



Biological Relevance of ID3EAL microRNA Knowledge Panels



Learn how key microRNA from the ID3EAL Knowledge Panels regulates a variety of transcripts active in vital pathways today!

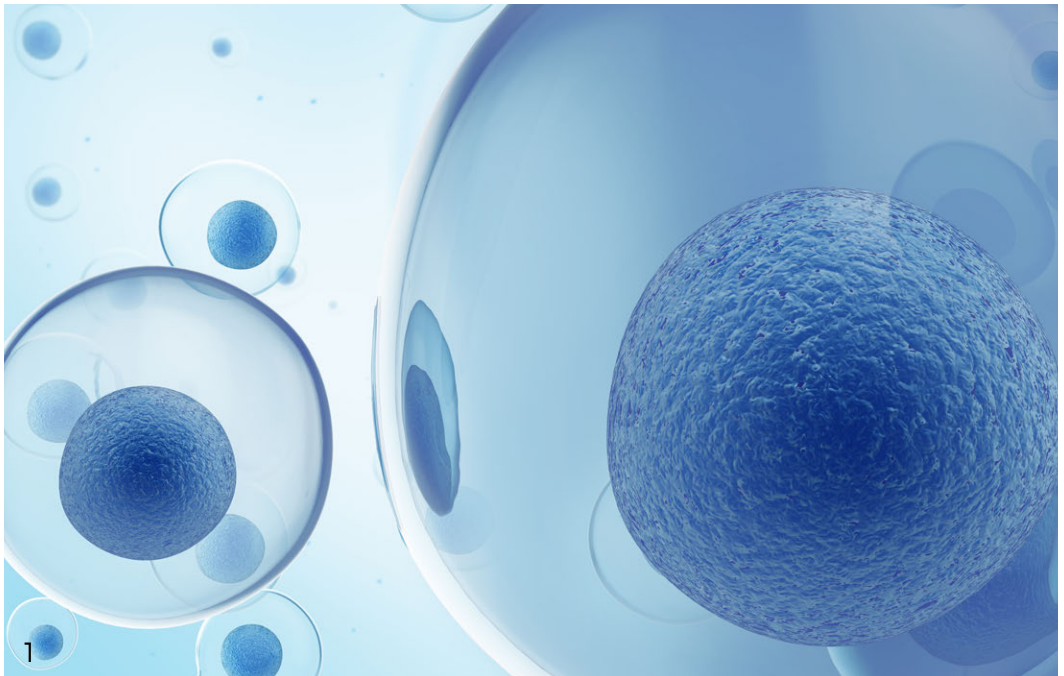
Biological pathways associated with Cancer

microRNAs are intimately involved in every hallmark of cancer. Detecting microRNA dysregulations could provide insights into cancer pathogenesis, drug response and recurrence.

The MiRXES ID3EAL Cancer microRNA Knowledge panel consists of 352 microRNAs strongly associated with various cancer types and regulate up to hundreds of key onco- and tumour suppressor genes and pathways. In this booklet, we have analysed and compiled up to eleven pathways relevant to cancer. These pathways were co-developed with Clarivate Analytics – Market leader in pharmaceutical and biotechnology intelligence.

For each pathway, there is a schematic representation of the vital genes and microRNA regulating the pathway. A short synopsis of the pathway and its involvement in cancer is provided – Furnished with citations. Isn't it great?

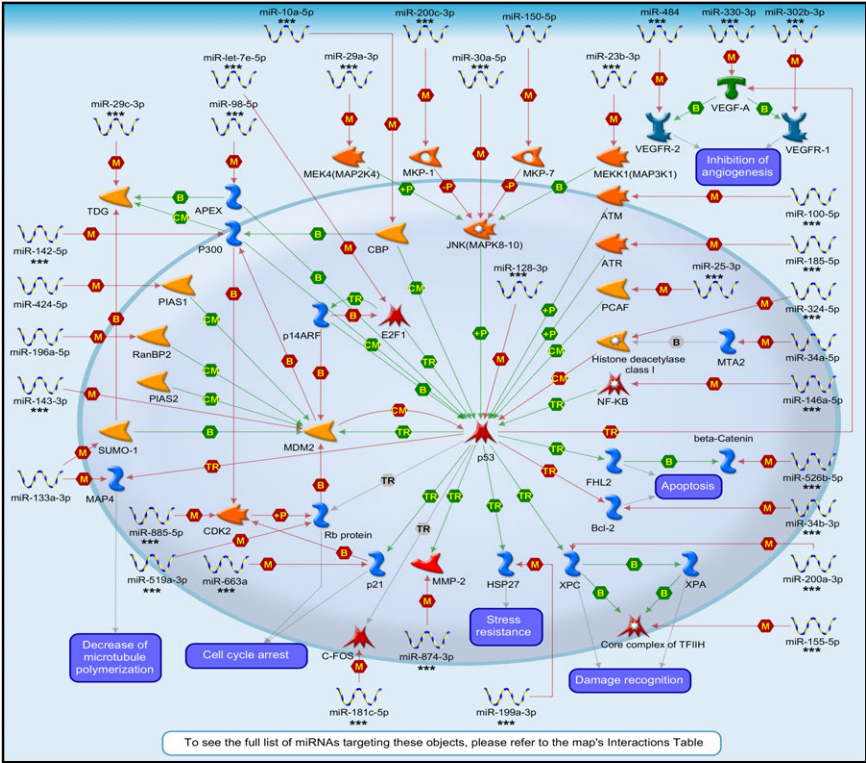
It gets better. We have a compilation of all the interactions between the respective microRNA and target transcripts within the pathways. It is also further segmented into interaction effects, mechanisms and methods these interactions were established. To further enable researchers in the analytics, each of these interactions are supported with publications – Pubmed ID.



