Medical Xpress

Important step forward in stem cell therapy for rare bowel disease

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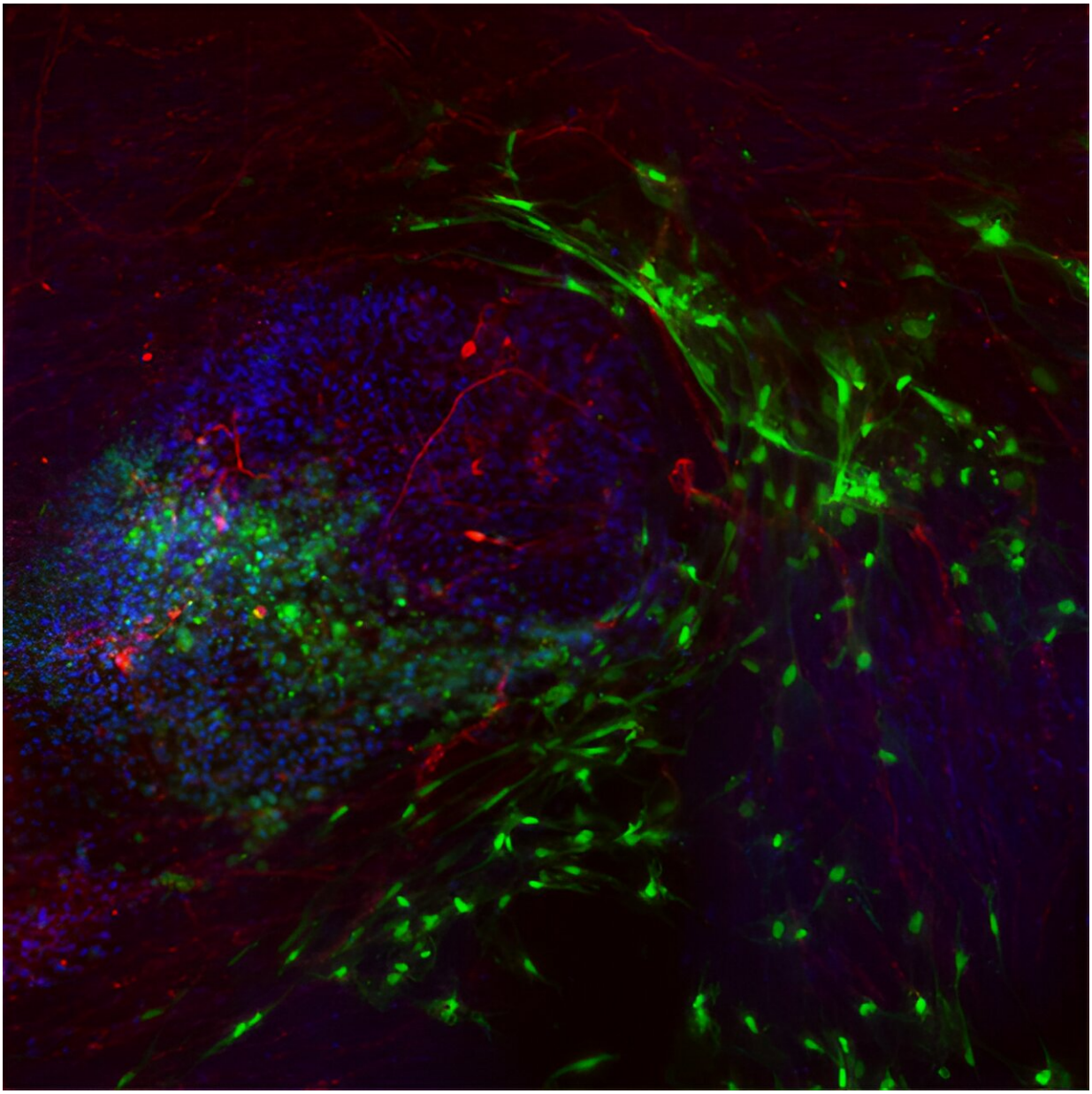


The cells given as a stem cell treatment can be seen in green—they are successfully implanting into the intestinal tissue donated by a patient with Hirschprung's disease. In this image, the overlap with red nerve cells shows that the donor cells are becoming new nerve cells. Credit: Conor J McCann et al

A new study led by researchers at UCL and the University of Sheffield, has demonstrated the potential of stem cell therapy to treat those with Hirschsprung disease.

Hirschsprung disease is a rare condition where some nerve cells are missing in the large intestine. This means the intestine doesn't contract and can't move stool, meaning that it can become blocked. This can cause constipation and sometimes lead to a serious bowel infection called enterocolitis.

