

Gut and Immune System

From Science Fiction To Reality: Building Baby Intestines



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Disclosures

- Abbott Nutrition (Research grant, speakers bureau)
- H&L Labs LLC
- Infant Bacterial Therapeutics (DSMB)
- US Patent Office





Butler County boy's cupcake dream motivates doctor

Austin Rath is almost 6 years old and never has had a drink of water. He hasn't eaten a cupcake, either. The kindergartener from Renfrew in ...

6-year-old raises cash in pursuit of 'tummy'



MEGAN GUZA | Friday, July 13, 2012, 10:24 p.m.



Austin Rath, 6, stands with a check for \$61,574.16 at a ceremony where he presented the check to Children's Hospital of Pittsburgh and UPMC Researcher Dr. David Hackam on Friday morning, July 13, 2012. The donation will help Dr. Hackam with his research into the development of an artificial intestine. Justin Merriman | Tribune-Review

Short bowel syndrome

- One of the most important and devastating childhood diseases that you have never heard of.
- Inadequate length of intestine (due to illness, injury, birth defect)
- Survival requires peripheral nutrition and intestinal transplantation
- 5000 cases per year.

Goal of this work

Short bowel syndrome causes tremendous hardship for children and families who suffer from this disease and there is no effective cure.

The goal of this research is to treat short bowel syndrome through the development of the world's first artificial intestine.

What causes short bowel syndrome?

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updated 8:49 p.m. EDT, Sun October 4, 2009



Report: 1M preemies die in first month annually

More than 1 million babies born prematurely die each year before they are a month old, the March of Dimes said Sunday in the first comprehensive global report on premature births. "Premature births are an enormous global problem that is exacting a huge toll emotionally, physically and financially on families, medical systems and economies," March of Dimes President Jennifer Howse said in a statement. [full story](#)

JUNE 2, 2014

India's New Leader / When Trains Explode / Plus: Love Me Tinder by Joel Stein

TIME

EMALYN WAS DUE IN JUNE.
SHE ARRIVED IN MARCH.

SAVING PREEMIES

BY JEFFREY KLUGER

A photograph of a newborn baby lying in a hospital bed, being held by a hand. The baby is wearing a green cap and is surrounded by medical equipment. The baby's hand is raised.

Emalyn Aubrey Randolph weighed 2 lb., 10 oz. when she was born at 29 weeks

time.com

Necrotizing enterocolitis

- Most common lethal disease affecting the GI tract of the premature infant.
- 3% of all neonatal deaths, 10% of all premature infants, 30% mortality
- Breast milk is protective, unclear why
- Associated with devastating neurological injury

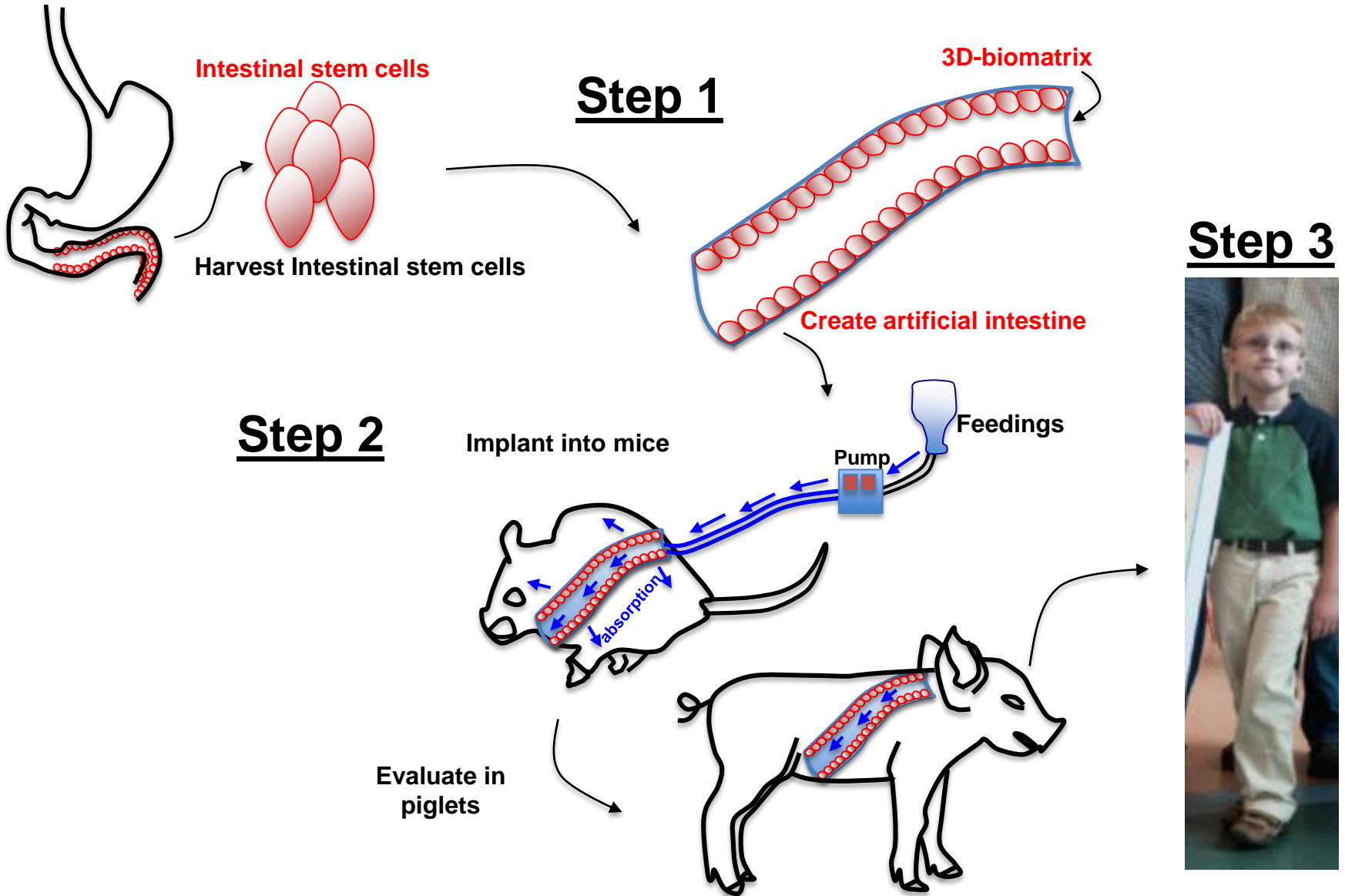


“This picture is the last one we ever took at home. It was taken on the way down to CHP for a doctors appointment. Freddie was admitted to the hospital but never came home”.

