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Researchers engineer miniature human livers in the lab

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Researchers at the Institute for Regenerative Medicine at Wake Forest University Baptist Medical Center have reached an early, but important, milestone in the quest to grow replacement livers in the lab. They are the first to use human liver cells to successfully engineer miniature livers that function – at least in a laboratory setting – like human livers. The next step is to see if the livers will continue to function after transplantation in an animal model.

The ultimate goal of the research, which will be presented Sunday at the annual meeting of the American Association for the Study of Liver Diseases in Boston, is to provide a solution to the shortage of donor livers available for patients who need transplants. Laboratory-engineered livers could also be used to test the safety of new drugs.

"We are excited about the possibilities this research represents, but must stress that we're at an early stage and many technical hurdles must be overcome before it could benefit patients," said Shay Soker, Ph.D., professor of regenerative medicine and project director. "Not only must we learn how to grow billions of liver cells at one time in order to engineer livers large enough for patients, but we must determine whether these organs are safe to use in patients."

Pedro Baptista, PharmD, Ph.D., lead author on the study, said the project is the first time that human liver cells have been used to engineer livers in the lab. "Our hope is that once these organs are transplanted, they will maintain and gain function as they continue to develop," he

said.

To engineer the organs, the scientists used animal livers that were treated with a mild detergent to remove all cells (a process called decellularization), leaving only the collagen "skeleton" or support structure. They then replaced the original cells with two types of human cells: immature liver cells known as progenitors, and endothelial cells that line blood vessels.

The cells were introduced into the liver skeleton through a large vessel that feeds a system of smaller vessels in the liver. This network of vessels remains intact after the decellularization process. The liver was next placed in a bioreactor, special equipment that provides a constant flow of nutrients and oxygen throughout the organ.

After a week in the bioreactor system, the scientists documented the progressive formation of human liver tissue, as well as liver-associated function. They observed widespread cell growth inside the bioengineered organ.

The ability to engineer a liver with animal cells had been demonstrated previously. However, the possibility of generating a functional human liver was still in question.

The researchers said the current study suggests a new approach to whole-organ bioengineering that might prove to be critical not only for treating liver disease, but for growing organs such as the kidney and pancreas. Scientists at the Wake Forest Institute for Regenerative Medicine are working on these projects, as well as many other tissues and organs, and also working to develop cell therapies to restore organ function.

Bioengineered livers could also be useful for evaluating the safety of new drugs. "This would more closely mimic drug metabolism in the

human liver, something that can be difficult to reproduce in animal models," said Baptista.

Provided by Wake Forest University Baptist Medical Center