

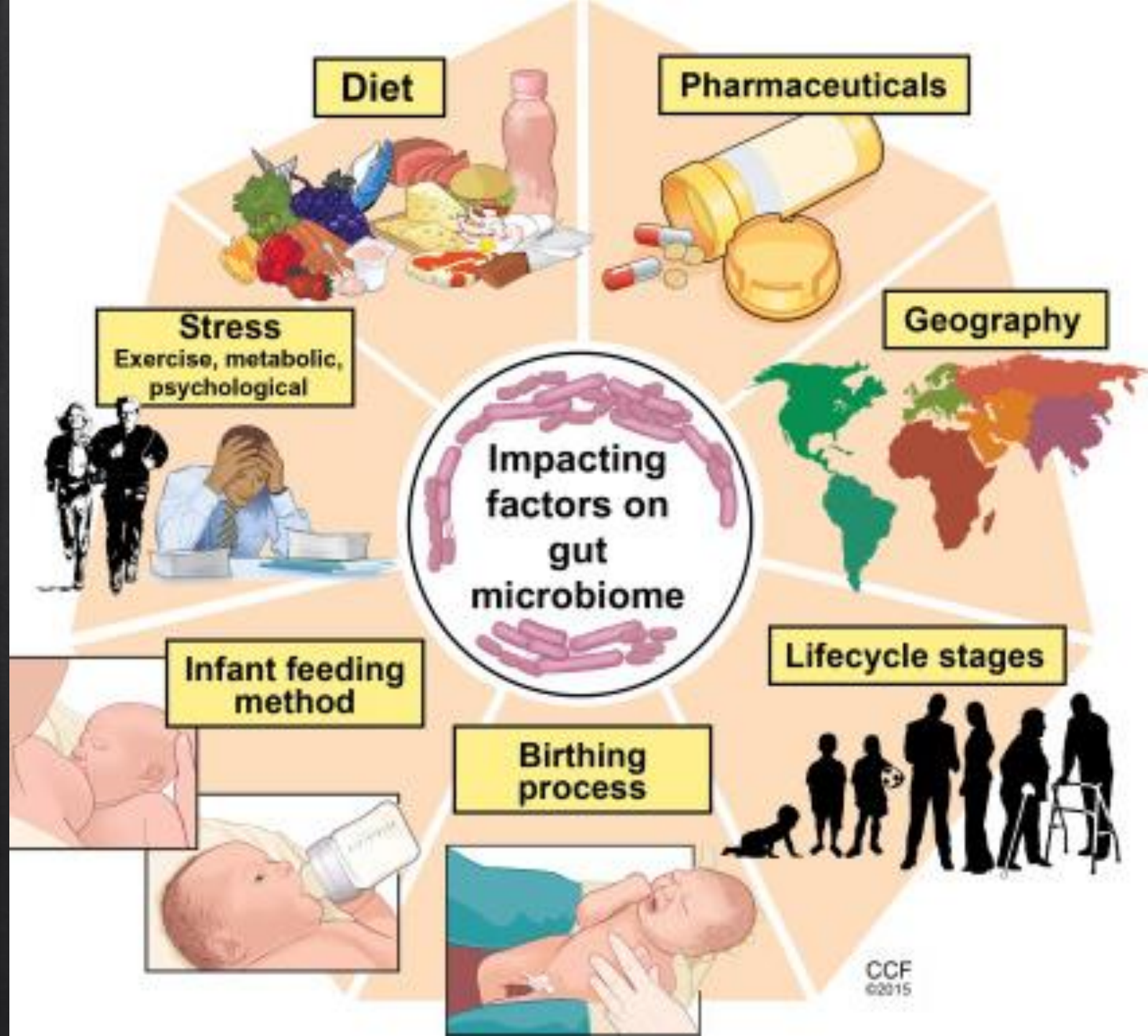
Does Diet Effect the Brain?

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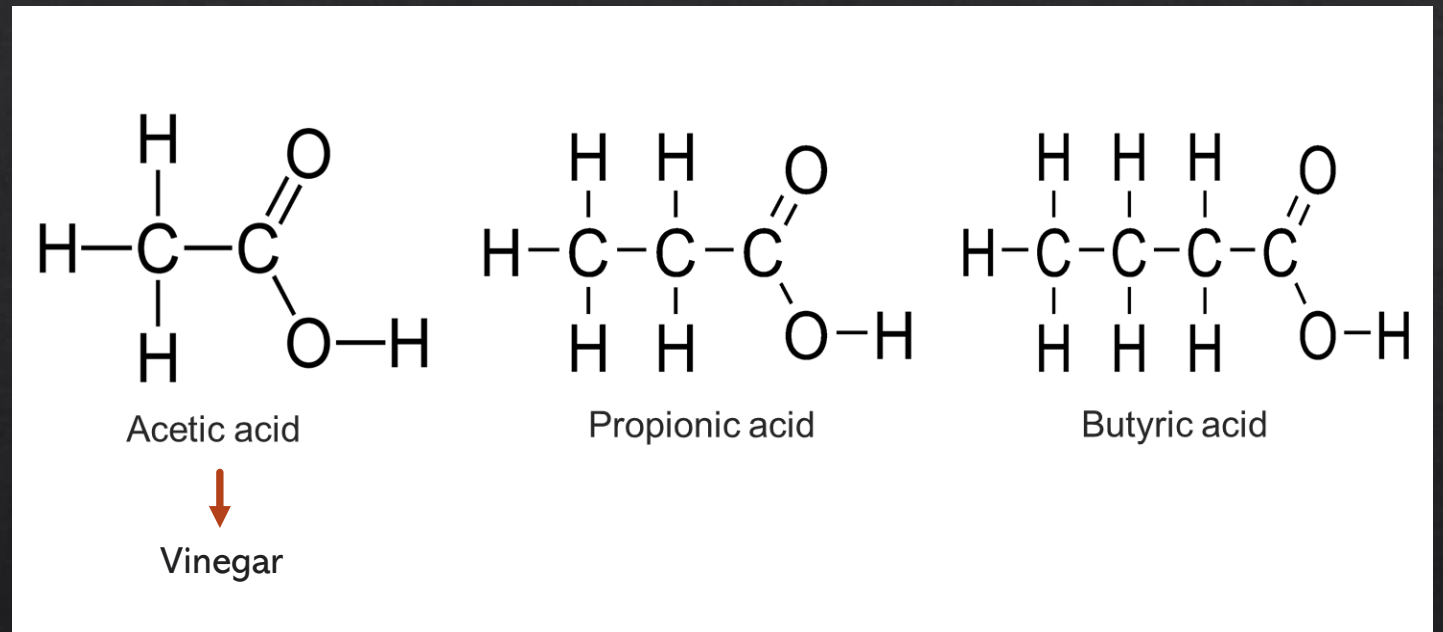
Freeman Lab