Featured Pathways

1. p53 signalling pathway
2. FAS signalling cascade
3. EGFR signalling pathway
4. VEGF-family signalling
5. WNT signalling pathway
6. Regulation of actin cytoskeleton organization by the kinase effectors of Rho GTPases
7. Regulation of immune cell differentiation by Notch signalling
8. Differentiation of natural regulatory T cells
9. Inhibitory PD-1 signalling in T cells
10. Macrophage-induced immunosuppression in the tumour microenvironment
11. Macrophage and dendritic cell phenotype shift in cancer

p53 signaling pathway



The Tumour protein p53 (p53) plays a critical role in safeguarding the integrity of the genome. Upon activation, p53 binds to the enhancer/promoter elements of downstream target genes and regulates their transcription, through which it initiates cellular programs that account for most of its tumour-suppressor functions. The signal transduction circuit of p53 consists of the upstream mediators, the core regulation components and the downstream effectors.

The core regulatory circuitry consists of Mdm2 p53 binding protein homolog (MDM2), Cyclin-dependent kinase inhibitor 2A (p14ARF) and E2F transcription factor 1 (E2F1). p53 activates MDM2 transcription. MDM2 in conjunction with Proteasome 26S subunit non-ATPase 10 (PSMD10 (Gankyrin)) mediates p53 ubiquitination and degradation. E2F1 activates transcription of p53 and p14ARF. p14ARF facilitates proteolytic degradation of E2F1 and MDM2-mediated p53 ubiquitination. Transcription of p53 is also mediated by nuclear factor kappaB (NF-KB) in a response to stress.

MIRXES has 234 miRNAs targeting 50 proteins on this signalling cascade, indicating that most proteins involved in the p53 pathway are miRNA targets and may therefore be affected by miRNA action.

Hi-resolution
Pathway Map



Full pathway
summary & Citations



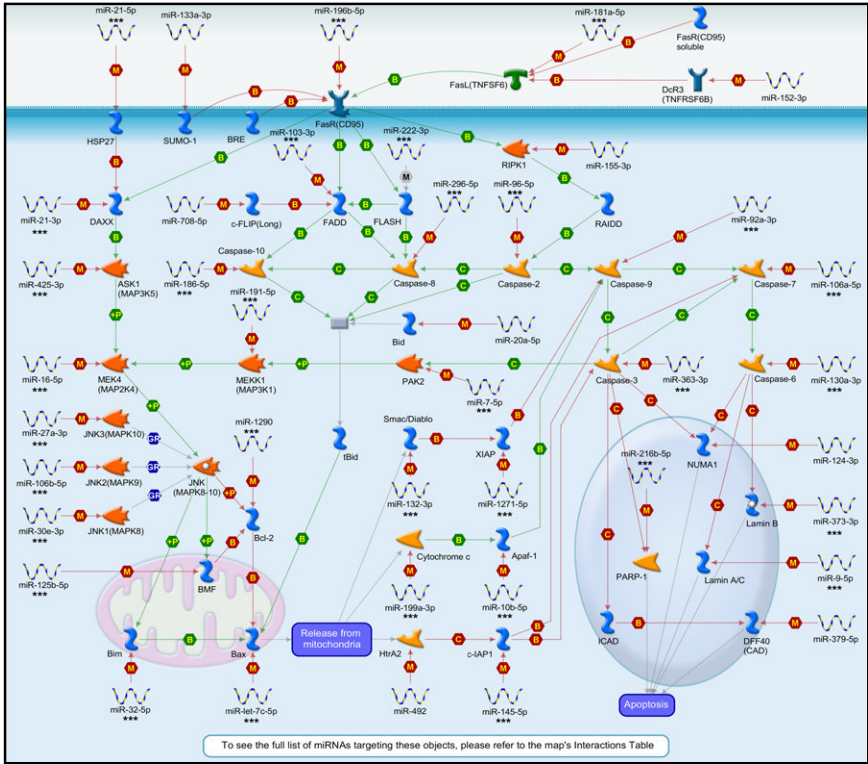
Relevant microRNA
and gene transcripts



Interactions Table



FAS signalling cascade



Death receptors such as FasR belong to a Tumour Necrosis Factor (TNF) superfamily of receptors involved in proliferation, differentiation and apoptosis. FasR is ubiquitously expressed in various tissues, but its ligand FasL is expressed mainly in activated T lymphocytes and natural killer cells. The binding of ligands to receptor induces receptor trimerisation. Clustering on the plasma membrane is required to initiate apoptosis in cells.

FasR have some splice variants and isoforms. Isoforms which are missing the transmembrane domain (soluble form), or the intracellular domain, (sFasR), can sequester FasL and inhibit apoptosis. In addition to death receptors, there are decoy receptors (DcR). DcR3 is a soluble receptor secreted by cells and binds with Fas ligand (FasL). Decoy receptors possess functional extracellular ligand binding domains but do not contain intracellular death domains and cannot recruit adaptor proteins required for apoptosis. The principle function of decoy receptors is modulating the sensitivity to death-receptor-mediated apoptosis in vivo. DcR3 sequesters and inactivates the membrane-bound Fas ligand on adjacent cells and prevents activation of Fas receptor (FasR). Activation of FasR lead to stimulation of several signal cascades: activation of caspase cascade, activation of intrinsic apoptotic pathway mediated by mitochondria, and activation of JNK-cascade.

MIRXES has 157 miRNAs targeting 41 proteins on this signalling cascade, indicating that most proteins involved in the FAS pathway are miRNA targets and may therefore be affected by miRNA action.

