

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



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**Wednesday, October 13, 2021**

1:00pm PT / 4:00pm ET



**THE FRONT ROW**  
at Scripps Research

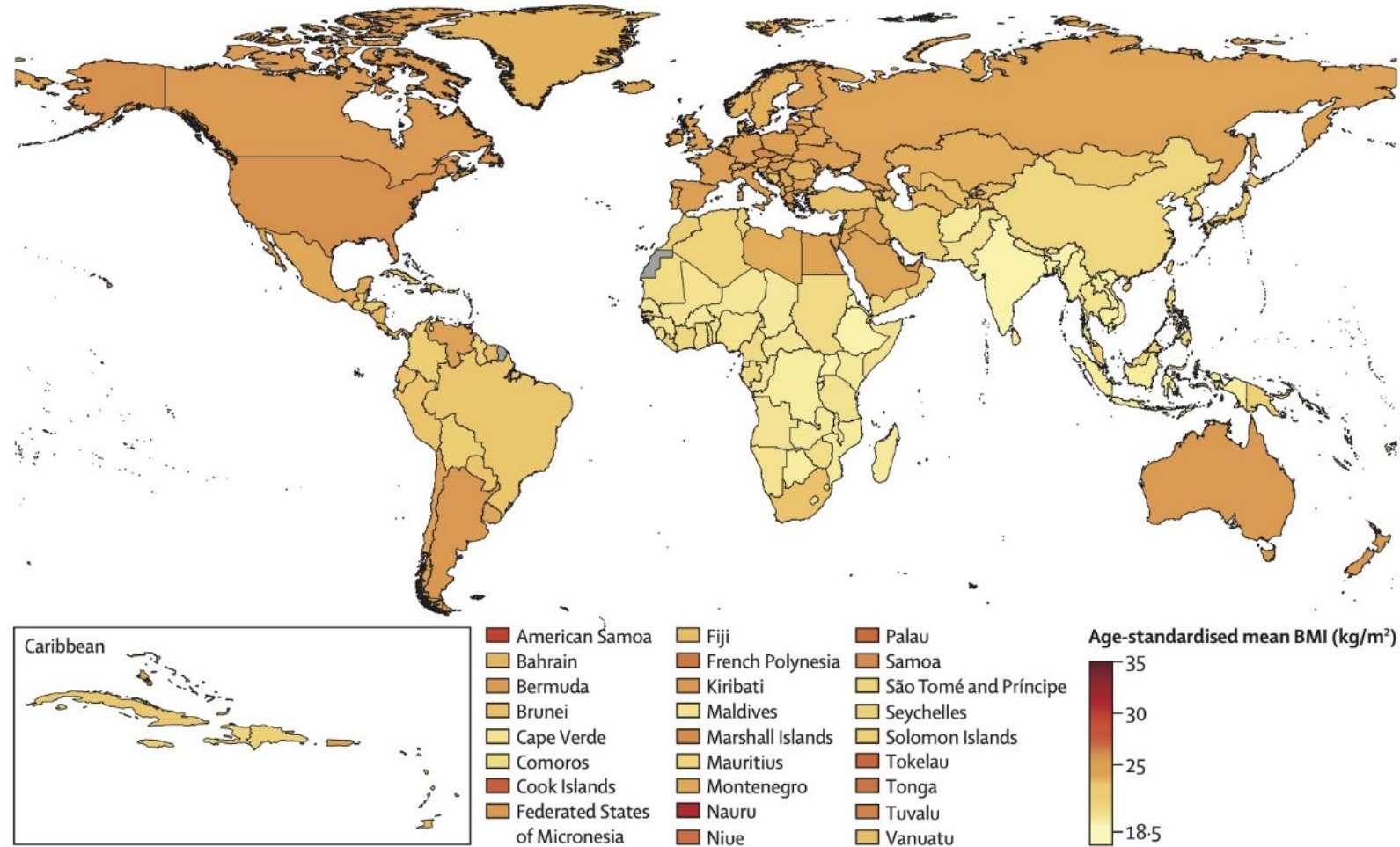
**FRONTROW.SCRIPPS.EDU**

# Genes control our metabolism



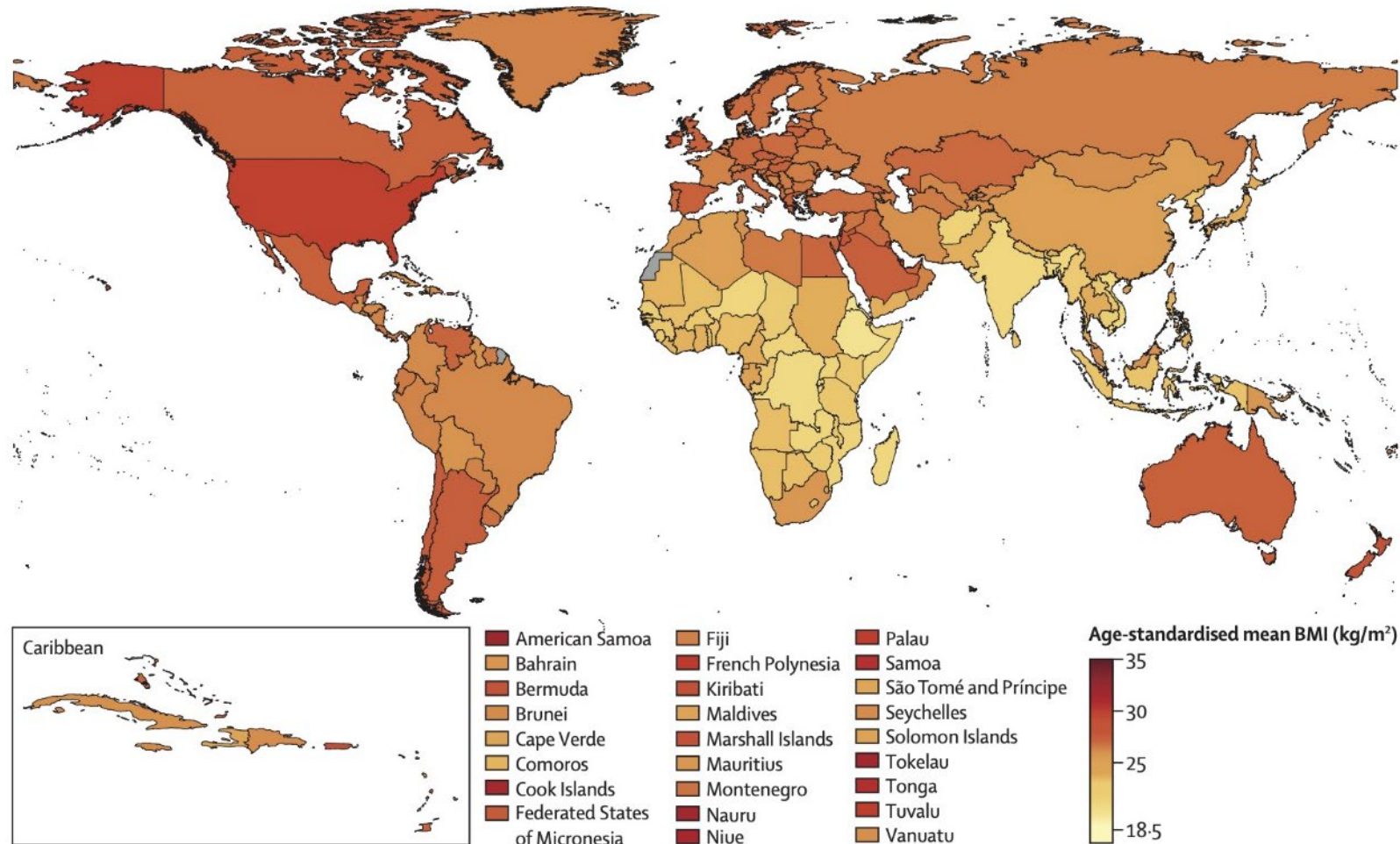
# The environment controls metabolism

1975

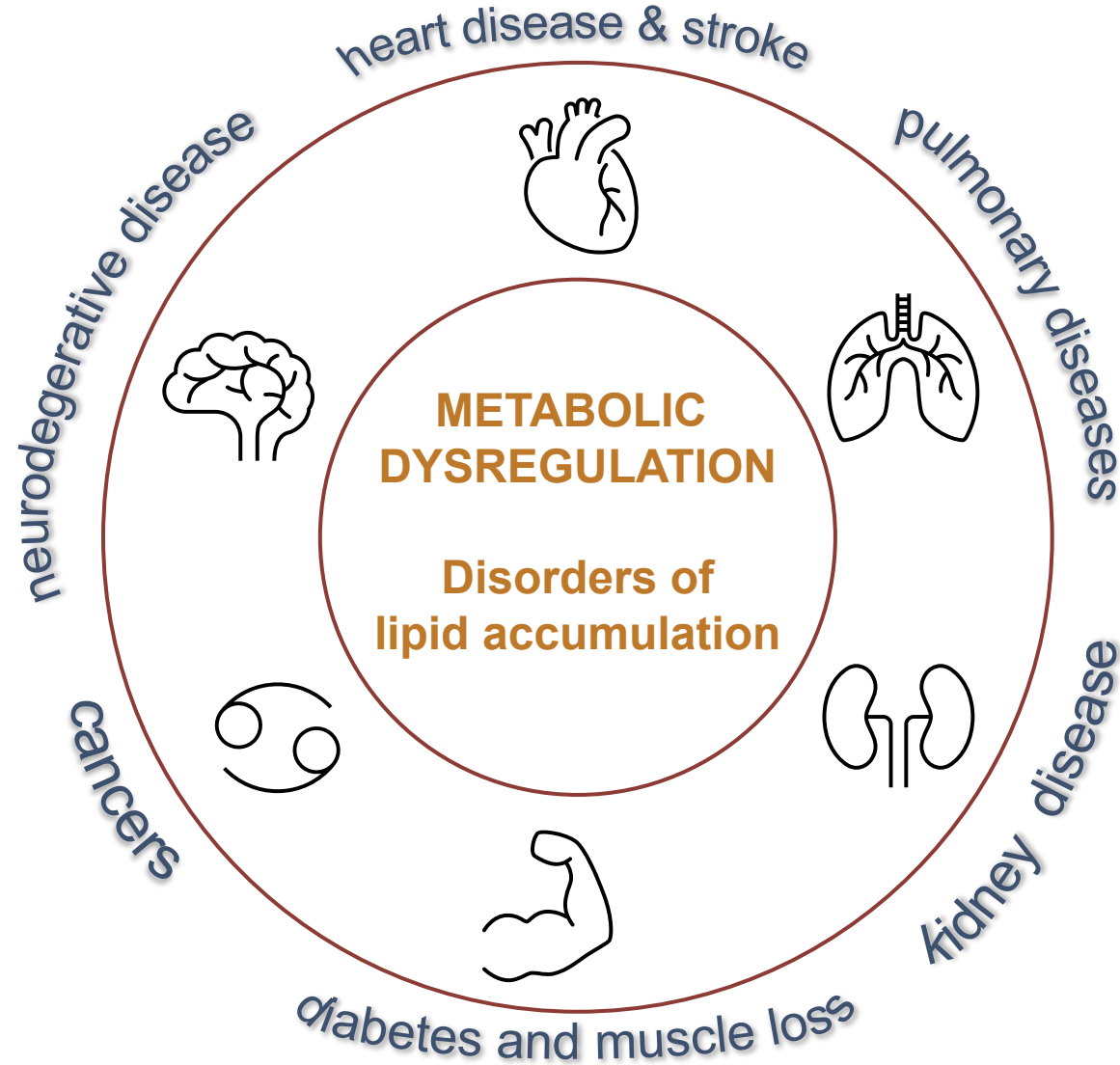