The Gut Microbiome



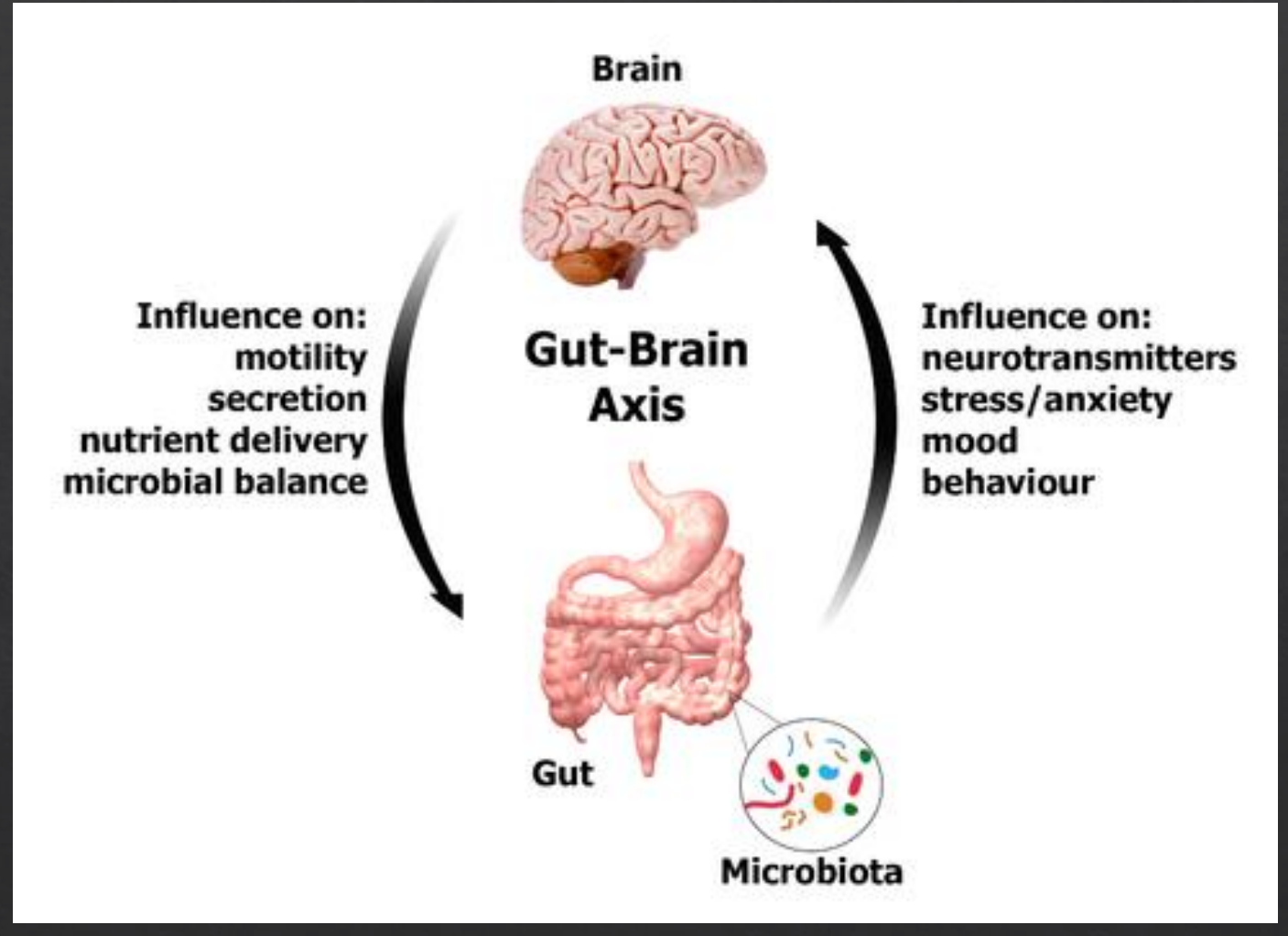
Short-Chain Fatty Acids (SCFAs) and the Gut Microbiome

