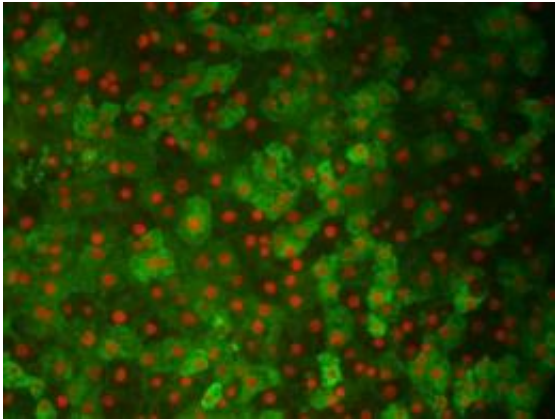


Liver cells grown from patients' skin cells

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These are liver cells generated from skin that are shown to make human liver proteins Albumin in green and HNF4 in red. Credit: Medical College of Wisconsin

Scientists at The Medical College of Wisconsin in Milwaukee have successfully produced liver cells from patients' skin cells opening the possibility of treating a wide range of diseases that affect liver function. The study was led by Stephen A. Duncan, D. Phil., Marcus Professor in Human and Molecular Genetics, and professor of cell biology, neurobiology and anatomy, along with postdoctoral fellow Karim Si-Tayeb, Ph.D., and graduate student Ms. Fallon Noto.

"This is a crucial step forward towards developing therapies that can potentially replace the need for scarce liver transplants, currently the only treatment for most advanced liver disease," says Dr. Duncan.

Liver disease is the fourth leading cause of death among middle aged adults in the United States. Loss of liver function can be caused by several factors, including genetic mutations, infections with hepatitis viruses, by excessive alcohol consumption, or chronic use of some prescription drugs. When liver function goes awry it can result in a wide variety of disorders including diabetes and atherosclerosis and in many cases is fatal.

The Medical College research team generated patient-specific liver cells by first repeating the work of James Thomson and colleagues at University of Wisconsin-Madison who showed that skin cells can be reprogrammed to become cells that resemble embryonic stem cells. They then tricked the skin-derived pluripotent stem cells into forming liver cells by mimicking the normal processes through which liver cells are made during embryonic development. [Pluripotent stem cells](#) are so named because of their capacity to develop into any one of eh more than 200 cell types in the human body.

At the end of this process, the researchers found that they were able to very easily produce large numbers of relatively pure liver cells in laboratory culture dishes. "We were excited to discover that the liver cells produced from human skin cells were able to perform many of the activities associated with healthy adult liver function and that the cells could be injected into mouse livers where they integrated and were capable of making human liver proteins," says Dr. Duncan.

Several studies have shown that liver cells generated from embryonic stem cells could potentially be used for therapy. However, the possible use of such cells is limited by ethical considerations associated with the generation of [embryonic stem cells](#) from preimplantation embryos and the fact that embryonic [stem cells](#) do not have the same genetic make-up as the patient.

Although the investigations are still at an early stage the researchers believe that the reprogrammed skin cells could be used to investigate and potentially treat metabolic liver disease. The liver may be particularly suitable for stem-cell based therapies because it has a remarkable capacity to regenerate. It is interesting to note that the regenerative nature of the liver was referenced in the ancient Greek tale of Prometheus. When Prometheus was caught stealing the gift of fire from Zeus, he was punished by having his liver eaten daily by an eagle. This provided the eagle with an everlasting meal because each night the liver of Prometheus would re-grow.

The liver is a central regulator of the body's metabolism and is responsible for controlling sugar and cholesterol levels, secretion of a variety of hormones, production of blood clotting factors, and has an essential role in preventing toxins from damaging other organs in the body.

It is possible that in the future a small piece of skin from a patient with loss of liver function could be used to produce healthy liver cells, replacing the diseased liver with normal tissue.

Recently, the National Institutes of Health's National Institute of Diabetes and Digestive and Kidney Diseases through the American Recovery and Reinvestment Act have provided the MCW researchers, in collaboration with Markus Grompe, M.D., at the Oregon Health and Science University, a \$1 million research grant to pursue the possibility of using reprogrammed [skin cells](#) to study and treat metabolic [liver disease](#). Using this support, as well as donations from individuals throughout Milwaukee, the Medical College researchers are currently producing reprogrammed cells from patients suffering from diabetes, hyperlipidemia, and hypercholesterolemia in an effort to identify new treatments for these diseases.

Source: Medical College of Wisconsin ([news](#) : [web](#))

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