Hopes high for a bioengineered liver

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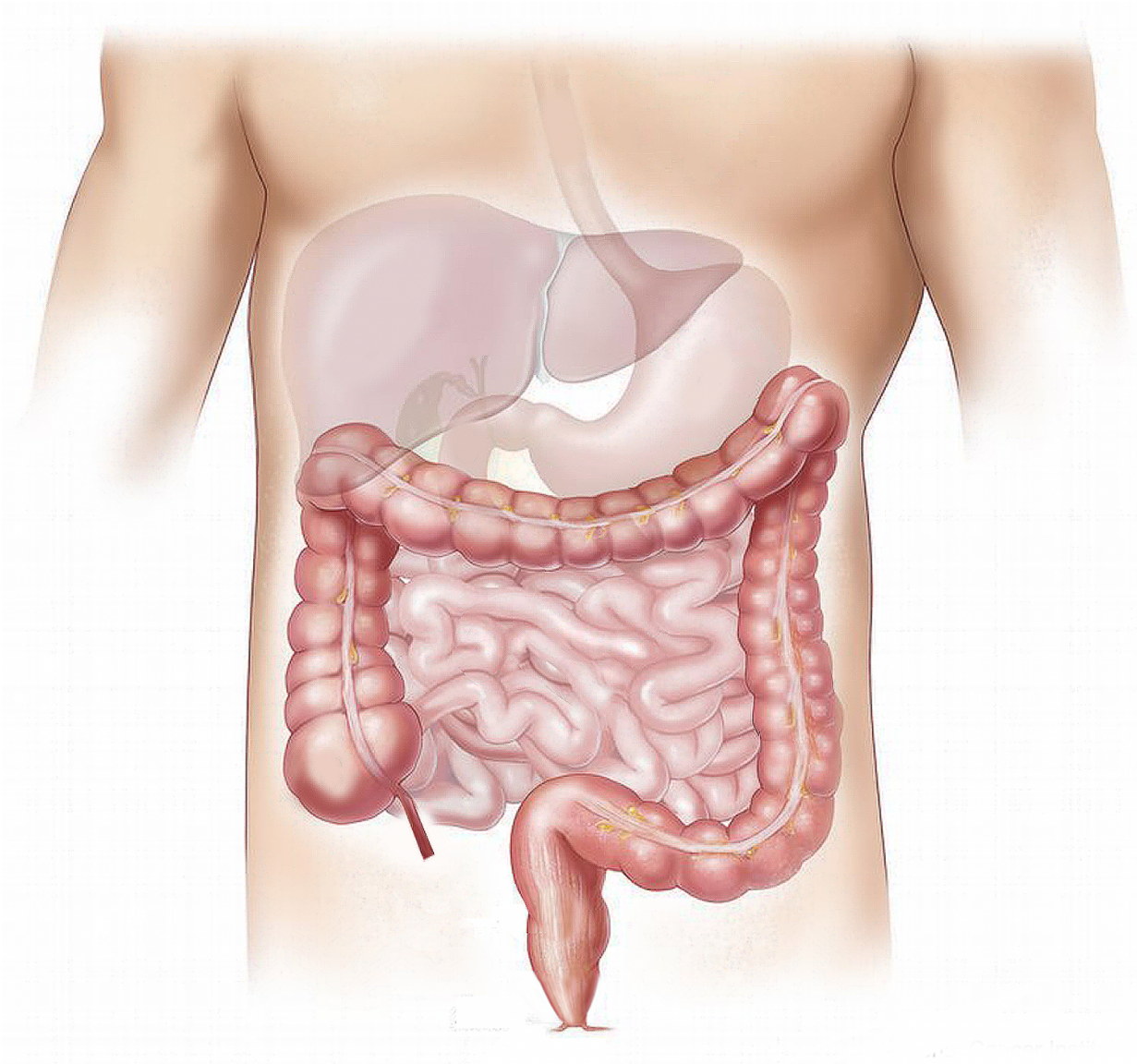

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Every year, at least 1,500 people die on the waiting list for a new liver because of a donor shortage.

