Wnt6 in Progenitor Maintenance During Hematopoiesis: A Potential Biomarker for Acute Myeloid Leukemia (AML)

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Hematopoiesis, or blood cell development, is a strictly regulated process and the maintenance of blood progenitors requires various pathways in cells within a microenvironment. Deregulation of these processes will result in hematopoietic malignancies, such as leukemia. I used Drosophila melanogaster, where hematopoietic development and functions are similar to those in vertebrate systems, including mammals, as a model system of hematopoiesis. Hematopoiesis in Drosophila takes place in a specialized organ called the lymph gland and within the lymph gland, blood progenitors can undergo a differentiation process or become quiescent. In this study, I investigated the role of the Wnt6 ligand in the progenitor maintenance pathway during hematopoiesis. RNA-interference mediated depletion of Wnt6 demonstrated a phenotype of over-differentiation and decreased progenitor and intermediate progenitor populations. Over-expression of Wnt6 resulted in a strong progenitor maintenance phenotype, indicating that Wnt6 is a crucial regulator of the progenitor maintenance pathway during the hematopoietic process. This study revealed that Wnt6 signaling can trigger progenitors into a G2 phase arrest and quiescence. Wnt6 was found to be involved in the ß-catenin mediated canonical pathway, which controls irregular ROS (reactive oxygen species), a signaling factor that promotes aberrant myeloid precursors. The involvement of Wnt6 in both progenitor and intermediate progenitor differentiation processes suggests Wnt6's potential as a molecular marker for Acute Myeloid Leukemia, a blood cancer characterized by excess immature blood cells. These new developments can lead to a better understanding of the pathogenesis of relevant hematologic malignancies and can have therapeutic applications.

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