

# Pre-transplant umbilical cord blood expansion speeds establishment of new blood supply in patients

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Donated umbilical cord blood establishes a new blood supply in patients more quickly after transplantation when it is first expanded in the lab on a bed of cells that mimics conditions in the bone marrow, researchers report in the Dec. 13 edition of the *New England Journal of Medicine*.

The phase 1/2 study led by scientists at The University of Texas MD Anderson Cancer Center addresses the main difficulty with using umbilical [cord blood stem cells](#) to replace the blood supply of patients who have had theirs destroyed by chemotherapy or radiation to treat leukemia, lymphoma and other blood-based diseases.

"You get fewer [cells](#) - blood stem cells, [immune cells](#) - from two umbilical cords than you do by collecting from a donor's bone marrow or peripheral blood," said senior author Elizabeth Shpall, M.D., professor in MD Anderson's Department of Stem Cell Transplantation and [Cellular Therapy](#).

That lengthens the time between infusion of the cord blood cells and establishment, or engraftment, of the new blood supply. "It's a high-risk time, patients don't have [white blood cells](#) to fight infection, they don't have platelets to keep them from bleeding," Shpall said.

### **Umbilical Cord Blood Transplantation**

About 75 percent of those who need a blood stem cell transplant do not have a matched donor.

Umbilical cord blood is readily available and does not have to be precisely matched to patient.

After a mother consents to donate her child's umbilical cord, it's harvested in the delivery room after she gives birth.

The [National Marrow Donor Program](#) has 9.5 million blood stem cell donors listed and 165,000 cord blood units.

Banks worldwide share cord blood units, more than 500,000 available.

### **MD Anderson Cord Blood Bank**

Is the world's fastest-growing bank.

Has stored 16,284 units

73 percent of cord donors are among racial, ethnic groups underrepresented in the marrow donor pool.

790 units transplanted worldwide

4,680 units not fit for use have been shared with scientists for research.

**To donate call: 713-563-8000 or 1-866-869-5100**

This shows Cord Blood Facts. Credit: MD Anderson

## **More cells transplanted, faster recovery**

By taking blood from one of the two donated umbilical cords and growing it in the laboratory on a bed of mesenchymal [precursor cells](#), the researchers greatly increased the number of cells transplanted, reduced

recovery time and increased the proportion of patients whose new blood became established.

"Expansion achieved a median 12-fold increase in total cells transplanted and a 40-fold increase in the number of CD34+ cells, which are crucial for engraftment," Shpall said. "This led to faster engraftment of white blood cells and platelets, which we believe enhances patient safety."

"Pre-transplant cord blood expansion on mesenchymal stromal cells could become the new standard of care if our findings are confirmed in a randomized clinical trial," Shpall said.

Shpall notes that readily available mesenchymal precursor cells provided by Australian regenerative medicine company Mesoblast Limited reduced the time it takes to expand the cord blood cells from more than a month to a few weeks.

Australian scientist and study co-author Paul Simmons, Ph.D., executive vice president for research at Mesoblast, led the research team that originally identified mesenchymal precursor cells and discovered a way to extract mesenchymal cells from the bone marrow for use in other settings.

Only about 25 percent of those needing a blood stem cell transplant have a matching donor - the ideal situation for a transplant. Double-cord blood transplant is one of the main options for the rest, which includes a higher proportion of those with African, Asian or Latino heritage, who are underrepresented among blood stem cell donors.

Patients who receive peripheral blood from a matched donor, the main method used in blood stem cell transplants, on average have their infection-fighting white blood cells (neutrophils) engraft in 11 days and their platelets in 13 days. For a double-cord blood transplant, the same

cells engraft in 26 days and 53 days, respectively.

"That isn't good enough," Shpall said. She and other researchers have long sought optimal ways to expand cord blood. The key cells are blood stem cells, which can differentiate into any type blood cell - platelets, white cells or red cells.

## **Expansion hastens white cell, platelet engraftment**

In 31 high-risk patients, the team expanded blood cells from one of the two cords transplanted. They compared outcomes to 80 cases of standard double-cord blood transplant reported to the Center for International Blood and Marrow Transplantation.

The study's composite endpoint of neutrophil engraftment within 26 days, platelet engraftment within 60 days and survival at 100 days was reached by 63 percent of the expanded cord blood group compared with 24 percent among controls.

Patients with expanded cord blood had:

- Median time to neutrophil engraftment of 15 days, compared to 24 for controls.
- Median time of platelet engraftment of 42 days, compared with 49 for controls.
- Cumulative neutrophil engraftment rate of 88 percent at 26 days, compared with 53 percent in control cases.
- Cumulative platelet engraftment rate of 71 percent at 60 days, compared with 31 percent in controls.

"In addition to the faster engraftment of neutrophils and platelets, the quality of engraftment was better than anything we've seen," said first

author Marcos de Lima, M.D., who led the study while on MD Anderson's faculty and is now professor of medicine at Case Western Reserve University School of Medicine in Cleveland.

Goals: Less bleeding, fewer infections, hospital stays and transfusions

"Cord blood transplant patients often need platelet transfusions for months," de Lima said. "Most of the control group did not start making their own platelets, while in the study group, 70 percent of patients engrafted within 60 days."

"From patients' perspective, these are things you want to see going forward: less bleeding, less infection, fewer trips to hospital and less dependence on transfusions," de Lima said.

Mesoblast is sponsoring a prospective, randomized Phase 3 trial led by Shpall in 15 centers that will compare 120 patients who receive one expanded and one regular cord blood transplant to 120 others who get the standard double cord transplant.

## **Recreating bone marrow environment in lab flasks**

Shpall and Ian McNiece, Ph.D., also a professor in [Stem Cell Transplantation](#) and Cellular Therapy, have been working on cord blood expansion for 15 years. They thought mesenchymal precursor cells, which form a supportive network in the bone marrow that allows blood cells to grow, would enhance cord blood cell expansion. The stromal cells do not provoke an immune response when donated.

They developed a technique to take mesenchymal stromal cells from a relative of the patient, cultivate those cells, and then expand cord blood on a layer of the cells in the lab. The logistics and time involved in this procedure limited enrollment in the clinical trial. They evaluated

Mesoblast's cells, found them to be superior to donor cells in terms of expansion of blood-forming precursors, and switched to the off-the-shelf cells.

"This really recapitulates what happens in our [bone marrow](#), where mesenchymal [stromal cells](#) provide the optimal environment for [blood stem cells](#) to proliferate and differentiate," McNiece said. "We also supplement growth factors to the media the cells are grown in to drive them in a direction of differentiation we think is optimal for patient treatment."

Provided by University of Texas M. D. Anderson Cancer Center

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