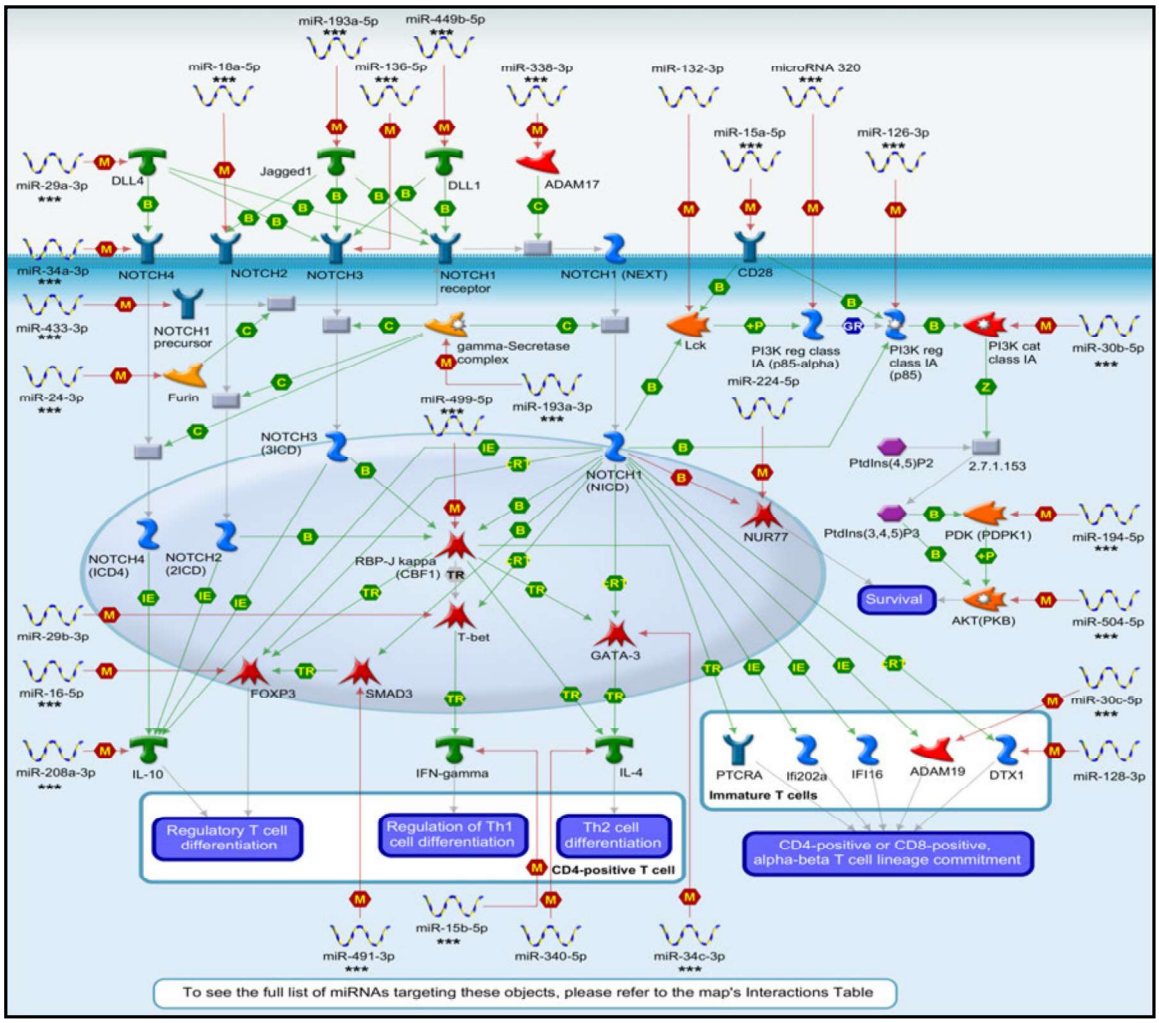
Regulation of immune cell differentiation by Notch signaling



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 CTF 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 metallopeptidase 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