A – P, ROC curve graphics showing AUC and *p*-values. On the -y axis is presented sensitivity versus 1-specificity on -x axis. Below each graph, the 95% CI value is presented.

2 Supplementary Tables

Table S1. Clinical-histopathological profile of patients with CaPe in this study (n=22).

Id patient	Age	Phimosis	Smoker	Alcoholism	HPV subtype	Anatomical site of tumor	Histological type	Lesion	Surgery type	Tu. size	Tu. grade	Tu. stage	Lymphatic invasion	Perineural invasion
1	62	no	N/A	N/A	16	glans	usual	ulcerated	total penectomy	2.5	2	pT3	yes	yes
2	80	N/A	smoker former	N/A	16	glans, foreskin and others areas	condilomatous	ulcerated	partial penectomy	10	2	pT2	no	no
3	81	yes	yes	N/A	18,53	glans and foreskin	condilomatous	ulcerated	partial penectomy	2.1	2	pT1	no	no
4	37	yes	no	yes	positive [a]	glans and foreskin	usual	nodular ulcerated	partial penectomy	5	3	pT3	no	yes
5	76	yes	no	yes	30	glans and foreskin	condilomatous	ulcerated	partial penectomy	3	1	pT1b	yes	no
6	54	yes	yes	yes	positive [a]	foreskin	usual	vegetative	partial penectomy	0.8	2	pT2	yes	no
7	74	yes	no	no	73,74	glans, foreskin and others areas	usual and basaloide	verrucous	partial penectomy	0.8	I	pT2	no	no
8	78	N/A	yes	yes	16,06	glans	usual and basaloid	vegetative	partial penectomy	4	3	pT1b	no	no
9	44	yes	no	yes	16	glans, foreskin and others areas	usual	ulcerated	partial penectomy	1.7	2	pT1	no	no
10	57	no	no	yes	58	glans	usual and condilomatous	nodular ulcerated	penectomia total	3	3	pT2	no	no
11	85	no	N/A	N/A	16	glans and foreskin	condilomatous	nodular ulcerated	partial penectomy	4	3	pT3	no	yes
12	83	no	smoker former	alcoholic former	16	glans and foreskin	usual	ulcerated	partial penectomy	4.5	3	pT3	no	yes
13	40	no	no	no	59,66	glans	condilomatous	ulcer-vegetative	partial penectomy	3	2	pT2	no	no
14	68	N/A	no	no	16,66	glans and foreskin	condilomatous	verrucous	partial penectomy	5.5	1	pT3	no	no
15	65	N/A	N/A	N/A	16,74	glans and foreskin	condilomatous	vegetative	partial penectomy	3.5	2	pT2	no	no

16	51	N/A	yes	sim	16,35,59	glande, foreskin and others areas	usual	ulcer-vegetative	partial penectomy	3	2	pT2	yes	no
17	74	no	yes	no	positive [a]	glans	condilomatous	ulcerated	partial penectomy	1.8	2	pT1a	no	no
18	32	no	yes	yes	16,44,74	glans	usual and condilomatous	ulcer-vegetative	partial penectomy	3.7	2	pT2	no	no
19	71	no	no	no	16	glans	usual	ulcerated	partial penectomy	3.2	3	pT3	no	no
20	69	no	no	no	16,30	glans	condilomatous	vegetative	partial penectomy	3.5	1	pT2	no	no
21	73	yes	smoker former	no	16	foreskin	usual	ulcerated	postectomy	N/A	2	pT1	N/A	N/A
22	59	yes	no	yes	positive [a]	glans	condilomatous	verrucous	partial penectomy	5.5	2	pT3	no	yes

N/A = not available; [a] = no information on the HPV genotype; Tu = tumor; Genotyping was conducted by nested-PCR and DNA sequencing, except for cases 04, 06, 17 and 22 because there was not enough DNA for both assays.

Table S2. All 507 miRDEs identified between 22 tumors *vs.* 5 non-tumor tissues of this study.

miRNA	ID	FC	Log FC	*p*-value	Adj.-*p*
hsa-let-7a-5p	MI0000061	4,68036	2,22662	0,001926	0,004355
hsa-miR-1178-3p	MI0006271	-3,74275	-1,9041	0,002912	0,005721
hsa-miR-1180-3p	MI0006273	-3,42988	-1,77816	0,000362	0,001556
hsa-miR-1183	MI0006276	-5,71202	-2,514	1,05E-05	0,00055
hsa-miR-1185-5p	MI0003844	-6,89567	-2,78569	0,000152	0,001045
hsa-miR-1193	MI0014205	-4,06628	-2,02371	0,00315	0,006028
hsa-miR-1197	MI0006656	-4,78364	-2,25811	0,001472	0,003752
hsa-miR-1200	MI0006332	-7,05619	-2,81889	1,98E-05	0,000599
hsa-miR-1202	MI0006334	-4,41575	-2,14266	0,002408	0,005043
hsa-miR-1203	MI0006335	-6,49833	-2,70007	0,000295	0,001434
hsa-miR-1204	MI0006337	-6,23466	-2,64031	0,000128	0,000993
hsa-miR-1205	MI0006338	-4,67495	-2,22495	0,001812	0,004265
hsa-miR-1206	MI0006339	-8,17387	-3,03102	9,48E-06	0,00054
hsa-miR-1224-3p	MI0003764	-4,40701	-2,1398	0,002513	0,005195
hsa-miR-1224-5p	MI0003764	-3,55983	-1,83181	0,002301	0,00491
hsa-miR-1226-3p	MI0006313	-7,1135	-2,83056	7,76E-06	0,00054
hsa-miR-1234-3p	MI0006324	-5,59412	-2,48391	4,84E-05	0,000655
hsa-miR-1236-3p	MI0006326	-3,95317	-1,98301	0,001401	0,003673
hsa-miR-124-3p	MI0000445	-5,67685	-2,50509	7,47E-05	0,000746
hsa-miR-1244	MI0015975	-3,89467	-1,9615	0,002572	0,00525
hsa-miR-1245a	MI0006380	-3,71366	-1,89284	0,005993	0,0098
hsa-miR-1245b-3p	MI0017431	-3,90258	-1,96443	0,001348	0,003604
hsa-miR-1249-3p	MI0006384	-6,41945	-2,68245	0,000431	0,001695
hsa-miR-1249-5p	MI0006384	-5,2317	-2,38728	0,000293	0,001434
hsa-miR-1250-5p	MI0006385	-4,1079	-2,0384	0,002097	0,004622
hsa-miR-1252-5p	MI0006434	-6,91678	-2,7901	0,000234	0,00127
hsa-miR-1254		-5,09146	-2,34808	0,000128	0,000993
hsa-miR-1255a	MI0006389	-6,09992	-2,60879	3,16E-05	0,000599
hsa-miR-1255b-5p	MI0006436	-3,44468	-1,78437	0,001746	0,004173
hsa-miR-1257	MI0006391	-4,0427	-2,01532	0,001826	0,004271
hsa-miR-1258	MI0006392	-4,01508	-2,00543	0,001235	0,003374
hsa-miR-125a-3p	MI0000469	-4,50576	-2,17177	0,00018	0,00112
hsa-miR-1260b	MI0014197	-4,0269	-2,00967	0,000998	0,002871
hsa-miR-1261	MI0006396	-5,22329	-2,38496	0,000258	0,001349
hsa-miR-1262	MI0006397	-6,5577	-2,71319	0,000173	0,001093
hsa-miR-1264	MI0003758	-3,56146	-1,83247	0,00201	0,004505
hsa-miR-1266-5p	MI0006403	-5,86349	-2,55176	0,000165	0,001067
hsa-miR-1268a	MI0006405	-4,30923	-2,10743	9,52E-05	0,000849
hsa-miR-1268b	MI0016748	-5,18675	-2,37483	0,00149	0,003786
hsa-miR-1269a	MI0006406	-4,85513	-2,27951	0,000187	0,001142
hsa-miR-1270	MI0006407	-4,94376	-2,30561	0,000262	0,001349
hsa-miR-1273c	MI0014171	-4,13618	-2,0483	0,002394	0,005027
hsa-miR-127-3p	MI0000472	-3,04438	-1,60615	0,00295	0,005771
hsa-miR-1275	MI0006415	-5,47129	-2,45188	0,000341	0,001529
hsa-miR-127-5p	MI0000472	-4,1833	-2,06464	0,002163	0,004718
hsa-miR-1277-3p	MI0006419	-4,71527	-2,23734	0,000414	0,001644
hsa-miR-1278	MI0006425	-4,59744	-2,20083	0,001256	0,00341
hsa-miR-128-1-5p	MI0000447	-3,8749	-1,95416	0,001177	0,003261
hsa-miR-128-2-5p	MI0000727	-4,14172	-2,05023	0,00382	0,00676
hsa-miR-1285-3p	MI0006347	-6,35288	-2,66741	2,09E-05	0,000599
hsa-miR-1286	MI0006348	-6,58398	-2,71896	2,05E-08	1,64E-05
hsa-miR-1287-5p	MI0006349	-4,43563	-2,14914	0,000851	0,002611
hsa-miR-1288-3p	MI0006432	-3,16547	-1,66242	0,003272	0,006145
hsa-miR-1289	MI0006350	-5,74418	-2,5221	0,000433	0,001695
hsa-miR-129-2-3p	MI0000473	-4,35711	-2,12337	0,003273	0,006145

hsa-miR-1293	MI0006355	-4,08116	-2,02898	0,001841	0,004271
hsa-miR-1295a	MI0006357	-4,97325	-2,31419	3,52E-05	0,000599
hsa-miR-129-5p	MI0000473	-3,46941	-1,79469	0,003028	0,005865
hsa-miR-1297	MI0006358	-6,94474	-2,79592	0,000303	0,001463
hsa-miR-1298-5p	MI0003938	-4,97936	-2,31596	3,18E-05	0,000599
hsa-miR-1299	MI0006359	-6,64952	-2,73325	9,60E-05	0,000849
hsa-miR-1302	MI0006363	-5,24023	-2,38963	0,000854	0,002611
hsa-miR-1303	MI0006370	-3,46946	-1,79471	0,003451	0,006317
hsa-miR-1304-3p	MI0006371	-4,03761	-2,0135	0,001742	0,004173
hsa-miR-1304-5p	MI0006371	-7,34463	-2,87669	0,000358	0,001553
hsa-miR-1305	MI0006372	-3,69243	-1,88457	0,000707	0,002321
hsa-miR-1307-3p	MI0006444	-2,76964	-1,4697	0,004551	0,007743
hsa-miR-1307-5p	MI0006444	-4,57817	-2,19477	0,000405	0,001616
hsa-miR-130a-3p	MI0000448	2,23499	1,16027	0,000756	0,002431
hsa-miR-1322	MI0006653	-4,89952	-2,29264	2,96E-05	0,000599
hsa-miR-1323	MI0003786	-3,80113	-1,92643	0,000771	0,002446
hsa-miR-133a-3p	MI0000450	-4,07336	-2,02622	0,001723	0,004173
hsa-miR-133a-5p	MI0000450	-5,31622	-2,4104	0,003536	0,006398
hsa-miR-134-5p		-5,54751	-2,47184	0,000161	0,001052
hsa-miR-136-5p	MI0000475	-5,45376	-2,44725	4,78E-05	0,000655
hsa-mir-137		-5,52912	-2,46705	0,001104	0,003112
hsa-miR-138-5p	MI0000455	-4,73384	-2,24301	0,000399	0,001616
hsa-miR-139-3p	MI0000261	-3,97719	-1,99175	0,000371	0,001575
hsa-miR-139-5p	MI0000261	-4,69342	-2,23064	0,000643	0,002184
hsa-miR-1-3p	MI0000437	-5,32219	-2,41202	0,000224	0,001243
hsa-miR-140-3p	MI0000456	-4,71377	-2,23688	1,90E-05	0,000599
hsa-miR-140-5p	MI0000456	-3,48276	-1,80023	6,22E-05	0,000701
hsa-miR-142-3p	MI0000458	2,74649	1,45759	0,005361	0,008949
hsa-miR-144-3p	MI0000460	-7,72471	-2,94948	3,04E-05	0,000599
hsa-miR-146b-3p	MI0003129	-3,42858	-1,77761	0,005753	0,009466
hsa-miR-146b-5p	MI0003129	-2,34375	-1,22882	0,002024	0,004515
hsa-mir-147b		-5,58319	-2,48109	0,000673	0,002256
hsa-miR-148b-3p	MI0000811	-2,56612	-1,35959	5,20E-05	0,000669
hsa-miR-151a-5p	MI0000809	-2,84672	-1,5093	0,00037	0,001575
hsa-miR-151b	MI0003772	-3,87412	-1,95387	0,004351	0,00745
hsa-miR-152-3p	MI0000462	-3,44965	-1,78645	0,001757	0,004185
hsa-miR-152-5p	MI0000462	-3,26427	-1,70676	0,004884	0,008292
hsa-miR-153-3p	MI0000463	-5,65043	-2,49836	0,000264	0,001352
hsa-miR-1537-3p	MI0007258	-3,71711	-1,89418	0,000243	0,001301
hsa-miR-15b-5p	MI0000438	3,14021	1,65086	3,89E-05	0,000623
hsa-miR-1-5p	MI0000651	-5,13595	-2,36063	0,000586	0,002054
hsa-miR-16-5p	MI0000070	2,38034	1,25117	0,00077	0,002446
hsa-miR-181b-2-3p	MI0000683	-5,52954	-2,46716	0,000135	0,00101
hsa-miR-182-3p	MI0000272	-3,54054	-1,82397	0,006127	0,00997
hsa-miR-1827	MI0008195	-6,82254	-2,77031	3,90E-05	0,000623
hsa-miR-184	MI0000481	-3,44497	-1,78449	0,005432	0,00905
hsa-miR-188-3p	MI0000484	-4,99111	-2,31936	0,002542	0,005222
hsa-miR-188-5p	MI0000484	-3,91736	-1,96988	0,001906	0,004347
hsa-miR-18a-5p	MI0000072	-2,7562	-1,46268	0,002243	0,004811
hsa-miR-18b-5p	MI0001518	-4,34718	-2,12008	0,000894	0,002692
hsa-miR-1908-3p	MI0008329	-3,49759	-1,80636	0,002501	0,005184
hsa-miR-1909-3p	MI0008330	-4,67851	-2,22605	0,001451	0,003746
hsa-miR-190a-3p	MI0000486	-4,68458	-2,22792	0,004273	0,007333
hsa-miR-190a-5p	MI0000486	-6,68937	-2,74187	6,00E-05	0,000701
hsa-mir-190b		-8,02466	-3,00444	2,71E-05	0,000599
hsa-miR-1910-5p	MI0008331	-4,64185	-2,2147	0,001076	0,003067
hsa-miR-192-5p	MI0000234	-3,49192	-1,80402	0,00337	0,006211

hsa-miR-193a-3p	MI0000487	-4,64159	-2,21462	5,55E-05	0,000701
hsa-miR-195-5p	MI0000489	-3,4808	-1,79942	0,002607	0,005308
hsa-miR-196a-3p	MI0000279	-6,13903	-2,61801	0,000132	0,00101
hsa-miR-196a-5p	MI0000279	-2,78557	-1,47797	0,001508	0,003798
hsa-mir-1973		-3,368	-1,75189	0,00331	0,006156
hsa-miR-198	MI0000240	-5,19632	-2,37749	6,52E-05	0,000706
hsa-miR-200a-3p	MI0000737	-4,11325	-2,04028	6,23E-05	0,000701
hsa-miR-200c-3p	MI0000650	2,38513	1,25407	0,002298	0,00491
hsa-miR-204-5p	MI0000284	-4,72269	-2,23961	0,000764	0,002446
hsa-miR-205-5p	MI0000285	2,75295	1,46098	0,001291	0,003492
hsa-miR-208a-3p	MI0000251	-3,21882	-1,68653	0,004516	0,0077
hsa-miR-208b-3p	MI0005570	-4,65987	-2,22029	0,001465	0,003747
hsa-miR-208b-5p	MI0005570	-4,48631	-2,16553	0,001337	0,003593
hsa-miR-2110	MI0010629	-3,9087	-1,96669	0,003428	0,006304
hsa-miR-212-3p	MI0000288	-5,16791	-2,36958	0,000171	0,001093
hsa-miR-215-5p	MI0000291	-5,23939	-2,3894	3,35E-05	0,000599
hsa-miR-21-5p	MI0000077	2,75668	1,46293	0,000401	0,001616
hsa-miR-216a-5p	MI0000292	-6,17809	-2,62716	4,39E-05	0,000649
hsa-miR-216b-5p	MI0005569	-3,42001	-1,774	0,001174	0,003261
hsa-mir-217		-5,94147	-2,57082	0,001905	0,004347
hsa-miR-218-5p	MI0000294	-5,17734	-2,37221	1,10E-05	0,00055
hsa-miR-219a-1-3p	MI0000296	-4,79689	-2,2621	0,000136	0,00101
hsa-miR-219a-2-3p	MI0000740	-3,43621	-1,78082	0,001441	0,00374
hsa-miR-219a-5p	MI0000296	-3,11888	-1,64103	0,002309	0,004914
hsa-miR-221-5p	MI0000298	-3,78562	-1,92053	0,003302	0,006156
hsa-miR-223-3p	MI0000300	4,06191	2,02216	0,002814	0,005584
hsa-miR-22-3p	MI0000078	2,08565	1,0605	0,001837	0,004271
hsa-miR-224-5p	MI0000301	-5,54855	-2,47211	2,70E-06	0,000431
hsa-miR-2278	MI0011285	-4,2007	-2,07063	0,001	0,002871
hsa-miR-23c	MI0016010	-3,90862	-1,96666	0,005567	0,009216
hsa-miR-25-3p	MI0000082	2,91756	1,54476	7,67E-05	0,00075
hsa-miR-27a-3p	MI0000085	-2,30478	-1,20463	0,000261	0,001349
hsa-miR-28-3p	MI0000086	-2,61794	-1,38843	0,00056	0,002017
hsa-miR-296-3p	MI0000747	-4,22916	-2,08037	0,003291	0,006156
hsa-miR-297	MI0005775	-3,88146	-1,9566	0,001901	0,004347
hsa-miR-299-5p	MI0000744	-4,06614	-2,02366	0,000584	0,002054
hsa-miR-301a-3p	MI0000745	-3,88814	-1,95908	6,49E-05	0,000706
hsa-miR-301a-5p	MI0000745	-3,9972	-1,99899	0,002857	0,005632
hsa-miR-301b-3p	MI0005568	-3,96173	-1,98613	0,000816	0,002528
hsa-miR-302a-3p	MI0000738	-4,12696	-2,04508	0,001952	0,0044
hsa-miR-302a-5p	MI0000738	-4,70534	-2,2343	0,000538	0,001954
hsa-miR-302b-3p	MI0000772	-4,66404	-2,22158	0,003098	0,005942
hsa-miR-302c-3p	MI0000773	-4,63465	-2,21246	0,001811	0,004265
hsa-miR-302e	MI0006417	-5,05773	-2,33849	0,000539	0,001954
hsa-miR-302f	MI0006418	-4,79148	-2,26047	0,000123	0,000971
hsa-miR-3065-3p	MI0014228	-4,19834	-2,06982	0,002546	0,005222
hsa-miR-3074-3p	MI0014181	-5,90841	-2,56277	2,98E-05	0,000599
hsa-miR-30b-5p	MI0000441	-2,48423	-1,3128	0,000591	0,002054
hsa-miR-30c-5p	MI0000736	-3,0361	-1,60222	2,91E-05	0,000599
hsa-miR-3130-3p	MI0014147	-3,79645	-1,92465	0,003165	0,006043
hsa-miR-3131	MI0014151	-3,76208	-1,91153	0,000386	0,001594
hsa-miR-3136-5p	MI0014158	-3,92663	-1,97329	0,000105	0,000881
hsa-miR-3140-3p	MI0014163	-4,06453	-2,02309	0,00135	0,003604
hsa-miR-3140-5p	MI0014163	-6,30703	-2,65696	4,65E-05	0,000655
hsa-miR-3147	MI0014173	-4,48609	-2,16546	0,002918	0,005721
hsa-miR-3150b-3p	MI0016426	-3,51579	-1,81385	0,004025	0,006989
hsa-miR-3151-5p	MI0014178	-5,83212	-2,54402	0,000232	0,001267
hsa-miR-31-5p	MI0000089	4,00341	2,00123	0,000567	0,002019

hsa-miR-3164	MI0014194	-6,5327	-2,70768	9,03E-05	0,000829
hsa-miR-3168	MI0014199	-5,00632	-2,32375	0,00112	0,003148
hsa-miR-3179	MI0014213	-4,06493	-2,02323	0,00122	0,003358
hsa-miR-3180	MI0016409	-4,45965	-2,15693	0,000938	0,00275
hsa-miR-3180-3p	MI0014214	-4,73847	-2,24442	0,000694	0,002288
hsa-miR-3180-5p	MI0014214	-3,87485	-1,95414	0,00098	0,00284
hsa-miR-3182	MI0014224	-5,01358	-2,32584	0,000223	0,001243
hsa-miR-3190-3p	MI0014235	-3,82156	-1,93416	0,002777	0,005554
hsa-miR-3196	MI0014241	-5,00753	-2,3241	0,000473	0,001796
hsa-mir-320a		-4,58395	-2,19659	0,00032	0,001501
hsa-miR-320b	MI0003776	-4,02517	-2,00905	0,001444	0,00374
hsa-miR-320d	MI0008190	-3,48059	-1,79933	0,005771	0,009476
hsa-miR-320e	MI0014234	-2,4748	-1,30731	0,005289	0,008852
hsa-miR-323a-3p	MI0000807	-4,09394	-2,03349	0,000509	0,001897
hsa-miR-323b-3p	MI0014206	-5,96313	-2,57607	0,000156	0,001052
hsa-miR-323b-5p	MI0014206	-3,99928	-1,99974	0,002718	0,005477
hsa-miR-324-3p	MI0000813	-3,25891	-1,70439	0,003067	0,005913
hsa-miR-325	MI0000824	-6,13724	-2,61759	6,59E-05	0,000706
hsa-miR-328-3p	MI0000804	-5,28858	-2,40288	0,000252	0,001339
hsa-miR-330-3p	MI0000803	-5,20281	-2,37929	9,89E-05	0,000849
hsa-miR-330-5p	MI0000803	-4,03954	-2,01419	0,000569	0,002019
hsa-miR-331-5p	MI0000812	-4,82216	-2,26968	0,000716	0,002342
hsa-miR-335-5p	MI0000816	-4,31551	-2,10953	0,003045	0,005884
hsa-miR-337-5p	MI0000806	-3,34061	-1,74011	0,003187	0,006067
hsa-miR-338-5p	MI0000814	-5,07497	-2,3434	0,00152	0,003798
hsa-miR-339-3p	MI0000815	-3,39488	-1,76336	0,003017	0,005865
hsa-miR-339-5p	MI0000815	-3,78502	-1,9203	0,003256	0,006145
hsa-miR-33a-5p	MI0000091	-5,34078	-2,41705	0,000328	0,001512
hsa-miR-342-5p	MI0000805	-4,1729	-2,06105	0,00187	0,004313
hsa-miR-345-3p	MI0000825	-4,65655	-2,21926	0,003843	0,006785
hsa-miR-346	MI0000826	-6,11936	-2,61338	6,24E-05	0,000701
hsa-miR-34b-3p	MI0000742	-4,89015	-2,28988	0,000512	0,0019
hsa-miR-34c-3p	MI0000743	-3,59579	-1,84631	0,000278	0,001397
hsa-miR-34c-5p	MI0000743	-3,12382	-1,64331	0,002481	0,005169
hsa-miR-3605-3p	MI0015995	-3,68828	-1,88295	0,004909	0,008318
hsa-miR-3605-5p	MI0015995	-4,59447	-2,1999	0,001798	0,004257
hsa-miR-3614-3p	MI0016004	-4,02983	-2,01072	0,001511	0,003798
hsa-miR-363-5p	MI0000764	-4,72639	-2,24074	0,002386	0,005024
hsa-miR-365b-5p	MI0000769	-5,13402	-2,36009	0,000214	0,001227
hsa-miR-367-3p	MI0000775	-5,05759	-2,33845	0,000268	0,001365
hsa-miR-3690	MI0016091	-4,03165	-2,01137	0,002005	0,004505
hsa-miR-370-3p	MI0000778	-5,27679	-2,39966	0,000197	0,001154
hsa-miR-371a-5p	MI0000779	-4,83773	-2,27433	0,000457	0,001762
hsa-miR-371b-5p	MI0017393	-6,12021	-2,61358	0,00046	0,001766
hsa-miR-372-3p	MI0000780	-4,39359	-2,1354	0,000619	0,002111
hsa-miR-374a-3p	MI0000782	-6,1426	-2,61885	0,000179	0,00112
hsa-miR-374c-5p	MI0016684	-3,58174	-1,84066	0,000789	0,00247
hsa-mir-375		-4,42522	-2,14575	0,003369	0,006211
hsa-miR-376a-2-5p	MI0003529	-4,07845	-2,02802	0,003669	0,00655
hsa-miR-376a-3p	MI0003529	-4,84666	-2,27699	9,89E-05	0,000849
hsa-miR-376b-3p	MI0002466	-7,92901	-2,98714	6,75E-06	0,00054
hsa-miR-376c-3p	MI0000776	-4,11505	-2,04091	0,00015	0,001045
hsa-miR-377-3p	MI0000785	-4,04027	-2,01445	0,000594	0,002054
hsa-miR-378c	MI0015825	-6,95823	-2,79872	9,26E-05	0,000839
hsa-miR-378d	MI0016749	-5,42292	-2,43907	0,000338	0,001529
hsa-miR-378f	MI0016756	-5,58199	-2,48078	0,000324	0,001505
hsa-miR-378i	MI0016902	-2,82482	-1,49816	0,001926	0,004355

hsa-miR-379-5p	MI0000787	-2,80191	-1,48641	0,001738	0,004173
hsa-miR-380-3p	MI0000788	-4,50523	-2,1716	0,000195	0,001152
hsa-miR-381-3p	MI0000789	-6,33217	-2,6627	2,71E-05	0,000599
hsa-miR-381-5p	MI0000789	-7,92236	-2,98593	1,19E-05	0,00055
hsa-miR-382-3p	MI0000790	-3,39949	-1,76532	0,003084	0,00593
hsa-miR-382-5p	MI0000790	-3,70982	-1,89135	6,98E-05	0,000733
hsa-miR-384	MI0001145	-6,604	-2,72334	0,000144	0,001034
hsa-miR-3916	MI0016422	-4,37438	-2,12908	0,001418	0,003699
hsa-miR-3918	MI0016424	-4,28421	-2,09903	0,002616	0,005312
hsa-miR-3928-3p	MI0016438	-4,02063	-2,00742	0,004124	0,007108
hsa-miR-409-5p	MI0001735	-4,04912	-2,01761	0,002119	0,004658
hsa-miR-410-3p	MI0002465	-4,0656	-2,02347	0,000335	0,001527
hsa-miR-411-3p		-5,54739	-2,47181	1,63E-05	0,000599
hsa-miR-411-5p	MI0003675	-5,08043	-2,34495	0,000223	0,001243
hsa-miR-421	MI0003685	-3,00141	-1,58564	0,001227	0,003366
hsa-miR-424-5p	MI0001446	-2,98827	-1,57931	0,003654	0,006539
hsa-miR-431-5p	MI0001721	-3,97187	-1,98982	0,000334	0,001527
hsa-miR-432-5p	MI0003133	-4,90768	-2,29504	0,000142	0,001034
hsa-miR-433-3p	MI0001723	-7,98582	-2,99744	1,41E-05	0,00059
hsa-miR-433-5p	MI0001723	-6,79216	-2,76387	5,69E-05	0,000701
hsa-miR-4421	MI0016758	-6,72675	-2,74991	0,000535	0,001954
hsa-miR-4435	MI0016775	-5,69588	-2,50992	8,48E-05	0,000799
hsa-miR-4448	MI0016791	-3,38295	-1,75828	0,002754	0,005526
hsa-miR-4451	MI0016797	-4,98195	-2,31671	0,001375	0,003649
hsa-miR-4455	MI0016801	-7,10498	-2,82883	5,83E-06	0,00054
hsa-miR-448	MI0001637	-4,79556	-2,2617	0,002206	0,004763
hsa-miR-4485-3p	MI0016846	-4,58299	-2,19629	0,002044	0,004532
hsa-miR-449b-5p	MI0003673	-5,20941	-2,38112	0,000166	0,001067
hsa-miR-449c-5p	MI0003823	-4,40194	-2,13814	0,002808	0,005584
hsa-miR-450a-2-3p	MI0003187	-4,74001	-2,24489	0,003697	0,006582
hsa-miR-450b-3p	MI0005531	-3,93739	-1,97724	0,000218	0,001236
hsa-miR-450b-5p	MI0005531	-4,26049	-2,09102	0,003193	0,006067
hsa-miR-4521	MI0016887	-4,26043	-2,091	0,000593	0,002054
hsa-miR-452-5p	MI0001733	-4,13719	-2,04865	0,000486	0,001831
hsa-mir-4532		-2,58184	-1,3684	0,002363	0,004988
hsa-miR-4647	MI0017274	-7,24999	-2,85798	5,04E-05	0,000666
hsa-miR-4707-5p	MI0017340	-5,03004	-2,33057	0,003619	0,006504
hsa-miR-4741	MI0017379	-3,90418	-1,96502	0,003957	0,006894
hsa-miR-4755-5p	MI0017395	-6,85031	-2,77617	3,17E-05	0,000599
hsa-miR-4787-5p	MI0017434	-7,10961	-2,82977	2,34E-05	0,000599
hsa-miR-4792		-6,67681	-2,73916	0,000309	0,001484
hsa-miR-483-3p	MI0002467	-4,13418	-2,0476	0,000519	0,001919
hsa-miR-483-5p	MI0002467	-6,18687	-2,62921	5,09E-05	0,000666
hsa-miR-485-5p	MI0002469	-4,63205	-2,21165	0,000564	0,002017
hsa-miR-486-3p	MI0002470	-3,66682	-1,87453	0,002756	0,005526
hsa-miR-487a-3p	MI0002471	-7,33746	-2,87528	2,74E-05	0,000599
hsa-miR-487b-3p	MI0003530	-3,75445	-1,9086	0,002646	0,005346
hsa-miR-488-3p	MI0003123	-6,06001	-2,59932	0,00019	0,001142
hsa-miR-491-3p	MI0003126	-4,18713	-2,06596	3,08E-05	0,000599
hsa-miR-491-5p	MI0003126	-3,4179	-1,77311	0,00104	0,002975
hsa-miR-492	MI0003131	-5,04471	-2,33477	0,001502	0,003798
hsa-miR-494-5p	MI0003134	-3,61168	-1,85267	0,005672	0,009371
hsa-miR-495-3p	MI0003135	-8,59644	-3,10374	4,73E-05	0,000655
hsa-miR-497-5p	MI0003138	-3,76216	-1,91156	0,000441	0,001717
hsa-mir-498		-4,16264	-2,0575	0,004104	0,007089
hsa-miR-499a-3p	MI0003183	-4,22061	-2,07745	0,000692	0,002288
hsa-miR-499a-5p	MI0003183	-4,79769	-2,26234	0,005727	0,009442
hsa-miR-499b-5p	MI0017396	-5,58242	-2,48089	0,00023	0,001267

hsa-miR-5001-5p	MI0017867	-4,40655	-2,13965	0,001461	0,003747
hsa-miR-5010-3p	MI0017878	-4,57668	-2,1943	0,004045	0,007003
hsa-miR-501-3p	MI0003185	-4,9622	-2,31098	6,64E-05	0,000706
hsa-miR-502-3p	MI0003186	-4,28909	-2,10067	0,002858	0,005632
hsa-miR-505-3p	MI0003190	-2,66538	-1,41434	0,001131	0,003167
hsa-miR-506-3p	MI0003193	-4,37296	-2,12861	0,00282	0,005584
hsa-miR-507	MI0003194	-4,97798	-2,31556	0,000778	0,002446
hsa-miR-508-3p	MI0003195	-7,70065	-2,94498	2,63E-05	0,000599
hsa-miR-509-3-5p	MI0005717	-7,68156	-2,9414	1,24E-05	0,00055
hsa-miR-509-3p	MI0005530	-8,27145	-3,04814	2,32E-05	0,000599
hsa-miR-510-5p	MI0003197	-4,34938	-2,12081	0,001204	0,003325
hsa-miR-511-5p	MI0003127	-6,34025	-2,66454	4,15E-05	0,000634
hsa-miR-512-3p	MI0003140	-4,06234	-2,02231	0,00146	0,003747
hsa-miR-512-5p	MI0003140	-3,82018	-1,93364	0,001678	0,00412
hsa-miR-513a-3p	MI0003191	-5,82166	-2,54143	0,000405	0,001616
hsa-miR-513a-5p	MI0003191	-5,38561	-2,42911	0,000394	0,001616
hsa-miR-513b-5p	MI0006648	-6,0635	-2,60015	9,08E-06	0,00054
hsa-miR-513c-3p	MI0006649	-4,41459	-2,14228	0,000133	0,00101
hsa-miR-513c-5p	MI0006649	-6,10842	-2,6108	0,000339	0,001529
hsa-miR-514a-3p	MI0003198	-7,21825	-2,85165	3,01E-05	0,000599
hsa-miR-514b-3p	MI0014251	-5,14774	-2,36394	0,000236	0,001274
hsa-miR-514b-5p	MI0014251	-5,08882	-2,34733	0,000207	0,001209
hsa-miR-515-3p	MI0003144	-6,51249	-2,70321	4,21E-05	0,000634
hsa-miR-515-5p	MI0003144	-4,47544	-2,16203	0,002031	0,004515
hsa-miR-516a-3p		-6,5294	-2,70695	7,40E-05	0,000746
hsa-miR-516a-5p	MI0003180	-5,29874	-2,40565	0,000381	0,001592
hsa-miR-516b-3p		-5,29874	-2,40565	0,000381	0,001592
hsa-miR-516b-5p	MI0003167	-4,8946	-2,29119	0,000293	0,001434
hsa-miR-517a-3p	MI0003161	-3,77891	-1,91797	0,001824	0,004271
hsa-miR-517b-3p	MI0003165	-3,43141	-1,7788	0,002182	0,004732
hsa-miR-517c-3p		-5,18491	-2,37432	0,00171	0,004172
hsa-miR-518a-5p		-3,40289	-1,76676	0,000592	0,002054
hsa-miR-518b	MI0003156	-2,87334	-1,52273	0,002317	0,004917
hsa-miR-518c-5p		-7,18376	-2,84474	8,14E-06	0,00054
hsa-miR-518d-3p	MI0003171	-6,20392	-2,63318	2,21E-05	0,000599
hsa-miR-518d-5p		-7,18376	-2,84474	8,14E-06	0,00054
hsa-miR-518e-3p	MI0003169	-4,08606	-2,03071	0,004438	0,007584
hsa-miR-518e-5p		-4,30511	-2,10605	0,000868	0,002633
hsa-miR-518f-3p	MI0003154	-4,10468	-2,03727	0,00096	0,002797
hsa-miR-5196-3p		-4,42946	-2,14713	3,91E-07	0,000156
hsa-miR-5196-5p	MI0018175	-5,38076	-2,42781	5,73E-05	0,000701
hsa-miR-519a-3p		-5,18491	-2,37432	0,00171	0,004172
hsa-miR-519a-5p		-4,30511	-2,10605	0,000868	0,002633
hsa-miR-519b-3p	MI0003151	-4,31991	-2,111	0,000742	0,002396
hsa-miR-519b-5p		-4,30511	-2,10605	0,000868	0,002633
hsa-miR-519c-5p		-4,30511	-2,10605	0,000868	0,002633
hsa-miR-519e-3p	MI0003145	-4,6901	-2,22962	0,001632	0,004019
hsa-miR-520a-3p	MI0003149	-5,95718	-2,57463	6,03E-05	0,000701
hsa-miR-520a-5p	MI0003149	-4,76207	-2,25159	0,00082	0,002528
hsa-mir-520b		-3,36568	-1,7509	0,003547	0,006404
hsa-miR-520c-3p	MI0003158	-5,66309	-2,50159	0,000314	0,001496
hsa-miR-520d-3p	MI0003164	-6,47774	-2,69549	8,22E-06	0,00054
hsa-miR-520d-5p		-3,40289	-1,76676	0,000592	0,002054
hsa-mir-520e		-3,75034	-1,90702	0,002209	0,004763
hsa-miR-520f-3p	MI0003146	-4,94013	-2,30455	0,000433	0,001695
hsa-miR-520g-3p	MI0003166	-3,23736	-1,69482	0,003858	0,006796
hsa-miR-521	MI0003163	-3,64243	-1,8649	0,00087	0,002633

hsa-miR-522-5p		-4,30511	-2,10605	0,000868	0,002633
hsa-miR-523-5p		-4,30511	-2,10605	0,000868	0,002633
hsa-miR-524-3p	MI0003160	-3,36559	-1,75086	0,00348	0,006321
hsa-miR-525-3p	MI0003152	-5,46	-2,4489	0,001329	0,003583
hsa-miR-525-5p	MI0003152	-6,19017	-2,62998	0,000345	0,001529
hsa-miR-526a		-7,18376	-2,84474	8,14E-06	0,00054
hsa-miR-527		-3,40289	-1,76676	0,000592	0,002054
hsa-miR-532-3p	MI0003205	-4,33821	-2,1171	0,001736	0,004173
hsa-miR-532-5p	MI0003205	-3,32801	-1,73466	0,000159	0,001052
hsa-miR-539-3p	MI0003514	-4,05401	-2,01935	0,00072	0,002344
hsa-miR-542-5p	MI0003686	-4,02018	-2,00726	0,000772	0,002446
hsa-miR-543	MI0005565	-2,84719	-1,50954	0,002221	0,004778
hsa-miR-544a	MI0003515	-8,44513	-3,07812	3,53E-05	0,000599
hsa-miR-545-3p	MI0003516	-4,16657	-2,05886	0,002431	0,005078
hsa-miR-548a-3p	MI0003593	-4,08943	-2,0319	0,000153	0,001045
hsa-miR-548ad-3p	MI0016770	-4,6985	-2,2322	0,00019	0,001142
hsa-miR-548ah-5p	MI0016796	-5,9341	-2,56903	4,11E-05	0,000634
hsa-miR-548ak	MI0016840	-5,72784	-2,51799	7,10E-05	0,000735
hsa-miR-548al	MI0016851	-4,92093	-2,29893	0,002177	0,004732
hsa-miR-548am-5p		-5,86349	-2,55176	7,47E-05	0,000746
hsa-miR-548ar-3p	MI0019131	-5,38371	-2,4286	0,000816	0,002528
hsa-miR-548b-3p	MI0003596	-4,34026	-2,11778	0,000617	0,002111
hsa-miR-548c-5p		-5,86349	-2,55176	7,47E-05	0,000746
hsa-miR-548e-3p	MI0006344	-3,569	-1,83552	0,002968	0,005791
hsa-miR-548e-5p	MI0006344	-6,00082	-2,58516	0,001855	0,004292
hsa-miR-548g-3p	MI0006395	-6,48947	-2,6981	0,000363	0,001556
hsa-miR-548h-3p		-5,81202	-2,53904	1,01E-06	0,000269
hsa-miR-548h-5p	MI0006411	-4,00558	-2,00201	0,000449	0,001739
hsa-miR-548i	MI0006421	-4,40164	-2,13804	0,000317	0,001496
hsa-miR-548j-5p	MI0006345	-3,17197	-1,66538	0,00093	0,00274
hsa-miR-548k	MI0006354	-6,05997	-2,59931	0,000152	0,001045
hsa-miR-548l	MI0006361	-3,50579	-1,80974	0,00016	0,001052
hsa-miR-548m	MI0006400	-3,39773	-1,76457	0,001404	0,003673
hsa-miR-548n	MI0006399	-3,54074	-1,82405	0,000186	0,001142
hsa-miR-548o-5p		-5,86349	-2,55176	7,47E-05	0,000746
hsa-miR-548v	MI0014174	-7,23293	-2,85458	2,54E-05	0,000599
hsa-miR-548y	MI0016595	-5,72887	-2,51825	0,000475	0,001796
hsa-miR-548z		-5,81202	-2,53904	1,01E-06	0,000269
hsa-mir-549a		-5,49965	-2,45934	3,87E-05	0,000623
hsa-miR-551a	MI0003556	-4,28674	-2,09988	0,000357	0,001553
hsa-miR-551b-3p	MI0003575	-7,12752	-2,8334	0,000137	0,00101
hsa-miR-552-3p	MI0003557	-5,18984	-2,37569	0,000505	0,001894
hsa-miR-554	MI0003559	-3,91679	-1,96967	0,003305	0,006156
hsa-miR-555	MI0003561	-3,63756	-1,86297	0,001605	0,003977
hsa-miR-556-3p	MI0003562	-6,26403	-2,64709	0,000257	0,001349
hsa-miR-556-5p	MI0003562	-5,2192	-2,38383	2,22E-06	0,000431
hsa-miR-561-5p	MI0003567	-7,35421	-2,87857	3,19E-05	0,000599
hsa-miR-562	MI0003568	-3,83493	-1,9392	0,005481	0,009112
hsa-miR-564	MI0003570	-4,47935	-2,16329	0,001392	0,003667
hsa-miR-567	MI0003573	-4,00791	-2,00285	0,000375	0,001575
hsa-miR-568	MI0003574	-4,68156	-2,22699	0,002153	0,004718
hsa-miR-571	MI0003578	-6,45573	-2,69058	0,000261	0,001349
hsa-miR-573	MI0003580	-3,82837	-1,93673	0,00171	0,004172
hsa-miR-575	MI0003582	-2,4754	-1,30766	0,003478	0,006321
hsa-miR-576-3p	MI0003583	-4,38218	-2,13165	0,000871	0,002633
hsa-miR-576-5p	MI0003583	-5,4807	-2,45436	0,000928	0,00274
hsa-miR-577	MI0003584	-5,28843	-2,40284	0,000562	0,002017
hsa-miR-578	MI0003585	-3,60985	-1,85194	0,005291	0,008852

hsa-miR-580-3p	MI0003587	-5,72855	-2,51817	8,30E-05	0,000798
hsa-miR-582-5p	MI0003589	-4,31249	-2,10852	0,001096	0,003102
hsa-miR-584-3p	MI0003591	-4,05446	-2,01951	0,004029	0,006989
hsa-miR-584-5p	MI0003591	-4,80844	-2,26557	0,000151	0,001045
hsa-miR-585-3p	MI0003592	-5,9664	-2,57686	0,002031	0,004515
hsa-miR-587	MI0003595	-5,22713	-2,38602	0,000373	0,001575
hsa-miR-589-5p	MI0003599	-4,26312	-2,09191	0,002803	0,005584
hsa-miR-590-3p	MI0003602	-4,89806	-2,29221	0,00069	0,002288
hsa-miR-591	MI0003603	-5,30422	-2,40714	0,001718	0,004173
hsa-miR-592	MI0003604	-3,89297	-1,96087	0,002079	0,004596
hsa-miR-593-3p	MI0003605	-3,42089	-1,77437	0,002538	0,005222
hsa-miR-595	MI0003607	-5,73654	-2,52018	0,00012	0,000971
hsa-miR-598-3p	MI0003610	-5,48587	-2,45572	6,13E-05	0,000701
hsa-miR-599	MI0003611	-3,23165	-1,69227	0,00387	0,006802
hsa-miR-600	MI0003613	-4,91224	-2,29638	0,001765	0,004192
hsa-miR-601	MI0003614	-3,15148	-1,65603	0,005526	0,009167
hsa-miR-604	MI0003617	-4,28006	-2,09763	0,00157	0,003903
hsa-miR-605-5p	MI0003618	-3,8179	-1,93278	0,003791	0,006722
hsa-miR-606	MI0003619	-3,46455	-1,79267	0,002635	0,005337
hsa-miR-607	MI0003620	-5,2423	-2,3902	0,001093	0,003102
hsa-miR-608	MI0003621	-3,70651	-1,89006	0,005134	0,008661
hsa-miR-615-3p	MI0003628	-3,47083	-1,79528	0,005091	0,008607
hsa-miR-615-5p	MI0003628	-4,04209	-2,0151	0,003468	0,006321
hsa-miR-616-3p	MI0003629	-5,21187	-2,3818	0,000661	0,002228
hsa-miR-617	MI0003631	-4,15463	-2,05472	0,001731	0,004173
hsa-miR-619-3p	MI0003633	-3,75216	-1,90772	0,00073	0,002369
hsa-miR-620	MI0003634	-3,70717	-1,89032	0,003888	0,006804
hsa-miR-624-3p	MI0003638	-3,96665	-1,98792	0,002495	0,005184
hsa-miR-626	MI0003640	-4,63192	-2,21161	0,000153	0,001045
hsa-miR-628-3p	MI0003642	-4,17458	-2,06163	0,000982	0,00284
hsa-miR-628-5p	MI0003642	-4,98513	-2,31763	0,000195	0,001152
hsa-miR-629-5p	MI0003643	-5,3336	-2,41511	0,000399	0,001616
hsa-miR-631	MI0003645	-6,76233	-2,75752	3,42E-05	0,000599
hsa-miR-637	MI0003652	-3,3686	-1,75215	0,00332	0,006158
hsa-miR-638	MI0003653	-3,78108	-1,9188	0,000779	0,002446
hsa-miR-639	MI0003654	-4,82711	-2,27116	0,001917	0,004355
hsa-miR-640	MI0003655	-6,6491	-2,73316	3,21E-05	0,000599
hsa-miR-641	MI0003656	-3,15949	-1,65969	0,005224	0,008794
hsa-miR-642a-3p	MI0003657	-2,81766	-1,4945	0,003222	0,006107
hsa-miR-642a-5p	MI0003657	-4,2797	-2,09751	0,000351	0,001542
hsa-miR-643	MI0003658	-5,32647	-2,41318	0,00012	0,000971
hsa-miR-644a	MI0003659	-3,79355	-1,92355	0,000315	0,001496
hsa-miR-648	MI0003663	-4,89996	-2,29277	0,000285	0,001415
hsa-miR-649	MI0003664	-5,0824	-2,34551	0,000677	0,00226
hsa-miR-650	MI0003665	-5,80095	-2,53629	0,00607	0,009906
hsa-miR-6511a-5p	MI0022223	-4,233	-2,08168	0,003326	0,006158
hsa-miR-651-5p	MI0003666	-5,12752	-2,35826	0,000344	0,001529
hsa-miR-652-5p	MI0003667	-3,66063	-1,87209	0,006134	0,00997
hsa-miR-654-3p	MI0003676	-3,89065	-1,96001	0,001905	0,004347
hsa-miR-654-5p	MI0003676	-5,25624	-2,39403	0,000323	0,001505
hsa-miR-655-3p	MI0003677	-5,09418	-2,34885	0,000898	0,002693
hsa-miR-656-3p	MI0003678	-5,38778	-2,42969	0,000401	0,001616
hsa-miR-660-3p	MI0003684	-4,76587	-2,25274	0,001376	0,003649
hsa-miR-661	MI0003669	-9,05805	-3,1792	3,33E-05	0,000599
hsa-miR-663a	MI0003672	-4,68478	-2,22798	0,000467	0,001783
hsa-miR-664b-5p	MI0019134	-4,93353	-2,30262	0,000908	0,002714
hsa-miR-665	MI0005563	-6,34927	-2,66659	7,71E-05	0,00075

hsa-miR-671-3p	MI0003760	-5,81948	-2,54089	0,000538	0,001954
hsa-miR-671-5p	MI0003760	-5,47823	-2,45371	0,000189	0,001142
hsa-miR-6728-5p		-5,54751	-2,47184	0,000161	0,001052
hsa-miR-6732-3p		-4,42946	-2,14713	3,91E-07	0,000156
hsa-miR-675-5p	MI0005416	-6,77993	-2,76127	0,000123	0,000971
hsa-miR-744-5p	MI0005559	-5,34045	-2,41696	8,52E-05	0,000799
hsa-miR-758-3p		-5,54739	-2,47181	1,63E-05	0,000599
hsa-miR-758-5p	MI0003757	-4,14502	-2,05138	0,002164	0,004718
hsa-miR-7-5p	MI0000264	-3,24323	-1,69743	0,002571	0,00525
hsa-miR-760	MI0005567	-4,33608	-2,11639	0,000352	0,001542
hsa-miR-764	MI0003944	-5,17687	-2,37208	0,001168	0,003258
hsa-miR-765	MI0005116	-6,37308	-2,67199	5,09E-06	0,00054
hsa-miR-766-3p	MI0003836	-6,64763	-2,73284	8,61E-05	0,000799
hsa-miR-766-5p	MI0003836	-5,2678	-2,3972	0,003446	0,006317
hsa-miR-767-3p	MI0003763	-4,38547	-2,13273	0,000931	0,00274
hsa-miR-767-5p	MI0003763	-4,94332	-2,30548	0,00139	0,003667
hsa-miR-769-3p	MI0003834	-4,27016	-2,09429	0,005855	0,009594
hsa-miR-769-5p	MI0003834	-3,24872	-1,69987	0,000143	0,001034
hsa-miR-770-5p	MI0005118	-5,15506	-2,36599	0,000158	0,001052
hsa-miR-802	MI0003906	-5,29481	-2,40458	0,000282	0,001408
hsa-miR-873-3p	MI0005564	-3,93745	-1,97726	0,001244	0,003389
hsa-miR-874-5p	MI0005532	-3,39683	-1,76419	0,005257	0,008833
hsa-miR-875-3p	MI0005541	-5,81875	-2,54071	0,0001	0,000853
hsa-miR-876-3p	MI0005542	-6,75558	-2,75608	4,68E-05	0,000655
hsa-miR-877-5p	MI0005561	-5,20955	-2,38116	9,68E-05	0,000849
hsa-miR-885-3p	MI0005560	-5,41875	-2,43796	0,00027	0,001365
hsa-miR-885-5p	MI0005560	-3,2676	-1,70823	0,003703	0,006582
hsa-miR-887-3p	MI0005562	-4,22025	-2,07733	0,003645	0,006536
hsa-miR-889-3p	MI0005540	-5,87301	-2,5541	7,30E-06	0,00054
hsa-miR-890	MI0005533	-2,98589	-1,57816	0,003485	0,006321
hsa-miR-891a-5p	MI0005524	-5,85805	-2,55042	0,001837	0,004271
hsa-miR-891b	MI0005534	-6,3844	-2,67455	0,000216	0,001233
hsa-miR-892a	MI0005528	-4,92147	-2,29909	0,000917	0,002729
hsa-miR-892b	MI0005538	-3,96362	-1,98682	0,004182	0,007192
hsa-miR-922	MI0005714	-5,52292	-2,46543	0,001523	0,003798
hsa-miR-92b-3p	MI0003560	-2,83697	-1,50435	0,003921	0,006846
hsa-miR-933	MI0005755	-4,78222	-2,25768	0,003884	0,006804
hsa-miR-934	MI0005756	-3,53319	-1,82097	0,003028	0,005865
hsa-miR-935	MI0005757	-3,69781	-1,88667	0,002336	0,004944
hsa-miR-93-5p	MI0000095	2,07415	1,05252	0,001615	0,00399
hsa-miR-936	MI0005758	-3,27522	-1,71159	0,000616	0,002111
hsa-miR-937-3p	MI0005759	-5,09856	-2,35009	0,000941	0,00275
hsa-miR-939-5p	MI0005761	-5,04362	-2,33446	0,000662	0,002228
hsa-miR-940	MI0005762	-4,78152	-2,25747	0,000112	0,000923
hsa-miR-941	MI0005763	-3,54577	-1,8261	0,003259	0,006145
hsa-miR-942-5p	MI0005767	-4,60047	-2,20178	0,001517	0,003798
hsa-miR-944	MI0005769	-3,39069	-1,76158	0,00021	0,001212
hsa-miR-9-5p	MI0000466	-3,49342	-1,80464	0,000384	0,001594
hsa-miR-96-5p	MI0000098	-3,33237	-1,73655	0,003613	0,006504
hsa-miR-98-3p	MI0000100	-6,35173	-2,66715	0,00011	0,000913

Table S3. All the 143 miRDEs between clinical groups (advanced disease *vs.* early disease).

