

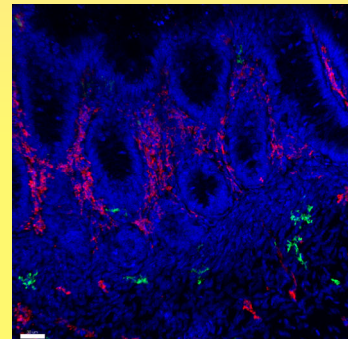
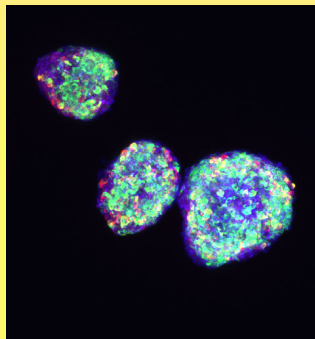
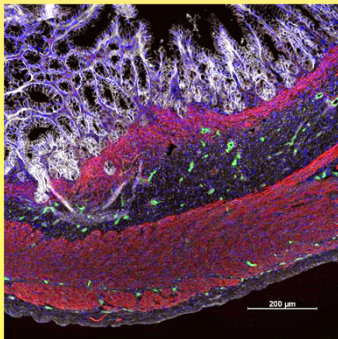
New ways to study human nutritional homeostasis using organoids

Jim Wells, PhD.

Center for Stem Cell and Organoid Medicine (CuSTOM)

Divisions of Developmental Biology and Endocrinology

Cincinnati Children's Hospital Medical Center, OH



NASEM workshop July 10, 2025



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Thanks!

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CuSTOM
Center for Stem Cell & Organoid Medicine
Translating Discovery to Human Health

