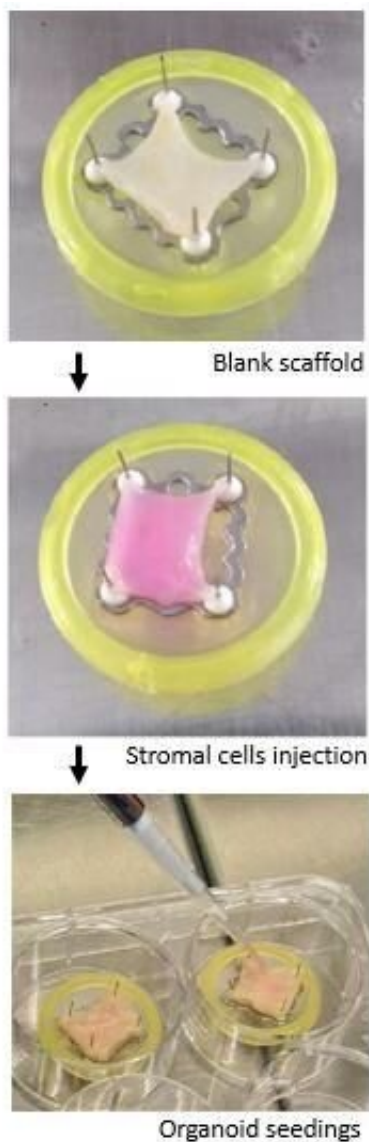


Personalized mini-organs could offer treatment hope for children with intestinal failure

September 8 2020



Credit: The Francis Crick Institute

Pioneering scientists at the Francis Crick Institute, Great Ormond Street Hospital (GOSH) and UCL Great Ormond Street Institute of Child Health (ICH) have grown human intestinal grafts using stem cells from patient tissue that could one day lead to personalized transplants for children with intestinal failure, according to a study published in *Nature Medicine*.

Children with [intestinal failure](#) cannot absorb the nutrients that are essential for their overall health and development. This may be due to a disease or injury to their small [intestine](#).

In these cases, children can be fed intravenously via a process called parenteral nutrition, however this is associated with severe complications such as line infections and liver failure. If complications arise or in severe cases these children may need a transplant. However, there is a shortage of suitable donor organs and problems can arise after surgery, such as the body rejecting the transplant.

In their proof-of-concept study, the research team showed how intestinal [stem cells](#) and small intestinal or colonic [tissue](#) taken from patients can be used to grow the important inner layer of small intestine in the laboratory with the capacity to digest and absorb peptides and digest sucrose in food.

This is the first step in efforts to engineer all the layers of the intestine for transplantation. The researchers hope that one day, laboratory grown organs could offer a safe and longer-lasting alternative to traditional donor transplants.

"It's urgent that we find new ways to care for children without a working intestine because, as they grow older, complications from parental

nutrition can arise," says Dr. Vivian Li, senior author and group leader of the Stem Cell and Cancer Biology Laboratory at the Crick.

"We've set out a process to grow one layer of intestine in the laboratory, moving us a step closer to being able to offer these patients a form of regenerative medicine, which uses materials created from their own tissue. This would reduce some of the risks that transplant patients face, such as their immune system attacking the transplant."

The researchers took small biopsies of intestine from 12 children who either had intestinal failure or were at risk of developing the condition. In the lab, they then stimulated the biopsy [cells](#) to grow into "mini-guts," also known as intestinal organoids, generating over 10 million [intestinal stem cells](#) from each patient over the course of four weeks.

The researchers also collected small intestine and colon tissue, that would otherwise have been discarded, from other children undergoing essential surgery to remove parts of their gut. Using laboratory techniques, cells were removed from these tissues leaving behind a skeleton structure which formed scaffolds.

The researchers placed the "mini-guts" onto these scaffolds, where they grew on this structure to form a living [graft](#). Due to specific culture conditions, the stem cells changed into many of the different types of cells that exist in the small intestine. The grafts were able to digest and absorb peptides, the building blocks of proteins, as well as digest sucrose into glucose sugars.

"Although this research is in the lab right now, we're concentrating on making this a realistic and safe treatment option," explains senior author NIHR Professor Paolo De Coppi, Consultant Pediatric Surgeon at GOSH and Head of Surgery, Stem Cells & Regenerative Medicine Section at the UCL Great Ormond Street Institute of Child Health

(ICH).

"What's significant here is we've shown that scaffolds can be created using tissue from the colon, not only tissue from the small intestine. In practice, it is often easier to obtain tissue from the colon, so this could make the approach much more feasible. It's an important step forward in regenerative medicine and we're optimistic about what this means for patients, but more research lies ahead before we can safely and effectively translate this approach to treatment."

As well as proving that biopsies taken from [children](#) could be used to grow functioning intestinal grafts, the researchers also demonstrated that the grafts survive and mature when transplanted into mice.

"By applying our basic science knowledge of intestinal stem cell biology, we have developed a time efficient and clinically relevant method for rebuilding human [small intestine](#) grafts for transplantation," says Laween Meran, lead author, Gastroenterology Registrar and Clinical Research Training Fellow at the Stem Cell and Cancer Biology Laboratory at the Crick and the ICH.

"Now that we've shown the grafts are successful on a small scale, the next crucial steps will be to start growing the other layers of the intestine such as muscle and blood vessels, whilst also scaling up our methods to create viable grafts relevant to individual patient needs."

More information: Laween Meran et al. Engineering transplantable jejunal mucosal grafts using patient-derived organoids from children with intestinal failure, *Nature Medicine* (2020). [DOI: 10.1038/s41591-020-1024-z](https://doi.org/10.1038/s41591-020-1024-z)

Provided by The Francis Crick Institute

Citation: Personalized mini-organs could offer treatment hope for children with intestinal failure (2020, September 8) retrieved 4 May 2024 from <https://medicalxpress.com/news/2020-09-personalized-mini-organs-treatment-children-intestinal.html>

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