# The environment controls metabolism

2014

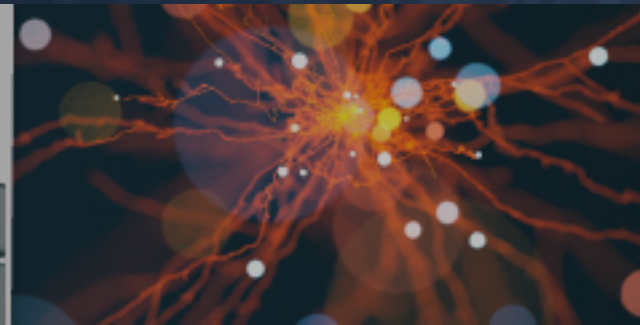


# Both genes, and the environment, control metabolism

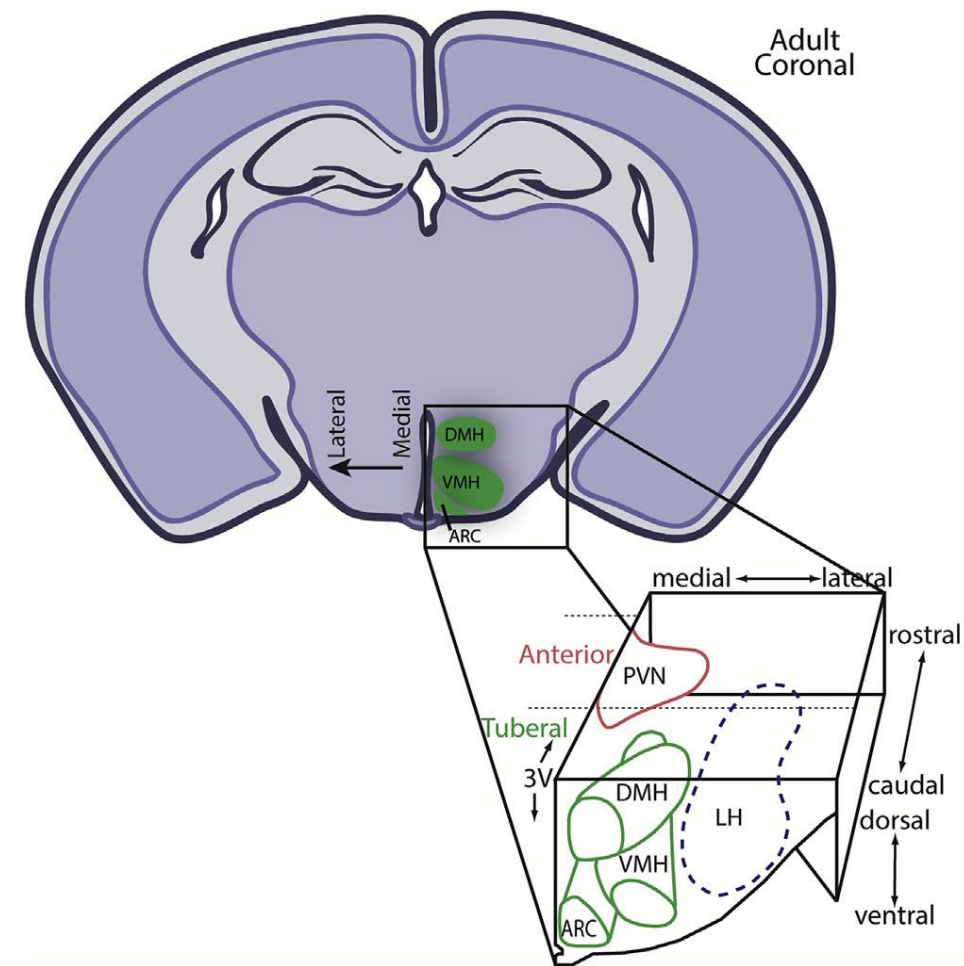
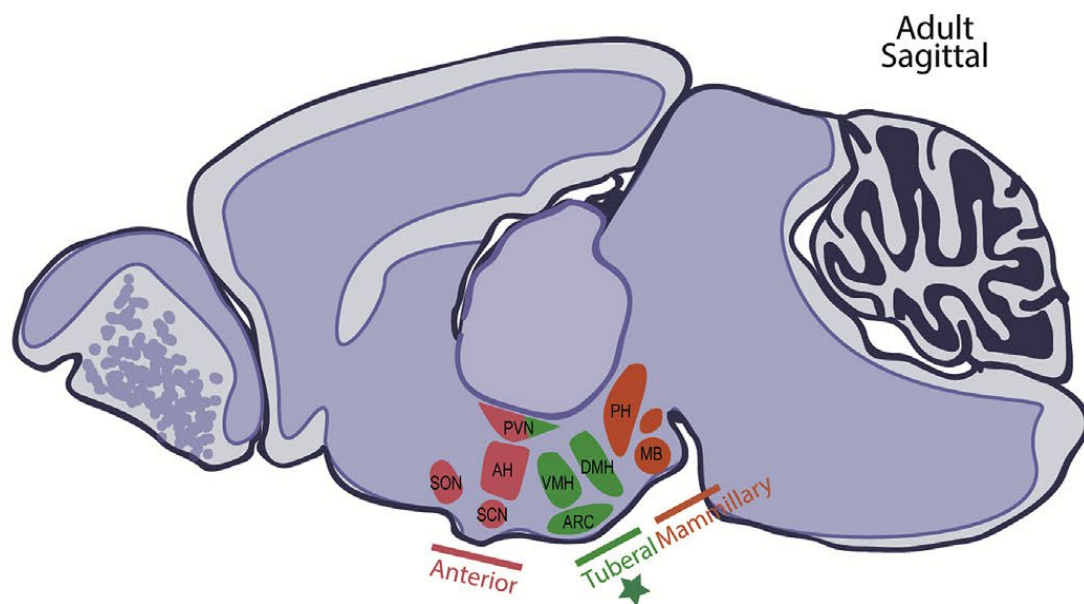




- Early studies on metabolism and body weight
- Finding new genes, brain-gut biology
- Applying discoveries



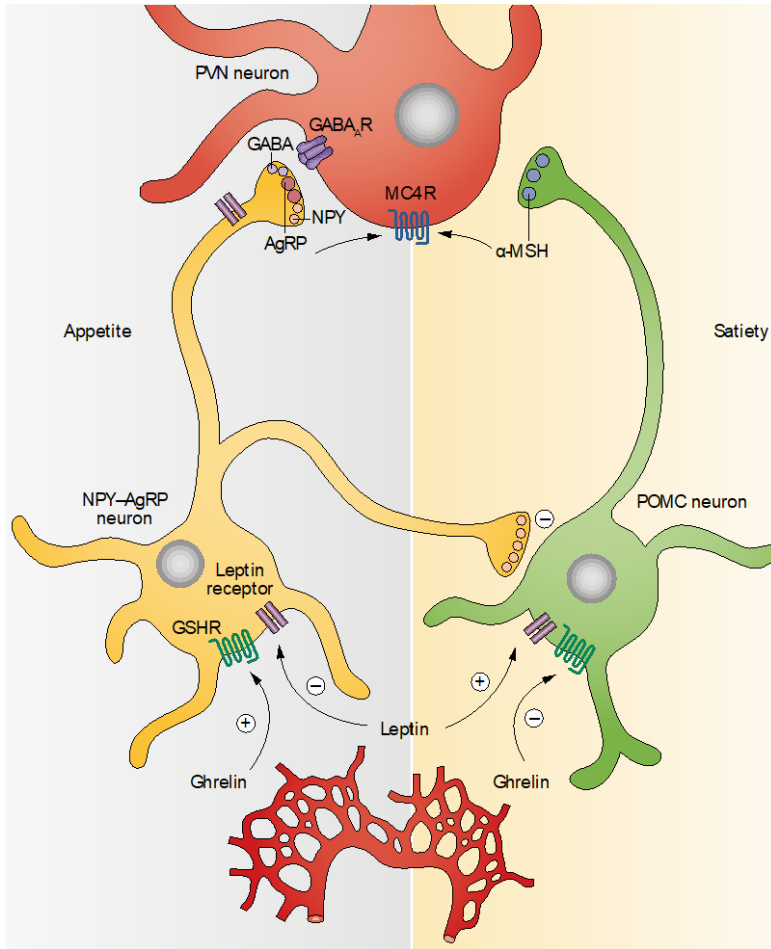
# Brain regions control metabolism: 1950s – 2000s



