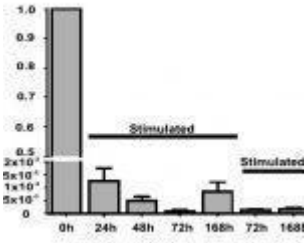
WNT7A: The new marker for resting T cells



The WNT signalling pathway regulates several processes involved in the homeostasis of hematopoietic cells, including self renewal, differentiation and proliferation. This pathway comprises 19 different ligands, at least 10 Frizzled receptors, 2 co-receptors and some molecules like the Dickkopf family that might regulate its activity. WNT signaling is often classified as canonical or WNT/β-catenin pathway and non-canonical pathways associated with Ca^{2+} signals of JNK kinases that are independent of β-catenin and are associated with cell movement.

WNT ligands are glycoproteins with conserved cysteine residues that can induce the canonical or non-canonical pathways after the interaction with Frizzled receptors. Among these, WNT7A is a 39-kDa protein that has been implicated in female reproductive tract development, maintenance of the blood-brain barrier, blood-retina barrier and corneal epithelium. Even though few reports have shown that WNT7A is expressed in some immature blood cells, its expression and role in mature leukocytes is not fully understood.

In this study, Barreto-Vargas, *et al.,* evaluated the WNT7A expression in different subpopulations of peripheral blood mononuclear cells (PBMCS) and have found that this ligand is mainly expressed by T cells and monocytes. Interestingly, after 2 hours of TCR activation, WNT7A expression (mRNA and protein) decreases by changes in the H3K4me2/3 occupancy and

histone deacetylases activity at its promoter. In fact, WNT7A expression is similar to other molecules that are regulated by TCR activation, including CD25, CD69 and CD71. In addition, a proliferative stimulus mediated by IL-2 keeps WNT7A expression at low levels but in the absence of this cytokine the expression of this gene tends to be restored. Furthermore, once WNT7A is downregulated, β-catenin is stabilized at the cytoplasm and translocates into the nucleus to induce the expression of WNT canonical target genes like MYC, CCND1 and MMP7. Moreover, WNT7A expression is abolished in the tumoral counterpart as a consequence of DNA hypermethylation of its promoter, which correlates with higher proliferation.

Altogether, these data implicate that WNT7A regulates cell proliferation and might act as a new marker for resting mature T cells.

Journal Article: Barreto-Vargas, C et al. WNT7A Expression is Downregulated in T Lymphocytes after T-Cell Receptor Activation Due to Histone Modifications and in T-ALL by DNA Methylation. Arch. Immunol. Ther. Exp.

Summary by Christian Barreto Vargas