Funding



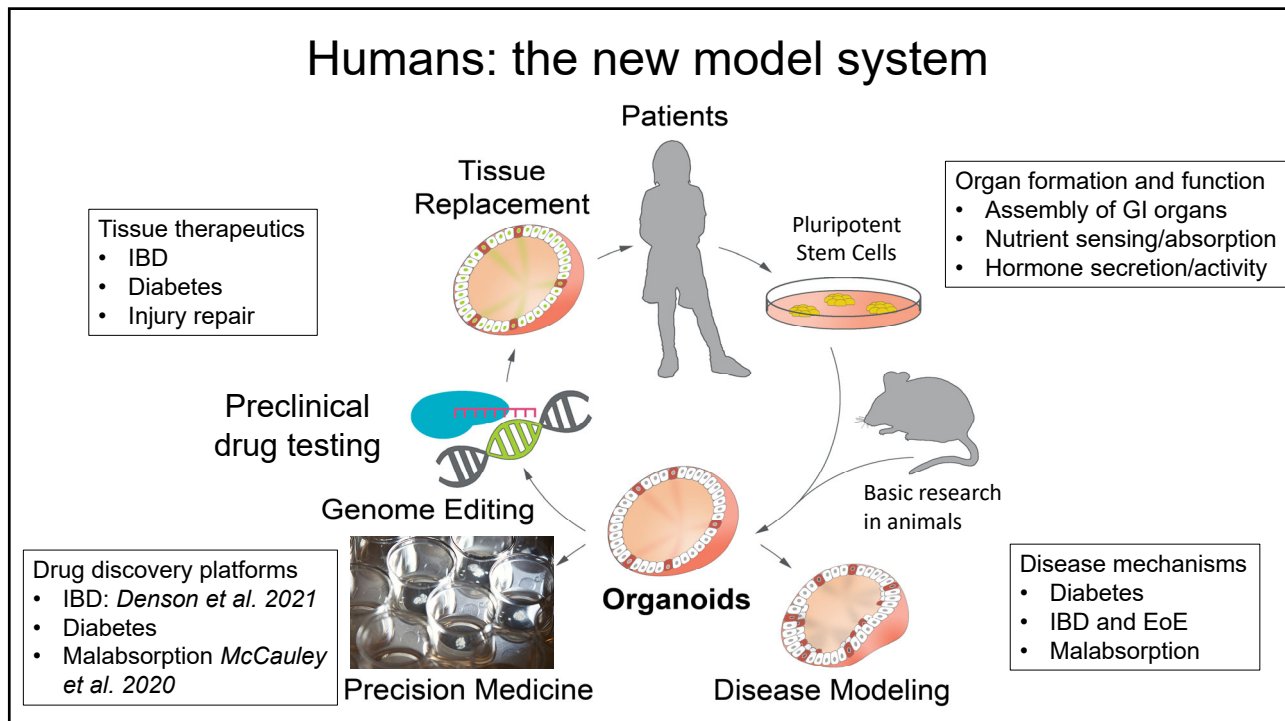

NIDDK 

NATIONAL CANCER INSTITUTE

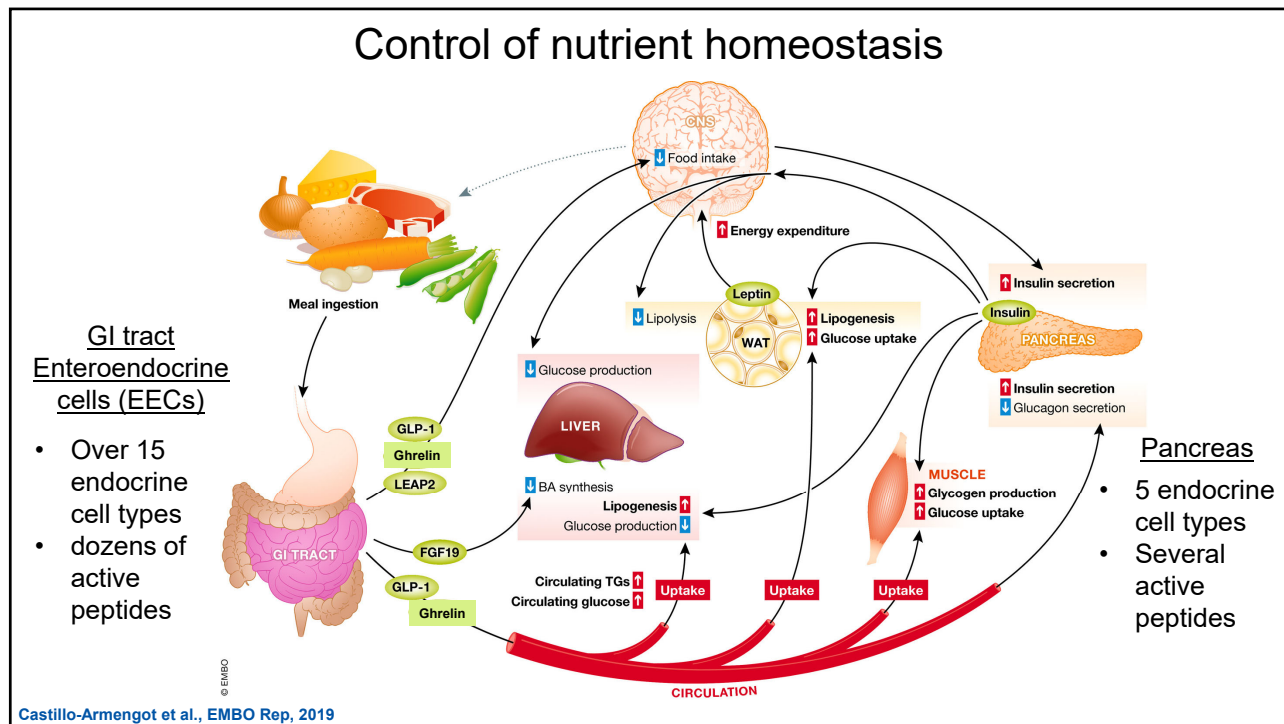
PAUL G. ALLEN FAMILY FOUNDATION


Shibley Foundation

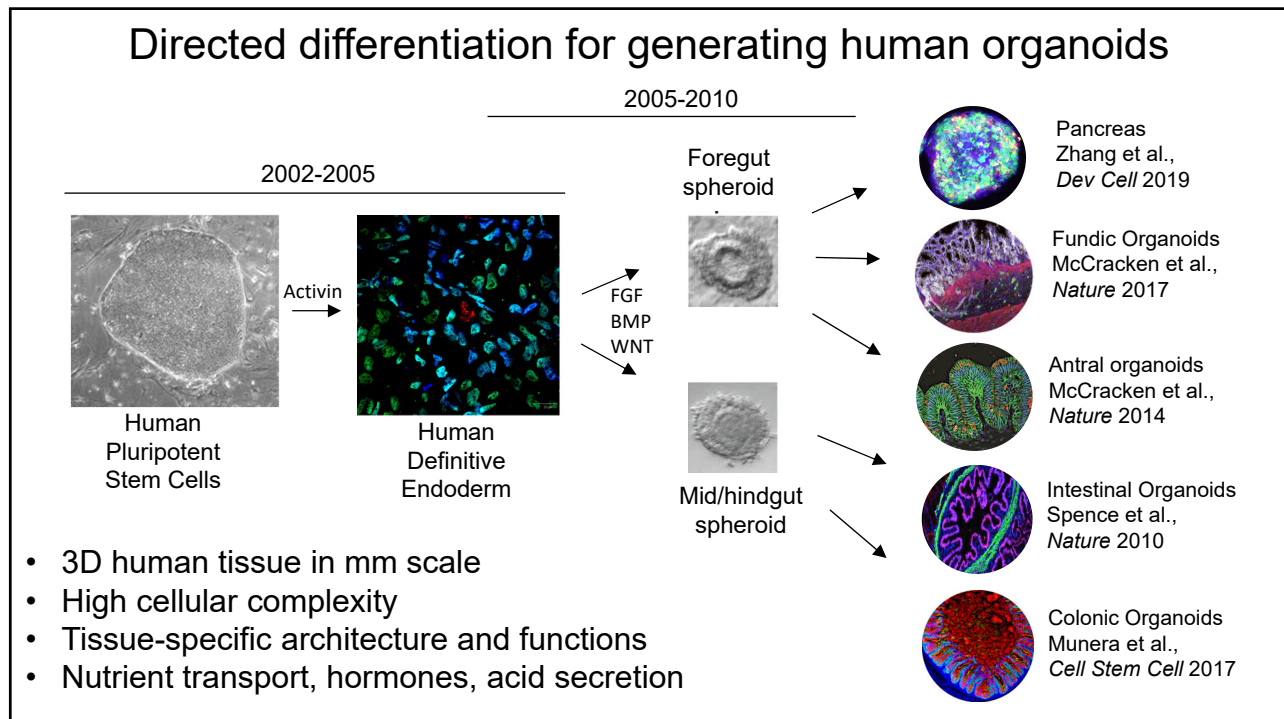
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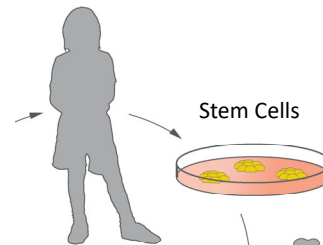
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Enteroendocrine cells control macronutrient absorption

- EEC deficiency causes malabsorptive diarrhea in mice and humans
- Patients require IV nutrition for survival
- Organoids phenocopy patients
- Use organoids to identify hormones that restore macronutrient absorption