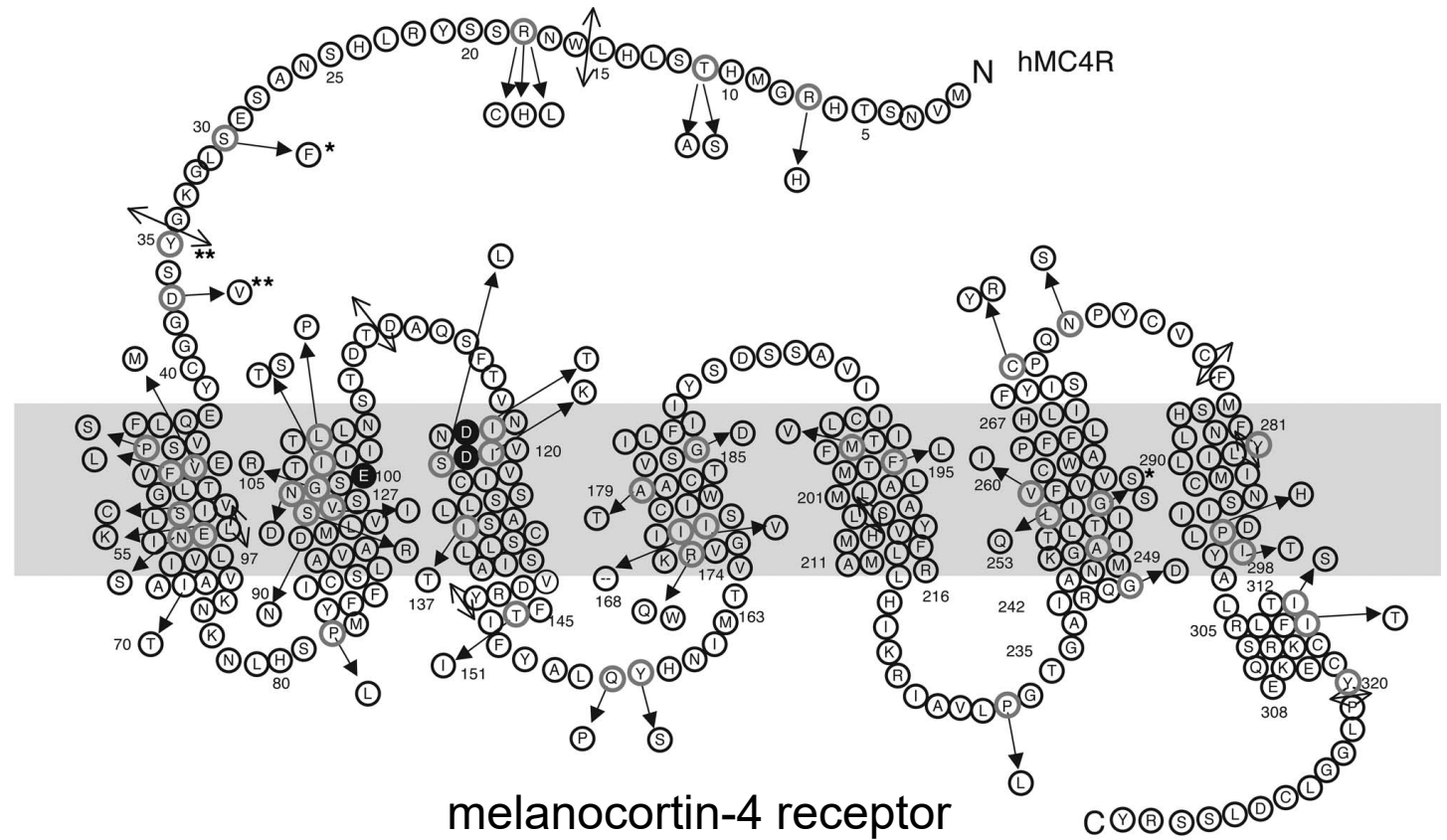
Nesan & Kurrasch, 2016



# Brain regions control metabolism: 1950s – 2000s



Nasrallah & Horvath, 2014



melanocortin-4 receptor

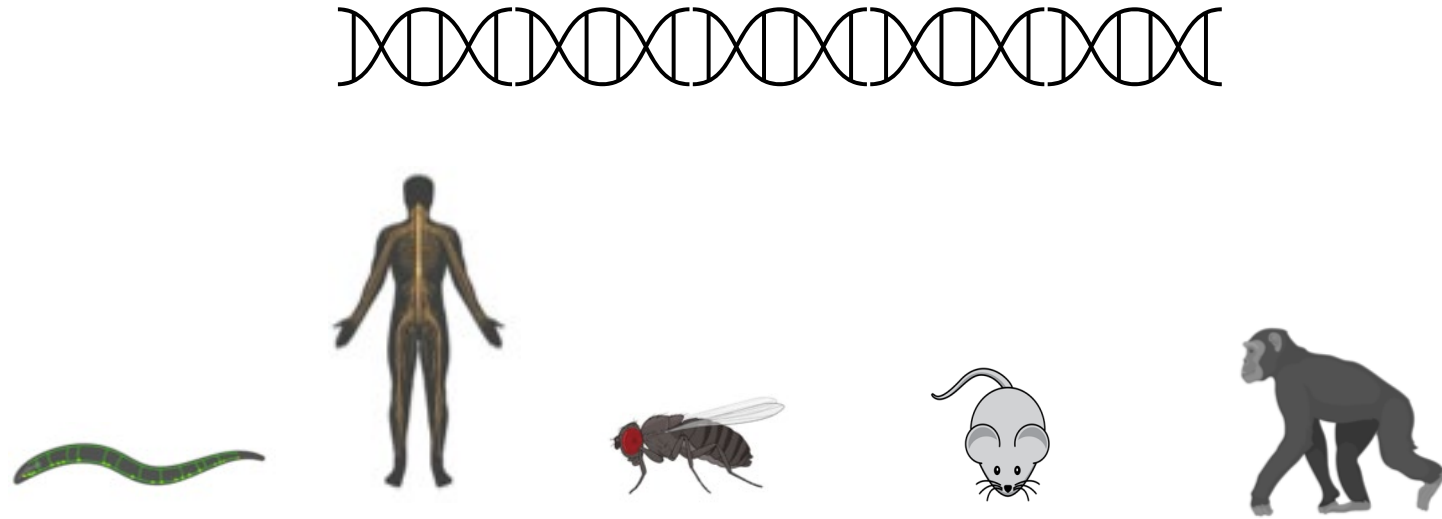
Srinivasan et al., 2004



# Genomic Revolution: ~ 1990s - date



*efttrends.com*



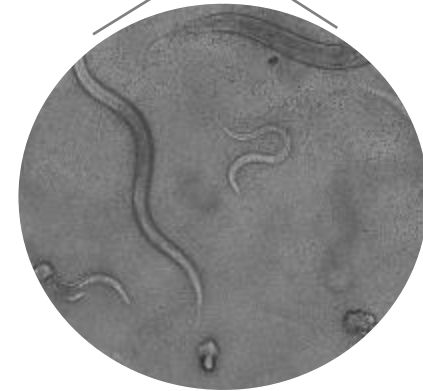
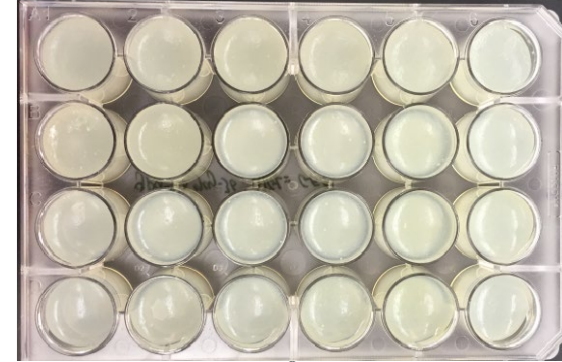
Shared genes and genetic ancestry between species!



# Uncovering the genes of fat metabolism, at scale



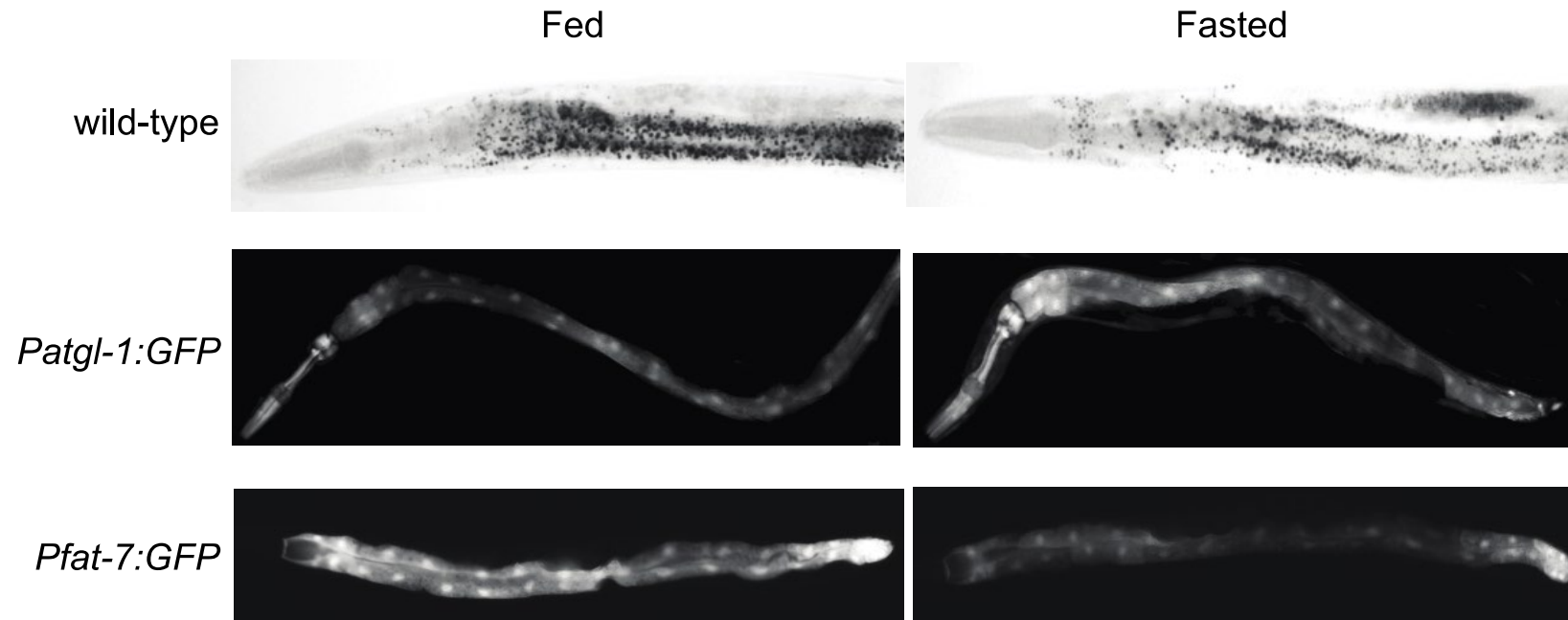
*Caenorhabditis elegans*



- ❖ Similar genomes, new genetic and molecular tools
- ❖ Speed – life cycle, lifespan, size
- ❖ Scale – genes x phenotype in living animals



