

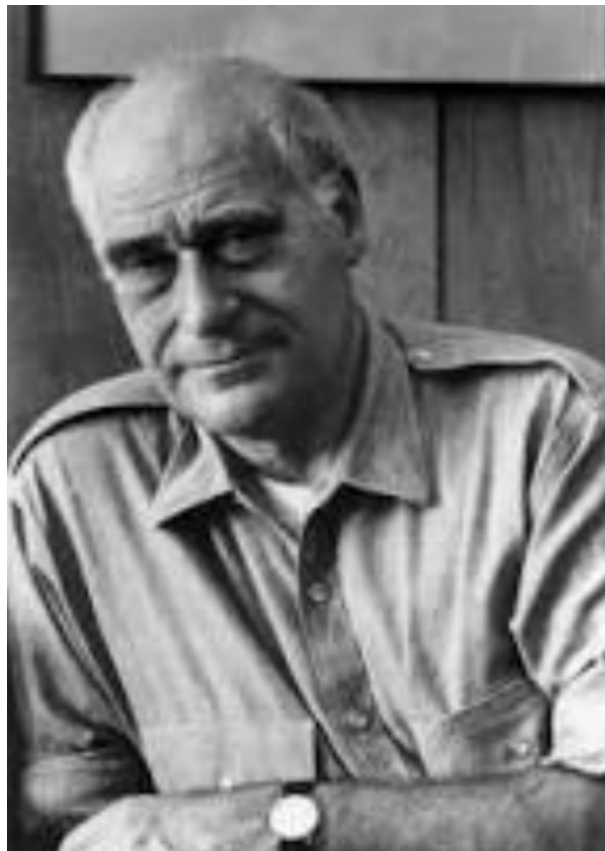
# How experiences shape the developing brain and impact neurological diseases

Hollis Cline, PhD

What changes in the  
brain as we grow up?

Is it Nature or Nurture?





