Tissue-engineered grafts composed of adult stem cells could 1 day replace synthetic vascular bypass grafts

April 8 2010

Using adult stem cells, researchers have created functional blood vessels that could one day replace synthetic grafts often required in various vascular bypass surgeries, according to research presented at the American Heart Association's Arteriosclerosis, Thrombosis and Vascular Biology Annual Conference 2010.

Bypass surgery is used to open blocked arteries in one part of the body by using a vessel from elsewhere in the body. However, up to 40 percent of patients don't have a vessel suitable for the procedure. In such cases, surgeons use synthetic grafts. But the artificial blood vessels often become clogged within one to three years at a higher rate than natural arteries often leading to serious infections.

"Our grafts have the potential to be used for peripheral artery disease bypass (mostly in the legs), and arteriovenous fistula (a type of vascular access for hemodialysis), and heart bypass surgery," said Stephen E. McIlhenny, Ph.D., lead author of the study and tissue engineer of Thomas Jefferson University Hospital in Philadelphia. "However, the first uses of the grafts would be for treatment of peripheral artery disease and dialysis access grafting."

McIlhenny and colleagues reported encouraging results from their first pre-clinical tests of the graphs.

"It was our idea to create a more biological conduit that would avoid the problems of synthetic grafts and give patients a better alternative," said McIlhenny. "The significant finding is that we can build a blood vessel from donor tissue and an animal's own adult stem cells. Potentially, patients requiring bypass surgery could receive optimized grafts that would reduce their future complications."

Researchers grew rabbit adult stem cells on human vein scaffolds in the laboratory. The team removed all cells from sections of human saphenous veins, which left a tube consisting only of the protein scaffolding that supported the cells. Because the scaffolding contains no cells; there is less risk the immune system will reject it.

The researchers derived adult stem cells from the fat cells of each rabbit that would receive the test graft. They grew the stem cells on pieces of scaffolding, and each rabbit received a graft with only its own stem cells on it.

"Fat cells are easily obtained with liposuction," McIlhenny said. "Bone-marrow-derived stem cells require going into the bone canal to take bone marrow out, which can be painful."

Surgeons cut the abdominal aorta of five male rabbits and inserted stem cell grafts into the large artery. In five other male rabbits, they similarly inserted grafts of the bare protein scaffolding. They examined the animals every two weeks for eight weeks with ultrasound, monitoring whether their inserted grafts were closing up.

After eight weeks, surgeons removed the grafts from the 10 animals. The five bare scaffolding grafts showed significant thickening akin to that seen in human cardiovascular disease, as well as evidence of blood clots.

As for the other five grafts, "we found that using the stem cells as a coating prevented clotting and thickening of the graft wall," McIlhenny said. "I would say those grafts were significantly better."

Considerably more work remains, including additional animal testing, before studies of the fat-cell-derived grafts can begin in human testing. The team is attempting to grow smooth muscle cells on the outer layer of the scaffolding. In arteries, this layer of cells strengthens the blood vessels and enables them to contract.

The group is also investigating a suspected but unproven function of nitric oxide in the success of the adult stem cell graft. Nitric oxide is known to inhibit platelet aggregation and blood-clot formation in blood vessels. "We are going to attempt to prove more definitely that this molecule is protecting our graft against wall thickening," McIlhenny said.

Provided by American Heart Association