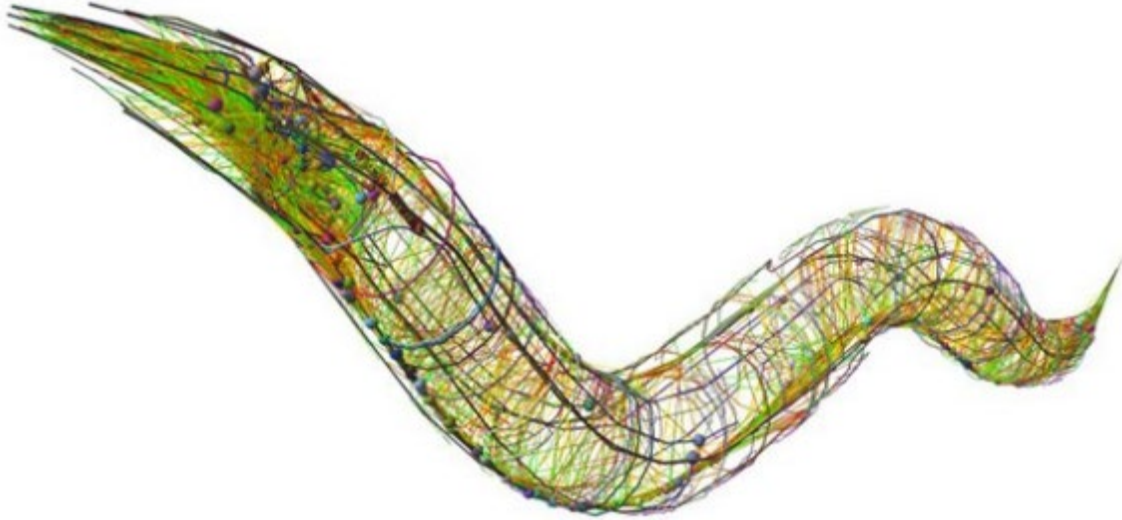
# Uncovering the genes of fat metabolism, at scale



Srinivasan, 2015



# Neurobiology of *C. elegans*



Yemini et al., 2021

- ❖ 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

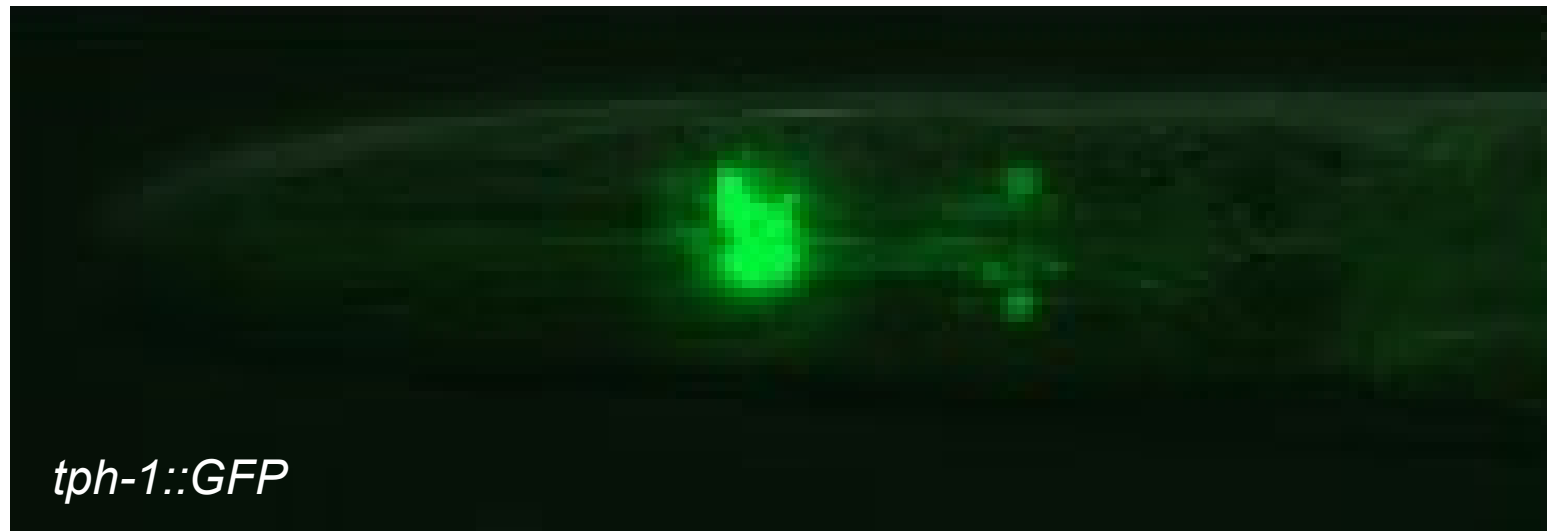
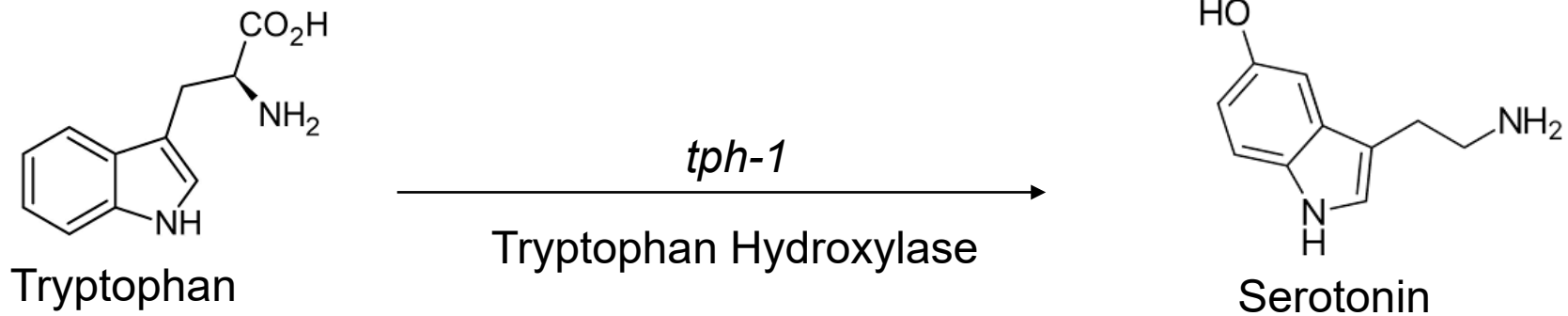




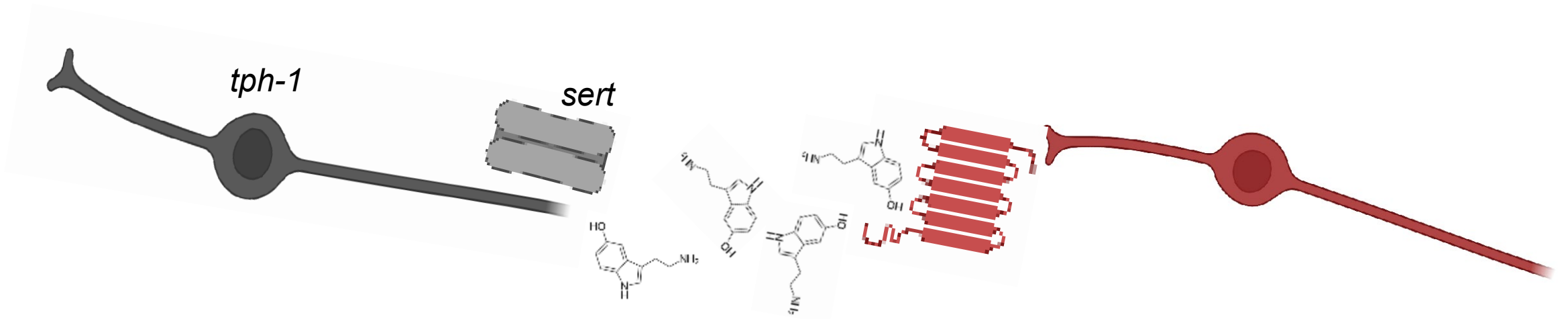
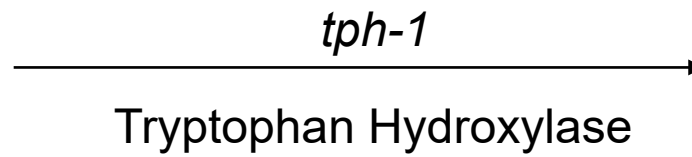
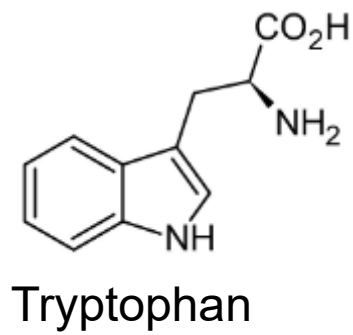
- #1. The neurotransmitter serotonin is a principal driver of fat loss
- #2. A brain-to-gut messenger: the Tachykinin peptide
- #3. Gut metabolism and longevity are intertwined
- #4. A twist: the gut talks back!
- #5. Applying new knowledge: the Tachykinin receptor in mammals