- ◆ Produced via fermentation
- ◆ Amount of SCFAs are based on:
 - ◆ Dietary fiber, microbiota, gut transit time
- ◆ Preventative of Type 1/2 diabetes, liver cirrhosis, IBDs



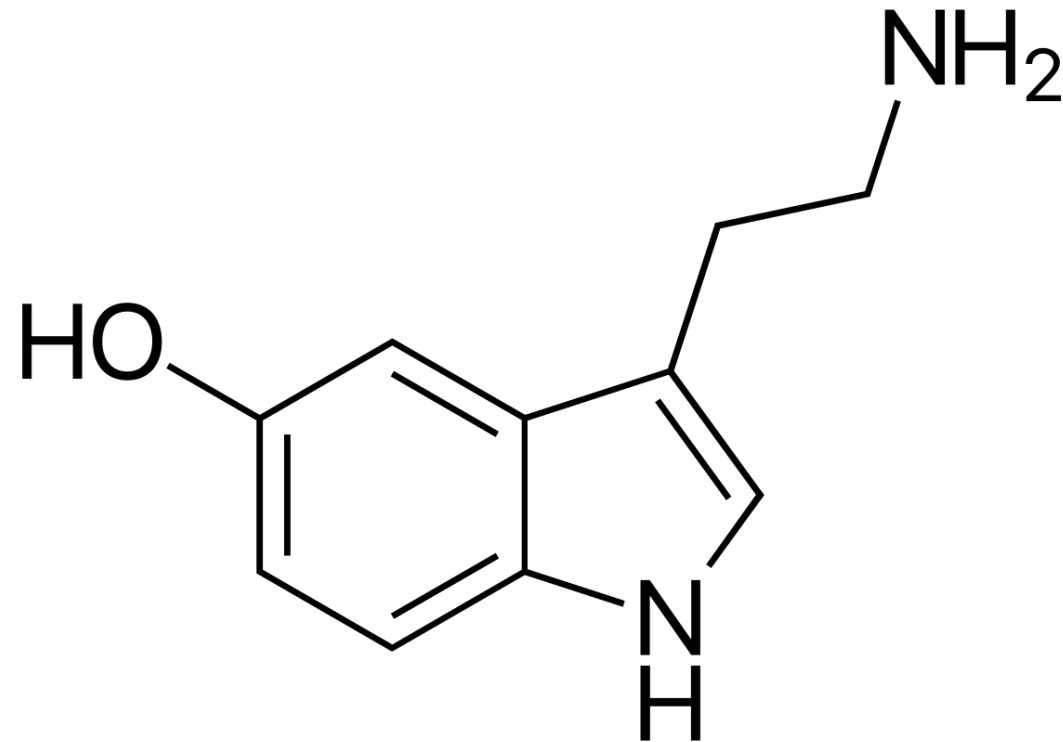
What does this have to do with the brain?

- ◆ Connected to...
- ◆ Anxiety
- ◆ Autism
- ◆ Schizophrenia
- ◆ Depression
- ◆ ADHD
- ◆ Alzheimer's
- ◆ Parkinson's
- ◆ Mood disorders