Hi-resolution
Pathway Map



Full pathway
summary & Citations



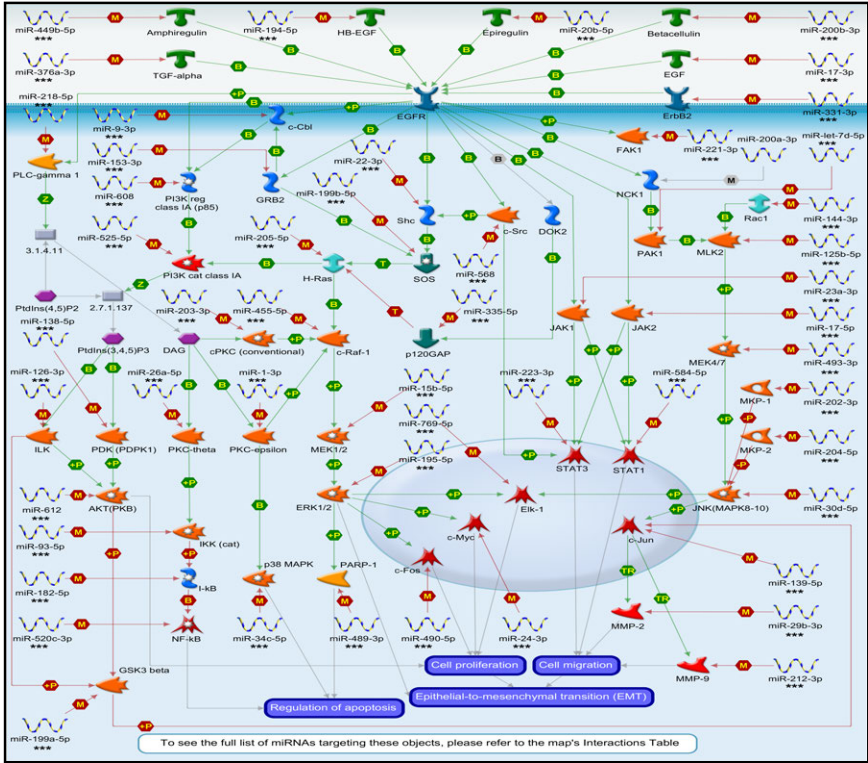
Relevant microRNA
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Interactions Table



EGFR signaling pathway



Epidermal growth factor receptor (EGFR) belongs to the ERBB family of receptor tyrosine kinases that contains four closely related members EGFR and ERBB2-4. They couple the binding of the extracellular growth factor ligands to intracellular signalling pathways that regulate diverse biologic responses, including proliferation, differentiation, cell motility, and survival. Six ligands of EGFR are known. These are Epidermal growth factor (EGF), Amphiregulin, Transforming growth factor alpha (TGF-alpha), Betacellulin, Heparin binding EGF-like growth factor (HB-EGF), and Epregrulin. ErbB2 is a unique member of the ERBB family in that it does not bind any of the known ligands with high affinity. However, it is the preferred heterodimeric partner for other EGFRs.

The ligand-induced receptor dimerization and subsequent autophosphorylation of distinct tyrosine residues creates docking sites for various membrane-targeted proteins. The cytoplasmic mediators that bind to EGFR phospho-tyrosine residues are either the adaptor proteins, such as SHC transforming protein 1 (Shc), Growth factor receptor-bound protein 2 (GRB2), Cas-Br-M ecotropic retroviral transforming sequence (c-Cbl), Docking protein 2 (DOK2) and NCK adaptor protein 1 (NCK1), or enzymes, such as Phospholipase C gamma 1 (PLC-gamma 1), v-Src sarcoma viral oncogene homolog (c-Src) and PTK2 protein tyrosine kinase 2 (FAK1).

MIRXES has 228 miRNAs targeting 71 proteins on this signalling cascade, indicating that most proteins involved in the EGFR pathway are miRNA targets and may therefore be affected by miRNA action.

Hi-resolution
Pathway Map



Full pathway
summary & Citations



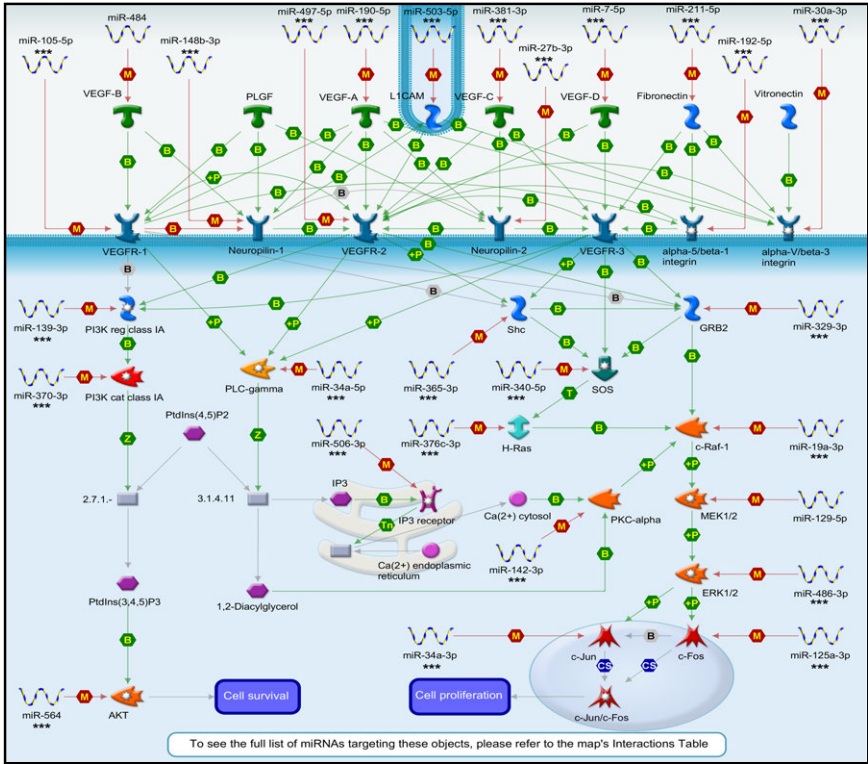
Relevant microRNA
and gene transcripts



Interactions Table



VEGF-family signalling



The vascular endothelial growth factor (VEGF) family of ligands and receptors is crucial for vascular development and neovascularization in physiological and pathological processes in both embryos, and in adults. VEGFs belong to a family of homo-dimeric glycoproteins that contains five members (VEGF-A, VEGF-B, VEGF-C, VEGF-D, and Placenta growth factor PLGF). VEGFs bind to three different VEGF-receptor tyrosine kinases (VEGFR-1, VEGFR-2 and VEGFR-3). Upon ligation, VEGF-receptors dimerize, auto-phosphorylate and, thereby transduce signals that direct cellular function.

