Selected cells from blood or bone marrow may provide a route to healing blood vessels

August 13 2010

Isolating cells from a patient's blood or bone marrow that nourish blood vessels may be a safer and less arduous route to treatment of cardiovascular disease than obtaining rare stem cells, according to research from Emory University School of Medicine.

In recent clinical trials, doctors in several countries have tested the ability of a patient's bone marrow cells to repair damage, such as heart attacks and peripheral artery disease, created by problems of blood flow.

"The focus has been on stem cells, but it looks like the main beneficial effects come from transplanted cells' ability to support the growth of nearby blood vessels," says senior author Young-sup Yoon, MD, PhD, associate professor of medicine (cardiology) at Emory University School of Medicine. "Based on this idea, we wanted to identify a population of cells enriched with the capacity to regenerate blood vessels."

The blood vessel-repairing properties of selected cells from human blood were described in the Aug. 10 issue of the *Journal of the American College of Cardiology*, with a related paper on cells derived from mouse bone marrow published online July 15 by the journal *Circulation Research*.

Yoon's team focused on the molecule CD31, also known as platelet endothelial cell adhesion molecule-1 or PECAM-1, because of its presence on endothelial cells—the cells that form the inner lining of blood vessels. In experiments with donated blood from human volunteers

or mouse bone marrow cells, the researchers showed that cells with CD31 on their surfaces secrete hormones that support the growth of blood vessels.

About a third of the cells in the blood or bone marrow have CD31 on their surfaces, including some differentiated immune cells. In culture, sorted cells displaying CD31 can form tubular structures mimicking the growth of blood vessels in the body.

"We can show that after transplantation, some CD31 positive cells do become endothelial cells, but their main effect is more to support other cells than to become the building blocks," Yoon says.

The researchers used antibodies against CD31 to sort human blood or mouse bone marrow cells into two groups: cells with CD31 and those without. They then tested these cells' ability to spur blood vessel regrowth in mice whose hind legs had a blocked blood supply.

In the project described in *Circulation Research*, after two weeks more than 80 percent of the mouse hind legs transplanted with CD31 positive bone marrow cells survived, while less than 15 percent of the legs transplanted with CD31 negative cells survived. In laser Doppler images, the mice with CD31 positive cells injected into their legs had greatly enhanced blood flow and an increased number of capillaries.

Yoon says harvesting CD31 positive cells may have several advantages compared to previous methods of treating cardiovascular disease. The cells can be prepared without the need to grow them in a dish for several days, and it may not be necessary to take large volumes of blood or bone marrow from the patient—an advantage with respect to safety. In addition, cells from mice used to simulate atherosclerosis (mutant for a gene that helps clear fat from the blood and given a high-fat diet) do not seem to lose their repair potential.

"Based on the insights gained from preclinical and clinical studies from several investigators, we view the use of CD31 positive cells as a second-generation cardiovascular cell therapy that could be a novel option for the treatment of peripheral artery disease," Yoon says.

He adds that CD31 positive cells may have potential for treating other conditions, including heart attack, heart failure and diabetic neuropathy, which his team is investigating in animal models.

More information: S.W. Kim, H. Kim, H.J. Cho, J.U. Lee, R. Levit, and Y. Yoon. Human Peripheral Blood-Derived CD31+ Cells Have Robust Angiogenic and Vasculogenic Properties and Are Effective for Treating Ischemic Vascular Disease. J. Am. Coll. Cardiol, 56: 593 - 607 (2010)

Provided by Emory University