Heather McCauley
Assistant Professor UNC

Collaborators:
Chip Montrose
Eitaro Aihara

Drug discovery platforms

- IBD
- NAFL
- Malabsorption



Precision Medicine

Organoids

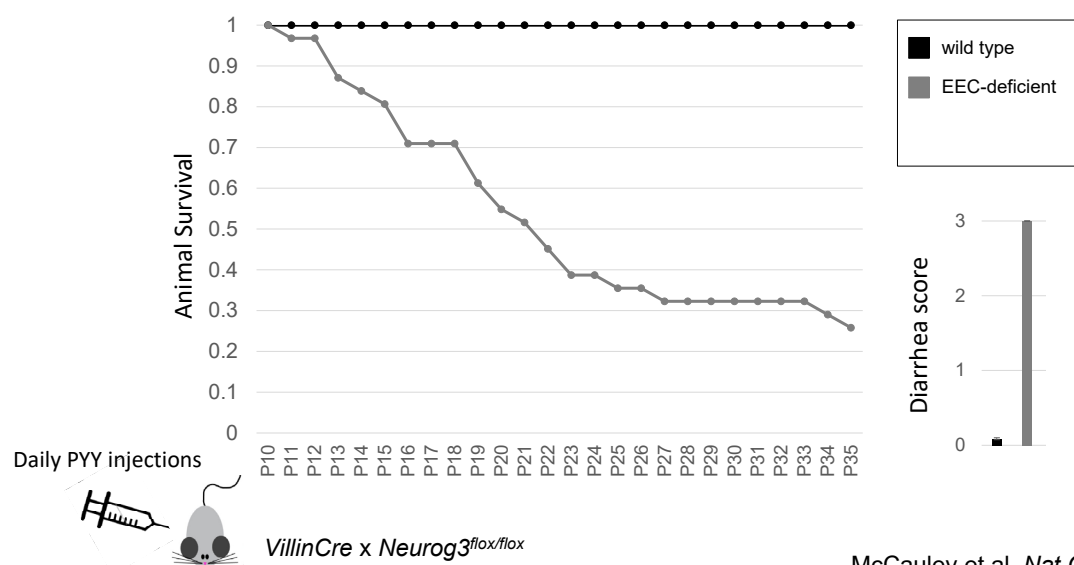
Disease Modeling

Basic research
in animals

PYY

7

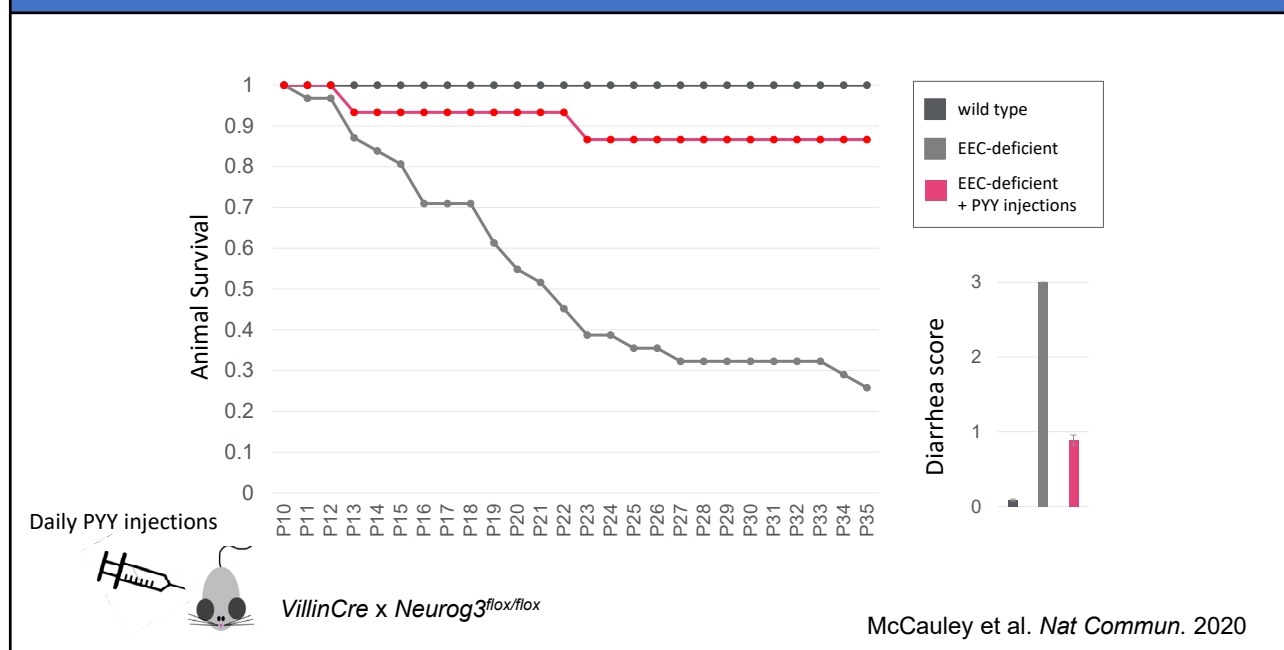
Preclinical testing of PYY as a treatment for severe malabsorption