# Brain Basics

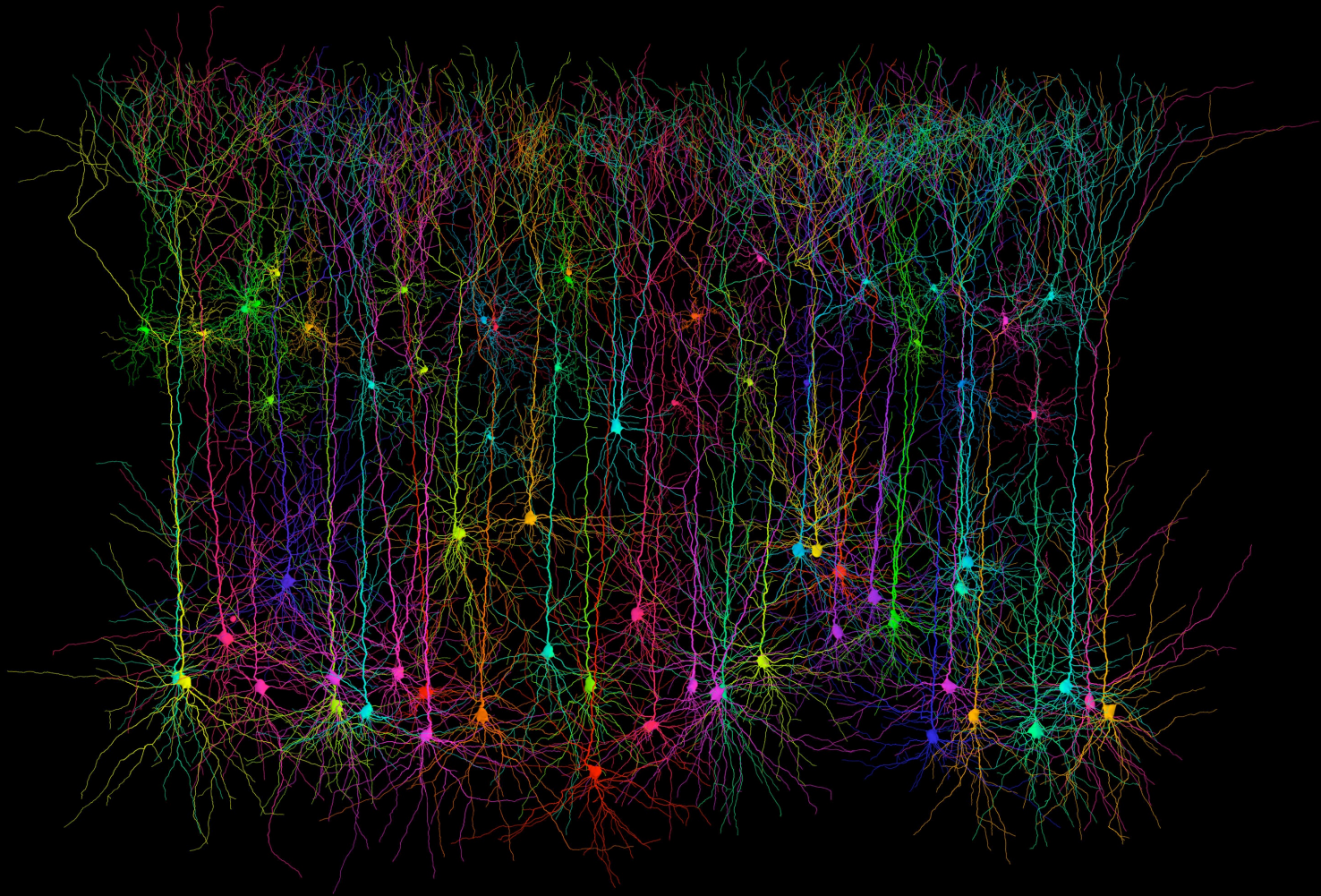


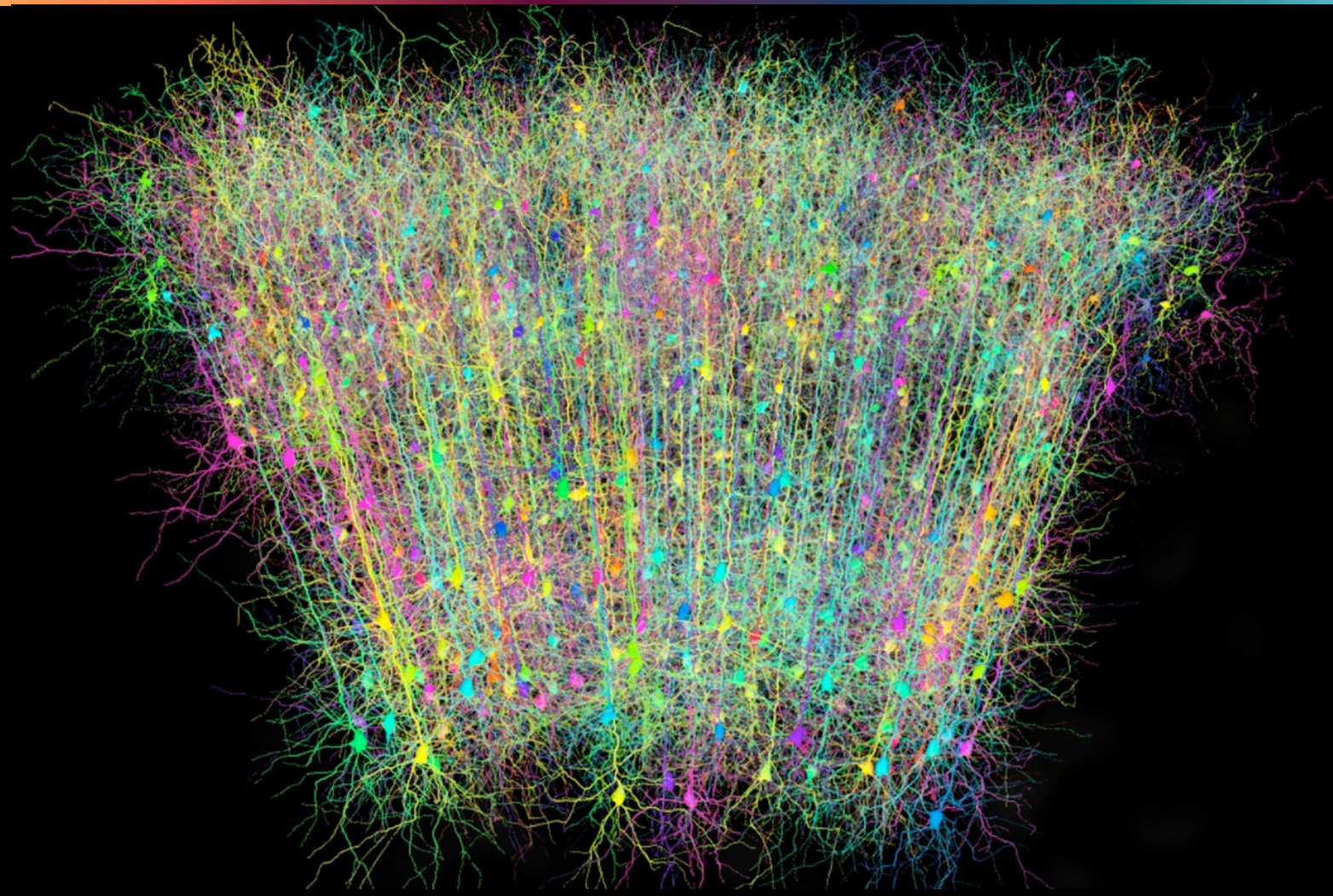
Your brain:

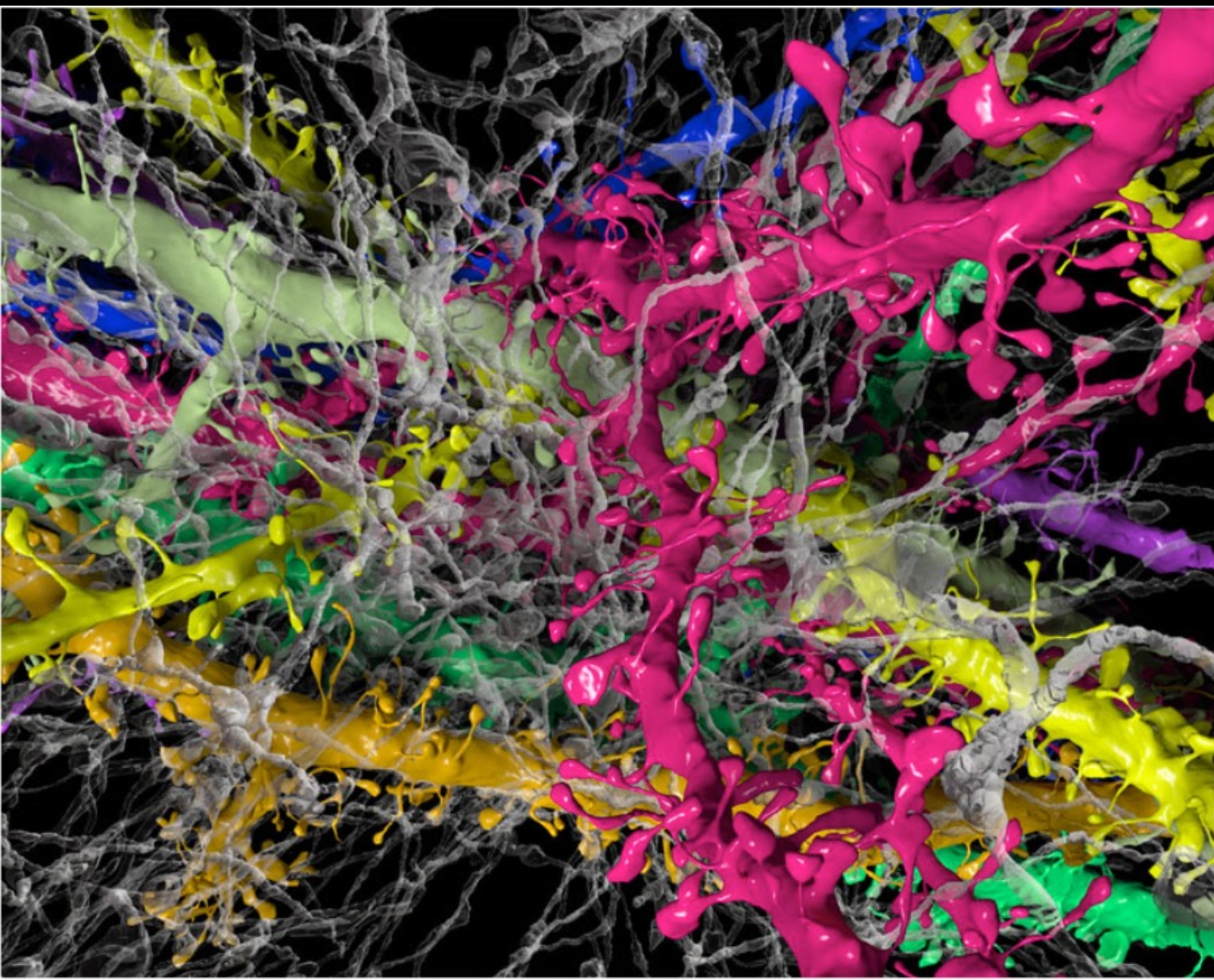
1,000,000,000 neurons

1,000,000,000 non-neuronal cells

1,000,000,000,000 connections









# What we know about visual system connections:



DaVinci  
~1500

- The optic nerve is the sole information pathway from the eyes to the brain
- People have 30 different parts of their brains that receive visual information
- Different parts of the brain use visual information in different ways
  - navigation
  - visuo-motor coordination
  - facial recognition

How does our visual system develop?

Is it Nature or Nurture?