Nome	ID	FC	Log FC	*p*-value	Adj.-*p*
hsa-miR-99a-5p	MI0000101	3,33591	1,7381	0,0351	0,195967
hsa-miR-150-5p	MI0000479	2,71752	1,4423	0,0324	0,187927
hsa-miR-155-5p	MI0000681	2,5818	1,3684	0,0264	0,185283
hsa-let-7c-5p	MI0000064	2,19757	1,1359	0,0280	0,185283
hsa-miR-342-3p	MI0000805	2,1823	1,1259	0,0077	0,160566
hsa-miR-524-3p	MI0003160	-2,00014	-1,0001	0,013512	0,160566
hsa-miR-367-3p	MI0000775	-2,00319	-1,0023	0,026766	0,185283
hsa-miR-516a-3p		-2,0034	-1,00245	0,020806	0,181748
hsa-miR-516b-3p		-2,0034	-1,00245	0,020806	0,181748
hsa-miR-5196-5p	MI0018175	-2,01254	-1,00902	0,04614	0,216585
hsa-miR-507	MI0003194	-2,04041	-1,02886	0,038966	0,204812
hsa-miR-1249-5p	MI0006384	-2,0463	-1,03302	0,015295	0,164936
hsa-miR-181a-3p	MI0000289	-2,05304	-1,03776	0,008833	0,160566
hsa-miR-1323	MI0003786	-2,07733	-1,05473	0,044648	0,216177
hsa-miR-548j-5p	MI0006345	-2,0805	-1,05693	0,012062	0,160566
hsa-miR-3127-5p	MI0014144	-2,08323	-1,05882	0,020953	0,181748
hsa-miR-1908-5p	MI0008329	-2,08782	-1,062	0,019358	0,180449
hsa-miR-767-3p	MI0003763	-2,08918	-1,06294	0,020213	0,181748
hsa-miR-641	MI0003656	-2,08958	-1,06321	0,010909	0,160566
hsa-miR-548c-5p		-2,1029	-1,07238	0,01185	0,160566
hsa-miR-548am-5p		-2,1029	-1,07238	0,01185	0,160566
hsa-miR-548o-5p		-2,1029	-1,07238	0,01185	0,160566
hsa-miR-655-3p	MI0003677	-2,1037	-1,07293	0,049019	0,223527
hsa-miR-548ai		-2,10812	-1,07596	0,028466	0,185283
hsa-miR-570-5p		-2,10812	-1,07596	0,028466	0,185283
hsa-miR-513a-5p	MI0003191	-2,13581	-1,09478	0,044393	0,216177
hsa-miR-410-3p	MI0002465	-2,13595	-1,09488	0,024705	0,185283
hsa-miR-506-3p	MI0003193	-2,13855	-1,09663	0,040567	0,210213
hsa-miR-421	MI0003685	-2,14147	-1,0986	0,019447	0,180449
hsa-miR-518f-3p	MI0003154	-2,14593	-1,1016	0,02178	0,184575
hsa-miR-190a-5p	MI0000486	-2,1475	-1,10266	0,026705	0,185283
hsa-miR-3164	MI0014194	-2,15739	-1,10929	0,009643	0,160566
hsa-miR-1278	MI0006425	-2,16124	-1,11186	0,013163	0,160566
hsa-miR-3131	MI0014151	-2,16242	-1,11265	0,047063	0,217088
hsa-miR-1279	MI0006426	-2,16711	-1,11577	0,033445	0,188186
hsa-miR-516b-5p	MI0003167	-2,16811	-1,11644	0,032754	0,187927
hsa-miR-552-3p	MI0003557	-2,16977	-1,11754	0,046856	0,217088
hsa-miR-455-5p	MI0003513	-2,17617	-1,12179	0,007469	0,160566
hsa-miR-1258	MI0006392	-2,1815	-1,12532	0,027927	0,185283
hsa-miR-3185	MI0014227	-2,18353	-1,12666	0,029385	0,185283
hsa-miR-520h	MI0003175	-2,1924	-1,13251	0,046571	0,217088
hsa-miR-4787-5p	MI0017434	-2,19441	-1,13383	0,009385	0,160566
hsa-miR-34c-3p	MI0000743	-2,19906	-1,13689	0,004168	0,133057

hsa-miR-4524a-5p	MI0016891	-2,2025	-1,13914	0,024223	0,185283
hsa-miR-501-3p	MI0003185	-2,20361	-1,13987	0,012335	0,160566
hsa-miR-208b-5p	MI0005570	-2,21269	-1,1458	0,010229	0,160566
hsa-miR-323a-3p	MI0000807	-2,22604	-1,15448	0,02372	0,185283
hsa-miR-519e-3p	MI0003145	-2,23612	-1,161	0,0191	0,180449
hsa-miR-18a-5p	MI0000072	-2,23648	-1,16123	0,01177	0,160566
hsa-miR-606	MI0003619	-2,24159	-1,16452	0,013642	0,160566
hsa-miR-566		-2,25391	-1,17243	0,021864	0,184575
hsa-miR-888-5p	MI0005537	-2,26392	-1,17882	0,038335	0,203941
hsa-miR-766-3p	MI0003836	-2,27319	-1,18472	0,023009	0,185283
hsa-miR-656-3p	MI0003678	-2,27467	-1,18566	0,025086	0,185283
hsa-miR-2278	MI0011285	-2,28387	-1,19148	0,005223	0,138762
hsa-miR-146b-3p	MI0003129	-2,28948	-1,19502	0,011901	0,160566
hsa-miR-1302	MI0006363	-2,29061	-1,19573	0,031627	0,187927
hsa-miR-548j-3p	MI0006345	-2,29223	-1,19675	0,016832	0,173254
hsa-miR-525-3p	MI0003152	-2,29625	-1,19928	0,027339	0,185283
hsa-miR-514a-3p	MI0003198	-2,29905	-1,20104	0,043623	0,216177
hsa-miR-338-5p	MI0000814	-2,30665	-1,2058	0,040286	0,210118
hsa-miR-3151-5p	MI0014178	-2,30899	-1,20726	0,026151	0,185283
hsa-miR-449a	MI0001648	-2,31306	-1,2098	0,041674	0,214551
hsa-miR-1205	MI0006338	-2,31755	-1,2126	0,028121	0,185283
hsa-miR-448	MI0001637	-2,32212	-1,21544	0,045627	0,216585
hsa-miR-181b-2-3p	MI0000683	-2,32758	-1,21883	0,011358	0,160566
hsa-miR-494-5p	MI0003134	-2,35507	-1,23577	0,013799	0,160566
hsa-miR-184	MI0000481	-2,35652	-1,23666	0,036378	0,196759
hsa-miR-1206	MI0006339	-2,35863	-1,23795	0,008291	0,160566
hsa-miR-548o-3p		-2,36723	-1,2432	0,011494	0,160566
hsa-miR-548av-3p		-2,36723	-1,2432	0,011494	0,160566
hsa-miR-548ah-3p		-2,36723	-1,2432	0,011494	0,160566
hsa-miR-514b-5p	MI0014251	-2,36817	-1,24377	0,032559	0,187927
hsa-miR-514a-5p	MI0003198	-2,37046	-1,24517	0,009308	0,160566
hsa-miR-548y	MI0016595	-2,37881	-1,25024	0,028049	0,185283
hsa-miR-483-5p	MI0002467	-2,43088	-1,28148	0,028931	0,185283
hsa-miR-651-5p	MI0003666	-2,43282	-1,28263	0,024514	0,185283
hsa-miR-378c	MI0015825	-2,44738	-1,29124	0,018409	0,180449
hsa-miR-3928-3p	MI0016438	-2,45849	-1,29777	0,018875	0,180449
hsa-miR-129-2-3p	MI0000473	-2,45932	-1,29826	0,02972	0,185283
hsa-miR-4425	MI0016764	-2,4643	-1,30118	0,02958	0,185283
hsa-miR-935	MI0005757	-2,47257	-1,30601	0,005564	0,138762
hsa-miR-142-5p	MI0000458	-2,48947	-1,31584	0,003486	0,131054
hsa-miR-6721-5p	MI0022556	-2,51347	-1,32968	0,013884	0,160566
hsa-miR-345-5p	MI0000825	-2,54923	-1,35006	0,003777	0,131054
hsa-miR-548a-5p	MI0003612	-2,55361	-1,35254	0,019023	0,180449
hsa-miR-152-5p	MI0000462	-2,55719	-1,35456	0,003534	0,131054
hsa-miR-301b-3p	MI0005568	-2,56189	-1,35721	0,005452	0,138762
hsa-miR-487a-3p	MI0002471	-2,56427	-1,35855	0,023137	0,185283

hsa-miR-103a-3p	MI0000108	-2,57994	-1,36734	0,003503	0,131054
hsa-miR-761	MI0003941	-2,58809	-1,37189	0,013668	0,160566
hsa-miR-135b-5p	MI0000810	-2,59113	-1,37358	0,016935	0,173254
hsa-miR-323b-5p	MI0014206	-2,60595	-1,38181	0,009727	0,160566
hsa-miR-649	MI0003664	-2,6142	-1,38637	0,044559	0,216177
hsa-miR-548ar-3p	MI0019131	-2,62349	-1,39149	0,00996	0,160566
hsa-miR-33a-5p	MI0000091	-2,62457	-1,39208	0,018563	0,180449
hsa-miR-519d-3p	MI0003162	-2,63337	-1,39691	0,00497	0,138762
hsa-miR-188-3p	MI0000484	-2,63911	-1,40005	0,023197	0,185283
hsa-miR-490-5p	MI0003125	-2,64851	-1,40518	0,00501	0,138762
hsa-miR-1262	MI0006397	-2,66121	-1,41208	0,033487	0,188186
hsa-miR-553	MI0003558	-2,68064	-1,42258	0,027741	0,185283
hsa-miR-1252-5p	MI0006434	-2,68822	-1,42665	0,012248	0,160566
hsa-miR-1203	MI0006335	-2,68911	-1,42713	0,02541	0,185283
hsa-miR-6511a-5p	MI0022223	-2,70984	-1,43821	0,010208	0,160566
hsa-miR-892b	MI0005538	-2,72786	-1,44777	0,00413	0,133057
hsa-miR-590-3p	MI0003602	-2,75731	-1,46326	0,013564	0,160566
hsa-miR-561-3p	MI0003567	-2,77787	-1,47398	0,003224	0,131054
hsa-miR-664b-5p	MI0019134	-2,77935	-1,47475	0,003439	0,131054
hsa-miR-4536-3p	MI0016906	-2,7896	-1,48006	0,020481	0,181748
hsa-miR-562	MI0003568	-2,79047	-1,48051	0,000905	0,131054
hsa-miR-1304-3p	MI0006371	-2,80782	-1,48945	0,016103	0,169085
hsa-miR-615-3p	MI0003628	-2,81062	-1,49089	0,000327	0,131054
hsa-miR-1273c	MI0014171	-2,84705	-1,50947	0,003496	0,131054
hsa-miR-924	MI0005716	-2,85081	-1,51137	0,032647	0,187927
hsa-miR-939-5p	MI0005761	-2,87077	-1,52144	0,00997	0,160566
hsa-miR-660-5p	MI0003684	-2,89676	-1,53444	0,039012	0,204812
hsa-miR-571	MI0003578	-2,90797	-1,54001	0,024308	0,185283
hsa-miR-1306-3p	MI0006443	-2,91071	-1,54137	0,000706	0,131054
hsa-miR-4451	MI0016797	-2,91517	-1,54358	0,004433	0,136066
hsa-miR-584-3p	MI0003591	-2,9548	-1,56306	0,003431	0,131054
hsa-miR-221-3p	MI0000298	-2,97766	-1,57418	0,000455	0,131054
hsa-miR-6503-3p	MI0022215	-2,9831	-1,57681	0,001432	0,131054
hsa-miR-5010-5p	MI0017878	-2,98436	-1,57742	0,010279	0,160566
hsa-miR-548d-3p	MI0003671	-3,02532	-1,59709	0,015714	0,167202
hsa-miR-450a-2-3p	MI0003187	-3,04426	-1,60609	0,029695	0,185283
hsa-miR-766-5p	MI0003836	-3,06815	-1,61737	0,009479	0,160566
hsa-miR-595	MI0003607	-3,08975	-1,62749	0,001371	0,131054
hsa-miR-196a-3p	MI0000279	-3,09813	-1,6314	0,014237	0,161229
hsa-miR-525-5p	MI0003152	-3,18287	-1,67033	0,002595	0,131054
hsa-miR-554	MI0003559	-3,20399	-1,67987	0,001223	0,131054
hsa-miR-190a-3p	MI0000486	-3,21712	-1,68577	0,043723	0,216177
hsa-miR-1271-5p	MI0003814	-3,29596	-1,7207	0,002966	0,131054
hsa-miR-6511a-3p	MI0022223	-3,29738	-1,72132	0,003145	0,131054
hsa-miR-579-5p	MI0003586	-3,30163	-1,72318	0,000549	0,131054

hsa-miR-616-3p	MI0003629	-3,3755	-1,7551	0,018321	0,180449
hsa-miR-620	MI0003634	-3,3887	-1,76073	0,008838	0,160566
hsa-miR-3934-5p	MI0016590	-3,40721	-1,76859	0,002001	0,131054
hsa-miR-568	MI0003574	-3,42554	-1,77633	0,008264	0,160566
hsa-miR-891a-5p	MI0005524	-3,55988	-1,8318	0,0077	0,160566
hsa-miR-376a-2-5p	MI0003529	-3,64543	-1,8661	0,0054	0,138762
hsa-miR-551b-3p	MI0003575	-3,8487	-1,9444	0,0020	0,131054
hsa-miR-1285-5p	MI0006346	-3,93908	-1,9779	0,0121	0,160566
hsa-miR-362-3p	MI0000762	-6,151	-2,6208	0,0091	0,160566

Table S4A. All the target genes on 24 miRDEs obtained by DIANA TOOLS and miRTarBase.

Gene	miRNA	Database	Gene	miRNA	Database
A1BG	*hsa-miR-661*	MirTarBase	*MPRIP*	*hsa-miR-22-3p*	DIANA TOOLS
AAED1	*hsa-miR-661*	MirTarBase	*MRM3*	*hsa-miR-661*	MirTarBase
AAED1	*hsa-miR-661*	MirTarBase	*MRPS10*	*hsa-miR-661*	MirTarBase
AARS	*hsa-miR-25-3p*	DIANA TOOLS	*MRPS10*	*hsa-miR-661*	MirTarBase
ABCA1	*hsa-miR-25-3p*	DIANA TOOLS	*MRPS14*	*hsa-miR-205-5p*	DIANA TOOLS
ABCB7	*hsa-miR-130a-3p*	DIANA TOOLS	*MRPS17*	*hsa-miR-661*	MirTarBase
ABCB7	*hsa-miR-661*	MirTarBase	*MRPS21*	*hsa-miR-661*	MirTarBase
ABCC5	*hsa-let-7a-5p*	DIANA TOOLS	*MRPS25*	*hsa-miR-433-3p*	MirTarBase
ABCC8	*hsa-let-7a-5p*	DIANA TOOLS	*MRS2*	*hsa-let-7a-5p*	DIANA TOOLS
ABCD3	*hsa-miR-21-5p*	DIANA TOOLS	*MSH6*	*hsa-let-7a-5p*	DIANA TOOLS
ABCF2	*hsa-miR-16-5p*	DIANA TOOLS	*MSL2*	*hsa-miR-22-3p*	DIANA TOOLS
ABCF3	*hsa-miR-661*	MirTarBase	*MSN*	*hsa-miR-200c-3p*	DIANA TOOLS
ABCF3	*hsa-miR-661*	MirTarBase	*MTA1*	*hsa-miR-661*	MirTarBase
ABCF3	*hsa-miR-661*	MirTarBase	*MTA2*	*hsa-miR-661*	MirTarBase
ABHD12	*hsa-miR-661*	MirTarBase	*MTCH1*	*hsa-miR-142-3p*	DIANA TOOLS
ABHD5	*hsa-miR-661*	MirTarBase	*MTCL1*	*hsa-miR-130a-3p*	DIANA TOOLS
ABHD5	*hsa-miR-661*	MirTarBase	*MTDH*	*hsa-miR-22-3p*	DIANA TOOLS
ABI2	*hsa-miR-15b-5p*	DIANA TOOLS	*MTDH*	*hsa-let-7a-5p*	DIANA TOOLS
ABI2	*hsa-miR-16-5p*	DIANA TOOLS	*MTERFD2*	*hsa-miR-93-5p*	DIANA TOOLS
ABI2	*hsa-miR-381-5p*	MirTarBase	*MTF1*	*hsa-miR-22-3p*	DIANA TOOLS
ABL2	*hsa-miR-16-5p*	DIANA TOOLS	*MTHFD1*	*hsa-miR-661*	MirTarBase
ABL2	*hsa-miR-15b-5p*	DIANA TOOLS	*MTMR3*	*hsa-miR-15b-5p*	DIANA TOOLS
ABL2	*hsa-let-7a-5p*	DIANA TOOLS	*MTMR3*	*hsa-miR-16-5p*	DIANA TOOLS
ABRAXAS1	*hsa-miR-661*	MirTarBase	*MTMR4*	*hsa-miR-130a-3p*	DIANA TOOLS
ABT1	*hsa-let-7a-5p*	DIANA TOOLS	*MTMR6*	*hsa-miR-130a-3p*	DIANA TOOLS
AC012123.1	*hsa-miR-142-3p*	DIANA TOOLS	*MTMR9*	*hsa-miR-130a-3p*	DIANA TOOLS
ACAD8	*hsa-miR-661*	MirTarBase	*MTMR9*	*hsa-miR-433-3p*	MirTarBase
ACAP2	*hsa-miR-661*	MirTarBase	*MTOR*	*hsa-miR-144-3p*	DIANA TOOLS
ACBD3	*hsa-miR-130a-3p*	DIANA TOOLS	*MTOR*	*hsa-miR-144-3p*	MirTarBase
ACP2	*hsa-miR-15b-5p*	DIANA TOOLS	*MTOR*	*hsa-miR-144-3p*	MirTarBase
ACP2	*hsa-miR-16-5p*	DIANA TOOLS	*MTSS1L*	*hsa-miR-200c-3p*	DIANA TOOLS
ACSL3	*hsa-miR-16-5p*	DIANA TOOLS	*MTSS1L*	*hsa-miR-661*	MirTarBase
ACSL3	*hsa-miR-15b-5p*	DIANA TOOLS	*MTUS1*	*hsa-miR-142-3p*	DIANA TOOLS
ACSL4	*hsa-miR-15b-5p*	DIANA TOOLS	*MTX3*	*hsa-miR-144-3p*	DIANA TOOLS
ACSL4	*hsa-miR-16-5p*	DIANA TOOLS	*MTX3*	*hsa-miR-661*	MirTarBase
ACTB	*hsa-let-7a-5p*	DIANA TOOLS	*MTX3*	*hsa-miR-661*	MirTarBase
ACTR2	*hsa-miR-15b-5p*	DIANA TOOLS	*MVB12B*	*hsa-miR-22-3p*	DIANA TOOLS
ACTR2	*hsa-miR-16-5p*	DIANA TOOLS	*MYB*	*hsa-miR-15b-5p*	DIANA TOOLS
ACVR1	*hsa-miR-130a-3p*	DIANA TOOLS	*MYB*	*hsa-miR-16-5p*	DIANA TOOLS
ACVR1B	*hsa-let-7a-5p*	DIANA TOOLS	*MYBL1*	*hsa-miR-16-5p*	DIANA TOOLS
ACVR1C	*hsa-let-7a-5p*	DIANA TOOLS	*MYBL1*	*hsa-miR-15b-5p*	DIANA TOOLS
ACVR2A	*hsa-miR-15b-5p*	DIANA TOOLS	*MYC*	*hsa-let-7a-5p*	MirTarBase
ACVR2A	*hsa-miR-16-5p*	DIANA TOOLS	*MYC*	*hsa-let-7a-5p*	MirTarBase
ACVR2B	*hsa-miR-16-5p*	DIANA TOOLS	*MYCBP*	*hsa-let-7a-5p*	DIANA TOOLS

Adamts1	*hsa-miR-144-3p*	MirTarBase	*MYCN*	*hsa-miR-200c-3p*	DIANA TOOLS
ADAMTS12	*hsa-let-7a-5p*	DIANA TOOLS	*MYCN*	*hsa-let-7a-5p*	DIANA TOOLS
ADAMTS17	*hsa-miR-661*	MirTarBase	*MYDGF*	*hsa-miR-661*	MirTarBase
ADAMTS5	*hsa-let-7a-5p*	DIANA TOOLS	*MYLIP*	*hsa-miR-25-3p*	DIANA TOOLS
ADIPOR2	*hsa-let-7a-5p*	DIANA TOOLS	*MYNN*	*hsa-miR-200c-3p*	DIANA TOOLS
ADM	*hsa-miR-25-3p*	DIANA TOOLS	*MYO18A*	*hsa-miR-25-3p*	DIANA TOOLS
ADNP	*hsa-miR-21-5p*	DIANA TOOLS	*MYO1B*	*hsa-miR-25-3p*	DIANA TOOLS
ADRB1	*hsa-miR-25-3p*	DIANA TOOLS	*MYO1G*	*hsa-miR-15b-5p*	DIANA TOOLS
ADRB2	*hsa-let-7a-5p*	DIANA TOOLS	*MYO1G*	*hsa-miR-16-5p*	DIANA TOOLS
AEN	*hsa-let-7a-5p*	DIANA TOOLS	*MYO5A*	*hsa-miR-15b-5p*	DIANA TOOLS
AFF3	*hsa-miR-509-3-5p*	DIANA TOOLS	*MYO5A*	*hsa-miR-16-5p*	DIANA TOOLS
AFMID	*hsa-miR-433-3p*	MirTarBase	*MYO5A*	*hsa-miR-25-3p*	DIANA TOOLS
AGAP1	*hsa-let-7a-5p*	DIANA TOOLS	*MYO5A*	*hsa-miR-190b*	DIANA TOOLS
AGFG1	*hsa-miR-130a-3p*	DIANA TOOLS	*MYO5B*	*hsa-miR-15b-5p*	DIANA TOOLS
AGFG2	*hsa-miR-93-5p*	DIANA TOOLS	*MYO9A*	*hsa-miR-200c-3p*	DIANA TOOLS
AGMAT	*hsa-miR-661*	MirTarBase	*MYPN*	*hsa-miR-661*	MirTarBase
AGO1	*hsa-miR-130a-3p*	DIANA TOOLS	*MYPN*	*hsa-miR-661*	MirTarBase
AGO1	*hsa-miR-15b-5p*	DIANA TOOLS	*MYPN*	*hsa-miR-661*	MirTarBase
AGO1	*hsa-miR-16-5p*	DIANA TOOLS	*N4BP1*	*hsa-miR-16-5p*	DIANA TOOLS
AGO1	*hsa-let-7a-5p*	MirTarBase	*N4BP1*	*hsa-miR-15b-5p*	DIANA TOOLS
AGO3	*hsa-miR-31-5p*	DIANA TOOLS	*N4BP1*	*hsa-miR-381-5p*	MirTarBase
AGO3	*hsa-let-7a-5p*	DIANA TOOLS	*N4BP2*	*hsa-miR-25-3p*	DIANA TOOLS
AGO3	*hsa-miR-15b-5p*	DIANA TOOLS	*NAA16*	*hsa-miR-200c-3p*	DIANA TOOLS
AGO3	*hsa-miR-16-5p*	DIANA TOOLS	*NAA25*	*hsa-miR-16-5p*	DIANA TOOLS
AGO4	*hsa-miR-15b-5p*	DIANA TOOLS	*NAA25*	*hsa-miR-15b-5p*	DIANA TOOLS
AGO4	*hsa-miR-16-5p*	DIANA TOOLS	*NAA30*	*hsa-let-7a-5p*	DIANA TOOLS
AGO4	*hsa-let-7a-5p*	DIANA TOOLS	*NABP1*	*hsa-miR-130a-3p*	DIANA TOOLS
AGO4	*hsa-let-7a-5p*	MirTarBase	*NAGA*	*hsa-miR-25-3p*	DIANA TOOLS
AGPAT5	*hsa-miR-190b*	DIANA TOOLS	*NANOS1*	*hsa-miR-381-5p*	MirTarBase
AHCTF1	*hsa-miR-93-5p*	DIANA TOOLS	*NAP1L1*	*hsa-let-7a-5p*	DIANA TOOLS
AHCYL2	*hsa-miR-16-5p*	DIANA TOOLS	*NAP1L5*	*hsa-miR-200c-3p*	DIANA TOOLS
AHCYL2	*hsa-miR-661*	MirTarBase	*NAPG*	*hsa-miR-15b-5p*	DIANA TOOLS
AKAP11	*hsa-miR-16-5p*	DIANA TOOLS	*NAPG*	*hsa-miR-16-5p*	DIANA TOOLS
AKAP11	*hsa-miR-15b-5p*	DIANA TOOLS	*NAT8L*	*hsa-miR-16-5p*	DIANA TOOLS
AKAP8	*hsa-let-7a-5p*	DIANA TOOLS	*NAT8L*	*hsa-miR-15b-5p*	DIANA TOOLS
AKIRIN2	*hsa-miR-142-3p*	DIANA TOOLS	*NAV1*	*hsa-miR-16-5p*	DIANA TOOLS
AKR7A2	*hsa-miR-661*	MirTarBase	*NAV1*	*hsa-miR-15b-5p*	DIANA TOOLS
AKR7A2	*hsa-miR-661*	MirTarBase	*NBEA*	*hsa-miR-21-5p*	DIANA TOOLS
AKT3	*hsa-miR-15b-5p*	DIANA TOOLS	*NBEA*	*hsa-miR-16-5p*	DIANA TOOLS
AKT3	*hsa-miR-16-5p*	DIANA TOOLS	*NBEA*	*hsa-miR-15b-5p*	DIANA TOOLS
AKT3	*hsa-miR-22-3p*	DIANA TOOLS	*NBL1*	*hsa-miR-93-5p*	DIANA TOOLS
ALDH1A3	*hsa-miR-16-5p*	DIANA TOOLS	*NBR1*	*hsa-miR-200c-3p*	DIANA TOOLS
ALDH1B1	*hsa-miR-661*	MirTarBase	*NCAPD2*	*hsa-miR-93-5p*	DIANA TOOLS
ALDH2	*hsa-miR-16-5p*	DIANA TOOLS	*NCDN*	*hsa-miR-22-3p*	DIANA TOOLS
ALDH2	*hsa-miR-15b-5p*	DIANA TOOLS	*NCKAP1*	*hsa-miR-130a-3p*	DIANA TOOLS
ALDH6A1	*hsa-miR-661*	MirTarBase	*NCKAP1*	*hsa-miR-142-3p*	DIANA TOOLS
ALDOA	*hsa-miR-433-3p*	MirTarBase	*NCKAP1*	*hsa-miR-144-3p*	DIANA TOOLS

ALDOA	*hsa-miR-661*	MirTarBase	*NCOA1*	*hsa-miR-22-3p*	DIANA TOOLS
ALG14	*hsa-miR-661*	MirTarBase	*NCOA2*	*hsa-miR-21-5p*	DIANA TOOLS
ALG3	*hsa-miR-16-5p*	DIANA TOOLS	*NCOA3*	*hsa-miR-200c-3p*	DIANA TOOLS
AMD1	*hsa-miR-661*	MirTarBase	*NCOA7*	*hsa-miR-93-5p*	DIANA TOOLS
AMFR	*hsa-miR-200c-3p*	DIANA TOOLS	*NCOR2*	*hsa-miR-200c-3p*	DIANA TOOLS
AMMECR1	*hsa-miR-190b*	DIANA TOOLS	*NCS1*	*hsa-miR-661*	MirTarBase
AMOTL1	*hsa-miR-15b-5p*	DIANA TOOLS	*NDEL1*	*hsa-miR-130a-3p*	DIANA TOOLS
AMOTL1	*hsa-miR-16-5p*	DIANA TOOLS	*NDST2*	*hsa-let-7a-5p*	DIANA TOOLS
ANGEL1	*hsa-miR-661*	MirTarBase	*NDUFA4*	*hsa-miR-205-5p*	DIANA TOOLS
ANGEL2	*hsa-miR-22-3p*	DIANA TOOLS	*NDUFB5*	*hsa-miR-661*	MirTarBase
ANGEL2	*hsa-miR-130a-3p*	DIANA TOOLS	*NDUFV3*	*hsa-miR-661*	MirTarBase
ANGPT4	*hsa-miR-661*	MirTarBase	*NECAP1*	*hsa-miR-25-3p*	DIANA TOOLS
ANGPT4	*hsa-miR-661*	MirTarBase	*NECTIN1*	*hsa-miR-661*	MirTarBase
ANKFY1	*hsa-miR-661*	MirTarBase	*NEDD1*	*hsa-miR-200c-3p*	DIANA TOOLS
ANKIB1	*hsa-miR-16-5p*	DIANA TOOLS	*NEDD4*	*hsa-miR-22-3p*	DIANA TOOLS
ANKIB1	*hsa-miR-15b-5p*	DIANA TOOLS	*NEFH*	*hsa-miR-25-3p*	DIANA TOOLS
ANKIB1	*hsa-miR-130a-3p*	DIANA TOOLS	*NEFL*	*hsa-miR-381-5p*	MirTarBase
ANKIB1	*hsa-miR-25-3p*	DIANA TOOLS	*NEK3*	*hsa-let-7a-5p*	DIANA TOOLS
ANKRD13C	*hsa-miR-93-5p*	DIANA TOOLS	*NEK7*	*hsa-miR-25-3p*	DIANA TOOLS
ANKRD17	*hsa-miR-16-5p*	DIANA TOOLS	*NEK9*	*hsa-miR-433-3p*	MirTarBase
ANKRD17	*hsa-miR-15b-5p*	DIANA TOOLS	*NEUROD1*	*hsa-miR-190b*	DIANA TOOLS
ANKRD40	*hsa-miR-200c-3p*	DIANA TOOLS	*NF2*	*hsa-let-7a-5p*	MirTarBase
ANKRD49	*hsa-let-7a-5p*	DIANA TOOLS	*NF2*	*hsa-miR-661*	MirTarBase
ANKRD50	*hsa-miR-142-3p*	DIANA TOOLS	*NFAT5*	*hsa-let-7a-5p*	DIANA TOOLS
ANKRD52	*hsa-miR-22-3p*	DIANA TOOLS	*NFAT5*	*hsa-miR-22-3p*	DIANA TOOLS
ANKRD52	*hsa-miR-130a-3p*	DIANA TOOLS	*NFAT5*	*hsa-miR-25-3p*	DIANA TOOLS
ANKRD62	*hsa-miR-661*	MirTarBase	*NFATC2IP*	*hsa-miR-661*	MirTarBase
ANKS4B	*hsa-miR-661*	MirTarBase	*NFATC3*	*hsa-miR-15b-5p*	DIANA TOOLS
ANLN	*hsa-miR-15b-5p*	DIANA TOOLS	*NFATC3*	*hsa-miR-16-5p*	DIANA TOOLS
ANLN	*hsa-miR-200c-3p*	DIANA TOOLS	*NFE2L1*	*hsa-miR-16-5p*	DIANA TOOLS
ANP32E	*hsa-miR-25-3p*	DIANA TOOLS	*NFE2L2*	*hsa-miR-144-3p*	MirTarBase
ANXA11	*hsa-miR-16-5p*	DIANA TOOLS	*NFE2L2*	*hsa-miR-144-3p*	MirTarBase
ANXA11	*hsa-miR-15b-5p*	DIANA TOOLS	*NFIA*	*hsa-miR-200c-3p*	DIANA TOOLS
AP1S2	*hsa-miR-200c-3p*	DIANA TOOLS	*NFIA*	*hsa-miR-223-3p*	DIANA TOOLS
AP2B1	*hsa-miR-15b-5p*	DIANA TOOLS	*NFIB*	*hsa-miR-25-3p*	DIANA TOOLS
AP2B1	*hsa-miR-16-5p*	DIANA TOOLS	*NFIB*	*hsa-miR-21-5p*	DIANA TOOLS
AP3M1	*hsa-miR-21-5p*	DIANA TOOLS	*NFKB1*	*hsa-let-7a-5p*	MirTarBase
APLN	*hsa-miR-16-5p*	DIANA TOOLS	*NFYA*	*hsa-miR-22-3p*	DIANA TOOLS
APOC3	*hsa-miR-661*	MirTarBase	*NFYA*	*hsa-miR-200c-3p*	DIANA TOOLS
APOC3	*hsa-miR-661*	MirTarBase	*NHLRC2*	*hsa-miR-16-5p*	DIANA TOOLS
APP	*hsa-let-7a-5p*	MirTarBase	*NHLRC2*	*hsa-miR-15b-5p*	DIANA TOOLS
APP	*hsa-miR-144-3p*	MirTarBase	*NHLRC3*	*hsa-let-7a-5p*	DIANA TOOLS
APPL1	*hsa-miR-25-3p*	DIANA TOOLS	*NIN*	*hsa-miR-200c-3p*	DIANA TOOLS
AQP6	*hsa-miR-661*	MirTarBase	*NINJ1*	*hsa-miR-433-3p*	MirTarBase
AR	*hsa-miR-16-5p*	DIANA TOOLS	*NIPA1*	*hsa-miR-93-5p*	DIANA TOOLS
ARAP2	*hsa-miR-130a-3p*	DIANA TOOLS	*NIPA1*	*hsa-let-7a-5p*	DIANA TOOLS
ARAP2	*hsa-miR-93-5p*	DIANA TOOLS	*NKAP*	*hsa-miR-661*	MirTarBase

AREL1	*hsa-miR-205-5p*	DIANA TOOLS	*NKIRAS2*	*hsa-let-7a-5p*	MirTarBase
AREL1	*hsa-miR-16-5p*	DIANA TOOLS	*NKX2-2*	*hsa-miR-661*	MirTarBase
AREL1	*hsa-miR-15b-5p*	DIANA TOOLS	*NKX3-1*	*hsa-miR-144-3p*	DIANA TOOLS
ARFGAP2	*hsa-miR-16-5p*	DIANA TOOLS	*NLK*	*hsa-miR-25-3p*	DIANA TOOLS
ARFIP2	*hsa-miR-22-3p*	DIANA TOOLS	*NLRP9*	*hsa-miR-661*	MirTarBase
ARG2	*hsa-let-7a-5p*	DIANA TOOLS	*NLRX1*	*hsa-miR-16-5p*	DIANA TOOLS
ARG2	*hsa-let-7a-5p*	MirTarBase	*NLRX1*	*hsa-miR-15b-5p*	DIANA TOOLS
ARHGAP1	*hsa-miR-130a-3p*	DIANA TOOLS	*NME1-NME2*	*hsa-miR-661*	MirTarBase
ARHGAP12	*hsa-miR-130a-3p*	DIANA TOOLS	*NME6*	*hsa-let-7a-5p*	DIANA TOOLS
ARHGAP24	*hsa-miR-21-5p*	DIANA TOOLS	*NNT*	*hsa-miR-16-5p*	DIANA TOOLS
ARHGAP28	*hsa-let-7a-5p*	DIANA TOOLS	*NOL4L*	*hsa-let-7a-5p*	DIANA TOOLS
ARHGDIA	*hsa-miR-661*	MirTarBase	*NOL4L*	*hsa-miR-15b-5p*	DIANA TOOLS
ARHGEF10	*hsa-miR-93-5p*	DIANA TOOLS	*NOL4L*	*hsa-miR-16-5p*	DIANA TOOLS
ARHGEF12	*hsa-miR-22-3p*	DIANA TOOLS	*NOLC1*	*hsa-miR-22-3p*	DIANA TOOLS
ARHGEF15	*hsa-let-7a-5p*	DIANA TOOLS	*NOM1*	*hsa-miR-661*	MirTarBase
ARHGEF2	*hsa-miR-31-5p*	DIANA TOOLS	*NOTCH1*	*hsa-miR-144-3p*	MirTarBase
ARHGEF7	*hsa-miR-21-5p*	DIANA TOOLS	*NOTCH1*	*hsa-miR-144-3p*	MirTarBase
ARID1B	*hsa-miR-25-3p*	DIANA TOOLS	*NOV*	*hsa-miR-130a-3p*	DIANA TOOLS
ARID3A	*hsa-let-7a-5p*	DIANA TOOLS	*NPEPL1*	*hsa-miR-130a-3p*	DIANA TOOLS
ARID3B	*hsa-let-7a-5p*	DIANA TOOLS	*NPFFR1*	*hsa-miR-661*	MirTarBase
ARID4A	*hsa-miR-200c-3p*	DIANA TOOLS	*NPNT*	*hsa-miR-200c-3p*	DIANA TOOLS
ARID4B	*hsa-miR-130a-3p*	DIANA TOOLS	*NPR1*	*hsa-miR-661*	MirTarBase
ARIH1	*hsa-miR-200c-3p*	DIANA TOOLS	*NPTN*	*hsa-miR-25-3p*	DIANA TOOLS
ARL10	*hsa-miR-16-5p*	DIANA TOOLS	*NPTN*	*hsa-miR-130a-3p*	DIANA TOOLS
ARL2	*hsa-miR-16-5p*	DIANA TOOLS	*NPTX1*	*hsa-miR-25-3p*	DIANA TOOLS
ARL2	*hsa-miR-15b-5p*	DIANA TOOLS	*NPY4R*	*hsa-miR-661*	MirTarBase
ARL2BP	*hsa-miR-200c-3p*	DIANA TOOLS	*NR1D2*	*hsa-miR-144-3p*	DIANA TOOLS
ARL4A	*hsa-miR-93-5p*	DIANA TOOLS	*NR1I2*	*hsa-let-7a-5p*	MirTarBase
ARL4C	*hsa-miR-93-5p*	DIANA TOOLS	*NR2F6*	*hsa-miR-142-3p*	DIANA TOOLS
ARL4C	*hsa-miR-144-3p*	DIANA TOOLS	*NR2F6*	*hsa-miR-661*	MirTarBase
ARL5A	*hsa-miR-200c-3p*	DIANA TOOLS	*NR3C1*	*hsa-miR-142-3p*	DIANA TOOLS
ARL5B	*hsa-miR-15b-5p*	DIANA TOOLS	*NR5A2*	*hsa-miR-200c-3p*	DIANA TOOLS
ARL5B	*hsa-miR-16-5p*	DIANA TOOLS	*NR6A1*	*hsa-let-7a-5p*	DIANA TOOLS
ARL5B	*hsa-miR-25-3p*	DIANA TOOLS	*NRAS*	*hsa-miR-22-3p*	DIANA TOOLS
ARL6IP1	*hsa-miR-130a-3p*	DIANA TOOLS	*NRAS*	*hsa-let-7a-5p*	DIANA TOOLS
ARL8B	*hsa-miR-130a-3p*	DIANA TOOLS	*NRAS*	*hsa-let-7a-5p*	MirTarBase
ARL8B	*hsa-miR-15b-5p*	DIANA TOOLS	*NRAS*	*hsa-let-7a-5p*	MirTarBase
ARL8B	*hsa-miR-16-5p*	DIANA TOOLS	*NRBF2*	*hsa-miR-130a-3p*	DIANA TOOLS
ARMC1	*hsa-miR-25-3p*	DIANA TOOLS	*NRBF2*	*hsa-miR-200c-3p*	DIANA TOOLS
ARMC8	*hsa-miR-93-5p*	DIANA TOOLS	*NRBP1*	*hsa-miR-16-5p*	DIANA TOOLS
ARNTL	*hsa-miR-142-3p*	DIANA TOOLS	*NRBP1*	*hsa-miR-200c-3p*	DIANA TOOLS
ARNTL2	*hsa-miR-93-5p*	DIANA TOOLS	*NRIP1*	*hsa-miR-200c-3p*	DIANA TOOLS
ARNTL2	*hsa-miR-25-3p*	DIANA TOOLS	*NRP1*	*hsa-miR-130a-3p*	DIANA TOOLS
ARPC5	*hsa-miR-22-3p*	DIANA TOOLS	*NRXN3*	*hsa-miR-25-3p*	DIANA TOOLS
ARPP19	*hsa-let-7a-5p*	DIANA TOOLS	*NSA2*	*hsa-miR-433-3p*	MirTarBase
ARPP19	*hsa-miR-15b-5p*	DIANA TOOLS	*NSD1*	*hsa-miR-144-3p*	DIANA TOOLS
ARPP19	*hsa-miR-16-5p*	DIANA TOOLS	*NSF*	*hsa-miR-25-3p*	DIANA TOOLS
ARRDC3	*hsa-miR-130a-3p*	DIANA TOOLS	*NT5C2*	*hsa-miR-661*	MirTarBase