McCauley et al. *Nat Commun.* 2020

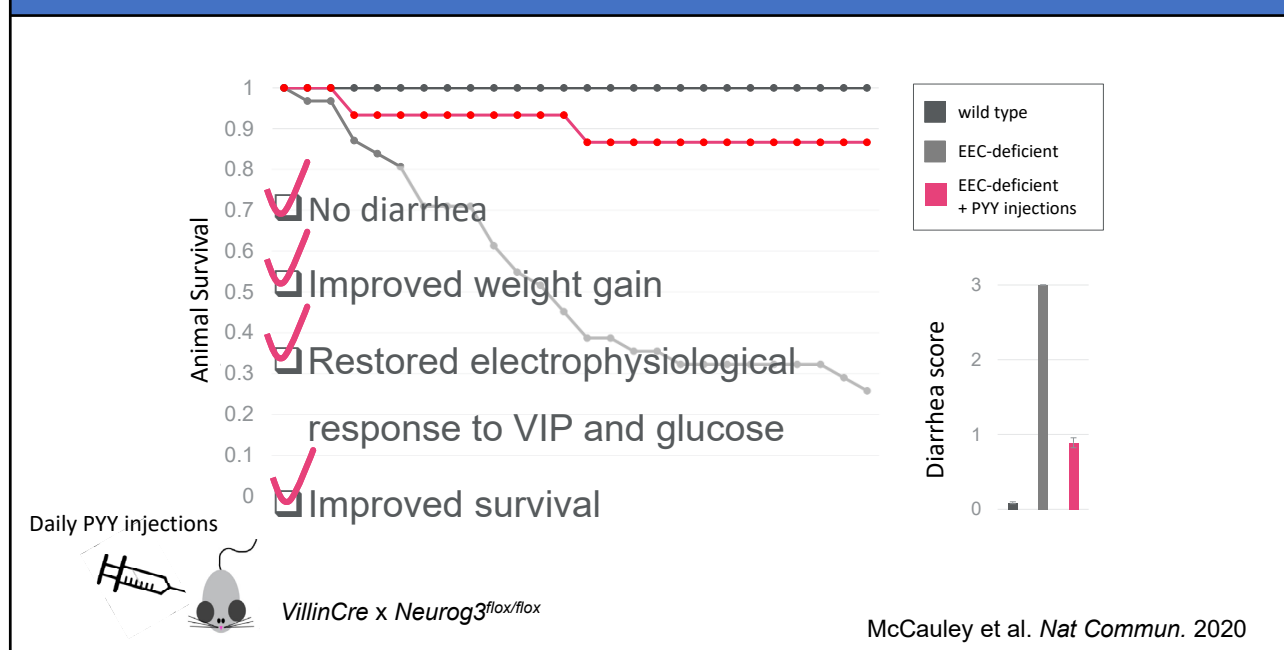
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Exogenous PYY rescues mutant mice from malabsorptive diarrhea



9

Exogenous PYY rescues mutant mice from malabsorptive diarrhea



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Modeling nutrient homeostasis using a microfluidic system

Patrizia Tornabene², Philip Lewis², J. Guillermo Sanchez², and **James Wells^{2*}**

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Masaki Kimura¹ and **Takanori Takebe^{1*}**

