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...
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.
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?

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
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

1. Harvest Intestinal stem cells
2. Implant into mice
3. Create artificial intestine
   - 3D-biomatrix

Evaluate in piglets
Feedings
Pump
Step 1
Step 2
Step 3
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
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.
Human intestinal stem cell scaffolds in a mouse

Hongpeng Jia, Shahab Shaffiey
Lab-grown guts show promise in mice and dogs

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

ADAPTED FROM S. A. SHAFFIEY ET AL., REGENERATIVE MEDICINE (2015)
Placement of the artificial intestine in dogs
Implantation of artificial intestine in dogs restores the mucosa
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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