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Mutational Analyses of IgVh genes in chronic lymphocytic leukemia

Technology Reference

R206

Keywords:

Diagnostic Tool

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Inventor

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Dr. Janet Plate's research interests are in the regulation of immune cell differentiation including the role that cell surface molecules play in transmitting signals that initiate molecular steps in the differentiation pathway. The manner in which alterations in normal signaling pathways contribute to disease states are being investigated. Dr. Plate's laboratory investigates two main diseases: Chronic Lymphocytic Leukemia (CLL), the most common adult leukemic disease of B-lymphocytes, and, pancreatic cancer - the fourth leading cause of cancer deaths. A variety of molecular and cellular biological approaches are being used in these studies.

PATENT

US Patent Pending

AREAS OF APPLICATION

- Chronic lymphocytic leukemia is now classified as one generic disease. This novel invention will provide a method for diagnosing subtypes of CLL.

ADVANTAGES

- More Accurately predict the disease course of CLL subtypes
- Allow physicians to develop different treatment strategies for their CLL patients based on a patients diagnostic subtype
- Less than 3 ml of blood is required from a patient

THE TECHNOLOGY

This discovery would make available the mutational analyses of IgVh genes in CLL patients to physicians who would like to know their patients CLL mutational status. The importance of determining mutational subtypes in CLL versus other phenotypes was recently confirmed in studies demonstrating that the mutational status of the leukemic cells is a more reliable prognostic indicator than other phenotypes including CD38 expression. ZAP70 gene expression appears to correlate better than CD38 with the unmutated subtype, but no census clinical assay for ZAP70 has been validated for use as a clinical diagnostic tool. This assay uses molecular biological techniques to isolate total RNA from leukemic peripheral blood cells, synthesize cDNA, then perform a round of PCR with a set of 7 primers to identify the IgVh gene family expressed in the monoclonal leukemic cells. A second PCR is then performed using a primer set for the 5' leader sequence of the identified IgVh family. The second PCR product is purified and DNA sequenced in both directions. The sequence is then compared with the genomic sequence through NCBI IgVbase, the number of changes in patient's IgVh gene sequence is recorded and the percentage of mutational changes calculated.

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