ARRDC3	*hsa-miR-25-3p*	DIANA TOOLS	*NT5DC2*	*hsa-miR-142-3p*	DIANA TOOLS
ARSK	*hsa-miR-381-5p*	MirTarBase	*NTMT1*	*hsa-miR-661*	MirTarBase
ASAP1	*hsa-miR-15b-5p*	DIANA TOOLS	*NTRK3*	*hsa-miR-509-3p*	DIANA TOOLS
ASAP1	*hsa-miR-16-5p*	DIANA TOOLS	*NTSR1*	*hsa-miR-661*	MirTarBase
ASAP1	*hsa-miR-25-3p*	DIANA TOOLS	*NUBPL*	*hsa-miR-433-3p*	MirTarBase
ASAP1	*hsa-miR-130a-3p*	DIANA TOOLS	*NUFIP2*	*hsa-miR-31-5p*	DIANA TOOLS
ASAP1	*hsa-miR-200c-3p*	DIANA TOOLS	*NUFIP2*	*hsa-miR-16-5p*	DIANA TOOLS
ASAP1	*hsa-miR-22-3p*	DIANA TOOLS	*NUFIP2*	*hsa-miR-15b-5p*	DIANA TOOLS
ASAP1	*hsa-let-7a-5p*	DIANA TOOLS	*NUFIP2*	*hsa-miR-661*	MirTarBase
ASB1	*hsa-miR-16-5p*	DIANA TOOLS	*NUP50*	*hsa-miR-15b-5p*	DIANA TOOLS
ASB1	*hsa-miR-15b-5p*	DIANA TOOLS	*NUP50*	*hsa-miR-16-5p*	DIANA TOOLS
ASCC3	*hsa-let-7a-5p*	DIANA TOOLS	*NUPL1*	*hsa-miR-142-3p*	DIANA TOOLS
ASH1L	*hsa-miR-15b-5p*	DIANA TOOLS	*NUPL2*	*hsa-miR-661*	MirTarBase
ASH1L	*hsa-miR-16-5p*	DIANA TOOLS	*NUPL2*	*hsa-miR-661*	MirTarBase
ASH1L	*hsa-miR-200c-3p*	DIANA TOOLS	*NXF1*	*hsa-miR-31-5p*	DIANA TOOLS
ASH1L	*hsa-miR-142-3p*	DIANA TOOLS	*NXPH3*	*hsa-miR-661*	MirTarBase
ATF6	*hsa-miR-16-5p*	DIANA TOOLS	*OCIAD2*	*hsa-miR-661*	MirTarBase
ATF6	*hsa-miR-15b-5p*	DIANA TOOLS	*OCIAD2*	*hsa-miR-661*	MirTarBase
ATG12	*hsa-miR-661*	MirTarBase	*OGFOD1*	*hsa-miR-142-3p*	DIANA TOOLS
ATG14	*hsa-miR-16-5p*	DIANA TOOLS	*OLFML2A*	*hsa-miR-661*	MirTarBase
ATG16L1	*hsa-miR-130a-3p*	DIANA TOOLS	*OLR1*	*hsa-miR-21-5p*	DIANA TOOLS
ATG9A	*hsa-miR-22-3p*	DIANA TOOLS	*OLR1*	*hsa-miR-661*	MirTarBase
ATL2	*hsa-miR-16-5p*	DIANA TOOLS	*ONECUT2*	*hsa-let-7a-5p*	DIANA TOOLS
ATL2	*hsa-miR-661*	MirTarBase	*ONECUT3*	*hsa-miR-661*	MirTarBase
ATL2	*hsa-miR-661*	MirTarBase	*OOEP*	*hsa-miR-16-5p*	DIANA TOOLS
ATL3	*hsa-miR-93-5p*	DIANA TOOLS	*OOEP*	*hsa-miR-15b-5p*	DIANA TOOLS
ATMIN	*hsa-miR-200c-3p*	DIANA TOOLS	*OPA3*	*hsa-miR-661*	MirTarBase
ATP11A	*hsa-miR-130a-3p*	DIANA TOOLS	*OPA3*	*hsa-miR-661*	MirTarBase
ATP13A3	*hsa-miR-200c-3p*	DIANA TOOLS	*OR7D2*	*hsa-miR-661*	MirTarBase
ATP13A3	*hsa-miR-16-5p*	DIANA TOOLS	*ORAI2*	*hsa-miR-661*	MirTarBase
ATP13A3	*hsa-miR-15b-5p*	DIANA TOOLS	*ORC1*	*hsa-miR-661*	MirTarBase
ATP13A4	*hsa-miR-661*	MirTarBase	*ORC1*	*hsa-miR-661*	MirTarBase
ATP1B1	*hsa-miR-144-3p*	DIANA TOOLS	*ORC6*	*hsa-miR-661*	MirTarBase
ATP2A2	*hsa-miR-16-5p*	DIANA TOOLS	*ORMDL3*	*hsa-miR-93-5p*	DIANA TOOLS
ATP2A2	*hsa-miR-15b-5p*	DIANA TOOLS	*OSGIN2*	*hsa-miR-25-3p*	DIANA TOOLS
ATP2A2	*hsa-let-7a-5p*	DIANA TOOLS	*OSTF1*	*hsa-let-7a-5p*	DIANA TOOLS
ATP2A2	*hsa-miR-25-3p*	DIANA TOOLS	*OSTM1*	*hsa-miR-200c-3p*	DIANA TOOLS
ATP2A2	*hsa-miR-142-3p*	DIANA TOOLS	*OTUD3*	*hsa-miR-130a-3p*	DIANA TOOLS
ATP2B4	*hsa-miR-21-5p*	DIANA TOOLS	*OTUD4*	*hsa-miR-144-3p*	DIANA TOOLS
ATP5G3	*hsa-miR-15b-5p*	DIANA TOOLS	*OTUD4*	*hsa-miR-16-5p*	DIANA TOOLS
ATP5G3	*hsa-miR-16-5p*	DIANA TOOLS	*OTUD4*	*hsa-miR-15b-5p*	DIANA TOOLS
ATP6V0D1	*hsa-miR-22-3p*	DIANA TOOLS	*OTUD4*	*hsa-miR-190b*	DIANA TOOLS
ATP6V0D1	*hsa-miR-130a-3p*	DIANA TOOLS	*OTUD6B*	*hsa-miR-22-3p*	DIANA TOOLS
ATP8B1	*hsa-miR-25-3p*	DIANA TOOLS	*OTUD7B*	*hsa-miR-661*	MirTarBase
ATP8B3	*hsa-miR-661*	MirTarBase	*OTULIN*	*hsa-miR-661*	MirTarBase
ATPAF1	*hsa-let-7a-5p*	DIANA TOOLS	*OXSR1*	*hsa-miR-31-5p*	DIANA TOOLS
ATXN1	*hsa-miR-130a-3p*	DIANA TOOLS	*P2RX3*	*hsa-miR-661*	MirTarBase

ATXN1	*hsa-miR-433-3p*	MirTarBase	*P4HA2*	*hsa-let-7a-5p*	DIANA TOOLS
ATXN10	*hsa-miR-21-5p*	DIANA TOOLS	*PAFAH1B1*	*hsa-miR-15b-5p*	DIANA TOOLS
ATXN3	*hsa-miR-130a-3p*	DIANA TOOLS	*PAFAH1B1*	*hsa-miR-16-5p*	DIANA TOOLS
ATXN3	*hsa-miR-25-3p*	DIANA TOOLS	*PAFAH1B2*	*hsa-miR-142-3p*	DIANA TOOLS
ATXN7L3	*hsa-miR-16-5p*	DIANA TOOLS	*PAFAH1B2*	*hsa-miR-15b-5p*	DIANA TOOLS
ATXN7L3	*hsa-miR-15b-5p*	DIANA TOOLS	*PAFAH1B2*	*hsa-miR-16-5p*	DIANA TOOLS
ATXN7L3B	*hsa-miR-16-5p*	DIANA TOOLS	*PAG1*	*hsa-miR-21-5p*	DIANA TOOLS
ATXN7L3B	*hsa-miR-15b-5p*	DIANA TOOLS	*PAG1*	*hsa-miR-16-5p*	DIANA TOOLS
AURKB	*hsa-let-7a-5p*	MirTarBase	*PAG1*	*hsa-miR-15b-5p*	DIANA TOOLS
AVL9	*hsa-miR-16-5p*	DIANA TOOLS	*PAG1*	*hsa-let-7a-5p*	DIANA TOOLS
AVL9	*hsa-miR-661*	MirTarBase	*PAICS*	*hsa-miR-661*	MirTarBase
AVL9	*hsa-miR-661*	MirTarBase	*PAIP2*	*hsa-miR-200c-3p*	DIANA TOOLS
AVL9	*hsa-miR-661*	MirTarBase	*PAK1*	*hsa-let-7a-5p*	MirTarBase
AXIN2	*hsa-miR-15b-5p*	DIANA TOOLS	*PAK2*	*hsa-miR-200c-3p*	DIANA TOOLS
AXIN2	*hsa-miR-16-5p*	DIANA TOOLS	*PALD1*	*hsa-let-7a-5p*	DIANA TOOLS
AXL	*hsa-miR-25-3p*	DIANA TOOLS	*PALLD*	*hsa-miR-25-3p*	DIANA TOOLS
AZIN1	*hsa-miR-433-3p*	MirTarBase	*PALM2-AKAP2*	*hsa-miR-16-5p*	DIANA TOOLS
B3GALTL	*hsa-miR-200c-3p*	DIANA TOOLS	*PAM*	*hsa-miR-200c-3p*	DIANA TOOLS
B3GNT1	*hsa-let-7a-5p*	DIANA TOOLS	*PANK3*	*hsa-miR-200c-3p*	DIANA TOOLS
B3GNT1	*hsa-miR-200c-3p*	DIANA TOOLS	*PANK3*	*hsa-miR-31-5p*	DIANA TOOLS
B4GALT5	*hsa-miR-130a-3p*	DIANA TOOLS	*PAPD5*	*hsa-miR-25-3p*	DIANA TOOLS
B4GALT6	*hsa-miR-200c-3p*	DIANA TOOLS	*PAPD7*	*hsa-miR-25-3p*	DIANA TOOLS
BACH1	*hsa-let-7a-5p*	DIANA TOOLS	*PAPLN*	*hsa-miR-661*	MirTarBase
BAG5	*hsa-miR-200c-3p*	DIANA TOOLS	*PAPOLA*	*hsa-let-7a-5p*	DIANA TOOLS
BAG6	*hsa-miR-200c-3p*	DIANA TOOLS	*PAPPA*	*hsa-miR-15b-5p*	DIANA TOOLS
BAP1	*hsa-miR-200c-3p*	DIANA TOOLS	*PAPPA*	*hsa-miR-16-5p*	DIANA TOOLS
BAP1	*hsa-miR-661*	MirTarBase	*PAPPA*	*hsa-let-7a-5p*	DIANA TOOLS
BAZ2B	*hsa-miR-25-3p*	DIANA TOOLS	*PARD3*	*hsa-miR-661*	MirTarBase
BBS2	*hsa-miR-433-3p*	MirTarBase	*PARD6B*	*hsa-miR-200c-3p*	DIANA TOOLS
BBS5	*hsa-miR-661*	MirTarBase	*PARD6B*	*hsa-miR-16-5p*	DIANA TOOLS
BCAP29	*hsa-let-7a-5p*	DIANA TOOLS	*PARD6B*	*hsa-miR-15b-5p*	DIANA TOOLS
BCAP29	*hsa-miR-15b-5p*	DIANA TOOLS	*PARD6B*	*hsa-miR-661*	MirTarBase
BCAP29	*hsa-miR-16-5p*	DIANA TOOLS	*PARP1*	*hsa-let-7a-5p*	MirTarBase
BCAT1	*hsa-miR-25-3p*	DIANA TOOLS	*PARP2*	*hsa-miR-661*	MirTarBase
BCAT1	*hsa-let-7a-5p*	DIANA TOOLS	*PARS2*	*hsa-let-7a-5p*	DIANA TOOLS
BCL11A	*hsa-miR-21-5p*	DIANA TOOLS	*PATZ1*	*hsa-miR-142-3p*	DIANA TOOLS
BCL11A	*hsa-miR-25-3p*	DIANA TOOLS	*PAX6*	*hsa-miR-223-3p*	DIANA TOOLS
BCL11B	*hsa-miR-25-3p*	DIANA TOOLS	*PBRM1*	*hsa-miR-21-5p*	DIANA TOOLS
BCL11B	*hsa-miR-93-5p*	DIANA TOOLS	*PBX1*	*hsa-miR-22-3p*	DIANA TOOLS
BCL2	*hsa-miR-15b-5p*	DIANA TOOLS	*PBX1*	*hsa-let-7a-5p*	DIANA TOOLS
BCL2	*hsa-miR-16-5p*	DIANA TOOLS	*PBX3*	*hsa-let-7a-5p*	DIANA TOOLS
BCL2	*hsa-let-7a-5p*	MirTarBase	*PCBD2*	*hsa-miR-661*	MirTarBase
BCL2L11	*hsa-miR-25-3p*	DIANA TOOLS	*PCBP1*	*hsa-miR-21-5p*	DIANA TOOLS
BCL2L11	*hsa-miR-130a-3p*	DIANA TOOLS	*PCDH7*	*hsa-miR-144-3p*	DIANA TOOLS
BCL2L2	*hsa-miR-16-5p*	DIANA TOOLS	*PCDH9*	*hsa-miR-16-5p*	DIANA TOOLS
BCL2L2	*hsa-miR-15b-5p*	DIANA TOOLS	*PCDH9*	*hsa-miR-15b-5p*	DIANA TOOLS
BCL7A	*hsa-miR-16-5p*	DIANA TOOLS	*PCGF3*	*hsa-let-7a-5p*	DIANA TOOLS
BCL7A	*hsa-miR-21-5p*	DIANA TOOLS	*PCGF5*	*hsa-miR-22-3p*	DIANA TOOLS

BCL9L	*hsa-miR-22-3p*	DIANA TOOLS	*PCGF5*	*hsa-miR-16-5p*	DIANA TOOLS
BDKRB2	*hsa-miR-200c-3p*	DIANA TOOLS	*PCLAF*	*hsa-miR-661*	MirTarBase
BDP1	*hsa-miR-200c-3p*	DIANA TOOLS	*PCLAF*	*hsa-miR-661*	MirTarBase
BFAR	*hsa-miR-16-5p*	DIANA TOOLS	*PCMT1*	*hsa-miR-16-5p*	DIANA TOOLS
BFAR	*hsa-miR-15b-5p*	DIANA TOOLS	*PCMTD1*	*hsa-miR-25-3p*	DIANA TOOLS
BICDL1	*hsa-miR-661*	MirTarBase	*PCNP*	*hsa-miR-661*	MirTarBase
BICDL1	*hsa-miR-661*	MirTarBase	*PCNP*	*hsa-miR-661*	MirTarBase
BICDL1	*hsa-miR-661*	MirTarBase	*PCSK1*	*hsa-miR-142-3p*	DIANA TOOLS
BMP3	*hsa-miR-661*	MirTarBase	*PCSK6*	*hsa-miR-21-5p*	DIANA TOOLS
BMP3	*hsa-miR-661*	MirTarBase	*PCTP*	*hsa-let-7a-5p*	DIANA TOOLS
BMPR2	*hsa-miR-130a-3p*	DIANA TOOLS	*PCYOX1*	*hsa-miR-661*	MirTarBase
BMPR2	*hsa-miR-21-5p*	DIANA TOOLS	*PDCD10*	*hsa-miR-200c-3p*	DIANA TOOLS
BNC2	*hsa-miR-16-5p*	DIANA TOOLS	*PDCD4*	*hsa-miR-21-5p*	DIANA TOOLS
BNC2	*hsa-miR-15b-5p*	DIANA TOOLS	*PDCD4*	*hsa-miR-15b-5p*	DIANA TOOLS
BNC2	*hsa-miR-142-3p*	DIANA TOOLS	*PDCD4*	*hsa-miR-16-5p*	DIANA TOOLS
BNIP2	*hsa-miR-21-5p*	DIANA TOOLS	*PDE12*	*hsa-let-7a-5p*	DIANA TOOLS
BNIP2	*hsa-miR-93-5p*	DIANA TOOLS	*PDE12*	*hsa-miR-661*	MirTarBase
BOD1	*hsa-miR-142-3p*	DIANA TOOLS	*PDE4C*	*hsa-miR-661*	MirTarBase
BRAF	*hsa-miR-25-3p*	DIANA TOOLS	*PDE4DIP*	*hsa-miR-130a-3p*	DIANA TOOLS
BRCA1	*hsa-miR-200c-3p*	DIANA TOOLS	*PDF*	*hsa-miR-661*	MirTarBase
BRD3	*hsa-let-7a-5p*	DIANA TOOLS	*PDIK1L*	*hsa-miR-22-3p*	DIANA TOOLS
BROX	*hsa-miR-661*	MirTarBase	*PDIK1L*	*hsa-miR-15b-5p*	DIANA TOOLS
BRWD1	*hsa-miR-130a-3p*	DIANA TOOLS	*PDLIM3*	*hsa-miR-433-3p*	MirTarBase
BRWD1	*hsa-miR-433-3p*	MirTarBase	*PDPR*	*hsa-let-7a-5p*	DIANA TOOLS
BRWD3	*hsa-let-7a-5p*	DIANA TOOLS	*PDS5A*	*hsa-miR-22-3p*	DIANA TOOLS
BRWD3	*hsa-miR-22-3p*	DIANA TOOLS	*PDXDC1*	*hsa-miR-25-3p*	DIANA TOOLS
BSDC1	*hsa-miR-25-3p*	DIANA TOOLS	*PDZD11*	*hsa-miR-130a-3p*	DIANA TOOLS
BSN	*hsa-miR-25-3p*	DIANA TOOLS	*PDZD8*	*hsa-miR-25-3p*	DIANA TOOLS
BTAF1	*hsa-miR-16-5p*	DIANA TOOLS	*PDZD8*	*hsa-miR-15b-5p*	DIANA TOOLS
BTAF1	*hsa-miR-15b-5p*	DIANA TOOLS	*PDZD8*	*hsa-miR-16-5p*	DIANA TOOLS
BTAF1	*hsa-miR-144-3p*	DIANA TOOLS	*PEAK1*	*hsa-miR-200c-3p*	DIANA TOOLS
BTBD3	*hsa-let-7a-5p*	DIANA TOOLS	*PELI1*	*hsa-miR-21-5p*	DIANA TOOLS
BTBD3	*hsa-miR-130a-3p*	DIANA TOOLS	*PER2*	*hsa-miR-25-3p*	DIANA TOOLS
BTBD3	*hsa-miR-144-3p*	DIANA TOOLS	*PEX11A*	*hsa-miR-661*	MirTarBase
BTBD9	*hsa-miR-15b-5p*	DIANA TOOLS	*PEX11B*	*hsa-miR-381-5p*	MirTarBase
BTBD9	*hsa-miR-16-5p*	DIANA TOOLS	*PEX2*	*hsa-miR-661*	MirTarBase
BTG1	*hsa-miR-130a-3p*	DIANA TOOLS	*PEX5L*	*hsa-miR-93-5p*	DIANA TOOLS
BTG2	*hsa-miR-21-5p*	DIANA TOOLS	*PFN2*	*hsa-miR-93-5p*	DIANA TOOLS
BTG2	*hsa-miR-15b-5p*	DIANA TOOLS	*PGM2L1*	*hsa-miR-130a-3p*	DIANA TOOLS
BTG2	*hsa-miR-16-5p*	DIANA TOOLS	*PGM2L1*	*hsa-miR-93-5p*	DIANA TOOLS
BTG2	*hsa-miR-25-3p*	DIANA TOOLS	*PGRMC1*	*hsa-let-7a-5p*	DIANA TOOLS
BTNL3	*hsa-miR-661*	MirTarBase	*PGRMC2*	*hsa-miR-144-3p*	DIANA TOOLS
BTRC	*hsa-miR-15b-5p*	DIANA TOOLS	*PGRMC2*	*hsa-miR-21-5p*	DIANA TOOLS
BTRC	*hsa-miR-16-5p*	DIANA TOOLS	*PHACTR2*	*hsa-miR-144-3p*	DIANA TOOLS
BZW1	*hsa-miR-15b-5p*	DIANA TOOLS	*PHACTR2*	*hsa-miR-16-5p*	DIANA TOOLS
BZW1	*hsa-miR-16-5p*	DIANA TOOLS	*PHACTR2*	*hsa-miR-15b-5p*	DIANA TOOLS
BZW1	*hsa-miR-661*	MirTarBase	*PHAX*	*hsa-miR-130a-3p*	DIANA TOOLS

BZW1	*hsa-miR-661*	MirTarBase	*PHC3*	*hsa-miR-200c-3p*	DIANA TOOLS
C10orf12	*hsa-miR-21-5p*	DIANA TOOLS	*PHF20*	*hsa-miR-130a-3p*	DIANA TOOLS
C11orf54	*hsa-miR-661*	MirTarBase	*PHF3*	*hsa-miR-144-3p*	DIANA TOOLS
C11orf84	*hsa-miR-381-5p*	MirTarBase	*PHF6*	*hsa-miR-21-5p*	DIANA TOOLS
C14orf28	*hsa-let-7a-5p*	DIANA TOOLS	*PHF7*	*hsa-miR-661*	MirTarBase
C15orf39	*hsa-let-7a-5p*	DIANA TOOLS	*PHF8*	*hsa-miR-22-3p*	DIANA TOOLS
C15orf40	*hsa-miR-661*	MirTarBase	*PHKA1*	*hsa-miR-15b-5p*	DIANA TOOLS
C15orf41	*hsa-let-7a-5p*	DIANA TOOLS	*PHKA1*	*hsa-miR-16-5p*	DIANA TOOLS
C16orf70	*hsa-miR-142-3p*	DIANA TOOLS	*PHLDA3*	*hsa-miR-15b-5p*	DIANA TOOLS
C16orf70	*hsa-miR-130a-3p*	DIANA TOOLS	*PHLDA3*	*hsa-miR-16-5p*	DIANA TOOLS
C16orf72	*hsa-miR-15b-5p*	DIANA TOOLS	*PHLDB2*	*hsa-let-7a-5p*	DIANA TOOLS
C16orf72	*hsa-miR-200c-3p*	DIANA TOOLS	*PHLPP2*	*hsa-miR-25-3p*	DIANA TOOLS
C17orf105	*hsa-miR-661*	MirTarBase	*PHTF1*	*hsa-miR-25-3p*	DIANA TOOLS
C18orf25	*hsa-miR-142-3p*	DIANA TOOLS	*PHTF2*	*hsa-miR-25-3p*	DIANA TOOLS
C18orf25	*hsa-miR-661*	MirTarBase	*PIAS2*	*hsa-miR-93-5p*	DIANA TOOLS
C18orf25	*hsa-miR-661*	MirTarBase	*PICALM*	*hsa-miR-205-5p*	DIANA TOOLS
C18orf25	*hsa-miR-661*	MirTarBase	*PIGA*	*hsa-miR-130a-3p*	DIANA TOOLS
C18orf32	*hsa-miR-93-5p*	DIANA TOOLS	*PIGB*	*hsa-miR-15b-5p*	DIANA TOOLS
C1GALT1	*hsa-let-7a-5p*	DIANA TOOLS	*PIGB*	*hsa-miR-16-5p*	DIANA TOOLS
C1orf35	*hsa-miR-661*	MirTarBase	*PIGR*	*hsa-miR-661*	MirTarBase
C20orf194	*hsa-let-7a-5p*	DIANA TOOLS	*PIK3C2A*	*hsa-miR-22-3p*	DIANA TOOLS
C2orf69	*hsa-miR-93-5p*	DIANA TOOLS	*PIK3CB*	*hsa-miR-25-3p*	DIANA TOOLS
C3	*hsa-miR-661*	MirTarBase	*PIK3IP1*	*hsa-let-7a-5p*	DIANA TOOLS
C3orf38	*hsa-let-7a-5p*	DIANA TOOLS	*PIK3R1*	*hsa-miR-21-5p*	DIANA TOOLS
C3orf70	*hsa-miR-661*	MirTarBase	*PIK3R5*	*hsa-miR-142-3p*	DIANA TOOLS
C4orf26	*hsa-miR-661*	MirTarBase	*PIKFYVE*	*hsa-miR-130a-3p*	DIANA TOOLS
C5AR2	*hsa-miR-661*	MirTarBase	*PIKFYVE*	*hsa-miR-25-3p*	DIANA TOOLS
C5orf22	*hsa-miR-433-3p*	MirTarBase	*PIKFYVE*	*hsa-miR-200c-3p*	DIANA TOOLS
C5orf24	*hsa-miR-22-3p*	DIANA TOOLS	*PIKFYVE*	*hsa-miR-508-3p*	MirTarBase
C5orf24	*hsa-miR-142-3p*	DIANA TOOLS	*PIM2*	*hsa-miR-200c-3p*	DIANA TOOLS
C5orf30	*hsa-miR-25-3p*	DIANA TOOLS	*PIP5K1C*	*hsa-miR-25-3p*	DIANA TOOLS
C5orf30	*hsa-miR-130a-3p*	DIANA TOOLS	*PISD*	*hsa-miR-16-5p*	DIANA TOOLS
C5orf51	*hsa-let-7a-5p*	DIANA TOOLS	*PISD*	*hsa-miR-15b-5p*	DIANA TOOLS
C6orf141	*hsa-miR-661*	MirTarBase	*PITPNA*	*hsa-miR-25-3p*	DIANA TOOLS
C6orf47	*hsa-miR-142-3p*	DIANA TOOLS	*PITPNM2*	*hsa-miR-25-3p*	DIANA TOOLS
C6orf62	*hsa-miR-25-3p*	DIANA TOOLS	*PITPNM3*	*hsa-miR-200c-3p*	DIANA TOOLS
C7orf60	*hsa-miR-130a-3p*	DIANA TOOLS	*PKD2*	*hsa-miR-93-5p*	DIANA TOOLS
C8orf58	*hsa-let-7a-5p*	DIANA TOOLS	*PKIA*	*hsa-miR-200c-3p*	DIANA TOOLS
C9orf40	*hsa-let-7a-5p*	DIANA TOOLS	*PKM*	*hsa-let-7a-5p*	MirTarBase
C9orf41	*hsa-miR-93-5p*	DIANA TOOLS	*PKM*	*hsa-let-7a-5p*	MirTarBase
C9orf72	*hsa-miR-142-3p*	DIANA TOOLS	*PKN2*	*hsa-miR-93-5p*	DIANA TOOLS
CA6	*hsa-miR-661*	MirTarBase	*PKP4*	*hsa-miR-25-3p*	DIANA TOOLS
CAB39	*hsa-miR-15b-5p*	DIANA TOOLS	*PLA2G15*	*hsa-miR-15b-5p*	DIANA TOOLS
CABLES1	*hsa-miR-381-5p*	MirTarBase	*PLAC8*	*hsa-miR-661*	MirTarBase
CACNA2D1	*hsa-miR-25-3p*	DIANA TOOLS	*PLAG1*	*hsa-miR-15b-5p*	DIANA TOOLS
CACNA2D1	*hsa-miR-16-5p*	DIANA TOOLS	*PLAG1*	*hsa-miR-16-5p*	DIANA TOOLS
CACNA2D1	*hsa-miR-15b-5p*	DIANA TOOLS	*PLAG1*	*hsa-miR-21-5p*	DIANA TOOLS
CACNB2	*hsa-miR-144-3p*	DIANA TOOLS	*PLAG1*	*hsa-miR-144-3p*	MirTarBase

CACUL1	*hsa-miR-93-5p*	DIANA TOOLS	*PLCG1*	*hsa-miR-200c-3p*	DIANA TOOLS
CACUL1	*hsa-miR-15b-5p*	DIANA TOOLS	*PLCXD3*	*hsa-miR-22-3p*	DIANA TOOLS
CACUL1	*hsa-miR-16-5p*	DIANA TOOLS	*PLEKHA1*	*hsa-miR-25-3p*	DIANA TOOLS
CAD	*hsa-miR-661*	MirTarBase	*PLEKHA1*	*hsa-miR-15b-5p*	DIANA TOOLS
CALD1	*hsa-miR-21-5p*	DIANA TOOLS	*PLEKHA1*	*hsa-miR-16-5p*	DIANA TOOLS
CALM2	*hsa-miR-130a-3p*	DIANA TOOLS	*PLEKHA1*	*hsa-miR-21-5p*	DIANA TOOLS
CAMK2N2	*hsa-miR-93-5p*	DIANA TOOLS	*PLEKHA1*	*hsa-miR-433-3p*	MirTarBase
CAMSAP2	*hsa-miR-200c-3p*	DIANA TOOLS	*PLEKHA3*	*hsa-miR-661*	MirTarBase
CAMSAP2	*hsa-miR-144-3p*	DIANA TOOLS	*PLEKHA8*	*hsa-miR-200c-3p*	DIANA TOOLS
CAMTA1	*hsa-miR-93-5p*	DIANA TOOLS	*PLEKHA8*	*hsa-let-7a-5p*	DIANA TOOLS
CAND1	*hsa-miR-144-3p*	DIANA TOOLS	*PLEKHB2*	*hsa-miR-25-3p*	DIANA TOOLS
CAND1	*hsa-miR-16-5p*	DIANA TOOLS	*PLEKHG2*	*hsa-miR-661*	MirTarBase
CAND1	*hsa-miR-15b-5p*	DIANA TOOLS	*PLEKHG3*	*hsa-miR-25-3p*	DIANA TOOLS
CAND1	*hsa-miR-25-3p*	DIANA TOOLS	*PLEKHO1*	*hsa-let-7a-5p*	DIANA TOOLS
CAPN15	*hsa-miR-93-5p*	DIANA TOOLS	*PLK2*	*hsa-miR-200c-3p*	DIANA TOOLS
CAPRIN1	*hsa-miR-16-5p*	DIANA TOOLS	*PLS3*	*hsa-miR-22-3p*	DIANA TOOLS
CAPRIN1	*hsa-miR-15b-5p*	DIANA TOOLS	*PLSCR4*	*hsa-miR-15b-5p*	DIANA TOOLS
CAPRIN1	*hsa-miR-22-3p*	DIANA TOOLS	*PLSCR4*	*hsa-miR-16-5p*	DIANA TOOLS
CAPRIN2	*hsa-let-7a-5p*	DIANA TOOLS	*PLXNA3*	*hsa-miR-661*	MirTarBase
CAPRIN2	*hsa-miR-200c-3p*	DIANA TOOLS	*PLXNA3*	*hsa-miR-661*	MirTarBase
CAPZA2	*hsa-miR-16-5p*	DIANA TOOLS	*PLXND1*	*hsa-let-7a-5p*	DIANA TOOLS
CAPZA2	*hsa-miR-15b-5p*	DIANA TOOLS	*PMAIP1*	*hsa-miR-200c-3p*	DIANA TOOLS
CAPZB	*hsa-miR-661*	MirTarBase	*PNISR*	*hsa-miR-25-3p*	DIANA TOOLS
CARD10	*hsa-miR-15b-5p*	DIANA TOOLS	*PNPLA6*	*hsa-miR-15b-5p*	DIANA TOOLS
CARD6	*hsa-miR-661*	MirTarBase	*PNPLA6*	*hsa-miR-16-5p*	DIANA TOOLS
CARD8	*hsa-miR-661*	MirTarBase	*POLR1A*	*hsa-miR-16-5p*	DIANA TOOLS
CASD1	*hsa-miR-25-3p*	DIANA TOOLS	*POLR1A*	*hsa-miR-15b-5p*	DIANA TOOLS
CASK	*hsa-miR-16-5p*	DIANA TOOLS	*POLR1B*	*hsa-miR-22-3p*	DIANA TOOLS
CASK	*hsa-miR-142-3p*	DIANA TOOLS	*POLR2D*	*hsa-let-7a-5p*	DIANA TOOLS
CASP3	*hsa-miR-144-3p*	DIANA TOOLS	*POLR2D*	*hsa-miR-661*	MirTarBase
CASP3	*hsa-let-7a-5p*	DIANA TOOLS	*POLR2E*	*hsa-miR-381-5p*	MirTarBase
CASP3	*hsa-let-7a-5p*	MirTarBase	*POLR3B*	*hsa-miR-21-5p*	DIANA TOOLS
CASP8	*hsa-let-7a-5p*	MirTarBase	*POLR3F*	*hsa-miR-15b-5p*	DIANA TOOLS
CASP9	*hsa-let-7a-5p*	MirTarBase	*POLR3F*	*hsa-miR-16-5p*	DIANA TOOLS
CAST	*hsa-miR-130a-3p*	DIANA TOOLS	*POLR3K*	*hsa-miR-661*	MirTarBase
CBFB	*hsa-miR-130a-3p*	DIANA TOOLS	*POLR3K*	*hsa-miR-661*	MirTarBase
CBL	*hsa-miR-22-3p*	DIANA TOOLS	*PON1*	*hsa-miR-661*	MirTarBase
CBL	*hsa-miR-200c-3p*	DIANA TOOLS	*PON1*	*hsa-miR-661*	MirTarBase
CBX1	*hsa-miR-205-5p*	DIANA TOOLS	*POTEG*	*hsa-miR-433-3p*	MirTarBase
CBX2	*hsa-miR-15b-5p*	DIANA TOOLS	*POTEG*	*hsa-miR-433-3p*	MirTarBase
CBX2	*hsa-miR-16-5p*	DIANA TOOLS	*POTEM*	*hsa-miR-433-3p*	MirTarBase
CBX4	*hsa-miR-200c-3p*	DIANA TOOLS	*POTEM*	*hsa-miR-433-3p*	MirTarBase
CBX4	*hsa-miR-15b-5p*	DIANA TOOLS	*POU2F1*	*hsa-let-7a-5p*	DIANA TOOLS
CBX4	*hsa-miR-16-5p*	DIANA TOOLS	*POU2F1*	*hsa-miR-223-3p*	DIANA TOOLS
CBX5	*hsa-miR-93-5p*	DIANA TOOLS	*POU2F1*	*hsa-miR-22-3p*	DIANA TOOLS
CBX5	*hsa-miR-200c-3p*	DIANA TOOLS	*POU2F3*	*hsa-miR-661*	MirTarBase
CBX5	*hsa-let-7a-5p*	DIANA TOOLS	*POU2F3*	*hsa-miR-661*	MirTarBase

CBX6	*hsa-miR-15b-5p*	DIANA TOOLS	*POU3F2*	*hsa-miR-130a-3p*	DIANA TOOLS
CBX6	*hsa-miR-16-5p*	DIANA TOOLS	*PPAP2A*	*hsa-miR-16-5p*	DIANA TOOLS
CC2D1B	*hsa-miR-16-5p*	DIANA TOOLS	*PPAP2B*	*hsa-miR-15b-5p*	DIANA TOOLS
CC2D1B	*hsa-miR-15b-5p*	DIANA TOOLS	*PPAP2B*	*hsa-miR-16-5p*	DIANA TOOLS
CCDC126	*hsa-miR-130a-3p*	DIANA TOOLS	*PPAPDC2*	*hsa-miR-15b-5p*	DIANA TOOLS
CCDC186	*hsa-miR-25-3p*	DIANA TOOLS	*PPAPDC2*	*hsa-miR-16-5p*	DIANA TOOLS
CCDC34	*hsa-miR-21-5p*	DIANA TOOLS	*PPARA*	*hsa-miR-21-5p*	DIANA TOOLS
CCDC47	*hsa-miR-22-3p*	DIANA TOOLS	*PPARGC1B*	*hsa-miR-144-3p*	DIANA TOOLS
CCDC50	*hsa-miR-22-3p*	DIANA TOOLS	*PPCS*	*hsa-miR-25-3p*	DIANA TOOLS
CCDC6	*hsa-miR-142-3p*	DIANA TOOLS	*PPEF2*	*hsa-miR-661*	MirTarBase
CCDC71L	*hsa-miR-93-5p*	DIANA TOOLS	*PPEF2*	*hsa-miR-661*	MirTarBase
CCDC71L	*hsa-let-7a-5p*	DIANA TOOLS	*PPEF2*	*hsa-miR-661*	MirTarBase
CCDC8	*hsa-miR-661*	MirTarBase	*PPIL4*	*hsa-miR-200c-3p*	DIANA TOOLS
CCDC85C	*hsa-miR-16-5p*	DIANA TOOLS	*PPIL4*	*hsa-miR-661*	MirTarBase
CCDC85C	*hsa-miR-15b-5p*	DIANA TOOLS	*PPIL4*	*hsa-miR-661*	MirTarBase
CCL20	*hsa-miR-21-5p*	DIANA TOOLS	*PPIL6*	*hsa-miR-661*	MirTarBase
CCL7	*hsa-let-7a-5p*	DIANA TOOLS	*PPM1A*	*hsa-miR-15b-5p*	DIANA TOOLS
CCNA2	*hsa-miR-22-3p*	DIANA TOOLS	*PPM1A*	*hsa-miR-16-5p*	DIANA TOOLS
CCND1	*hsa-miR-16-5p*	DIANA TOOLS	*PPM1D*	*hsa-miR-15b-5p*	DIANA TOOLS
CCND1	*hsa-miR-15b-5p*	DIANA TOOLS	*PPM1D*	*hsa-miR-16-5p*	DIANA TOOLS
CCND2	*hsa-let-7a-5p*	DIANA TOOLS	*PPM1F*	*hsa-miR-200c-3p*	DIANA TOOLS
CCND2	*hsa-miR-93-5p*	DIANA TOOLS	*PPM1K*	*hsa-miR-661*	MirTarBase
CCND2	*hsa-miR-15b-5p*	DIANA TOOLS	*PPP1R10*	*hsa-miR-200c-3p*	DIANA TOOLS
CCND2	*hsa-miR-16-5p*	DIANA TOOLS	*PPP1R10*	*hsa-miR-142-3p*	DIANA TOOLS
CCND2	*hsa-let-7a-5p*	MirTarBase	*PPP1R11*	*hsa-miR-16-5p*	DIANA TOOLS
CCND2	*hsa-let-7a-5p*	MirTarBase	*PPP1R11*	*hsa-miR-15b-5p*	DIANA TOOLS
CCND3	*hsa-miR-15b-5p*	DIANA TOOLS	*PPP1R12A*	*hsa-miR-25-3p*	DIANA TOOLS
CCND3	*hsa-miR-16-5p*	DIANA TOOLS	*PPP1R12B*	*hsa-miR-15b-5p*	DIANA TOOLS
CCNE1	*hsa-miR-15b-5p*	DIANA TOOLS	*PPP1R12B*	*hsa-miR-16-5p*	DIANA TOOLS
CCNE1	*hsa-miR-16-5p*	DIANA TOOLS	*PPP1R12C*	*hsa-miR-25-3p*	DIANA TOOLS
CCNE2	*hsa-miR-200c-3p*	DIANA TOOLS	*PPP1R15B*	*hsa-miR-130a-3p*	DIANA TOOLS
CCNF	*hsa-miR-16-5p*	DIANA TOOLS	*PPP1R15B*	*hsa-miR-22-3p*	DIANA TOOLS
CCNF	*hsa-miR-22-3p*	DIANA TOOLS	*PPP1R15B*	*hsa-let-7a-5p*	DIANA TOOLS
CCNF	*hsa-let-7a-5p*	DIANA TOOLS	*PPP1R18*	*hsa-miR-200c-3p*	DIANA TOOLS
CCNG1	*hsa-miR-661*	MirTarBase	*PPP1R37*	*hsa-miR-25-3p*	DIANA TOOLS
CCNG2	*hsa-miR-130a-3p*	DIANA TOOLS	*PPP2R1A*	*hsa-miR-15b-5p*	DIANA TOOLS
CCNJ	*hsa-miR-142-3p*	DIANA TOOLS	*PPP2R1A*	*hsa-miR-16-5p*	DIANA TOOLS
CCNJ	*hsa-let-7a-5p*	DIANA TOOLS	*PPP2R1B*	*hsa-miR-200c-3p*	DIANA TOOLS
CCNJ	*hsa-miR-205-5p*	DIANA TOOLS	*PPP2R1B*	*hsa-miR-16-5p*	DIANA TOOLS
CCNJL	*hsa-miR-22-3p*	DIANA TOOLS	*PPP2R1B*	*hsa-miR-15b-5p*	DIANA TOOLS
CCNT2	*hsa-miR-142-3p*	DIANA TOOLS	*PPP2R2A*	*hsa-miR-31-5p*	DIANA TOOLS
CCNT2	*hsa-miR-15b-5p*	DIANA TOOLS	*PPP2R2A*	*hsa-miR-93-5p*	DIANA TOOLS
CCNT2	*hsa-miR-16-5p*	DIANA TOOLS	*PPP2R5C*	*hsa-miR-15b-5p*	DIANA TOOLS
CCNT2	*hsa-miR-144-3p*	DIANA TOOLS	*PPP2R5C*	*hsa-miR-16-5p*	DIANA TOOLS
CCR7	*hsa-let-7a-5p*	DIANA TOOLS	*PPP2R5E*	*hsa-miR-200c-3p*	DIANA TOOLS
CCR7	*hsa-let-7a-5p*	MirTarBase	*PPP4C*	*hsa-let-7a-5p*	DIANA TOOLS
CCT4	*hsa-miR-661*	MirTarBase	*PPP4R1*	*hsa-miR-22-3p*	DIANA TOOLS
CCT6A	*hsa-miR-25-3p*	DIANA TOOLS	*PPP6C*	*hsa-miR-16-5p*	DIANA TOOLS