# #1. Serotonin is a principal driver of fat loss



# #1. Serotonin is made in neurons ...



# #1. ... and elicits fat loss in the intestine



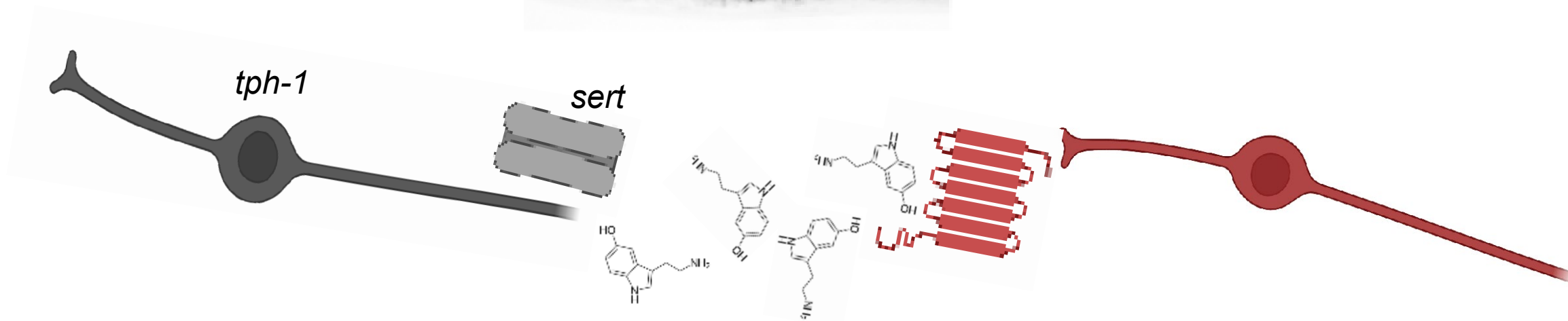
control



*tph-1* -/-

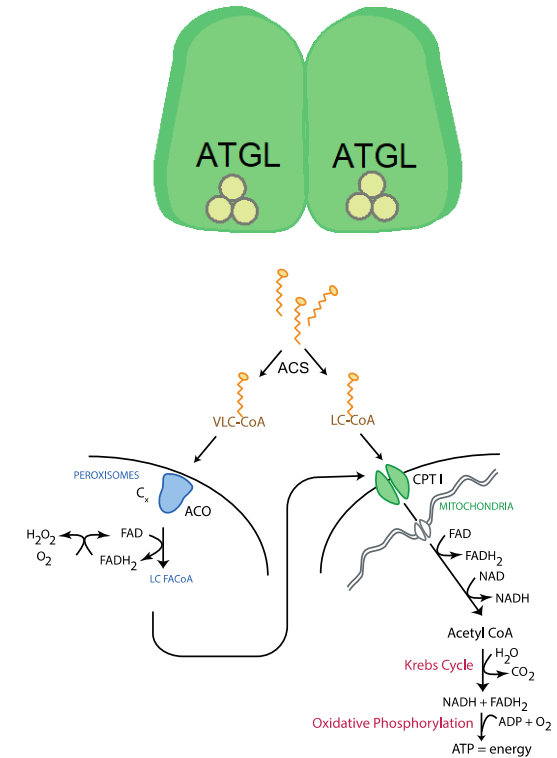
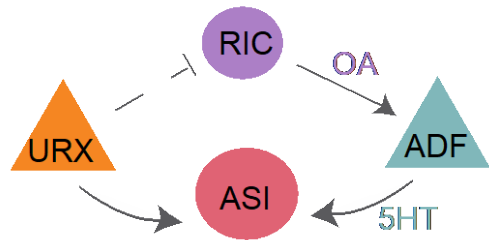


*sert* -/-





# #1. Serotonin is a principal driver of fat loss



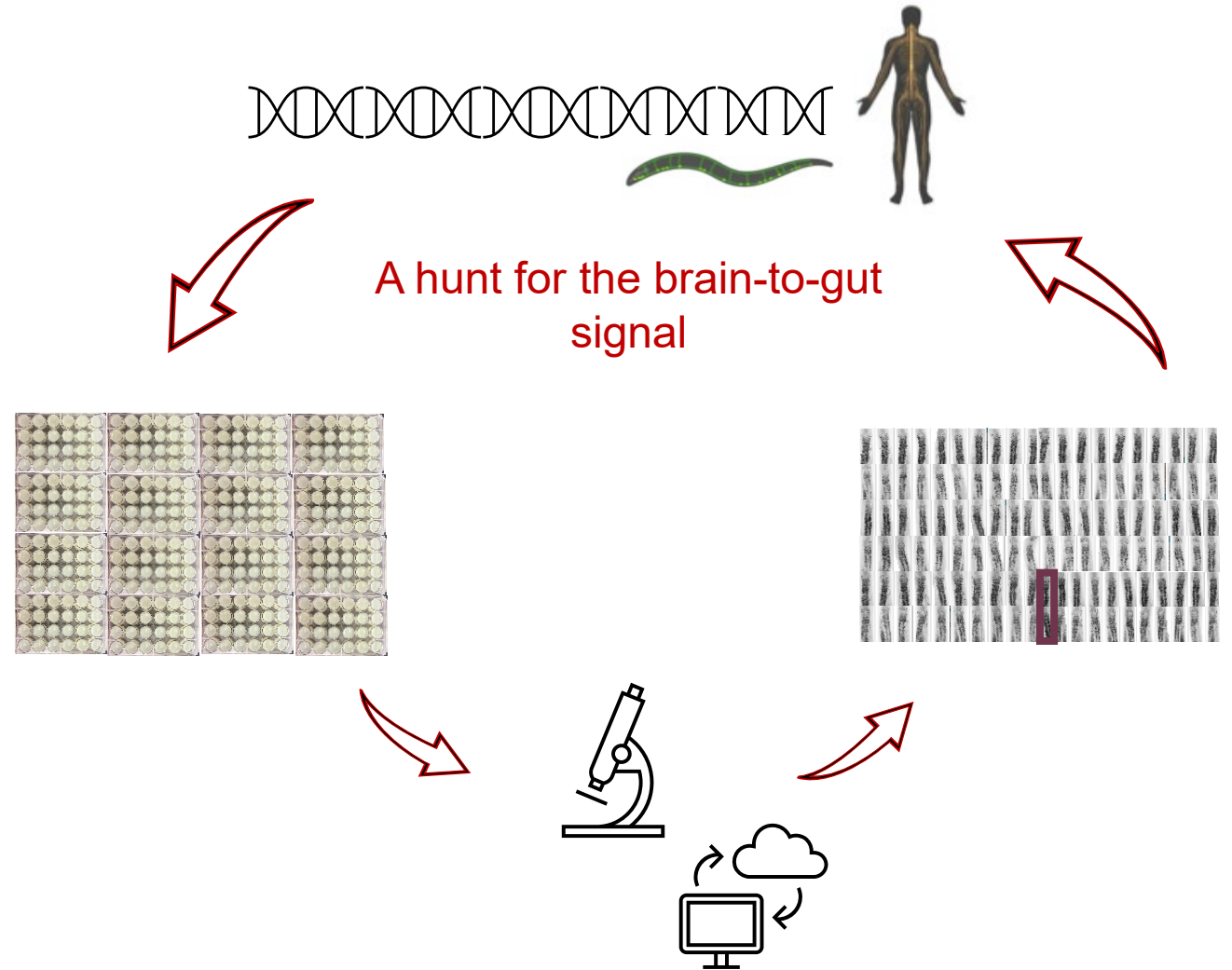
Srinivasan et al, 2008

Noble et al, 2013

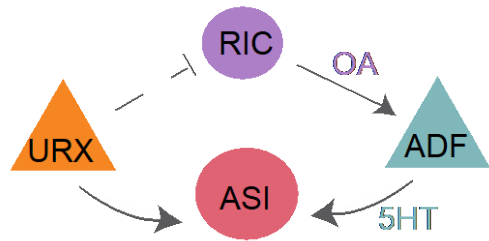
# #2. Searching for the brain-to-gut messenger



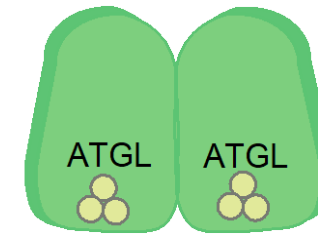
*efttrends.com*



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

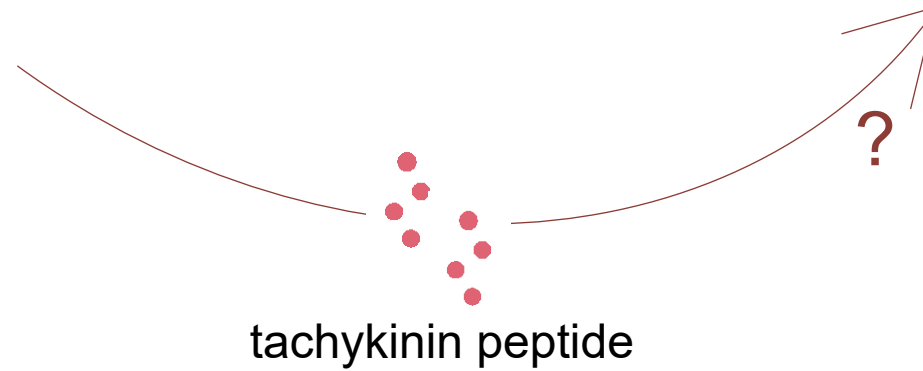
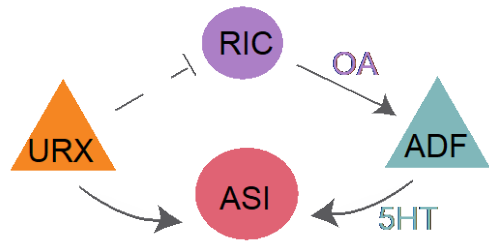