Short bowel syndrome is caused by NEC



Making baby intestines



Stem cells in the gut

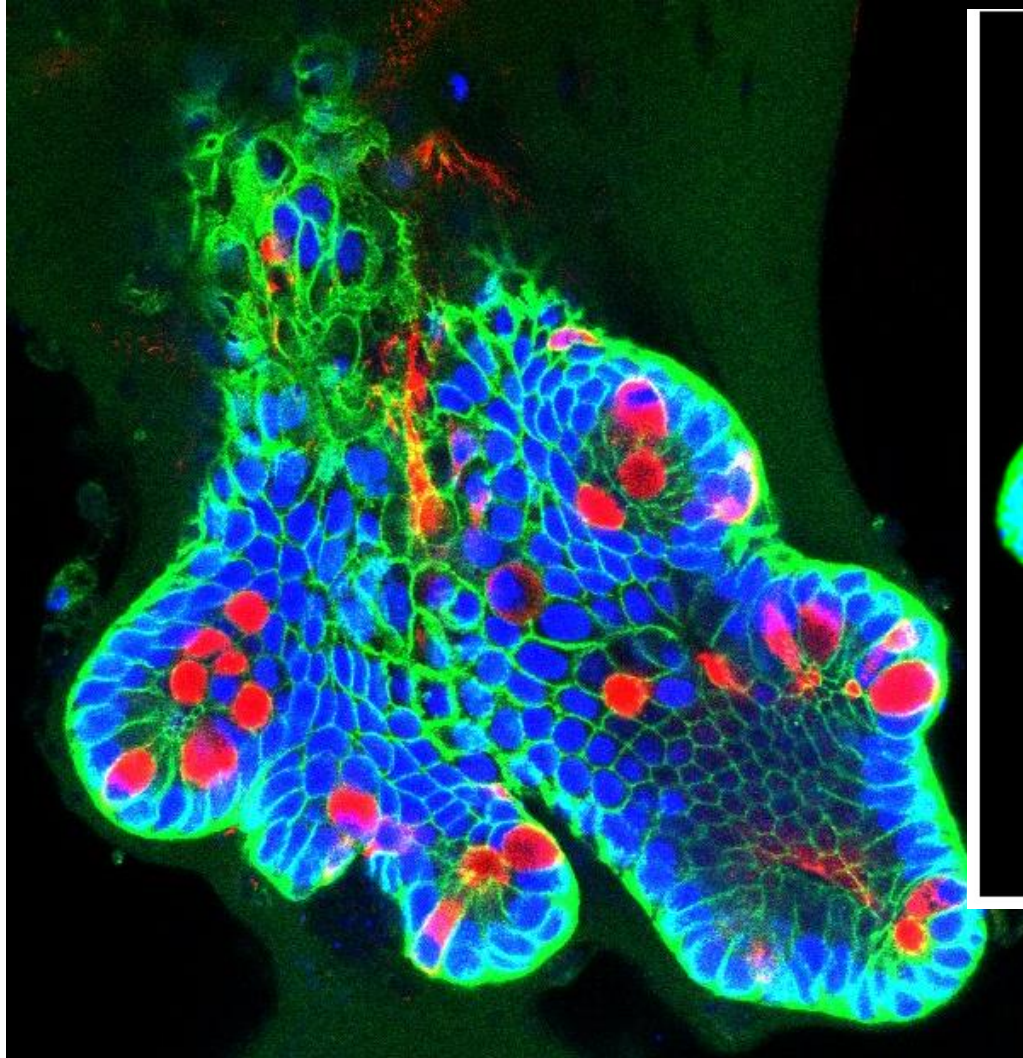
- The intestine turns over every 3-5 days due to stem cells at the base of the crypts.
- Markers to identify the intestinal epithelial stem cells have very recently been identified.



