Immunotherapy Protects Against CMV After Cord Blood Transplant

Megan Brooks May 05, 2015

A novel adoptive immunotherapy offers a way to protect against potentially lethal cytomegalovirus (CMV) infection after hematopoietic stem cell transplant from umbilical cord blood or CMV-seronegative adult donors, hint the results of a phase 1 pilot study.

In a first, researchers were able to create CMV-specific T-cells from CMV-naive T-cells derived from umbilical cord blood and adult CMV-seronegative donors. They infused the novel T-cells into three consecutive children who had undergone cord blood transplant and were at high risk for CMV infection. The procedure appeared safe and potentially protective.

There was no infusion-related toxicity or graft-vs-host disease, and the children remain free of CMV more than 2 years after cord blood transplant, the researchers report. One patient experienced a reactivation of both CMV, which resolved with treatment; the other two patients have shown no signs of infection.

The study was published [online](http://stm.sciencemag.org/content/7/285/285ra63) April 29 in *Science Translational Medicine.*

**Proof of Principle**

"It's the first time that we know of that antigen-specific T-cells from cord blood have been given to anyone," first author Patrick J. Hanley, PhD, of the Division of Blood and Marrow Transplantation at Children's National Medical Center, in Washington, DC, noted in an interview with *Medscape Medical News.*

Umbilical cord blood is a "rich source of stem cells" for stem cell transplant, but virtually all of the cells are naive, and until now, no one has been able to grow virus-specific T-cells for CMV in the clinical setting, explained Dr Hanley, who conducted most of the work during his postdoctoral training in the Center for Cell and Gene Therapy at Baylor College of Medicine, in Houston, Texas.

CMV is one of the most problematic viruses after bone marrow transplant. "When the donor has had CMV, it's less of a problem. We can make CMV-specific cells from memory T-cells and give them to the recipient. But when the donor has not had CMV and the recipient is CMV-seropositive, that creates a big risk factor. In fact, a lot of transplanters will choose a different donor if they can," Dr Hanley said.

"We were able to expand T-cells from umbilical cord blood and also from adult donors who were CMV-seronegative, and in the case of the cord blood T-cells, give them to cord blood transplant recipients," Dr Hanley said. A "fun basic science fact," he said, is that CMV-specific T-cells generated from naive T-cells from cord blood and CMV-seronegative adult donors recognize and respond differently to different parts of CMV than memory T-cells. The researchers are now looking into why this is so.

"We've been quite good at generating T-cells against viruses, and hopefully, that will become standard of care in the next 5 to 10 years, but the limitation has been that we can only make those cells when people have had the virus before, if they are seropositive," Dr Hanley explained.

This research provides "proof of principle [that] we are no longer limited by T-cell memory," Dr Hanley added in a news release. "This gives us a platform to generate T-cells against tumors, additional viruses, or any antigen where we do not have enriched T-cell precursors."

"This work is exciting because we may ultimately be able to use this treatment as a 'prophylactic vaccine' to improve outcomes for all high-risk transplant recipients, including patients after solid organ transplantation," added Catherine Bollard, MD, director of the Program for Emerging Technologies in Immune Cell Therapies at Children's National Medical Center, who is corresponding author of the study.

*The study was supported by a postdoctoral fellowship to Dr Hanley from the American Cancer Society, the Cancer Prevention Research Institute of Texas, and the National Cancer Institute. The authors have disclosed no relevant financial relationships. Dr Hanley and Dr Bolland have filed a provisional patent application for expansion of CMV-specific T-cells from CMV-seronegative donors.*

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