It would be convenient to just press the "new liver" button on a 3-D printer and watch the organ take shape on a plate. Unfortunately, that technology does not yet exist. But an Eden Prairie, Minn., company called Miromatrix is taking a different approach, working from the premise that humans don't have to invent a new way to grow organs - nature does that just fine, thanks. The trick, rather, is in taking a liver from one body and implanting it inside another without triggering rejection.

Scientists at Miromatrix think they may have the answer. It involves taking the liver from a pig that was slaughtered for food, washing away the living cells in a mild detergent, and then "reseeding" the resulting white collagen shell with human cells that can transform the pig liver into a functioning human organ.

It may sound like science fiction, but the first attempt at this will take place before the year is out: A pig at the Mayo Clinic will have its liver removed, and a new liver "recellularized" with human and pig cells implanted in its place, to test whether a Miromatrix bioengineered liver can keep the pig alive for at least two days. Results of the experiment should be in by this time next year, and that may clear the way for the first human implant around 2020.

"This has really been the promise of regenerative medicine: How do you create products that can cure disease?" said Jeff Ross, a longtime biomedical researcher who became CEO of Miromatrix during a shake-up at the company earlier this year. "This would be the first product of its kind."

Although other companies and academic labs have figured out how to

strip away living cells from an organic structure to leave behind only the "decellularized" matrix, Miromatrix relies on a patented process invented at the University of Minnesota called "perfusion decellularization."

Typically, decellularization is accomplished by soaking the organ in a special solution, but Ross says this method of "immersion perfusion" penetrates only a few millimeters into tissue. That's why other decellularized tissue matrices on the market tend to be thin, like skin-matrix products.

Perfusion decellularization, in contrast, involves mechanically pumping a cleaning solution through an organ's natural internal vasculature continuously for a day or two, until all that's left is the inert white "matrix" of collagen and other proteins that can be preserved in a refrigerator for months at a time. Critically, the resulting matrix still retains tiny tunnels from the original blood vessels, allowing new cells to grow their own vascular system inside the existing structure.

"I like to say perfusion decellularization is analogous to remodeling a house," Ross says. "Essentially we go in and remove all the drywall. What you are left with is the structure of that house. ... A kitchen is still a kitchen; all the plumbing is still intact. The same is true with an organ. When you remove all the cellular material, all that architecture is still there, the microenvironments are still there, the vasculature channels are still there. So then we are able to go in and recellularize."

Miromatrix already has validated this part of the process, earning approval by the Food and Drug Administration to sell two types of meshlike products derived from decellularized pig liver tissue. Ross said thousands of these thin "Miromesh" and "Miroderm" products have been implanted in humans to treat hernias and wounds, with no reported immunological issues from rejection. The 25-employee company had

more than $1 million in sales last year from these two products.

The much larger prize lay in repopulating a decellularized pig liver with human endothelial cells to create the slippery lining inside natural vessels that allows blood to flow without clotting. In theory, a person's own stem cells could be used to recellularize a pig liver matrix, creating a new organ perfectly suited for the donor's immune system, but that's a long-term goal.

If some of this sounds familiar, it may be because Miromatrix made news several years ago by announcing an effort to create bioengineered hearts through the same process. The work on a recellularized heart is still progressing, but Ross said the liver work has taken precedence because it led to the smaller products such as Miromesh that could be commercialized quickly and because liver-failure patients have very limited medical options today.

On April 19, Miromatrix announced a new CEO and three new board members. Miromatrix is also preparing to announce that its founder, Doris Taylor - who pioneered perfusion decellularization techniques at the U but left the company in 2011 - is rejoining as a scientific adviser.

"I believe the company's new leadership, combined with my intimate knowledge of this leading-edge technology, will help Miromatrix realize its goal of bringing whole organs to patients worldwide," Taylor said in a statement.