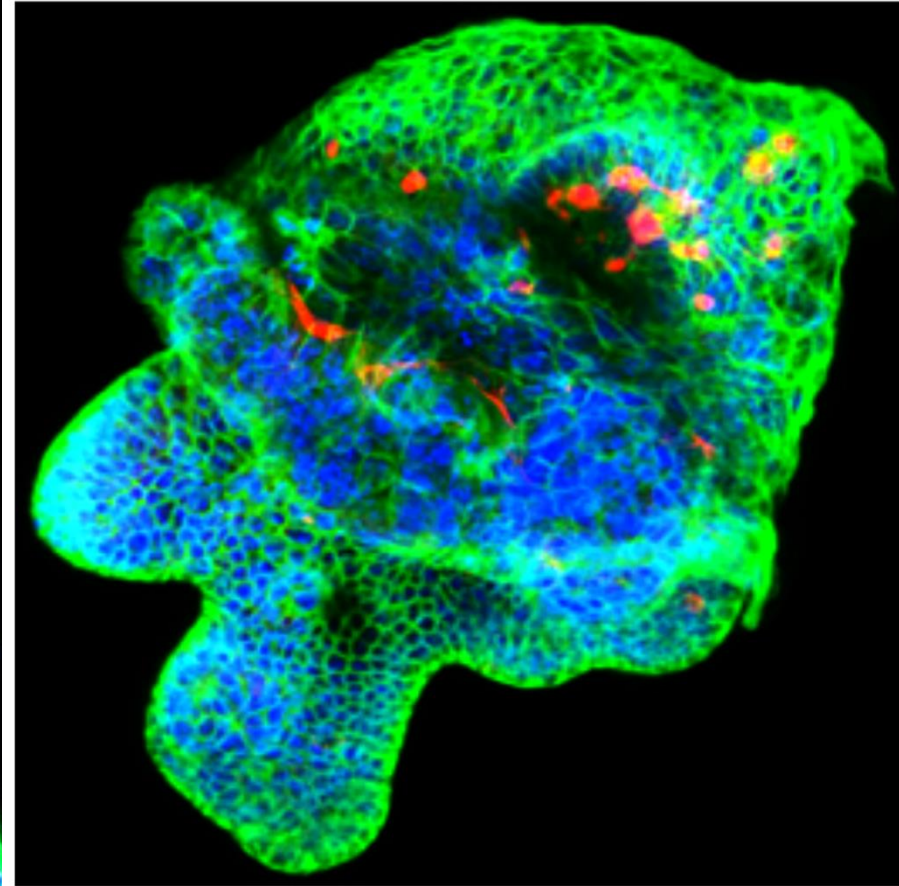
Hackam, J Biol Chem 2004

Growing stem cells into mini-guts in the lab

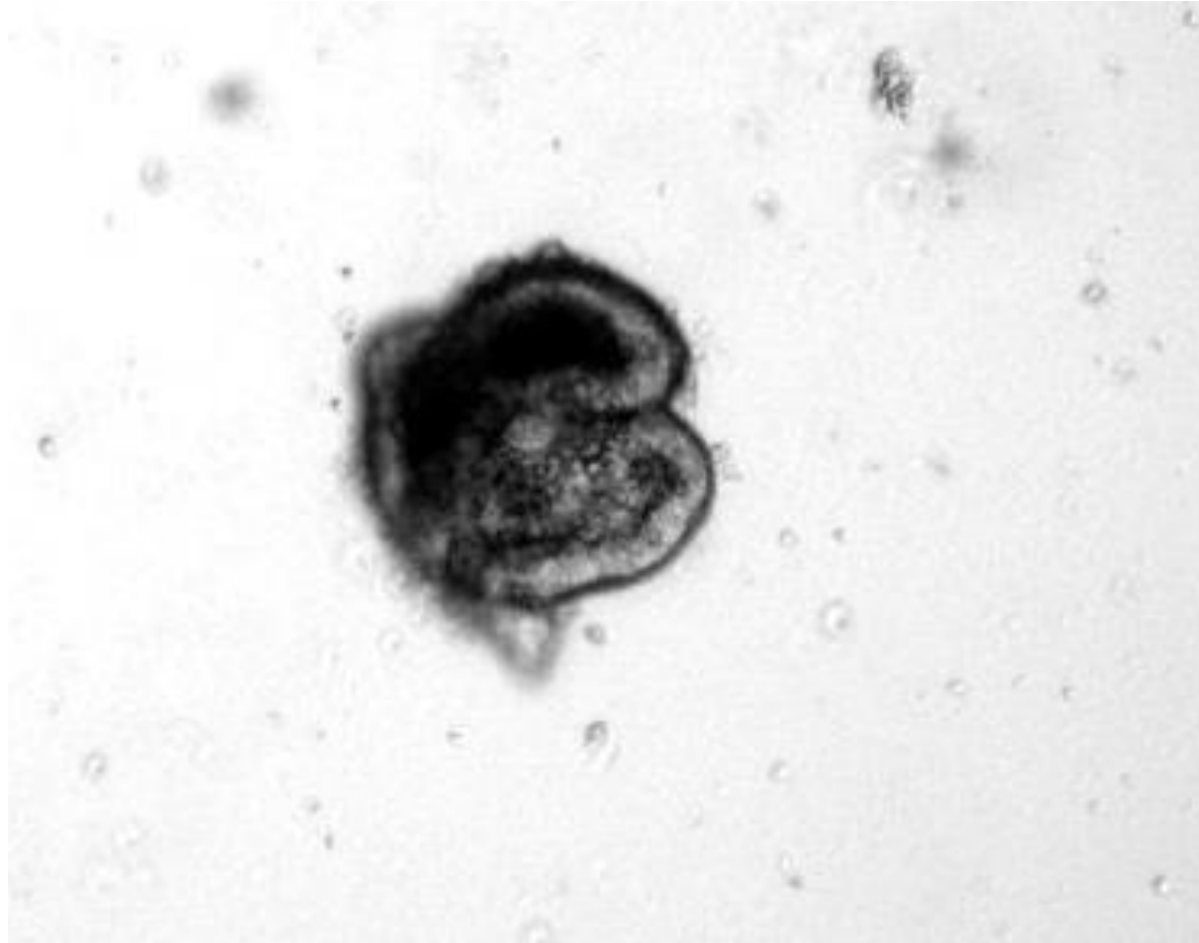
