# Stem cells could set up future transplant therapies

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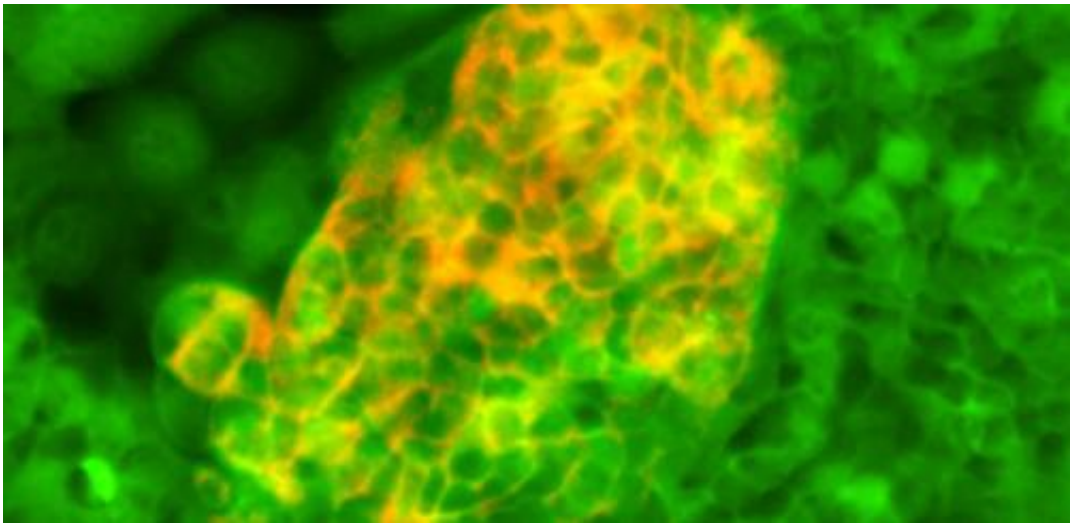

Foregut stem cells (green) differentiated into pancreatic cells expressing insulin. The development method pioneered by Cambridge researchers enables the production of an uncontaminated population of foregut cells, which could then be further differentiated as pancreatic cells for therapeutic use. Credit: University of Cambridge

(Medical Xpress)—Scientists have developed a new method for creating stem cells for the human liver and pancreas. This method could enable both cell types to be grown in sufficient quantities for clinical use.

Using the technique, researchers have for the first time been able to grow a pure, self-renewing population of stem cells specific to the

human foregut - the section of the digestive system that includes the liver and pancreas. These digestive cells could then be developed further to produce liver or pancreatic cells.

Stem cells have the potential to be used to replace dying or damaged cells with healthy cells and have potential wide-ranging uses in medicine such as organ replacement, bone replacement and treatment of neurodegenerative diseases.

This method significantly improves on existing techniques for cultivating these stem cells and raises the possibility that, with further work, they could be grown in large numbers. That would make it possible to use them for regenerative therapies, such as repairing damaged organs or tissues in the body.

"We have developed a cell culture system which allows us to specifically isolate foregut cells in the lab," Dr Nicholas Hannan, from the University of Cambridge Wellcome Trust MRC Stem Cell Institute, Department for Surgery, explained. Hannan led the study, which was carried out in the lab of Dr Ludovic Vallier, joint Faculty member of the Wellcome Trust Sanger Institute and the University of Cambridge.

"These cells have huge implications for regenerative medicine, because they are the precursors to the thyroid, upper airways, lungs, liver, pancreas, stomach and biliary systems. We now have a system where we may be able to create all these cell types from the same starting population."

To grow pancreatic or liver cells, stem cells are differentiated into the endoderm - the primary tissue layer associated with the digestive and respiratory systems. This provides a base population of cells that researchers can then try to develop as more specialised cells, such as heart or lung cells. Unfortunately, other cell types can grow, making it

difficult to identify the target cells in the lab and complicating the application of these cells in transplant therapies.

The new approach overcomes some of these problems that currently limit scientists' ability to grow cells associated with this region in sufficiently large numbers for clinical use.

By manipulating the signal pathways of the cells and varying the environment in which the cells were developed, researchers were able to isolate the precise treatments needed to drive differentiation of cells associated with the foregut itself. When heavily contaminated stem cell populations were developed under these conditions, the contaminating cells eventually died out.

The universal nature of this culture system takes a step towards a universal system that could be used to treat any patient requiring cells for transplantation purposes.

The cells generated are true stem cells because they are able to self-renew and can differentiate towards any part of the foregut. Because they are also still at the stage where they can self-renew, they can be grown in large enough numbers to be used in clinical therapies. The team was also able to show that these human foregut stem cells do not form tumours, which means that they could be safely injected for therapeutic purposes, without having adverse side effects.

"What we have now is a better starting point - a sustainable platform for producing liver and pancreatic cells," Dr Ludovic Vallier, senior author of the study, said. "It will improve the quality of the cells that we produce and it will allow us to produce the large number of uncontaminated cells we need for the clinical application of stem cell therapy."

**More information:** Hannan, N. et al. Generation of Multipotent Foregut Stem Cells from Human Pluripotent Stem Cells, *Stem Cell Reports*, 2013. DOI: 10.1016/j.stemcr.2013.09.003