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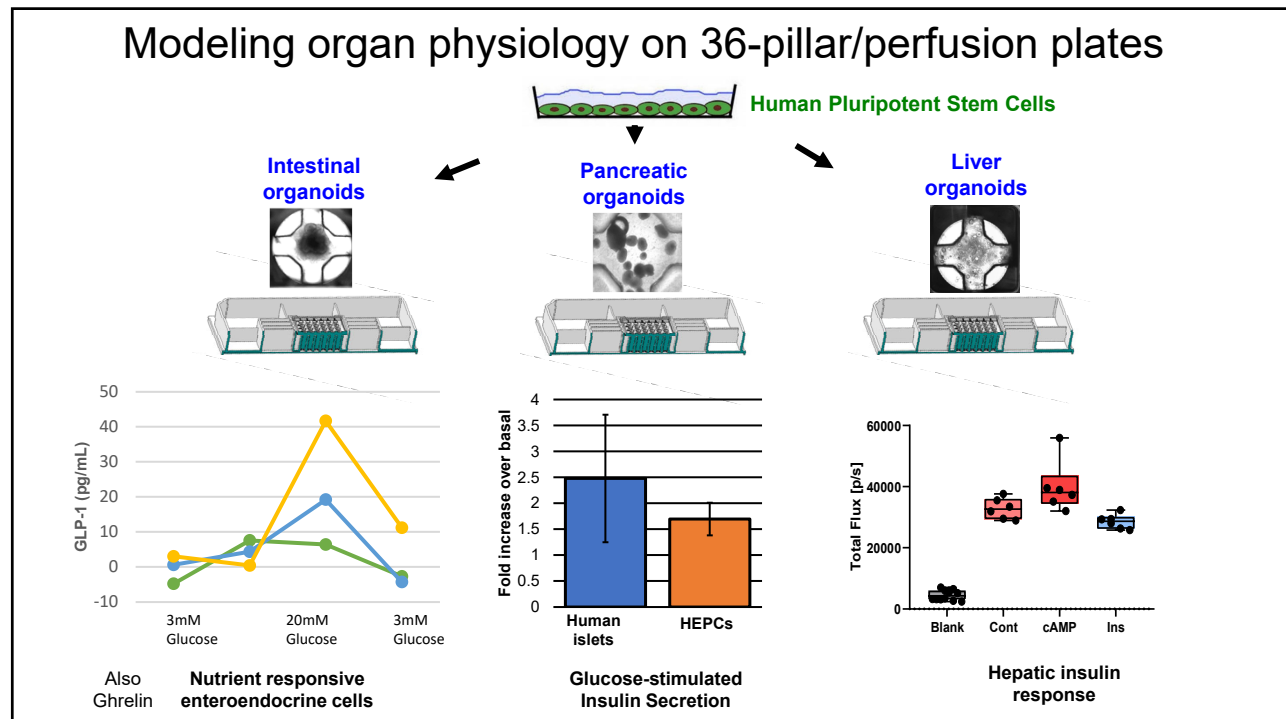
³Department of Chemical and Biomedical Engineering, Cleveland State University

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⁴Department of Bioengineering and Orthopedics, University of Illinois at Chicago

[UH3DK119982](#)

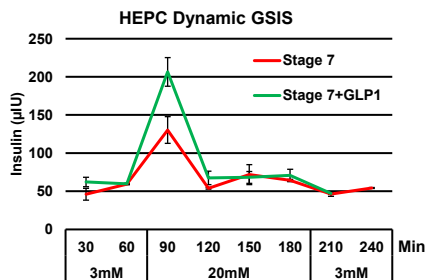
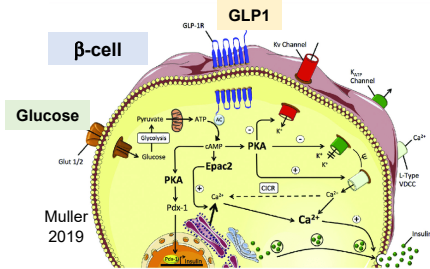
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Testing T2D drugs on Pillar/Perfusion plate

GLP1 augments insulin secretion



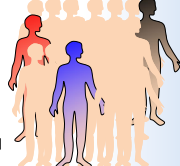
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Village in a dish: diverse responses to nutrients and therapeutics

