Study of two sisters sheds light on lymphoma evolution

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When a 41-year-old woman was diagnosed with chronic-phase chronic myeloid leukemia, she received a bone marrow transplant and subsequent leukocyte infusion from her sister. These treatments controlled her leukemia, but seven years later, both sisters developed follicular lymphoma.

Although the phenomenon of a donor passing a malignancy to a recipient is well documented and considered a minimal risk to those in the transplant community, this case gave scientists the unique opportunity to understand the genetic abnormalities that led to follicular lymphoma in both cases.

"We were able to combine clinical activity with laboratory expertise to gain a real insight into the biology involved," said David Weinstock, M.D., an assistant professor of medicine at Dana-Farber Cancer Institute, who published the case study in a recent issue of *Cancer Discovery*, the newest journal of the American Association for Cancer Research.

The study was funded by a Stand Up To Cancer Innovative Research Grant.

Both sisters are now in remission after standard chemotherapy treatment. Weinstock's research group will present their findings at the 2011 American Society of Hematology Annual Meeting and Exposition in San Diego on Dec. 12, 2011, at 6:00 p.m. PT.

Weinstock and his colleagues sequenced the DNA of samples derived from the two sisters as well as a frozen sample of the leukocyte infusion to determine the genetic lesions that led to the lymphoma.

They found that both sisters had identical BCL2/IGH rearrangements and the same V(D)J rearrangement. They also identified 15 mutations that were present in both lymphomas. Researchers recovered 14 of these mutations from the donor lymphocyte infusions using ultra-deep sequencing — a finding that indicates that a lymphoma ancestor harboring these mutations was passed from the donor to the recipient seven years before clinical presentation.

Weinstock said this sort of knowledge could one day lead to an early treatment for follicular lymphoma.

"Currently the only curative approach is stem cell transplantation, but the more we understand about the genetic aberrations that lead to follicular lymphoma, the better we'll be able to manage the disease," said Weinstock.

Provided by American Association for Cancer Research