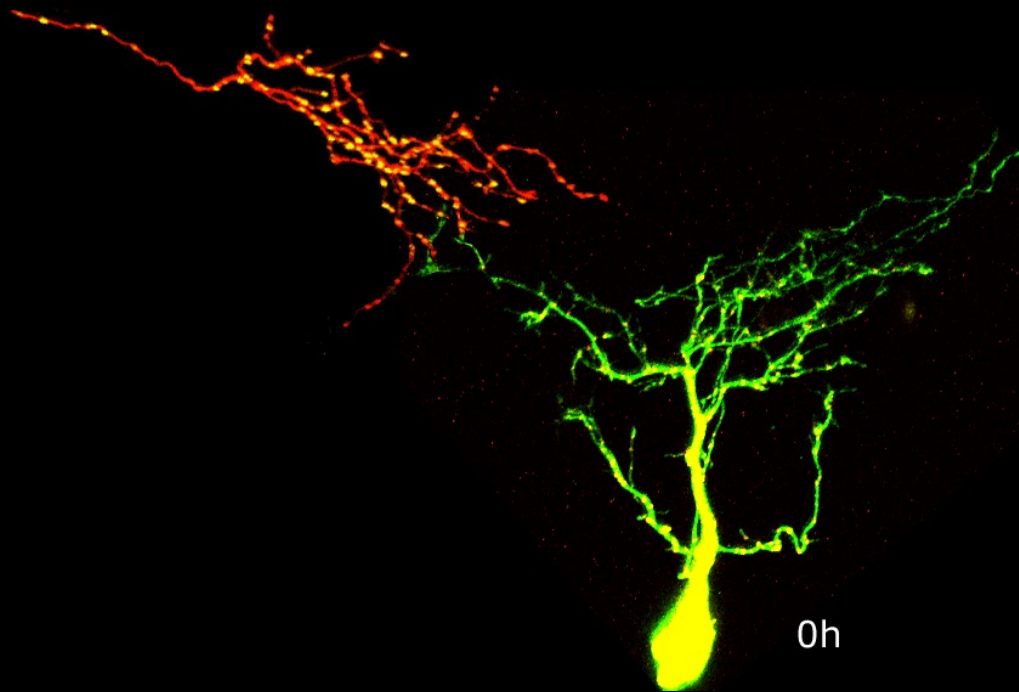


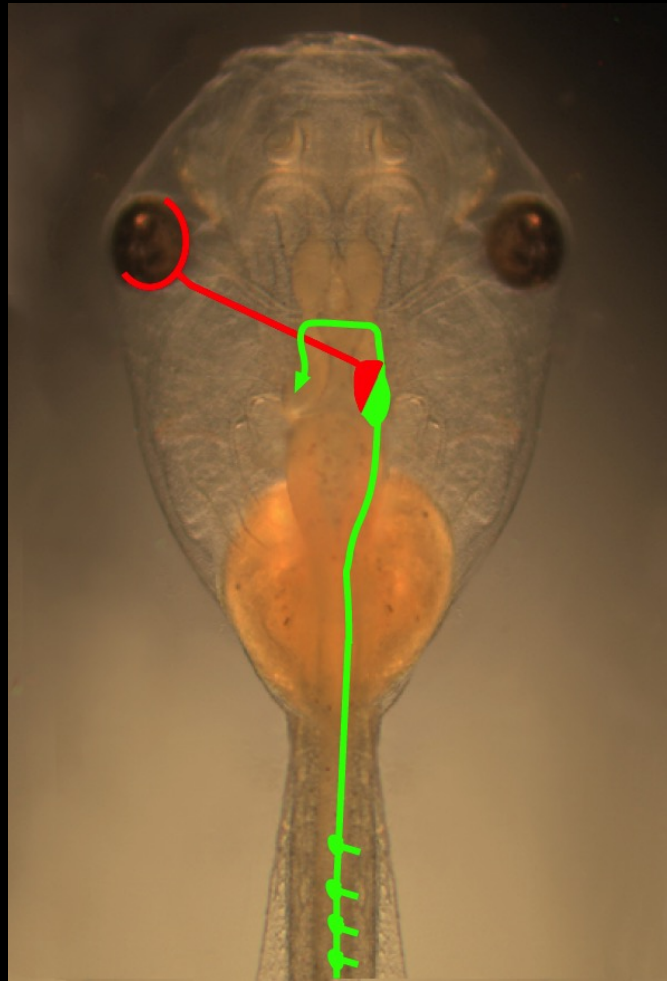


# How do brain circuits get hooked up and what does that have to do with Nature and Nurture?

You can see a lot just by looking

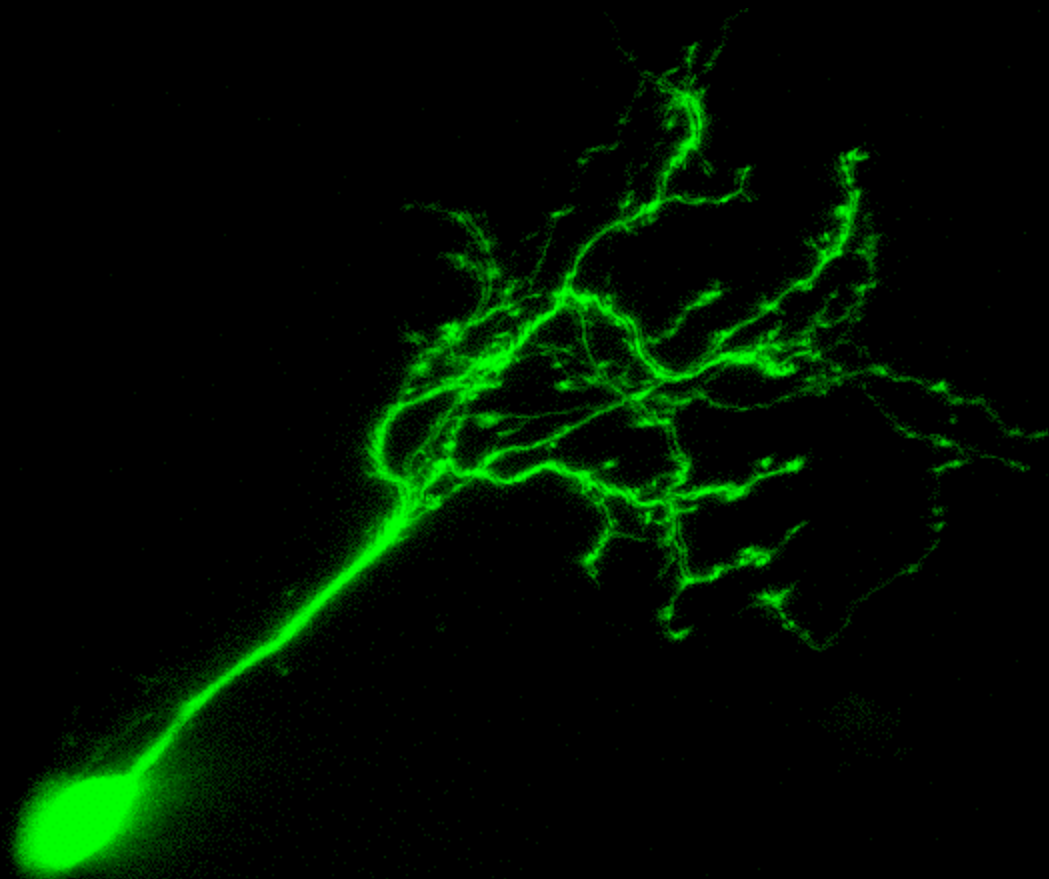
