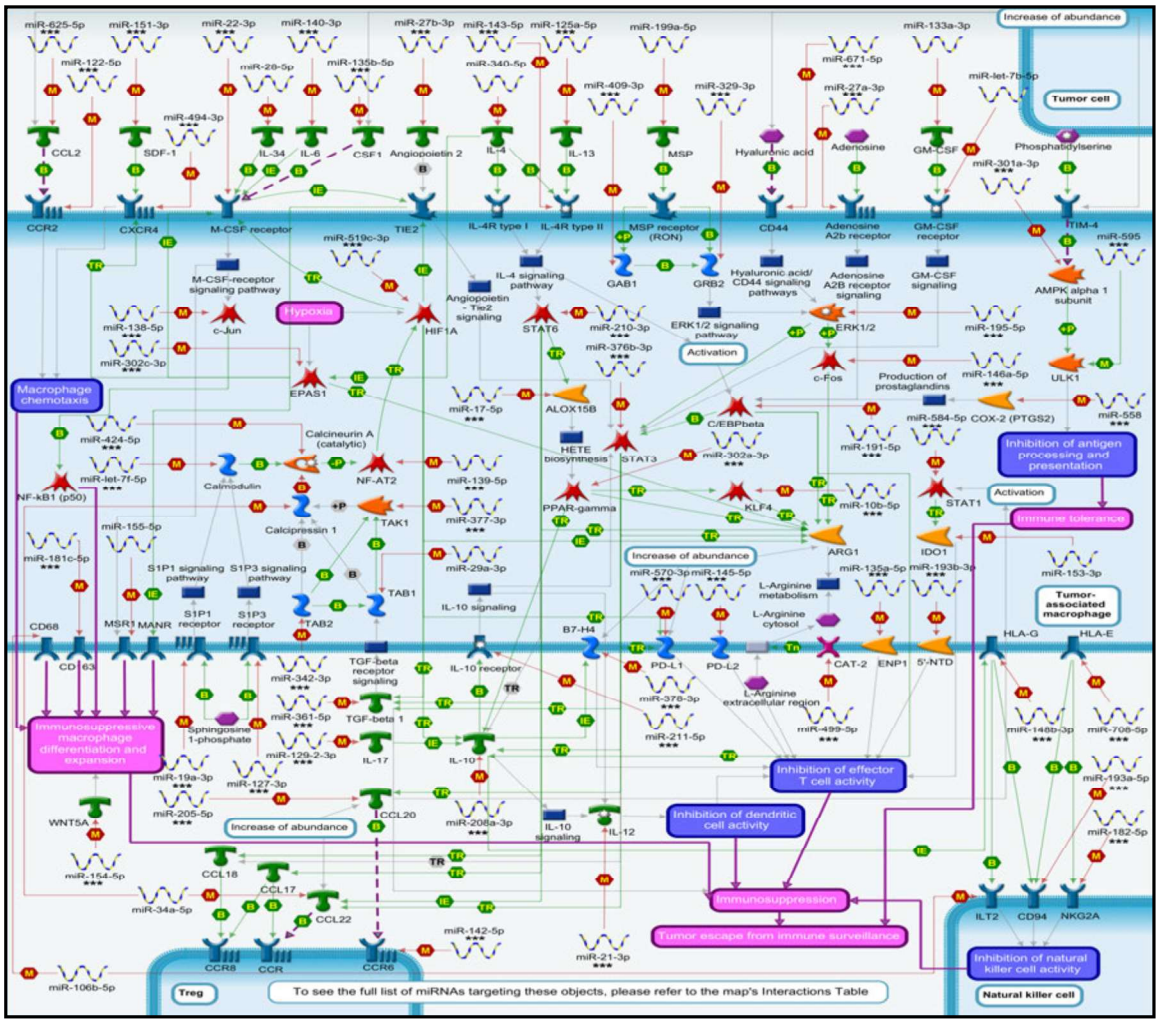
Macrophage-induced immunosuppression in the tumour microenvironment



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.

MiRXES 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