CCT6A	*hsa-miR-130a-3p*	DIANA TOOLS	*PPP6C*	*hsa-miR-15b-5p*	DIANA TOOLS
CD200R1	*hsa-let-7a-5p*	DIANA TOOLS	*PPP6R1*	*hsa-miR-130a-3p*	DIANA TOOLS
CD2AP	*hsa-miR-25-3p*	DIANA TOOLS	*PPT1*	*hsa-miR-16-5p*	DIANA TOOLS
CD2AP	*hsa-miR-15b-5p*	DIANA TOOLS	*PPT1*	*hsa-miR-15b-5p*	DIANA TOOLS
CD2AP	*hsa-miR-16-5p*	DIANA TOOLS	*PPT2*	*hsa-miR-16-5p*	DIANA TOOLS
CD300LD	*hsa-miR-661*	MirTarBase	*PPT2*	*hsa-miR-15b-5p*	DIANA TOOLS
CD36	*hsa-miR-661*	MirTarBase	*PPTC7*	*hsa-miR-190b*	DIANA TOOLS
CD47	*hsa-miR-21-5p*	DIANA TOOLS	*PPWD1*	*hsa-miR-22-3p*	DIANA TOOLS
CD55	*hsa-miR-31-5p*	DIANA TOOLS	*PQLC2*	*hsa-miR-16-5p*	DIANA TOOLS
CD69	*hsa-miR-25-3p*	DIANA TOOLS	*PRDM1*	*hsa-miR-223-3p*	DIANA TOOLS
CDC14A	*hsa-miR-16-5p*	DIANA TOOLS	*PRDM1*	*hsa-let-7a-5p*	MirTarBase
CDC14A	*hsa-miR-15b-5p*	DIANA TOOLS	*PRDM1*	*hsa-let-7a-5p*	MirTarBase
CDC25A	*hsa-miR-21-5p*	DIANA TOOLS	*PRDM4*	*hsa-miR-15b-5p*	DIANA TOOLS
CDC25A	*hsa-miR-15b-5p*	DIANA TOOLS	*PRDM4*	*hsa-miR-16-5p*	DIANA TOOLS
CDC25A	*hsa-miR-16-5p*	DIANA TOOLS	*PRDX3*	*hsa-miR-31-5p*	DIANA TOOLS
CDC27	*hsa-miR-15b-5p*	DIANA TOOLS	*PREB*	*hsa-let-7a-5p*	DIANA TOOLS
CDC27	*hsa-miR-16-5p*	DIANA TOOLS	*PRKAA1*	*hsa-miR-130a-3p*	DIANA TOOLS
CDC27	*hsa-miR-25-3p*	DIANA TOOLS	*PRKAB2*	*hsa-miR-16-5p*	DIANA TOOLS
CDC34	*hsa-let-7a-5p*	DIANA TOOLS	*PRKAR2A*	*hsa-let-7a-5p*	DIANA TOOLS
CDC34	*hsa-let-7a-5p*	MirTarBase	*PRKAR2A*	*hsa-miR-15b-5p*	DIANA TOOLS
CDC37L1	*hsa-miR-93-5p*	DIANA TOOLS	*PRKAR2A*	*hsa-miR-16-5p*	DIANA TOOLS
CDC37L1	*hsa-miR-15b-5p*	DIANA TOOLS	*PRKAR2B*	*hsa-miR-93-5p*	DIANA TOOLS
CDC37L1	*hsa-miR-16-5p*	DIANA TOOLS	*PRKD3*	*hsa-miR-130a-3p*	DIANA TOOLS
CDC40	*hsa-miR-93-5p*	DIANA TOOLS	*PRKRA*	*hsa-miR-200c-3p*	DIANA TOOLS
CDC42SE2	*hsa-miR-144-3p*	DIANA TOOLS	*PRLR*	*hsa-let-7a-5p*	DIANA TOOLS
CDC42SE2	*hsa-miR-15b-5p*	DIANA TOOLS	*PRNP*	*hsa-miR-130a-3p*	DIANA TOOLS
CDC42SE2	*hsa-miR-16-5p*	DIANA TOOLS	*PRPF38B*	*hsa-let-7a-5p*	DIANA TOOLS
CDC73	*hsa-miR-661*	MirTarBase	*PRR15*	*hsa-miR-93-5p*	DIANA TOOLS
CDCA4	*hsa-miR-16-5p*	DIANA TOOLS	*PRRC2B*	*hsa-miR-22-3p*	DIANA TOOLS
CDCA4	*hsa-miR-15b-5p*	DIANA TOOLS	*PRRC2C*	*hsa-miR-22-3p*	DIANA TOOLS
CDCA7	*hsa-miR-661*	MirTarBase	*PRRC2C*	*hsa-miR-16-5p*	DIANA TOOLS
CDCA7	*hsa-miR-661*	MirTarBase	*PRRC2C*	*hsa-miR-15b-5p*	DIANA TOOLS
CDK13	*hsa-miR-22-3p*	DIANA TOOLS	*PRRG1*	*hsa-miR-93-5p*	DIANA TOOLS
CDK16	*hsa-miR-25-3p*	DIANA TOOLS	*PRRG4*	*hsa-miR-93-5p*	DIANA TOOLS
CDK17	*hsa-miR-16-5p*	DIANA TOOLS	*PRRG4*	*hsa-miR-661*	MirTarBase
CDK17	*hsa-miR-15b-5p*	DIANA TOOLS	*PRRG4*	*hsa-miR-661*	MirTarBase
CDK19	*hsa-miR-130a-3p*	DIANA TOOLS	*PRSS21*	*hsa-miR-661*	MirTarBase
CDK2	*hsa-miR-200c-3p*	DIANA TOOLS	*PRTG*	*hsa-let-7a-5p*	DIANA TOOLS
CDK5R1	*hsa-miR-130a-3p*	DIANA TOOLS	*PSAP*	*hsa-miR-130a-3p*	DIANA TOOLS
CDK5R1	*hsa-miR-25-3p*	DIANA TOOLS	*PSAT1*	*hsa-miR-15b-5p*	DIANA TOOLS
CDK5R1	*hsa-miR-15b-5p*	DIANA TOOLS	*PSAT1*	*hsa-miR-16-5p*	DIANA TOOLS
CDK5R1	*hsa-miR-16-5p*	DIANA TOOLS	*PSKH1*	*hsa-miR-15b-5p*	DIANA TOOLS
CDK6	*hsa-miR-15b-5p*	DIANA TOOLS	*PSKH1*	*hsa-miR-16-5p*	DIANA TOOLS
CDK6	*hsa-miR-16-5p*	DIANA TOOLS	*PSMA6*	*hsa-miR-22-3p*	DIANA TOOLS
CDK6	*hsa-miR-22-3p*	DIANA TOOLS	*PSMD2*	*hsa-miR-205-5p*	DIANA TOOLS
CDK6	*hsa-let-7a-5p*	MirTarBase	*PSMD9*	*hsa-miR-661*	MirTarBase
CDKN1A	*hsa-let-7a-5p*	DIANA TOOLS	*PSMF1*	*hsa-miR-661*	MirTarBase

CDKN1A	*hsa-miR-130a-3p*	DIANA TOOLS	*PSMG4*	*hsa-miR-661*	MirTarBase
CDKN1A	*hsa-miR-93-5p*	DIANA TOOLS	*PTAR1*	*hsa-miR-200c-3p*	DIANA TOOLS
CDKN1A	*hsa-let-7a-5p*	MirTarBase	*PTAR1*	*hsa-miR-25-3p*	DIANA TOOLS
CDS1	*hsa-miR-130a-3p*	DIANA TOOLS	*PTCD3*	*hsa-miR-16-5p*	DIANA TOOLS
CDV3	*hsa-let-7a-5p*	DIANA TOOLS	*PTEN*	*hsa-miR-130a-3p*	DIANA TOOLS
CDYL	*hsa-miR-200c-3p*	DIANA TOOLS	*PTEN*	*hsa-miR-22-3p*	DIANA TOOLS
CELF1	*hsa-miR-22-3p*	DIANA TOOLS	*PTEN*	*hsa-miR-205-5p*	DIANA TOOLS
CELF2	*hsa-miR-93-5p*	DIANA TOOLS	*PTGER4*	*hsa-miR-25-3p*	DIANA TOOLS
CELF2	*hsa-miR-144-3p*	DIANA TOOLS	*PTGES3*	*hsa-miR-130a-3p*	DIANA TOOLS
CENPL	*hsa-miR-661*	MirTarBase	*PTGS2*	*hsa-miR-144-3p*	MirTarBase
CEP19	*hsa-miR-381-5p*	MirTarBase	*PTK2*	*hsa-miR-200c-3p*	DIANA TOOLS
CEP350	*hsa-miR-144-3p*	DIANA TOOLS	*PTK6*	*hsa-miR-661*	MirTarBase
CEP41	*hsa-miR-200c-3p*	DIANA TOOLS	*PTPDC1*	*hsa-miR-93-5p*	DIANA TOOLS
CEP55	*hsa-miR-130a-3p*	DIANA TOOLS	*PTPN12*	*hsa-miR-200c-3p*	DIANA TOOLS
CEP55	*hsa-miR-144-3p*	DIANA TOOLS	*PTPN14*	*hsa-miR-31-5p*	DIANA TOOLS
CEP97	*hsa-miR-381-5p*	MirTarBase	*PTPN14*	*hsa-miR-21-5p*	DIANA TOOLS
CEP97	*hsa-miR-661*	MirTarBase	*PTPN14*	*hsa-miR-130a-3p*	DIANA TOOLS
CERCAM	*hsa-let-7a-5p*	DIANA TOOLS	*PTPN3*	*hsa-miR-16-5p*	DIANA TOOLS
CERS6	*hsa-miR-93-5p*	DIANA TOOLS	*PTPN3*	*hsa-miR-15b-5p*	DIANA TOOLS
CERS6	*hsa-miR-200c-3p*	DIANA TOOLS	*PTPN4*	*hsa-miR-130a-3p*	DIANA TOOLS
CFL2	*hsa-miR-200c-3p*	DIANA TOOLS	*PTPN4*	*hsa-miR-15b-5p*	DIANA TOOLS
CFTR	*hsa-miR-433-3p*	MirTarBase	*PTPN4*	*hsa-miR-16-5p*	DIANA TOOLS
CHAC1	*hsa-miR-15b-5p*	DIANA TOOLS	*PTPRD*	*hsa-miR-130a-3p*	DIANA TOOLS
CHAC1	*hsa-miR-16-5p*	DIANA TOOLS	*PUM1*	*hsa-miR-142-3p*	DIANA TOOLS
CHAC1	*hsa-miR-661*	MirTarBase	*PURA*	*hsa-miR-21-5p*	DIANA TOOLS
CHAF1B	*hsa-miR-661*	MirTarBase	*PURA*	*hsa-miR-16-5p*	DIANA TOOLS
CHAF1B	*hsa-miR-661*	MirTarBase	*PURA*	*hsa-miR-15b-5p*	DIANA TOOLS
CHCHD10	*hsa-miR-25-3p*	DIANA TOOLS	*PURB*	*hsa-miR-21-5p*	DIANA TOOLS
CHD2	*hsa-miR-16-5p*	DIANA TOOLS	*PURG*	*hsa-miR-130a-3p*	DIANA TOOLS
CHD2	*hsa-miR-15b-5p*	DIANA TOOLS	*PVRL1*	*hsa-miR-15b-5p*	DIANA TOOLS
CHD6	*hsa-miR-15b-5p*	DIANA TOOLS	*PVRL1*	*hsa-miR-16-5p*	DIANA TOOLS
CHD6	*hsa-miR-16-5p*	DIANA TOOLS	*PVRL4*	*hsa-miR-200c-3p*	DIANA TOOLS
CHD9	*hsa-miR-130a-3p*	DIANA TOOLS	*PWWP2B*	*hsa-miR-15b-5p*	DIANA TOOLS
CHD9	*hsa-miR-21-5p*	DIANA TOOLS	*PWWP2B*	*hsa-miR-16-5p*	DIANA TOOLS
CHD9	*hsa-miR-22-3p*	DIANA TOOLS	*PXDN*	*hsa-let-7a-5p*	DIANA TOOLS
CHD9	*hsa-miR-433-3p*	MirTarBase	*PXMP4*	*hsa-miR-661*	MirTarBase
CHEK1	*hsa-miR-15b-5p*	DIANA TOOLS	*PXT1*	*hsa-let-7a-5p*	DIANA TOOLS
CHEK1	*hsa-miR-16-5p*	DIANA TOOLS	*QKI*	*hsa-miR-130a-3p*	DIANA TOOLS
CHIC1	*hsa-miR-93-5p*	DIANA TOOLS	*QKI*	*hsa-miR-200c-3p*	DIANA TOOLS
CHKA	*hsa-miR-25-3p*	DIANA TOOLS	*QRFPR*	*hsa-miR-661*	MirTarBase
CHMP2B	*hsa-miR-200c-3p*	DIANA TOOLS	*QTRT2*	*hsa-miR-661*	MirTarBase
CHN2	*hsa-miR-200c-3p*	DIANA TOOLS	*QTRT2*	*hsa-miR-661*	MirTarBase
CHRFAM7A	*hsa-miR-661*	MirTarBase	*RAB10*	*hsa-miR-15b-5p*	DIANA TOOLS
CHRNA10	*hsa-miR-15b-5p*	DIANA TOOLS	*RAB10*	*hsa-miR-16-5p*	DIANA TOOLS
CHST6	*hsa-miR-661*	MirTarBase	*RAB11A*	*hsa-miR-21-5p*	DIANA TOOLS
CHTOP	*hsa-miR-31-5p*	DIANA TOOLS	*RAB11FIP2*	*hsa-let-7a-5p*	DIANA TOOLS
CIC	*hsa-miR-93-5p*	DIANA TOOLS	*RAB11FIP2*	*hsa-miR-21-5p*	DIANA TOOLS
CIC	*hsa-miR-25-3p*	DIANA TOOLS	*RAB11FIP2*	*hsa-miR-15b-5p*	DIANA TOOLS

CLCN5	*hsa-miR-142-3p*	DIANA TOOLS	*RAB11FIP2*	*hsa-miR-16-5p*	DIANA TOOLS
CLCN5	*hsa-miR-16-5p*	DIANA TOOLS	*RAB11FIP2*	*hsa-miR-200c-3p*	DIANA TOOLS
CLCN5	*hsa-miR-15b-5p*	DIANA TOOLS	*RAB11FIP4*	*hsa-miR-661*	MirTarBase
CLDN11	*hsa-miR-25-3p*	DIANA TOOLS	*RAB12*	*hsa-miR-142-3p*	DIANA TOOLS
CLDN12	*hsa-miR-142-3p*	DIANA TOOLS	*RAB1A*	*hsa-miR-144-3p*	DIANA TOOLS
CLDN12	*hsa-miR-16-5p*	DIANA TOOLS	*RAB22A*	*hsa-miR-661*	MirTarBase
CLDN12	*hsa-let-7a-5p*	DIANA TOOLS	*RAB23*	*hsa-miR-25-3p*	DIANA TOOLS
CLDN12	*hsa-miR-15b-5p*	DIANA TOOLS	*RAB30*	*hsa-miR-16-5p*	DIANA TOOLS
CLIC4	*hsa-miR-142-3p*	DIANA TOOLS	*RAB30*	*hsa-miR-130a-3p*	DIANA TOOLS
CLIC4	*hsa-miR-200c-3p*	DIANA TOOLS	*RAB34*	*hsa-miR-130a-3p*	DIANA TOOLS
CLIC4	*hsa-miR-22-3p*	DIANA TOOLS	*RAB3D*	*hsa-miR-661*	MirTarBase
CLIP1	*hsa-miR-130a-3p*	DIANA TOOLS	*RAB3GAP2*	*hsa-let-7a-5p*	DIANA TOOLS
CLK4	*hsa-miR-661*	MirTarBase	*RAB40C*	*hsa-let-7a-5p*	MirTarBase
CLOCK	*hsa-miR-142-3p*	DIANA TOOLS	*RAB42*	*hsa-miR-661*	MirTarBase
CLPP	*hsa-miR-661*	MirTarBase	*RAB5B*	*hsa-miR-22-3p*	DIANA TOOLS
CLTC	*hsa-miR-130a-3p*	DIANA TOOLS	*RAB5C*	*hsa-miR-433-3p*	MirTarBase
CLTC	*hsa-miR-205-5p*	DIANA TOOLS	*RAB6A*	*hsa-miR-21-5p*	DIANA TOOLS
CMC4	*hsa-miR-16-5p*	DIANA TOOLS	*RAB7A*	*hsa-miR-25-3p*	DIANA TOOLS
CMC4	*hsa-miR-15b-5p*	DIANA TOOLS	*RAB8B*	*hsa-miR-93-5p*	DIANA TOOLS
CMPK1	*hsa-miR-16-5p*	DIANA TOOLS	*RAC1*	*hsa-miR-142-3p*	DIANA TOOLS
CMTM4	*hsa-miR-16-5p*	DIANA TOOLS	*RAD21*	*hsa-miR-25-3p*	DIANA TOOLS
CMTM4	*hsa-miR-15b-5p*	DIANA TOOLS	*RAD51C*	*hsa-miR-15b-5p*	DIANA TOOLS
CNEP1R1	*hsa-miR-25-3p*	DIANA TOOLS	*RAD51C*	*hsa-miR-16-5p*	DIANA TOOLS
CNEP1R1	*hsa-miR-200c-3p*	DIANA TOOLS	*RALGAPB*	*hsa-miR-381-5p*	MirTarBase
CNIH1	*hsa-miR-25-3p*	DIANA TOOLS	*RALGAPB*	*hsa-miR-381-5p*	MirTarBase
CNIH4	*hsa-miR-142-3p*	DIANA TOOLS	*RANBP2*	*hsa-let-7a-5p*	DIANA TOOLS
CNKSR3	*hsa-miR-15b-5p*	DIANA TOOLS	*RANBP9*	*hsa-miR-144-3p*	DIANA TOOLS
CNKSR3	*hsa-miR-16-5p*	DIANA TOOLS	*RANBP9*	*hsa-miR-200c-3p*	DIANA TOOLS
CNOT4	*hsa-miR-130a-3p*	DIANA TOOLS	*RAP1B*	*hsa-miR-200c-3p*	DIANA TOOLS
CNOT6	*hsa-miR-21-5p*	DIANA TOOLS	*RAP2B*	*hsa-miR-144-3p*	DIANA TOOLS
CNOT6	*hsa-miR-130a-3p*	DIANA TOOLS	*RAP2C*	*hsa-miR-130a-3p*	DIANA TOOLS
CNOT6L	*hsa-miR-22-3p*	DIANA TOOLS	*RAP2C*	*hsa-miR-200c-3p*	DIANA TOOLS
CNOT6L	*hsa-miR-15b-5p*	DIANA TOOLS	*RARG*	*hsa-miR-142-3p*	DIANA TOOLS
CNOT6L	*hsa-miR-16-5p*	DIANA TOOLS	*RARS*	*hsa-miR-16-5p*	DIANA TOOLS
CNOT7	*hsa-miR-93-5p*	DIANA TOOLS	*RARS*	*hsa-miR-15b-5p*	DIANA TOOLS
CNTN4	*hsa-miR-661*	MirTarBase	*RASA2*	*hsa-miR-200c-3p*	DIANA TOOLS
CNTN4	*hsa-miR-661*	MirTarBase	*RASGRP1*	*hsa-miR-223-3p*	DIANA TOOLS
CNTRL	*hsa-let-7a-5p*	DIANA TOOLS	*RASGRP1*	*hsa-miR-21-5p*	DIANA TOOLS
COA4	*hsa-miR-661*	MirTarBase	*RASL11B*	*hsa-miR-93-5p*	DIANA TOOLS
COIL	*hsa-let-7a-5p*	DIANA TOOLS	*RASSF9*	*hsa-miR-661*	MirTarBase
COL12A1	*hsa-miR-16-5p*	DIANA TOOLS	*RASSF9*	*hsa-miR-661*	MirTarBase
COL12A1	*hsa-miR-15b-5p*	DIANA TOOLS	*RAVER2*	*hsa-miR-21-5p*	DIANA TOOLS
COL12A1	*hsa-miR-25-3p*	DIANA TOOLS	*RAVER2*	*hsa-let-7a-5p*	MirTarBase
COL15A1	*hsa-let-7a-5p*	DIANA TOOLS	*RBFOX2*	*hsa-miR-22-3p*	DIANA TOOLS
COL18A1	*hsa-miR-661*	MirTarBase	*RBFOX2*	*hsa-let-7a-5p*	DIANA TOOLS
COL1A1	*hsa-let-7a-5p*	DIANA TOOLS	*RBL2*	*hsa-miR-25-3p*	DIANA TOOLS
COL1A2	*hsa-let-7a-5p*	DIANA TOOLS	*RBM12*	*hsa-miR-16-5p*	DIANA TOOLS

COL1A2	*hsa-miR-25-3p*	DIANA TOOLS	*RBM12*	*hsa-miR-15b-5p*	DIANA TOOLS
COL27A1	*hsa-let-7a-5p*	DIANA TOOLS	*RBM12B*	*hsa-miR-200c-3p*	DIANA TOOLS
COL3A1	*hsa-let-7a-5p*	DIANA TOOLS	*RBM23*	*hsa-miR-661*	MirTarBase
COL4A1	*hsa-miR-21-5p*	DIANA TOOLS	*RBM25*	*hsa-miR-144-3p*	DIANA TOOLS
COL4A1	*hsa-let-7a-5p*	DIANA TOOLS	*RBM25*	*hsa-miR-130a-3p*	DIANA TOOLS
COPG1	*hsa-miR-142-3p*	DIANA TOOLS	*RBM25*	*hsa-miR-22-3p*	DIANA TOOLS
COPS2	*hsa-miR-200c-3p*	DIANA TOOLS	*RBM27*	*hsa-miR-25-3p*	DIANA TOOLS
COPS7A	*hsa-miR-15b-5p*	DIANA TOOLS	*RBM27*	*hsa-miR-142-3p*	DIANA TOOLS
COPS7A	*hsa-miR-16-5p*	DIANA TOOLS	*RBM28*	*hsa-miR-661*	MirTarBase
COPS8	*hsa-miR-200c-3p*	DIANA TOOLS	*RBM34*	*hsa-miR-93-5p*	DIANA TOOLS
COX11	*hsa-miR-200c-3p*	DIANA TOOLS	*RBM47*	*hsa-miR-142-3p*	DIANA TOOLS
COX18	*hsa-miR-661*	MirTarBase	*RBM47*	*hsa-miR-25-3p*	DIANA TOOLS
COX18	*hsa-miR-661*	MirTarBase	*RBM6*	*hsa-miR-15b-5p*	DIANA TOOLS
COX6B1	*hsa-miR-433-3p*	MirTarBase	*RBM6*	*hsa-miR-16-5p*	DIANA TOOLS
COX6B1	*hsa-miR-433-3p*	MirTarBase	*RBMS1*	*hsa-miR-15b-5p*	DIANA TOOLS
COX6B1	*hsa-miR-661*	MirTarBase	*RBMS1*	*hsa-miR-16-5p*	DIANA TOOLS
COX8A	*hsa-miR-433-3p*	MirTarBase	*RBMS1*	*hsa-let-7a-5p*	DIANA TOOLS
CPD	*hsa-miR-16-5p*	DIANA TOOLS	*RBMXL1*	*hsa-miR-22-3p*	DIANA TOOLS
CPD	*hsa-let-7a-5p*	DIANA TOOLS	*RBPJ*	*hsa-miR-25-3p*	DIANA TOOLS
CPEB2	*hsa-miR-15b-5p*	DIANA TOOLS	*RBPJ*	*hsa-miR-21-5p*	DIANA TOOLS
CPEB2	*hsa-miR-16-5p*	DIANA TOOLS	*RC3H2*	*hsa-miR-22-3p*	DIANA TOOLS
CPEB2	*hsa-miR-25-3p*	DIANA TOOLS	*RC3H2*	*hsa-miR-130a-3p*	DIANA TOOLS
CPEB3	*hsa-miR-200c-3p*	DIANA TOOLS	*RCOR1*	*hsa-miR-22-3p*	DIANA TOOLS
CPEB3	*hsa-miR-21-5p*	DIANA TOOLS	*RDX*	*hsa-miR-200c-3p*	DIANA TOOLS
CPEB3	*hsa-miR-25-3p*	DIANA TOOLS	*RDX*	*hsa-let-7a-5p*	DIANA TOOLS
CPEB3	*hsa-miR-93-5p*	DIANA TOOLS	*RECK*	*hsa-miR-21-5p*	DIANA TOOLS
CPEB3	*hsa-miR-15b-5p*	DIANA TOOLS	*RECK*	*hsa-miR-16-5p*	DIANA TOOLS
CPEB3	*hsa-miR-16-5p*	DIANA TOOLS	*RECK*	*hsa-miR-15b-5p*	DIANA TOOLS
CPEB4	*hsa-let-7a-5p*	DIANA TOOLS	*RECK*	*hsa-miR-200c-3p*	DIANA TOOLS
CPEB4	*hsa-miR-16-5p*	DIANA TOOLS	*RELA*	*hsa-miR-22-3p*	DIANA TOOLS
CPEB4	*hsa-miR-15b-5p*	DIANA TOOLS	*RELN*	*hsa-miR-205-5p*	DIANA TOOLS
CPEB4	*hsa-miR-130a-3p*	DIANA TOOLS	*RELN*	*hsa-miR-200c-3p*	DIANA TOOLS
CPEB4	*hsa-miR-25-3p*	DIANA TOOLS	*RERE*	*hsa-miR-142-3p*	DIANA TOOLS
CPM	*hsa-miR-661*	MirTarBase	*RETREG3*	*hsa-miR-661*	MirTarBase
CRCP	*hsa-miR-661*	MirTarBase	*REV3L*	*hsa-miR-25-3p*	DIANA TOOLS
CREB1	*hsa-miR-205-5p*	DIANA TOOLS	*REV3L*	*hsa-miR-15b-5p*	DIANA TOOLS
CREB1	*hsa-miR-433-3p*	MirTarBase	*REV3L*	*hsa-miR-16-5p*	DIANA TOOLS
CREBRF	*hsa-miR-21-5p*	DIANA TOOLS	*REV3L*	*hsa-let-7a-5p*	DIANA TOOLS
CREBRF	*hsa-miR-15b-5p*	DIANA TOOLS	*REXO1*	*hsa-miR-25-3p*	DIANA TOOLS
CREBRF	*hsa-miR-16-5p*	DIANA TOOLS	*RFK*	*hsa-miR-15b-5p*	DIANA TOOLS
CREBRF	*hsa-miR-144-3p*	DIANA TOOLS	*RFK*	*hsa-miR-190b*	DIANA TOOLS
CREG1	*hsa-miR-31-5p*	DIANA TOOLS	*RFK*	*hsa-miR-16-5p*	DIANA TOOLS
CRIPT	*hsa-miR-190b*	DIANA TOOLS	*RFX1*	*hsa-miR-25-3p*	DIANA TOOLS
CRISPLD2	*hsa-miR-661*	MirTarBase	*RFX3*	*hsa-miR-16-5p*	DIANA TOOLS
CRK	*hsa-miR-15b-5p*	DIANA TOOLS	*RFX3*	*hsa-miR-15b-5p*	DIANA TOOLS
CRK	*hsa-miR-93-5p*	DIANA TOOLS	*RFX7*	*hsa-miR-22-3p*	DIANA TOOLS
CRKL	*hsa-miR-200c-3p*	DIANA TOOLS	*RFX7*	*hsa-miR-130a-3p*	DIANA TOOLS
CRKL	*hsa-miR-661*	MirTarBase	*RGL1*	*hsa-miR-25-3p*	DIANA TOOLS

CRLF3	*hsa-miR-661*	MirTarBase	*RGL1*	*hsa-miR-190b*	DIANA TOOLS
CRLF3	*hsa-miR-661*	MirTarBase	*RGL1*	*hsa-miR-200c-3p*	DIANA TOOLS
CRLS1	*hsa-miR-22-3p*	DIANA TOOLS	*RGL2*	*hsa-miR-142-3p*	DIANA TOOLS
CROT	*hsa-miR-190b*	DIANA TOOLS	*RGMB*	*hsa-miR-93-5p*	DIANA TOOLS
CRTAP	*hsa-let-7a-5p*	DIANA TOOLS	*RGS16*	*hsa-let-7a-5p*	DIANA TOOLS
CRTAP	*hsa-miR-200c-3p*	DIANA TOOLS	*RGS2*	*hsa-miR-22-3p*	DIANA TOOLS
CSDE1	*hsa-miR-15b-5p*	DIANA TOOLS	*RGS4*	*hsa-miR-31-5p*	DIANA TOOLS
CSDE1	*hsa-miR-16-5p*	DIANA TOOLS	*RHNO1*	*hsa-miR-661*	MirTarBase
CSF1	*hsa-miR-130a-3p*	DIANA TOOLS	*RHOBTB3*	*hsa-miR-142-3p*	DIANA TOOLS
CSNK1G3	*hsa-miR-200c-3p*	DIANA TOOLS	*RHPN2*	*hsa-miR-661*	MirTarBase
CSNK2A1	*hsa-let-7a-5p*	DIANA TOOLS	*RIC8B*	*hsa-miR-16-5p*	DIANA TOOLS
CTDSP1	*hsa-miR-661*	MirTarBase	*RICTOR*	*hsa-let-7a-5p*	DIANA TOOLS
CTDSPL2	*hsa-miR-200c-3p*	DIANA TOOLS	*RICTOR*	*hsa-miR-142-3p*	DIANA TOOLS
CTDSPL2	*hsa-let-7a-5p*	DIANA TOOLS	*RIF1*	*hsa-miR-15b-5p*	DIANA TOOLS
CTNNBL1	*hsa-miR-661*	MirTarBase	*RIF1*	*hsa-miR-16-5p*	DIANA TOOLS
CTPS1	*hsa-miR-381-5p*	MirTarBase	*RIMKLA*	*hsa-let-7a-5p*	DIANA TOOLS
CTPS2	*hsa-let-7a-5p*	DIANA TOOLS	*RIN2*	*hsa-miR-144-3p*	DIANA TOOLS
CTSA	*hsa-let-7a-5p*	DIANA TOOLS	*RLIM*	*hsa-miR-190b*	DIANA TOOLS
CTTNBP2	*hsa-miR-15b-5p*	DIANA TOOLS	*RMDN3*	*hsa-miR-22-3p*	DIANA TOOLS
CTTNBP2	*hsa-miR-16-5p*	DIANA TOOLS	*RMND5A*	*hsa-miR-21-5p*	DIANA TOOLS
CUX1	*hsa-miR-25-3p*	DIANA TOOLS	*RNASEH2B*	*hsa-miR-661*	MirTarBase
CUX1	*hsa-miR-200c-3p*	DIANA TOOLS	*RNF11*	*hsa-miR-25-3p*	DIANA TOOLS
CXCL10	*hsa-miR-661*	MirTarBase	*RNF111*	*hsa-miR-16-5p*	DIANA TOOLS
CXCL12	*hsa-miR-144-3p*	DIANA TOOLS	*RNF115*	*hsa-miR-661*	MirTarBase
CXCL6	*hsa-miR-130a-3p*	DIANA TOOLS	*RNF125*	*hsa-miR-661*	MirTarBase
CXXC5	*hsa-miR-25-3p*	DIANA TOOLS	*RNF135*	*hsa-miR-661*	MirTarBase
CYC1	*hsa-miR-661*	MirTarBase	*RNF138*	*hsa-miR-15b-5p*	DIANA TOOLS
CYLD	*hsa-miR-15b-5p*	DIANA TOOLS	*RNF138*	*hsa-miR-16-5p*	DIANA TOOLS
CYP20A1	*hsa-miR-661*	MirTarBase	*RNF141*	*hsa-miR-25-3p*	DIANA TOOLS
CYP26B1	*hsa-miR-16-5p*	DIANA TOOLS	*RNF144B*	*hsa-miR-16-5p*	DIANA TOOLS
CYP26B1	*hsa-miR-15b-5p*	DIANA TOOLS	*RNF144B*	*hsa-miR-15b-5p*	DIANA TOOLS
CYP2R1	*hsa-let-7a-5p*	DIANA TOOLS	*RNF19A*	*hsa-miR-200c-3p*	DIANA TOOLS
CYP4F3	*hsa-miR-661*	MirTarBase	*RNF2*	*hsa-miR-200c-3p*	DIANA TOOLS
CYR61	*hsa-miR-22-3p*	DIANA TOOLS	*RNF20*	*hsa-miR-661*	MirTarBase
CYTH3	*hsa-miR-22-3p*	DIANA TOOLS	*RNF213*	*hsa-miR-16-5p*	DIANA TOOLS
DAB2IP	*hsa-miR-25-3p*	DIANA TOOLS	*RNF213*	*hsa-miR-15b-5p*	DIANA TOOLS
DAD1	*hsa-miR-22-3p*	DIANA TOOLS	*RNF217*	*hsa-miR-15b-5p*	DIANA TOOLS
DAND5	*hsa-miR-661*	MirTarBase	*RNF217*	*hsa-let-7a-5p*	DIANA TOOLS
DARS2	*hsa-miR-661*	MirTarBase	*RNF219*	*hsa-miR-130a-3p*	DIANA TOOLS
DAZAP2	*hsa-miR-381-5p*	MirTarBase	*RNF222*	*hsa-miR-661*	MirTarBase
DAZAP2	*hsa-miR-381-5p*	MirTarBase	*RNF24*	*hsa-miR-21-5p*	DIANA TOOLS
DAZAP2	*hsa-miR-381-5p*	MirTarBase	*RNF38*	*hsa-miR-130a-3p*	DIANA TOOLS
DBT	*hsa-miR-25-3p*	DIANA TOOLS	*RNF38*	*hsa-miR-25-3p*	DIANA TOOLS
DCAF15	*hsa-let-7a-5p*	DIANA TOOLS	*RNF4*	*hsa-miR-25-3p*	DIANA TOOLS
DCAF16	*hsa-miR-22-3p*	DIANA TOOLS	*RNF41*	*hsa-miR-130a-3p*	DIANA TOOLS
DCAF17	*hsa-miR-15b-5p*	DIANA TOOLS	*RNF43*	*hsa-miR-16-5p*	DIANA TOOLS
DCAF7	*hsa-miR-15b-5p*	DIANA TOOLS	*RNF43*	*hsa-miR-15b-5p*	DIANA TOOLS

DCAF7	*hsa-miR-16-5p*	DIANA TOOLS	*RNF44*	*hsa-let-7a-5p*	DIANA TOOLS
DCAF7	*hsa-miR-21-5p*	DIANA TOOLS	*RNF44*	*hsa-miR-25-3p*	DIANA TOOLS
DCAF8	*hsa-miR-15b-5p*	DIANA TOOLS	*RNFT1*	*hsa-let-7a-5p*	DIANA TOOLS
DCAF8	*hsa-miR-16-5p*	DIANA TOOLS	*ROCK1*	*hsa-miR-190b*	DIANA TOOLS
DCBLD2	*hsa-miR-31-5p*	DIANA TOOLS	*ROCK2*	*hsa-miR-93-5p*	DIANA TOOLS
DCBLD2	*hsa-miR-433-3p*	MirTarBase	*ROCK2*	*hsa-miR-142-3p*	DIANA TOOLS
DCP2	*hsa-miR-144-3p*	DIANA TOOLS	*RORA*	*hsa-miR-25-3p*	DIANA TOOLS
DCP2	*hsa-miR-130a-3p*	DIANA TOOLS	*RP2*	*hsa-miR-21-5p*	DIANA TOOLS
DCUN1D3	*hsa-miR-130a-3p*	DIANA TOOLS	*RPA2*	*hsa-miR-130a-3p*	DIANA TOOLS
DDIT4	*hsa-miR-223-3p*	DIANA TOOLS	*RPE*	*hsa-miR-142-3p*	DIANA TOOLS
DDIT4	*hsa-miR-22-3p*	DIANA TOOLS	*RPL12*	*hsa-miR-661*	MirTarBase
DDX19B	*hsa-miR-661*	MirTarBase	*RPL14*	*hsa-miR-16-5p*	DIANA TOOLS
DDX26B	*hsa-let-7a-5p*	DIANA TOOLS	*RPL14*	*hsa-miR-15b-5p*	DIANA TOOLS
DDX3X	*hsa-miR-25-3p*	DIANA TOOLS	*RPL23*	*hsa-miR-661*	MirTarBase
DDX3X	*hsa-miR-15b-5p*	DIANA TOOLS	*RPL24*	*hsa-miR-433-3p*	MirTarBase
DDX3X	*hsa-miR-16-5p*	DIANA TOOLS	*RPL28*	*hsa-miR-661*	MirTarBase
DDX3X	*hsa-miR-495-3p*	DIANA TOOLS	*RPL7L1*	*hsa-miR-661*	MirTarBase
DDX3Y	*hsa-miR-200c-3p*	DIANA TOOLS	*RPLP0*	*hsa-miR-16-5p*	DIANA TOOLS
DDX3Y	*hsa-miR-16-5p*	DIANA TOOLS	*RPRD2*	*hsa-miR-25-3p*	DIANA TOOLS
DDX5	*hsa-miR-93-5p*	DIANA TOOLS	*RPRD2*	*hsa-miR-661*	MirTarBase
DDX52	*hsa-miR-661*	MirTarBase	*RPS15A*	*hsa-miR-661*	MirTarBase
DDX6	*hsa-miR-130a-3p*	DIANA TOOLS	*RPS19*	*hsa-miR-661*	MirTarBase
DEDD	*hsa-miR-16-5p*	DIANA TOOLS	*RPS6KA3*	*hsa-miR-21-5p*	DIANA TOOLS
DEFB105A	*hsa-miR-661*	MirTarBase	*RPS6KA3*	*hsa-miR-200c-3p*	DIANA TOOLS
DEFB105A	*hsa-miR-661*	MirTarBase	*RPS6KA3*	*hsa-miR-16-5p*	DIANA TOOLS
DEFB105B	*hsa-miR-661*	MirTarBase	*RPS6KA3*	*hsa-miR-15b-5p*	DIANA TOOLS
DEFB105B	*hsa-miR-661*	MirTarBase	*RPS6KB2*	*hsa-let-7a-5p*	DIANA TOOLS
DENND1B	*hsa-miR-25-3p*	DIANA TOOLS	*RPS6KC1*	*hsa-miR-22-3p*	DIANA TOOLS
DENND4B	*hsa-miR-25-3p*	DIANA TOOLS	*RRAGA*	*hsa-miR-16-5p*	DIANA TOOLS
DENND5B	*hsa-miR-190b*	DIANA TOOLS	*RRAGA*	*hsa-miR-15b-5p*	DIANA TOOLS
DENND5B	*hsa-miR-93-5p*	DIANA TOOLS	*RRAGD*	*hsa-miR-130a-3p*	DIANA TOOLS
DENND6A	*hsa-miR-144-3p*	DIANA TOOLS	*RRBP1*	*hsa-miR-25-3p*	DIANA TOOLS
DENND6A	*hsa-miR-190b*	DIANA TOOLS	*RREB1*	*hsa-miR-142-3p*	DIANA TOOLS
DENND6A	*hsa-miR-200c-3p*	DIANA TOOLS	*RREB1*	*hsa-miR-16-5p*	DIANA TOOLS
DEPDC1B	*hsa-miR-15b-5p*	DIANA TOOLS	*RREB1*	*hsa-miR-15b-5p*	DIANA TOOLS
DESI1	*hsa-miR-200c-3p*	DIANA TOOLS	*RRM2*	*hsa-let-7a-5p*	DIANA TOOLS
DESI1	*hsa-miR-15b-5p*	DIANA TOOLS	*RRM2*	*hsa-let-7a-5p*	MirTarBase
DESI1	*hsa-miR-16-5p*	DIANA TOOLS	*RRN3*	*hsa-miR-25-3p*	DIANA TOOLS
DFFB	*hsa-miR-661*	MirTarBase	*RSBN1*	*hsa-miR-25-3p*	DIANA TOOLS
DGCR2	*hsa-miR-16-5p*	DIANA TOOLS	*RSBN1*	*hsa-miR-16-5p*	DIANA TOOLS
DGCR6L	*hsa-miR-661*	MirTarBase	*RSBN1*	*hsa-miR-15b-5p*	DIANA TOOLS
DGKE	*hsa-miR-433-3p*	MirTarBase	*RSBN1*	*hsa-miR-93-5p*	DIANA TOOLS
DGKH	*hsa-miR-130a-3p*	DIANA TOOLS	*RSL1D1*	*hsa-miR-661*	MirTarBase
DHRS7	*hsa-miR-16-5p*	DIANA TOOLS	*RTCA*	*hsa-miR-130a-3p*	DIANA TOOLS
DHX30	*hsa-miR-22-3p*	DIANA TOOLS	*RTCB*	*hsa-miR-661*	MirTarBase
DICER1	*hsa-miR-31-5p*	DIANA TOOLS	*RTL8C*	*hsa-miR-661*	MirTarBase
DICER1	*hsa-let-7a-5p*	DIANA TOOLS	*RTN3*	*hsa-miR-205-5p*	DIANA TOOLS
DICER1	*hsa-let-7a-5p*	MirTarBase	*RTN4*	*hsa-miR-130a-3p*	DIANA TOOLS

DIEXF	*hsa-miR-15b-5p*	DIANA TOOLS	*RTN4*	*hsa-miR-21-5p*	DIANA TOOLS
DIEXF	*hsa-miR-16-5p*	DIANA TOOLS	*RUFY2*	*hsa-miR-22-3p*	DIANA TOOLS
DIXDC1	*hsa-miR-15b-5p*	DIANA TOOLS	*RUNX1*	*hsa-miR-93-5p*	DIANA TOOLS
DIXDC1	*hsa-miR-16-5p*	DIANA TOOLS	*RUNX2*	*hsa-miR-433-3p*	MirTarBase
DIXDC1	*hsa-miR-200c-3p*	DIANA TOOLS	*RUNX3*	*hsa-miR-130a-3p*	DIANA TOOLS
DLC1	*hsa-let-7a-5p*	DIANA TOOLS	*RUSC2*	*hsa-miR-661*	MirTarBase
DLD	*hsa-miR-15b-5p*	DIANA TOOLS	*RXRB*	*hsa-miR-31-5p*	DIANA TOOLS
DLGAP4	*hsa-let-7a-5p*	DIANA TOOLS	*S100PBP*	*hsa-miR-200c-3p*	DIANA TOOLS
DLL1	*hsa-miR-130a-3p*	DIANA TOOLS	*S1PR2*	*hsa-miR-661*	MirTarBase
DLL1	*hsa-miR-15b-5p*	DIANA TOOLS	*SALL1*	*hsa-miR-15b-5p*	DIANA TOOLS
DLL1	*hsa-miR-16-5p*	DIANA TOOLS	*SALL1*	*hsa-miR-16-5p*	DIANA TOOLS
DMKN	*hsa-miR-661*	MirTarBase	*SALL4*	*hsa-miR-661*	MirTarBase
DMKN	*hsa-miR-661*	MirTarBase	*SAMD12*	*hsa-miR-142-3p*	DIANA TOOLS
DMKN	*hsa-miR-661*	MirTarBase	*SAMD12*	*hsa-miR-93-5p*	DIANA TOOLS
DMTF1	*hsa-miR-15b-5p*	DIANA TOOLS	*SAR1B*	*hsa-miR-130a-3p*	DIANA TOOLS
DMTF1	*hsa-miR-16-5p*	DIANA TOOLS	*SASH1*	*hsa-miR-130a-3p*	DIANA TOOLS
DMTF1	*hsa-miR-142-3p*	DIANA TOOLS	*SASH1*	*hsa-miR-661*	MirTarBase
DMXL1	*hsa-miR-25-3p*	DIANA TOOLS	*SATB1*	*hsa-miR-21-5p*	DIANA TOOLS
DNA2	*hsa-let-7a-5p*	DIANA TOOLS	*SATB2*	*hsa-miR-22-3p*	DIANA TOOLS
DNA2	*hsa-miR-661*	MirTarBase	*SBF2*	*hsa-miR-130a-3p*	DIANA TOOLS
DNAH10OS	*hsa-miR-661*	MirTarBase	*SBNO1*	*hsa-miR-25-3p*	DIANA TOOLS
DNAJA2	*hsa-let-7a-5p*	DIANA TOOLS	*SC5D*	*hsa-miR-661*	MirTarBase
DNAJB12	*hsa-miR-25-3p*	DIANA TOOLS	*SCAI*	*hsa-miR-15b-5p*	DIANA TOOLS
DNAJB4	*hsa-miR-142-3p*	DIANA TOOLS	*SCAI*	*hsa-miR-16-5p*	DIANA TOOLS
DNAJB4	*hsa-miR-16-5p*	DIANA TOOLS	*SCAMP1*	*hsa-miR-433-3p*	MirTarBase
DNAJB4	*hsa-miR-15b-5p*	DIANA TOOLS	*SCAMP4*	*hsa-miR-661*	MirTarBase
DNAJB9	*hsa-miR-200c-3p*	DIANA TOOLS	*SCARB1*	*hsa-miR-223-3p*	DIANA TOOLS
DNAJC10	*hsa-miR-15b-5p*	DIANA TOOLS	*SCD*	*hsa-miR-200c-3p*	DIANA TOOLS
DNAJC10	*hsa-miR-16-5p*	DIANA TOOLS	*SCD*	*hsa-let-7a-5p*	DIANA TOOLS
DNAJC22	*hsa-miR-661*	MirTarBase	*SCFD1*	*hsa-miR-190b*	DIANA TOOLS
DNAJC27	*hsa-miR-25-3p*	DIANA TOOLS	*SCML2*	*hsa-miR-381-5p*	MirTarBase
DNAJC28	*hsa-miR-661*	MirTarBase	*SCNN1G*	*hsa-miR-433-3p*	MirTarBase
DNAJC30	*hsa-miR-25-3p*	DIANA TOOLS	*SDHAF2*	*hsa-miR-661*	MirTarBase
DNAJC5	*hsa-miR-200c-3p*	DIANA TOOLS	*SEC14L1*	*hsa-let-7a-5p*	DIANA TOOLS
DNM1L	*hsa-miR-15b-5p*	DIANA TOOLS	*SEC16A*	*hsa-miR-544a*	DIANA TOOLS
DNM1L	*hsa-miR-16-5p*	DIANA TOOLS	*SEC23A*	*hsa-miR-190b*	DIANA TOOLS
DOCK5	*hsa-miR-22-3p*	DIANA TOOLS	*SEC23A*	*hsa-miR-200c-3p*	DIANA TOOLS
DOCK5	*hsa-miR-16-5p*	DIANA TOOLS	*SEC24A*	*hsa-miR-16-5p*	DIANA TOOLS
DOK3	*hsa-let-7a-5p*	DIANA TOOLS	*SECISBP2L*	*hsa-miR-200c-3p*	DIANA TOOLS
DPF2	*hsa-miR-22-3p*	DIANA TOOLS	*SECISBP2L*	*hsa-miR-130a-3p*	DIANA TOOLS
DPF3	*hsa-miR-25-3p*	DIANA TOOLS	*SEH1L*	*hsa-miR-205-5p*	DIANA TOOLS
DPH3	*hsa-let-7a-5p*	DIANA TOOLS	*SEL1L3*	*hsa-miR-130a-3p*	DIANA TOOLS
DSEL	*hsa-miR-661*	MirTarBase	*SEL1L3*	*hsa-miR-16-5p*	DIANA TOOLS
DST	*hsa-miR-130a-3p*	DIANA TOOLS	*SELT*	*hsa-let-7a-5p*	DIANA TOOLS
DSTYK	*hsa-miR-25-3p*	DIANA TOOLS	*SELT*	*hsa-miR-25-3p*	DIANA TOOLS
DSTYK	*hsa-miR-661*	MirTarBase	*SEMA3A*	*hsa-miR-16-5p*	DIANA TOOLS
DSTYK	*hsa-miR-661*	MirTarBase	*SEMA3A*	*hsa-miR-15b-5p*	DIANA TOOLS