--Yogi Berra



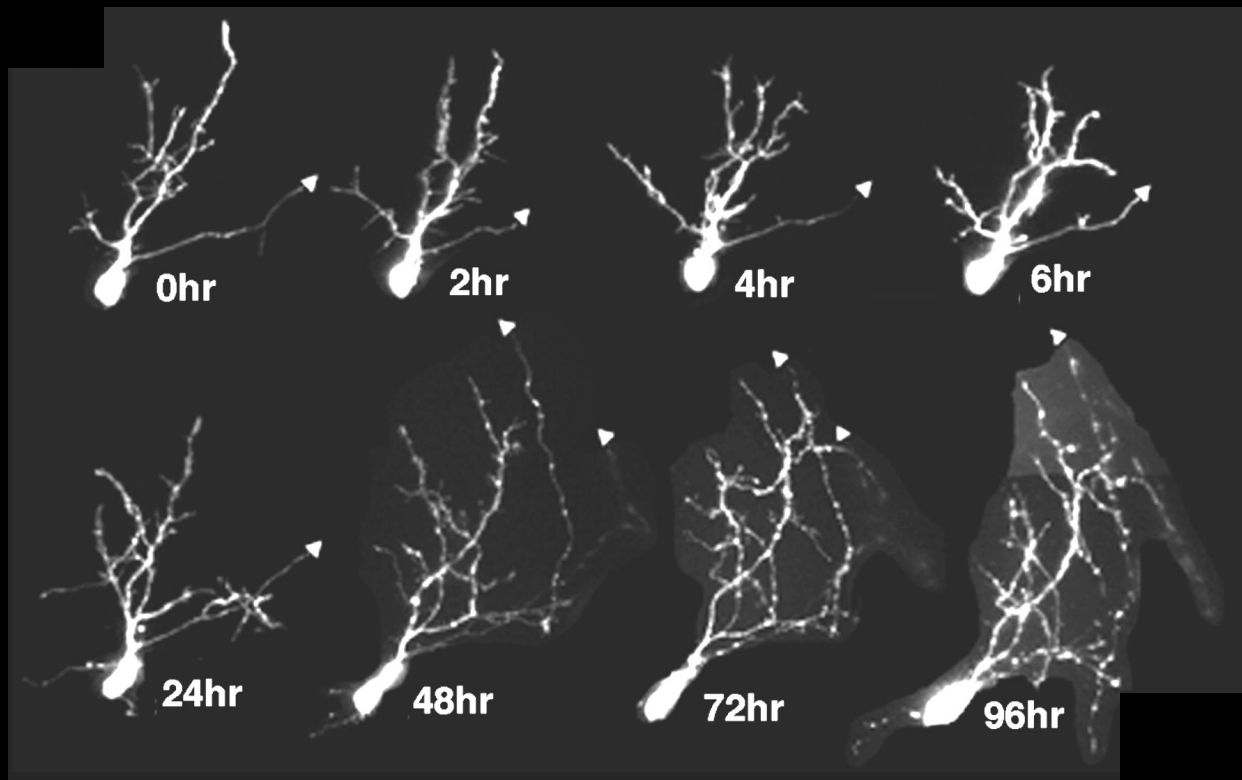


Scott Fraser  
Nancy O'Rourke

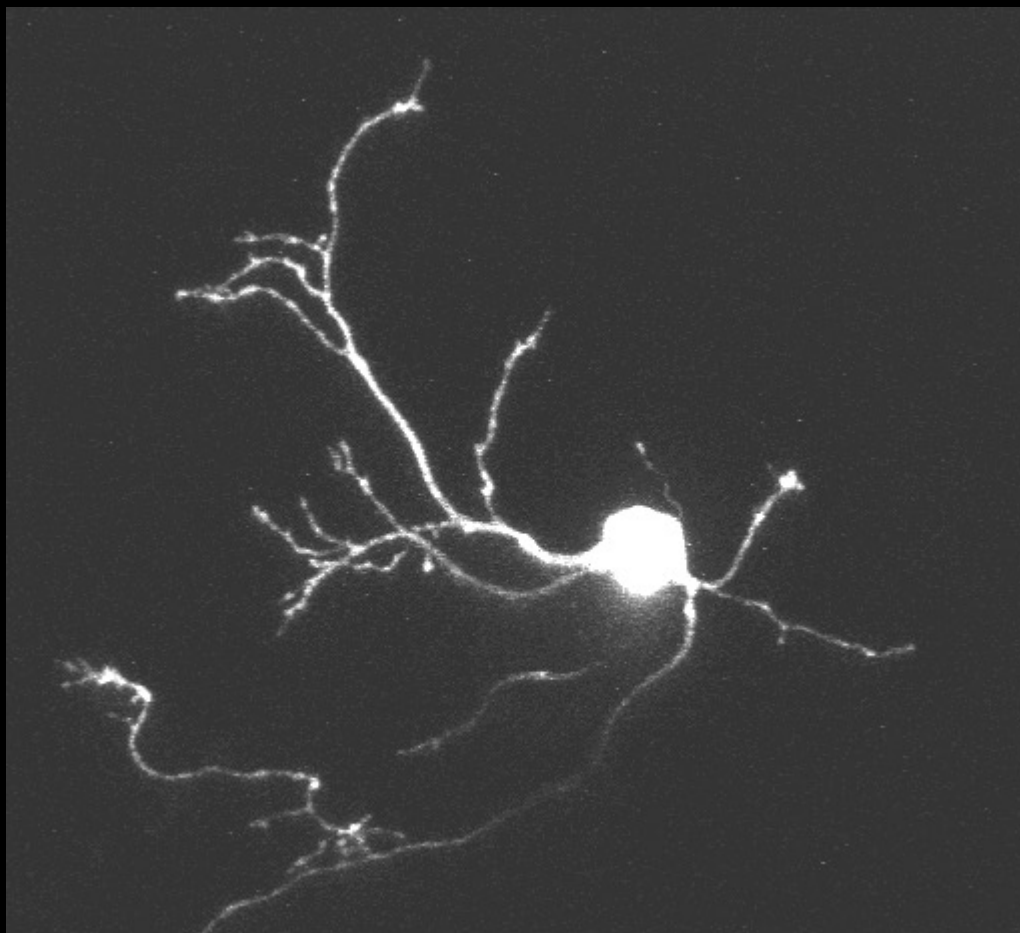




Haas, Sin



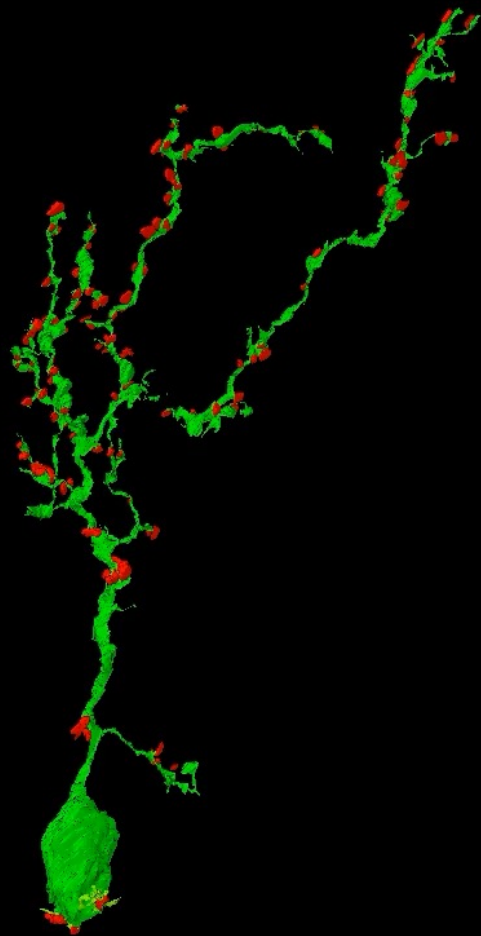
Jen Bestman



10 min  
intervals