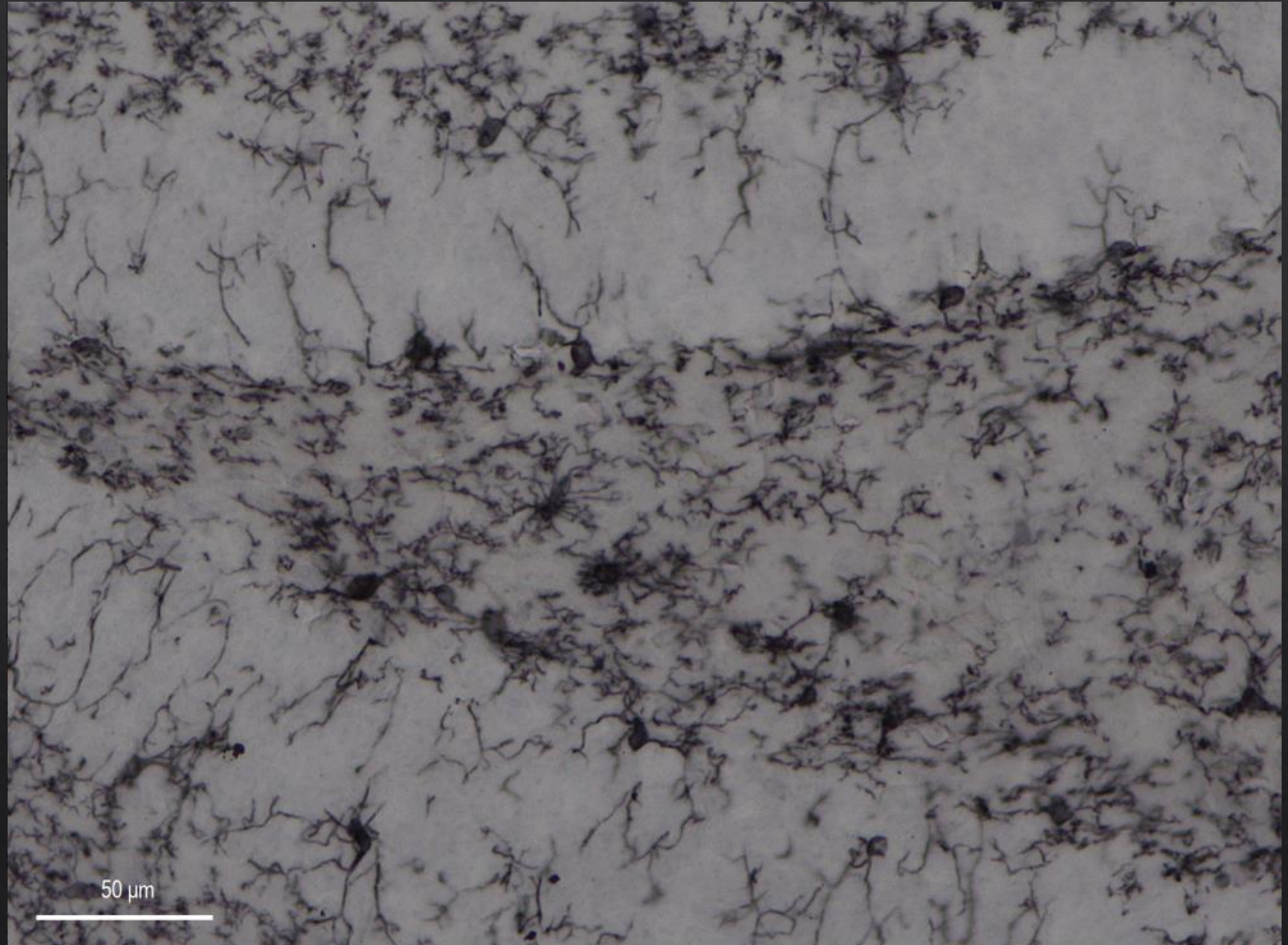
Serotonin

- ◇ Neurotransmitter important for:
 - ◇ Mood stabilization
 - ◇ Learning and memory
 - ◇ Appetite
 - ◇ Motor control
 - ◇ Sleep
- ◇ ~95% produced in the gut
 - ◇ Found in raphe nuclei in the brain



Microglia

- ◆ Immune cells of the brain
 - ◆ Help with brain development
 - ◆ Sensitive to environment
 - ◆ Dysregulation: Alzheimer's, Parkinson's, behavioral issues
- ◆ Inflammation in the gut is correlated with inflammation in the brain.



The current study

- ❖ Collaboration with Hintze and Ward Labs
- ❖ 7 groups of 12 mice were fed the diets shown here for 16 weeks
- ❖ Euthanized and brains were extracted and fixed
- ❖ Brains were sectioned at 40 um on a cryostat and mounted to slides.
- ❖ Slides were refrigerated prior to use in gene expression assays.

Diet	Fat Content	Ingredients	Description
CHOW	5%	whole food	50g /1000 kcal fiber (Negative Control)
LFC	5%	semi purified	Cellulose only (Negative Control)

Diet	Fat Content	Ingredients	Description
DIO	45%	semi purified	58g/kg cellulose only (Positive Control)
HFI	45%	semi purified	14g/1000 kcal fiber (80:20 insoluble: soluble)
HFS	45%	semi purified	14g/1000 kcal fiber (20:80 insoluble: soluble)
LFI	45%	semi purified	8.4g/1000 kcal fiber (80:20 insoluble: soluble)
LFS	45%	semi purified	8.4g/1000 kcal fiber (20:80 insoluble: soluble)