DUSP1	*hsa-let-7a-5p*	DIANA TOOLS	*SEMA4C*	*hsa-let-7a-5p*	DIANA TOOLS
DUSP1	*hsa-miR-200c-3p*	DIANA TOOLS	*SEMA6D*	*hsa-miR-16-5p*	DIANA TOOLS
DUSP10	*hsa-miR-25-3p*	DIANA TOOLS	*SEMA7A*	*hsa-miR-205-5p*	DIANA TOOLS
DUSP10	*hsa-miR-223-3p*	DIANA TOOLS	*SENP1*	*hsa-miR-93-5p*	DIANA TOOLS
DUSP22	*hsa-let-7a-5p*	DIANA TOOLS	*SENP5*	*hsa-miR-16-5p*	DIANA TOOLS
DUSP5	*hsa-miR-25-3p*	DIANA TOOLS	*SENP5*	*hsa-miR-15b-5p*	DIANA TOOLS
DUSP6	*hsa-let-7a-5p*	DIANA TOOLS	*SENP5*	*hsa-let-7a-5p*	DIANA TOOLS
DUSP8	*hsa-miR-21-5p*	DIANA TOOLS	*SENP6*	*hsa-miR-200c-3p*	DIANA TOOLS
DYNC1LI2	*hsa-miR-130a-3p*	DIANA TOOLS	*SEPT10*	*hsa-miR-21-5p*	DIANA TOOLS
DYNC1LI2	*hsa-miR-93-5p*	DIANA TOOLS	*SEPT2*	*hsa-miR-16-5p*	DIANA TOOLS
DYNLL2	*hsa-miR-16-5p*	DIANA TOOLS	*SEPT2*	*hsa-miR-15b-5p*	DIANA TOOLS
DYNLL2	*hsa-miR-130a-3p*	DIANA TOOLS	*SERBP1*	*hsa-miR-433-3p*	MirTarBase
DYNLL2	*hsa-miR-15b-5p*	DIANA TOOLS	*SERINC1*	*hsa-miR-200c-3p*	DIANA TOOLS
DYRK1B	*hsa-miR-15b-5p*	DIANA TOOLS	*SERP1*	*hsa-miR-93-5p*	DIANA TOOLS
DYRK1B	*hsa-miR-16-5p*	DIANA TOOLS	*SERPING1*	*hsa-miR-661*	MirTarBase
DYRK2	*hsa-miR-25-3p*	DIANA TOOLS	*SERPINI1*	*hsa-miR-200c-3p*	DIANA TOOLS
DYRK2	*hsa-let-7a-5p*	DIANA TOOLS	*SERTAD2*	*hsa-miR-31-5p*	DIANA TOOLS
DZIP1	*hsa-miR-200c-3p*	DIANA TOOLS	*SERTAD2*	*hsa-miR-93-5p*	DIANA TOOLS
E2F1	*hsa-miR-205-5p*	DIANA TOOLS	*SERTAD2*	*hsa-miR-25-3p*	DIANA TOOLS
E2F1	*hsa-let-7a-5p*	MirTarBase	*SESN1*	*hsa-miR-200c-3p*	DIANA TOOLS
E2F2	*hsa-miR-130a-3p*	DIANA TOOLS	*SESN1*	*hsa-miR-22-3p*	DIANA TOOLS
E2F2	*hsa-let-7a-5p*	MirTarBase	*SESN1*	*hsa-miR-16-5p*	DIANA TOOLS
E2F3	*hsa-miR-21-5p*	DIANA TOOLS	*SESN1*	*hsa-miR-15b-5p*	DIANA TOOLS
E2F3	*hsa-miR-200c-3p*	DIANA TOOLS	*SESN3*	*hsa-miR-93-5p*	DIANA TOOLS
E2F3	*hsa-miR-16-5p*	DIANA TOOLS	*SESN3*	*hsa-miR-25-3p*	DIANA TOOLS
E2F3	*hsa-miR-15b-5p*	DIANA TOOLS	*SESTD1*	*hsa-let-7a-5p*	DIANA TOOLS
E2F5	*hsa-let-7a-5p*	DIANA TOOLS	*SESTD1*	*hsa-miR-130a-3p*	DIANA TOOLS
E2F6	*hsa-let-7a-5p*	DIANA TOOLS	*SETD1B*	*hsa-miR-15b-5p*	DIANA TOOLS
E2F7	*hsa-miR-130a-3p*	DIANA TOOLS	*SETD1B*	*hsa-miR-16-5p*	DIANA TOOLS
E2F7	*hsa-miR-16-5p*	DIANA TOOLS	*SETD2*	*hsa-miR-25-3p*	DIANA TOOLS
E2F7	*hsa-miR-15b-5p*	DIANA TOOLS	*SETD5*	*hsa-miR-142-3p*	DIANA TOOLS
EDA	*hsa-miR-15b-5p*	DIANA TOOLS	*SETD7*	*hsa-miR-200c-3p*	DIANA TOOLS
EDA	*hsa-miR-16-5p*	DIANA TOOLS	*SF3A1*	*hsa-miR-661*	MirTarBase
EDEM1	*hsa-miR-25-3p*	DIANA TOOLS	*SF3A1*	*hsa-miR-661*	MirTarBase
EDEM3	*hsa-let-7a-5p*	DIANA TOOLS	*SFSWAP*	*hsa-let-7a-5p*	DIANA TOOLS
EDEM3	*hsa-miR-200c-3p*	DIANA TOOLS	*SFXN1*	*hsa-miR-16-5p*	DIANA TOOLS
EDN1	*hsa-miR-130a-3p*	DIANA TOOLS	*SFXN1*	*hsa-miR-15b-5p*	DIANA TOOLS
EDN1	*hsa-let-7a-5p*	DIANA TOOLS	*SFXN1*	*hsa-miR-22-3p*	DIANA TOOLS
EDN1	*hsa-miR-433-3p*	MirTarBase	*SFXN1*	*hsa-miR-25-3p*	DIANA TOOLS
EDNRA	*hsa-miR-200c-3p*	DIANA TOOLS	*SFXN1*	*hsa-miR-200c-3p*	DIANA TOOLS
EFCAB14	*hsa-miR-93-5p*	DIANA TOOLS	*SGK1*	*hsa-miR-25-3p*	DIANA TOOLS
EFNA1	*hsa-miR-200c-3p*	DIANA TOOLS	*SGK3*	*hsa-miR-25-3p*	DIANA TOOLS
EFNB2	*hsa-miR-130a-3p*	DIANA TOOLS	*SGPP1*	*hsa-miR-25-3p*	DIANA TOOLS
EFR3A	*hsa-miR-25-3p*	DIANA TOOLS	*SGSM2*	*hsa-miR-661*	MirTarBase
EGFR	*hsa-let-7a-5p*	MirTarBase	*SH3BGRL2*	*hsa-miR-16-5p*	DIANA TOOLS
EGLN2	*hsa-let-7a-5p*	DIANA TOOLS	*SH3BGRL2*	*hsa-miR-15b-5p*	DIANA TOOLS
EHD4	*hsa-miR-661*	MirTarBase	*SH3D19*	*hsa-miR-25-3p*	DIANA TOOLS
EHD4	*hsa-miR-661*	MirTarBase	*SH3D19*	*hsa-miR-661*	MirTarBase

EHHADH	*hsa-miR-661*	MirTarBase	*SH3GL1*	*hsa-miR-200c-3p*	DIANA TOOLS
EIF1	*hsa-miR-25-3p*	DIANA TOOLS	*SH3PXD2A*	*hsa-miR-200c-3p*	DIANA TOOLS
EIF2A	*hsa-miR-142-3p*	DIANA TOOLS	*SH3PXD2A*	*hsa-miR-25-3p*	DIANA TOOLS
EIF2S1	*hsa-miR-93-5p*	DIANA TOOLS	*SH3PXD2A*	*hsa-miR-544a*	DIANA TOOLS
EIF2S3L	*hsa-miR-200c-3p*	DIANA TOOLS	*SH3TC1*	*hsa-let-7a-5p*	DIANA TOOLS
EIF3F	*hsa-miR-661*	MirTarBase	*SHANK2*	*hsa-miR-144-3p*	DIANA TOOLS
EIF3H	*hsa-miR-661*	MirTarBase	*SHE*	*hsa-miR-661*	MirTarBase
EIF3H	*hsa-miR-661*	MirTarBase	*SHISA5*	*hsa-miR-15b-5p*	DIANA TOOLS
EIF4A2	*hsa-miR-93-5p*	DIANA TOOLS	*SHISA5*	*hsa-miR-16-5p*	DIANA TOOLS
EIF4B	*hsa-miR-16-5p*	DIANA TOOLS	*SHKBP1*	*hsa-miR-22-3p*	DIANA TOOLS
EIF4B	*hsa-miR-376b-3p*	DIANA TOOLS	*SHOC2*	*hsa-miR-16-5p*	DIANA TOOLS
EIF4E	*hsa-miR-16-5p*	DIANA TOOLS	*SHOC2*	*hsa-miR-661*	MirTarBase
EIF4E2	*hsa-miR-200c-3p*	DIANA TOOLS	*SIAH1*	*hsa-miR-200c-3p*	DIANA TOOLS
EIF4EBP1	*hsa-miR-661*	MirTarBase	*SIK1*	*hsa-miR-25-3p*	DIANA TOOLS
EIF4EBP2	*hsa-miR-31-5p*	DIANA TOOLS	*SIK2*	*hsa-miR-31-5p*	DIANA TOOLS
EIF4ENIF1	*hsa-let-7a-5p*	DIANA TOOLS	*SIK2*	*hsa-miR-25-3p*	DIANA TOOLS
EIF4G2	*hsa-miR-93-5p*	DIANA TOOLS	*SIKE1*	*hsa-miR-31-5p*	DIANA TOOLS
EIF4G2	*hsa-miR-144-3p*	DIANA TOOLS	*SIKE1*	*hsa-miR-200c-3p*	DIANA TOOLS
EIF5	*hsa-miR-661*	MirTarBase	*SIPA1*	*hsa-miR-661*	MirTarBase
ELF4	*hsa-let-7a-5p*	DIANA TOOLS	*SIPA1L2*	*hsa-miR-16-5p*	DIANA TOOLS
ELK4	*hsa-let-7a-5p*	DIANA TOOLS	*SIPA1L2*	*hsa-miR-15b-5p*	DIANA TOOLS
ELK4	*hsa-miR-200c-3p*	DIANA TOOLS	*SIRT1*	*hsa-miR-200c-3p*	DIANA TOOLS
ELL	*hsa-miR-16-5p*	DIANA TOOLS	*SIRT1*	*hsa-miR-22-3p*	DIANA TOOLS
ELL2	*hsa-miR-16-5p*	DIANA TOOLS	*SIX4*	*hsa-miR-130a-3p*	DIANA TOOLS
ELL2	*hsa-miR-15b-5p*	DIANA TOOLS	*SIX4*	*hsa-miR-661*	MirTarBase
ELOVL6	*hsa-miR-661*	MirTarBase	*SKI*	*hsa-miR-16-5p*	DIANA TOOLS
ELOVL6	*hsa-miR-661*	MirTarBase	*SKI*	*hsa-miR-15b-5p*	DIANA TOOLS
ELOVL7	*hsa-miR-15b-5p*	DIANA TOOLS	*SKI*	*hsa-miR-21-5p*	DIANA TOOLS
ELOVL7	*hsa-miR-16-5p*	DIANA TOOLS	*SKIL*	*hsa-let-7a-5p*	DIANA TOOLS
EMC1	*hsa-miR-661*	MirTarBase	*SKIL*	*hsa-miR-16-5p*	DIANA TOOLS
EMC1	*hsa-miR-661*	MirTarBase	*SKIL*	*hsa-miR-15b-5p*	DIANA TOOLS
EMC1	*hsa-miR-661*	MirTarBase	*SKIL*	*hsa-miR-144-3p*	DIANA TOOLS
ENAH	*hsa-miR-21-5p*	DIANA TOOLS	*SKIV2L2*	*hsa-miR-142-3p*	DIANA TOOLS
ENAH	*hsa-miR-16-5p*	DIANA TOOLS	*SKP2*	*hsa-miR-142-3p*	DIANA TOOLS
ENAH	*hsa-miR-15b-5p*	DIANA TOOLS	*SKP2*	*hsa-miR-21-5p*	DIANA TOOLS
ENPP5	*hsa-miR-93-5p*	DIANA TOOLS	*SLAIN1*	*hsa-miR-130a-3p*	DIANA TOOLS
ENPP5	*hsa-miR-130a-3p*	DIANA TOOLS	*SLC11A2*	*hsa-miR-15b-5p*	DIANA TOOLS
ENSA	*hsa-miR-16-5p*	DIANA TOOLS	*SLC11A2*	*hsa-miR-16-5p*	DIANA TOOLS
ENSA	*hsa-miR-15b-5p*	DIANA TOOLS	*SLC11A2*	*hsa-miR-661*	MirTarBase
ENTPD1	*hsa-miR-661*	MirTarBase	*SLC12A2*	*hsa-miR-16-5p*	DIANA TOOLS
ENTPD4	*hsa-miR-25-3p*	DIANA TOOLS	*SLC12A5*	*hsa-miR-25-3p*	DIANA TOOLS
ENTPD4	*hsa-miR-433-3p*	MirTarBase	*SLC15A4*	*hsa-miR-16-5p*	DIANA TOOLS
EOGT	*hsa-let-7a-5p*	DIANA TOOLS	*SLC15A4*	*hsa-miR-15b-5p*	DIANA TOOLS
EOGT	*hsa-miR-130a-3p*	DIANA TOOLS	*SLC16A10*	*hsa-let-7a-5p*	DIANA TOOLS
EP400	*hsa-miR-142-3p*	DIANA TOOLS	*SLC16A10*	*hsa-miR-21-5p*	DIANA TOOLS
EPB41	*hsa-miR-190b*	DIANA TOOLS	*SLC16A14*	*hsa-miR-22-3p*	DIANA TOOLS
EPG5	*hsa-miR-25-3p*	DIANA TOOLS	*SLC16A4*	*hsa-miR-661*	MirTarBase

EPHA4	*hsa-let-7a-5p*	DIANA TOOLS	*SLC16A9*	*hsa-let-7a-5p*	DIANA TOOLS
EPHA7	*hsa-miR-93-5p*	DIANA TOOLS	*SLC1A5*	*hsa-miR-433-3p*	MirTarBase
EPHB4	*hsa-miR-130a-3p*	DIANA TOOLS	*SLC1A5*	*hsa-miR-433-3p*	MirTarBase
EPHB4	*hsa-miR-93-5p*	DIANA TOOLS	*SLC20A2*	*hsa-miR-15b-5p*	DIANA TOOLS
EPS15	*hsa-miR-130a-3p*	DIANA TOOLS	*SLC20A2*	*hsa-miR-16-5p*	DIANA TOOLS
ERBB3	*hsa-miR-22-3p*	DIANA TOOLS	*SLC22A23*	*hsa-miR-93-5p*	DIANA TOOLS
ERBB3	*hsa-miR-205-5p*	DIANA TOOLS	*SLC24A2*	*hsa-miR-93-5p*	DIANA TOOLS
ERBIN	*hsa-miR-433-3p*	MirTarBase	*SLC24A4*	*hsa-miR-661*	MirTarBase
ERCC4	*hsa-miR-130a-3p*	DIANA TOOLS	*SLC24A4*	*hsa-miR-661*	MirTarBase
ERCC6	*hsa-let-7a-5p*	DIANA TOOLS	*SLC25A12*	*hsa-miR-130a-3p*	DIANA TOOLS
ERGIC2	*hsa-miR-25-3p*	DIANA TOOLS	*SLC25A16*	*hsa-miR-661*	MirTarBase
ERI1	*hsa-miR-200c-3p*	DIANA TOOLS	*SLC25A17*	*hsa-miR-22-3p*	DIANA TOOLS
ERO1L	*hsa-let-7a-5p*	DIANA TOOLS	*SLC25A22*	*hsa-miR-15b-5p*	DIANA TOOLS
ESR1	*hsa-miR-22-3p*	DIANA TOOLS	*SLC25A22*	*hsa-miR-16-5p*	DIANA TOOLS
ETF1	*hsa-miR-93-5p*	DIANA TOOLS	*SLC25A27*	*hsa-let-7a-5p*	DIANA TOOLS
ETNK1	*hsa-miR-15b-5p*	DIANA TOOLS	*SLC25A36*	*hsa-miR-200c-3p*	DIANA TOOLS
ETS1	*hsa-miR-144-3p*	MirTarBase	*SLC25A44*	*hsa-miR-130a-3p*	DIANA TOOLS
ETV1	*hsa-miR-22-3p*	DIANA TOOLS	*SLC28A1*	*hsa-miR-433-3p*	MirTarBase
ETV1	*hsa-miR-93-5p*	DIANA TOOLS	*SLC29A2*	*hsa-miR-15b-5p*	DIANA TOOLS
ETV3	*hsa-let-7a-5p*	DIANA TOOLS	*SLC29A2*	*hsa-miR-16-5p*	DIANA TOOLS
EVC	*hsa-miR-661*	MirTarBase	*SLC2A3*	*hsa-miR-15b-5p*	DIANA TOOLS
EVI5	*hsa-miR-25-3p*	DIANA TOOLS	*SLC2A3*	*hsa-miR-16-5p*	DIANA TOOLS
EVI5	*hsa-miR-200c-3p*	DIANA TOOLS	*SLC30A1*	*hsa-miR-144-3p*	DIANA TOOLS
EWSR1	*hsa-let-7a-5p*	MirTarBase	*SLC30A8*	*hsa-miR-15b-5p*	DIANA TOOLS
EXOC5	*hsa-miR-130a-3p*	DIANA TOOLS	*SLC30A8*	*hsa-miR-16-5p*	DIANA TOOLS
EXOSC2	*hsa-miR-661*	MirTarBase	*SLC31A1*	*hsa-miR-509-3-5p*	DIANA TOOLS
EXOSC2	*hsa-miR-661*	MirTarBase	*SLC33A1*	*hsa-miR-661*	MirTarBase
EXOSC3	*hsa-miR-200c-3p*	DIANA TOOLS	*SLC35B4*	*hsa-miR-200c-3p*	DIANA TOOLS
EXT2	*hsa-miR-15b-5p*	DIANA TOOLS	*SLC35D2*	*hsa-let-7a-5p*	DIANA TOOLS
EXT2	*hsa-miR-16-5p*	DIANA TOOLS	*SLC35E2*	*hsa-miR-661*	MirTarBase
EZH1	*hsa-miR-15b-5p*	DIANA TOOLS	*SLC35F5*	*hsa-miR-190b*	DIANA TOOLS
EZH1	*hsa-miR-16-5p*	DIANA TOOLS	*SLC35F5*	*hsa-miR-142-3p*	DIANA TOOLS
EZH2	*hsa-miR-144-3p*	DIANA TOOLS	*SLC35F6*	*hsa-miR-661*	MirTarBase
EZH2	*hsa-let-7a-5p*	MirTarBase	*SLC36A1*	*hsa-miR-381-5p*	MirTarBase
F2RL2	*hsa-miR-661*	MirTarBase	*SLC38A2*	*hsa-let-7a-5p*	DIANA TOOLS
F8A2	*hsa-miR-661*	MirTarBase	*SLC38A2*	*hsa-miR-200c-3p*	DIANA TOOLS
F8A3	*hsa-miR-661*	MirTarBase	*SLC39A10*	*hsa-miR-16-5p*	DIANA TOOLS
FAHD1	*hsa-miR-661*	MirTarBase	*SLC39A10*	*hsa-miR-15b-5p*	DIANA TOOLS
FAM104A	*hsa-let-7a-5p*	DIANA TOOLS	*SLC41A1*	*hsa-miR-93-5p*	DIANA TOOLS
FAM104A	*hsa-miR-130a-3p*	DIANA TOOLS	*SLC41A2*	*hsa-miR-15b-5p*	DIANA TOOLS
FAM110C	*hsa-miR-130a-3p*	DIANA TOOLS	*SLC41A2*	*hsa-miR-16-5p*	DIANA TOOLS
FAM110C	*hsa-miR-15b-5p*	DIANA TOOLS	*SLC44A1*	*hsa-miR-130a-3p*	DIANA TOOLS
FAM110C	*hsa-miR-25-3p*	DIANA TOOLS	*SLC5A3*	*hsa-miR-15b-5p*	DIANA TOOLS
FAM110C	*hsa-miR-16-5p*	DIANA TOOLS	*SLC5A3*	*hsa-miR-16-5p*	DIANA TOOLS
FAM114A1	*hsa-miR-142-3p*	DIANA TOOLS	*SLC5A5*	*hsa-miR-661*	MirTarBase
FAM117B	*hsa-miR-661*	MirTarBase	*SLC5A6*	*hsa-let-7a-5p*	DIANA TOOLS
FAM118A	*hsa-let-7a-5p*	DIANA TOOLS	*SLC7A11*	*hsa-miR-93-5p*	DIANA TOOLS

FAM126B	*hsa-miR-25-3p*	DIANA TOOLS	*SLC9A7*	*hsa-miR-661*	MirTarBase
FAM126B	*hsa-miR-433-3p*	MirTarBase	*SLCO5A1*	*hsa-let-7a-5p*	DIANA TOOLS
FAM127A	*hsa-miR-142-3p*	DIANA TOOLS	*SLIT2*	*hsa-miR-15b-5p*	DIANA TOOLS
FAM134A	*hsa-miR-15b-5p*	DIANA TOOLS	*SLIT2*	*hsa-miR-16-5p*	DIANA TOOLS
FAM134A	*hsa-miR-16-5p*	DIANA TOOLS	*SLK*	*hsa-miR-21-5p*	DIANA TOOLS
FAM135A	*hsa-miR-16-5p*	DIANA TOOLS	*SLX4*	*hsa-miR-25-3p*	DIANA TOOLS
FAM135A	*hsa-miR-15b-5p*	DIANA TOOLS	*SMAD2*	*hsa-miR-200c-3p*	DIANA TOOLS
FAM160B1	*hsa-miR-25-3p*	DIANA TOOLS	*SMAD4*	*hsa-miR-144-3p*	MirTarBase
FAM175B	*hsa-miR-130a-3p*	DIANA TOOLS	*SMAD5*	*hsa-miR-200c-3p*	DIANA TOOLS
FAM179B	*hsa-miR-130a-3p*	DIANA TOOLS	*SMAD5*	*hsa-miR-130a-3p*	DIANA TOOLS
FAM208B	*hsa-miR-142-3p*	DIANA TOOLS	*SMAD7*	*hsa-miR-25-3p*	DIANA TOOLS
FAM20C	*hsa-miR-25-3p*	DIANA TOOLS	*SMAD7*	*hsa-miR-21-5p*	DIANA TOOLS
FAM212B	*hsa-miR-661*	MirTarBase	*SMAD7*	*hsa-miR-15b-5p*	DIANA TOOLS
FAM214A	*hsa-miR-15b-5p*	DIANA TOOLS	*SMAD7*	*hsa-miR-16-5p*	DIANA TOOLS
FAM214A	*hsa-miR-16-5p*	DIANA TOOLS	*SMAP1*	*hsa-let-7a-5p*	DIANA TOOLS
FAM222B	*hsa-let-7a-5p*	DIANA TOOLS	*SMARCA5*	*hsa-miR-661*	MirTarBase
FAM234B	*hsa-miR-661*	MirTarBase	*SMARCAD1*	*hsa-miR-200c-3p*	DIANA TOOLS
FAM234B	*hsa-miR-661*	MirTarBase	*SMARCAD1*	*hsa-let-7a-5p*	DIANA TOOLS
FAM3C	*hsa-miR-21-5p*	DIANA TOOLS	*SMARCC1*	*hsa-let-7a-5p*	DIANA TOOLS
FAM3C	*hsa-miR-433-3p*	MirTarBase	*SMARCD2*	*hsa-miR-130a-3p*	DIANA TOOLS
FAM3C	*hsa-miR-433-3p*	MirTarBase	*SMC1A*	*hsa-let-7a-5p*	DIANA TOOLS
FAM43A	*hsa-miR-130a-3p*	DIANA TOOLS	*SMG1*	*hsa-miR-142-3p*	DIANA TOOLS
FAM46A	*hsa-miR-25-3p*	DIANA TOOLS	*SMG7*	*hsa-miR-22-3p*	DIANA TOOLS
FAM49B	*hsa-miR-22-3p*	DIANA TOOLS	*SMIM3*	*hsa-let-7a-5p*	DIANA TOOLS
FAM60A	*hsa-miR-200c-3p*	DIANA TOOLS	*SMOC1*	*hsa-miR-130a-3p*	DIANA TOOLS
FAM63B	*hsa-miR-130a-3p*	DIANA TOOLS	*SMTNL2*	*hsa-miR-661*	MirTarBase
FAM63B	*hsa-miR-190b*	DIANA TOOLS	*SMU1*	*hsa-miR-433-3p*	MirTarBase
FAM63B	*hsa-miR-21-5p*	DIANA TOOLS	*SMU1*	*hsa-miR-661*	MirTarBase
FAM73A	*hsa-miR-15b-5p*	DIANA TOOLS	*SMURF1*	*hsa-miR-15b-5p*	DIANA TOOLS
FAM73A	*hsa-miR-16-5p*	DIANA TOOLS	*SMURF1*	*hsa-miR-16-5p*	DIANA TOOLS
FAM73A	*hsa-miR-130a-3p*	DIANA TOOLS	*SMURF2*	*hsa-miR-16-5p*	DIANA TOOLS
FAM81A	*hsa-miR-16-5p*	DIANA TOOLS	*SMURF2*	*hsa-miR-15b-5p*	DIANA TOOLS
FAM83F	*hsa-miR-661*	MirTarBase	*SNAP23*	*hsa-let-7a-5p*	DIANA TOOLS
FAM83F	*hsa-miR-661*	MirTarBase	*SNAP25*	*hsa-miR-130a-3p*	DIANA TOOLS
FAM8A1	*hsa-miR-200c-3p*	DIANA TOOLS	*SNAPC1*	*hsa-miR-25-3p*	DIANA TOOLS
FAR1	*hsa-miR-25-3p*	DIANA TOOLS	*SNCG*	*hsa-miR-16-5p*	DIANA TOOLS
FAS	*hsa-let-7a-5p*	DIANA TOOLS	*SNN*	*hsa-miR-144-3p*	DIANA TOOLS
FASLG	*hsa-miR-21-5p*	DIANA TOOLS	*SNN*	*hsa-miR-25-3p*	DIANA TOOLS
FASN	*hsa-miR-16-5p*	DIANA TOOLS	*SNRK*	*hsa-miR-16-5p*	DIANA TOOLS
FASN	*hsa-miR-15b-5p*	DIANA TOOLS	*SNRK*	*hsa-miR-15b-5p*	DIANA TOOLS
FBXL16	*hsa-miR-200c-3p*	DIANA TOOLS	*SNRNP48*	*hsa-miR-15b-5p*	DIANA TOOLS
FBXO21	*hsa-miR-130a-3p*	DIANA TOOLS	*SNRPD3*	*hsa-miR-661*	MirTarBase
FBXO21	*hsa-miR-15b-5p*	DIANA TOOLS	*SNTB2*	*hsa-miR-16-5p*	DIANA TOOLS
FBXO21	*hsa-miR-16-5p*	DIANA TOOLS	*SNTB2*	*hsa-miR-15b-5p*	DIANA TOOLS
FBXO22	*hsa-miR-200c-3p*	DIANA TOOLS	*SNTB2*	*hsa-miR-144-3p*	DIANA TOOLS
FBXO28	*hsa-miR-142-3p*	DIANA TOOLS	*SNW1*	*hsa-miR-205-5p*	DIANA TOOLS
FBXO28	*hsa-miR-130a-3p*	DIANA TOOLS	*SNX16*	*hsa-let-7a-5p*	DIANA TOOLS

FBXO3	*hsa-miR-142-3p*	DIANA TOOLS	*SNX20*	*hsa-miR-661*	MirTarBase
FBXO3	*hsa-miR-16-5p*	DIANA TOOLS	*SNX25*	*hsa-miR-93-5p*	DIANA TOOLS
FBXO3	*hsa-miR-15b-5p*	DIANA TOOLS	*SNX25*	*hsa-let-7a-5p*	DIANA TOOLS
FBXO30	*hsa-miR-200c-3p*	DIANA TOOLS	*SNX27*	*hsa-miR-22-3p*	DIANA TOOLS
FBXO47	*hsa-miR-661*	MirTarBase	*SNX29*	*hsa-miR-21-5p*	DIANA TOOLS
FBXW11	*hsa-miR-200c-3p*	DIANA TOOLS	*SNX30*	*hsa-miR-200c-3p*	DIANA TOOLS
FBXW7	*hsa-miR-16-5p*	DIANA TOOLS	*SOBP*	*hsa-miR-16-5p*	DIANA TOOLS
FBXW7	*hsa-miR-223-3p*	DIANA TOOLS	*SOBP*	*hsa-miR-15b-5p*	DIANA TOOLS
FBXW7	*hsa-miR-15b-5p*	DIANA TOOLS	*SOCS5*	*hsa-miR-661*	MirTarBase
FBXW7	*hsa-miR-200c-3p*	DIANA TOOLS	*SOCS6*	*hsa-miR-15b-5p*	DIANA TOOLS
FBXW7	*hsa-miR-25-3p*	DIANA TOOLS	*SOCS6*	*hsa-miR-16-5p*	DIANA TOOLS
FCHO2	*hsa-miR-93-5p*	DIANA TOOLS	*SOD2*	*hsa-miR-509-3-5p*	DIANA TOOLS
FCRL2	*hsa-miR-661*	MirTarBase	*SOD2*	*hsa-miR-130a-3p*	DIANA TOOLS
FEM1C	*hsa-miR-93-5p*	DIANA TOOLS	*SOGA1*	*hsa-miR-31-5p*	DIANA TOOLS
FEZ2	*hsa-miR-200c-3p*	DIANA TOOLS	*SON*	*hsa-miR-130a-3p*	DIANA TOOLS
FGA	*hsa-miR-144-3p*	MirTarBase	*SON*	*hsa-miR-15b-5p*	DIANA TOOLS
FGB	*hsa-miR-144-3p*	MirTarBase	*SON*	*hsa-miR-16-5p*	DIANA TOOLS
FGD6	*hsa-let-7a-5p*	DIANA TOOLS	*SOX4*	*hsa-miR-25-3p*	DIANA TOOLS
FGF2	*hsa-miR-15b-5p*	DIANA TOOLS	*SOX5*	*hsa-miR-16-5p*	DIANA TOOLS
FGF2	*hsa-miR-16-5p*	DIANA TOOLS	*SOX5*	*hsa-miR-15b-5p*	DIANA TOOLS
FGF20	*hsa-miR-433-3p*	MirTarBase	*SP1*	*hsa-miR-31-5p*	DIANA TOOLS
FGF9	*hsa-miR-433-3p*	MirTarBase	*SP4*	*hsa-miR-205-5p*	DIANA TOOLS
FGFR1	*hsa-miR-16-5p*	DIANA TOOLS	*SPATA7*	*hsa-miR-93-5p*	DIANA TOOLS
FGFR1	*hsa-miR-15b-5p*	DIANA TOOLS	*SPATS2L*	*hsa-miR-200c-3p*	DIANA TOOLS
FHL2	*hsa-miR-25-3p*	DIANA TOOLS	*SPATS2L*	*hsa-miR-433-3p*	MirTarBase
FHL2	*hsa-miR-661*	MirTarBase	*SPC24*	*hsa-miR-661*	MirTarBase
FHL2	*hsa-miR-661*	MirTarBase	*SPEN*	*hsa-miR-130a-3p*	DIANA TOOLS
FICD	*hsa-miR-130a-3p*	DIANA TOOLS	*SPEN*	*hsa-miR-15b-5p*	DIANA TOOLS
FICD	*hsa-miR-93-5p*	DIANA TOOLS	*SPEN*	*hsa-miR-16-5p*	DIANA TOOLS
FIGN	*hsa-let-7a-5p*	DIANA TOOLS	*SPG20*	*hsa-miR-130a-3p*	DIANA TOOLS
FIGN	*hsa-miR-200c-3p*	DIANA TOOLS	*SPOPL*	*hsa-miR-130a-3p*	DIANA TOOLS
FIGNL1	*hsa-miR-661*	MirTarBase	*SPRED1*	*hsa-miR-16-5p*	DIANA TOOLS
FILIP1L	*hsa-miR-21-5p*	DIANA TOOLS	*SPRED1*	*hsa-miR-15b-5p*	DIANA TOOLS
FKBP14	*hsa-miR-661*	MirTarBase	*SPRTN*	*hsa-miR-16-5p*	DIANA TOOLS
FKBP1A	*hsa-miR-433-3p*	MirTarBase	*SPRTN*	*hsa-miR-15b-5p*	DIANA TOOLS
FKBP1C	*hsa-miR-433-3p*	MirTarBase	*SPRYD3*	*hsa-miR-16-5p*	DIANA TOOLS
FKBP1C	*hsa-miR-433-3p*	MirTarBase	*SPRYD3*	*hsa-miR-15b-5p*	DIANA TOOLS
FKBP8	*hsa-miR-661*	MirTarBase	*SPRYD4*	*hsa-miR-25-3p*	DIANA TOOLS
FKTN	*hsa-let-7a-5p*	DIANA TOOLS	*SPRYD4*	*hsa-miR-433-3p*	MirTarBase
FLNA	*hsa-let-7a-5p*	DIANA TOOLS	*SPRYD4*	*hsa-miR-661*	MirTarBase
FLNA	*hsa-miR-22-3p*	DIANA TOOLS	*SPSB4*	*hsa-miR-15b-5p*	DIANA TOOLS
FLT1	*hsa-miR-200c-3p*	DIANA TOOLS	*SPTBN2*	*hsa-miR-16-5p*	DIANA TOOLS
FMC1	*hsa-miR-661*	MirTarBase	*SPTBN2*	*hsa-miR-15b-5p*	DIANA TOOLS
FMN2	*hsa-miR-25-3p*	DIANA TOOLS	*SPTSSA*	*hsa-miR-200c-3p*	DIANA TOOLS
FMN2	*hsa-miR-144-3p*	DIANA TOOLS	*SPTY2D1*	*hsa-miR-130a-3p*	DIANA TOOLS
FMNL3	*hsa-miR-22-3p*	DIANA TOOLS	*SQSTM1*	*hsa-miR-93-5p*	DIANA TOOLS
FN1	*hsa-miR-200c-3p*	DIANA TOOLS	*SREK1*	*hsa-miR-15b-5p*	DIANA TOOLS

FNBP4	*hsa-miR-200c-3p*	DIANA TOOLS	*SREK1*	*hsa-miR-16-5p*	DIANA TOOLS
FNDC3A	*hsa-miR-142-3p*	DIANA TOOLS	*SRGAP1*	*hsa-miR-93-5p*	DIANA TOOLS
FNDC3A	*hsa-let-7a-5p*	DIANA TOOLS	*SRGN*	*hsa-miR-661*	MirTarBase
FNDC3A	*hsa-miR-190b*	DIANA TOOLS	*SRP72*	*hsa-miR-16-5p*	DIANA TOOLS
FNDC3A	*hsa-miR-144-3p*	DIANA TOOLS	*SRP72*	*hsa-miR-200c-3p*	DIANA TOOLS
FNDC3B	*hsa-miR-200c-3p*	DIANA TOOLS	*SRPK1*	*hsa-miR-16-5p*	DIANA TOOLS
FNDC3B	*hsa-miR-16-5p*	DIANA TOOLS	*SRPK1*	*hsa-miR-15b-5p*	DIANA TOOLS
FNDC3B	*hsa-miR-15b-5p*	DIANA TOOLS	*SRPR*	*hsa-miR-15b-5p*	DIANA TOOLS
FNDC3B	*hsa-miR-25-3p*	DIANA TOOLS	*SRPR*	*hsa-miR-25-3p*	DIANA TOOLS
FNIP1	*hsa-miR-25-3p*	DIANA TOOLS	*SRPR*	*hsa-miR-16-5p*	DIANA TOOLS
FNIP1	*hsa-miR-190b*	DIANA TOOLS	*SRPRB*	*hsa-miR-16-5p*	DIANA TOOLS
FNIP2	*hsa-miR-21-5p*	DIANA TOOLS	*SRPRB*	*hsa-miR-15b-5p*	DIANA TOOLS
FNIP2	*hsa-miR-25-3p*	DIANA TOOLS	*SRPX2*	*hsa-miR-661*	MirTarBase
FNTA	*hsa-miR-16-5p*	DIANA TOOLS	*SRSF2*	*hsa-miR-130a-3p*	DIANA TOOLS
FOSL2	*hsa-miR-130a-3p*	DIANA TOOLS	*SRSF7*	*hsa-miR-661*	MirTarBase
FOSL2	*hsa-miR-15b-5p*	DIANA TOOLS	*SSBP2*	*hsa-miR-661*	MirTarBase
FOSL2	*hsa-miR-16-5p*	DIANA TOOLS	*SSC5D*	*hsa-miR-433-3p*	MirTarBase
FOXA1	*hsa-let-7a-5p*	MirTarBase	*SSC5D*	*hsa-miR-433-3p*	MirTarBase
FOXJ3	*hsa-miR-661*	MirTarBase	*SSC5D*	*hsa-miR-433-3p*	MirTarBase
FOXL2NB	*hsa-miR-661*	MirTarBase	*SSC5D*	*hsa-miR-433-3p*	MirTarBase
FOXM1	*hsa-miR-509-3-5p*	MirTarBase	*SSFA2*	*hsa-miR-25-3p*	DIANA TOOLS
FOXN2	*hsa-miR-25-3p*	DIANA TOOLS	*SSH1*	*hsa-miR-25-3p*	DIANA TOOLS
FOXO1	*hsa-miR-16-5p*	DIANA TOOLS	*SSH2*	*hsa-miR-661*	MirTarBase
FOXP2	*hsa-let-7a-5p*	DIANA TOOLS	*SSH3*	*hsa-miR-661*	MirTarBase
FOXQ1	*hsa-miR-93-5p*	DIANA TOOLS	*SSR1*	*hsa-miR-16-5p*	DIANA TOOLS
FRAT2	*hsa-miR-22-3p*	DIANA TOOLS	*SSTR2*	*hsa-miR-661*	MirTarBase
FRMD6	*hsa-miR-130a-3p*	DIANA TOOLS	*ST13*	*hsa-miR-661*	MirTarBase
FRMD6	*hsa-miR-200c-3p*	DIANA TOOLS	*ST6GAL1*	*hsa-miR-21-5p*	DIANA TOOLS
FRMD8	*hsa-miR-661*	MirTarBase	*ST6GAL2*	*hsa-miR-25-3p*	DIANA TOOLS
FRS2	*hsa-miR-15b-5p*	DIANA TOOLS	*ST8SIA3*	*hsa-miR-15b-5p*	DIANA TOOLS
FRS2	*hsa-miR-200c-3p*	DIANA TOOLS	*ST8SIA3*	*hsa-miR-16-5p*	DIANA TOOLS
FRS2	*hsa-miR-21-5p*	DIANA TOOLS	*STAG2*	*hsa-miR-22-3p*	DIANA TOOLS
FSD1L	*hsa-miR-200c-3p*	DIANA TOOLS	*STAG2*	*hsa-miR-21-5p*	DIANA TOOLS
FUS	*hsa-miR-661*	MirTarBase	*STARD10*	*hsa-miR-661*	MirTarBase
FUT1	*hsa-miR-661*	MirTarBase	*STARD13*	*hsa-miR-16-5p*	DIANA TOOLS
FUT1	*hsa-miR-661*	MirTarBase	*STARD13*	*hsa-miR-15b-5p*	DIANA TOOLS
FUT1	*hsa-miR-661*	MirTarBase	*STARD13*	*hsa-miR-31-5p*	DIANA TOOLS
FUT1	*hsa-miR-661*	MirTarBase	*STARD13*	*hsa-let-7a-5p*	DIANA TOOLS
FUT1	*hsa-miR-661*	MirTarBase	*STARD7*	*hsa-miR-433-3p*	MirTarBase
FUT9	*hsa-miR-661*	MirTarBase	*STARD7*	*hsa-miR-433-3p*	MirTarBase
FXR1	*hsa-miR-25-3p*	DIANA TOOLS	*STAT3*	*hsa-miR-21-5p*	DIANA TOOLS
FXR1	*hsa-miR-130a-3p*	DIANA TOOLS	*STAT3*	*hsa-miR-93-5p*	DIANA TOOLS
FYCO1	*hsa-miR-130a-3p*	DIANA TOOLS	*STAT3*	*hsa-let-7a-5p*	MirTarBase
FZD3	*hsa-let-7a-5p*	DIANA TOOLS	*STAU1*	*hsa-miR-142-3p*	DIANA TOOLS
G3BP2	*hsa-miR-25-3p*	DIANA TOOLS	*STEAP2*	*hsa-miR-661*	MirTarBase
GAB1	*hsa-miR-142-3p*	DIANA TOOLS	*STEAP4*	*hsa-miR-130a-3p*	DIANA TOOLS

GAB1	*hsa-miR-200c-3p*	DIANA TOOLS	*STK24*	*hsa-let-7a-5p*	DIANA TOOLS
GAB1	*hsa-miR-93-5p*	DIANA TOOLS	*STK32A*	*hsa-miR-661*	MirTarBase
GABARAPL1	*hsa-miR-15b-5p*	DIANA TOOLS	*STK33*	*hsa-miR-15b-5p*	DIANA TOOLS
GABARAPL1	*hsa-miR-16-5p*	DIANA TOOLS	*STK33*	*hsa-miR-16-5p*	DIANA TOOLS
GABPB1	*hsa-miR-433-3p*	MirTarBase	*STK38*	*hsa-miR-433-3p*	MirTarBase
GABPB1	*hsa-miR-661*	MirTarBase	*STK39*	*hsa-miR-25-3p*	DIANA TOOLS
GABPB2	*hsa-miR-661*	MirTarBase	*STK4*	*hsa-miR-200c-3p*	DIANA TOOLS
GADD45A	*hsa-miR-130a-3p*	DIANA TOOLS	*STK4*	*hsa-miR-661*	MirTarBase
GALC	*hsa-let-7a-5p*	DIANA TOOLS	*STMP1*	*hsa-miR-661*	MirTarBase
GALNT1	*hsa-let-7a-5p*	DIANA TOOLS	*STMP1*	*hsa-miR-661*	MirTarBase
GAN	*hsa-let-7a-5p*	DIANA TOOLS	*STON2*	*hsa-miR-130a-3p*	DIANA TOOLS
GAN	*hsa-miR-25-3p*	DIANA TOOLS	*STON2*	*hsa-miR-661*	MirTarBase
GAN	*hsa-miR-661*	MirTarBase	*STRBP*	*hsa-miR-190b*	DIANA TOOLS
GAPVD1	*hsa-miR-661*	MirTarBase	*STRIP1*	*hsa-miR-16-5p*	DIANA TOOLS
GAREM	*hsa-let-7a-5p*	DIANA TOOLS	*STRIP1*	*hsa-miR-15b-5p*	DIANA TOOLS
GAREM	*hsa-miR-130a-3p*	DIANA TOOLS	*STRN*	*hsa-miR-21-5p*	DIANA TOOLS
GAREM	*hsa-miR-15b-5p*	DIANA TOOLS	*STRN3*	*hsa-miR-200c-3p*	DIANA TOOLS
GAREM	*hsa-miR-16-5p*	DIANA TOOLS	*STRN3*	*hsa-miR-142-3p*	DIANA TOOLS
GATA2	*hsa-miR-25-3p*	DIANA TOOLS	*STX16*	*hsa-miR-200c-3p*	DIANA TOOLS
GATA6	*hsa-miR-25-3p*	DIANA TOOLS	*STX3*	*hsa-let-7a-5p*	DIANA TOOLS
GATAD2B	*hsa-miR-21-5p*	DIANA TOOLS	*STX4*	*hsa-miR-661*	MirTarBase
GATAD2B	*hsa-miR-25-3p*	DIANA TOOLS	*STX6*	*hsa-miR-130a-3p*	DIANA TOOLS
GATM	*hsa-let-7a-5p*	DIANA TOOLS	*STX6*	*hsa-miR-22-3p*	DIANA TOOLS
GATM	*hsa-miR-22-3p*	DIANA TOOLS	*STXBP3*	*hsa-miR-15b-5p*	DIANA TOOLS
GBP2	*hsa-miR-433-3p*	MirTarBase	*STXBP3*	*hsa-miR-16-5p*	DIANA TOOLS
GCC1	*hsa-miR-544a*	DIANA TOOLS	*STYX*	*hsa-miR-22-3p*	DIANA TOOLS
GDAP2	*hsa-miR-190b*	DIANA TOOLS	*STYX*	*hsa-miR-15b-5p*	DIANA TOOLS
GDAP2	*hsa-let-7a-5p*	DIANA TOOLS	*STYX*	*hsa-miR-16-5p*	DIANA TOOLS
GDI2	*hsa-miR-200c-3p*	DIANA TOOLS	*STYX*	*hsa-miR-200c-3p*	DIANA TOOLS
GFPT1	*hsa-miR-200c-3p*	DIANA TOOLS	*SUCO*	*hsa-miR-15b-5p*	DIANA TOOLS
GFPT2	*hsa-miR-144-3p*	DIANA TOOLS	*SUCO*	*hsa-miR-16-5p*	DIANA TOOLS
GFPT2	*hsa-miR-25-3p*	DIANA TOOLS	*SUGT1*	*hsa-miR-130a-3p*	DIANA TOOLS
GFRA1	*hsa-miR-22-3p*	DIANA TOOLS	*SULF1*	*hsa-miR-130a-3p*	DIANA TOOLS
GID4	*hsa-miR-21-5p*	DIANA TOOLS	*SURF4*	*hsa-miR-200c-3p*	DIANA TOOLS
GID4	*hsa-miR-25-3p*	DIANA TOOLS	*SUSD5*	*hsa-miR-661*	MirTarBase
GIT2	*hsa-miR-25-3p*	DIANA TOOLS	*SUV420H1*	*hsa-miR-93-5p*	DIANA TOOLS
GJC1	*hsa-let-7a-5p*	DIANA TOOLS	*SUV420H1*	*hsa-miR-25-3p*	DIANA TOOLS
GK5	*hsa-miR-661*	MirTarBase	*SUZ12*	*hsa-miR-200c-3p*	DIANA TOOLS
GLB1L3	*hsa-miR-661*	MirTarBase	*SV2A*	*hsa-miR-22-3p*	DIANA TOOLS
GLCCI1	*hsa-miR-21-5p*	DIANA TOOLS	*SVIL*	*hsa-let-7a-5p*	DIANA TOOLS
GLCCI1	*hsa-miR-144-3p*	DIANA TOOLS	*SYBU*	*hsa-miR-130a-3p*	DIANA TOOLS
GLCE	*hsa-miR-15b-5p*	DIANA TOOLS	*SYNCRIP*	*hsa-let-7a-5p*	DIANA TOOLS
GLI3	*hsa-miR-200c-3p*	DIANA TOOLS	*SYNCRIP*	*hsa-miR-93-5p*	DIANA TOOLS
GLYR1	*hsa-miR-25-3p*	DIANA TOOLS	*SYNCRIP*	*hsa-miR-200c-3p*	DIANA TOOLS
GMFB	*hsa-miR-200c-3p*	DIANA TOOLS	*SYNJ1*	*hsa-miR-15b-5p*	DIANA TOOLS
GMPR	*hsa-miR-661*	MirTarBase	*SYNJ2*	*hsa-miR-31-5p*	DIANA TOOLS
GNA12	*hsa-miR-15b-5p*	DIANA TOOLS	*SYT7*	*hsa-let-7a-5p*	DIANA TOOLS
GNA12	*hsa-miR-16-5p*	DIANA TOOLS	*SYVN1*	*hsa-miR-200c-3p*	DIANA TOOLS

