Targeting the Wnt and Notch signaling pathway as a therapeutic strategy against leukemia

Once thought to serve a purely structural role in the body, the bone has recently been shown to play a crucial role in the regulation of many important physiological processes, from metabolism to male fertility to the production of white and red blood cells. When these precisely coordinated physiological processes are perturbed, serious diseases can arise such as Acute Myelogenous Leukemia (AML) and Myelodysplastic Syndrome (MDS). AML is one of the most common acute leukemias affecting adults, and accounts for up to 1% of cancer deaths in the United States. This technology identifies potential causes and biomarkers for these debilitating diseases. The technology demonstrates that overstimulation of the Wnt signaling pathway in osteoblasts (bone-forming cells) of mice rapidly and reliably induces both AML and MDS. Additionally, by following the downstream consequences of this pathway overstimulation, biomarkers for AML and MDS are identified as potential targets for disease diagnostics.

Treatment of leukemia by targeting osteoblasts rather than hematopoietic cells

Much of the research effort on AML and MDS has been focused on the hematopoietic (blood-forming) cells in the bone marrow. This technology focuses on a different signaling pathway involving abnormal Wnt signaling and subsequent increased expression of Notch ligands. The increased expression of Notch ligands induced proliferative activity that led to the development of AML and MDS in mouse models. Furthermore, it was found that an excess of associated proteins called b-catenin indicated disease pathogenesis as well. Thus, inhibitors of Wnt or Notch signaling may be a viable treatment strategy for leukemia patients while excess b-catenin nuclear staining in osteoblasts may be used as a diagnostic biomarker.

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Applications:

• Targeting Wnt and notch pathway for leukemia treatment
• Biomarker for diagnosing AML and MDS development

Advantages:

• Potential for using already-existing Notch and Wnt inhibitors to treat AML
• Reliable biomarker for AML and MDS diagnosis
• Dual Wnt-Notch inhibition as a treatment for AML and MDS

Patent information:

Patent Pending
Tech Ventures Reference: IR CU12342

Related Publications:


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