Gene Targets

SCFAs → FFAR3

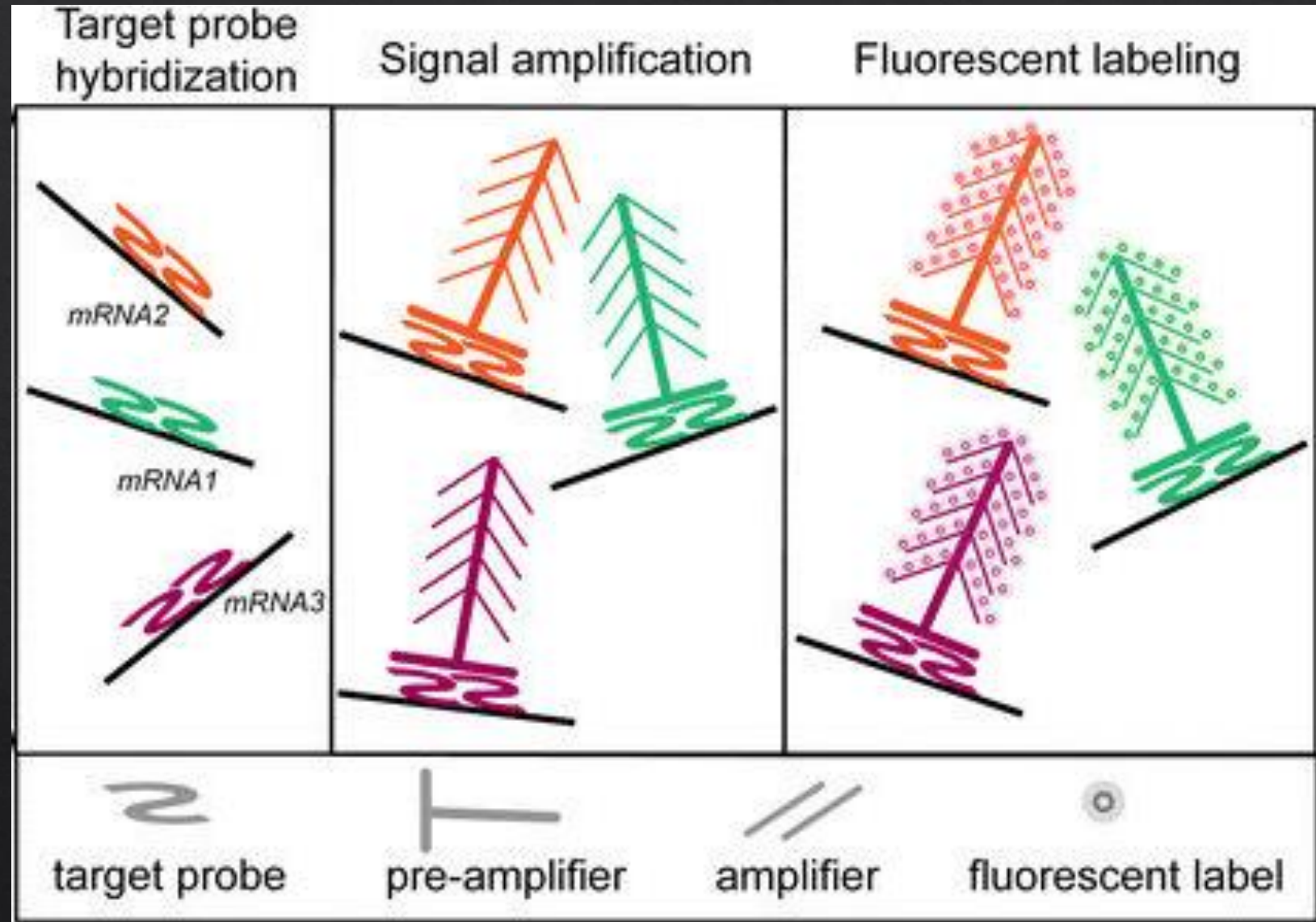
Serotonin → TPH-2

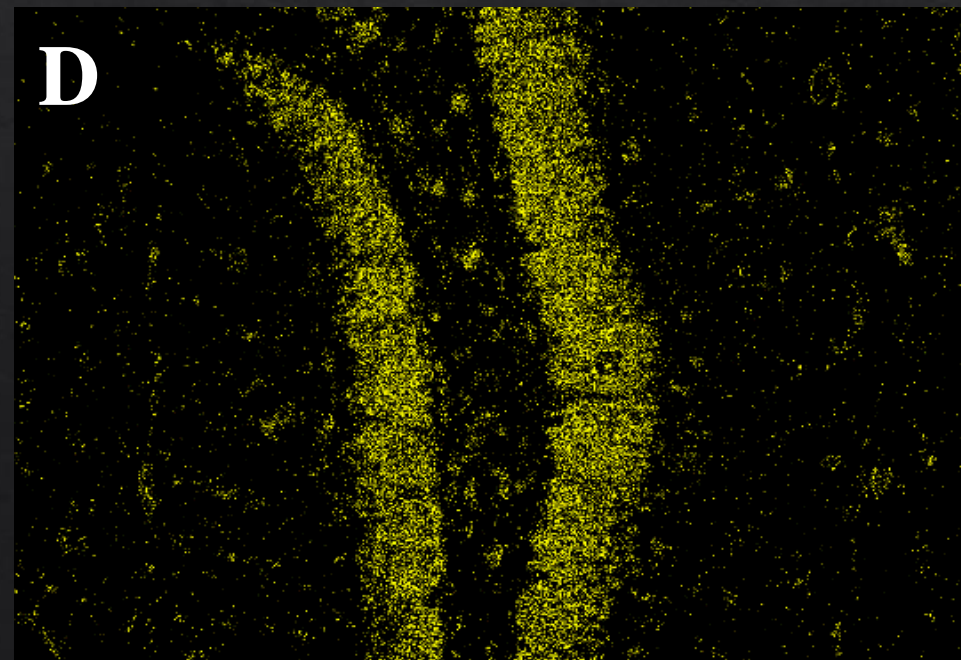