tachykinin peptide

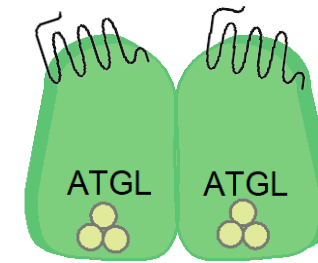


*Palamiuc et al, 2017*

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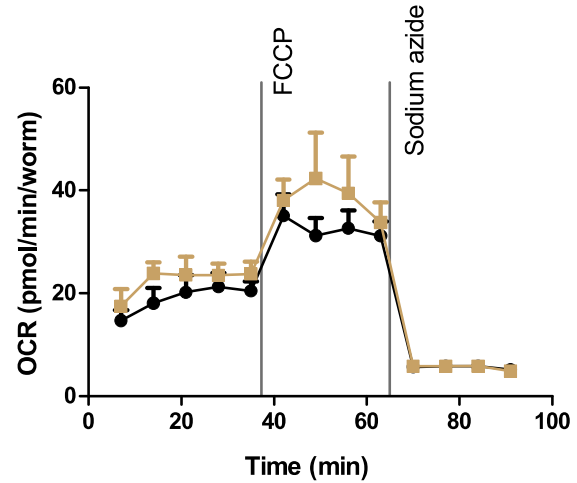
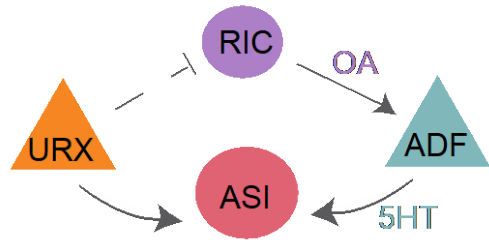


tachykinin receptor

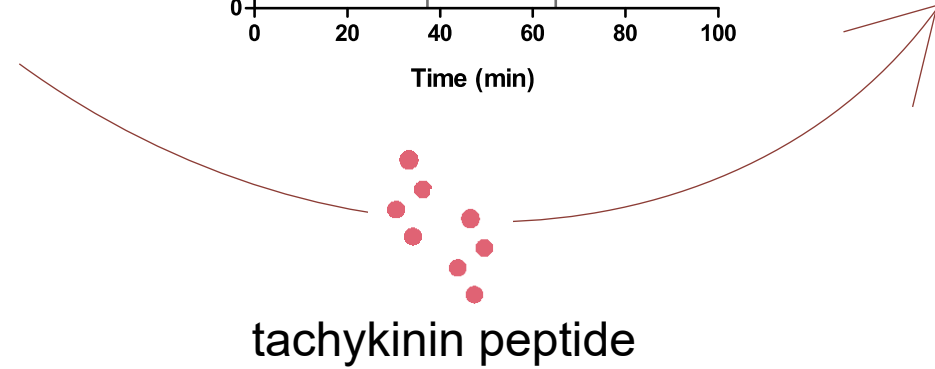
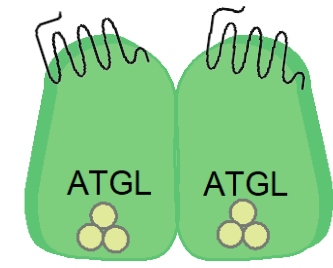


*Palamiuc et al, 2017*

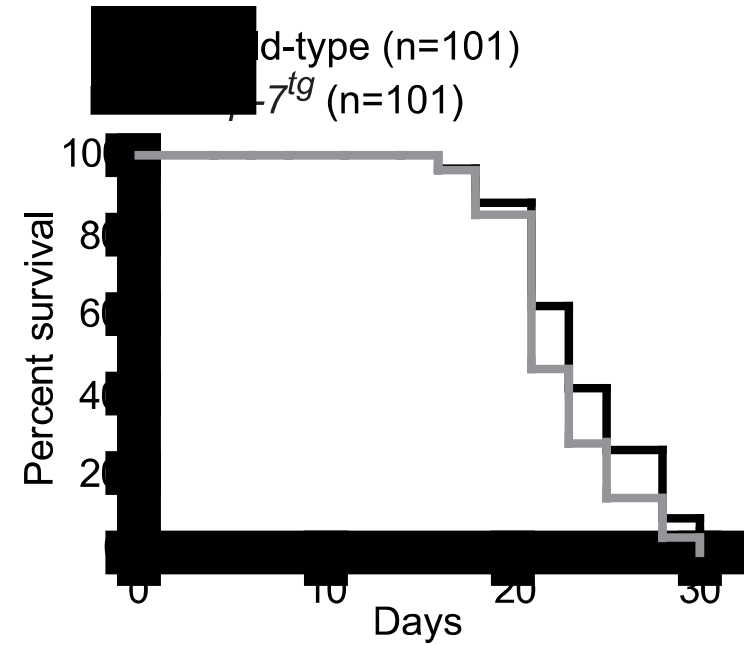
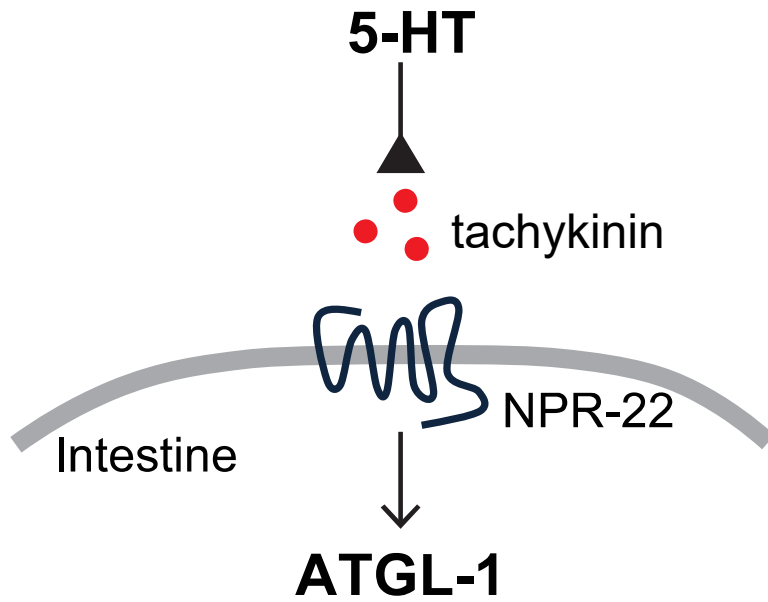
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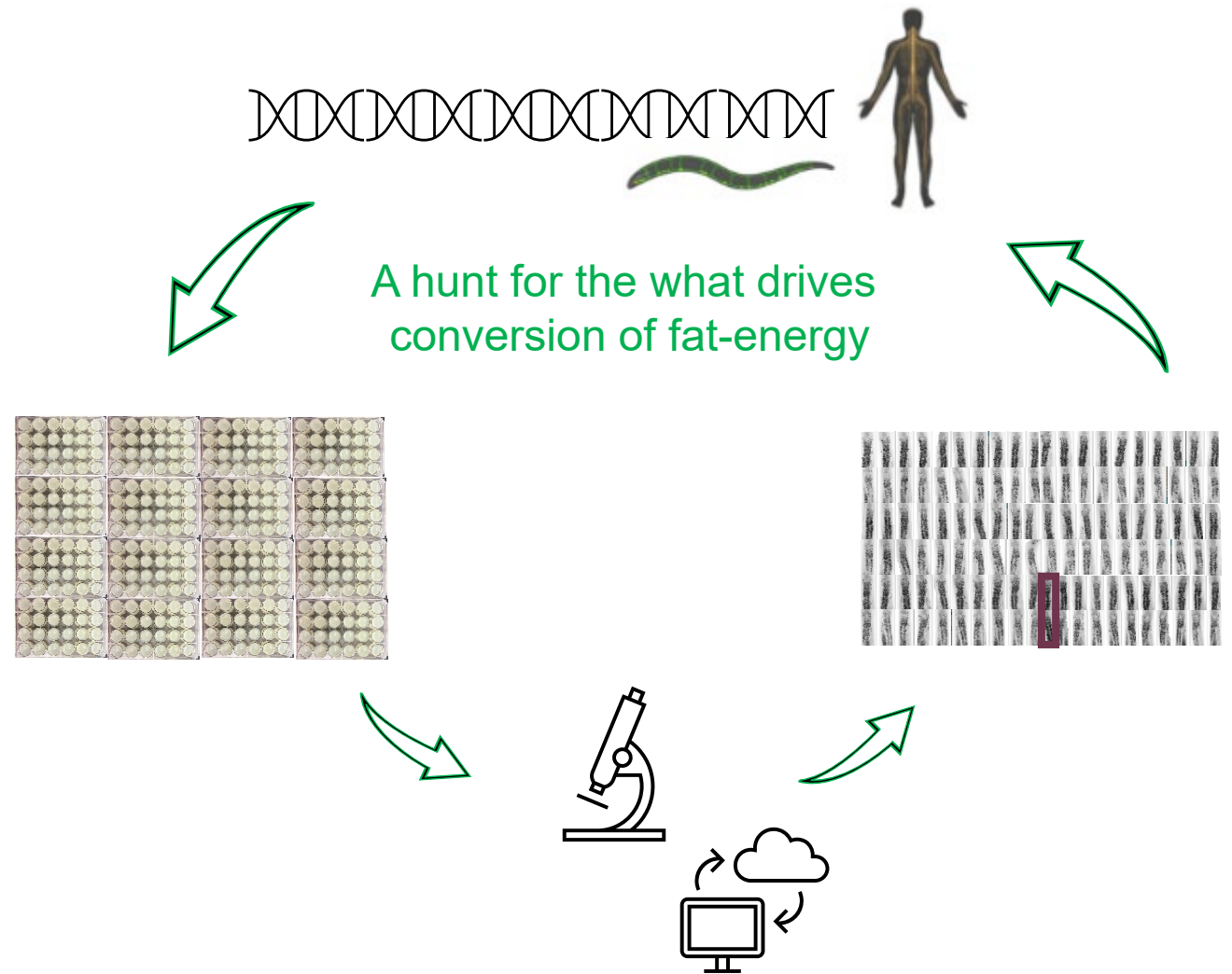
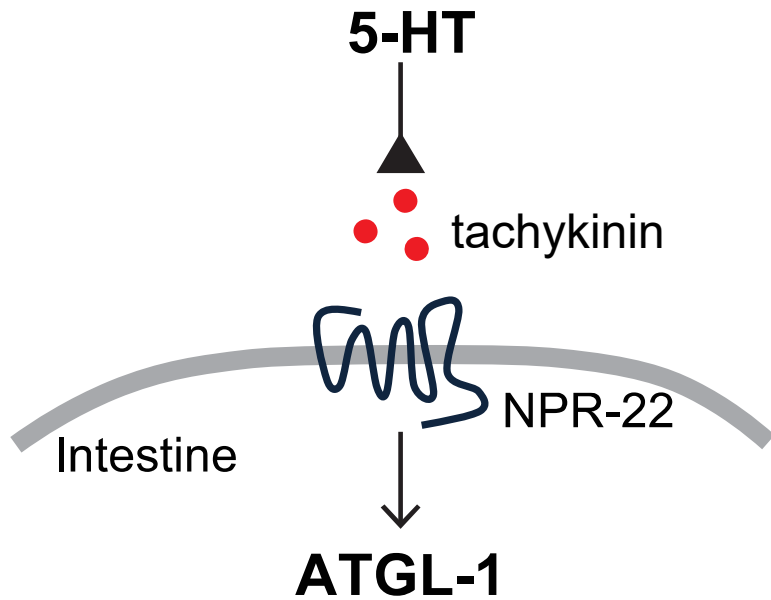
tachykinin receptor