VEGFR-1 is a high-affinity receptor for VEGF-A, VEGF-B and PLGF. It is expressed in vascular endothelial and some non-endothelial cells including haematopoietic stem cells, macrophages and monocytes. VEGFR-2 is highly specific towards VEGF-A. However, it also binds the processed forms of VEGF-C and VEGF-D [7]. VEGFR-2 is expressed in both vascular endothelial and lymphatic endothelial cells. Its expression has also been demonstrated in several other cell types such as megakaryocytes and haematopoietic stem cells. VEGFR-3 is highly specific towards VEGF-C and VEGF-D. It is expressed at high levels in lymphatic endothelial cells, but also is important for vascular development. VEGF-receptor function is enhanced by interaction with co-receptors of VEGFs Neuropilin-1 and Neuropilin-2. VEGF-A, VEGF-B and PLGF bind to Neuropilin-1, whereas VEGF-A, VEGF-C and PLGF bind to Neuropilin-2. Neuropilin-2 stabilizes the VEGFR-2 complex with VEGF-A, whereas Neuropilin-2 might be required for stabilizing the complex of VEGFR-3 with its ligands.

MIRXES has 201 miRNAs targeting 40 proteins on this signalling cascade, indicating that most proteins involved in the VEGF pathway are miRNA targets and may therefore be affected by miRNA action.

Hi-resolution
Pathway Map



Full pathway
summary & Citations



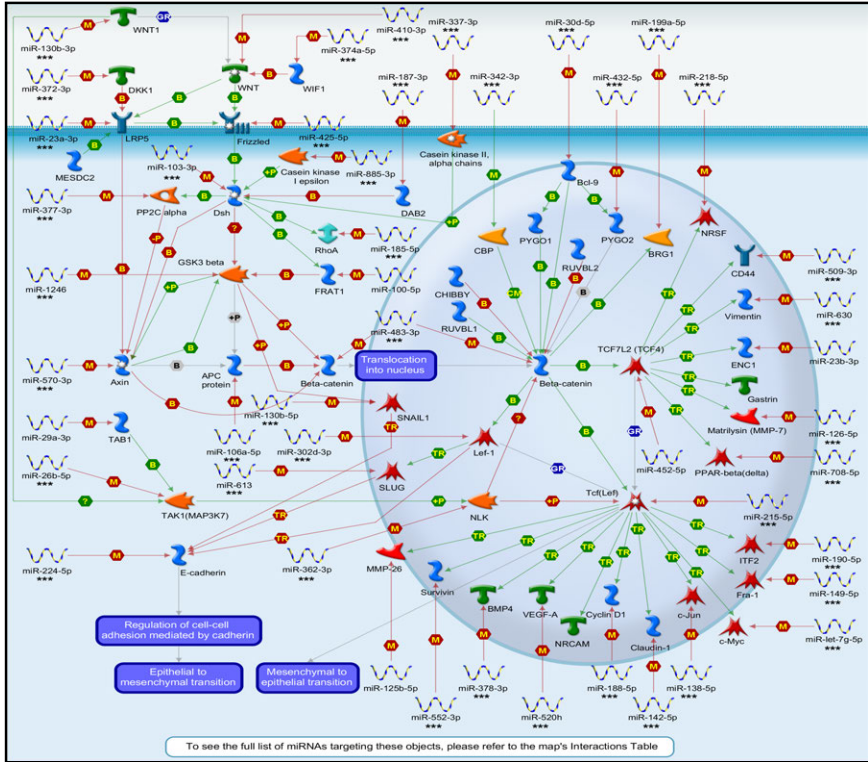
Relevant microRNA
and gene transcripts



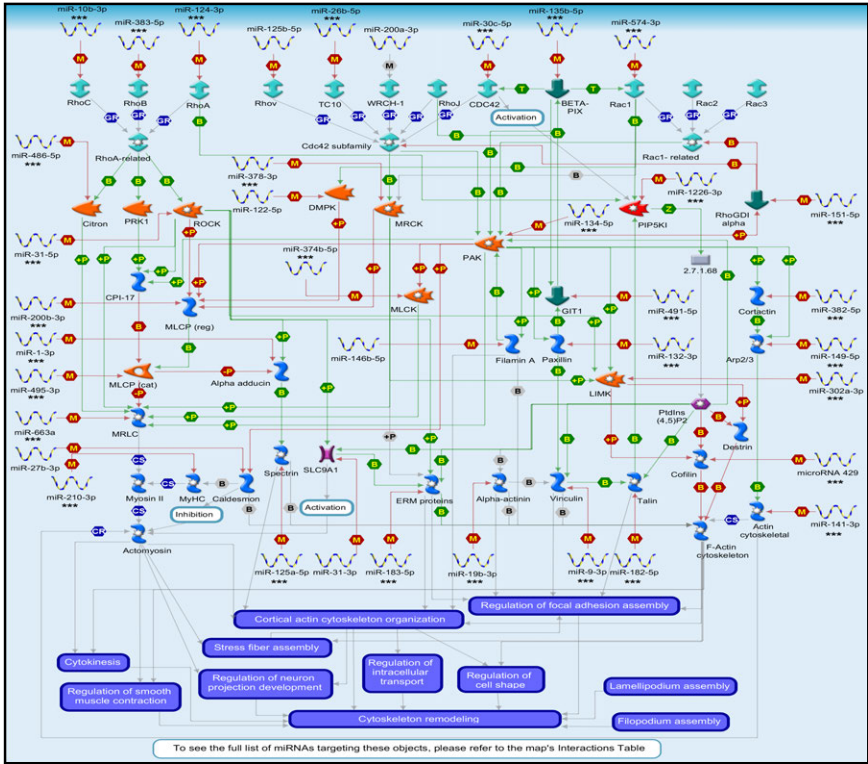
Interactions Table



WNT signaling pathway



Regulation of actin cytoskeleton organization by the kinase effectors of Rho GTPases



Ras-homologous (Rho) GTPases are well-known regulators of the actin cytoskeleton, which is involved in many important processes, such as cell migration, cell adhesion, regulation of cell shape and intracellular transport. Among Rho GTPases, members of the RhoA, Rac1 and CDC42 subfamilies have been most extensively studied. Activated Rho GTPases recruit a series of kinase effectors (e.g. ROCK, PAK and MRCK) that regulate the organization and dynamics of diverse F-actin cytoskeleton structures.