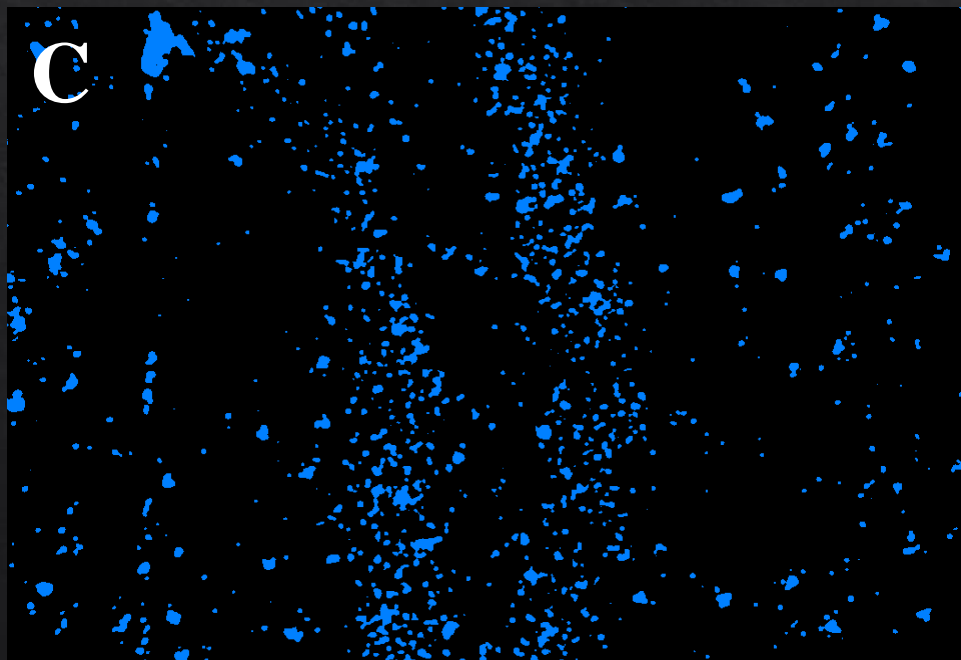
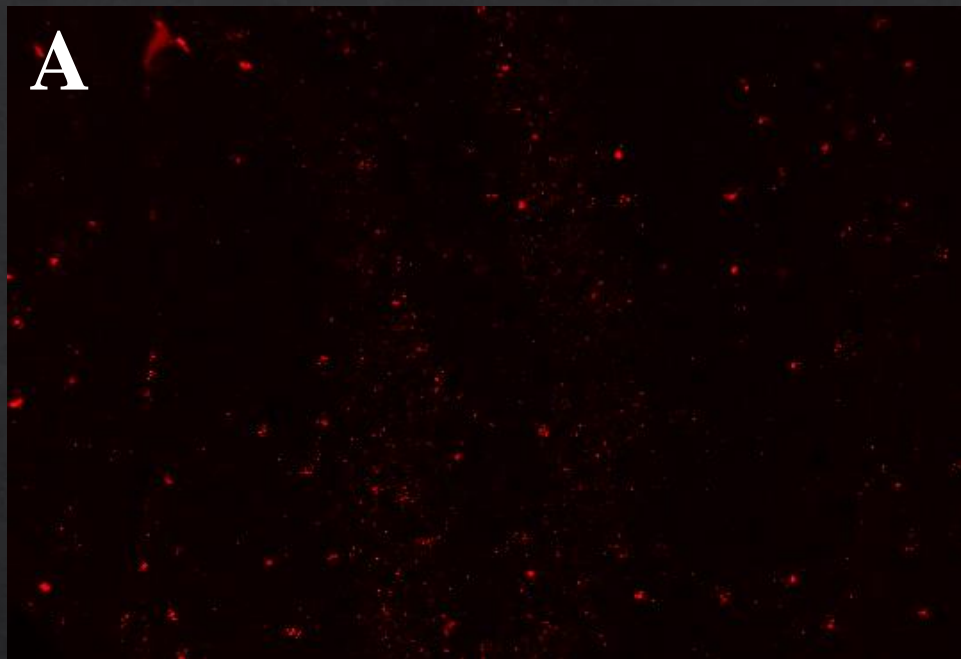
Microglia → AIF-1

