

Stem cells turned into complex, functioning intestinal tissue in lab

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For the first time, scientists have created functioning human intestinal tissue in the laboratory from pluripotent stem cells.

In a study posted online Dec. 12 by *Nature*, scientists from Cincinnati Children's Hospital Medical Center say their findings will open the door to unprecedented studies of human intestinal development, function and disease. The process is also a significant step toward generating intestinal tissue for transplantation, researchers say.

"This is the first study to demonstrate that human pluripotent stem cells in a [petri dish](#) can be instructed to efficiently form human tissue with three-dimensional architecture and cellular composition remarkably similar to intestinal tissue," said James Wells, Ph.D., senior investigator on the study and a researcher in the division of Developmental Biology at Cincinnati Children's.

"The hope is that our ability to turn stem cells into intestinal tissue will eventually be therapeutically beneficial for people with diseases such as necrotizing enterocolitis, [inflammatory bowel disease](#) and short bowel syndromes," he added.

In the study, a team of scientists led by Dr. Wells and study first author Jason Spence, Ph.D. – a member of Dr. Wells' laboratory – used two types of pluripotent cells: human embryonic stem cells (hESCs) and induced pluripotent stem cells (iPSCs). iPSCs were generated by reprogramming biopsied human skin cells into pluripotent stem cells.

This was done in collaboration with Cincinnati Children's researchers Susanne Wells, Ph.D., and Chris Mayhew, Ph.D., co-director of the institution's Pluripotent Stem Cell Facility.

hESCs are called pluripotent because of their ability to become any of the more than 200 different cell types in the human body. iPSCs can be generated from the cells of individual patients, and therapeutic cells derived from those iPSCs would have that person's genetic makeup and not be at risk of rejection. Because iPSC technology is new, it remains unknown if these cells have all of the potential of hESCs, Dr. Wells explained. This prompted the researchers to use both iPSCs and human embryonic stem cells in this study so they could further test and compare the transformative capabilities of each.

To turn pluripotent stem cells into intestinal tissue, scientists performed a timed series of cell manipulations using chemicals and proteins called growth factors to mimic embryonic intestinal development in the laboratory.

The first step turned [pluripotent stem cells](#) into an embryonic cell type called definitive endoderm, which gives rise to the lining of the esophagus, stomach and intestines as well as the lungs, pancreas and liver. Next, endoderm cells were instructed to become one those organ cell types, specifically embryonic intestinal cells called a "hindgut progenitors". The researchers then subjected the cells to what they describe as a "pro-intestinal" cell culture system that promoted intestinal growth.

Within 28 days, these steps resulted in the formation of three-dimensional tissue resembling fetal intestine that contained all the major intestinal cell types – including enterocytes, goblet, Paneth and enteroendocrine cells. The tissue continued to mature and acquire both the absorptive and secretory functionality of normal human intestinal

tissues and also formed intestine-specific [stem cells](#).

Dr. Wells said his team and other researchers around the world will be able to build on these findings. The process will be used as a tool to study normal intestinal development in humans and what goes wrong with the intestine in people with diseases.

Another important next step is to determine if the intestinal tissue is effective in transplant-based treatments of intestinal diseases such as short bowel syndrome. This approach is first being tested in animals in collaboration with co-author Noah Shroyer, Ph.D., and Michael Helmuth, M.S., M.D., a [transplant](#) surgeon at Cincinnati Children's. Ultimately, the researchers want to translate those methods into treatment for people.

The researchers said the study's findings will also facilitate studies to design better drugs that are more easily taken up by the body, since the intestine absorbs most drugs taken orally.

More information: [dx.doi.org/10.1038/nature09691](https://doi.org/10.1038/nature09691)

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