

SPEED SCIENCE 2024

Session Two



Longling (Silvia) Shui in Westcott Lab @CSHL



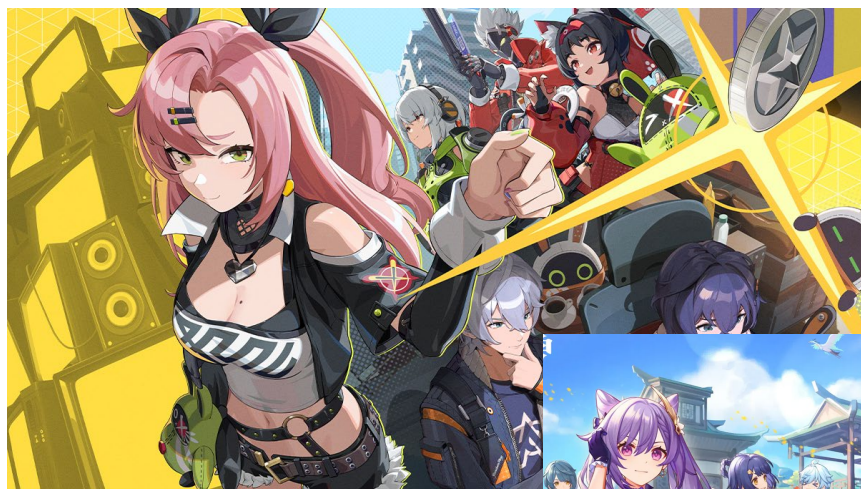
ENTJ 

Commander

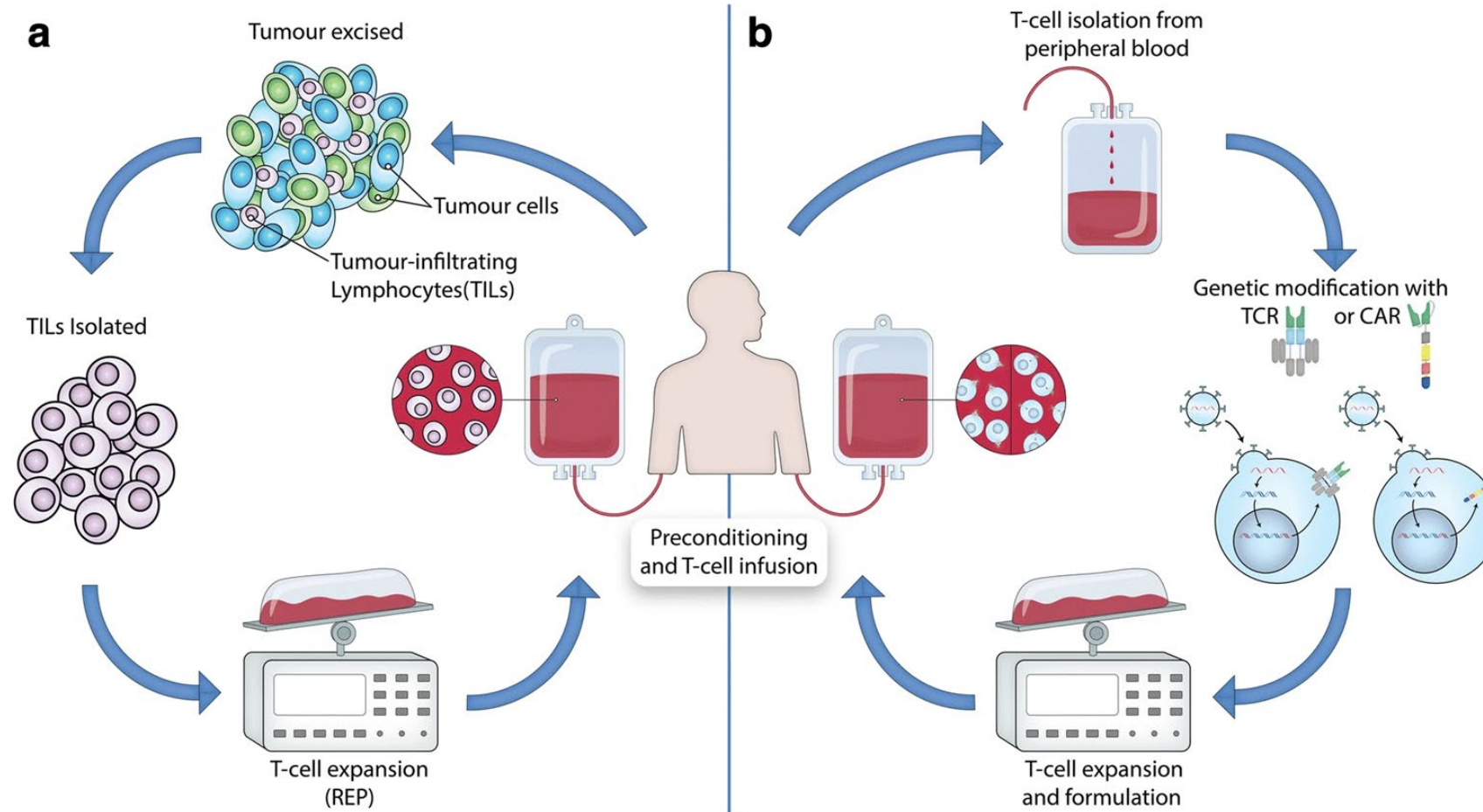
aka Strategist, Mobilizer,
The CEO

Role: Analyst / Rational

Happiness Lies in the Joy of Achievement



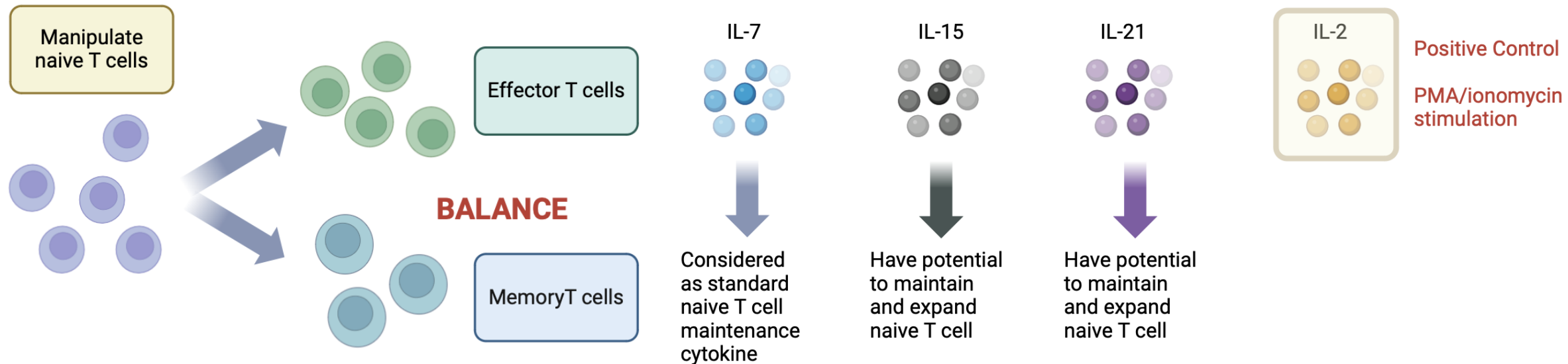
Adopted Cell Transfer (ACT) Treatment



1. Adoptive cell therapy has limitations on short-lived responses and limited efficacy in solid tumors
2. The fate of T cells can be determined in the first division after T cell priming.

Need strategies to manipulate T cells before priming

- Directly manipulate naive T cells
- Allow flexible priming and activation of manipulated naive T cells in vivo, with therapies that enhance priming.



