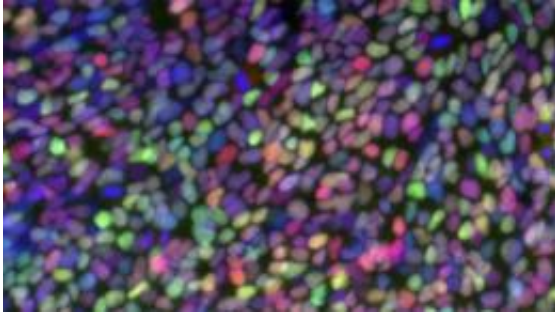


# Teaching old cells new tricks

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Stem cells. Credit: Candy Cho

Much hyped by the media, stem cells have tremendous power to improve human health. As part of the Cambridge Stem Cell Initiative, Dr Ludovic Vallier's research in the Anne McLaren Laboratory for Regenerative Medicine shows how stem cells can further our understanding of disease and help deliver much-needed new treatments.

How do you study a human disease that has no equivalent in animals and where the human cells in question are so hard to grow outside the body they cannot be tested in the laboratory? The answer, until now, was with great difficulty. But by using a new stem cell technique, that is set to change.

Dr. Ludovic Vallier, who holds an MRC Senior Fellowship in the Anne McLaren Laboratory for Regenerative Medicine, Department of Surgery at Cambridge in collaboration with Professor David Lomas (Cambridge

Institute for Medical Research and Department of Medicine), works on a group of devastating genetic diseases affecting the liver.

“We target metabolic diseases of the liver, diseases such as alpha 1 antitrypsin deficiency. It’s one of the most common single genetic disorders and the protein it affects – which is only produced by the liver – is really important because it controls activity of elastase in the lung. Without this control, people develop serious lung problems and the disease also affects the liver, so these patients develop liver failure,” he explained.

The problem is that these diseases cannot be studied in vitro – in a dish – in the laboratory, he said: “You can’t take cells from the liver of these very sick patients, and if you could they wouldn’t grow, which means you don’t have any way of screening drugs that could help treat these diseases.”

Without effective drugs, the only current treatment is a liver transplant. “There is a huge shortage of organs and transplantation involves taking immunosuppressive drugs, which is heavy treatment especially in already fragile patients,” Dr. Vallier said. “And the disease is progressive so it’s very complicated to manage.” Understandably, Dr. Vallier is excited that a new method of producing stem cells developed in Japan has given him and other researchers a way of studying these diseases and screening potential drugs to treat them.

“The new technology consists of taking cells from skin and reprogramming them so that they become stem cells – cells that are capable of proliferating and differentiating into almost all tissue types,” he said.

This reprogramming means a cell with a previously fixed identity can be taught a new one – in this case taking [skin cells](#) and reprogramming

them to become liver cells. When the skin cells come from a patient with liver disease, these skin-turned-liver cells also have the disease, making them ideal for studying the disease and screening potential drugs to treat it.

According to Dr. Vallier: “Because we can generate liver cells that mimic the disease of the original patient in vitro, that allows us to do basic studies that were impossible by biopsy or primary culture and also to do drug screening.” And because the skin cells can come from a whole range of people, it gives researchers access to a broad diversity of patients as well as overcoming some of the ethical concerns associated with embryonic stem cells.

“That’s a very important step because it solves the problems associated with a limited stock of stem cells,” he said, “and because it’s a simple method, it’s easily accessible to a wide number of laboratories.”

Showing this can be done in a small number of liver patients in Cambridge is an important proof of concept, and supports the possibility that a similar approach might be applicable to a wide range of other serious diseases that still lack effective treatments, including neurodegenerative diseases such as Parkinson’s and Alzheimer’s Disease as well as heart diseases.

And Cambridge – which now has almost 30 groups doing stem cell research and strong links between academic researchers and clinicians – is perfectly positioned to make the most of this new technique.

“The Laboratory for Regenerative Medicine is starting to become an expert in this disease modelling and we are all part of a larger consortium, the Cambridge Stem Cell Initiative (SCI),” said Dr. Vallier. “Together, we are putting together resources and scientific interest to really develop [stem cells](#) and their clinical application. The SCI is a

unique consortium because it brings together a wealth of complementary expertise.”

While this first revolution involves in vitro disease modelling and drug screening, Dr. Vallier hopes this work will ultimately lead to personalized cell-based therapies where liver cells reprogrammed from a patient’s own skin [cells](#) could be used in place of a [liver](#) transplant. “It will take time for us to assess this clinical use and show that it is safe as well as effective,” he explained, “but if you ask me again in five years I should be able to tell you whether we are going to do it.”

Provided by University of Cambridge

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