10  $\mu\text{m}$

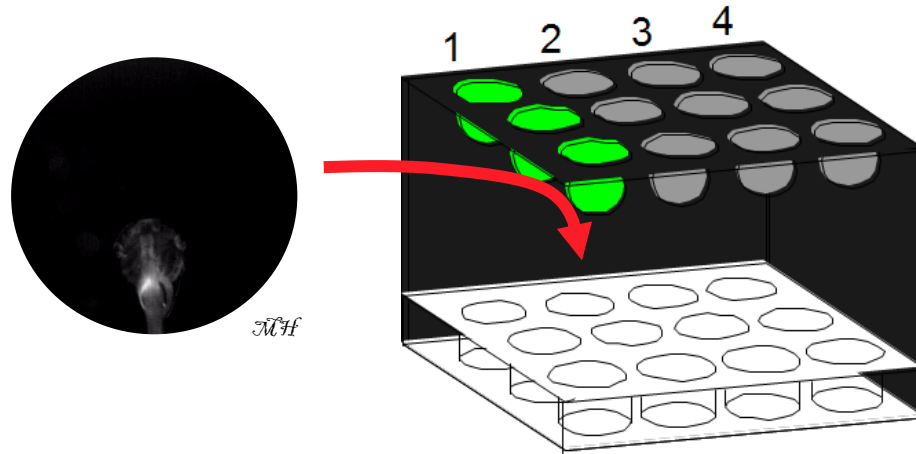




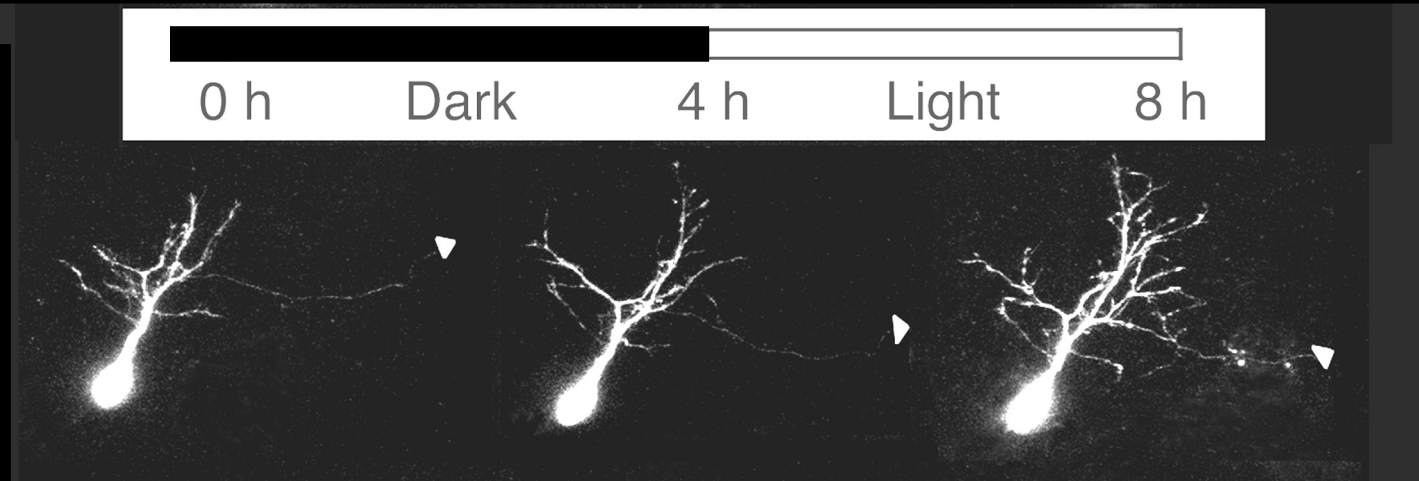
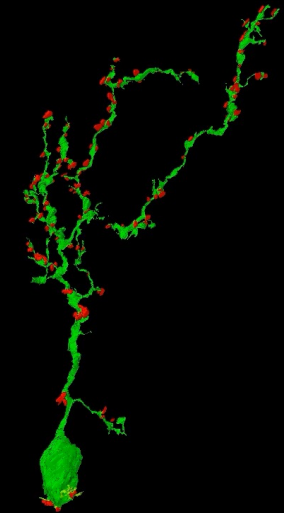
Jianli Li



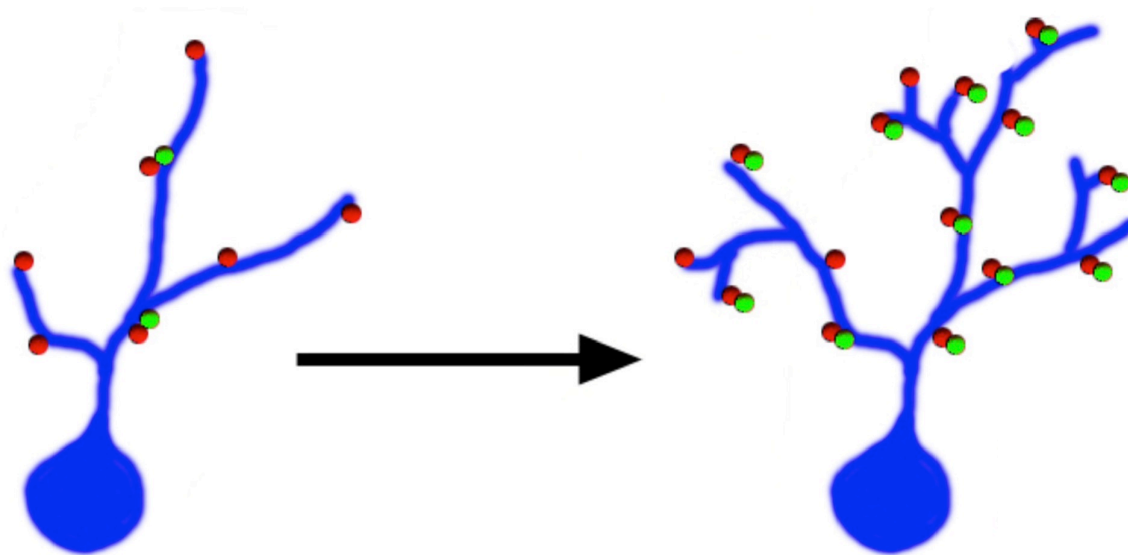
## Visual Experience for Freely Swimming Tadpoles