Ras-homologous (Rho) GTPases are well-known regulators of the actin cytoskeleton, which serves as a scaffold for the spatial distribution of a large set of cellular components. Activated Rho GTPases recruit a series of kinases that regulate assembly and organization of diverse F-Actin cytoskeleton structures needed for many important processes [1], such as cell migration [2], [3], [4] cell adhesion [2], cytokinesis [5], regulation of cell shape [6] and intracellular transport, [7], [8], [9]. Among Rho GTPases, members of the RhoA, Rac1 and CDC42 subfamilies have been widely studied for their effects on actin organization, being classically associated with stress fibre assembly, filopodium assembly and lamellipodium assembly

MIRXES has 163 miRNAs targeting 74 proteins on this signalling cascade, indicating that most proteins involved in the Rho pathway are miRNA targets and may therefore be affected by miRNA action.

Hi-resolution
Pathway Map



Full pathway
summary & Citations



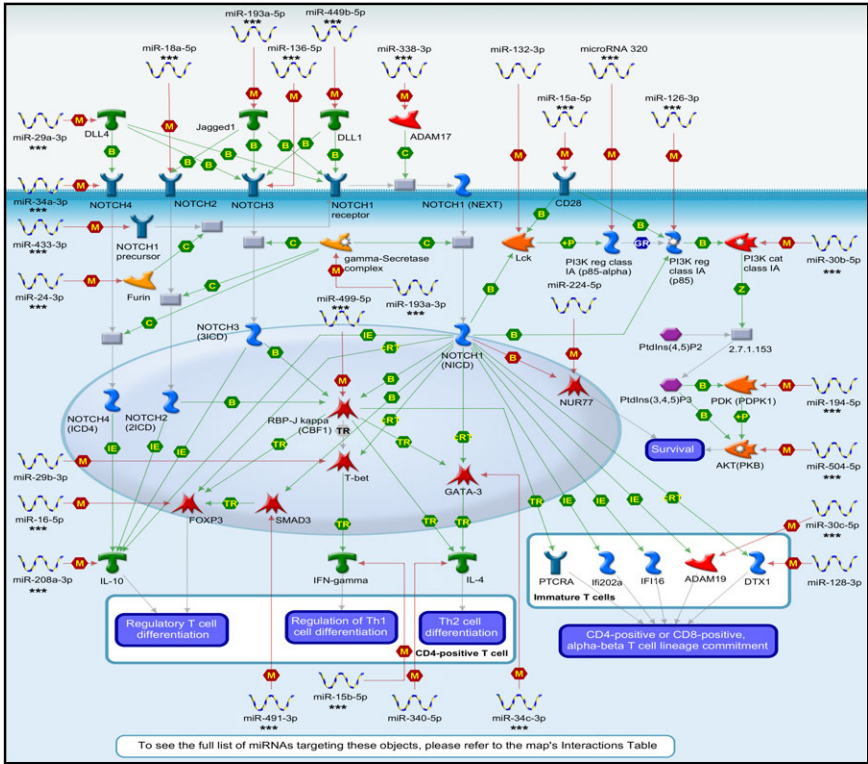
Relevant microRNA
and gene transcripts



Interactions Table



Regulation of immune cell differentiation by Notch signaling



Notch proteins are a family of evolutionarily-conserved transmembrane receptors: Notch homolog 1, translocation-associated (NOTCH1 receptor), Notch homologs 2, 3 and 4 (NOTCH2, NOTCH3, NOTCH4). Regulated intramembrane proteolysis mediated by Gamma-Secretase complex plays a critical role in Notch signalling. Ligand binding to Notch receptors stimulates ectodomain shedding mediated by metalloprotease, leaving the protein C-terminal fragment (CTF) consisting of transmembrane and intracytoplasmic domains. Gamma-Secretase complex cleaves CT of all Notch receptors, releasing active Notch intracytoplasmic domain (ICD) from the membrane. Notch signalling regulated by Gamma-Secretase complex has multiple, critical regulatory functions in immune cell development and function.

Notch signalling regulates immature and mature T cell differentiation. Delta-like 1 (DLL1) and Jagged 1 binding to NOTCH1 receptor in immature T cells promotes the two-step cleavage of NOTCH1 receptor by ADAM metalloprotease domain 17 (ADAM17) and Gamma-Secretase complex, generating the active intracellular fragment NOTCH1 (NICD). Notch signalling also prevents immune cells from apoptosis. Activated by DLL1 and Jagged1, NOTCH1 receptor signalling leads to the release of NOTCH1 (NICD).

MIRXES has 167 miRNAs targeting 36 proteins on this signalling cascade, indicating that most proteins involved in the NOTCH pathway are miRNA targets and may therefore be affected by miRNA action.

