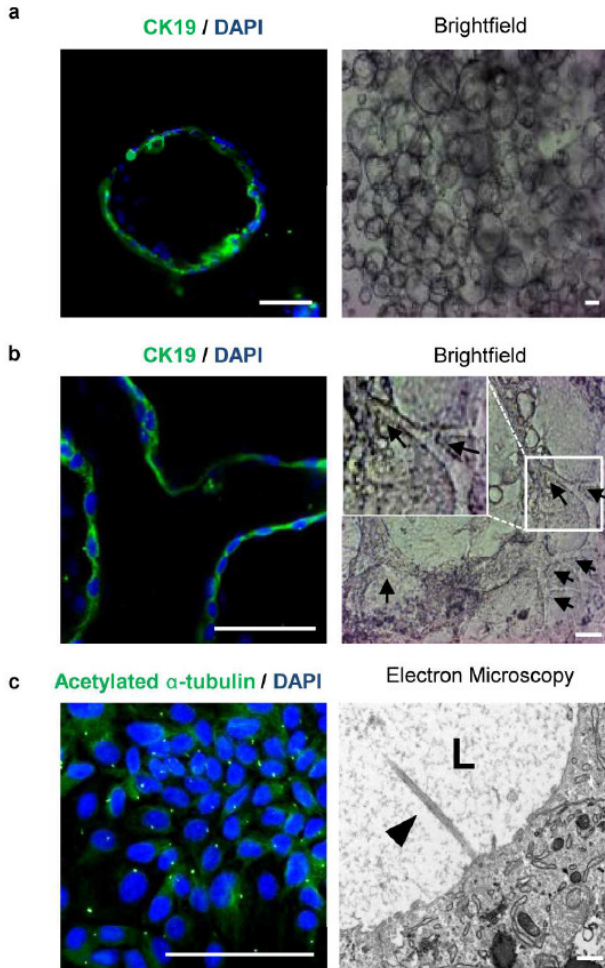


# Cystic fibrosis treatment tested on lab-grown bile ducts

14 July 2015



Images a and b show immunofluorescence (left) and light microscopy (right) images of organoids, demonstrating the formation of cystic and branching (arrows) tubular structures. Image c shows Transmitted electron microscopy images (right) and Immunofluorescence analyses (left) demonstrating the presence of cilia (arrow). [DOI: 10.1038/nbt.3275]

An experimental cystic fibrosis drug has been shown prevent the disease's damage to the liver, thanks to a world-first where scientists grew mini bile ducts in the lab.

For the first time, researchers led by scientists from the Wellcome Trust-Medical Research Council Stem Cell Institute and the Wellcome Trust Sanger Institute in Cambridge, used [stem cells](#) to grow fully functional three-dimensional bile ducts in the lab. Bile ducts act as the liver's waste disposal system, and dysfunctioning bile ducts are implicated in a third of adult and 70 per cent of children's liver transplantations.

The researchers used their lab-grown miniature bile ducts to test new drugs for biliary disease, leading to the discovery that VX809 - an experimental compound originally designed to treat the effects of [cystic fibrosis](#) in the lungs- could be the first therapeutic agent to prevent the damage cystic fibrosis causes to the liver and [bile duct](#).

Dr Fotios Sampaziotis, first author from the Wellcome Trust-Medical Research Council Stem Cell Institute and MRC-Sparks Clinical Research Fellow in hepatology, said: "Treating liver complications caused by bile duct disorders constitutes a major challenge - with the only treatment option often being liver transplantation. We were delighted to identify a new experimental drug that could prevent patients with cystic fibrosis, one of the most common inherited disorders in Europe, from undergoing a [liver transplantation](#), a major and life changing operation. But, this treatment will need to be tested in clinical trials before it can be recommended to patients."

Until now there has been no way of generating large numbers of fully functional bile ducts that mimic disease in the lab, which has limited our understanding of biliary disorders and restricted the development of new drugs. Using their bile duct replicas the researchers reproduced key features of two more bile duct diseases - polycystic liver disease and Alagille syndrome - and tested the effects of additional drugs, such as octreotide.

Professor Ludovic Vallier, Principal Investigator and

corresponding author from the Wellcome Trust-Medical Research Council Stem Cell Institute and the Sanger Institute, said: "The pharmaceutical applications of our system are particularly important as we don't have many human samples of this type of tissue to work on. This system could provide a unique resource for identifying new therapeutic agents."

Dr Nicholas Hannan a senior author from the Wellcome Trust-Medical Research Council Stem Cell Institute, said: "The bile duct cells we have generated represent an invaluable tool to understand not only how healthy bile ducts develop and function, but to also understand how diseased bile ducts behave and how they may respond to therapeutic treatment. This platform opens up the possibility of modelling complex liver diseases and will certainly progress our understanding of biliary disease in the future."

To demonstrate that the cells they had grown were in fact forming bile ducts the researchers looked for characteristic markers and functions of the cells. They then compared the signature of these cells with those from human donors and found that they were almost identical.

Dr Paul Colville-Nash, Programme Manager for Stem Cell, Developmental Biology and Regenerative Medicine at the MRC, said: "The approach developed in this work will enable a vast range of work, from understanding how organs grow and develop to a greater understanding of disease and testing new drugs. This work could also one day lead to functioning spare [liver](#) parts being grown to replace damaged areas."

**More information:** "Cholangiocytes derived from human induced pluripotent stem cells for disease modelling and drug validation." *Nature Biotechnology* 2015 [DOI: 10.1038/nbt.3275](https://doi.org/10.1038/nbt.3275)

Provided by Wellcome Trust Sanger Institute

APA citation: Cystic fibrosis treatment tested on lab-grown bile ducts (2015, July 14) retrieved 2 December 2021 from <https://medicalxpress.com/news/2015-07-cystic-fibrosis-treatment-lab-grown-bile.html>

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