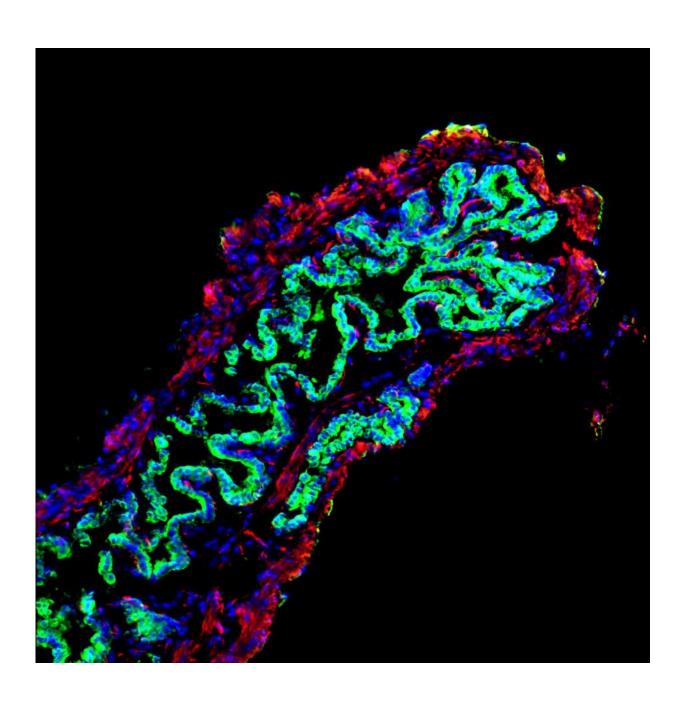


Artificial bile ducts grown in lab, transplanted into mice could help treat liver disease

July 3 2017





An image of a mouse gallbladder following repair with a bioengineered patch of tissue incorporating human 'bile duct' cells, shown in green. The human bile duct cells have fully repaired and replaced the damaged mouse epithelium. Credit: Fotis Sampaziotis

Cambridge scientists have developed a new method for growing and transplanting artificial bile ducts that could in future be used to help treat liver disease in children, reducing the need for liver transplantation.

In research published in the journal *Nature Medicine*, the researchers grew 3D cellular structure which, once transplanted into mice, developed into normal, functioning <u>bile ducts</u>.

Bile ducts are long, tube-like structures that carry bile, which is secreted by the liver andis essential for helping us digest food. If the ducts do not work correctly, for example in the childhood disease biliary atresia, this can lead to damaging build of bile in the liver.

The study suggests that it will be feasible to generate and transplant artificial human bile ducts using a combination of cell transplantation and tissue engineering technology. This approach provides hope for the future treatment of diseases of the bile duct; at present, the only option is a <u>liver</u> transplant.

The University of Cambridge research team, led by Professor Ludovic Vallier and Dr Fotios Sampaziotis from the Wellcome-MRC Cambridge Stem Cell Institute and Dr Kourosh Saeb-Parsy from the Department of Surgery, extracted healthy cells (cholangiocytes) from bile ducts and grew these into functioning 3D duct structures known as biliary



organoids. When transplanted into mice, the biliary organoids assembled into intricate tubular structures, resembling bile ducts.

The researchers, in collaboration with Mr Alex Justin and Dr Athina Markaki from the Department of Engineering, then investigated whether the biliary organoids could be grown on a 'biodegradable collagen scaffold', which could be shaped into a tube and used to repair damaged bile ducts in the body. After four weeks, the cells had fully covered the miniature scaffolding resulting in artificial tubes which exhibited key features of a normal, functioning bile duct. These artificial ducts were then used to replace damaged bile ducts in mice. The artificial duct transplants were successful, with the animals surviving without further complications.

"Our work has the potential to transform the treatment of bile duct disorders," explains Professor Vallier. "At the moment, our only option is <u>liver transplantation</u>, so we are limited by the availability of healthy organs for transplantation. In future, we believe it will be possible to generate large quantities of bioengineered tissue that could replace diseased bile ducts and provide a powerful new therapeutic option without this reliance on organ transplants."

"This demonstrates the power of tissue engineering and regenerative medicine," adds Dr Sampaziotis. "These artificial bile ducts will not only be useful for transplanting, but could also be used to model other diseases of the bile duct and potentially develop and test new drug treatments."

More information: Reconstruction of the mouse extrahepatic biliary tree using primary human extrahepatic cholangiocyte organoids, *Nature Medicine* (2017). DOI: 10.1038/nm.4360



Provided by University of Cambridge

Citation: Artificial bile ducts grown in lab, transplanted into mice could help treat liver disease (2017, July 3) retrieved 23 April 2024 from https://medicalxpress.com/news/2017-07-artificial-bile-ducts-grown-lab.html

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