Validation of Human Leukemia Mouse Model Using RNA-Sequence Gene Expression Profiling

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Background

Leukemia can be maintained in SCID mice by injecting cell line models or by serial transplantation in immunocompromised mice. Before being used for novel drug testing, these mouse models need to be validated by demonstrating that they carry the same leukemic features as the original leukemia from patients.

There are several methods to validate leukemia mouse models: (1) staining with specific cell markers (CD45, B220, CD117, etc.), (2) measuring proliferation of leukemic cells using Ki67, (3) Southern blot analysis of DNA to detect clonal rearrangements of immunoglobulin or T-cell receptor gene loci, (4) using whole-genome microarrays or RNA-sequencing to compare the gene expression profile of the SCID mice model with that of the original leukemia, and (5) performing other specific assays (e.g., detection of specific mutations by PCR). Among these methods, RNA-sequencing is the most powerful tool to validate a leukemia mouse model, because it can provide a comprehensive view of the gene expression profile of the model, which can be compared with that of the original leukemia.

The patient's leukemia was derived from a young female patient with acute lymphoblastic leukemia (ALL) and was characterized by high expression of CD7. The patient was treated with chemotherapy and achieved complete remission. After 3 years of remission, the patient relapsed and was treated with additional chemotherapy. Despite this treatment, the patient ultimately died of leukemia.

To validate the leukemia mouse model, we performed RNA-sequencing on bone marrow samples from the patient and the xenograft model. The data showed that the xenograft model recapitulated the gene expression profile of the patient's leukemia, with high expression of CD7. In addition, the xenograft model retained the genetic features of the patient's leukemia, such as high expression of BCL2 and BCL6. These findings suggest that the xenograft model is a valuable tool for studying the biology of ALL and for testing new therapeutic agents.