Determinants of the Tuft Cell Lineage in Small Cell Carcinomas

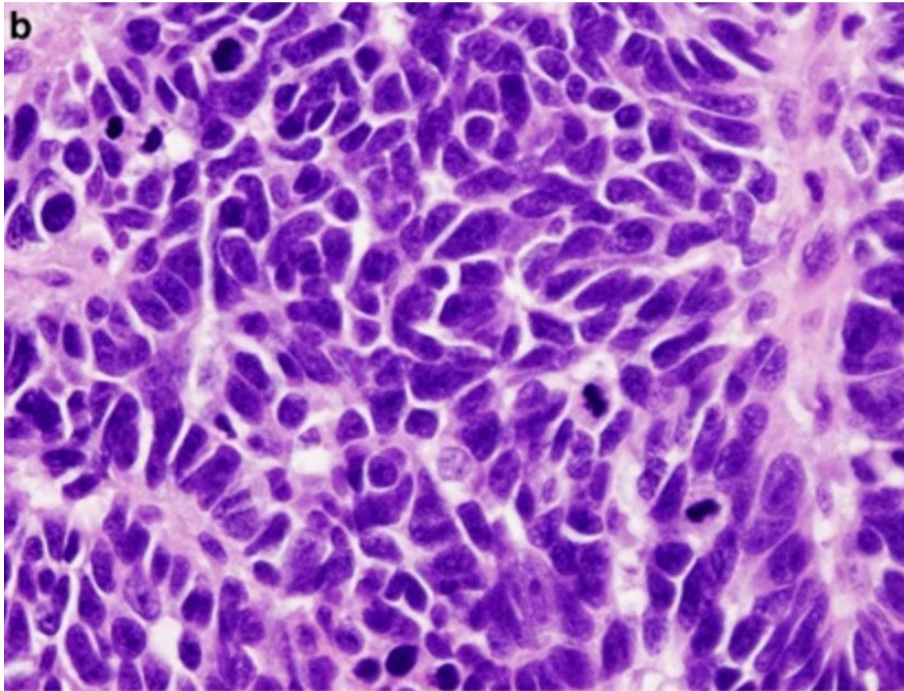
Kamil Taneja

Vakoc Lab

Cold Spring Harbor Lab

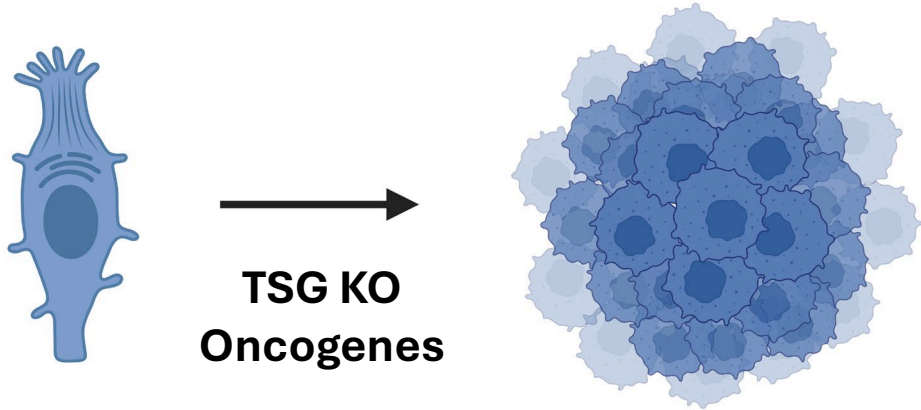
Genetics Speed Science 2024

Small Cell Carcinomas



1. Neuroendocrine
2. Tuft