Hi-resolution
Pathway Map



Full pathway
summary & Citations



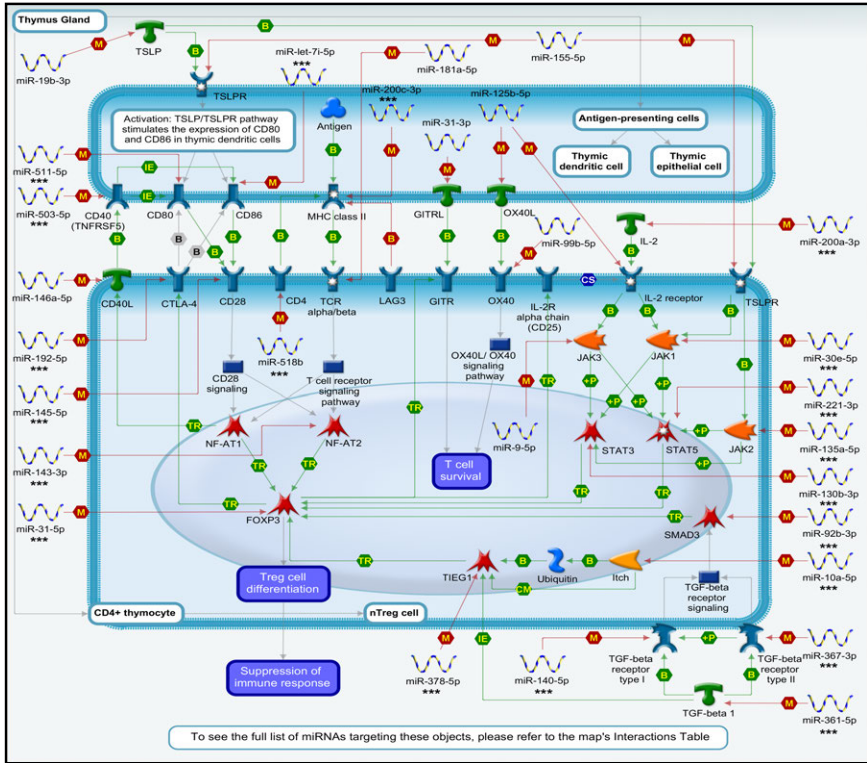
Relevant microRNA
and gene transcripts



Interactions Table



Differentiation of natural regulatory T cells



Natural regulatory T (nTreg) cells are a critical subset of T cells that mediate peripheral tolerance. nTreg cells undergo their lineage commitment and maturation in the thymus, where thymic dendritic cells and/or thymic epithelial cells act as antigen-presenting cells (APCs) to induce differentiation of thymocytes. nTreg cells are characterized by expression of FOXP3. Differentiation of nTreg cells is regulated by coordinated action of several signaling cascades: (1) TCR alpha/beta stimulation by Antigen-MHC class II complex presented by APCs, (2) CD28 signaling induced by CD80 and CD86 expressed in APCs, and (3) IL-2 and, probably, TGF-beta 1 signaling pathways. These signaling cascades lead to expression of FOXP3. In turn, FOXP3 up-regulates IL-2R alpha chain (CD25), CTLA-4 and GITR gene expression. FOXP3 is a master regulator for the nTreg cell lineage and is required to maintain the lineage identity and immunomodulatory functions of peripheral mature nTreg cells.

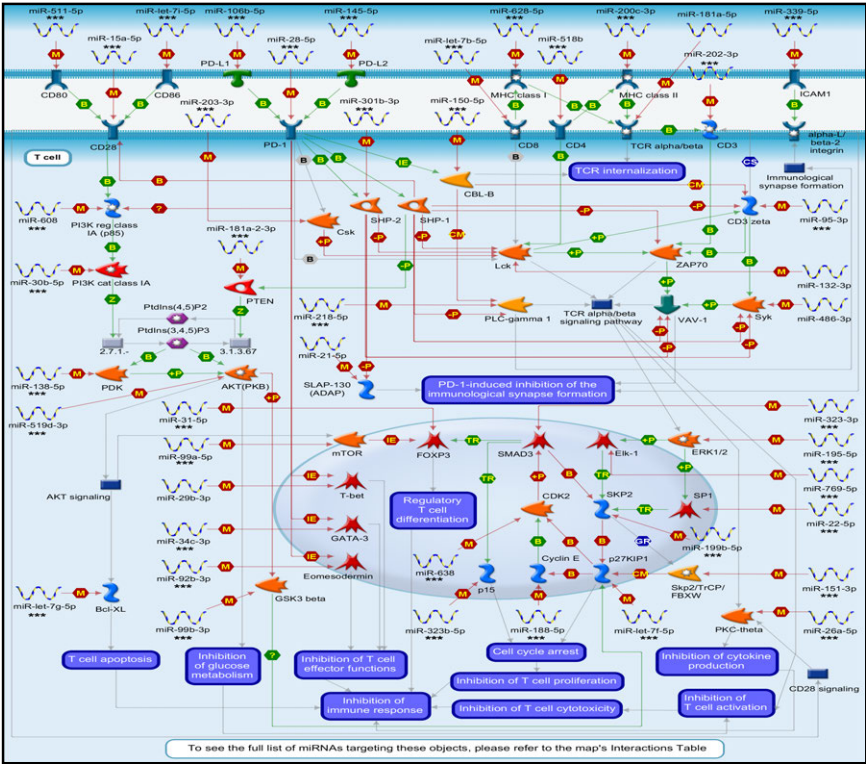
MIRXES has 145 miRNAs targeting 30 proteins on this signaling cascade, indicating that most proteins involved in the natural regulatory T cells signaling are miRNA targets and may therefore be affected by miRNA action.

Hi-resolution
Pathway MapFull pathway
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and gene transcripts

Interactions Table



Inhibitory PD-1 signalling in T cells



PD-1 is a cell surface receptor that suppresses the adaptive immune response. Engagement of PD-1 by its ligands PD-L1 or PD-L2 transduces a signal that inhibits proximal TCR alpha/beta signalling and CD28-mediated co-stimulation required for T cell activation, proliferation, cytokine production, and cytolytic function. In addition, PD-1 signalling promotes the development of regulatory T cells, and inhibits the expression of transcription factors that are associated with T cell effector functions.

MIRXES has 134 miRNAs targeting 23 proteins on this signalling cascade, indicating that most proteins involved in Inhibitory PD-1 signalling in T cells are miRNA targets and may therefore be affected by miRNA action.

