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Wnt signaling in red blood cells

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Introduction & Aim: Red blood cells (RBCs) are the most common cell type in the human body. These cells deliver oxygen to the body's tissues and are composed of a cytoplasm that is rich in hemoglobin and is surrounded by a membrane that is essential for the cells function by providing properties such as stability and deformability. The membrane is composed of a lipid bilayer, transmembrane proteins and a filamentous meshwork of proteins such as actin and adducin that forms the cells cytoskeleton along the entire cytoplasmic surface of the membrane. RBCs lack a nucleus and other cellular organelles that enable gene expression. Thus, it has been assumed that signaling cascades such as the Wnt signaling pathway are not active in RBCs. The Wnt pathways are fundamental for normal development and homeostasis and regulate among other, cell growth, motility and differentiation. Although there is no functional data connecting between Wnt signaling and RBCs, previous proteomic studies have shown that some of the non-canonical Wnt signaling components, such as specific small GTPases and kinases are present in RBCs. In this study, we show for the first time that Wnt ligands activate signaling cascades in RBCs.

Methods: RBCs were collected from healthy donors and treated with different Wnt ligands. A large number of methods were used to evaluate the RBCs morphological properties, life span, vitality, flexibility and protein expression patterns.

Results: Our results clearly show that different Wnt ligands can dramatically increase the live span of RBCs by affecting the cells membrane cytoskeleton. Some of the Wnts affects include activation of GTPases such as Rac, JNK and RhoA, which lead to actin modification. These changes in the actin cytoskeleton result in increased membrane stability. In parallel, treating RBCs with Wnts leads to activation of PKC and RhoA resulting in phosphorylation of adducin which in turn increases the cells membrane flexibility and improves the vitality of the cell.

Conclusion: Our novel findings indicate that the non-canonical Wnt signaling pathway in RBCs is active and can stabilize the RBCs cytoskeleton enhancing the vitality, deformability and life span of the cell. These novel findings may help in the development of new therapeutic strategies for people suffering from different hemolytic disease that affects the RBCs cytoskeleton and provide new insights into the improvement of stored RBC units.

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Prognostic value of T-cell CD38 expression in B-chronic lymphocytic leukemia

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B-cell chronic lymphocytic leukemia (B-CLL) is a heterogeneous disease with some patients having an indolent course never needs treatment, while others having rapidly progressive one requires intensive treatment. In recent decades, numerous prognostic markers, such as IgVH mutational status, ZAP-70 and the expression of CD38 on leukemic cells were introduced to screen for patients likely to have progressive course of B-CLL bearing the potential to facilitate risk-adapted treatment strategies. In B-CLL, T cell function is shown to be dysregulated. CD38 has been demonstrated to be an important transmembrane signaling molecule of T cell with a direct effect on its function. The present study was conducted to analyze CD38 expression on T cells by flow cytometry to evaluate its impact on the clinical course of 88 unselected B-CLL patients and correlate it with other risk factors. CD38 expression level on T cells was shown to predict the clinical course of B-CLL in male patients but not in female patients. Male patients showed CD38 expression on T cells in a stage-dependent manner, in contrast to female patients who showed higher expression irrespective to clinical staging. CD38 expression on T cells negatively interacted with treatment-free survival in male patients. Multivariate analysis revealed that CD38 expression level on T cells is an independent prognostic factor in B-CLL male patients. A simultaneous evaluation of CD38 expression on both B-CLL cells and T cells allowed predicting male patient groups with the most favorable prognosis as well as those with the worst.

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