Mouse

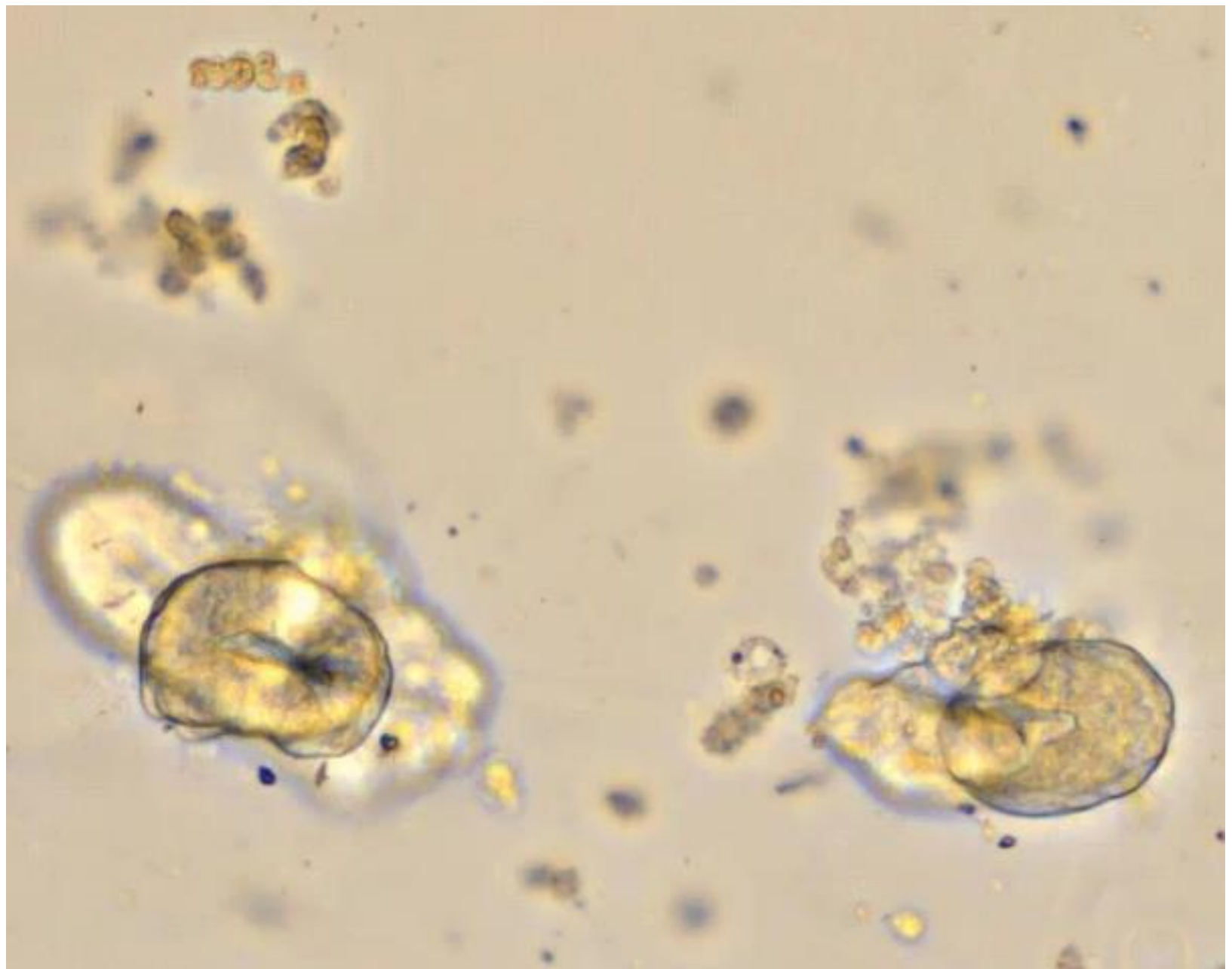


Human

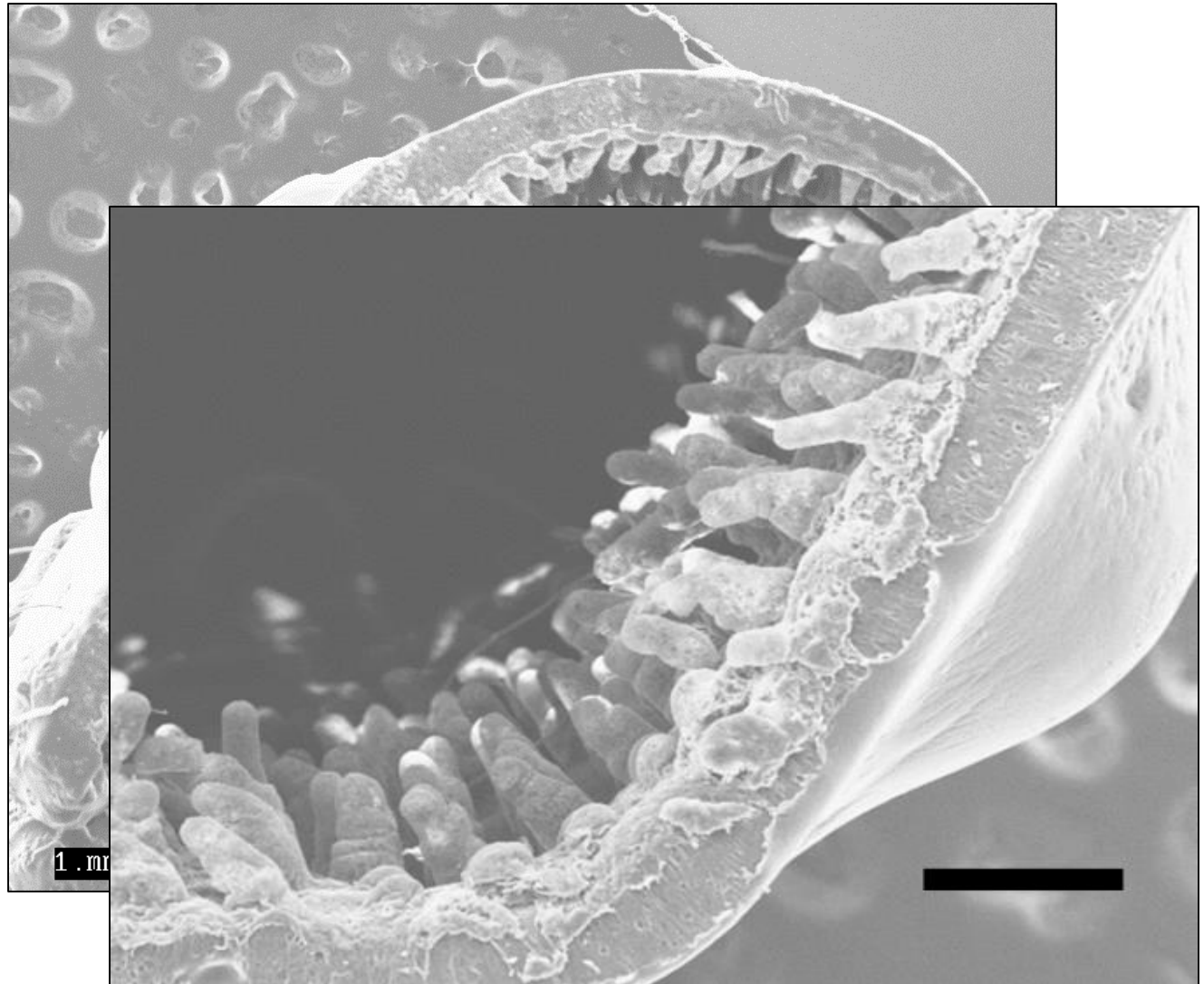
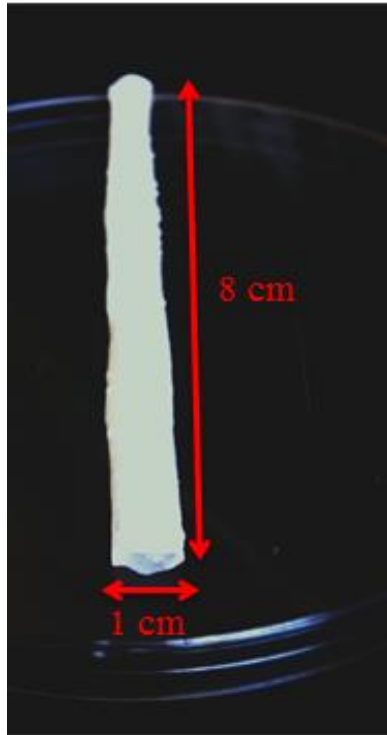