# What we Learn from Watching Neurons Grow



# Visual stimulation promotes dendritic arbor growth and synaptogenesis





Visual stimulation increases neuron development, circuit assembly, visually-guided behaviors, recovery from injury

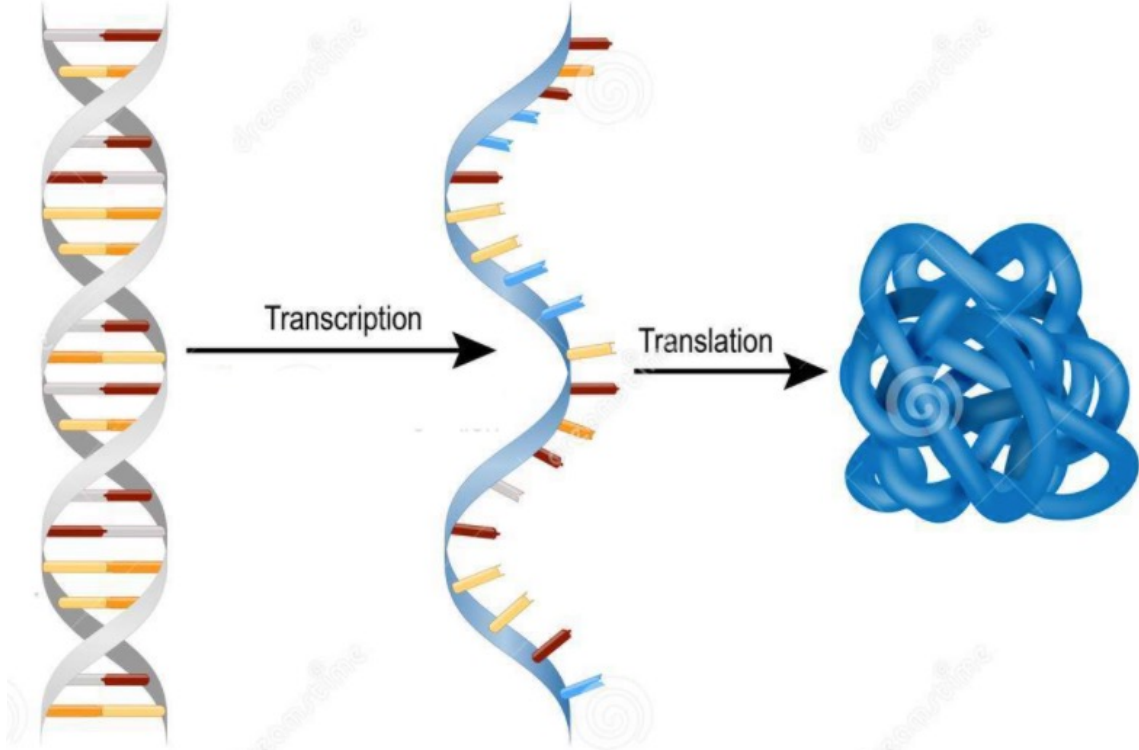
 How does this happen?

# The Central Dogma

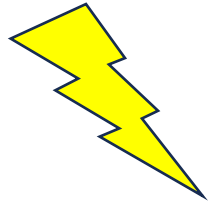
DNA

mRNA

Protein

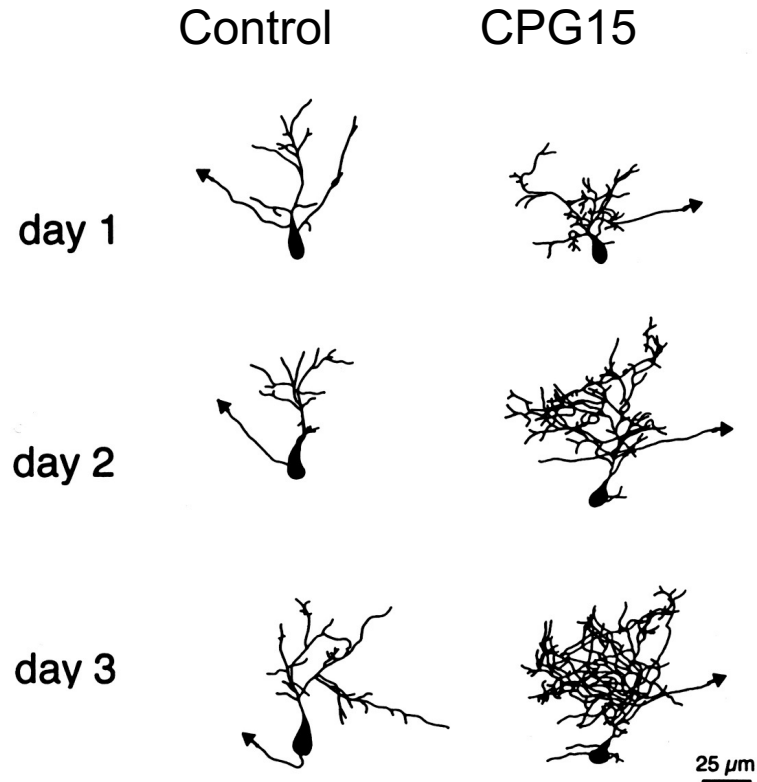


# Active brain cells turn on special genes “candidate plasticity genes”



DNA → mRNA → Protein

# CPG15 increases neuron growth



Sensory experience (brain activity) increases expression of activity-regulated genes. These genes generate proteins which build brain circuits.



What proteins are synthesized in  
response to brain activity?

Why does this matter?

# Screen for Visual Experience-induced Newly-Synthesized Brain Proteins V1.0

- 25% of candidate plasticity proteins are from Autism Spectrum Disorder-risk genes and FMRP targets

