Tiny human stomachs have been created from stem cells

Three-dimensional "mini-stomachs" have been created from human stem cells. The tiny organs measure about 3 millimeters in diameter and can be used as models for the infections that are often precursors to peptic ulcers and stomach cancer.

"This represents the first in vitro model of the human stomach," says James Wells, a stem cell biologist at Cincinnati Children’s and a co-author of [the study, which is published in*Nature* today](http://dx.doi.org/10.1038/nature13863). And "it’s not a cute little term — they really do look like ‘mini stomachs.’"

When the researchers first tried to grow these tissues, they did so using embryonic stem cells — cells that originate from a human embryo. The growth process, from start to finish, took about a month, Wells says, and the end product was a small organ that contained human stomach tissue made of at least eight different cell types. But before the researchers could celebrate, they had to make sure the technique could be deployed using cells from adults as well, a critical step in ensuring that the technique can be tailored to fit a specific patient. It worked in those cells too. "We were gobsmacked," Wells says. "It’s really amazing that these tissues will undergo their normal [growth patterns] in a dish."

Usually, researchers study infections in humans by observing tissue that’s already infected. The problem with that approach is that the moment when the infection takes hold remains a mystery. But the researchers in this study were able to look at what happens when bacteria encounters "healthy" gastric tissue in a petri dish, Wells explains. The new technique might one day help them identify the genes and cell signaling patterns that allow bacteria like *Helicobacter pylori —* the primary cause of peptic ulcer disease — to wreak havoc in our gastrointestinal tracts. The gastric tissues could also enhance the way pharmaceutical companies test the drugs that treat infections, Wells says. And since stomach cancer is the second leading cause of cancer-related deaths, investigating how these sorts of cancer precursors develop might one day help extend patients’ lives.

"We’re now planning to really dissect how these infections happen, which of the stomach cells are really being adversely impacted by the stomach bacteria, and how can we use chemicals to attenuate or shut off this response," Wells says.

Unfortunately, Wells and his team of researchers were only able to grow part of the human stomach: the lower end, which goes by the name of "antrum" and connects to the intestine. The upper part of the stomach — the part that manufactures most of the digestive enzymes and acid — will take more time to produce. This means that right now, the engineered organoids are more like tiny, self-contained antrums than complete human stomachs. It's not ideal, since infections in the stomach play out differently depending on where they start, Wells says. Still, it’s a step in the right direction, and the researchers are working on engineering the rest of the stomach tissues as well. And the antrum tissues are already a lot to work with.

For instance, Wells and his team have started exploring whether this tissue could be used to patch ulcers in mice. Stomach ulcers are essentially defects in the lining of the organs; in severe cases, they can be "patched" to avoid pain and internal bleeding. Right now, patching ulcers involves growing gastric tissues from a sample removed during a biopsy. This, Wells says, can be invasive. But growing tissues from stem cells would allow researchers to bypass that step altogether, because they could start with cells taken from a patient’s blood. "I think if our animal trials go well we could certainly scale up," Wells says, "and start patching ulcers within the next ten years."

Jason Mills, a developmental biologist at Washington University, says that the study is "beautiful" and "innovative." "You can do more experiments and manipulate individual genes more than you can in a mouse," he says, "because it’s easier to do this in a dish and incubator rather than in a living creature." But there are no immune cells or blood in the system, he says — key elements in any infection — so it’s not a perfect model. And Wells himself points out that the tissues that his team produced are "immature," meaning that their architecture and function doesn’t perfectly mimic that of adult gastric tissue. Still, the organoids look "more like a mini-organ than anything else that’s ever come before," Wells says.

This is the "perfect illustration" of the power of using adult stem cells for disease modelling, says Melissa Little, a developmental biologist at The University of Queensland in Australia. A model like this one "will increase our understanding of the association between *H. pylori* and gastric cancer" in humans, she says, and it might provide us with the means of tailoring treatments to specific patients.

Individualized treatments are still a long way off, however. So Wells says that he would like this work to be used as an example of the value of basic research — the kind of research that isn’t always popular with the public. "If we didn’t have a basic understanding of developmental biology, these studies would never have been possible — or it would have been extraordinarily difficult," he says. "This whole thing, it’s a testimony to the importance of basic research."