Human stem cells used to repair intestines of rats

Oliver Moody Science Correspondent

Gut tissue cultivated from a human cells has been used to repair the intestines of rats in an advance towards laboratory-grown transplants.

Until now, the largest structures grown from human stem cells in a living body have been "organoids" a few millimetres in diameter. A US-Chinese experiment is thought to be the first to show that the transplanted tissue can form part of a fully functioning organ.

In the latter stages of several gut disorders, including Crohn's disease, which affects 115,000 people in the UK, patients sometimes lose the use of a portion of their small intestine. The condition, known as small bowel syndrome, can lead to pain, weight loss and diarrhoea.

While it can be treated by transplanting a section of small intestine from a donor, the grafts fail about 40 per cent of the time, largely because the patient's immune system rejects the alien tissue. The answer to this, according to Harald Ott, associate professor of surgery at Harvard Medical School, is to grow "on-demand" grafts with cells culled from another part of the patient's body. These cells can be stripped of their adult identity and turned into induced pluripotent stem (iPS) cells, which are then chemically coaxed to form tissue that can replace almost any organ.

Dr Ott and his colleagues took iPS cells and grew them on a "living scaffold" into two forms, the epithelial cells that form the lining of the intestine and the endothelial cells that form blood vessels.

After being cultured for a little more than a fortnight, the structure developed the characteristics of a section of the small intestine, including blood flow and the ability to take up nutrients. "While previously studies have reported successful differentiation of organoids — millimetre-small units of tissue — from iPS cells, we describe a technology that enables these smaller units of tissue to form larger-scale grafts that someday could be used as implanted replacement organs," Dr Ott said.

When the human gut patches were sewn into rats whose immune systems had been knocked out, they appeared to do their job and to grow as though they had been there from birth.

"The next steps will be to further mature these grafts and to scale the construct to a human size ... ideally growing 'on-demand' patient-specific grafts that would not require immunosuppressive drugs," Dr Ott said.

The findings were published in the journal *Nature Communications*.

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