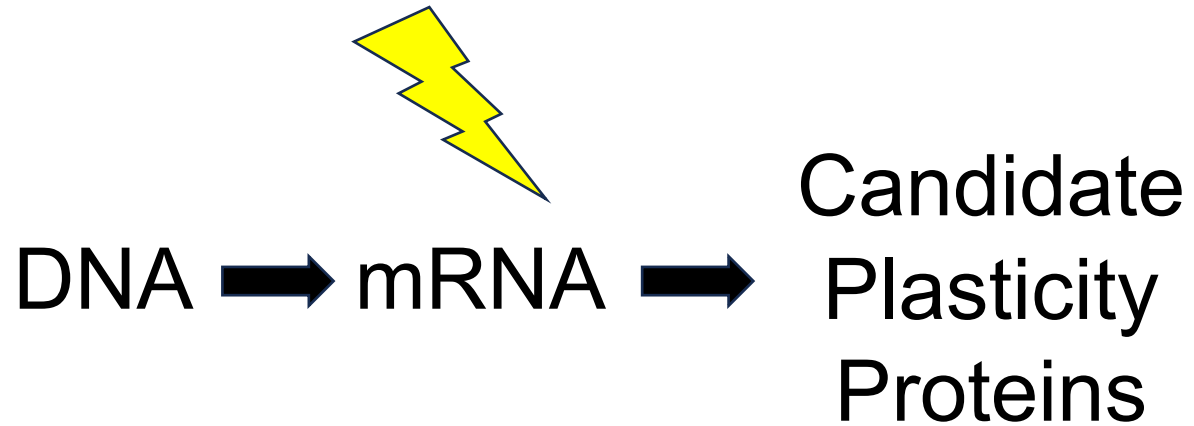


Han-Hsuan Liu   Lucio Schiapparelli

John Yates, Dan McClatchy

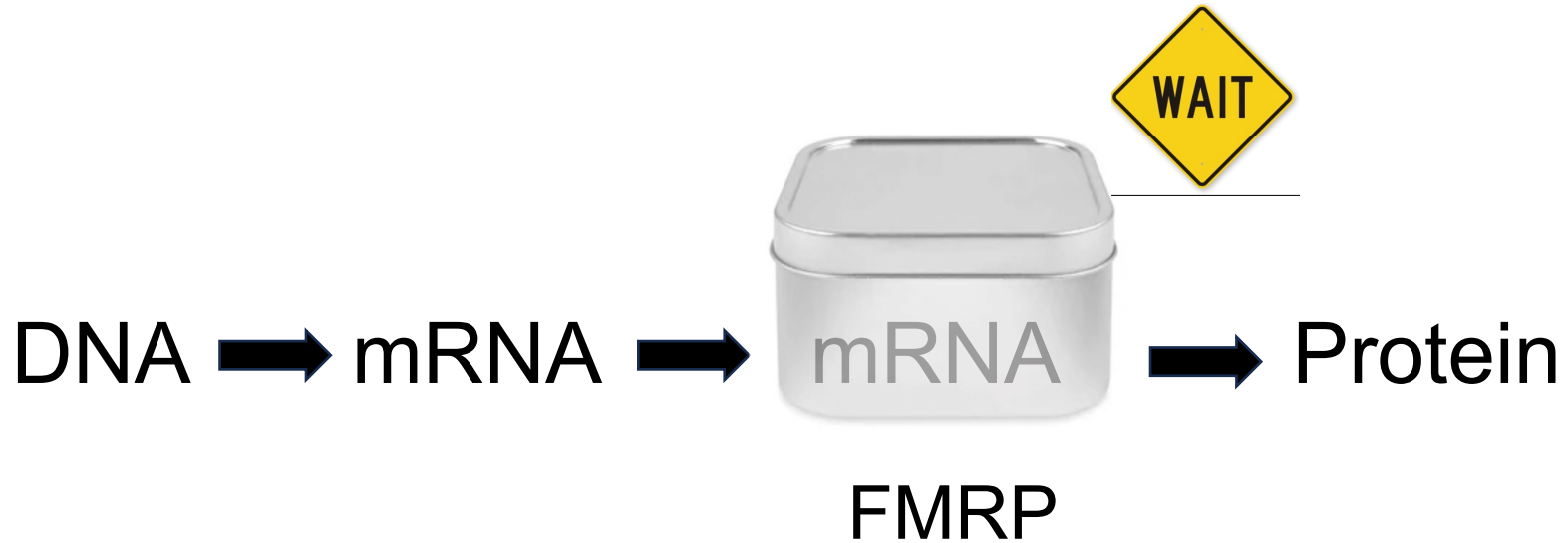
 **Skaggs Graduate School**  
at Scripps Research

Visual experience increases  
“candidate plasticity proteins”

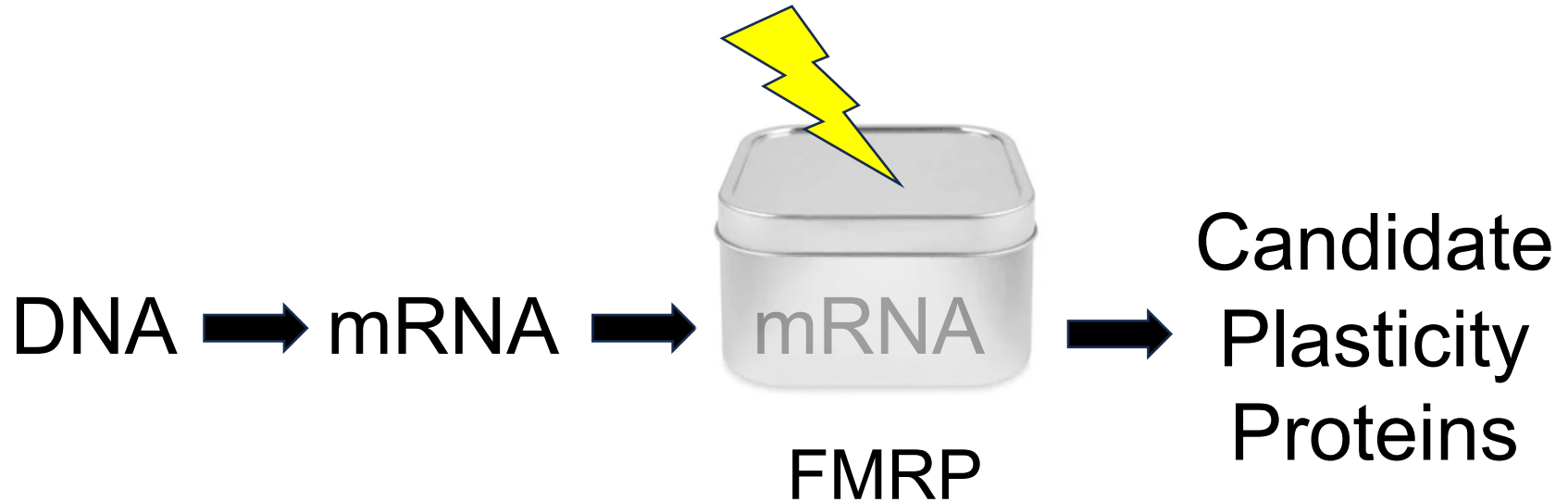




# FMRP sequesters mRNA

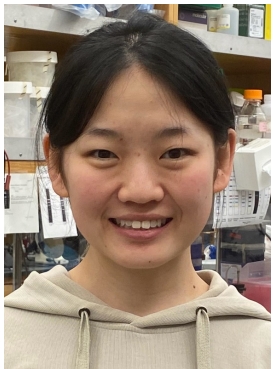


# Visual experience affects FMRP function



# Screen for Neuron Class Specific Visual Experience-induced Newly-Synthesized Brain Proteins V2.0

- Optimize pipeline, Improve technology → Higher Yield (>10X)