Methods:

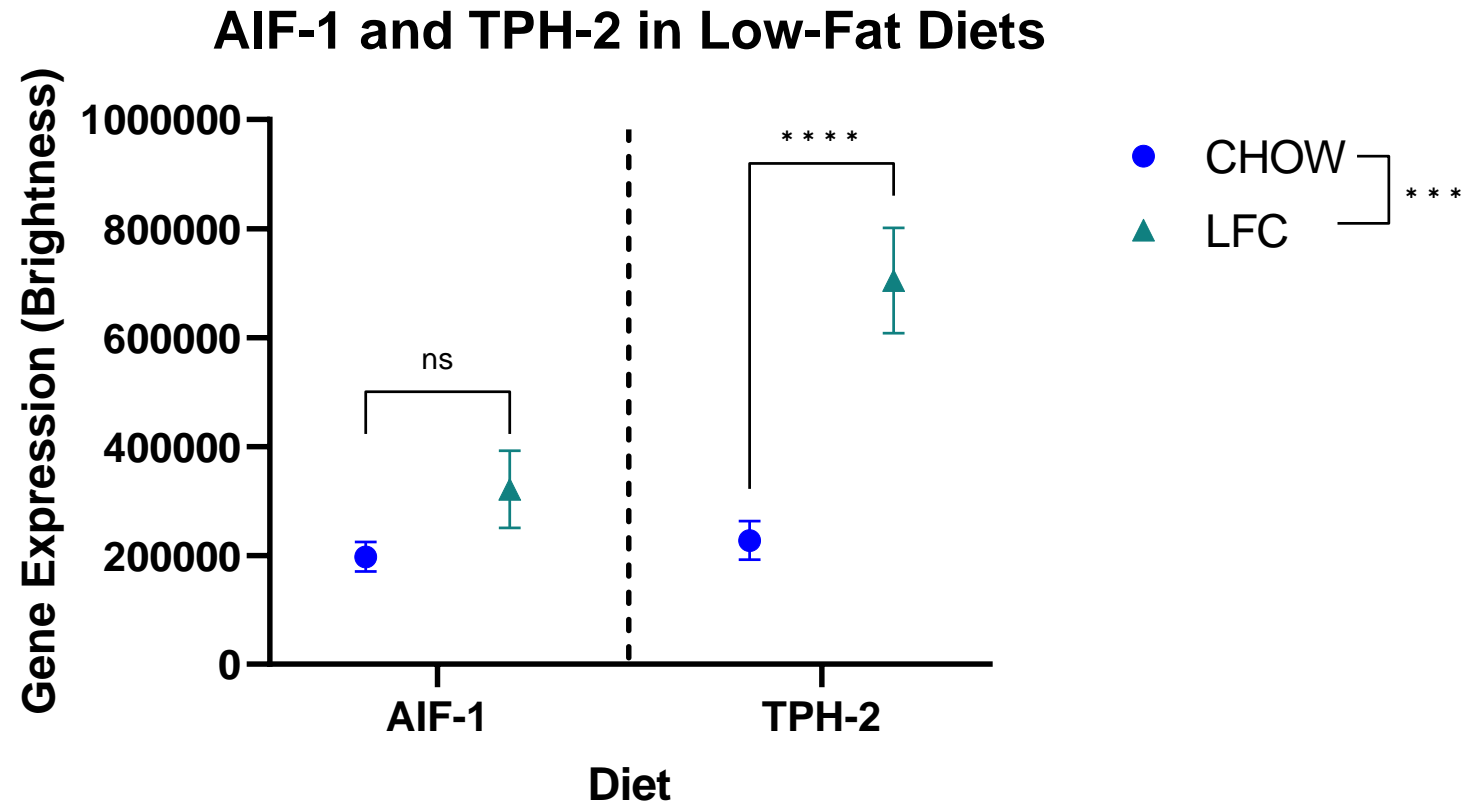
Fluorescent *in situ* Hybridization

- Visualizes mRNA for genes of interest in tissue sections
- Used to measure gene expression
- Can visualize multiple targets in the same tissue
- TPH-2 (red) + FFAR3 (green)
- AIF-1 (red) + FFAR3 (green)