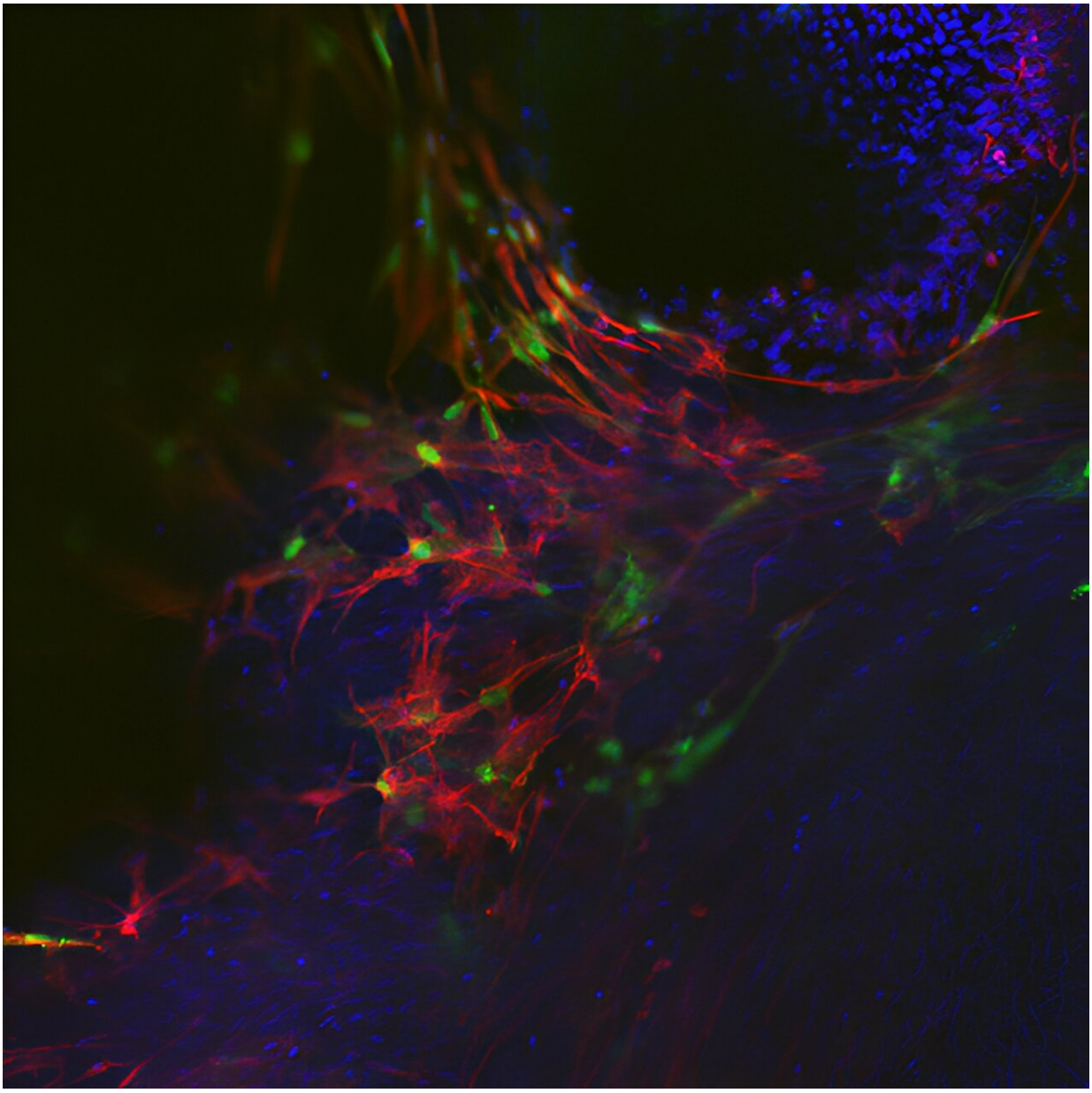
Around 1 in 5000 babies are born with Hirschsprung disease. The condition is usually picked up soon after birth and treated with surgery as soon as possible however patients frequently suffer debilitating, lifelong symptoms, with multiple surgical procedures often required.

Alternative treatment options are therefore crucial. One option that has been explored by researchers involves using stem cell therapy to generate nerve cell precursors, which then produce the missing nerves in the intestine of those with Hirschsprung disease after transplantation. This in turn should improve the intestine's functionality.

However, this procedure has not been carried out on human tissue from people with Hirschsprung disease until now.

The research, published in *Gut* is a collaborative effort between researchers at UCL and the University of Sheffield which began in

2017.



The red cells are the cells that support the nervous system and the overlap with the green cells (the cells given as a stem cell treatment) shows that the stem cell treatment can also form this crucial support system. Credit: Conor J McCann et al

Researchers at the University of Sheffield focused on the production and analysis of nerve precursors from stem cells. These were then shipped to the UCL team, who prepared the patient gut tissue, undertook the transplantation and maintenance of the tissue and then tested the function of the tissue segments.

The study involved taking tissue samples donated by GOSH patients with Hirschsprung disease as a part of their routine treatment which were then cultured in the lab. The samples were then transplanted with stem cell-derived nerve cell precursors which then developed into the crucial nerve cells within the gut tissue.

Importantly the transplanted gut samples showed increased ability to contract compared to control tissue suggesting improved functionality of the gut in those with the disease.

Principal Investigator, Dr. Conor McCann (UCL Great Ormond Street Institute of Child Health) said, "This study is a real breakthrough in our cell therapy work for Hirschsprung disease. It really shows the benefit of bringing the expertise of different groups together which will hopefully benefit children and adults living with Hirschsprung disease in the future."

Dr. Anestis Tsakiridis, Principal Investigator at University of Sheffield said, "This has been a fantastic collaboration, led by two talented early career scientists, Dr. Ben Jevans and Fay Cooper. Our findings have laid the foundations for the future development of a cell therapy against Hirschsprung disease and we will continue our efforts to bring this to the clinic in the next few years."

The results of this study demonstrate for the first time the potential of stem cell therapy to improve the functionality of the intestine in those with Hirschsprung disease which, in turn, could lead to improved

symptoms and better outcomes for individuals with the disease.

More information: Benjamin Jevans et al, Human enteric nervous system progenitor transplantation improves functional responses in Hirschsprung disease patient-derived tissue, *Gut* (2024). DOI: 10.1136/gutjnl-2023-331532

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