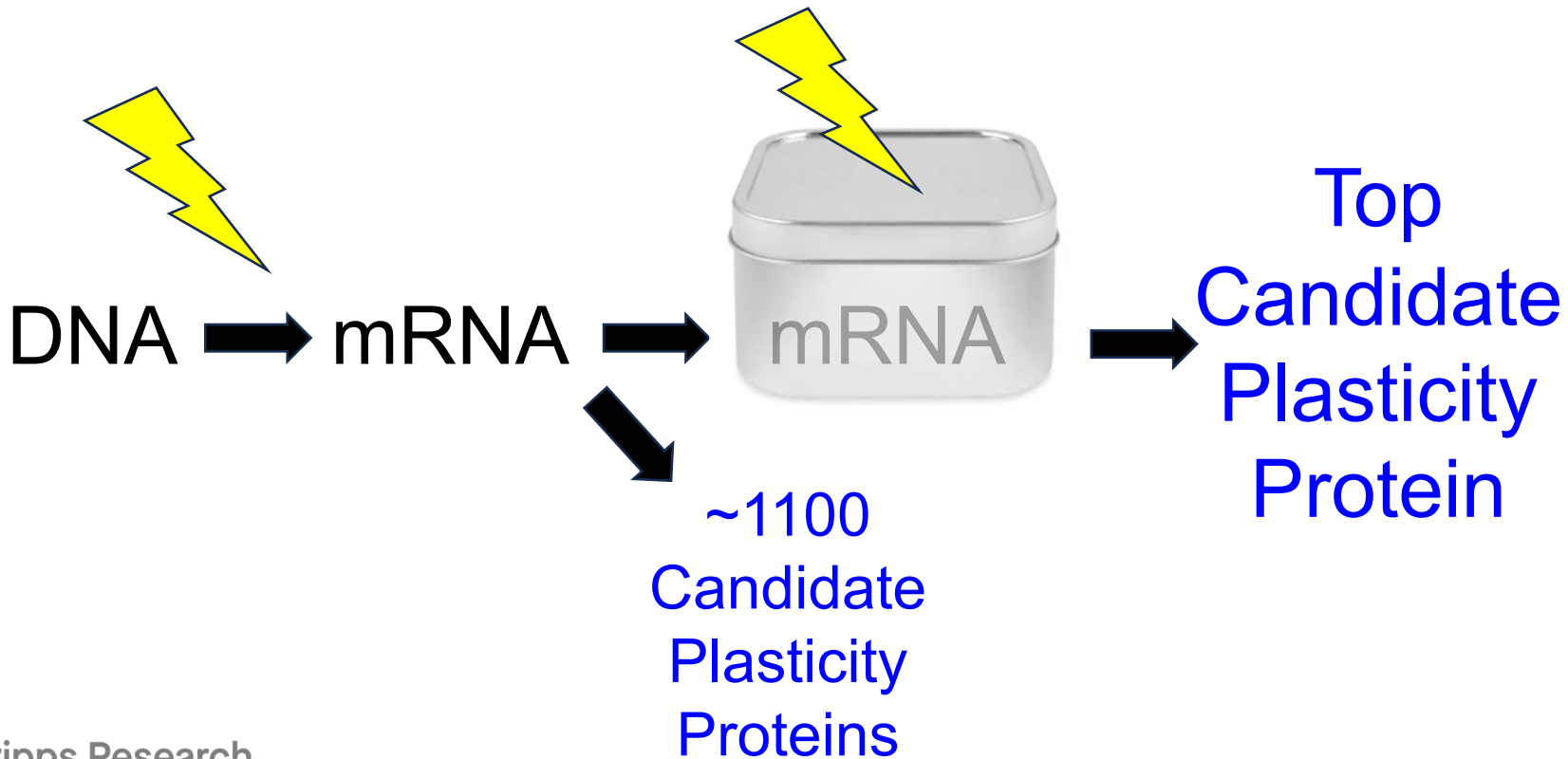
Ruoxi Wang



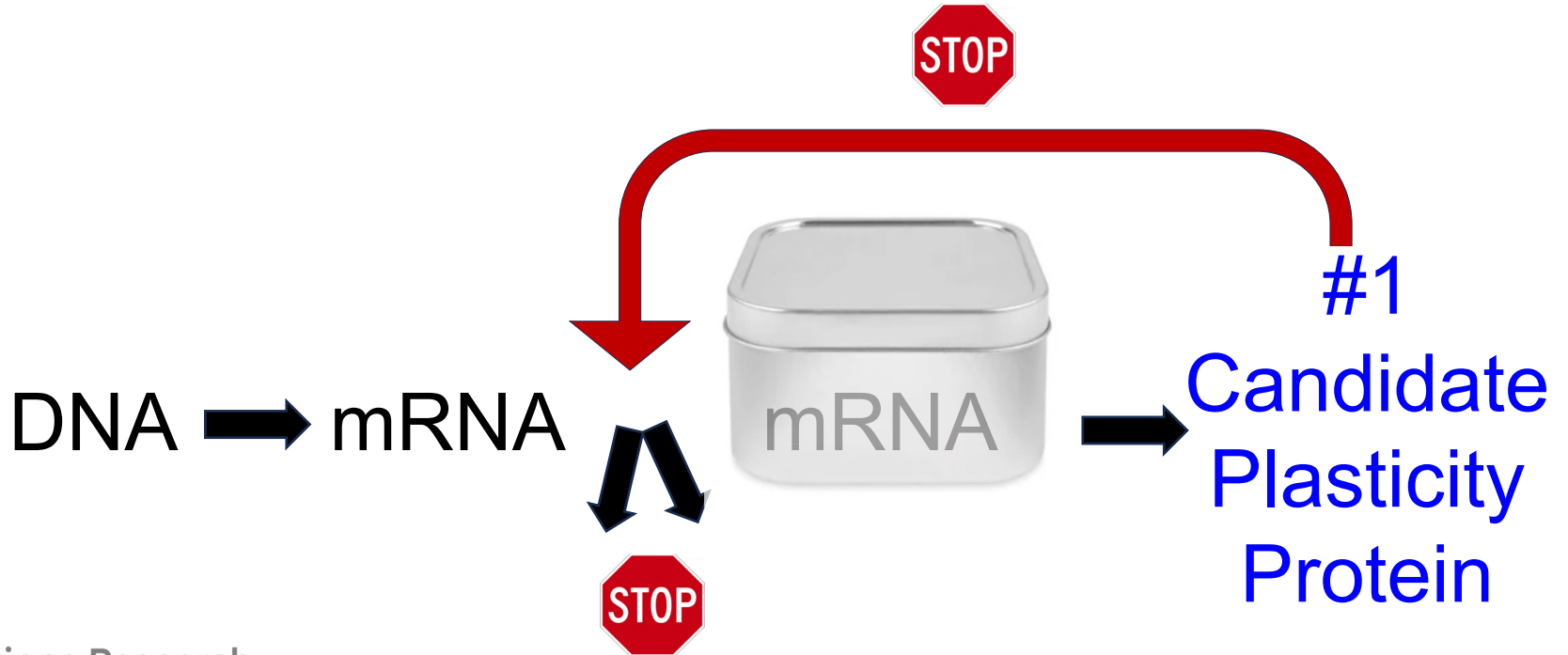
Yi Xie

John Yates, Dan McClatchy

 **Skaggs Graduate School**  
at Scripps Research



# Tight Temporal Control over Activity-dependent Protein Translation



# #1 CPP

- regulates synapse formation and maturation
- is required for vision
- is required for depth perception (i.e. visual information processing)

Your experiences (Nurture) activate your genes (Nature) which build and fine tune your brain and body.

# THANKS!

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Dan McClatchy  
Yuanhui Ma