3. Triple Negative/Inflammatory

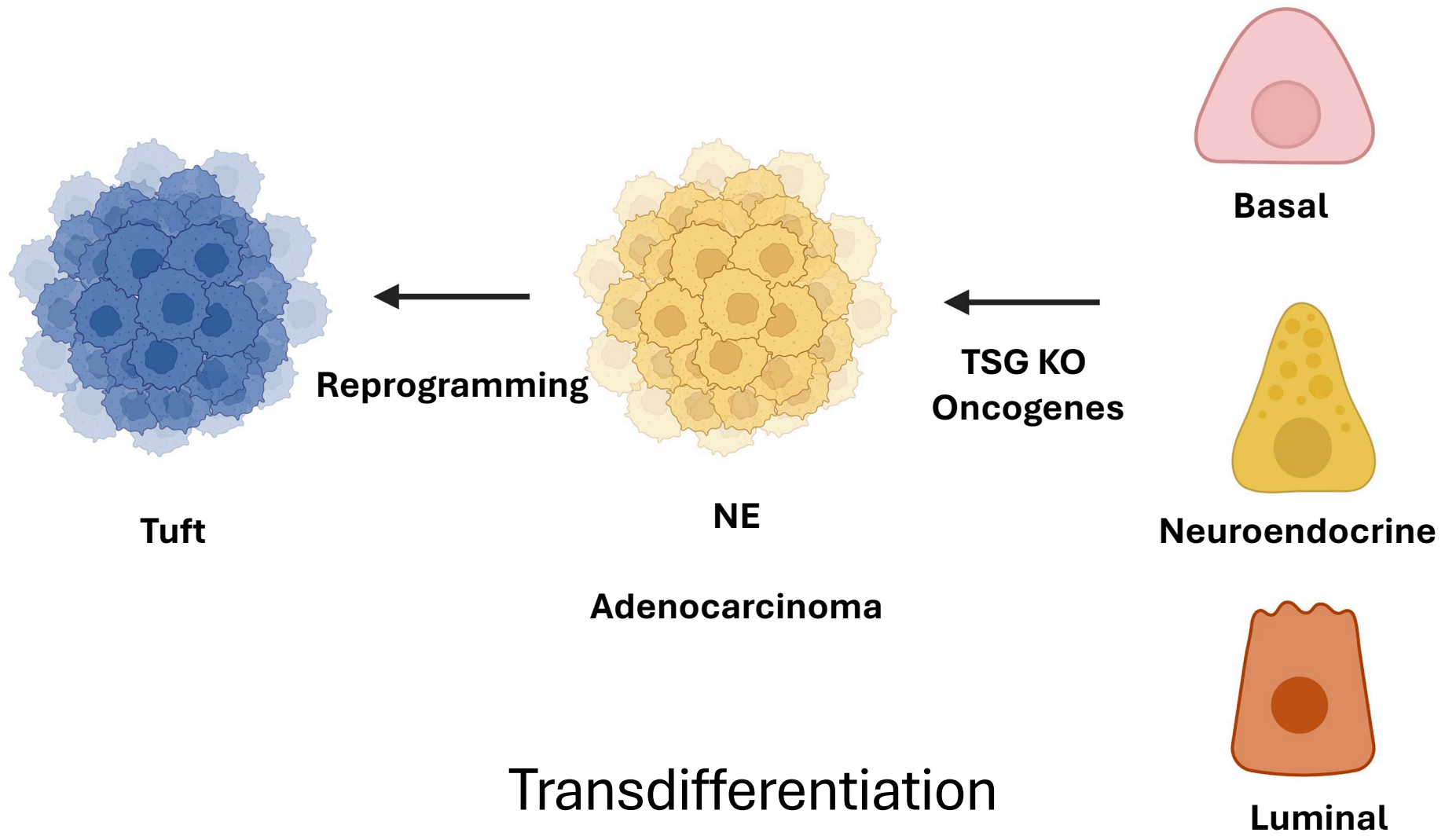
Goal: Genetic and Epigenetic Requirements of the Tuft Cell Lineage



Tuft

Tuft

Cell of Origin





Cell of Origin Model

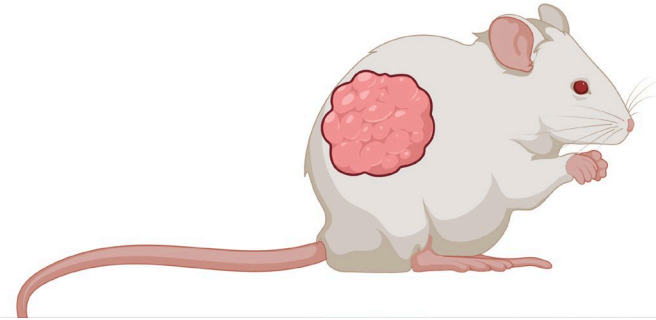
In Vivo

Tuft Cell Specific

Universal Mutations (p53 and rb1)

