

Skin cells morph to liver cells

Medical College team reports advance

By [Mark Johnson](#) of the Journal Sentinel

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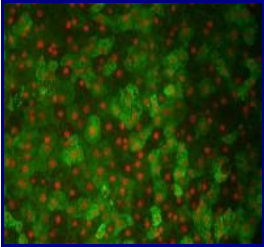


Photo courtesy of Medical College of Wisconsin

Researchers at the Medical College of Wisconsin released this image of liver cells that were generated from human skin cells.

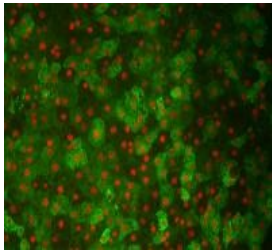


Photo courtesy of Medical College of Wisconsin

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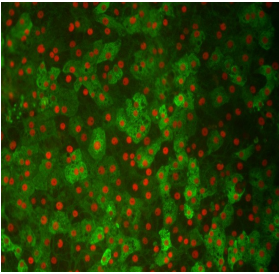


Targeting the Good Cell

In a fresh demonstration of science's newfound ability to alter the basic units of human life, researchers at the Medical College of Wisconsin have turned the cells in human skin into those in the liver, work that opens new avenues for treating diseases of the liver without relying on organ transplants.

Professor and stem cell researcher Stephen A. Duncan and other scientists in his lab reported this week in the journal *Hepatology* that they have created reprogrammed human liver cells that were identical to those grown in nature and were able to integrate and grow alongside those in a mouse liver.

Duncan and his fellow researchers also showed that human liver cells made through reprogramming are



virtually the same as those grown from embryonic stem cells, though both appear to differ from adult liver cells in one respect. Those grown with reprogrammed or embryonic stem cells in the lab had fewer of the enzymes that fulfill the liver's function of filtering out toxins than adult liver cells that have developed in the body.

The Medical College experiments, which represent roughly 2½ years of work, also showed that scientists have a reliable and efficient method of turning primitive cells into liver cells, a finding that could offer pharmaceutical companies opportunities to test drugs and provide researchers with a window that will allow them to observe liver diseases progress at the cellular level.

The cells the scientists made are called hepatocytes and make up about 70% of all the cells in the liver.

"You can now make hepatocytes from (the skin cells of) individuals with a liver disease. Then you can start screening for drugs and molecular approaches to reverse the disease or treat the disease," Duncan said.

Karim Si-Tayeb, a post-doctoral researcher in Duncan's lab, said it may still be five to 10 years before liver cells made using reprogramming are "clinical grade" and approved for use in people. He and Duncan, however, envision the possibility that liver cells made in the lab can be injected into an unhealthy liver and replace damaged cells.

Much of the mouse work for the new paper was done by Fallon Noto, a graduate student in Duncan's lab.

"It's really very impressive. Only a few elite labs in the world have done what Duncan's lab has done," said Kenneth Zaret, associate director of the Institute for Regenerative Medicine at the University of Pennsylvania School of Medicine. Zaret was not involved in the research.

Duncan's team had hoped to become the first group to provide published evidence that reprogramming could be used to make liver cells, but two other groups have succeeded in making liver cells in this manner. Chinese scientists published their results in late September, and this week a group led by Scottish scientist Ian Wilmut published similar work online.

However, the Medical College work in both human and mouse cells suggests treatment strategies right out of the pages of science fiction. For example, both Duncan and Si-Tayeb talked about the possibility of growing livers in mice that contain mostly human cells.

"I could make a mouse that has your liver. That's incredibly valuable," Duncan said.

Such a technique would help doctors solve the problems created by drugs that are generally safe but in a small number of people have devastating side effects.

In theory, here's how the procedure would work:

Scientists would take a skin biopsy from you and reprogram the cells back to the embryonic state, then coax them into becoming liver cells. They would then inject these liver cells into a mouse's liver until most of the mouse's liver was made up of your cells. Before they gave a drug to you they would give it to the mouse, which has a liver very similar to yours. If the drug harmed the mouse's liver, doctors would know not to use it on you.

Since some drugs have serious side effects in a small percentage of patients, this technique would allow scientists to create a model of your liver in a mouse, then use that specific mouse to determine whether a drug will be safe for you.

Duncan's team also will be looking to build on the new work by collecting skin cells from patients with liver diseases and reprogramming them into liver cells. Diseases they hope to examine using this method include mature onset diabetes of the young, mutations that affect cholesterol levels and hypercholesterolemia, a metabolic problem.

The Medical College work also could one day help people whose livers have been damaged by hepatitis C, alcohol or large amounts of certain drugs. Such ailments could be addressed by the injection of healthy liver cells to replace those that have been damaged or destroyed.