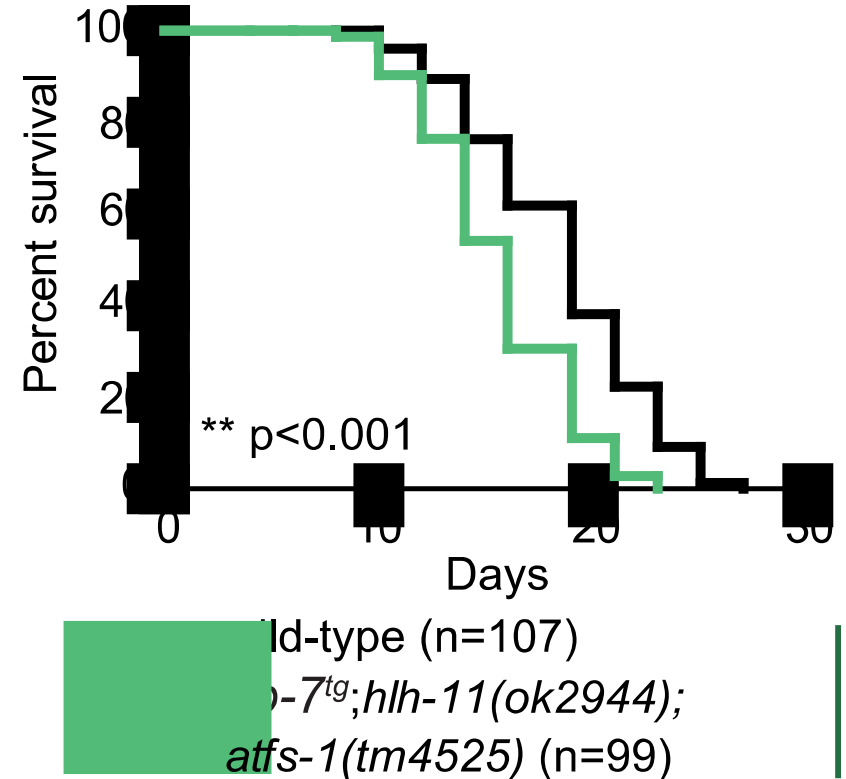
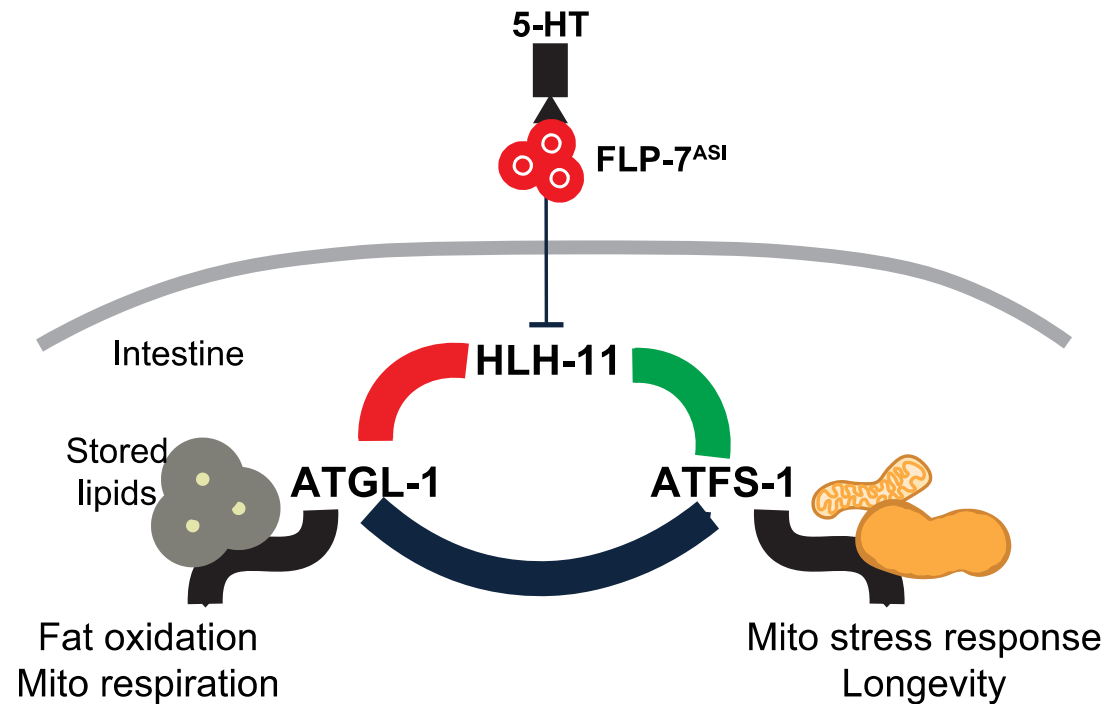
# #3. Metabolism and longevity are intertwined



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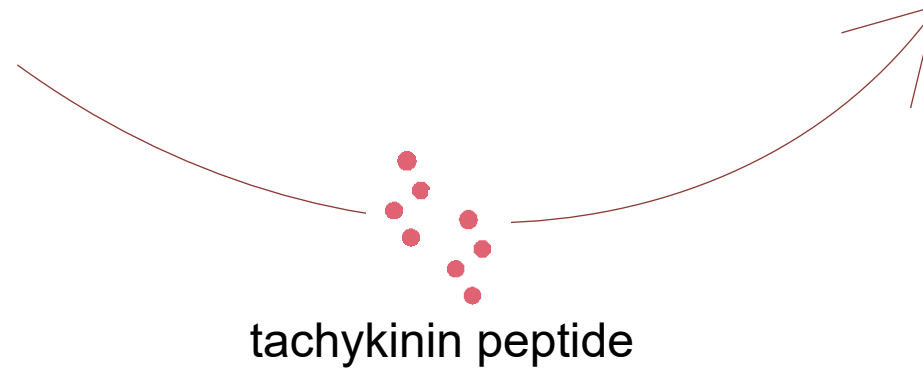
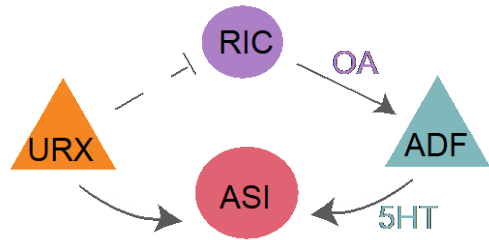
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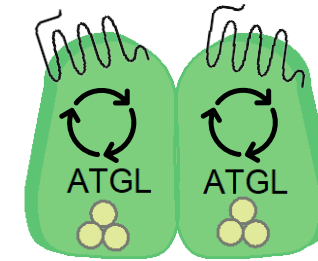
Littlejohn et al, 2020



# #3. Metabolism and longevity are intertwined



tachykinin receptor



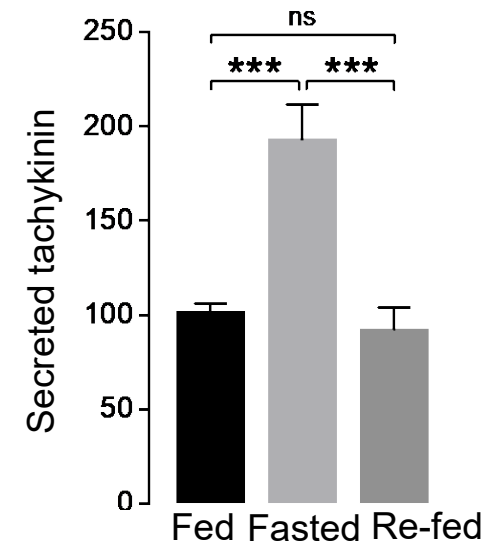
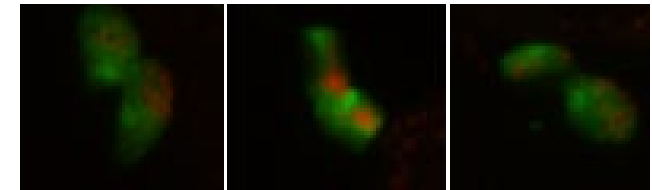
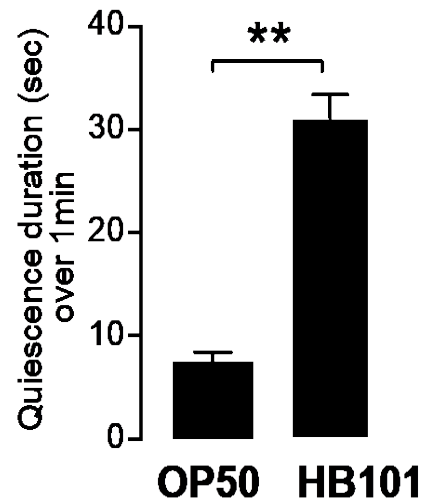
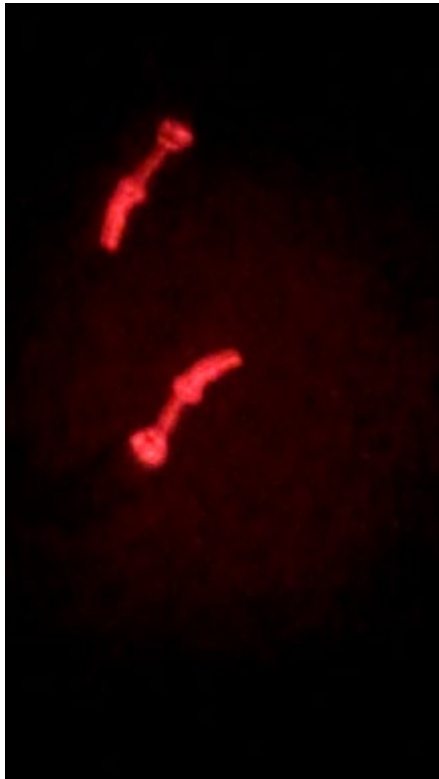
*Littlejohn et al, 2020*



