

Certain donors with high T cell counts make better match for stem-cell transplant patients

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Using a simple blood test to measure the T lymphocyte count in donors for stem cell transplants may help identify the best match for patients in need of an allogeneic stem cell transplant, suggests a new study in the *Journal of Clinical Oncology* from researchers at the Abramson Cancer Center (ACC) of the University of Pennsylvania. Typically, matched siblings have been preferred over unrelated donors. This study shows that older patients who received stem cells from younger, unrelated donors with higher numbers of so-called killer T cells (CD8 cells) had significantly reduced risk of disease relapse and improved survival compared to those who received stem-cells from donors with low numbers of CD8 cells, including older matched siblings.

The study, led by Ran Reshef, MD, an assistant professor in the division of Hematology/Oncology and a member of the Hematologic Malignancies Research Program in the ACC, and David Porter, MD, the Jodi Fisher Horowitz Professor in Leukemia Care Excellence and Director of Blood and Marrow Transplantation in the ACC, suggests that screening for donor T cell characteristics will optimize donor selection and ultimately lead to more successful transplants in an older population.

Older individuals with blood cancers are often treated with reduced-intensity allogeneic stem cell transplants, in which the chemotherapy or radiation dose is reduced, resulting in fewer side effects for patients. Such transplants rely heavily on the ability of donor T cells to kill [cancer cells](#), an effect known as "graft-vs-tumor" activity. More and more elderly patients are receiving these types of transplants—but the biggest

barrier to long-term survival is disease relapse, which occurs in more than a third of the patients, presumably because the donor T-cells fail to eradicate the malignant cells.

"Developing better tools to identify ideal donors is an exciting prospect—and fundamental to improving transplant outcomes," Reshef said. "There may be suitable donors out there who are overlooked because they are considered a poorer match by today's donor selection algorithms. Refining the screening method could greatly increase the chances of finding the most appropriate donor, one that will induce the most potent graft-vs-tumor response."

Today, about a third of patients find themselves with a matched sibling or relative. Otherwise, the search is widened to unrelated donor registries. Identifying the best donor has so far focused primarily on human leukocyte antigen (HLA) matching, because other criteria that predict the potency of the donor immune system have not been available.

In the new study, the researchers retrospectively evaluated associations between T cell doses present in the transplant graft and outcomes in 200 patients from the ACC with blood cancers (acute myeloid leukemia, myelodysplastic syndrome, non-Hodgkin lymphoma, and others). Knowing that CD8 cells can kill cancer cells, while CD4 cells help suppress or regulate immune responses, the investigators examined these two types of T-cells closely and found that the numbers of CD8 cells in the stem-cell graft had a dramatic impact on survival. They also found that high CD8 cell counts were much more common among young donors.

Consequently, the four-year overall survival rates were 59 percent for younger, unrelated donor grafts with high CD8 counts, 18 percent for younger, unrelated donor grafts (50). This suggests it would be better to use a younger unrelated donor graft with high CD8 cells instead of an

older sibling donor.

Additionally, the CD8 cell content of the graft could be predicted by measuring the proportion of CD8 [cells](#) in a blood test from potential stem cell donors, providing a simple way to screen for the best donor even before the stem cell graft was collected.

The next step is to determine how well these strategies translate into better outcomes in a prospective trial.

"This is a method deserving additional investigation, which could refine the standardized matching system used by registries, such as Be the Match and others, and ultimately optimize the [donor](#) pool for older patients undergoing these transplants," said Reshef.

Provided by University of Pennsylvania School of Medicine

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