GNAI3	*hsa-miR-544a*	DIANA TOOLS	*SZRD1*	*hsa-miR-130a-3p*	DIANA TOOLS
GNAI3	*hsa-miR-16-5p*	DIANA TOOLS	*TACC1*	*hsa-miR-15b-5p*	DIANA TOOLS
GNAI3	*hsa-miR-15b-5p*	DIANA TOOLS	*TACC1*	*hsa-miR-16-5p*	DIANA TOOLS
GNAQ	*hsa-miR-25-3p*	DIANA TOOLS	*TACO1*	*hsa-miR-661*	MirTarBase
GNAQ	*hsa-miR-142-3p*	DIANA TOOLS	*TACR2*	*hsa-miR-661*	MirTarBase
GNG5	*hsa-let-7a-5p*	DIANA TOOLS	*TAF1*	*hsa-miR-25-3p*	DIANA TOOLS
GNL3	*hsa-miR-661*	MirTarBase	*TAF12*	*hsa-miR-200c-3p*	DIANA TOOLS
GNL3	*hsa-miR-661*	MirTarBase	*TAF5*	*hsa-miR-21-5p*	DIANA TOOLS
GOLGA1	*hsa-miR-25-3p*	DIANA TOOLS	*TAF5*	*hsa-let-7a-5p*	DIANA TOOLS
GOLGA1	*hsa-miR-15b-5p*	DIANA TOOLS	*TAGAP*	*hsa-miR-93-5p*	DIANA TOOLS
GOLGA1	*hsa-miR-16-5p*	DIANA TOOLS	*TANC1*	*hsa-miR-130a-3p*	DIANA TOOLS
GOLGA3	*hsa-miR-25-3p*	DIANA TOOLS	*TANGO2*	*hsa-miR-661*	MirTarBase
GOLGA4	*hsa-let-7a-5p*	DIANA TOOLS	*TAOK1*	*hsa-miR-16-5p*	DIANA TOOLS
GOLGA4	*hsa-miR-25-3p*	DIANA TOOLS	*TAOK1*	*hsa-miR-15b-5p*	DIANA TOOLS
GOLGB1	*hsa-miR-93-5p*	DIANA TOOLS	*TAOK1*	*hsa-miR-93-5p*	DIANA TOOLS
GOLGB1	*hsa-miR-544a*	DIANA TOOLS	*TAOK1*	*hsa-miR-200c-3p*	DIANA TOOLS
GOLIM4	*hsa-miR-200c-3p*	DIANA TOOLS	*TAOK1*	*hsa-miR-142-3p*	DIANA TOOLS
GOLT1B	*hsa-miR-130a-3p*	DIANA TOOLS	*TARDBP*	*hsa-miR-200c-3p*	DIANA TOOLS
GOLT1B	*hsa-let-7a-5p*	DIANA TOOLS	*TATDN3*	*hsa-miR-661*	MirTarBase
GON7	*hsa-miR-661*	MirTarBase	*TBC1D13*	*hsa-miR-661*	MirTarBase
GOSR1	*hsa-miR-661*	MirTarBase	*TBC1D14*	*hsa-miR-190b*	DIANA TOOLS
GPATCH2L	*hsa-miR-190b*	DIANA TOOLS	*TBC1D15*	*hsa-miR-93-5p*	DIANA TOOLS
GPATCH8	*hsa-let-7a-5p*	DIANA TOOLS	*TBC1D15*	*hsa-miR-661*	MirTarBase
GPBP1L1	*hsa-miR-25-3p*	DIANA TOOLS	*TBC1D24*	*hsa-miR-661*	MirTarBase
GPCPD1	*hsa-let-7a-5p*	DIANA TOOLS	*TBC1D9*	*hsa-miR-93-5p*	DIANA TOOLS
GPM6A	*hsa-miR-200c-3p*	DIANA TOOLS	*TBCCD1*	*hsa-miR-661*	MirTarBase
GPR135	*hsa-miR-433-3p*	MirTarBase	*TBCCD1*	*hsa-miR-661*	MirTarBase
GPR137C	*hsa-miR-25-3p*	DIANA TOOLS	*TBL1XR1*	*hsa-miR-130a-3p*	DIANA TOOLS
GPR153	*hsa-miR-661*	MirTarBase	*TBL1XR1*	*hsa-miR-200c-3p*	DIANA TOOLS
GPR157	*hsa-let-7a-5p*	DIANA TOOLS	*TBP*	*hsa-miR-15b-5p*	DIANA TOOLS
GPR180	*hsa-miR-25-3p*	DIANA TOOLS	*TBP*	*hsa-miR-16-5p*	DIANA TOOLS
GPR63	*hsa-miR-15b-5p*	DIANA TOOLS	*TBPL1*	*hsa-miR-16-5p*	DIANA TOOLS
GPR63	*hsa-miR-16-5p*	DIANA TOOLS	*TBPL1*	*hsa-miR-15b-5p*	DIANA TOOLS
GPR63	*hsa-miR-93-5p*	DIANA TOOLS	*TBX1*	*hsa-miR-144-3p*	DIANA TOOLS
GPR64	*hsa-miR-21-5p*	DIANA TOOLS	*TBXA2R*	*hsa-miR-661*	MirTarBase
GPR75	*hsa-miR-661*	MirTarBase	*TC2N*	*hsa-miR-21-5p*	DIANA TOOLS
GPSM2	*hsa-miR-22-3p*	DIANA TOOLS	*TCEB3*	*hsa-miR-142-3p*	DIANA TOOLS
GRAMD1B	*hsa-miR-25-3p*	DIANA TOOLS	*TCF20*	*hsa-miR-433-3p*	MirTarBase
GRAMD3	*hsa-miR-25-3p*	DIANA TOOLS	*TCF4*	*hsa-miR-25-3p*	DIANA TOOLS
GRB2	*hsa-miR-433-3p*	MirTarBase	*TCF4*	*hsa-miR-130a-3p*	DIANA TOOLS
GREB1L	*hsa-let-7a-5p*	DIANA TOOLS	*TCP1*	*hsa-miR-16-5p*	DIANA TOOLS
GRHL1	*hsa-miR-25-3p*	DIANA TOOLS	*TCP1*	*hsa-miR-15b-5p*	DIANA TOOLS
GSKIP	*hsa-miR-200c-3p*	DIANA TOOLS	*TECPR2*	*hsa-miR-661*	MirTarBase
GSTCD	*hsa-miR-16-5p*	DIANA TOOLS	*TEF*	*hsa-miR-25-3p*	DIANA TOOLS
GSTCD	*hsa-miR-15b-5p*	DIANA TOOLS	*TERF1*	*hsa-miR-661*	MirTarBase
GTF2E1	*hsa-miR-200c-3p*	DIANA TOOLS	*TERF2*	*hsa-miR-130a-3p*	DIANA TOOLS
GTF2H1	*hsa-miR-130a-3p*	DIANA TOOLS	*TERF2*	*hsa-miR-661*	MirTarBase

GXYLT1	*hsa-let-7a-5p*	DIANA TOOLS	*TET1*	*hsa-miR-21-5p*	DIANA TOOLS
GYLTL1B	*hsa-miR-16-5p*	DIANA TOOLS	*TET1*	*hsa-miR-93-5p*	DIANA TOOLS
GYLTL1B	*hsa-miR-15b-5p*	DIANA TOOLS	*TET2*	*hsa-let-7a-5p*	DIANA TOOLS
H3F3B	*hsa-miR-22-3p*	DIANA TOOLS	*TET3*	*hsa-let-7a-5p*	DIANA TOOLS
H3F3C	*hsa-miR-22-3p*	DIANA TOOLS	*TET3*	*hsa-miR-93-5p*	DIANA TOOLS
HACD2	*hsa-miR-661*	MirTarBase	*TEX2*	*hsa-miR-142-3p*	DIANA TOOLS
HACD3	*hsa-miR-433-3p*	MirTarBase	*TFAP2A*	*hsa-let-7a-5p*	DIANA TOOLS
HACE1	*hsa-miR-661*	MirTarBase	*TFAP2A*	*hsa-miR-433-3p*	MirTarBase
HAND1	*hsa-let-7a-5p*	DIANA TOOLS	*TFG*	*hsa-miR-142-3p*	DIANA TOOLS
HAS2	*hsa-let-7a-5p*	MirTarBase	*TFPI*	*hsa-miR-661*	MirTarBase
HAUS2	*hsa-miR-433-3p*	MirTarBase	*TGFB1*	*hsa-miR-144-3p*	MirTarBase
HAUS3	*hsa-miR-16-5p*	DIANA TOOLS	*TGFBI*	*hsa-miR-21-5p*	DIANA TOOLS
HAUS3	*hsa-miR-661*	MirTarBase	*TGFBR1*	*hsa-miR-142-3p*	DIANA TOOLS
HBP1	*hsa-miR-21-5p*	DIANA TOOLS	*TGFBR1*	*hsa-let-7a-5p*	DIANA TOOLS
HBP1	*hsa-miR-93-5p*	DIANA TOOLS	*TGFBR2*	*hsa-miR-21-5p*	DIANA TOOLS
HDLBP	*hsa-let-7a-5p*	DIANA TOOLS	*TGFBR2*	*hsa-miR-130a-3p*	DIANA TOOLS
HDX	*hsa-let-7a-5p*	DIANA TOOLS	*TGFBR3*	*hsa-let-7a-5p*	MirTarBase
HEATR5A	*hsa-miR-15b-5p*	DIANA TOOLS	*TGIF1*	*hsa-miR-25-3p*	DIANA TOOLS
HECA	*hsa-miR-130a-3p*	DIANA TOOLS	*TGIF2*	*hsa-miR-130a-3p*	DIANA TOOLS
HECTD1	*hsa-miR-16-5p*	DIANA TOOLS	*TGIF2*	*hsa-miR-15b-5p*	DIANA TOOLS
HECTD1	*hsa-miR-15b-5p*	DIANA TOOLS	*TGIF2*	*hsa-miR-16-5p*	DIANA TOOLS
HECTD1	*hsa-miR-142-3p*	DIANA TOOLS	*TGIF2LX*	*hsa-miR-433-3p*	MirTarBase
HECTD2	*hsa-miR-93-5p*	DIANA TOOLS	*TGOLN2*	*hsa-miR-93-5p*	DIANA TOOLS
HECTD4	*hsa-miR-16-5p*	DIANA TOOLS	*TGOLN2*	*hsa-miR-130a-3p*	DIANA TOOLS
HECTD4	*hsa-miR-15b-5p*	DIANA TOOLS	*THBS1*	*hsa-let-7a-5p*	DIANA TOOLS
HEG1	*hsa-miR-200c-3p*	DIANA TOOLS	*THOC1*	*hsa-miR-544a*	DIANA TOOLS
HELLS	*hsa-let-7a-5p*	DIANA TOOLS	*THOC2*	*hsa-let-7a-5p*	DIANA TOOLS
HERPUD1	*hsa-miR-661*	MirTarBase	*TIAL1*	*hsa-miR-205-5p*	DIANA TOOLS
HERPUD2	*hsa-miR-31-5p*	DIANA TOOLS	*TIFA*	*hsa-miR-200c-3p*	DIANA TOOLS
HERPUD2	*hsa-miR-25-3p*	DIANA TOOLS	*TIMM10B*	*hsa-miR-661*	MirTarBase
HERPUD2	*hsa-miR-661*	MirTarBase	*TIMM29*	*hsa-miR-661*	MirTarBase
HES1	*hsa-miR-381-5p*	MirTarBase	*TIMM8A*	*hsa-miR-661*	MirTarBase
HGS	*hsa-miR-142-3p*	DIANA TOOLS	*TIMP2*	*hsa-miR-200c-3p*	DIANA TOOLS
HIAT1	*hsa-miR-31-5p*	DIANA TOOLS	*TIMP3*	*hsa-miR-21-5p*	DIANA TOOLS
HIC2	*hsa-let-7a-5p*	DIANA TOOLS	*TIRAP*	*hsa-miR-661*	MirTarBase
HIC2	*hsa-miR-661*	MirTarBase	*TK2*	*hsa-miR-16-5p*	DIANA TOOLS
HIF1A	*hsa-miR-93-5p*	DIANA TOOLS	*TLCD2*	*hsa-miR-661*	MirTarBase
HIF1A	*hsa-miR-433-3p*	MirTarBase	*TLCD2*	*hsa-miR-661*	MirTarBase
HIF1AN	*hsa-let-7a-5p*	DIANA TOOLS	*TLK1*	*hsa-miR-15b-5p*	DIANA TOOLS
HIF1AN	*hsa-miR-31-5p*	DIANA TOOLS	*TLK1*	*hsa-miR-16-5p*	DIANA TOOLS
HIF3A	*hsa-let-7a-5p*	DIANA TOOLS	*TM2D3*	*hsa-miR-22-3p*	DIANA TOOLS
HIPK1	*hsa-miR-31-5p*	DIANA TOOLS	*TM4SF5*	*hsa-miR-433-3p*	MirTarBase
HIPK1	*hsa-miR-200c-3p*	DIANA TOOLS	*TMCC1*	*hsa-miR-16-5p*	DIANA TOOLS
HIPK1	*hsa-miR-25-3p*	DIANA TOOLS	*TMCC1*	*hsa-miR-15b-5p*	DIANA TOOLS
HIPK1	*hsa-miR-22-3p*	DIANA TOOLS	*TMCO1*	*hsa-miR-661*	MirTarBase
HIPK1	*hsa-miR-509-3-5p*	DIANA TOOLS	*TMED4*	*hsa-let-7a-5p*	DIANA TOOLS
HIPK2	*hsa-miR-15b-5p*	DIANA TOOLS	*TMED7*	*hsa-let-7a-5p*	MirTarBase

HIPK2	*hsa-miR-16-5p*	DIANA TOOLS	*TMEM100*	*hsa-miR-15b-5p*	DIANA TOOLS
HIPK3	*hsa-miR-200c-3p*	DIANA TOOLS	*TMEM100*	*hsa-miR-16-5p*	DIANA TOOLS
HIPK3	*hsa-miR-25-3p*	DIANA TOOLS	*TMEM120B*	*hsa-miR-661*	MirTarBase
HIPK3	*hsa-miR-15b-5p*	DIANA TOOLS	*TMEM123*	*hsa-miR-93-5p*	DIANA TOOLS
HIPK3	*hsa-miR-130a-3p*	DIANA TOOLS	*TMEM126A*	*hsa-miR-16-5p*	DIANA TOOLS
HIPK3	*hsa-miR-21-5p*	DIANA TOOLS	*TMEM165*	*hsa-miR-22-3p*	DIANA TOOLS
HIPK3	*hsa-miR-144-3p*	DIANA TOOLS	*TMEM167A*	*hsa-miR-93-5p*	DIANA TOOLS
HIST1H2AG	*hsa-miR-661*	MirTarBase	*TMEM167A*	*hsa-let-7a-5p*	DIANA TOOLS
HIST1H2BN	*hsa-miR-661*	MirTarBase	*TMEM169*	*hsa-miR-661*	MirTarBase
HIVEP1	*hsa-miR-433-3p*	MirTarBase	*TMEM170A*	*hsa-miR-130a-3p*	DIANA TOOLS
HIVEP1	*hsa-miR-433-3p*	MirTarBase	*TMEM183A*	*hsa-miR-15b-5p*	DIANA TOOLS
HIVEP1	*hsa-miR-433-3p*	MirTarBase	*TMEM183A*	*hsa-miR-16-5p*	DIANA TOOLS
HIVEP1	*hsa-miR-433-3p*	MirTarBase	*TMEM184B*	*hsa-miR-16-5p*	DIANA TOOLS
HIVEP3	*hsa-miR-31-5p*	DIANA TOOLS	*TMEM184C*	*hsa-miR-661*	MirTarBase
HM13	*hsa-miR-661*	MirTarBase	*TMEM184C*	*hsa-miR-661*	MirTarBase
HM13	*hsa-miR-661*	MirTarBase	*TMEM189-UBE2V1*	*hsa-miR-15b-5p*	DIANA TOOLS
HMGA1	*hsa-miR-142-3p*	DIANA TOOLS	*TMEM189-UBE2V1*	*hsa-miR-16-5p*	DIANA TOOLS
HMGA1	*hsa-miR-16-5p*	DIANA TOOLS	*TMEM194A*	*hsa-let-7a-5p*	DIANA TOOLS
HMGA1	*hsa-miR-15b-5p*	DIANA TOOLS	*TMEM209*	*hsa-miR-661*	MirTarBase
HMGA1	*hsa-let-7a-5p*	MirTarBase	*TMEM229B*	*hsa-miR-433-3p*	MirTarBase
HMGA1	*hsa-let-7a-5p*	MirTarBase	*TMEM229B*	*hsa-miR-433-3p*	MirTarBase
HMGA1	*hsa-let-7a-5p*	MirTarBase	*TMEM229B*	*hsa-miR-433-3p*	MirTarBase
HMGA2	*hsa-let-7a-5p*	MirTarBase	*TMEM245*	*hsa-miR-15b-5p*	DIANA TOOLS
HMGA2	*hsa-let-7a-5p*	MirTarBase	*TMEM245*	*hsa-miR-16-5p*	DIANA TOOLS
HMGA2	*hsa-let-7a-5p*	MirTarBase	*TMEM245*	*hsa-miR-661*	MirTarBase
HMGA2	*hsa-let-7a-5p*	MirTarBase	*TMEM39B*	*hsa-miR-205-5p*	DIANA TOOLS
HMGA2	*hsa-let-7a-5p*	MirTarBase	*TMEM43*	*hsa-miR-22-3p*	DIANA TOOLS
HMGA2	*hsa-let-7a-5p*	MirTarBase	*TMEM55A*	*hsa-miR-130a-3p*	DIANA TOOLS
HMGA2	*hsa-let-7a-5p*	MirTarBase	*TMEM55A*	*hsa-miR-15b-5p*	DIANA TOOLS
HMGA2	*hsa-let-7a-5p*	MirTarBase	*TMEM55A*	*hsa-miR-16-5p*	DIANA TOOLS
HMGB3	*hsa-miR-93-5p*	DIANA TOOLS	*TMEM55B*	*hsa-miR-16-5p*	DIANA TOOLS
HMX3	*hsa-miR-661*	MirTarBase	*TMEM55B*	*hsa-miR-15b-5p*	DIANA TOOLS
HN1	*hsa-miR-93-5p*	DIANA TOOLS	*TMEM59*	*hsa-miR-142-3p*	DIANA TOOLS
HNRNPA0	*hsa-miR-376b-3p*	DIANA TOOLS	*TMEM59*	*hsa-miR-661*	MirTarBase
HNRNPAB	*hsa-miR-144-3p*	DIANA TOOLS	*TMEM65*	*hsa-miR-661*	MirTarBase
HNRNPD	*hsa-miR-200c-3p*	DIANA TOOLS	*TMEM65*	*hsa-miR-661*	MirTarBase
HNRNPF	*hsa-miR-144-3p*	DIANA TOOLS	*TMEM87A*	*hsa-miR-25-3p*	DIANA TOOLS
HNRNPH1	*hsa-miR-22-3p*	DIANA TOOLS	*TMEM9B*	*hsa-miR-130a-3p*	DIANA TOOLS
HNRNPH3	*hsa-miR-205-5p*	DIANA TOOLS	*TMOD1*	*hsa-miR-544a*	DIANA TOOLS
HNRNPUL1	*hsa-miR-22-3p*	DIANA TOOLS	*TMOD3*	*hsa-miR-200c-3p*	DIANA TOOLS
HOMER2	*hsa-let-7a-5p*	DIANA TOOLS	*TMPPE*	*hsa-let-7a-5p*	DIANA TOOLS
HOXA1	*hsa-let-7a-5p*	DIANA TOOLS	*TMPRSS11BNL*	*hsa-miR-661*	MirTarBase
HOXA10	*hsa-miR-15b-5p*	DIANA TOOLS	*TMPRSS6*	*hsa-miR-661*	MirTarBase
HOXA10	*hsa-miR-16-5p*	DIANA TOOLS	*TMX4*	*hsa-miR-25-3p*	DIANA TOOLS
HOXA10	*hsa-miR-144-3p*	DIANA TOOLS	*TMX4*	*hsa-miR-200c-3p*	DIANA TOOLS

HOXA3	*hsa-miR-130a-3p*	DIANA TOOLS	*TNFAIP3*	*hsa-let-7a-5p*	MirTarBase
HOXA9	*hsa-let-7a-5p*	DIANA TOOLS	*TNFAIP8*	*hsa-miR-205-5p*	DIANA TOOLS
HPRT1	*hsa-miR-130a-3p*	DIANA TOOLS	*TNFRSF10B*	*hsa-let-7a-5p*	MirTarBase
HPS5	*hsa-miR-200c-3p*	DIANA TOOLS	*TNFRSF13B*	*hsa-miR-661*	MirTarBase
HRAS	*hsa-let-7a-5p*	MirTarBase	*TNFRSF1B*	*hsa-miR-130a-3p*	DIANA TOOLS
HRAS	*hsa-let-7a-5p*	MirTarBase	*TNFSF9*	*hsa-let-7a-5p*	DIANA TOOLS
HRAS	*hsa-let-7a-5p*	MirTarBase	*TNKS*	*hsa-miR-142-3p*	DIANA TOOLS
HRH4	*hsa-miR-433-3p*	MirTarBase	*TNKS2*	*hsa-miR-22-3p*	DIANA TOOLS
HRK	*hsa-miR-21-5p*	DIANA TOOLS	*TNKS2*	*hsa-miR-144-3p*	DIANA TOOLS
HRK	*hsa-miR-130a-3p*	DIANA TOOLS	*TNPO1*	*hsa-miR-661*	MirTarBase
HSBP1	*hsa-miR-661*	MirTarBase	*TNRC6A*	*hsa-miR-16-5p*	DIANA TOOLS
HSDL2	*hsa-miR-16-5p*	DIANA TOOLS	*TNRC6A*	*hsa-miR-15b-5p*	DIANA TOOLS
HSDL2	*hsa-miR-15b-5p*	DIANA TOOLS	*TNRC6A*	*hsa-miR-130a-3p*	DIANA TOOLS
HSP90B1	*hsa-miR-433-3p*	MirTarBase	*TNRC6A*	*hsa-miR-190b*	DIANA TOOLS
HSP90B1	*hsa-miR-433-3p*	MirTarBase	*TNRC6A*	*hsa-miR-144-3p*	DIANA TOOLS
HSPA13	*hsa-miR-200c-3p*	DIANA TOOLS	*TNRC6A*	*hsa-miR-142-3p*	DIANA TOOLS
HSPA14	*hsa-let-7a-5p*	DIANA TOOLS	*TNRC6B*	*hsa-miR-21-5p*	DIANA TOOLS
HSPA1B	*hsa-miR-142-3p*	DIANA TOOLS	*TNRC6B*	*hsa-miR-509-3-5p*	DIANA TOOLS
HSPA4L	*hsa-miR-93-5p*	DIANA TOOLS	*TNRC6B*	*hsa-miR-144-3p*	DIANA TOOLS
HSPA4L	*hsa-miR-16-5p*	DIANA TOOLS	*TNRC6B*	*hsa-miR-130a-3p*	DIANA TOOLS
HSPA8	*hsa-miR-93-5p*	DIANA TOOLS	*TNRC6B*	*hsa-miR-93-5p*	DIANA TOOLS
HSPA8	*hsa-miR-130a-3p*	DIANA TOOLS	*TNRC6B*	*hsa-miR-15b-5p*	DIANA TOOLS
HSPA9	*hsa-miR-205-5p*	DIANA TOOLS	*TNRC6B*	*hsa-miR-16-5p*	DIANA TOOLS
IDE	*hsa-let-7a-5p*	DIANA TOOLS	*TOB1*	*hsa-miR-25-3p*	DIANA TOOLS
IDE	*hsa-miR-661*	MirTarBase	*TOB1*	*hsa-miR-200c-3p*	DIANA TOOLS
IFITM10	*hsa-let-7a-5p*	DIANA TOOLS	*TOM1L2*	*hsa-miR-130a-3p*	DIANA TOOLS
IFNAR1	*hsa-miR-381-5p*	MirTarBase	*TOR1AIP1*	*hsa-miR-661*	MirTarBase
IFNAR1	*hsa-miR-381-5p*	MirTarBase	*TOR4A*	*hsa-miR-661*	MirTarBase
IFNAR1	*hsa-miR-381-5p*	MirTarBase	*TP53*	*hsa-let-7a-5p*	DIANA TOOLS
IFNAR1	*hsa-miR-381-5p*	MirTarBase	*TP53INP1*	*hsa-miR-200c-3p*	DIANA TOOLS
IFNAR2	*hsa-miR-381-5p*	MirTarBase	*TP53INP1*	*hsa-miR-93-5p*	DIANA TOOLS
IFNAR2	*hsa-miR-381-5p*	MirTarBase	*TP53INP1*	*hsa-miR-22-3p*	DIANA TOOLS
IFRD2	*hsa-miR-16-5p*	DIANA TOOLS	*TPD52*	*hsa-miR-144-3p*	DIANA TOOLS
IGDCC3	*hsa-let-7a-5p*	DIANA TOOLS	*TPGS1*	*hsa-miR-661*	MirTarBase
IGDCC4	*hsa-let-7a-5p*	DIANA TOOLS	*TPP1*	*hsa-let-7a-5p*	DIANA TOOLS
IGF1R	*hsa-miR-22-3p*	DIANA TOOLS	*TRAF3*	*hsa-miR-25-3p*	DIANA TOOLS
IGF1R	*hsa-miR-15b-5p*	DIANA TOOLS	*TRAF3IP1*	*hsa-miR-661*	MirTarBase
IGF1R	*hsa-miR-16-5p*	DIANA TOOLS	*TRAM1*	*hsa-miR-190b*	DIANA TOOLS
IGF1R	*hsa-let-7a-5p*	DIANA TOOLS	*TRAM1*	*hsa-miR-15b-5p*	DIANA TOOLS
IGF2	*hsa-let-7a-5p*	MirTarBase	*TRAM1*	*hsa-miR-16-5p*	DIANA TOOLS
IGF2BP1	*hsa-let-7a-5p*	DIANA TOOLS	*TRAM2*	*hsa-miR-25-3p*	DIANA TOOLS
IGF2BP1	*hsa-let-7a-5p*	MirTarBase	*TRANK1*	*hsa-let-7a-5p*	DIANA TOOLS
IGF2BP2	*hsa-let-7a-5p*	DIANA TOOLS	*TRAPPC1*	*hsa-let-7a-5p*	DIANA TOOLS
IGF2BP3	*hsa-let-7a-5p*	DIANA TOOLS	*TRAPPC2B*	*hsa-miR-661*	MirTarBase
IGFBP7	*hsa-miR-31-5p*	DIANA TOOLS	*TRAPPC8*	*hsa-miR-200c-3p*	DIANA TOOLS
IKBKB	*hsa-miR-15b-5p*	DIANA TOOLS	*TRERF1*	*hsa-miR-130a-3p*	DIANA TOOLS
IKBKB	*hsa-miR-16-5p*	DIANA TOOLS	*TRIB1*	*hsa-miR-144-3p*	DIANA TOOLS

IKZF3	*hsa-miR-661*	MirTarBase	*TRIM16L*	*hsa-miR-661*	MirTarBase
IKZF3	*hsa-miR-661*	MirTarBase	*TRIM16L*	*hsa-miR-661*	MirTarBase
IKZF3	*hsa-miR-661*	MirTarBase	*TRIM33*	*hsa-miR-142-3p*	DIANA TOOLS
IKZF4	*hsa-miR-22-3p*	DIANA TOOLS	*TRIM33*	*hsa-miR-200c-3p*	DIANA TOOLS
IL12A	*hsa-miR-21-5p*	DIANA TOOLS	*TRIM36*	*hsa-miR-15b-5p*	DIANA TOOLS
IL17RB	*hsa-miR-661*	MirTarBase	*TRIM37*	*hsa-miR-16-5p*	DIANA TOOLS
IL17REL	*hsa-miR-661*	MirTarBase	*TRIM59*	*hsa-miR-200c-3p*	DIANA TOOLS
IL6	*hsa-let-7a-5p*	MirTarBase	*TRIM71*	*hsa-let-7a-5p*	DIANA TOOLS
IL6R	*hsa-let-7a-5p*	DIANA TOOLS	*TRIM71*	*hsa-miR-200c-3p*	DIANA TOOLS
IL6ST	*hsa-miR-223-3p*	DIANA TOOLS	*TRIM71*	*hsa-let-7a-5p*	MirTarBase
INHBA	*hsa-miR-130a-3p*	DIANA TOOLS	*TRIM71*	*hsa-let-7a-5p*	MirTarBase
INHBB	*hsa-miR-22-3p*	DIANA TOOLS	*TRIOBP*	*hsa-miR-661*	MirTarBase
INO80D	*hsa-let-7a-5p*	DIANA TOOLS	*TRIP11*	*hsa-miR-22-3p*	DIANA TOOLS
INO80D	*hsa-miR-200c-3p*	DIANA TOOLS	*TRMO*	*hsa-miR-661*	MirTarBase
INO80E	*hsa-miR-22-3p*	DIANA TOOLS	*TRMT2B*	*hsa-miR-661*	MirTarBase
INSIG1	*hsa-miR-130a-3p*	DIANA TOOLS	*TROVE2*	*hsa-miR-200c-3p*	DIANA TOOLS
INSIG1	*hsa-miR-25-3p*	DIANA TOOLS	*TRPM7*	*hsa-miR-21-5p*	DIANA TOOLS
INSR	*hsa-let-7a-5p*	DIANA TOOLS	*TRPV1*	*hsa-miR-661*	MirTarBase
INTS7	*hsa-miR-661*	MirTarBase	*TSC1*	*hsa-let-7a-5p*	DIANA TOOLS
IP6K1	*hsa-miR-16-5p*	DIANA TOOLS	*TSC1*	*hsa-miR-130a-3p*	DIANA TOOLS
IP6K1	*hsa-miR-15b-5p*	DIANA TOOLS	*TSC22D2*	*hsa-miR-15b-5p*	DIANA TOOLS
IPO4	*hsa-miR-16-5p*	DIANA TOOLS	*TSC22D2*	*hsa-miR-16-5p*	DIANA TOOLS
IPO7	*hsa-miR-142-3p*	DIANA TOOLS	*TSC22D2*	*hsa-miR-200c-3p*	DIANA TOOLS
IPO7	*hsa-miR-22-3p*	DIANA TOOLS	*TSHZ1*	*hsa-miR-130a-3p*	DIANA TOOLS
IPO7	*hsa-miR-200c-3p*	DIANA TOOLS	*TSHZ2*	*hsa-miR-144-3p*	DIANA TOOLS
IPO7	*hsa-miR-16-5p*	DIANA TOOLS	*TSN*	*hsa-miR-15b-5p*	DIANA TOOLS
IPO7	*hsa-miR-15b-5p*	DIANA TOOLS	*TSPAN18*	*hsa-miR-130a-3p*	DIANA TOOLS
IPPK	*hsa-miR-16-5p*	DIANA TOOLS	*TSPEAR-AS2*	*hsa-miR-661*	MirTarBase
IPPK	*hsa-miR-15b-5p*	DIANA TOOLS	*TSPYL2*	*hsa-miR-15b-5p*	DIANA TOOLS
IQGAP2	*hsa-miR-25-3p*	DIANA TOOLS	*TSPYL2*	*hsa-miR-16-5p*	DIANA TOOLS
IRAK1	*hsa-miR-142-3p*	DIANA TOOLS	*TSTD2*	*hsa-miR-661*	MirTarBase
IRAK1BP1	*hsa-miR-661*	MirTarBase	*TTC26*	*hsa-let-7a-5p*	DIANA TOOLS
IRAK1BP1	*hsa-miR-661*	MirTarBase	*TTF2*	*hsa-miR-93-5p*	DIANA TOOLS
IRAK2	*hsa-miR-661*	MirTarBase	*TTLL4*	*hsa-let-7a-5p*	DIANA TOOLS
IREB2	*hsa-miR-144-3p*	DIANA TOOLS	*TTN*	*hsa-miR-144-3p*	MirTarBase
IRF1	*hsa-miR-130a-3p*	DIANA TOOLS	*TUBA1B*	*hsa-miR-22-3p*	DIANA TOOLS
IRGQ	*hsa-let-7a-5p*	DIANA TOOLS	*TUFT1*	*hsa-miR-661*	MirTarBase
IRGQ	*hsa-miR-661*	MirTarBase	*TUFT1*	*hsa-miR-661*	MirTarBase
IRS1	*hsa-miR-144-3p*	MirTarBase	*TUG1*	*hsa-miR-144-3p*	MirTarBase
IRS2	*hsa-miR-25-3p*	DIANA TOOLS	*TULP4*	*hsa-miR-25-3p*	DIANA TOOLS
IRS2	*hsa-let-7a-5p*	DIANA TOOLS	*TUSC2*	*hsa-miR-93-5p*	DIANA TOOLS
ISCA1	*hsa-miR-661*	MirTarBase	*TVP23C*	*hsa-miR-661*	MirTarBase
ISG20L2	*hsa-miR-661*	MirTarBase	*TWF1*	*hsa-miR-142-3p*	DIANA TOOLS
IST1	*hsa-miR-15b-5p*	DIANA TOOLS	*TXNDC16*	*hsa-miR-661*	MirTarBase
IST1	*hsa-miR-16-5p*	DIANA TOOLS	*TXNDC16*	*hsa-miR-661*	MirTarBase
ITGA5	*hsa-miR-25-3p*	DIANA TOOLS	*TYMS*	*hsa-miR-433-3p*	MirTarBase
ITGA8	*hsa-miR-144-3p*	DIANA TOOLS	*U2SURP*	*hsa-miR-16-5p*	DIANA TOOLS

ITGAV	*hsa-miR-142-3p*	DIANA TOOLS	*U2SURP*	*hsa-miR-15b-5p*	DIANA TOOLS
ITGAV	*hsa-miR-25-3p*	DIANA TOOLS	*UBA6*	*hsa-miR-200c-3p*	DIANA TOOLS
ITGB3	*hsa-let-7a-5p*	MirTarBase	*UBC*	*hsa-miR-130a-3p*	DIANA TOOLS
ITGB8	*hsa-miR-130a-3p*	DIANA TOOLS	*UBC*	*hsa-miR-661*	MirTarBase
ITGB8	*hsa-miR-142-3p*	DIANA TOOLS	*UBE2I*	*hsa-miR-200c-3p*	DIANA TOOLS
ITIH5	*hsa-miR-433-3p*	MirTarBase	*UBE2Q1*	*hsa-miR-15b-5p*	DIANA TOOLS
ITPA	*hsa-miR-661*	MirTarBase	*UBE2Q1*	*hsa-miR-16-5p*	DIANA TOOLS
ITPR1	*hsa-miR-25-3p*	DIANA TOOLS	*UBE2Q2*	*hsa-miR-93-5p*	DIANA TOOLS
ITPRIPL2	*hsa-miR-544a*	DIANA TOOLS	*UBE2R2*	*hsa-miR-200c-3p*	DIANA TOOLS
ITSN2	*hsa-miR-200c-3p*	DIANA TOOLS	*UBE2V1*	*hsa-miR-16-5p*	DIANA TOOLS
JADE1	*hsa-miR-25-3p*	DIANA TOOLS	*UBE2W*	*hsa-miR-130a-3p*	DIANA TOOLS
JADE1	*hsa-miR-130a-3p*	DIANA TOOLS	*UBE2W*	*hsa-miR-25-3p*	DIANA TOOLS
JAG1	*hsa-miR-21-5p*	DIANA TOOLS	*UBE2W*	*hsa-miR-93-5p*	DIANA TOOLS
JARID2	*hsa-miR-130a-3p*	DIANA TOOLS	*UBE2W*	*hsa-miR-200c-3p*	DIANA TOOLS
JARID2	*hsa-miR-15b-5p*	DIANA TOOLS	*UBE2Z*	*hsa-miR-25-3p*	DIANA TOOLS
JARID2	*hsa-miR-16-5p*	DIANA TOOLS	*UBE4A*	*hsa-miR-16-5p*	DIANA TOOLS
JAZF1	*hsa-miR-200c-3p*	DIANA TOOLS	*UBE4B*	*hsa-miR-15b-5p*	DIANA TOOLS
JMJD4	*hsa-miR-661*	MirTarBase	*UBE4B*	*hsa-miR-16-5p*	DIANA TOOLS
JMY	*hsa-miR-25-3p*	DIANA TOOLS	*UBN2*	*hsa-miR-130a-3p*	DIANA TOOLS
JOSD1	*hsa-miR-93-5p*	DIANA TOOLS	*UBN2*	*hsa-miR-200c-3p*	DIANA TOOLS
JUN	*hsa-miR-200c-3p*	DIANA TOOLS	*UBN2*	*hsa-miR-15b-5p*	DIANA TOOLS
KANK1	*hsa-miR-15b-5p*	DIANA TOOLS	*UBN2*	*hsa-miR-16-5p*	DIANA TOOLS
KANK1	*hsa-miR-16-5p*	DIANA TOOLS	*UBR3*	*hsa-miR-16-5p*	DIANA TOOLS
KANK2	*hsa-miR-200c-3p*	DIANA TOOLS	*UBR3*	*hsa-miR-15b-5p*	DIANA TOOLS
KAT6A	*hsa-miR-144-3p*	DIANA TOOLS	*UBXN2A*	*hsa-miR-661*	MirTarBase
KATNAL1	*hsa-miR-16-5p*	DIANA TOOLS	*UBXN7*	*hsa-miR-22-3p*	DIANA TOOLS
KATNAL1	*hsa-miR-15b-5p*	DIANA TOOLS	*UCHL5*	*hsa-miR-25-3p*	DIANA TOOLS
KBTBD2	*hsa-miR-15b-5p*	DIANA TOOLS	*UGCG*	*hsa-miR-22-3p*	DIANA TOOLS
KBTBD2	*hsa-miR-16-5p*	DIANA TOOLS	*UGCG*	*hsa-miR-200c-3p*	DIANA TOOLS
KBTBD6	*hsa-miR-200c-3p*	DIANA TOOLS	*UGDH*	*hsa-miR-661*	MirTarBase
KBTBD6	*hsa-miR-21-5p*	DIANA TOOLS	*UGDH*	*hsa-miR-661*	MirTarBase
KBTBD7	*hsa-miR-21-5p*	DIANA TOOLS	*UGDH*	*hsa-miR-661*	MirTarBase
KCNE4	*hsa-miR-661*	MirTarBase	*UGDH*	*hsa-miR-661*	MirTarBase
KCNH8	*hsa-miR-93-5p*	DIANA TOOLS	*UGT2B4*	*hsa-miR-433-3p*	MirTarBase
KCNK6	*hsa-miR-661*	MirTarBase	*UGT2B4*	*hsa-miR-433-3p*	MirTarBase
KCNN3	*hsa-miR-661*	MirTarBase	*UGT8*	*hsa-miR-130a-3p*	DIANA TOOLS
KCNN4	*hsa-miR-16-5p*	DIANA TOOLS	*UHMK1*	*hsa-miR-15b-5p*	DIANA TOOLS
KCNN4	*hsa-miR-15b-5p*	DIANA TOOLS	*UHMK1*	*hsa-miR-16-5p*	DIANA TOOLS
KCTD20	*hsa-miR-130a-3p*	DIANA TOOLS	*UHRF1*	*hsa-let-7a-5p*	MirTarBase
KDELR2	*hsa-miR-142-3p*	DIANA TOOLS	*UHRF2*	*hsa-let-7a-5p*	MirTarBase
KDM2A	*hsa-miR-130a-3p*	DIANA TOOLS	*ULBP2*	*hsa-miR-433-3p*	MirTarBase
KDM6B	*hsa-miR-22-3p*	DIANA TOOLS	*ULK1*	*hsa-miR-93-5p*	DIANA TOOLS
KDM6B	*hsa-miR-381-5p*	MirTarBase	*ULK2*	*hsa-miR-130a-3p*	DIANA TOOLS
KDM7A	*hsa-miR-200c-3p*	DIANA TOOLS	*ULK3*	*hsa-let-7a-5p*	DIANA TOOLS
KDR	*hsa-miR-16-5p*	DIANA TOOLS	*UNC5B*	*hsa-miR-16-5p*	DIANA TOOLS
KDR	*hsa-miR-200c-3p*	DIANA TOOLS	*UNC5B*	*hsa-miR-15b-5p*	DIANA TOOLS
KDSR	*hsa-miR-200c-3p*	DIANA TOOLS	*UQCRFS1*	*hsa-miR-661*	MirTarBase
KDSR	*hsa-miR-15b-5p*	DIANA TOOLS	*USF3*	*hsa-miR-661*	MirTarBase