Growth of a mini intestine in a dish

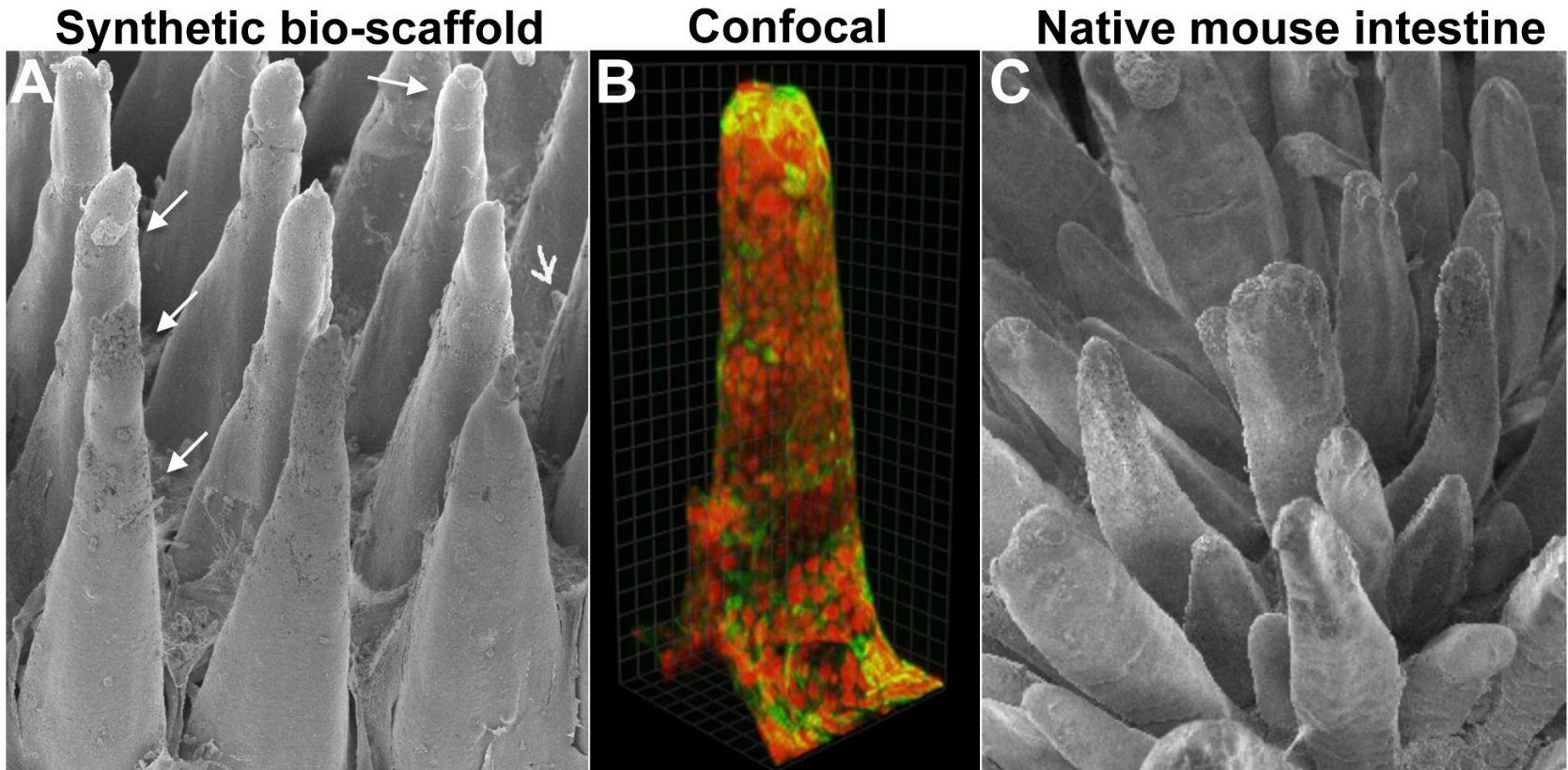




Creation of a bio-scaffold



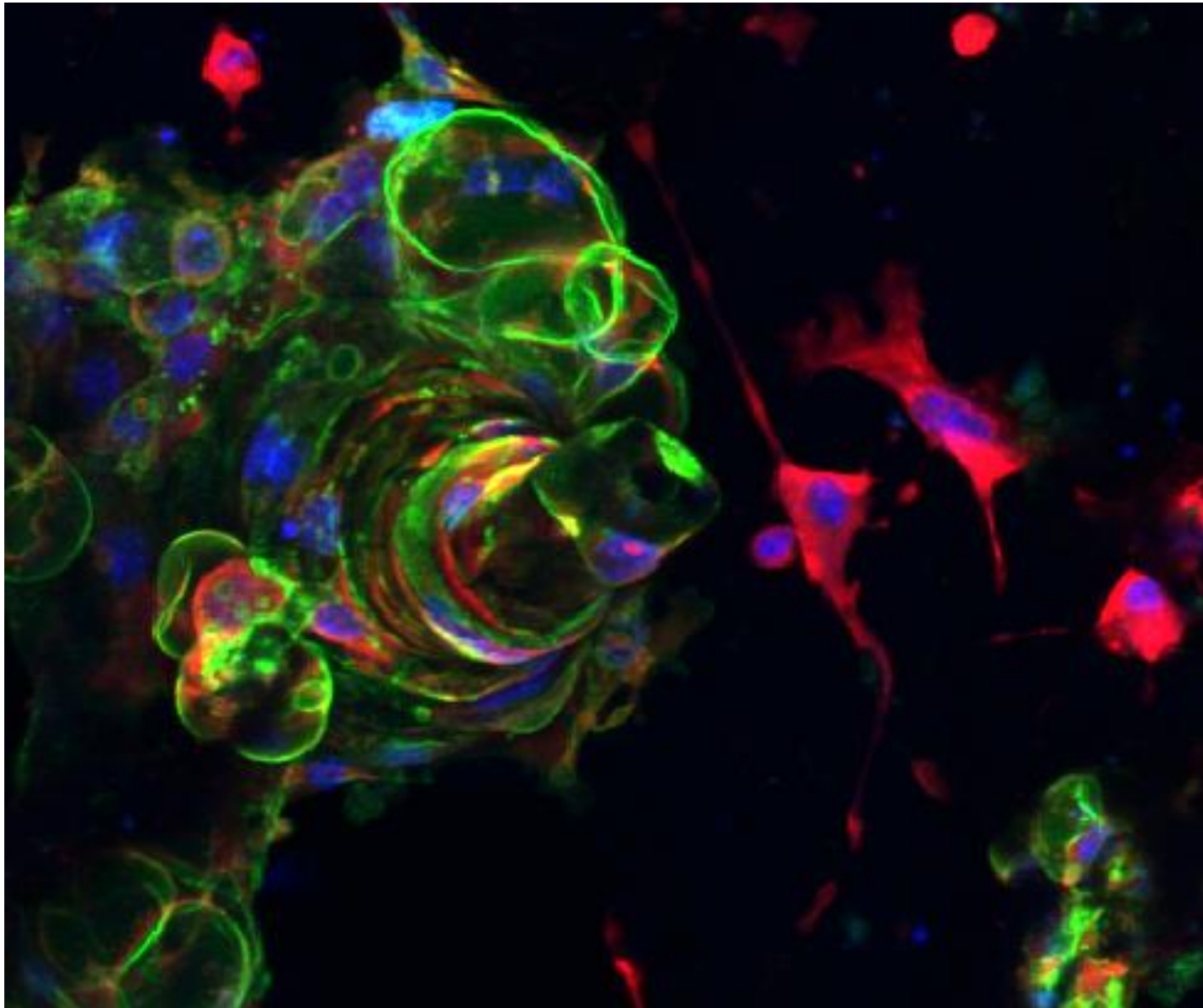
Seeding of the scaffold with intestinal stem cells