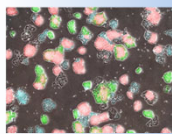
Ted Denson
Taka Takebe

Genetic factors

Population iPSC-panel



Low Middle High risk



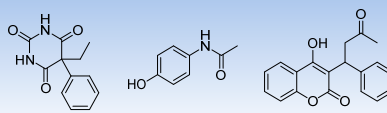
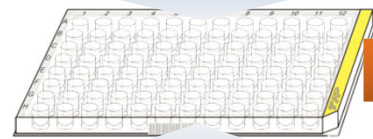
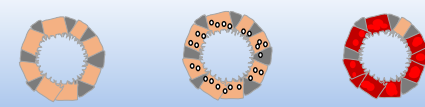
Population rep.
iPSC-organoid panel

Environmental factors

Balanced diet

HFD

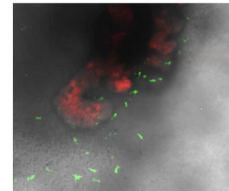
HCD



Screen drugs

Organoid Screen

High Content Imaging (Macs)



Drug Safety Screen
• Toxicity

Drugs screening platforms

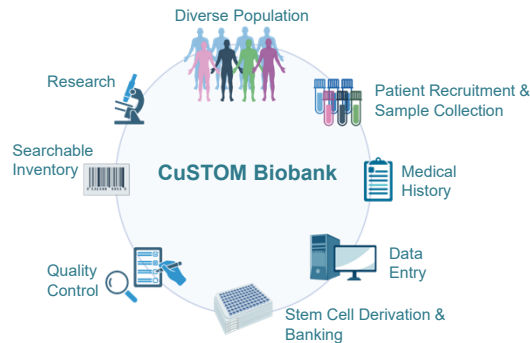
- IBD
- MASLD
- Diabetes

Slide adapted from Taka Takebe

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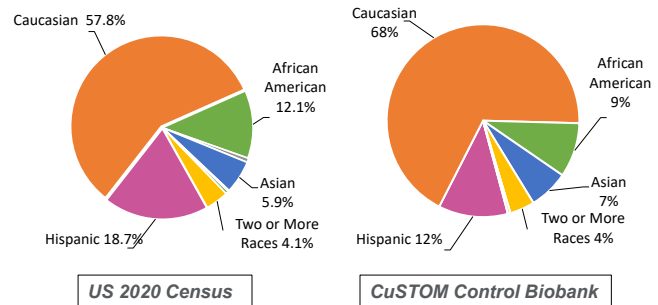
CuSTOM Biobank: Modeling nutrient homeostasis and disease

End-to-End Stem Cell Research



- Patient recruitment and sample collection
- Consenting allows for genome sequencing, sharing and commercialization
- Barcode linked to patient's clinical data
- Generation of pluripotent stem cell lines
- Extensive quality control

Stem Cell Line Banking

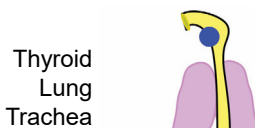


- CuSTOM 2020 control biobank
 - 450 consented donors
 - 300 collected blood samples
 - 135 stem cell lines generated
- Disease banks for IBD, Diabetes, Malabsorption, Liver Disease (MASH/MAFLD)

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Human organoids for modeling nutrient homeostasis

Population studies



- High throughput capacity in vitro
- PSC banks for population studies of nutrient handling
- Quantitative comparison to patient data

Bladder

Zorn and We

Disease modeling

Enteric neurons and glia

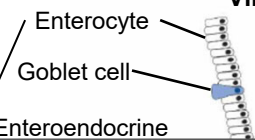
- Structure-function
- Patient mutations
- Personalized medicine
- Reversal of malabsorption in preclinical model

th
le
ium
cosa

Immune cells

Cell formation/function

VILLUS



- Control of endocrine cell formation and homeostasis
- Endocrine control of nutrient absorption