KDSR	*hsa-miR-16-5p*	DIANA TOOLS	*USP1*	*hsa-miR-661*	MirTarBase
KHNYN	*hsa-miR-16-5p*	DIANA TOOLS	*USP1*	*hsa-miR-661*	MirTarBase
KHNYN	*hsa-miR-15b-5p*	DIANA TOOLS	*USP12*	*hsa-let-7a-5p*	DIANA TOOLS
KHNYN	*hsa-miR-22-3p*	DIANA TOOLS	*USP14*	*hsa-miR-16-5p*	DIANA TOOLS
KIAA0101	*hsa-miR-200c-3p*	DIANA TOOLS	*USP14*	*hsa-miR-15b-5p*	DIANA TOOLS
KIAA0430	*hsa-miR-130a-3p*	DIANA TOOLS	*USP15*	*hsa-miR-16-5p*	DIANA TOOLS
KIAA1109	*hsa-miR-25-3p*	DIANA TOOLS	*USP21*	*hsa-let-7a-5p*	DIANA TOOLS
KIAA1279	*hsa-miR-25-3p*	DIANA TOOLS	*USP24*	*hsa-let-7a-5p*	DIANA TOOLS
KIAA1430	*hsa-miR-200c-3p*	DIANA TOOLS	*USP25*	*hsa-miR-16-5p*	DIANA TOOLS
KIAA1432	*hsa-miR-200c-3p*	DIANA TOOLS	*USP25*	*hsa-miR-15b-5p*	DIANA TOOLS
KIAA1432	*hsa-miR-15b-5p*	DIANA TOOLS	*USP31*	*hsa-miR-130a-3p*	DIANA TOOLS
KIAA1432	*hsa-miR-25-3p*	DIANA TOOLS	*USP33*	*hsa-miR-130a-3p*	DIANA TOOLS
KIAA1432	*hsa-miR-16-5p*	DIANA TOOLS	*USP44*	*hsa-miR-16-5p*	DIANA TOOLS
KIAA1468	*hsa-miR-130a-3p*	DIANA TOOLS	*USP44*	*hsa-miR-15b-5p*	DIANA TOOLS
KIAA1551	*hsa-miR-661*	MirTarBase	*USP47*	*hsa-let-7a-5p*	DIANA TOOLS
KIAA2018	*hsa-miR-200c-3p*	DIANA TOOLS	*USP47*	*hsa-miR-130a-3p*	DIANA TOOLS
KIF16B	*hsa-miR-15b-5p*	DIANA TOOLS	*USP47*	*hsa-miR-144-3p*	DIANA TOOLS
KIF16B	*hsa-miR-16-5p*	DIANA TOOLS	*USP6NL*	*hsa-miR-142-3p*	DIANA TOOLS
KIF18B	*hsa-miR-15b-5p*	DIANA TOOLS	*USP9X*	*hsa-miR-16-5p*	DIANA TOOLS
KIF18B	*hsa-miR-16-5p*	DIANA TOOLS	*UTRN*	*hsa-let-7a-5p*	DIANA TOOLS
KIF1B	*hsa-miR-25-3p*	DIANA TOOLS	*UTRN*	*hsa-miR-142-3p*	DIANA TOOLS
KIF1B	*hsa-miR-16-5p*	DIANA TOOLS	*VAMP3*	*hsa-miR-381-5p*	MirTarBase
KIF1B	*hsa-miR-15b-5p*	DIANA TOOLS	*VAPB*	*hsa-miR-15b-5p*	DIANA TOOLS
KIF1C	*hsa-miR-16-5p*	DIANA TOOLS	*VAPB*	*hsa-miR-16-5p*	DIANA TOOLS
KIF1C	*hsa-miR-15b-5p*	DIANA TOOLS	*VASH2*	*hsa-miR-21-5p*	DIANA TOOLS
KIF5A	*hsa-miR-16-5p*	DIANA TOOLS	*VAT1L*	*hsa-miR-200c-3p*	DIANA TOOLS
KIF5A	*hsa-miR-15b-5p*	DIANA TOOLS	*VCL*	*hsa-miR-21-5p*	DIANA TOOLS
KIF5B	*hsa-miR-144-3p*	DIANA TOOLS	*VCL*	*hsa-miR-661*	MirTarBase
KIF5B	*hsa-miR-15b-5p*	DIANA TOOLS	*VDR*	*hsa-let-7a-5p*	MirTarBase
KIF5B	*hsa-miR-16-5p*	DIANA TOOLS	*VEGFA*	*hsa-miR-16-5p*	DIANA TOOLS
KIF5B	*hsa-miR-142-3p*	DIANA TOOLS	*VEGFA*	*hsa-miR-205-5p*	DIANA TOOLS
KIF5B	*hsa-miR-25-3p*	DIANA TOOLS	*VEGFA*	*hsa-miR-15b-5p*	DIANA TOOLS
KIF5B	*hsa-miR-661*	MirTarBase	*VEGFC*	*hsa-miR-661*	MirTarBase
KIF5C	*hsa-miR-15b-5p*	DIANA TOOLS	*VEZF1*	*hsa-miR-200c-3p*	DIANA TOOLS
KIF6	*hsa-miR-661*	MirTarBase	*VEZT*	*hsa-miR-15b-5p*	DIANA TOOLS
KLC1	*hsa-miR-15b-5p*	DIANA TOOLS	*VEZT*	*hsa-miR-16-5p*	DIANA TOOLS
KLC1	*hsa-miR-16-5p*	DIANA TOOLS	*VEZT*	*hsa-let-7a-5p*	DIANA TOOLS
KLF10	*hsa-miR-661*	MirTarBase	*VGLL4*	*hsa-miR-130a-3p*	DIANA TOOLS
KLF13	*hsa-miR-200c-3p*	DIANA TOOLS	*VHL*	*hsa-miR-661*	MirTarBase
KLF13	*hsa-miR-142-3p*	DIANA TOOLS	*VHLL*	*hsa-miR-661*	MirTarBase
KLF2	*hsa-miR-25-3p*	DIANA TOOLS	*VLDLR*	*hsa-miR-200c-3p*	DIANA TOOLS
KLF3	*hsa-miR-144-3p*	DIANA TOOLS	*VPS13B*	*hsa-miR-142-3p*	DIANA TOOLS
KLF3	*hsa-miR-21-5p*	DIANA TOOLS	*VPS26A*	*hsa-miR-93-5p*	DIANA TOOLS
KLF4	*hsa-miR-142-3p*	DIANA TOOLS	*VPS26B*	*hsa-miR-31-5p*	DIANA TOOLS
KLF4	*hsa-miR-200c-3p*	DIANA TOOLS	*VPS33A*	*hsa-let-7a-5p*	DIANA TOOLS
KLF4	*hsa-miR-25-3p*	DIANA TOOLS	*VPS33B*	*hsa-miR-16-5p*	DIANA TOOLS
KLF5	*hsa-miR-21-5p*	DIANA TOOLS	*VPS37C*	*hsa-miR-15b-5p*	DIANA TOOLS

KLF6	*hsa-miR-25-3p*	DIANA TOOLS	*VPS37C*	*hsa-miR-16-5p*	DIANA TOOLS
KLHDC10	*hsa-miR-25-3p*	DIANA TOOLS	*VPS53*	*hsa-miR-661*	MirTarBase
KLHDC8B	*hsa-let-7a-5p*	DIANA TOOLS	*VPS54*	*hsa-miR-25-3p*	DIANA TOOLS
KLHL11	*hsa-miR-661*	MirTarBase	*VTCN1*	*hsa-miR-15b-5p*	DIANA TOOLS
KLHL15	*hsa-miR-21-5p*	DIANA TOOLS	*VTI1B*	*hsa-miR-16-5p*	DIANA TOOLS
KLHL2	*hsa-miR-93-5p*	DIANA TOOLS	*VTI1B*	*hsa-miR-15b-5p*	DIANA TOOLS
KLHL20	*hsa-miR-130a-3p*	DIANA TOOLS	*VWA7*	*hsa-miR-661*	MirTarBase
KLHL21	*hsa-miR-661*	MirTarBase	*WAPAL*	*hsa-miR-15b-5p*	DIANA TOOLS
KLHL3	*hsa-miR-130a-3p*	DIANA TOOLS	*WAPAL*	*hsa-miR-16-5p*	DIANA TOOLS
KLHL3	*hsa-miR-661*	MirTarBase	*WAPAL*	*hsa-miR-22-3p*	DIANA TOOLS
KLHL4	*hsa-miR-433-3p*	MirTarBase	*WASL*	*hsa-let-7a-5p*	DIANA TOOLS
KMT2C	*hsa-miR-130a-3p*	DIANA TOOLS	*WASL*	*hsa-miR-130a-3p*	DIANA TOOLS
KMT2C	*hsa-miR-200c-3p*	DIANA TOOLS	*WASL*	*hsa-miR-142-3p*	DIANA TOOLS
KMT2D	*hsa-miR-15b-5p*	DIANA TOOLS	*WBP11*	*hsa-miR-16-5p*	DIANA TOOLS
KMT2D	*hsa-let-7a-5p*	DIANA TOOLS	*WBP11*	*hsa-miR-661*	MirTarBase
KMT2E	*hsa-miR-144-3p*	DIANA TOOLS	*WBP11*	*hsa-miR-661*	MirTarBase
KMT2E	*hsa-let-7a-5p*	DIANA TOOLS	*WDFY3*	*hsa-miR-144-3p*	DIANA TOOLS
KPNA3	*hsa-miR-16-5p*	DIANA TOOLS	*WDR11*	*hsa-let-7a-5p*	DIANA TOOLS
KPNA5	*hsa-miR-190b*	DIANA TOOLS	*WDR13*	*hsa-miR-661*	MirTarBase
KRAS	*hsa-let-7a-5p*	MirTarBase	*WDR45B*	*hsa-miR-433-3p*	MirTarBase
KRAS	*hsa-let-7a-5p*	MirTarBase	*WDR47*	*hsa-miR-130a-3p*	DIANA TOOLS
KRAS	*hsa-let-7a-5p*	MirTarBase	*WDR82*	*hsa-miR-200c-3p*	DIANA TOOLS
KRAS	*hsa-let-7a-5p*	MirTarBase	*WDR82*	*hsa-miR-93-5p*	DIANA TOOLS
KRAS	*hsa-miR-433-3p*	MirTarBase	*WDR82*	*hsa-miR-22-3p*	DIANA TOOLS
KRIT1	*hsa-miR-21-5p*	DIANA TOOLS	*WDR82*	*hsa-miR-509-3-5p*	DIANA TOOLS
KRR1	*hsa-miR-200c-3p*	DIANA TOOLS	*WDTC1*	*hsa-miR-16-5p*	DIANA TOOLS
KSR1	*hsa-miR-200c-3p*	DIANA TOOLS	*WEE1*	*hsa-miR-15b-5p*	DIANA TOOLS
LACTB2	*hsa-miR-144-3p*	DIANA TOOLS	*WEE1*	*hsa-miR-16-5p*	DIANA TOOLS
LAMC3	*hsa-miR-661*	MirTarBase	*WHSC1*	*hsa-miR-200c-3p*	DIANA TOOLS
LANCL3	*hsa-miR-661*	MirTarBase	*WIPI2*	*hsa-miR-15b-5p*	DIANA TOOLS
LAPTM4A	*hsa-miR-495-3p*	DIANA TOOLS	*WIPI2*	*hsa-miR-16-5p*	DIANA TOOLS
LASP1	*hsa-miR-31-5p*	DIANA TOOLS	*WNK1*	*hsa-miR-22-3p*	DIANA TOOLS
LATS1	*hsa-miR-15b-5p*	DIANA TOOLS	*WNK1*	*hsa-miR-130a-3p*	DIANA TOOLS
LATS1	*hsa-miR-16-5p*	DIANA TOOLS	*WNT1*	*hsa-let-7a-5p*	MirTarBase
LATS1	*hsa-miR-509-3p*	DIANA TOOLS	*WNT3A*	*hsa-miR-15b-5p*	DIANA TOOLS
LATS1	*hsa-miR-200c-3p*	DIANA TOOLS	*WNT3A*	*hsa-miR-16-5p*	DIANA TOOLS
LATS1	*hsa-miR-21-5p*	DIANA TOOLS	*WNT9A*	*hsa-let-7a-5p*	DIANA TOOLS
LATS2	*hsa-miR-16-5p*	DIANA TOOLS	*WRNIP1*	*hsa-miR-22-3p*	DIANA TOOLS
LATS2	*hsa-miR-15b-5p*	DIANA TOOLS	*WRNIP1*	*hsa-miR-25-3p*	DIANA TOOLS
LATS2	*hsa-miR-25-3p*	DIANA TOOLS	*WSB1*	*hsa-miR-200c-3p*	DIANA TOOLS
LAX1	*hsa-miR-661*	MirTarBase	*WSB1*	*hsa-miR-15b-5p*	DIANA TOOLS
LBR	*hsa-let-7a-5p*	DIANA TOOLS	*WSB1*	*hsa-miR-16-5p*	DIANA TOOLS
LCLAT1	*hsa-miR-130a-3p*	DIANA TOOLS	*WT1*	*hsa-miR-661*	MirTarBase
LCOR	*hsa-let-7a-5p*	DIANA TOOLS	*WT1*	*hsa-miR-661*	MirTarBase
LCOR	*hsa-miR-130a-3p*	DIANA TOOLS	*XIAP*	*hsa-miR-200c-3p*	DIANA TOOLS
LDLR	*hsa-miR-130a-3p*	DIANA TOOLS	*XIAP*	*hsa-miR-661*	MirTarBase
LDOC1L	*hsa-miR-31-5p*	DIANA TOOLS	*XIST*	*hsa-miR-144-3p*	MirTarBase

LEMD2	*hsa-miR-433-3p*	MirTarBase	*XK*	*hsa-let-7a-5p*	DIANA TOOLS
LEPREL1	*hsa-miR-16-5p*	DIANA TOOLS	*XPO1*	*hsa-miR-200c-3p*	DIANA TOOLS
LEPREL1	*hsa-miR-15b-5p*	DIANA TOOLS	*XPO1*	*hsa-miR-223-3p*	DIANA TOOLS
LETM1	*hsa-miR-661*	MirTarBase	*XPO1*	*hsa-miR-142-3p*	DIANA TOOLS
LETM1	*hsa-miR-661*	MirTarBase	*XPO7*	*hsa-miR-16-5p*	DIANA TOOLS
LGALS1	*hsa-miR-22-3p*	DIANA TOOLS	*XPO7*	*hsa-miR-15b-5p*	DIANA TOOLS
LGALSL	*hsa-miR-130a-3p*	DIANA TOOLS	*XPOT*	*hsa-let-7a-5p*	DIANA TOOLS
LHFP	*hsa-miR-200c-3p*	DIANA TOOLS	*XRCC2*	*hsa-miR-661*	MirTarBase
LHFPL2	*hsa-miR-25-3p*	DIANA TOOLS	*XRCC5*	*hsa-miR-16-5p*	DIANA TOOLS
LHFPL4	*hsa-miR-661*	MirTarBase	*XRCC5*	*hsa-miR-15b-5p*	DIANA TOOLS
LIFR	*hsa-miR-21-5p*	DIANA TOOLS	*XRN1*	*hsa-miR-190b*	DIANA TOOLS
LIMD1	*hsa-miR-661*	MirTarBase	*XRN1*	*hsa-let-7a-5p*	DIANA TOOLS
LIMD1	*hsa-miR-661*	MirTarBase	*XYLT2*	*hsa-let-7a-5p*	DIANA TOOLS
LIN28A	*hsa-let-7a-5p*	MirTarBase	*YAP1*	*hsa-miR-21-5p*	DIANA TOOLS
LIN28B	*hsa-let-7a-5p*	DIANA TOOLS	*YAP1*	*hsa-miR-205-5p*	DIANA TOOLS
LIN28B	*hsa-let-7a-5p*	MirTarBase	*YARS*	*hsa-miR-22-3p*	DIANA TOOLS
LIN9	*hsa-miR-661*	MirTarBase	*YES1*	*hsa-miR-205-5p*	DIANA TOOLS
LIN9	*hsa-miR-661*	MirTarBase	*YIPF6*	*hsa-miR-433-3p*	MirTarBase
LIPA	*hsa-miR-130a-3p*	DIANA TOOLS	*YOD1*	*hsa-let-7a-5p*	DIANA TOOLS
LIPH	*hsa-let-7a-5p*	DIANA TOOLS	*YOD1*	*hsa-miR-21-5p*	DIANA TOOLS
LIX1L	*hsa-miR-661*	MirTarBase	*YOD1*	*hsa-miR-661*	MirTarBase
LIX1L	*hsa-miR-661*	MirTarBase	*YOD1*	*hsa-miR-661*	MirTarBase
LMAN1	*hsa-miR-200c-3p*	DIANA TOOLS	*YOD1*	*hsa-miR-661*	MirTarBase
LMBR1	*hsa-miR-130a-3p*	DIANA TOOLS	*YRDC*	*hsa-miR-15b-5p*	DIANA TOOLS
LMBR1L	*hsa-miR-25-3p*	DIANA TOOLS	*YRDC*	*hsa-miR-16-5p*	DIANA TOOLS
LMBR1L	*hsa-miR-16-5p*	DIANA TOOLS	*YTHDC1*	*hsa-miR-15b-5p*	DIANA TOOLS
LMO2	*hsa-miR-223-3p*	DIANA TOOLS	*YTHDC1*	*hsa-miR-16-5p*	DIANA TOOLS
LMO7	*hsa-miR-200c-3p*	DIANA TOOLS	*YWHAE*	*hsa-miR-31-5p*	DIANA TOOLS
LNPEP	*hsa-miR-200c-3p*	DIANA TOOLS	*YWHAG*	*hsa-miR-200c-3p*	DIANA TOOLS
LONRF1	*hsa-miR-130a-3p*	DIANA TOOLS	*YWHAH*	*hsa-miR-25-3p*	DIANA TOOLS
LONRF2	*hsa-miR-433-3p*	MirTarBase	*YWHAZ*	*hsa-miR-381-5p*	MirTarBase
LONRF3	*hsa-miR-433-3p*	MirTarBase	*YWHAZ*	*hsa-miR-661*	MirTarBase
LPGAT1	*hsa-let-7a-5p*	DIANA TOOLS	*YY1*	*hsa-let-7a-5p*	DIANA TOOLS
LPIN3	*hsa-miR-661*	MirTarBase	*ZADH2*	*hsa-miR-661*	MirTarBase
LRCH1	*hsa-miR-25-3p*	DIANA TOOLS	*ZADH2*	*hsa-miR-661*	MirTarBase
LRIF1	*hsa-miR-661*	MirTarBase	*ZADH2*	*hsa-miR-661*	MirTarBase
LRIG1	*hsa-miR-15b-5p*	DIANA TOOLS	*ZADH2*	*hsa-miR-661*	MirTarBase
LRIG1	*hsa-miR-16-5p*	DIANA TOOLS	*ZBTB10*	*hsa-let-7a-5p*	DIANA TOOLS
LRIG1	*hsa-miR-130a-3p*	DIANA TOOLS	*ZBTB18*	*hsa-miR-130a-3p*	DIANA TOOLS
LRIG2	*hsa-let-7a-5p*	DIANA TOOLS	*ZBTB20*	*hsa-miR-142-3p*	DIANA TOOLS
LRIG2	*hsa-miR-15b-5p*	DIANA TOOLS	*ZBTB26*	*hsa-let-7a-5p*	DIANA TOOLS
LRIG2	*hsa-miR-16-5p*	DIANA TOOLS	*ZBTB34*	*hsa-miR-15b-5p*	DIANA TOOLS
LRIG3	*hsa-miR-433-3p*	MirTarBase	*ZBTB34*	*hsa-miR-16-5p*	DIANA TOOLS
LRRC1	*hsa-miR-22-3p*	DIANA TOOLS	*ZBTB37*	*hsa-let-7a-5p*	DIANA TOOLS
LRRC57	*hsa-miR-21-5p*	DIANA TOOLS	*ZBTB38*	*hsa-miR-200c-3p*	DIANA TOOLS
LRRC58	*hsa-miR-200c-3p*	DIANA TOOLS	*ZBTB39*	*hsa-miR-22-3p*	DIANA TOOLS
LRRC59	*hsa-miR-31-5p*	DIANA TOOLS	*ZBTB39*	*hsa-miR-16-5p*	DIANA TOOLS

LRRK1	*hsa-miR-16-5p*	DIANA TOOLS	*ZBTB39*	*hsa-miR-15b-5p*	DIANA TOOLS
LRRK1	*hsa-miR-15b-5p*	DIANA TOOLS	*ZBTB4*	*hsa-miR-130a-3p*	DIANA TOOLS
LSM11	*hsa-miR-15b-5p*	DIANA TOOLS	*ZBTB4*	*hsa-miR-93-5p*	DIANA TOOLS
LSM11	*hsa-miR-16-5p*	DIANA TOOLS	*ZBTB44*	*hsa-miR-661*	MirTarBase
LSM11	*hsa-miR-661*	MirTarBase	*ZBTB46*	*hsa-miR-15b-5p*	DIANA TOOLS
LTBP3	*hsa-miR-16-5p*	DIANA TOOLS	*ZBTB46*	*hsa-miR-16-5p*	DIANA TOOLS
LUZP1	*hsa-miR-16-5p*	DIANA TOOLS	*ZBTB5*	*hsa-miR-200c-3p*	DIANA TOOLS
LUZP1	*hsa-miR-15b-5p*	DIANA TOOLS	*ZBTB7A*	*hsa-miR-130a-3p*	DIANA TOOLS
LY9	*hsa-miR-16-5p*	DIANA TOOLS	*ZBTB7A*	*hsa-miR-93-5p*	DIANA TOOLS
LY9	*hsa-miR-15b-5p*	DIANA TOOLS	*ZBTB8B*	*hsa-miR-661*	MirTarBase
LYRM4	*hsa-miR-661*	MirTarBase	*ZBTB8B*	*hsa-miR-661*	MirTarBase
LYRM4	*hsa-miR-661*	MirTarBase	*ZC3H4*	*hsa-miR-200c-3p*	DIANA TOOLS
LYRM7	*hsa-miR-21-5p*	DIANA TOOLS	*ZC3HAV1*	*hsa-miR-661*	MirTarBase
LYZ	*hsa-miR-661*	MirTarBase	*ZCCHC14*	*hsa-miR-130a-3p*	DIANA TOOLS
M6PR	*hsa-miR-130a-3p*	DIANA TOOLS	*ZCCHC14*	*hsa-miR-142-3p*	DIANA TOOLS
M6PR	*hsa-miR-93-5p*	DIANA TOOLS	*ZCCHC9*	*hsa-let-7a-5p*	DIANA TOOLS
MACF1	*hsa-let-7a-5p*	DIANA TOOLS	*ZDHHC15*	*hsa-miR-544a*	DIANA TOOLS
MACF1	*hsa-miR-544a*	DIANA TOOLS	*ZDHHC16*	*hsa-miR-16-5p*	DIANA TOOLS
MAFB	*hsa-miR-130a-3p*	DIANA TOOLS	*ZDHHC18*	*hsa-miR-661*	MirTarBase
MAFF	*hsa-miR-130a-3p*	DIANA TOOLS	*ZDHHC21*	*hsa-miR-15b-5p*	DIANA TOOLS
MAFK	*hsa-miR-15b-5p*	DIANA TOOLS	*ZDHHC23*	*hsa-miR-15b-5p*	DIANA TOOLS
MAFK	*hsa-miR-16-5p*	DIANA TOOLS	*ZDHHC23*	*hsa-miR-130a-3p*	DIANA TOOLS
MAFK	*hsa-miR-433-3p*	MirTarBase	*ZEB1*	*hsa-miR-200c-3p*	DIANA TOOLS
MAGI3	*hsa-miR-661*	MirTarBase	*ZEB1*	*hsa-miR-144-3p*	MirTarBase
MAGI3	*hsa-miR-661*	MirTarBase	*ZEB2*	*hsa-miR-200c-3p*	DIANA TOOLS
MAGI3	*hsa-miR-661*	MirTarBase	*ZEB2*	*hsa-miR-142-3p*	DIANA TOOLS
MALT1	*hsa-miR-21-5p*	DIANA TOOLS	*ZEB2*	*hsa-miR-144-3p*	MirTarBase
MAN2A1	*hsa-miR-25-3p*	DIANA TOOLS	*ZER1*	*hsa-miR-661*	MirTarBase
MANBAL	*hsa-miR-142-3p*	DIANA TOOLS	*ZFAND6*	*hsa-miR-200c-3p*	DIANA TOOLS
MAP1B	*hsa-miR-31-5p*	DIANA TOOLS	*ZFC3H1*	*hsa-miR-25-3p*	DIANA TOOLS
MAP1B	*hsa-miR-190b*	DIANA TOOLS	*ZFHX3*	*hsa-miR-16-5p*	DIANA TOOLS
MAP1B	*hsa-miR-25-3p*	DIANA TOOLS	*ZFHX3*	*hsa-miR-25-3p*	DIANA TOOLS
MAP1S	*hsa-miR-16-5p*	DIANA TOOLS	*ZFHX3*	*hsa-miR-15b-5p*	DIANA TOOLS
MAP2K1	*hsa-miR-16-5p*	DIANA TOOLS	*ZFHX4*	*hsa-let-7a-5p*	DIANA TOOLS
MAP2K1	*hsa-miR-15b-5p*	DIANA TOOLS	*ZFHX4*	*hsa-miR-15b-5p*	DIANA TOOLS
MAP2K4	*hsa-miR-25-3p*	DIANA TOOLS	*ZFHX4*	*hsa-miR-16-5p*	DIANA TOOLS
MAP3K1	*hsa-let-7a-5p*	DIANA TOOLS	*ZFP36L2*	*hsa-miR-144-3p*	DIANA TOOLS
MAP3K5	*hsa-miR-93-5p*	DIANA TOOLS	*ZFP36L2*	*hsa-miR-142-3p*	DIANA TOOLS
MAP3K8	*hsa-miR-144-3p*	MirTarBase	*ZFP69B*	*hsa-miR-661*	MirTarBase
MAP3K9	*hsa-miR-130a-3p*	DIANA TOOLS	*ZFP91*	*hsa-miR-22-3p*	DIANA TOOLS
MAP3K9	*hsa-miR-93-5p*	DIANA TOOLS	*ZFPM2*	*hsa-miR-200c-3p*	DIANA TOOLS
MAP4K3	*hsa-let-7a-5p*	DIANA TOOLS	*ZFX*	*hsa-miR-144-3p*	MirTarBase
MAP4K4	*hsa-let-7a-5p*	MirTarBase	*ZFYVE20*	*hsa-miR-16-5p*	DIANA TOOLS
MAP7	*hsa-miR-15b-5p*	DIANA TOOLS	*ZFYVE20*	*hsa-miR-15b-5p*	DIANA TOOLS
MAP7	*hsa-miR-16-5p*	DIANA TOOLS	*ZFYVE21*	*hsa-miR-25-3p*	DIANA TOOLS
MAPK6	*hsa-let-7a-5p*	DIANA TOOLS	*ZFYVE26*	*hsa-miR-93-5p*	DIANA TOOLS
MAPK8	*hsa-miR-15b-5p*	DIANA TOOLS	*ZFYVE26*	*hsa-let-7a-5p*	DIANA TOOLS
MAPK8	*hsa-miR-16-5p*	DIANA TOOLS	*ZFYVE9*	*hsa-miR-130a-3p*	DIANA TOOLS

MAPK8	*hsa-let-7a-5p*	DIANA TOOLS	*ZHX1*	*hsa-miR-25-3p*	DIANA TOOLS
MAPK8	*hsa-miR-433-3p*	MirTarBase	*ZIC5*	*hsa-miR-130a-3p*	DIANA TOOLS
MAPRE1	*hsa-miR-200c-3p*	DIANA TOOLS	*ZKSCAN1*	*hsa-miR-144-3p*	DIANA TOOLS
MAPRE3	*hsa-miR-93-5p*	DIANA TOOLS	*ZMAT3*	*hsa-miR-200c-3p*	DIANA TOOLS
MARCH1	*hsa-miR-190b*	DIANA TOOLS	*ZMAT3*	*hsa-miR-15b-5p*	DIANA TOOLS
MARCH6	*hsa-miR-661*	MirTarBase	*ZMAT3*	*hsa-miR-130a-3p*	DIANA TOOLS
MARCH8	*hsa-miR-22-3p*	DIANA TOOLS	*ZMAT3*	*hsa-miR-16-5p*	DIANA TOOLS
MARCH8	*hsa-miR-25-3p*	DIANA TOOLS	*ZMYM4*	*hsa-miR-22-3p*	DIANA TOOLS
MARCH8	*hsa-miR-200c-3p*	DIANA TOOLS	*ZMYND8*	*hsa-miR-142-3p*	DIANA TOOLS
MARS2	*hsa-let-7a-5p*	DIANA TOOLS	*ZNF101*	*hsa-miR-661*	MirTarBase
MAST4	*hsa-miR-25-3p*	DIANA TOOLS	*ZNF12*	*hsa-miR-93-5p*	DIANA TOOLS
MAX	*hsa-miR-22-3p*	DIANA TOOLS	*ZNF148*	*hsa-miR-93-5p*	DIANA TOOLS
MB21D2	*hsa-miR-130a-3p*	DIANA TOOLS	*ZNF157*	*hsa-miR-661*	MirTarBase
MBD3	*hsa-miR-661*	MirTarBase	*ZNF200*	*hsa-let-7a-5p*	DIANA TOOLS
MBD6	*hsa-miR-142-3p*	DIANA TOOLS	*ZNF207*	*hsa-miR-144-3p*	DIANA TOOLS
MBNL1	*hsa-miR-130a-3p*	DIANA TOOLS	*ZNF217*	*hsa-miR-144-3p*	DIANA TOOLS
MBNL1	*hsa-miR-144-3p*	DIANA TOOLS	*ZNF217*	*hsa-miR-130a-3p*	DIANA TOOLS
MBNL1	*hsa-miR-433-3p*	MirTarBase	*ZNF217*	*hsa-miR-142-3p*	DIANA TOOLS
MBNL2	*hsa-miR-15b-5p*	DIANA TOOLS	*ZNF217*	*hsa-miR-200c-3p*	DIANA TOOLS
MBNL2	*hsa-miR-16-5p*	DIANA TOOLS	*ZNF250*	*hsa-miR-130a-3p*	DIANA TOOLS
MBOAT7	*hsa-miR-15b-5p*	DIANA TOOLS	*ZNF277*	*hsa-miR-661*	MirTarBase
MBOAT7	*hsa-miR-16-5p*	DIANA TOOLS	*ZNF277*	*hsa-miR-661*	MirTarBase
MCCC2	*hsa-miR-661*	MirTarBase	*ZNF280B*	*hsa-miR-661*	MirTarBase
MCCC2	*hsa-miR-661*	MirTarBase	*ZNF281*	*hsa-miR-200c-3p*	DIANA TOOLS
MCF2L2	*hsa-miR-661*	MirTarBase	*ZNF292*	*hsa-miR-661*	MirTarBase
MCFD2	*hsa-miR-200c-3p*	DIANA TOOLS	*ZNF3*	*hsa-miR-130a-3p*	DIANA TOOLS
MCL1	*hsa-miR-661*	MirTarBase	*ZNF302*	*hsa-miR-200c-3p*	DIANA TOOLS
MCRS1	*hsa-miR-22-3p*	DIANA TOOLS	*ZNF317*	*hsa-miR-661*	MirTarBase
MCTS1	*hsa-miR-661*	MirTarBase	*ZNF326*	*hsa-miR-21-5p*	DIANA TOOLS
MDFIC	*hsa-miR-130a-3p*	DIANA TOOLS	*ZNF331*	*hsa-miR-661*	MirTarBase
MDM2	*hsa-miR-661*	MirTarBase	*ZNF343*	*hsa-let-7a-5p*	DIANA TOOLS
MDM2	*hsa-miR-661*	MirTarBase	*ZNF367*	*hsa-miR-21-5p*	DIANA TOOLS
MDM4	*hsa-let-7a-5p*	DIANA TOOLS	*ZNF367*	*hsa-miR-15b-5p*	DIANA TOOLS
MDM4	*hsa-miR-130a-3p*	DIANA TOOLS	*ZNF367*	*hsa-miR-16-5p*	DIANA TOOLS
MDM4	*hsa-miR-433-3p*	MirTarBase	*ZNF367*	*hsa-miR-144-3p*	DIANA TOOLS
MDM4	*hsa-miR-661*	MirTarBase	*ZNF383*	*hsa-miR-661*	MirTarBase
MECP2	*hsa-miR-130a-3p*	DIANA TOOLS	*ZNF41*	*hsa-miR-25-3p*	DIANA TOOLS
MED1	*hsa-miR-200c-3p*	DIANA TOOLS	*ZNF417*	*hsa-miR-661*	MirTarBase
MED13	*hsa-miR-200c-3p*	DIANA TOOLS	*ZNF43*	*hsa-miR-661*	MirTarBase
MED28	*hsa-miR-509-3-5p*	DIANA TOOLS	*ZNF43*	*hsa-miR-661*	MirTarBase
MED28	*hsa-let-7a-5p*	DIANA TOOLS	*ZNF430*	*hsa-miR-25-3p*	DIANA TOOLS
MED28	*hsa-miR-661*	MirTarBase	*ZNF451*	*hsa-let-7a-5p*	DIANA TOOLS
MED28	*hsa-miR-661*	MirTarBase	*ZNF451*	*hsa-miR-130a-3p*	DIANA TOOLS
MED4	*hsa-miR-190b*	DIANA TOOLS	*ZNF451*	*hsa-miR-661*	MirTarBase
MED8	*hsa-let-7a-5p*	DIANA TOOLS	*ZNF460*	*hsa-miR-661*	MirTarBase
MEDAG	*hsa-miR-142-3p*	DIANA TOOLS	*ZNF460*	*hsa-miR-661*	MirTarBase

MEF2D	*hsa-miR-25-3p*	DIANA TOOLS	*ZNF460*	*hsa-miR-661*	MirTarBase
MEOX2	*hsa-miR-130a-3p*	DIANA TOOLS	*ZNF507*	*hsa-miR-144-3p*	DIANA TOOLS
MET	*hsa-miR-130a-3p*	DIANA TOOLS	*ZNF512B*	*hsa-let-7a-5p*	DIANA TOOLS
MET	*hsa-miR-433-3p*	MirTarBase	*ZNF543*	*hsa-let-7a-5p*	DIANA TOOLS
MET	*hsa-miR-144-3p*	MirTarBase	*ZNF543*	*hsa-miR-661*	MirTarBase
METTL8	*hsa-miR-661*	MirTarBase	*ZNF554*	*hsa-miR-661*	MirTarBase
MFAP3L	*hsa-miR-93-5p*	DIANA TOOLS	*ZNF555*	*hsa-miR-661*	MirTarBase
MFN2	*hsa-miR-93-5p*	DIANA TOOLS	*ZNF584*	*hsa-miR-433-3p*	MirTarBase
MFSD12	*hsa-let-7a-5p*	DIANA TOOLS	*ZNF584*	*hsa-miR-433-3p*	MirTarBase
MFSD14C	*hsa-miR-661*	MirTarBase	*ZNF607*	*hsa-miR-381-5p*	MirTarBase
MFSD4	*hsa-let-7a-5p*	DIANA TOOLS	*ZNF610*	*hsa-miR-661*	MirTarBase
MGA	*hsa-miR-200c-3p*	DIANA TOOLS	*ZNF614*	*hsa-miR-130a-3p*	DIANA TOOLS
MGA	*hsa-let-7a-5p*	DIANA TOOLS	*ZNF616*	*hsa-miR-25-3p*	DIANA TOOLS
MGAT4A	*hsa-miR-15b-5p*	DIANA TOOLS	*ZNF622*	*hsa-miR-16-5p*	DIANA TOOLS
MGAT4A	*hsa-miR-142-3p*	DIANA TOOLS	*ZNF622*	*hsa-miR-15b-5p*	DIANA TOOLS
MGAT4A	*hsa-let-7a-5p*	DIANA TOOLS	*ZNF638*	*hsa-miR-144-3p*	DIANA TOOLS
MGAT4A	*hsa-miR-144-3p*	DIANA TOOLS	*ZNF641*	*hsa-miR-661*	MirTarBase
MGAT4A	*hsa-miR-16-5p*	DIANA TOOLS	*ZNF644*	*hsa-let-7a-5p*	DIANA TOOLS
MGEA5	*hsa-miR-93-5p*	DIANA TOOLS	*ZNF646*	*hsa-miR-661*	MirTarBase
MGMT	*hsa-miR-661*	MirTarBase	*ZNF646*	*hsa-miR-661*	MirTarBase
MGST1	*hsa-miR-130a-3p*	DIANA TOOLS	*ZNF675*	*hsa-miR-190b*	DIANA TOOLS
MIA3	*hsa-miR-25-3p*	DIANA TOOLS	*ZNF689*	*hsa-let-7a-5p*	DIANA TOOLS
MIB1	*hsa-miR-15b-5p*	DIANA TOOLS	*ZNF695*	*hsa-miR-661*	MirTarBase
MIB1	*hsa-miR-16-5p*	DIANA TOOLS	*ZNF695*	*hsa-miR-661*	MirTarBase
MID1IP1	*hsa-miR-130a-3p*	DIANA TOOLS	*ZNF697*	*hsa-miR-16-5p*	DIANA TOOLS
MIDN	*hsa-miR-381-5p*	MirTarBase	*ZNF697*	*hsa-miR-15b-5p*	DIANA TOOLS
MIEF1	*hsa-miR-509-3p*	DIANA TOOLS	*ZNF697*	*hsa-miR-200c-3p*	DIANA TOOLS
MIEF1	*hsa-miR-200c-3p*	DIANA TOOLS	*ZNF704*	*hsa-miR-93-5p*	DIANA TOOLS
MIER1	*hsa-miR-130a-3p*	DIANA TOOLS	*ZNF710*	*hsa-let-7a-5p*	DIANA TOOLS
MIER3	*hsa-miR-25-3p*	DIANA TOOLS	*ZNF711*	*hsa-miR-130a-3p*	DIANA TOOLS
MIGA1	*hsa-miR-661*	MirTarBase	*ZNF711*	*hsa-miR-200c-3p*	DIANA TOOLS
MINK1	*hsa-miR-16-5p*	DIANA TOOLS	*ZNF716*	*hsa-miR-661*	MirTarBase
MKL1	*hsa-miR-130a-3p*	DIANA TOOLS	*ZNF721*	*hsa-miR-25-3p*	DIANA TOOLS
MKL2	*hsa-miR-200c-3p*	DIANA TOOLS	*ZNF730*	*hsa-miR-661*	MirTarBase
MKLN1	*hsa-miR-200c-3p*	DIANA TOOLS	*ZNF766*	*hsa-miR-661*	MirTarBase
MKNK2	*hsa-miR-93-5p*	DIANA TOOLS	*ZNF780A*	*hsa-miR-433-3p*	MirTarBase
MLH1	*hsa-miR-661*	MirTarBase	*ZNF800*	*hsa-miR-130a-3p*	DIANA TOOLS
MLLT1	*hsa-miR-661*	MirTarBase	*ZNF800*	*hsa-miR-144-3p*	DIANA TOOLS
MLLT1	*hsa-miR-661*	MirTarBase	*ZNF827*	*hsa-miR-144-3p*	DIANA TOOLS
MLLT10	*hsa-let-7a-5p*	DIANA TOOLS	*ZNF835*	*hsa-miR-661*	MirTarBase
MLLT10	*hsa-miR-130a-3p*	DIANA TOOLS	*ZNF850*	*hsa-miR-661*	MirTarBase
MLXIP	*hsa-miR-142-3p*	DIANA TOOLS	*ZNF865*	*hsa-miR-661*	MirTarBase
MMD	*hsa-miR-15b-5p*	DIANA TOOLS	*ZNF865*	*hsa-miR-661*	MirTarBase
MMD	*hsa-miR-25-3p*	DIANA TOOLS	*ZNF865*	*hsa-miR-661*	MirTarBase
MMD	*hsa-miR-200c-3p*	DIANA TOOLS	*ZNF865*	*hsa-miR-661*	MirTarBase
MMS19	*hsa-miR-16-5p*	DIANA TOOLS	*ZNF865*	*hsa-miR-661*	MirTarBase
MNT	*hsa-miR-16-5p*	DIANA TOOLS	*ZNF878*	*hsa-miR-661*	MirTarBase
MNT	*hsa-miR-15b-5p*	DIANA TOOLS	*ZNF880*	*hsa-miR-15b-5p*	DIANA TOOLS

MOAP1	*hsa-miR-25-3p*	DIANA TOOLS	*ZNF880*	*hsa-miR-16-5p*	DIANA TOOLS
MOB3B	*hsa-miR-15b-5p*	DIANA TOOLS	*ZNFX1*	*hsa-miR-93-5p*	DIANA TOOLS
MOB3B	*hsa-miR-16-5p*	DIANA TOOLS	*ZNRF2*	*hsa-miR-15b-5p*	DIANA TOOLS
MOB4	*hsa-miR-142-3p*	DIANA TOOLS	*ZNRF2*	*hsa-miR-16-5p*	DIANA TOOLS
MOB4	*hsa-miR-15b-5p*	DIANA TOOLS	*ZNRF3*	*hsa-miR-16-5p*	DIANA TOOLS
MOB4	*hsa-miR-16-5p*	DIANA TOOLS	*ZNRF3*	*hsa-miR-15b-5p*	DIANA TOOLS
MON2	*hsa-miR-16-5p*	DIANA TOOLS	*ZSWIM6*	*hsa-miR-31-5p*	DIANA TOOLS
MON2	*hsa-miR-15b-5p*	DIANA TOOLS	*ZSWIM6*	*hsa-miR-21-5p*	DIANA TOOLS
MON2	*hsa-miR-661*	MirTarBase	*ZYG11A*	*hsa-miR-661*	MirTarBase
MORC3	*hsa-miR-200c-3p*	DIANA TOOLS	*ZYG11B*	*hsa-miR-200c-3p*	DIANA TOOLS
MORF4L2	*hsa-miR-142-3p*	DIANA TOOLS	*ZYX*	*hsa-miR-16-5p*	DIANA TOOLS
MPHOSPH9	*hsa-miR-130a-3p*	DIANA TOOLS	*ZYX*	*hsa-miR-15b-5p*	DIANA TOOLS
MPL	*hsa-let-7a-5p*	MirTarBase			

Table S4B. All the pathways KEGG identified by algorithm microT-CDS (v.5) (DIANA-miRPath v.3) involved on miRDE.

KEGG Pathways	*p*-Value
Fatty acid biosynthesis (hsa00061)	$1.99x10^{-20}$
Prion diseases (hsa05020)	$9.48x10^{-20}$
FoxO signaling pathway (hsa04068)	$6.60x10^{-09}$
Proteoglycans in cancer (hsa05205)	$1.30x10^{-06}$
mTOR signaling pathway (hsa04150)	$3.09x10^{-06}$
Pathways in cancer (hsa05200)	$5.21x10^{-06}$
Viral carcinogenesis (hsa05203)	$5.94x10^{-06}$
Glioma (hsa05214)	$1.11x10^{-05}$
p53 signaling pathway (hsa04115)	$1.14x10^{-05}$
Prostate cancer (hsa05215)	$4.35x10^{-05}$
PI3K-Akt signaling pathway (hsa04151)	$5.79x10^{-05}$
Pancreatic cancer (hsa05212)	$7.24x10^{-05}$
TGF-beta signaling pathway (hsa04350)	$8.51x10^{-05}$
Chronic myeloid leukemia (hsa05220)	0.0001317
Small cell lung cancer (hsa05222)	0.0001311
Hippo signaling pathway (hsa04390)	0.0001311
Lysine degradation (hsa00310)	0.0001340
Oocyte meiosis (hsa04114)	0.0001840
Focal adhesion (hsa04510)	0.0003299
Signaling pathways regulating pluripotency of stem cells (hsa04550)	0.0003899
Colorectal cancer (hsa05210)	0.0008778
Non-small cell lung cancer (hsa05223)	0.0016059
Endocytosis (hsa04144)	0.0016498
Melanoma (hsa05218)	0.0016498
Hepatitis B (hsa05161)	0.0023706
ErbB signaling pathway (hsa04012)	0.0025655
Cell cycle (hsa04110)	0.0046496
Renal cell carcinoma (hsa05211)	0.0067122
Sphingolipid signaling pathway (hsa04071)	0.0067648
Bacterial invasion of epithelial cells (hsa05100)	0.0070238
Axon guidance (hsa04360)	0.0079788
MAPK signaling pathway (hsa04010)	0.0087827
Regulation of actin cytoskeleton (hsa04810)	0.0087827
Neurotrophin signaling pathway (hsa04722)	0.0089922
Fatty acid metabolism (hsa01212)	0.0104633
Sphingolipid metabolism (hsa00600)	0.0111284
AMPK signaling pathway (hsa04152)	0.0115611
MicroRNAs in cancer (hsa05206)	0.0123909
Circadian rhythm (hsa04710)	0.0130263
Insulin signaling pathway (hsa04910)	0.0130263
Ubiquitin mediated proteolysis (hsa04120)	0.0185432
Progesterone-mediated oocyte maturation (hsa04914)	0.0415534
Adherens junction (hsa04520)	0.0458059

Table S4C. Top pathways KEGG identified by microT-CDS (v.5) (DIANA-miRPath v.3) involved on top miRDE.

