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Dana-Farber to present new research on stem cell transplantation for myeloid cancers

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Improving outcomes for patients with myeloid cancers who undergo stem cell transplantation is a focus of several studies to be presented by Dana-Farber Cancer Institute scientists at the American Society of Hematology (ASH) Annual Meeting Dec. 1-4. The research points to new opportunities for preventing relapse after transplantation and determining which patients should be considered for lower-intensity chemotherapy in preparation for transplant.

Here are two examples of this research:

Loss of HLA protein linked to relapse of acute myeloid leukemia after stem cell transplant from matched unrelated donors

Genetic changes that cause tumor cells to lose HLA proteins can spur relapses in patients with myeloid cancers who undergo stem cell transplants from matched, unrelated donors, Dana-Farber researchers report in a new study. The findings indicate that the loss of HLA proteins—which are used by the immune system cell to distinguish healthy cells from diseased ones—enable tumor cells to evade detection by the immune system and resume their proliferation.

The findings, to be reported in an oral presentation at Session 723 on Monday, Dec. 3, at 2:45 p.m. PST in Grand Hall D of the Manchester Grand Hyatt San Diego, suggest new avenues for immunological

approaches to preventing relapse following transplant.

While stem cell transplants often produce remissions in patients with myeloid malignancies such as acute myeloid leukemia (AML) and myelodysplastic syndrome (MDS), some patients relapse a year or more after transplant. Researchers sought to determine if these late relapses are the result of genetic alterations in tumor cells that prevent transplanted immune system cells from recognizing and attacking the cancer.

The investigators conducted a genomic analysis of tumor tissue from 25 patients with AML or MDS who had relapsed after undergoing a transplant with stem cells from a fully or partially matched donor. Samples were collected prior to transplant, 100 days after transplant, and at the time of relapse. Each sample was analyzed for abnormalities in any of 187 genes involved in myeloid malignancies or suspected of enabling cells to escape detection by the immune system.

Researchers identified three patients whose tumor cells lost HLA following transplant. Two of the patients had received stem cells from fully matched donors; the other had received them from a partially matched, unrelated donor. The findings suggest that HLA loss may enable tumor cells to foil the donor immune system's ability to detect important minor discrepancies in recipient leukemia cells.

"The donor's immune system is essential to cure after bone marrow transplantation," said R. Coleman Lindsley, MD, Ph.D., Dana-Farber physician and assistant professor of medicine at Harvard Medical School, who helped lead the study. "We show how some leukemias relapse by evading donor immune attack."

Telomere length linked to risk of death from toxicity

of high-dose chemotherapy in stem cell transplantation for myelodysplastic syndrome

Patients with myelodysplastic syndrome (MDS) whose blood cells have short telomeres—structures that protect the tips of chromosomes—have a greater risk of dying from the high-dose chemotherapy used in preparation for a stem cell transplant than do patients with longer telomeres, Dana-Farber physicians report in a new study. Treating such patients with lower-intensity chemotherapy regimens may reduce that risk.

The study findings are based on a measurement of telomere lengths in whole blood DNA samples from 1,514 patients who received donor stem cell transplants for MDS. Investigators found that patients age 40 or older who had short or intermediate-length telomeres had poorer overall survival than those with long telomeres. The association between telomere length and transplant-related death held only for patients who received high-intensity chemotherapy in preparation for transplant, not for those who received reduced-intensity regimens.

To explore genetic connections to telomere length, the researchers sequenced seven genes known to be involved in telomere maintenance. They found that mutations in three of those genes—TERT, TERC, and DKC1—are associated with patients with MDS who have short telomeres and poor transplant outcomes.

"This study identifies a group of MDS patients with shorter telomeres who are most vulnerable to the toxicities of bone marrow transplantation and points the way towards a more tailored approach to treatment," said Lindsley, the senior author of the study.

The findings will be discussed in an oral presentation at Session 637 on

Monday, Dec. 3, at 3:30 p.m. in Grand Hall A of the Manchester Grand Hyatt Sand Diego.

Provided by Dana-Farber Cancer Institute