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Pathway Map



Full pathway
summary & Citations



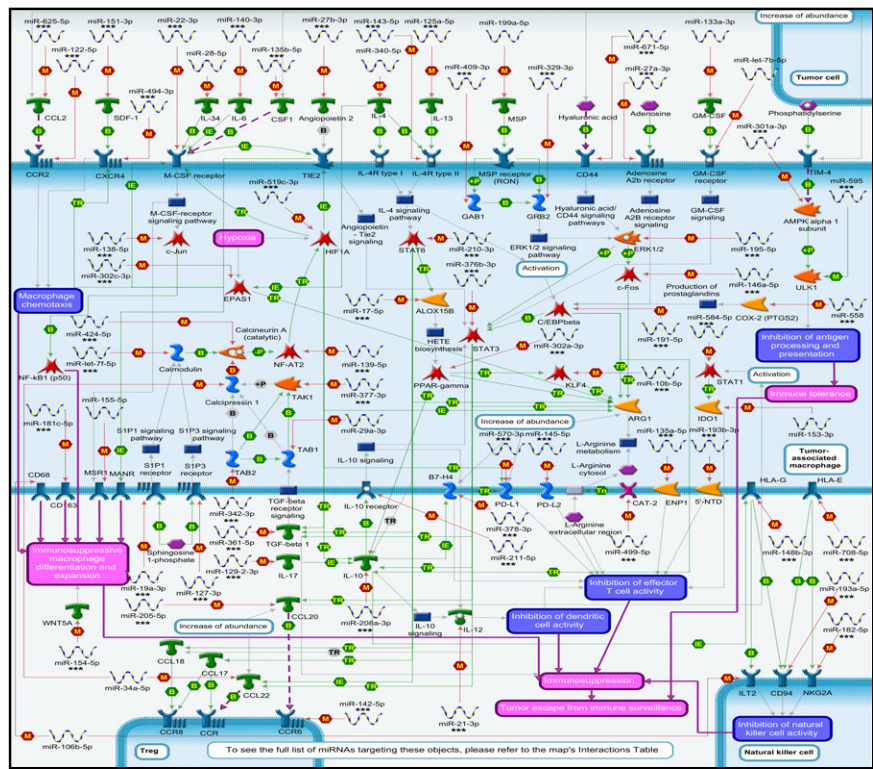
Relevant microRNA
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Interactions Table



Macrophage-induced immunosuppression in the tumour microenvironment



Tumour-associated macrophages (TAMs) form an important component of the tumour stroma, which is able to regulate tumour immune responses, tumour invasion and metastasis. The tumour microenvironment recruits monocytes and educates them towards a tumour-promoting immunosuppressive TAM phenotype via various stimuli, such as cytokines (IL-4, IL-13, IL-10, CSF1), chemokines (CCL2), and other tumour-derived factors (Adenosine, Hyaluronic acid, (R)-Lactic acid).

TAMs are able to promote inhibition of anti-tumour T cell response by both direct and indirect mechanisms. TAMs express increased levels of IL-10 and TGF-beta 1, and thus promote downregulation of IL-12 expression and disruption of dendritic cell functions, and activation of suppressive regulatory T cells (Treg) cells. Moreover, TAMs upregulate the expression of T cell suppressive molecules PD-L1, PD-L2 and B7-H4, and natural killer (NK) cell suppressive receptors HLA-G and HLA-E. TAMs express ARG1, which depletes L-arginine from microenvironment and thus inhibits T cell receptor re-expression. Also, TAMs express CCL17, CCL18, CCL20 and CCL22, which promote recruitment of Treg to tumour site.

MIRES has 203 miRNAs targeting 69 proteins on this signalling cascade, indicating that most proteins involved in macrophage-induced immunosuppression in the tumour microenvironment are miRNA targets and may therefore be affected by miRNA action.

Hi-resolution
Pathway Map



Full pathway
summary & Citations



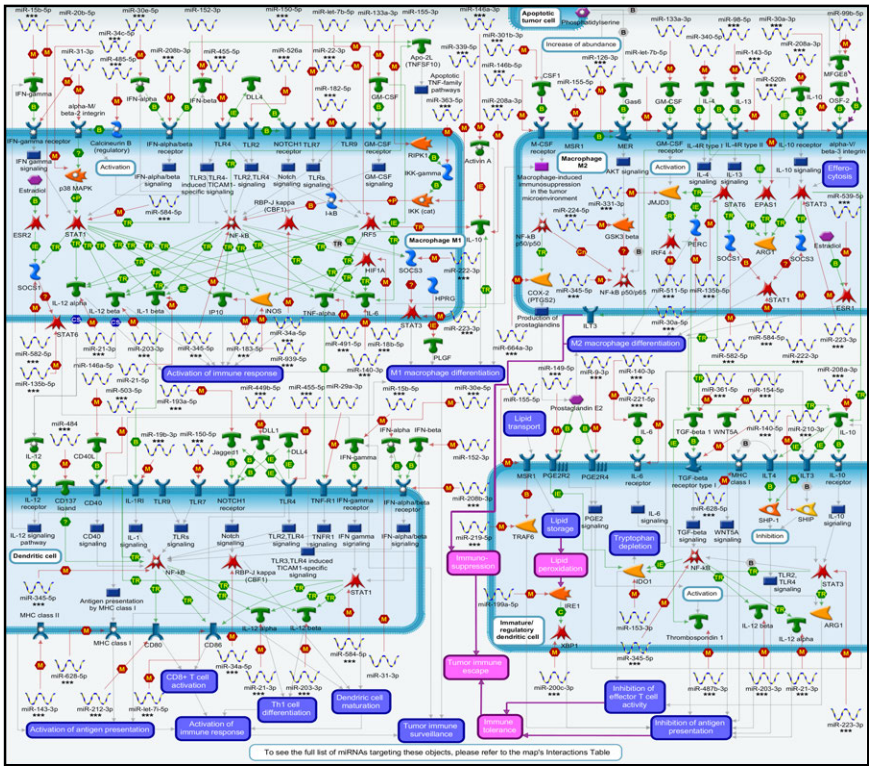
Relevant microRNA
and gene transcripts



Interactions Table



Macrophage and dendritic cell phenotype shift in cancer



Tumour-associated macrophages (TAMs) and dendritic cells (DCs) play an important role in the regulation of tumour immune responses. During tumour progression, circulating monocytes and macrophages are actively recruited into tumours where they alter the tumour microenvironment. Based on their function, macrophages are divided broadly into two phenotypes: M1 macrophages, which are involved in the inflammatory response, pathogen clearance, and antitumour immunity, and M2 macrophages, which influence an anti-inflammatory response, and pro-tumorigenic properties. TAMs shift their functional phenotypes in response to various microenvironmental stimuli generated from tumour and other cells, and polarize into immunosuppressive M2-like macrophages. Mature DCs have the ability for antigen cross-presentation and promotion of the activation of effector T cells that target tumour cells. However, the tumour microenvironment can polarize DCs, either inhibiting DCs maturation, or transforming them into immunosuppressive regulatory DCs, a tolerogenic phenotype which limits the activity of effector T cells and supports tumour growth and progression.

miRXES has 210 miRNAs targeting 93 proteins on this signalling cascade, indicating that most proteins involved in Macrophage and dendritic cell phenotype shift in cancer are miRNA targets and may therefore be affected by miRNA action.