KEGG Pathways	*p*-Value	genes	miRNAs	Name miRDE
Fatty acid biosynthesis (hsa00061)	<1e-325	3	2	hsa-miR-15b-5p, hsa-miR-16-5p
Prion Diseases (hsa05020)	<1e-325	1	2	hsa-miR-130a-3p, hsa-miR-495-3p
MicroRNAs in cancer (hsa05206)	<1e-325	38	8	*hsa-miR-130a-3p, hsa-miR-200c-3p, hsa-miR-205-5p, hsa-miR-21-5p, hsa-miR-22-3p, hsa-miR-495-3p, hsa-miR-508-3p, hsa-miR-509-3-5p*
Hippo signaling pathway (hsa04390)	<1e-325	21	9	*hsa-miR-15b-5p, hsa-miR-16-5p, hsa-miR-205-5p, hsa-miR-21-5p, hsa-miR-1206, hsa-miR-433-3p, hsa-miR-495-3p, hsa-miR-509-3-5p, hsa-miR-509-3p*
TGF-beta signaling pathway (hsa04350)	3.35e-10	15	9	*hsa-miR-130a-3p, hsa-miR-15b-5p, hsa-miR-16-5p, hsa-miR-200c-3p, hsa-miR-21-5p, hsa-miR-1206, hsa-miR-433-3p, hsa-miR-495-3p, hsa-miR-509-3-5p*
Oocyte meiosis (hsa04114)	5.1e-12	22	9	*hsa-let-7a-5p, hsa-miR-15b-5p, hsa-miR-16-5p, hsa-miR-200c-3p, hsa-miR-205-5p, hsa-miR-25-3p, hsa-miR-433-3p, hsa-miR-495-3p, hsa-miR-509-3-5p*
Lysine Degradation (hsa00310)	5.82e-12	9	6	*hsa-miR-15b-5p, hsa-miR-200c-3p, hsa-miR-1206, hsa-miR-190b, hsa-miR-495-3p, hsa-miR-508-3p*
Glioma (hsa05214)	4.7e-09	13	7	*hsa-miR-15b-5p, hsa-miR-16-5p, hsa-miR-205-5p, hsa-miR-22-3p, hsa-miR-144-3p, hsa-miR-495-3p, hsa-miR-509-3-5p*
FoxO signaling pathway (hsa04068)	4.49e-09	33	8	*hsa-let-7a-5p, hsa-miR-130a-3p, hsa-miR-16-5p, hsa-miR-200c-3p, hsa-miR-21-5p, hsa-miR-223-3p, hsa-miR-495-3p, hsa-miR-509-3-5p*
Signaling pathways that regulate stem cell pluripotency (hsa04550)	2.28e-07	24	8	*hsa-let-7a-5p, hsa-miR-15b-5p, hsa-miR-16-5p, hsa-miR-21-5p, hsa-miR-1206, hsa-miR-495-3p, hsa-miR-509-3-5p, hsa-miR-544a*
Prostate cancer (hsa05215)	8.31e-07	19	5	*hsa-miR-15b-5p, hsa-miR-16-5p, hsa-miR-205-5p, hsa-miR-495-3p, hsa-miR-509-3-5p*
Proteoglycans in cancer (hsa05205)	1.5e-06	35	8	*hsa-miR-15b-5p, hsa-miR-16-5p, hsa-miR-200c-3p, hsa-miR-205-5p, hsa-miR-22-3p, hsa-miR-93-5p, hsa-miR-144-3p, hsa-miR-495-3p*
P53 signaling pathway (hsa04115)	3.58e-05	20	6	hsa-miR-130a-3p, hsa-miR-15b-5p, hsa-miR-16-5p, hsa-miR-200c-3p, hsa-miR-22-3p, hsa-miR-495-3p
mTOR signaling pathway (hsa04150)	0.000147	18	5	*hsa-miR-130a-3p, hsa-miR-15b-5p, hsa-miR-16-5p, hsa-miR-22-3p, hsa-miR-495-3p*
Fatty Acid Metabolism (hsa01212)	0.000170	5	2	*hsa-miR-15b-5p, hsa-miR-16-5p*
Pathways in cancer (hsa05200)	0.000216	46	5	*hsa-miR-15b-5p, hsa-miR-16-5p, hsa-miR-93-5p, hsa-miR-495-3p, hsa-miR-509-3-5p*
Progesterone-mediated oocyte maturation (hsa04914)	0.003416	12	4	*hsa-let-7a-5p, hsa-miR-15b-5p, hsa-miR-16-5p, hsa-miR-21-5p*
Melanoma (hsa05218)	0.004781	12	5	hsa-miR-15b-5p, hsa-miR-16-5p, hsa-miR-22-3p, hsa-miR-495-3p, hsa-miR-509-3-5p
Pancreatic cancer (hsa05212)	0.005685	15	6	hsa-miR-15b-5p, hsa-miR-16-5p, hsa-miR-21-5p, hsa-miR-22-3p, hsa-miR-144-3p, hsa-miR-495-3p
PI3K-Akt signaling pathway (hsa04151)	0.008609	36	4	hsa-miR-15b-5p, hsa-miR-16-5p, hsa-miR-495-3p, hsa-miR-509-3p
Chronic myeloid leukemia (hsa05220)	0.019080	15	4	hsa-miR-15b-5p, hsa-miR-22-3p, hsa-miR-93-5p, hsa-miR-495-3p
Endocytosis (hsa04144)	0.036855	16	2	hsa-miR-130a-3p, hsa-miR-509-3-5p

Anexo D - Demais Publicações

Molecular Carcinogenesis; Qualis: A1 | IF: 5.139

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RESEARCH ARTICLE

Molecular Carcinogenesis WILEY

Genomic profiling reveals the pivotal role of hrHPV driving copy number and gene expression alterations, including mRNA downregulation of *TP53* and *RB1* in penile cancer

Juliana Macedo[1] | Elis Silva[2] | Leudivan Nogueira[3] | Ronald Coelho[3] | Jenilson da Silva[1,2] | Alcione dos Santos[4] | Antônio Augusto Teixeira-Júnior[5] | Marta Belfort[1] | Gyl Silva[5] | André Khayat[6] | Edivaldo de Oliveira[7] | Ana Paula dos Santos[8] | Luciane R. Cavalli[9,10] | Silma Regina Pereira[2]

[1]Postgraduate Program in Health Science, Federal University of Maranhão, São Luís, Maranhão, Brazil

[2]Laboratory of Genetics and Molecular Biology, Department of Biology, Federal University of Maranhão, São Luís, Maranhão, Brazil

[3]Aldenora Bello Cancer Hospital, São Luís, Maranhão, Brazil

[4]Public Health Department, Federal University of Maranhão, São Luís, Maranhão, Brazil

[5]Biology Undergraduate Course, Department of Pathology, Federal University of Maranhão, São Luís, Maranhão, Brazil

[6]Oncology Research Center, Federal University of Pará, Belém, Pará, Brazil

[7]Tissue Culture and Cytogenetics Laboratory, Institute of Evandro Chagas, Belém, Pará, Brazil

[8]Department of Physiological Sciences, Federal University of Maranhão, São Luís, Maranhão, Brazil

[9]Faculdades Pequeno Príncipe, Instituto de Pesquisa Pelé Pequeno Príncipe, Curitiba, Paraná, Brazil

[10]Department of Oncology, Georgetown Lombardi Comprehensive Cancer Center, Washington, District of Columbia, United States

Correspondence
Silma Regina Pereira, Department of Biology, Federal University of Maranhão, Avenida dos Portugueses, 1966 Bacanga, CEP: 65080-805, São Luís, Brazil.
Email: silmaregina@yahoo.com.br

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Abstract

The incidence of penile cancer (PeCa) is increasing worldwide, however, the highest rates are reported in underdeveloped countries. The molecular mechanisms that underly the onset and progression of these tumors are still unclear. Therefore, our goal was to determine the genome-wide copy number alterations and the involvement of human papiloma virus (HPV) (*TP53* and *RB1*), inflammatory (*COX2* and *EGFR*), and PI3K/AKT pathway (*AKT1*, *AKT2*, *EGFR*, *ERBB3*, *ERBB4*, *PIK3CA*, and *PTEN*) associated genes in patients with PeCa from a high incidence region in Brazil (Maranhão). HPV genotyping was performed by nest-PCR and genome sequencing, copy number alterations (CNAs) by array comparative genomic hybridization and gene copy number *status*, gene, and protein expression by quantitative polymerase chain reaction, reverse transcriptase-quantitative polymerase chain reaction, and immunohistochemistry, respectively. HPV genotyping revealed one of the highest frequencies of HPV reported in PeCa, affecting 96.4% of the cases. The most common CNAs observed were located at the HPV integration sites, such as 2p12-p11.2 and 14q32.33, where

Abbreviations: aCGH, array comparative genomic hybridization; CNA, copy number alteration; Cq, quantification cycle; FFPE, formalin-fixed paraffin-embedded; HPV, human papiloma virus; HrHPV, High risk HPV; IHCi, mmunohistochemistry; PCR, polymerase chain reaction; PeCa, penile cancer; qPCR, quantitative polymerase chain reaction; RT-qPCR, reverse transcriptase-quantitative polymerase chain reaction; TMA, tissue microarray.

Cancers; | Qualis: A1; IF: 6.575

cancers

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Article

Mutational Signature and Integrative Genomic Analysis of Human Papillomavirus-Associated Penile Squamous Cell Carcinomas from Latin American Patients

Luisa Matos do Canto [1,†], Jenilson Mota da Silva [2,3,†], Patrícia Valéria Castelo-Branco [3], Ingrid Monteiro da Silva [3], Jenilson Mota da Silva [2,3,†], Leudivan Nogueira [4], Carlos Eduardo Fonseca-Alves [5], André Khayat [6], Alexander Birbrair [7,8,9] and Silma Regina Pereira [3,*]

1 Clinical Genetics Department, University Hospital of Southern Denmark, 7100 Vejle, Denmark; luisaamatos@gmail.com
2 Postgraduate Program in Health Science, Federal University of Maranhão, São Luis 65080-805, MA, Brazil; jenilson.motadasilva@gmail.com
3 Laboratory of Genetics and Molecular Biology, Department of Biology, Federal University of Maranhão, São Luis 65080-805, MA, Brazil; patricia.valeria@ufma.br (J.V.C.-S.); ingrid.monteiro@discente.ufma.br (I.M.d.S.)
4 Aldenora Bello Cancer Hospital, São Luis 65031-630, MA, Brazil; leudivan.nogueira@gmail.com
5 Health Science Institute, Paulista University, Bauru 186085-500, SP, Brazil; carloseduardofa@hotmail.com
6 Oncology Research Center, Federal University of Pará, Belém 66073-005, PA, Brazil; andresk@ufpa.br
7 Department of Dermatology, School of Medicine and Public Health, University of Wisconsin-Madison, Madison, WI 53706, USA; birbrair@wisc.edu
8 Department of Pathology, Federal University of Minas Gerais, Belo Horizonte 31270-901, MG, Brazil
9 Department of Radiology, Columbia University Medical Center, New York, NY 10032, USA
* Correspondence: silma.pereira@ufma.br; Tel.: +55-98-32728543
† These authors contributed equally to this paper.

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Simple Summary: DNA sequencing has been crucial to comprehending cancer mutational patterns, leading to the identification of driver genes and altered signaling pathways. Thus, identifying new pathogenic variants and their impact on tumor onset, progression, and treatment response has fueled tumor biology research. Here, we present novel findings addressing the first whole-exome sequencing (WES) of human papillomavirus (HPV)-associated penile squamous cell carcinoma (PSCC) from Latin Americans and its association with pathogenesis. We also compared the molecular profile of the tumors to that of three previous studies from populations with different genetic and socioeconomic backgrounds, the majority of which was HPV-negative. We describe the most altered genes and the main pathogenic variants found in the Latin Americans, ten of which are exclusive to our study sample. The data allowed us to identify molecular pathways and druggable targets with potential treatment value for this still-neglected HPV-associated carcinoma.

Abstract: High-throughput DNA sequencing has allowed for the identification of genomic alterations and their impact on tumor development, progression, and therapeutic responses. In PSCC, for which the incidence has progressively increased worldwide, there are still limited data on the molecular mechanisms involved in the disease pathogenesis. In this study, we characterized the mutational signature of 30 human papillomavirus (HPV)-associated PSCC cases from Latin Americans, using whole-exome sequencing. Copy number variations (CNVs) were also identified and compared to previous array-generated data. Enrichment analyses were performed to reveal disrupted pathways and to identify alterations mapped to HPV integration sites (HPVis) and miRNA–mRNA hybridization regions. Among the most frequently mutated genes were *NOTCH1*, *TERT*, *TTN*, *FAT1*, *TP53*, *CDKN2A*, *RYR2*, *CASP8*, *FBXW7*, *HMCN2*, and *ITGA8*. Of note, 92% of these altered genes were localized at HPVis. We also found mutations in ten novel genes (*KMT2C*, *SMARCA4*, *PTPRB*, *AJUBA*, *CR1*, *KMT2D*, *NBEA*, *FAM135B*, *GTF2I*, and *CIC*), thus increasing our understanding of the potential HPV-disrupted pathways. Therefore, our study reveals innovative targets with potential therapeutic benefits for HPV-associated PSCCs. The CNV analysis by sequencing (CNV-seq) revealed five cancer-associated genes as the most frequent with gains (*NOTCH1*, *MYC*, *NUMA1*, *PLAG1*, and

Anexo E - Parecer de Aprovação do Comitê de Ética

COMISSÃO NACIONAL DE ÉTICA EM PESQUISA

Plataforma Brasil

PARECER CONSUBSTANCIADO DA CONEP

DADOS DA EMENDA

Título da Pesquisa: ANÁLISE DE ALTERAÇÕES GENÔMICAS E NA EXPRESSÃO GÊNICA E PROTEICA EM CÂNCER PENIANO

Pesquisador: SILMA REGINA FERREIRA PEREIRA

Área Temática: Genética Humana:
(Haverá envio para o exterior de material genético ou qualquer material biológico humano para obtenção de material genético, salvo nos casos em que houver cooperação com o Governo Brasileiro;);
Pesquisas com coordenação e/ou patrocínio originados fora do Brasil, excetuadas aquelas com copatrocínio do Governo Brasileiro;

Versão: 5

CAAE: 46371515.5.0000.5087

Instituição Proponente: FUNDACAO UNIVERSIDADE FEDERAL DO MARANHAO

Patrocinador Principal: FUNDACAO UNIVERSIDADE FEDERAL DO MARANHAO

DADOS DO PARECER

Número do Parecer: 3.123.125

Apresentação do Projeto:

As informações elencadas nos campos "Apresentação do Projeto", "Objetivo da Pesquisa" e "Avaliação dos Riscos e Benefícios" foram retiradas do arquivo Informações Básicas da Pesquisa (PB_INFORMAÇÕES_BÁSICAS_1192694_E1.pdf gerado em 20/01/2019).

INTRODUÇÃO

O câncer de pênis (CP) é uma neoplasia rara em países desenvolvidos. No entanto, sua incidência é mais elevada em países em desenvolvimento, como o Brasil, sendo mais prevalente nas regiões Norte e Nordeste. Segundo o Instituto Nacional de Câncer (INCA) esse tipo de tumor representa 2% de todos os tipos de câncer que atingem o homem, tendo sido registrados 363 mortes no ano de 2010. De acordo com a SBU, em 2007, o Maranhão teve 10,7% dos casos de câncer de pênis notificados no Brasil, estando entre os cinco estados onde há maior prevalência, sendo superior até mesmo que o câncer de próstata. No entanto, faz-se necessário a realização de um estudo epidemiológico mais robusto e atualizado para que seja conhecida a realidade sobre a ocorrência dessa patologia no Estado. A etiologia é heterogênea, mas estudos mostram uma relação com

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UF: DF **Município:** BRASILIA
Telefone: (61)3315-5877 **E-mail:** conep@saude.gov.br

participarão desta casuística, aqueles com indicação para procedimento cirúrgico como forma de tratamento e que assinarem Termo de Consentimento Livre e Esclarecido (TCLE) aprovado pelo Comitê de Ética em Pesquisa com Seres Humanos através da Plataforma Brasil.

Após o consentimento formal do sujeito da pesquisa, será utilizado como instrumento de coleta de dados, um formulário (anexo 1), no qual serão obtidas informações tais como: idade, estado civil, hábito de fumo, ingestão de álcool e dados histológicos do tumor. As amostras de tumores penianos serão avaliadas quanto à presença de papilomavírus humano (HPV) por método de genotipagem por sequenciamento direto. Os tumores serão analisados por métodos de análises genômicas e de expressão gênica globais. Para isso, DNA e RNA serão extraídos da mesma amostra para as análises de alterações do número de cópias pelas técnicas de array-CGH e reação em cadeia da polimerase quantitativa (qPCR), para análise de expressão gênica por RT-PCR e para a determinação do perfil de expressão de miRNAs.

Os dados de expressão de proteínas serão obtidos a partir de métodos imunohistoquímicos e por citometria de fluxo. Os dados dessas análises serão integrados para a identificação de alvos específicos para cada miRNA. Os principais miRNAs e seus respectivos alvos de mRNA serão avaliados quanto a sua função, através dos programas e bancos de dados publicamente disponíveis, tais como Medscan, Pubmed e Oncomine. Os principais alvos identificados serão validados por análises gênicas específicas e funcionais, incluindo as principais vias de sinalização celular identificadas. Após a identificação dos marcadores que apresentam associação importante com o prognóstico e progressão da doença, serão realizadas análises de sistemas biológicos downstream de alvos conhecidos e possíveis alvos de tais miRNAs (GUSEV et al, 2007; GUSEV, 2008).

Os programas utilizados para estas análises incluem o Pathway Studio, Ariadne, e Ingenuity Pathway e bancos de dados publicamente disponíveis, tais como Medscan, Pubmed e Oncomine. Os marcadores moleculares identificados serão validados em relação a alterações do número de cópias gênicas, variação de expressão gênica e proteica, utilizando-se métodos como Hibridização In Situ por Fluorescência (FISH), amplificação quantitativa (qPCR), amplificação a partir de RNA mensageiro (RT-PCR), imunohistoquímica e citometria de fluxo. Os dados que apresentarem distribuição normal, serão comparados por t-test, caso contrário será usado um teste não-paramétrico. Os genes que apresentarem uma amplificação estatisticamente significativa (em pelo menos 50% dos casos) serão analisados pelo software Ingenuity Pathways para identificar sua via funcional.

O número de amostras será de conveniência de acordo com número de casos por mês/ano.

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Estima-se 100 casos nos próximos dois anos (2019 a 2021).
A análise de exoma será feita no Laboratório do Departament of Clinical Genetics Department, Vejle Hospital e Institute of Regional Health Research, University of Southern Denmark, sob a responsabilidade da Dra. Silvia Rogatto.

CRITÉRIOS DE INCLUSÃO
Serão incluídos pacientes maiores de 18 anos, atendidos no Instituto Maranhense de Oncologia Aldenora Belo, em São Luís, Maranhão, com diagnóstico clínico e anatomopatológico de câncer de pênis, e que tenham indicação de procedimento cirúrgico como forma de tratamento. Além disso, somente serão incluídos na pesquisa, aqueles que concordarem em participar da pesquisa e assinar o Termo de Consentimento Livre e Esclarecido (TCLE) aprovado pelo Comitê de Ética em Pesquisa da UFMA, obedecendo a Resolução n.º 466/12.

CRITÉRIOS DE EXCLUSÃO
Pacientes que não se enquadrarem nos critérios de inclusão acima descritos e/ou não concordarem assinar o Termo de Consentimento Livre e Esclarecido. Também não serão incluídos os pacientes com diagnóstico de câncer peniano que já tiverem iniciado tratamento quimioterápico ou radioterápico.

Objetivo da Pesquisa:
OBJETIVO PRIMÁRIO
Identificar alterações genômicas e na expressão gênica e proteica em câncer de pênis, buscando a identificação de marcadores moleculares para este tipo de tumor.

OBJETIVOS SECUNDÁRIOS
• Caracterizar os portadores de carcinomas penianos do Estado do Maranhão para o desenvolvimento de um registro epidemiológico específico para os homens do estado, a fim de identificar os principais fatores de risco e promover e incentivar ações preventivas.
• Identificar a presença de papilomavírus humano (HPV) e genotipar os subtipos virais.
• Identificar o perfil de alterações genômicas através do método de array-CGH.
• Identificar o perfil de expressão de miRNAs.
• Identificar alterações no número de cópias gênicas (CNA) por meio de qPCR.
• Integrar os dados de alterações de número de cópias de DNA com os de expressão de miRNA nas mesmas amostras tumorais.

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Telefone: (61)3315-5877 **E-mail:** conep@saude.gov.br

• Avaliar alterações na expressão de genes específicos por meio de RT-PCR.
• Identificar, por citometria de fluxo e imunohistoquímica, variações na expressão de proteínas relacionadas às alterações genéticas detectadas nas células tumorais.
• Correlacionar as alterações observadas com parâmetros clínico-patológicos dos pacientes (tipo histológico, grau de estadiamento, tamanho do tumor), incluindo dados de seguimento clínico (tempo livre da doença, recorrência tumoral, sobrevida, entre outros).
• Determinar a assinatura mutacional de carcinomas de pênis utilizando o sequenciamento de alta performance de regiões codificantes (exoma).
• Estabelecer e caracterizar culturas celulares de tumores de pênis a partir de amostras a fresco.

Avaliação dos Riscos e Benefícios:

RISCOS

Este projeto confere riscos mínimos aos pacientes uma vez não será realizada nenhuma intervenção direta ou indireta para fins exclusivos desta pesquisa, mas somente aquelas previstas para o diagnóstico e tratamento dos sujeitos da pesquisa. As amostras biológicas a serem utilizadas serão provenientes de procedimentos cirúrgicos prescritos para os casos com diagnóstico clínico e anatomopatológico de câncer de pênis. A coleta dos fragmentos de tumor não implicará em riscos adicionais no tratamento ou na cirurgia, e nem tampouco, em aumento no tempo de operação ou extensão da mesma. Sob o aspecto emocional, os pacientes serão informados pela equipe médica, que sua participação na pesquisa não terá nenhuma influência sobre seu tratamento, de modo que eles devem se sentir livres para escolher entre participar, ou não, da pesquisa. Assim, é garantida a continuidade do acompanhamento, tratamento, assistência integral e orientação dos pacientes independentemente destes concordarem ou não em participar da pesquisa. É garantida a manutenção do sigilo e da privacidade dos participantes da pesquisa durante todas as fases da pesquisa. Todos os dados da paciente são absolutamente confidenciais e, portanto, serão comunicados somente à paciente ou ao médico que a acompanha. As amostras biológicas, bem como as informações clínico-laboratoriais, serão codificadas para registro em programa computacional específico, cujo aceso somente é possível através de senha de identificação única. Os resultados das análises genéticas para fins de divulgação científica sempre serão feitos considerando-se o grupo amostral, e não individualmente. Esses procedimentos garantem a confidencialidade e a privacidade, a proteção da imagem e a não estigmatização dos participantes da pesquisa, garantindo a não utilização das informações em prejuízo das pessoas e/ou das comunidades, inclusive em termos de autoestima, de prestígio e/ou de aspectos econômico-financeiros, conforme previsto na resolução nº 466, de 12 de dezembro de 2012.

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Telefone: (61)3315-5877 **E-mail:** conep@saude.gov.br

BENEFÍCIOS

O material biológico será processado para análise de alterações moleculares e este trabalho deverá produzir resultados que não beneficiarão diretamente o sujeito da pesquisa, mas contribuirá para produção de conhecimento sobre a patologia para futuras investigações sobre possíveis marcadores genéticos moleculares diagnósticos e prognósticos. Os resultados obtidos nesta pesquisa serão comparados aos já existentes na literatura científica e serão tornados públicos, sejam eles favoráveis ou não.

Comentários e Considerações sobre a Pesquisa:

Projeto de pesquisa para identificar alterações genômicas e analisar a expressão gênica e proteica em uma coorte prospectiva de câncer de pênis. Serão incluídos pacientes maiores de 18 anos, atendidos no Instituto Maranhense de Oncologia Aldenora Belo, em São Luís, Maranhão, com diagnóstico clínico e anatomopatológico de câncer de pênis, e que tenham indicação de procedimento cirúrgico como forma de tratamento. Estima-se um tamanho amostral de 100 casos nos próximos dois anos de projeto.

Projeto de pesquisa inicialmente aprovado pelo CEP da Universidade Federal do Maranhão (UFMA) em 04/11/2015 (PB_PARECER_CONSUBSTANCIADO_CEP_1308275.pdf). Na presente emenda, foi incorporada a análise de exoma no Laboratório do Departament of Clinical Genetics Department, Vejle Hospital e Institute of Regional Health Research, University of Southern Denmark, sob a responsabilidade da Dra. Silvia Rogatto.

Haverá constituição de biorrepositório de material biológico humano no Laboratório de Genética e Biologia Molecular do Departamento de Biologia da UFMA, e no exterior (Dinamarca).

Considerações sobre os Termos de apresentação obrigatória:

Vide item "Conclusões ou Pendências e Lista de Inadequações".

Conclusões ou Pendências e Lista de Inadequações:

Análise de respostas ao Parecer Consubstanciado CONEP nº 3.096.206 de 21/12/2018:

1. Todos os protocolos de pesquisa devem conter demonstrativo da existência de INFRAESTRUTURA NECESSÁRIA E APTA AO DESENVOLVIMENTO DA PESQUISA, BEM COMO PARA ATENDER EVENTUAIS PROBLEMAS DELA RESULTANTES, com documento que expresse a

concordância da instituição e/ou organização por meio de seu responsável maior com competência. Diante do exposto, embora tenham sido apresentadas declarações de infraestrutura dos laboratórios onde serão desenvolvidas as análises genéticas aqui no Brasil, solicita-se apresentar demonstrativo detalhado da existência de infraestrutura necessária e apta ao desenvolvimento da pesquisa no hospital onde serão coletadas as amostras (biópsias), assinada pelo responsável maior do local onde se dará a pesquisa (Norma Operacional CNS n° 001 de 2013, item 3.3.h).
RESPOSTA: Encaminho, via Plataforma Brasil, a declaração de infraestrutura do Hospital Aldenora Belo assinada pelo responsável.
ANÁLISE: PENDÊNCIA ATENDIDA.

2. Tendo em vista que o sigilo e a confidencialidade são direitos dos participantes de pesquisa:

2.1. Solicita-se descrever no projeto de pesquisa como as informações serão anonimizadas antes de serem encaminhados para qualquer outra instância.
RESPOSTA: As informações sobre a anonimização das amostras foram acrescentadas no projeto, item 4.1.4 (página 7).
ANÁLISE: PENDÊNCIA ATENDIDA.

2.2. Quanto ao instrumento de coleta de dados (documento "FichaSujeitodapesquisa.pdf", postado em 28/10/2015) é importante ressaltar que sob nenhuma circunstância poderá constar informações tais como nome, prontuário médico, endereço, telefone, etc. que permitam a identificação dos participantes de pesquisa. O pesquisador principal deverá garantir a anonimização dos dados antes de serem encaminhados para qualquer outra instância, por exemplo, através do uso de formulários específicos. Solicita-se adequação.
RESPOSTA: O instrumento de pesquisa foi readequado seguindo as instruções do parecer e encaminho via Plataforma Brasil.
ANÁLISE: PENDÊNCIA ATENDIDA.

3. Quanto aos documentos necessários para armazenamento de material biológico humano em biorrepositório, todos os aspectos relativos à formação de biorrepositório ao longo da execução de uma pesquisa deverão ser seguidos conforme explicitado na Resolução CNS n° 441 de 2011 e Portaria MS n° 2201 de 2011, ainda que o armazenamento do material biológico seja temporário

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sem previsão de uso futuro. Solicita-se uma revisão das referidas normativas e apresentar:

3.1. Justificativa quanto à necessidade e oportunidade para utilização futura das amostras biológicas armazenadas no estudo em tela (Resolução CNS n° 441 de 2011, item 2.I).
RESPOSTA: Encaminho justificativa via Plataforma Brasil.
ANÁLISE: PENDÊNCIA ATENDIDA.

3.2. Declaração de que toda nova pesquisa a ser realizada com o material armazenado em biorrepositório será submetida para aprovação do Comitê de Ética em Pesquisa (CEP) institucional e, quando for o caso, da Comissão Nacional de Ética em Pesquisa (CONEP) (Resolução CNS n° 441 de 2011, Item 2.III).
RESPOSTA: Encaminho declaração via Plataforma Brasil.
ANÁLISE: PENDÊNCIA ATENDIDA.

3.3. Regulamento dos laboratórios envolvidos no armazenamento do material biológico com o detalhamento operacional e de infraestrutura, bem como as condições de armazenamento do material, que podem estar contidos no projeto de pesquisa detalhado ou em forma de declaração. Cabe ressaltar que o prazo de armazenamento de material biológico humano em biorrepositório deve estar de acordo com o cronograma da pesquisa correspondente e pode ser autorizado por até dez anos.
RESPOSTA: Encaminho declaração via Plataforma Brasil.
ANÁLISE: PENDÊNCIA ATENDIDA.

3.4. Termo de Acordo em Pesquisa envolvendo mais de uma instituição, firmado entre as instituições participantes no exterior, contemplando formas de operacionalização, compartilhamento e utilização do material biológico humano armazenado em biorrepositório, inclusive a possibilidade de dissolução futura da parceria e a consequente partilha e destinação dos dados e materiais armazenados, conforme previsto no TCLE. Explicitando ainda o tipo e a quantidade dos materiais compartilhados, informando sua destinação após a utilização (Resolução CNS n° 441 de 2012, itens 13 e 13.I).
RESPOSTA: Encaminho, via Plataforma Brasil, Termo de Acordo assinado pelas instituições colaboradoras.
ANÁLISE: PENDÊNCIA ATENDIDA.

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3.5. Declaração de compromisso dos pesquisadores no exterior, garantindo aos pesquisadores e às instituições brasileiras o direito ao acesso e utilização do material biológico humano armazenado no exterior (Resolução CNS n° 441 de 2011, item 14).
RESPOSTA: Encaminho, via Plataforma Brasil, Declaração do pesquisador no exterior.
ANÁLISE: PENDÊNCIA ATENDIDA.

3.6. Compromisso dos pesquisadores no exterior quanto à vedação do patenteamento e da utilização comercial do material biológico humano armazenado em Biorrepositório (Resolução CNS n° 441 de 2011, Item 16).
RESPOSTA: Encaminho, via Plataforma Brasil, Declaração do pesquisador no exterior.
ANÁLISE: PENDÊNCIA ATENDIDA.

4. Quanto ao Termo de Consentimento Livre e Esclarecido (versão de 28.10.2015) referente ao arquivo "TCLE.docx", postado na Plataforma Brasil em 28.10.2015:

4.1. O TCLE deve ser conciso e de fácil compreensão por um indivíduo LEIGO, não sendo desejável a utilização de construções gramaticais complexas. Diante do exposto, solicita-se que o TCLE seja revisado, utilizando-se linguagem CLARA E ACESSÍVEL. Salienta-se que é necessário substituir os termos técnicos (tais como "marcadores genéticos moleculares diagnósticos e prognósticos", por exemplo), por palavras de fácil entendimento ou adicionar breve explicação sobre o termo empregado no texto (Resolução CNS n° 466 de 2012, itens II.23 e IV.1.b).
RESPOSTA: Encaminho, via Plataforma Brasil, nova versão do TCLE atendendo a solicitação do parecerista.
ANÁLISE: PENDÊNCIA ATENDIDA.

4.2. Não consta a garantia de ressarcimento de despesas como transporte e alimentação do participante e seus acompanhantes, quando houver (Resolução CNS n° 466 de 2012, item IV.3.g). Solicita-se adequação.
RESPOSTA: Encaminho, via Plataforma Brasil, nova versão do TCLE atendendo a solicitação do parecerista.
ANÁLISE: PENDÊNCIA ATENDIDA.

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4.3. O Termo de Consentimento Livre e Esclarecido não deve conter ressalva que negue a responsabilidade do pesquisador ou que implique ao participante da pesquisa abrir mão de seus direitos, incluindo o direito de buscar indenização por danos eventuais. Diante do exposto, solicita-se inserir no TCLE a explicitação acerca do direito de buscar indenização diante de eventuais danos decorrentes da pesquisa (Resolução CNS n° 466 de 2012, item IV.3.h).
RESPOSTA: Encaminho, via Plataforma Brasil, nova versão do TCLE atendendo a solicitação do parecerista.
ANÁLISE: PENDÊNCIA ATENDIDA.

4.4. Foram apresentadas formas de contato com o CEP responsável pela aprovação e pelo acompanhamento do estudo, tais como nome, endereço, contato telefônico. Entretanto, solicita-se constar no TCLE o HORÁRIO DE FUNCIONAMENTO do CEP responsável pelo estudo.
RESPOSTA: Encaminho, via Plataforma Brasil, nova versão do TCLE atendendo a solicitação do parecerista.
ANÁLISE: PENDÊNCIA ATENDIDA.

4.5. Solicita-se incluir ao final do TCLE o campo de assinatura do pesquisador responsável/ pessoa por ele delegada. Solicita-se ainda que os campos de assinatura ao final do TCLE constem da mesma página de assinatura, de forma integrada ao restante do texto (Resolução CNS n° 466 de 2012, item IV.5.d).
RESPOSTA: Encaminho, via Plataforma Brasil, nova versão do TCLE atendendo a solicitação do parecerista.
ANÁLISE: PENDÊNCIA ATENDIDA.

4.6. O TCLE apresenta a numeração nas páginas. Porém, com o objetivo de garantir a integridade do documento, solicita-se que sejam inseridos os números de cada página, bem com a quantidade total delas, como por exemplo: "1 de 3" e assim sucessivamente, até a página "X de X".
RESPOSTA: Encaminho, via Plataforma Brasil, nova versão do TCLE atendendo a solicitação do parecerista.
ANÁLISE: PENDÊNCIA ATENDIDA.

4.7. Para melhor esclarecer ao participante da pesquisa, solicita-se informar no TCLE o nome e o país onde está localizado o laboratório em que as amostras biológicas coletadas no estudo serão

processadas e também armazenadas. Adicionalmente, solicita-se adequação à Resolução CNS n° 441 de 2011 e à Portaria MS n° 2201 de 2011 em todos os documentos que possuem informações sobre o armazenamento e uso de material biológico no projeto.
RESPOSTA: Encaminho, via Plataforma Brasil, nova versão do TCLE atendendo a solicitação do parecerista, bem como foram adicionadas informações sobre o armazenamento e uso de material biológico no projeto.
ANÁLISE: PENDÊNCIA ATENDIDA.

4.8. Solicita-se que seja informado no TCLE que a retirada do consentimento de guarda dos dados genéticos humanos armazenados em bancos deverá ser realizada POR ESCRITO E ASSINADA, podendo dar-se a qualquer tempo, sem prejuízo ao participante da pesquisa, com validade a partir da data da comunicação da decisão, esclarecendo também que o participante de pesquisa tem o direto de retirar seus dados genéticos de bancos onde se encontrem armazenados (Resolução CNS nº 340 de 2004, itens III.6 e III.7; Resolução CNS nº 441 de 2011, item 10.I).
RESPOSTA: Encaminho, via Plataforma Brasil, nova versão do TCLE atendendo a solicitação do parecerista.
ANÁLISE: PENDÊNCIA ATENDIDA.

4.9. As pesquisas, em qualquer área do conhecimento envolvendo seres humanos, deverão observar as seguintes exigências: utilizar o material biológico e os dados obtidos na pesquisa exclusivamente para a finalidade prevista no seu protocolo, ou conforme o consentimento do participante. Não é adequado realizar testes adicionais nas amostras biológicas sem que o participante da pesquisa tenha conhecimento e consentido com a sua realização. Solicita-se descrever, em linguagem clara e de fácil compreensão, todos os procedimentos da pesquisa, com o detalhamento dos métodos a serem utilizados, isto é, descrever todos os procedimentos e exames que serão realizados no estudo, como por exemplo, o número de amostras biológicas que serão colhidas, o local onde será realizada a coleta das amostras, o laboratório onde serão realizados os exames, quais exames serão realizados, etc. (Item IV.3.a, da Resolução CNS n° 466 de 2012).
RESPOSTA: Encaminho, via Plataforma Brasil, nova versão do TCLE atendendo a solicitação do parecerista.
ANÁLISE: PENDÊNCIA ATENDIDA.

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Telefone: (61)3315-5877 **E-mail:** conep@saude.gov.br

4.10. As amostras biológicas armazenadas podem ser utilizadas em pesquisas futuras, desde que previamente aprovadas pelo Sistema CEP/Conep. Sendo assim, solicita-se descrever NESSE ITEM do TCLE que cada nova pesquisa realizada pelo patrocinador ou por PESQUISADORES INDEPENDENTES está condicionada a: (a) apresentação de novo projeto de pesquisa para ser analisado e aprovado pelo Sistema CEP/Conep e (b) reconsentimento do participante de pesquisa por meio de um TCLE específico referente ao novo projeto de pesquisa (ou, quando devidamente justificado, a obtenção de aprovação da dispensa do Termo pelo Comitê). Ressalta-se ainda que, se houver intenção de pesquisa futura com o material biológico, essa informação deverá constar claramente do TCLE (Resolução CNS n° 441 de 2011, item 6; Portaria MS n° 2.201 de 2011, capítulo IV, seção II, artigos 17, 18 e 22 e capítulo II, artigo 5°).
RESPOSTA: Encaminho, via Plataforma Brasil, nova versão do TCLE atendendo a solicitação do parecerista.
ANÁLISE: PENDÊNCIA ATENDIDA.

4.11. Considerando a necessidade de serem observados a proteção dos direitos humanos, das liberdades fundamentais e do respeito à dignidade humana na coleta, processamento, uso e armazenamento de dados genéticos humanos, solicita-se informar sobre o local e o responsável pelo armazenamento dos dados genéticos obtidos no estudo (Resolução CNS n° 340 de 2004, Preâmbulo).
RESPOSTA: Encaminho, via Plataforma Brasil, nova versão do TCLE atendendo a solicitação do parecerista.
ANÁLISE: PENDÊNCIA ATENDIDA.

4.12. Solicita-se que conste a informação quanto a medidas de proteção contra qualquer tipo de discriminação ou estigmatização, individual ou coletiva aos participantes atendidos nesse estudo (Resolução CNS n° 340 de 2004, item V.1.g).
RESPOSTA: Encaminho, via Plataforma Brasil, nova versão do TCLE atendendo a solicitação do parecerista.
ANÁLISE: PENDÊNCIA ATENDIDA.

Considerações Finais a critério da CONEP:
Diante do exposto, a Comissão Nacional de Ética em Pesquisa - Conep, de acordo com as atribuições definidas na Resolução CNS nº 466 de 2012 e na Norma Operacional nº 001 de 2013 do CNS, manifesta-se pela aprovação da emenda proposta ao projeto de pesquisa.

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Telefone: (61)3315-5877 **E-mail:** conep@saude.gov.br

Situação: Emenda aprovada.

Este parecer foi elaborado baseado nos documentos abaixo relacionados:

Tipo Documento	Arquivo	Postagem	Autor	Situação
Informações Básicas do Projeto	PB_INFORMAÇÕES_BÁSICAS_1192694_E1.pdf	20/01/2019 23:49:04		Aceito
Declaração de Manuseio Material Biológico / Biorepositório / Biobanco	Justificativa_Futura_Utilizacao_Material.pdf	20/01/2019 23:29:20	SILMA REGINA FERREIRA PEREIRA	Aceito
Declaração de Manuseio Material Biológico / Biorepositório / Biobanco	Justificativa_Futura_Utilizacao_Material.docx	20/01/2019 23:29:01	SILMA REGINA FERREIRA PEREIRA	Aceito
Declaração de Manuseio Material Biológico / Biorepositório / Biobanco	DECLARACAO_NOVAS_PESQUISAS_MATERIALBIORREPOSITORIO.docx	20/01/2019 23:28:13	SILMA REGINA FERREIRA PEREIRA	Aceito
Declaração de Manuseio Material Biológico / Biorepositório / Biobanco	DECLARACAO_NOVAS_PESQUISAS_MATERIALBIORREPOSITORIO.pdf	20/01/2019 23:27:40	SILMA REGINA FERREIRA PEREIRA	Aceito
Declaração de Manuseio Material Biológico / Biorepositório / Biobanco	DECLARACAO_BIORREPOSITORIO.pdf	20/01/2019 23:24:19	SILMA REGINA FERREIRA PEREIRA	Aceito
Declaração de Manuseio Material Biológico / Biorepositório / Biobanco	DECLARACAO_BIORREPOSITORIO.docx	20/01/2019 23:23:53	SILMA REGINA FERREIRA PEREIRA	Aceito
Declaração de Instituição e Infraestrutura	INFRAESTRUTURA_HOSPITAL.jpg	20/01/2019 23:17:44	SILMA REGINA FERREIRA PEREIRA	Aceito
Outros	Declaracao_Nao_Patenteamennto.pdf	20/01/2019 23:14:32	SILMA REGINA FERREIRA	Aceito
Outros	Declaracao_Acesso_Material.pdf	20/01/2019	SILMA REGINA	Aceito

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UF: DF **Município:** BRASILIA
Telefone: (61)3315-5877 **E-mail:** conep@saude.gov.br

Outros	Declaracao_Acesso_Material.pdf	23:13:11	FERREIRA	Aceito
Outros	TERMO_ACORDO_PORTUGUES.pdf	20/01/2019 22:55:12	SILMA REGINA FERREIRA	Aceito
Outros	TERMO_ACORDO_INGLES.pdf	20/01/2019 22:52:47	SILMA REGINA FERREIRA	Aceito
Outros	TERMO_ACORDO_INGLES.docx	20/01/2019 22:51:46	SILMA REGINA FERREIRA	Aceito
Outros	TERMO_ACORDO_PORTUGUES.docx	20/01/2019 22:50:54	SILMA REGINA FERREIRA	Aceito
Outros	INSTRUMENTO_DE_PESQUISA.pdf	20/01/2019 22:42:09	SILMA REGINA FERREIRA	Aceito
Outros	INSTRUMENTO_DE_PESQUISA.docx	20/01/2019 22:40:50	SILMA REGINA FERREIRA	Aceito
TCLE / Termos de Assentimento / Justificativa de Ausência	NOVO_TCLE_CONEP_LIMPA.pdf	20/01/2019 22:39:19	SILMA REGINA FERREIRA PEREIRA	Aceito
TCLE / Termos de Assentimento / Justificativa de Ausência	NOVO_TCLE_CONEP_DESTAQUES.pdf	20/01/2019 22:38:58	SILMA REGINA FERREIRA PEREIRA	Aceito
TCLE / Termos de Assentimento / Justificativa de Ausência	NOVO_TCLE_CONEP_DESTAQUES.docx	20/01/2019 22:36:47	SILMA REGINA FERREIRA PEREIRA	Aceito
TCLE / Termos de Assentimento / Justificativa de Ausência	NOVO_TCLE_CONEP_LIMPA.docx	20/01/2019 22:34:45	SILMA REGINA FERREIRA PEREIRA	Aceito
Outros	RESPOSTA_CONEP2018_EMENDA.pdf	20/01/2019 17:08:55	SILMA REGINA FERREIRA	Aceito
Outros	RESPOSTA_CONEP2018_EMENDA.docx	20/01/2019 17:07:39	SILMA REGINA FERREIRA	Aceito
Projeto Detalhado / Brochura Investigador	EMENDA_RESPOSTA_CONEP2018_VERSAO_LIMPA.pdf	20/01/2019 16:58:43	SILMA REGINA FERREIRA PEREIRA	Aceito
Projeto Detalhado / Brochura Investigador	EMENDARESPOSTA_CONEP2018DESTAQUE.pdf	20/01/2019 16:58:19	SILMA REGINA FERREIRA PEREIRA	Aceito
Projeto Detalhado / Brochura Investigador	EMENDA_RESPOSTA_CONEP2018_VERSAO_LIMPA.docx	20/01/2019 16:56:24	SILMA REGINA FERREIRA PEREIRA	Aceito
Projeto Detalhado / Brochura Investigador	EMENDARESPOSTA_CONEP2018DESTAQUE.docx	20/01/2019 16:55:43	SILMA REGINA FERREIRA PEREIRA	Aceito
Declaração de Pesquisadores	TRADUCAOCARTA_Letter_SilviaRogatto.pdf	03/12/2018 20:10:12	SILMA REGINA FERREIRA	Aceito

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UF: DF **Município:** BRASILIA
Telefone: (61)3315-5877 **E-mail:** conep@saude.gov.br

Declaração de Instituição e Infraestrutura	TRADUCAOLetterDeptUniversityofSouthernDenmark.pdf	03/12/2018 20:08:57	SILMA REGINA FERREIRA PEREIRA	Aceito
Folha de Rosto	FolhadeRosto22nov2018.pdf	22/11/2018 15:30:06	SILMA REGINA FERREIRA	Aceito
Declaração de Instituição e Infraestrutura	EmendaInfraestrutura_LABGEM.pdf	17/09/2018 15:30:33	SILMA REGINA FERREIRA PEREIRA	Aceito
Declaração de Instituição e Infraestrutura	EMENDACarta_AldenoraBelo.pdf	17/09/2018 14:15:05	SILMA REGINA FERREIRA PEREIRA	Aceito
Declaração de Pesquisadores	Letter_SilviaRogatto.pdf	17/09/2018 13:58:51	SILMA REGINA FERREIRA	Aceito
Declaração de Pesquisadores	Carta_RossyEricSoares.pdf	17/09/2018 13:58:35	SILMA REGINA FERREIRA	Aceito
Declaração de Pesquisadores	Carta_RonaldCoelho.pdf	17/09/2018 13:58:19	SILMA REGINA FERREIRA	Aceito
Declaração de Pesquisadores	Carta_MirtesRocha.pdf	17/09/2018 13:58:07	SILMA REGINA FERREIRA	Aceito
Declaração de Pesquisadores	Carta_MayaraLima.pdf	17/09/2018 13:57:56	SILMA REGINA FERREIRA	Aceito
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Declaração de Pesquisadores	Carta_AndreVale.pdf	17/09/2018 13:57:33	SILMA REGINA FERREIRA	Aceito
Declaração de Pesquisadores	Carta_AlcionedosSantos.pdf	17/09/2018 13:54:15	SILMA REGINA FERREIRA	Aceito
Declaração de Pesquisadores	Carta_AnaPaulaAzevedo.pdf	17/09/2018 13:53:39	SILMA REGINA FERREIRA	Aceito
Declaração de Instituição e Infraestrutura	LetterDeptUniversityofSouthernDenmark.pdf	17/09/2018 13:45:49	SILMA REGINA FERREIRA PEREIRA	Aceito
Outros	TERMODEOUTORGA_BrasilDinamarca.pdf	17/09/2018 13:35:59	SILMA REGINA FERREIRA	Aceito
Projeto Detalhado / Brochura Investigador	EMENDA_BrasilDinamarca2017FINALPlaraformaBrasil.pdf	17/09/2018 13:27:50	SILMA REGINA FERREIRA PEREIRA	Aceito
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Declaração de Instituição e Infraestrutura	CARTALABGEM.pdf	29/10/2015 12:37:35	SILMA REGINA FERREIRA PEREIRA	Aceito
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Declaração de Pesquisadores	CARTAAnaPaula.pdf	29/10/2015 12:29:12	SILMA REGINA FERREIRA	Aceito

Endereço: SRNTV 701, Via W 5 Norte - Edifício PO 700, 3º andar
Bairro: Asa Norte **CEP:** 70.719-049
UF: DF **Município:** BRASILIA
Telefone: (61)3315-5877 **E-mail:** conep@saude.gov.br

Declaração de Pesquisadores	CARTALEUDIVAN.pdf	29/10/2015 12:23:15	SILMA REGINA FERREIRA	Aceito
Outros	RESPOSTAAOPARECERcapeniano.pdf	28/10/2015 19:20:31	SILMA REGINA FERREIRA	Aceito
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Projeto Detalhado / Brochura Investigador	ProjetoCancerPenianoPlataformaBrasil2015FINAL.pdf	28/10/2015 18:33:19	SILMA REGINA FERREIRA PEREIRA	Aceito
Projeto Detalhado / Brochura Investigador	ProjetoCancerPenianoPlataformaBrasil2015FINAL.docx	28/10/2015 18:33:05	SILMA REGINA FERREIRA PEREIRA	Aceito
Projeto Detalhado / Brochura Investigador	Projeto Cancer Peniano Plataforma Brasil 2015 FINAL.pdf	09/06/2015 11:24:15		Aceito
Projeto Detalhado / Brochura Investigador	Projeto Cancer Peniano Plataforma Brasil 2015 FINAL.docx	09/06/2015 11:24:01		Aceito
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Outros	Carta- Ronald.pdf	18/05/2015 12:18:01		Aceito
Declaração de Instituição e Infraestrutura	Carta IMOAB.pdf	18/05/2015 12:08:33		Aceito
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Outros	CARTAS DE ANUENCIA_CALIXTO (1).pdf	18/05/2015 11:59:50		Aceito

Situação do Parecer:
Aprovado

BRASILIA, 28 de Janeiro de 2019

Assinado por:
Jorge Alves de Almeida Venancio
(Coordenador(a))