Testing in mice, dogs and piglets

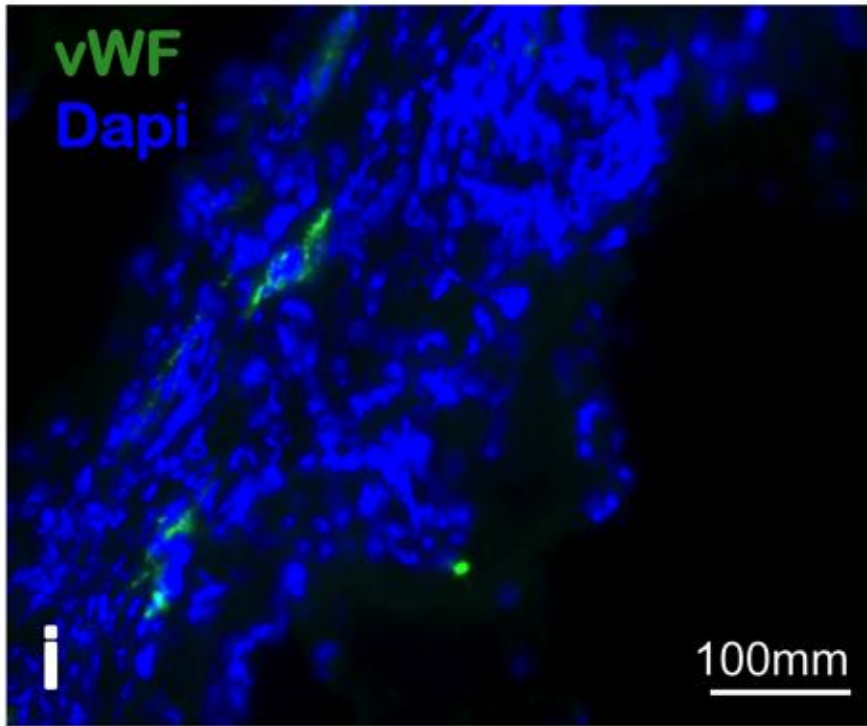


The engineered intestine survives in the mouse

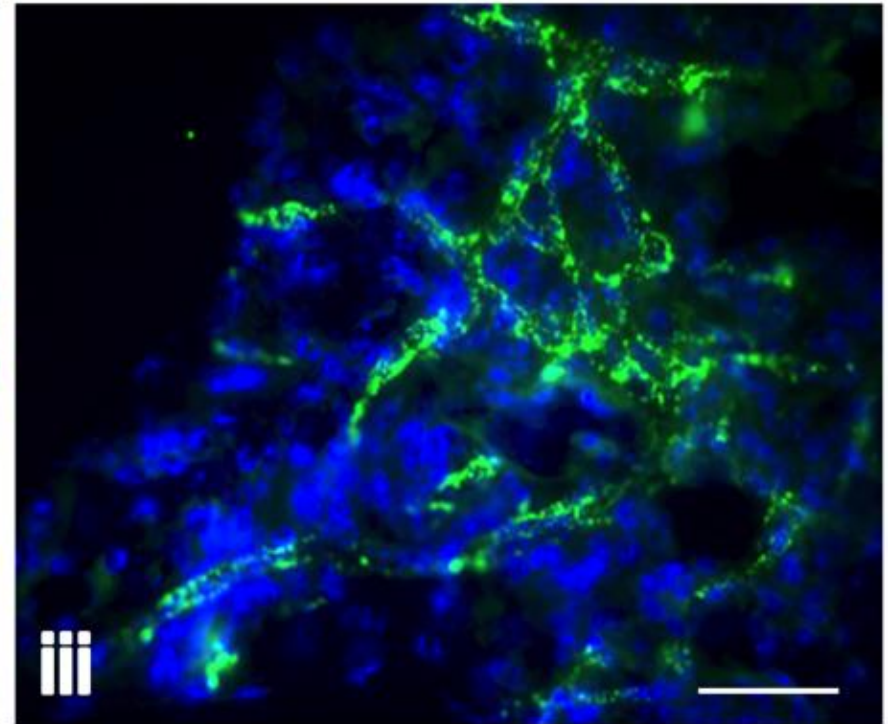


Recruitment of a blood supply to the neo-intestine

Day 0

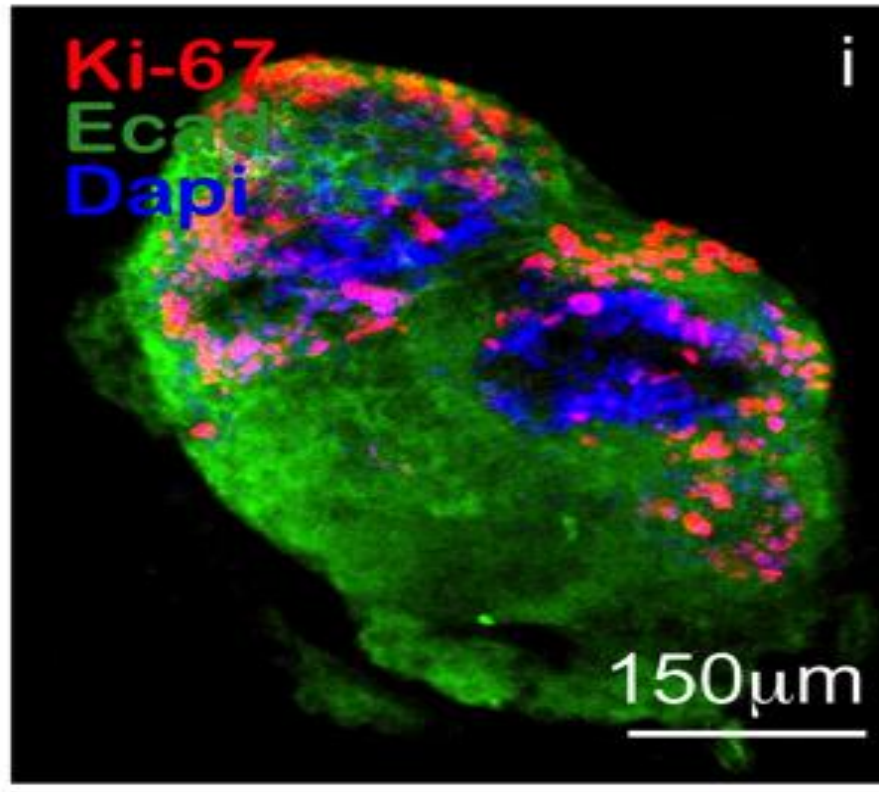


Day 28

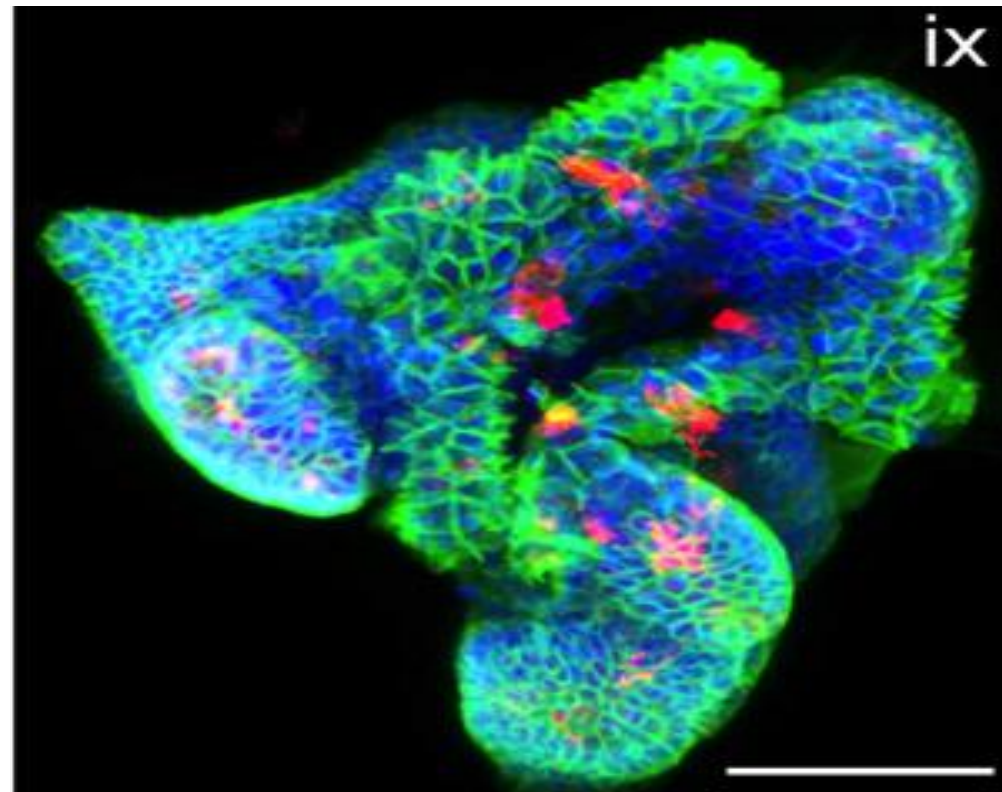


Probiotic bacteria promote intestinal growth

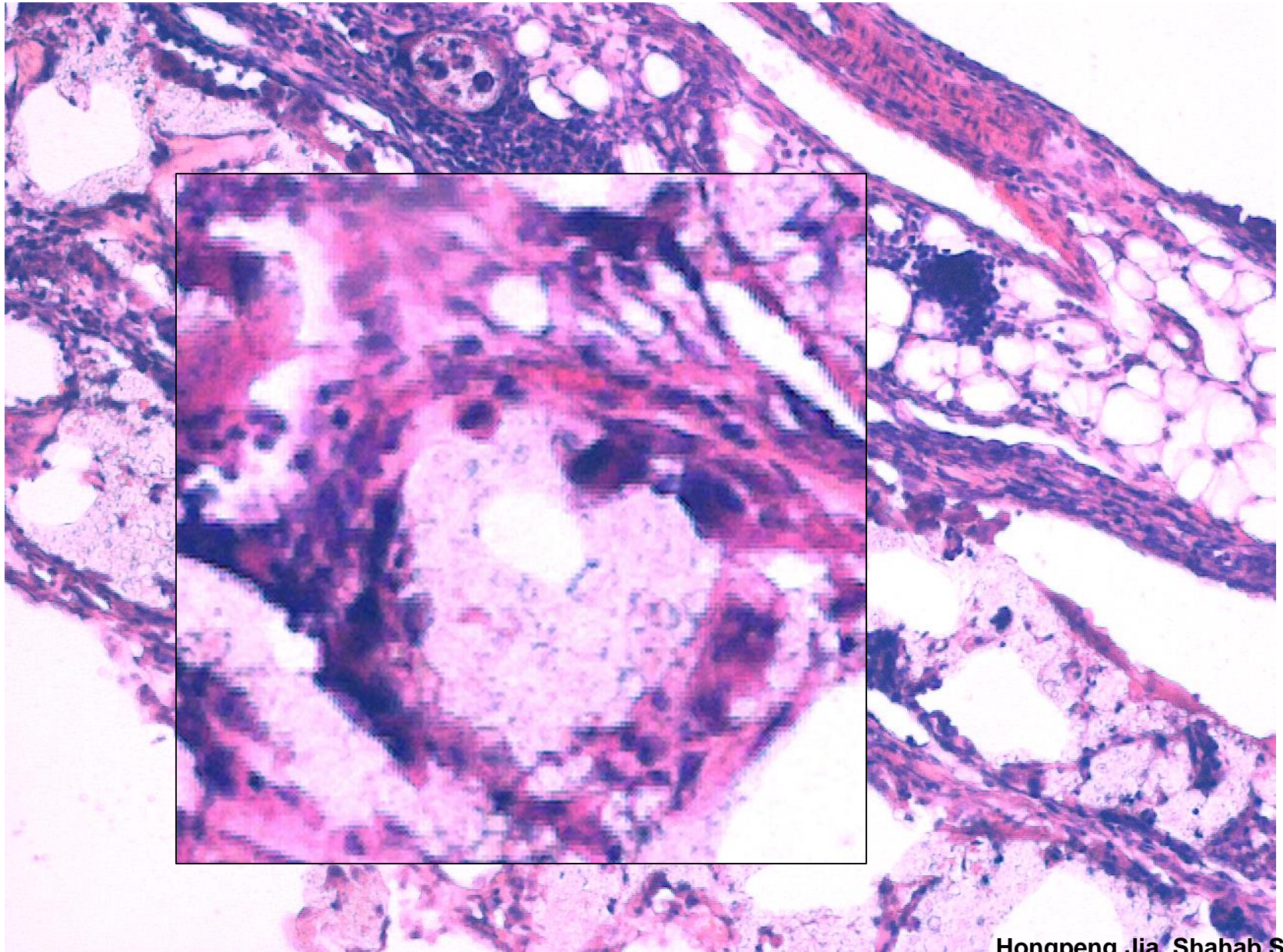
Control



Probiotic



Human intestinal stem cell scaffolds in a mouse