+

Subtype Specific Alterations (myc, PTEN)



Transdifferentiation Model

Xenograft

Basal Cells

Oncogenic Alterations

Transdifferentiation Specific Alterations

Lineage Tracing

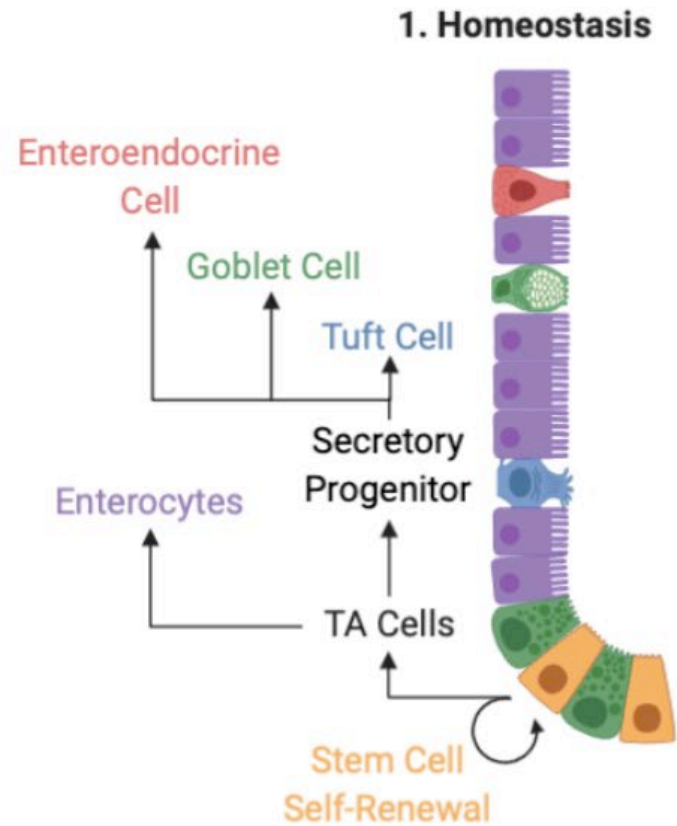
Speed Science

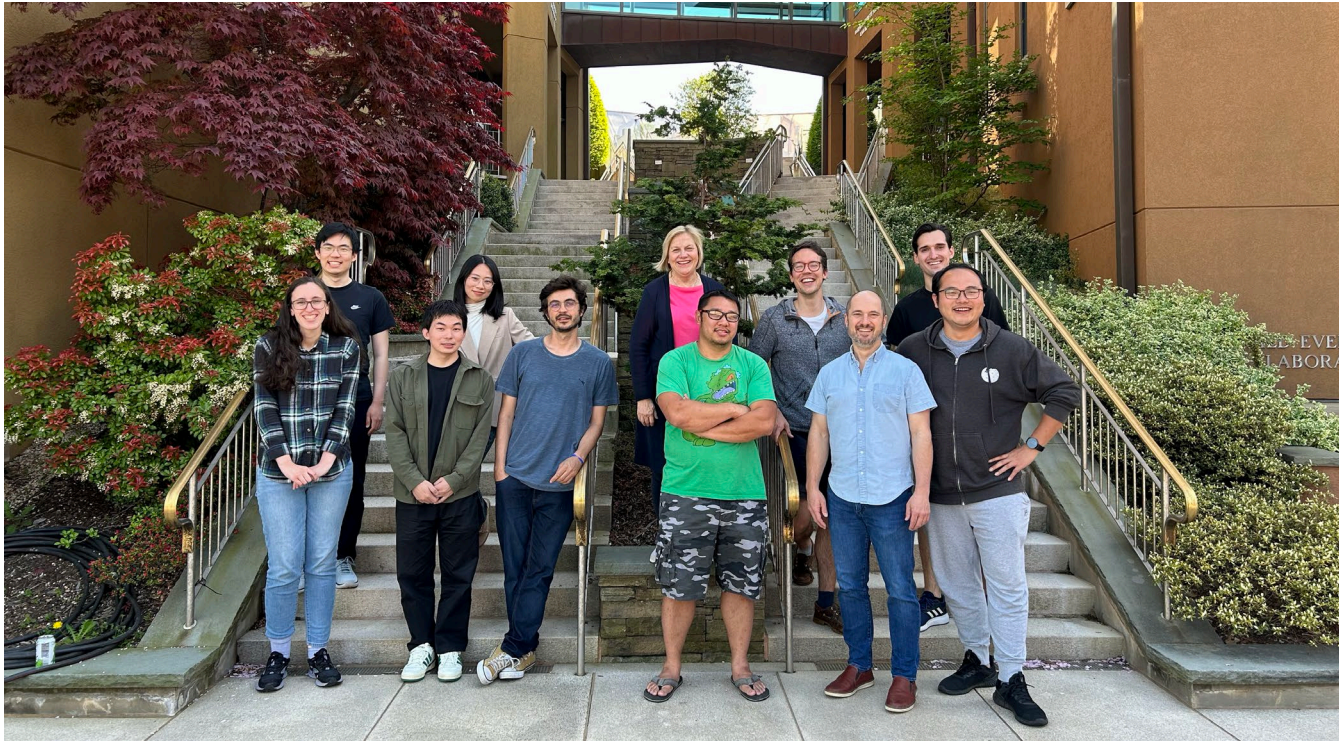
Cold Spring Harbor Laboratory / SBU