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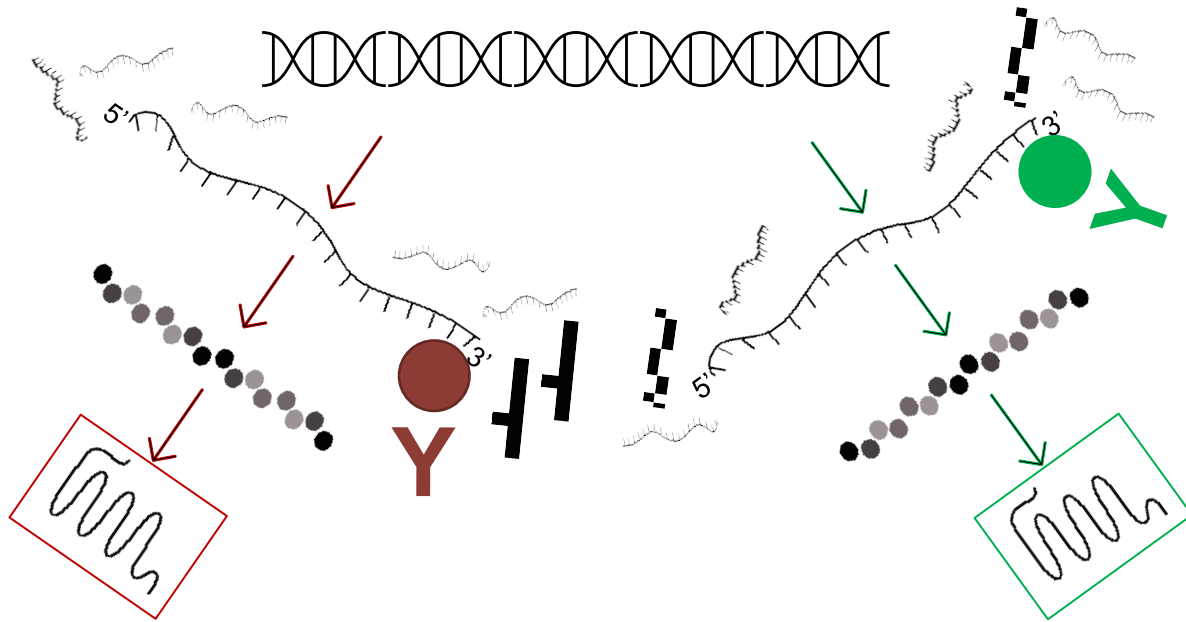
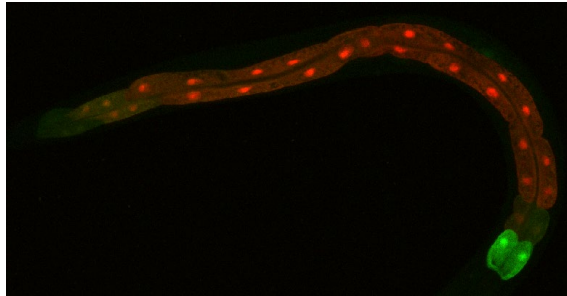


# #4. Does the gut talk back?



Chung-Chih Liu  
Nicolas Seban

# #4. Looking at genes of the gut



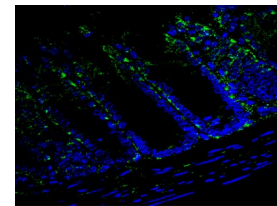
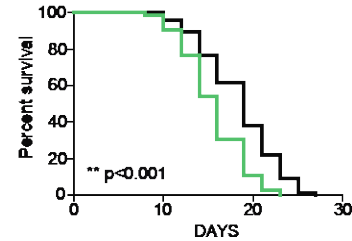
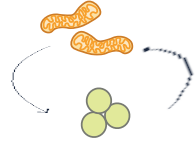
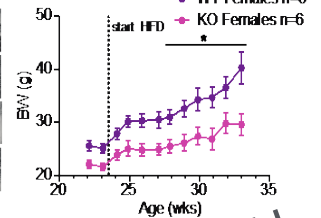
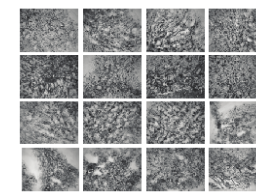
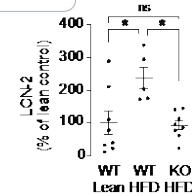
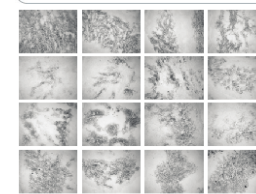
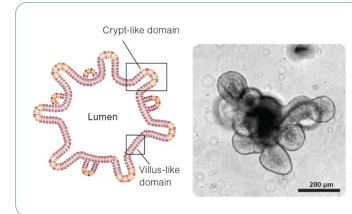
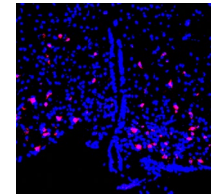
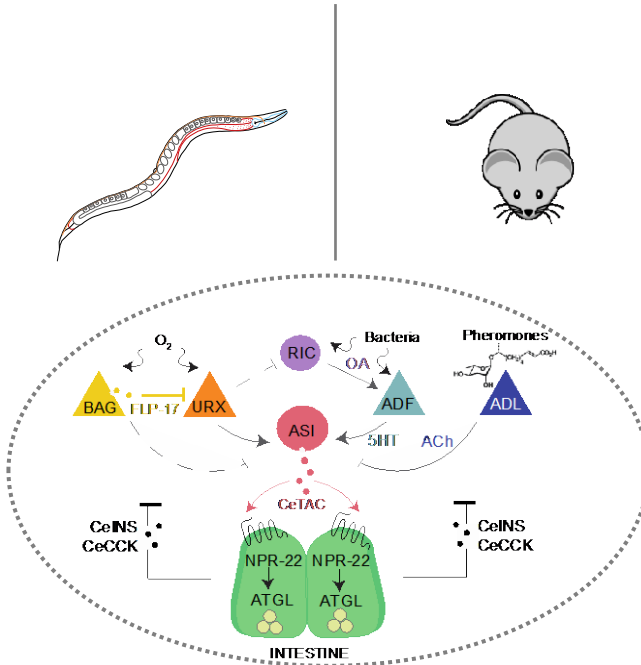
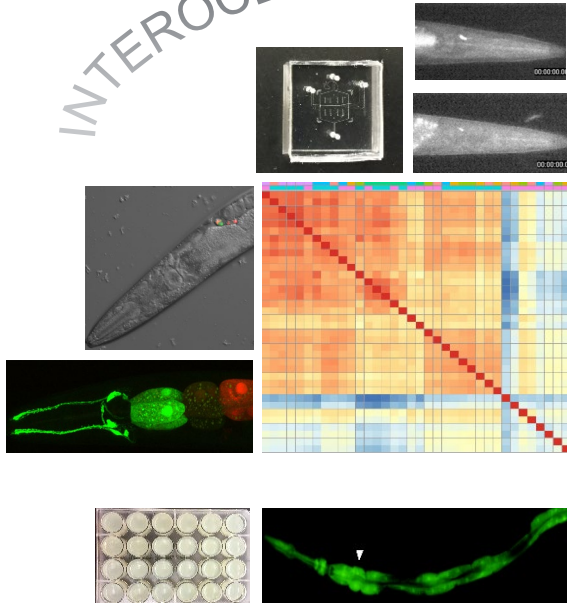


- Early studies on metabolism and body weight
- Finding new genes, brain-gut biology
- Applying discoveries



# Summary

## INTEROCEPTION: SENSING THE INTERNAL METABOLIC STATE OF THE BODY

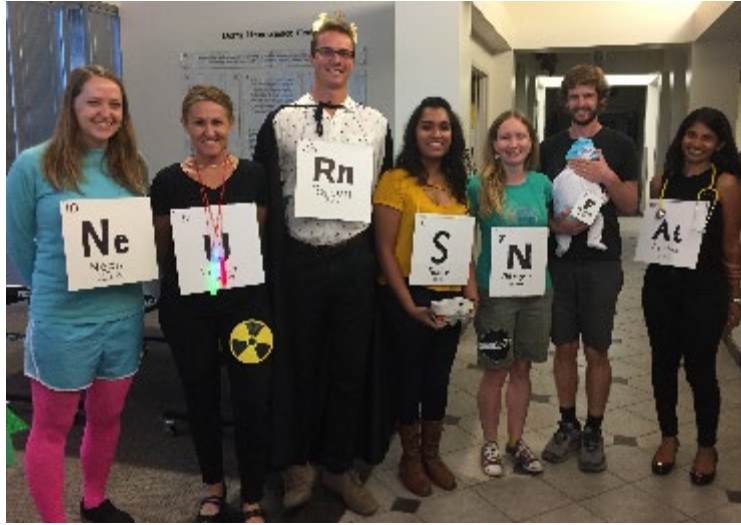


## METABOLIC DISEASES, INFLAMMATION, AGING, NEURODEGENERATION

# Acknowledgements

## Former Postdocs, Students, Associates

Claudio Comunian  
Emily Witham  
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Nicole Littlejohn  
Cheryl Park  
Shubhi Srivastava  
Tallie Noble  
Harry Ratanpal  
Erik Vanstrum  
Nicole Littlejohn  
Nicolas Seban



## Current Lab Members

Anthony Perez  
Chung-Chih Liu  
Ayub Khan  
Elizabeth Velez  
Vineeth Daniel  
Angela Glenn Hosac  
Jen Hawkins

## Scripps Research

Benjamin Cravatt  
Enrique Saez  
DNC Colleagues



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## Collaborators

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Cori Bargmann, Rockefeller  
Frank Schroeder, Cornell  
Cole Haynes, UMass Worcester  
Sreekanth Chalasani, Salk