Lab-grown guts show promise in mice and dogs

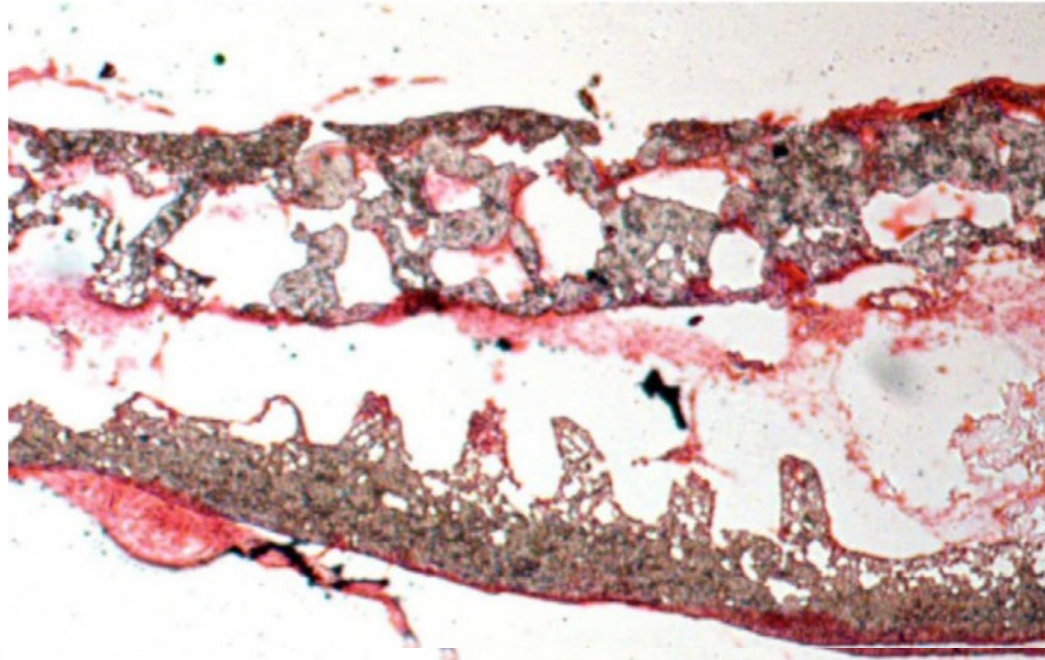
Science

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ADAPTED FROM S. A. SHAFFIEY ET AL., REGENERATIVE MEDICINE (2015)

Researchers have created artificial intestines complete with nutrient-absorbing villi that could one day help humans with gut disorders.

Placement of the artificial intestine in dogs



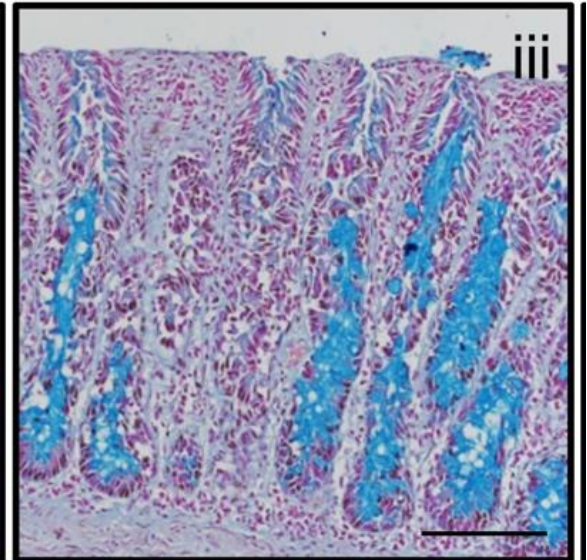
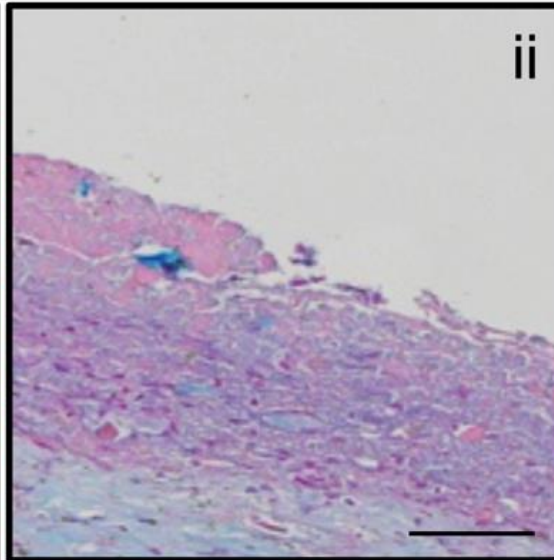