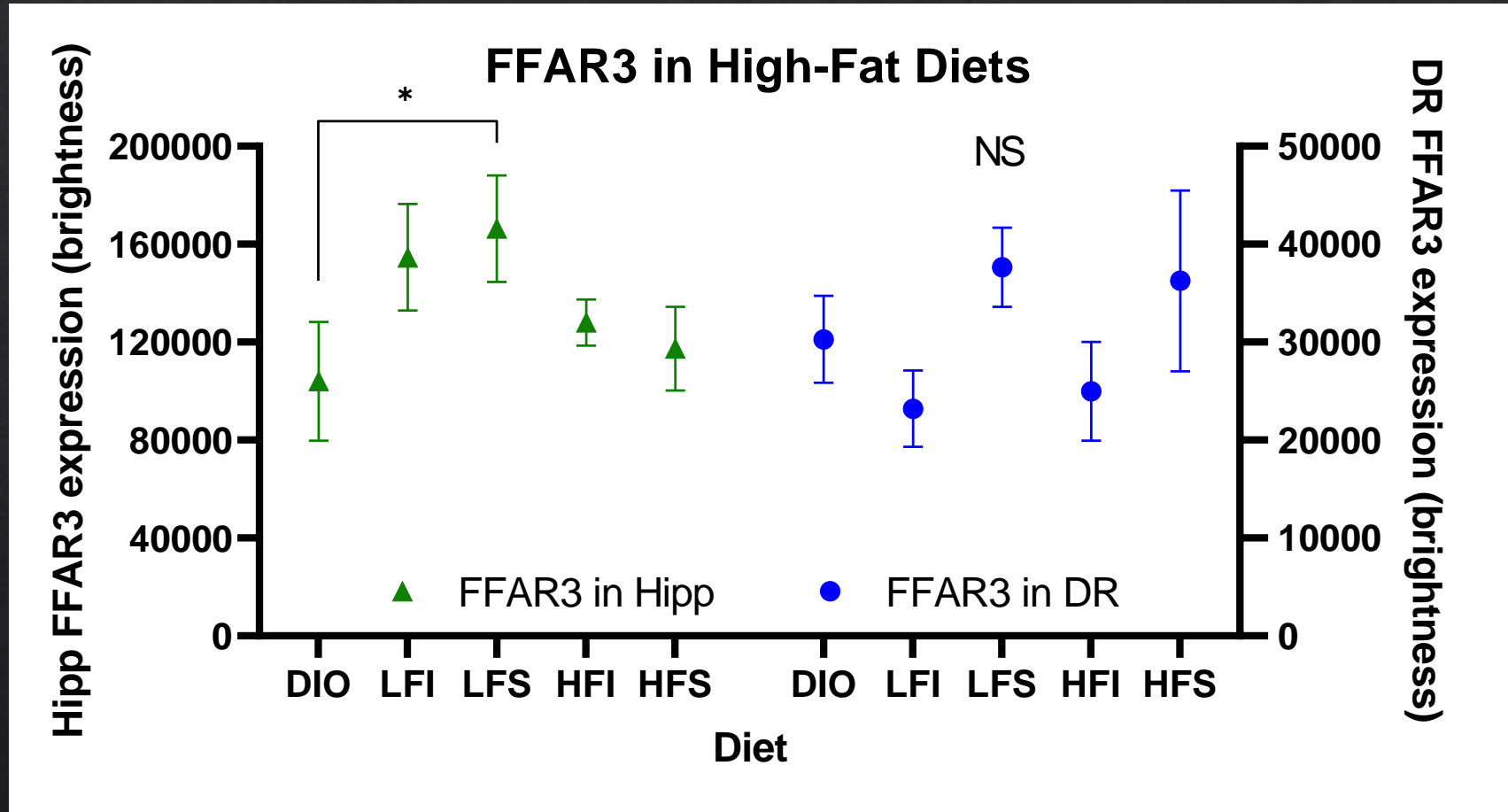




What We Found

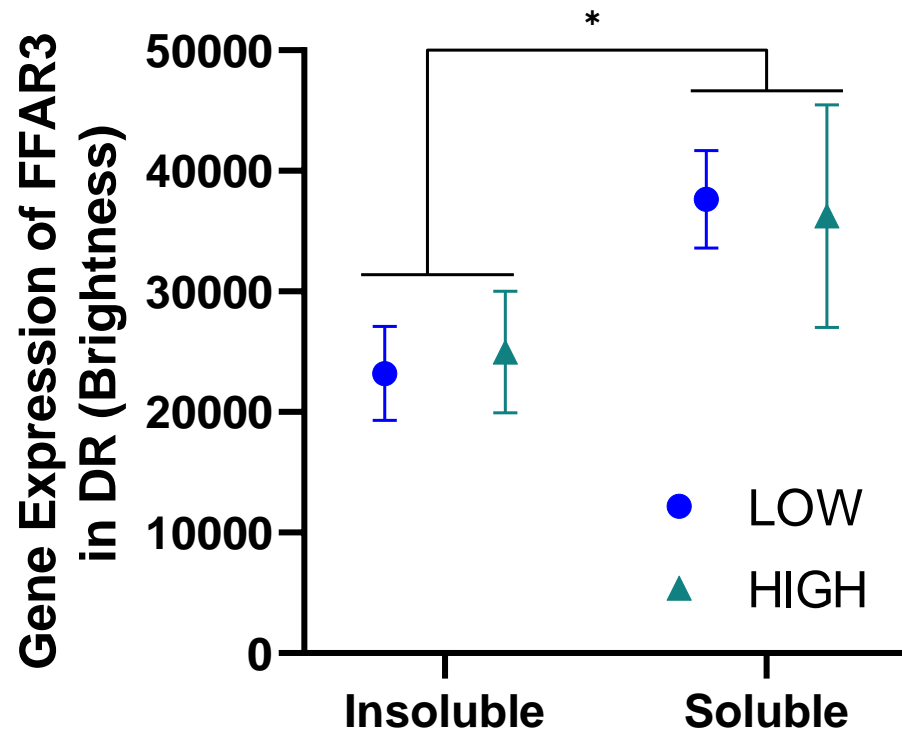


What We Found

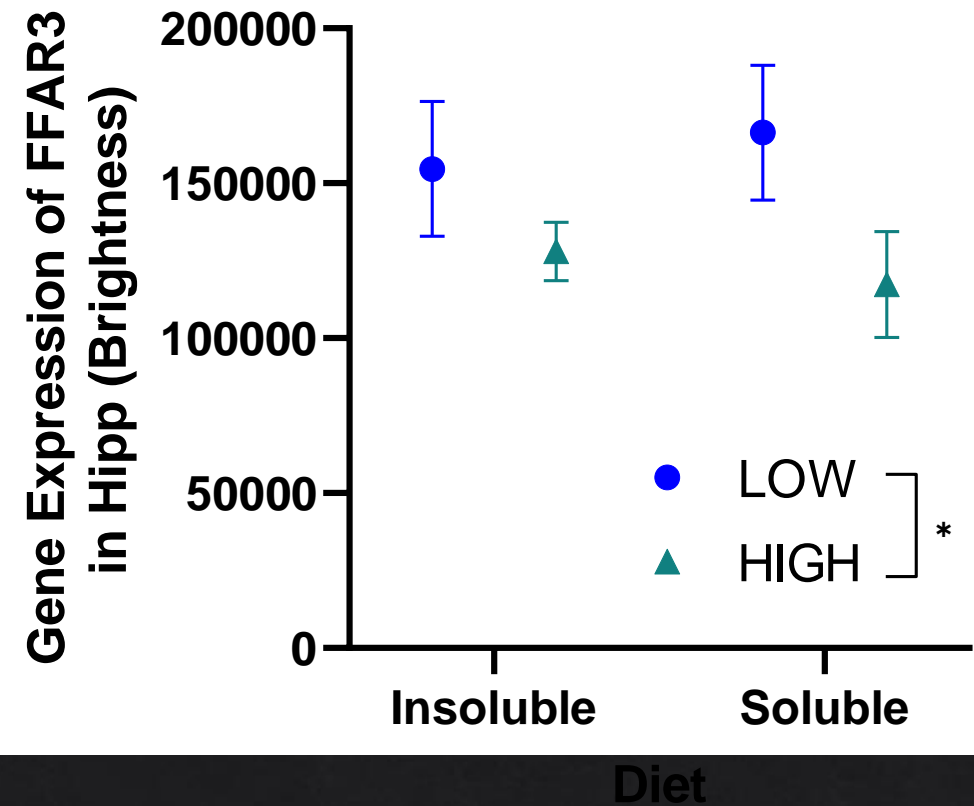


What We Found

FFAR3 mRNA in the DR



FFAR3 mRNA in the Hippocampus



So what does it all mean?



SCFA receptors are in the hippocampus and dorsal raphe

Found on important cells for brain health



Dietary fiber can be used to change the brain

Treatments for mental health