Hi-resolution
Pathway Map



Full pathway
summary & Citations



Relevant microRNA
and gene transcripts



Interactions Table



Purchasing information

Product	Description	Catalogue No.
ID3EAL miRNA Knowledge Panel 192 Targets, 96-well (2)	ID3EAL Biofluid A-B miRNA Knowledge Panel 192 Targets for 2 samples, 2 x 24 µl of ID3EAL miRNA RT Primers 96-plex, 1 x Panel RNA Spike-in, 4 x 96-well PCR plates	1105251
ID3EAL miRNA Knowledge Panel 192 Targets, 96-well (6)	ID3EAL Biofluid A-B miRNA Knowledge Panel 192 Targets for 6 samples, 2 x 24 µl of ID3EAL miRNA RT Primers 96-plex, 1 x Panel RNA Spike-in, 12 x 96-well PCR plates	1105252
ID3EAL miRNA Knowledge Panel 192 Targets, 96-well (12)	Qty of 2 x #1105252, ID3EAL Biofluid A-B miRNA Knowledge Panel 192 Targets for 12 samples, 2 x 24 µl of ID3EAL miRNA RT Primers 96-plex, 2 x Panel RNA Spike-in, 24 x 96-well PCR plates	1105253
ID3EAL miRNA Knowledge Panel 192 Targets, 96-well (24)	Qty of 4 x #1105252, ID3EAL Biofluid A-B miRNA Knowledge Panel 192 Targets for 24 samples, 4 x 24 µl of ID3EAL miRNA RT Primers 96-plex, 4 x Panel RNA Spike-in, 48 x 96-well PCR plates	1105254
ID3EAL miRNA Knowledge Panel 384 Targets, 96-well (2)	ID3EAL Cancer A-D miRNA Knowledge Panel 384 Targets for 2 samples, 4 x 24 µl of ID3EAL miRNA RT Primers 96-plex, 1 x Panel RNA Spike-in, 8 x 96-well PCR plates	1105261
ID3EAL miRNA Knowledge Panel 384 Targets, 96-well (6)	ID3EAL Cancer A-D miRNA Knowledge Panel 384 Targets for 6 samples, 4 x 24 µl of ID3EAL miRNA RT Primers 96-plex, 2 x Panel RNA Spike-in, 24 x 96-well PCR plates	1105262
ID3EAL miRNA Knowledge Panel 384 Targets, 96-well (12)	Qty of 2 x #1105252, ID3EAL Cancer A-D miRNA Knowledge Panel 384 Targets for 12 samples, 4 x 24 µl of ID3EAL miRNA RT Primers 96-plex, 4 x Panel RNA Spike-in, 48 x 96-well PCR plates	1105263
ID3EAL miRNA Knowledge Panel 384 Targets, 96-well (24)	Qty of 4 x #1105252, ID3EAL Cancer A-D miRNA Knowledge Panel 384 Targets for 24 samples, 8 x 24 µl of ID3EAL miRNA RT Primers 96-plex, 8 x Panel RNA Spike-in, 96 x 96-well PCR plates	1105264
ID3EAL miRNA Knowledge Panel 192 Targets, 384-well (2)	ID3EAL Biofluid A-B miRNA Knowledge Panel 192 Targets for 2 samples, 2 x 24 µl of ID3EAL miRNA RT Primers 96-plex, 1 x Panel RNA Spike-in, 1 x 384-well PCR plates	1105351
ID3EAL miRNA Knowledge Panel 192 Targets, 384-well (6)	ID3EAL Biofluid A-B miRNA Knowledge Panel 192 Targets for 6 samples, 2 x 24 µl of ID3EAL miRNA RT Primers 96-plex, 1 x Panel RNA Spike-in, 3 x 384-well PCR plates	1105352
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ID3EAL miRNA Knowledge Panel 192 Targets, 384-well (24)	Qty of 4 x #1105252, ID3EAL Biofluid A-B miRNA Knowledge Panel 192 Targets for 24 samples, 4 x 24 µl of ID3EAL miRNA RT Primers 96-plex, 4 x Panel RNA Spike-in, 12 x 384-well PCR plates	1105354
ID3EAL miRNA Knowledge Panel 384 Targets, 384-well (2)	ID3EAL Cancer A-D miRNA Knowledge Panel 384 Targets for 2 samples, 4 x 24 µl of ID3EAL miRNA RT Primers 96-plex, 1 x Panel RNA Spike-in, 2 x 384-well PCR plates	1105361
ID3EAL miRNA Knowledge Panel 384 Targets, 384-well (6)	ID3EAL Cancer A-D miRNA Knowledge Panel 384 Targets for 6 samples, 4 x 24 µl of ID3EAL miRNA RT Primers 96-plex, 2 x Panel RNA Spike-in, 6 x 384-well PCR plates	1105362
ID3EAL miRNA Knowledge Panel 384 Targets, 384-well (12)	Qty of 2 x #1105252, ID3EAL Cancer A-D miRNA Knowledge Panel 384 Targets for 12 samples, 4 x 24 µl of ID3EAL miRNA RT Primers 96-plex, 4 x Panel RNA Spike-in, 12 x 384-well PCR plates	1105363
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