Making human textiles: Research team ups the ante with development of blood vessels woven

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A lot of people were skeptical when two young California-based researchers set out more than a decade ago to create a completely human-derived alternative to the synthetic blood vessels commonly used in dialysis patients. Since then, they've done that and more.

"There were a lot of doubts in the field that you could make a blood vessel, which is something that needs to resist pressure constantly, 24-7, without any synthetic materials in it," explains Nicolas L'Heureux, a co-founder and the chief scientific officer of Cytograft Tissue Engineering Inc. "They didn't think that was possible at all." But they were wrong.

Cytograft, which L'Heureux and Todd McAllister co-founded in 2000, has indeed developed vessels that are "completely biological, completely human and living, which is the Cadillac of treatments … and it seems to work really well," L'Heureux says.

First the team created blood vessels from patients' own skin cells. Then, in June, the company announced that three dialysis patients had received the world's first lab-grown blood vessels made from skin cells from donors, which eliminates the long lead time needed for making vessels from a patient's own cells. And now Cytograft has developed a new technique for making human textiles that promises to reduce the production cost of these vessels by half.

L'Heureux will present his team's latest findings Monday, April 23, at the annual meeting of the American Association of Anatomists, which is being held in conjunction with the Experimental Biology 2012 meeting in San Diego.

Laying the foundation for a human textile

Cytograft's new approach builds on what already has been proved successful. In 2005, the team began extracting fibroblasts from patients' own skin, cultured those cells into thin sheets, rolled up those sheets, cultured them some more so that they would fuse together, and implanted the lab-grown cylindrical vessels. The vessel-growing process was lengthy, at about seven months, but, because the vessels were derived from the patients' own cells, the implants were easily accepted by the patients' bodies, and they held up to the rigors of dialysis, which requires repeated punctures with large-gauge needles.

Then the researchers created allogeneic vessels — ones grown from donor cells — with the hope that they were laying the foundation for an off-the-shelf stockpile of 100 percent human replacement parts.

"By combining these two methods we could make something that is allogeneic, cheaper to produce, and that you could store forever, meaning that the clinician can pull it off the shelves whenever they want," L'Heureux explains. "If it is frozen and allogeneic, that is kind of the homerun."

Those donor-based vessels were implanted into three patients in Poland, and they have performed well with no signs of rejection. That accomplishment was a big one, from a manufacturing standpoint, L'Heureux says, because "it is very, very costly to segregate all the patients' cells at all the steps with all the material and all the media and the culturing zones."

Though using donor cells dramatically reduces costs, putting the price tag of a lab-grown human vessel somewhere between $6,000 to $10,000 (although this will come down with automation and volume), it doesn't cut down the manufacturing time all that much, because the culturing of the cells so that they fuse together takes many months. So the researchers decided it was time to try out an idea they'd been kicking around for some years: human textiles.

Not your grandmother's knitting

Today the Cytograft team is deconstructing the sheets of cultured cells into threads and then using a variety of medical-textile-making techniques to weave together blood vessels. Most medical textiles used today are made of permanent synthetic fibers, such as polyester.

"They weave synthetic threads to create patches, for example, for blood vessels … and they can make a large blood-vessel replacement conduit that they use for arterial repair. They can use patches for hernia repair," L'Heureux explains. "What we are doing here is using a completely biological, completely human – and chemically nonprocessed in any way – fiber from which we can now build all kinds of structures by weaving, knitting, braiding or a combination of techniques."

L'Heureux says that, once the cell sheets are grown, the weaving of these human textiles into a vessel takes only a couple of days, even with the prototype loom currently in use at the Cytograft lab. And the threads of cells, while more delicate than synthetic fibers, are strong.

"It is not like your grandmother with the little knitting pins," L'Heureux says. "It is much faster than that. Basically, the time it takes for making the threads and assembling them in a blood vessel is negligible compared to the time that it took you to make the sheet."

The time is now

L'Heureux notes that, having shown that vessels grown from donor cells are a good, natural alternative to synthetic vessels, it's time to roll out "a treatment that is more streamlined and more cost effective," and this third-generation woven allogeneic blood vessel could be the solution.

"We just came to a point where we had proved a lot of what we could do with our blood vessels and it made sense to find a way to make it faster. And this weaving method that makes the vessel out of the same material that we used in the sheet makes it ready in about a third of the time that it took before," he says.

Additionally, he says, weaving actually produces a more robust vessel than one that has been cultured in a cylindrical shape. "There is no seam, which is a problem when you roll something – there's always a flap on the inside and a flap on the outside, and you need to be sure that these flaps are really well fused with the rest, and that takes a long time for the cells to do," he says.

The work remains in the early stages, and an animal trial showed promising results. For one thing, the woven vessel has proved to resist puncture, "which is important for dialysis," he says.

Next steps

From the beginning, Cytograft's team has focused primarily on the lab-grown vessels' use in dialysis patients, "because that's where the largest need is," L'Heureux says. But they could be used in a variety of patients. Babies with congenital heart defects, for instance, need replacement vessels that can grow and change. Heart bypass patients today endure the often-painful recovery associated with removing a vessel from one part of the body for implantation elsewhere, and a lab-grown and -woven one could eliminate the need for the first surgery.

Also, human-based replacement vessels are far less susceptible to infection than synthetic ones, L'Heureux emphasizes. "With synthetics, one of the big drawbacks is that they get easily infected. What happens is that the synthetic harbors microbes, and immune cells can't deal with the synthetic. They can't grab it. It's like chasing a dog on an ice rink." Immune cells, meanwhile, can recognize and interact with the lab-grown tissue since it is completely biological.

Despite the doubts about Cytograft's work in the early days, there is a push nowadays for finding natural alternatives to synthetics, in part because of the infection risk, L'Heureux says. "Today, 15 years later, the goal of eliminating synthetic materials from tissue-engineered products has become pretty mainstream."

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