Unlocking new insights into brain-gut communication, metabolism and longevity

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1:00pm PT / 4:00pm ET

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Genes control our metabolism
The environment controls metabolism
Both genes, and the environment, control metabolism.
- Early studies on metabolism and body weight
- Finding new genes, brain-gut biology
- Applying discoveries
Brain regions control metabolism: 1950s – 2000s

Nesan & Kurrasch, 2016
Brain regions control metabolism: 1950s – 2000s

Nasrallah & Horvath, 2014

Srinivasan et al., 2004
Genomic Revolution: ~ 1990s - date

Shared genes and genetic ancestry between species!
Uncovering the genes of fat metabolism, at scale

- **Caenorhabditis elegans**
  - Similar genomes, new genetic and molecular tools
  - Speed – life cycle, lifespan, size
  - Scale – genes x phenotype in living animals
Uncovering the genes of fat metabolism, at scale

Srinivasan, 2015
Identity of every single neuron is known

Genetic tools to monitor, manipulate and edit functions of neurons

Can study the effect of genes in the *C. elegans* brain, on metabolism

*Neurobiology of C. elegans*

Yemini et al., 2021
#1. The neurotransmitter serotonin is a principal driver of fat loss
#2. A brain-to-gut messenger: the Tachykinin peptide
#3. Gut metabolism and longevity are intertwined
#4. A twist: the gut talks back!
#5. Applying new knowledge: the Tachykinin receptor in mammals
#1. Serotonin is a principal driver of fat loss

Tryptophan Hydroxylase (tph-1)

Tryptophan → Serotonin

\( \text{tph-1::GFP} \)
#1. Serotonin is made in neurons …
#1. ... and elicits fat loss in the intestine

control

tph-1 -/-

sert -/-
#1. Serotonin is a principal driver of fat loss

Srinivasan et al, 2008
Noble et al, 2013
#2. Searching for the brain-to-gut messenger

A hunt for the brain-to-gut signal
#2. A brain-to-gut messenger: the Tachykinin peptide

Palamiuc et al, 2017
#2. A brain-to-gut messenger: the Tachykinin peptide

Palamiuc et al, 2017
#2. A brain-to-gut messenger: the Tachykinin peptide
#3. Metabolism and longevity are intertwined
#3. Metabolism and longevity are intertwined

A hunt for the what drives conversion of fat-energy

5-HT

- tachykinin

Intestine

NPR-22

ATGL-1
#3. Metabolism and longevity are intertwined

Littlejohn et al, 2020

![Diagram showing the relationship between metabolism and longevity.](image-url)
#3. Metabolism and longevity are intertwined

Littlejohn et al, 2020
#1. The neurotransmitter serotonin is a principal driver of fat loss

#2. A brain-to-gut messenger: the Tachykinin peptide

#3. Gut metabolism and longevity are intertwined

#4. A twist: the gut talks back!

#5. Applying new knowledge: the Tachykinin receptor in mammals
#4. Does the gut talk back?

Chung-Chih Liu
Nicolas Seban

Fed  Re-fed  Fasted

Available tachykinin

OP50  HB101

Quiescence duration (sec) over 1 min

press

Secreted tachykinin

ns  ***  ***
#4. Looking at genes of the gut
- Early studies on metabolism and body weight
- Finding new genes, brain-gut biology
- Applying discoveries
Summary

INTEROCEPTION: SENSING THE INTERNAL METABOLIC STATE OF THE BODY

METABOLIC DISEASES, INFLAMMATION, AGING, NEURODEGENERATION
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