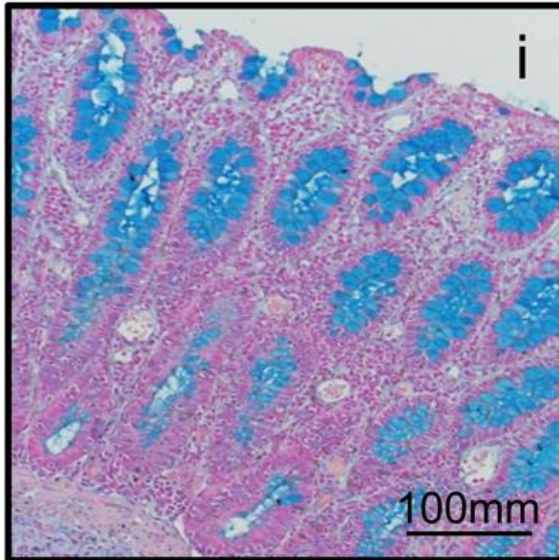
Implantation of artificial intestine in dogs restores the mucosa

Normal Colon

No Scaffold 8 wks

Scaffold 4 wks

A



Summary

- We have established proof of concept for the development of an artificial intestine for humans with short bowel syndrome
- We believe that eventually, we can make science fiction a reality.

“If you want to go fast, go alone. If you want to go far, go together”

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