Stem cells
Paneth cell
CRYPT

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Pluripotent Stem Cell Facility



pscf@cchmc.org

Transgenic Animal and Genome Editing Facility



transgenics@cchmc.org

iPSC generation:

- PBMCs, fibroblasts...
- Integration-free reprogramming
- Ethnically-diverse control iPSCs

iPSC gene editing:

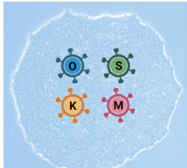
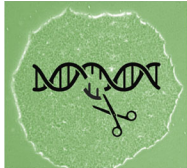
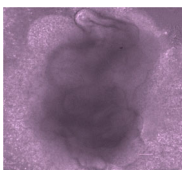
- INDELS
- Single base changes
- Affinity tag knockin
- Reporter knockin
- Inducible overexpression

hPSC QC and authentication:

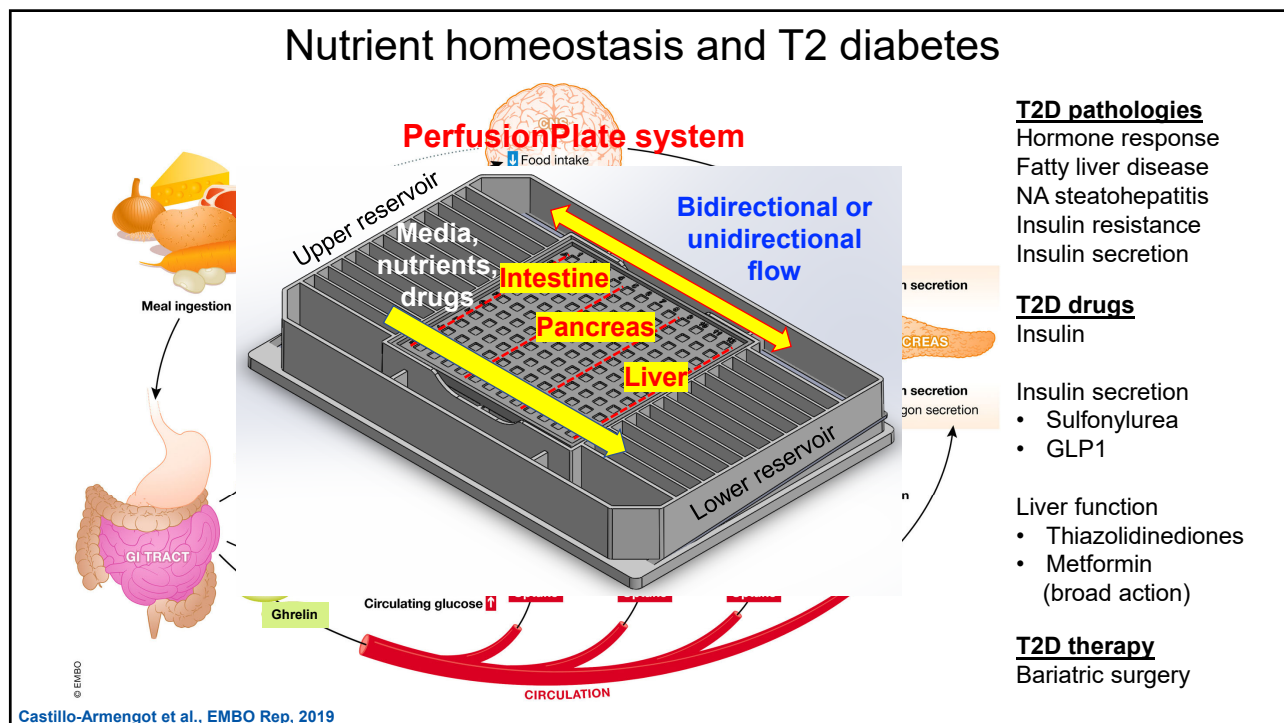
- Identity analysis
- Genetic stability
- Stemness marker expression
- Functional pluripotency

Hands-on training:

- hPSC culture techniques
- GI organoid generation

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