Onur Eskiocak-Beyaz LAB

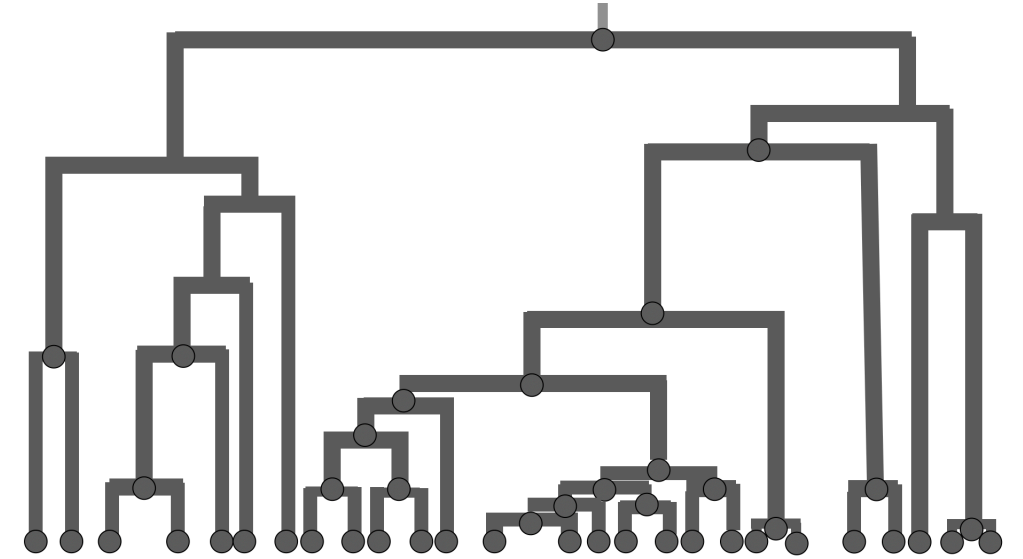
09/04/2024

Mechanisms of intestinal regeneration?





Siepel Lab



Develop probabilistic and mathematical models to address questions in evolutionary biology, human health, agriculture, and the environment

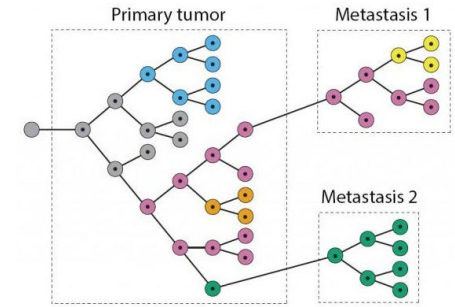
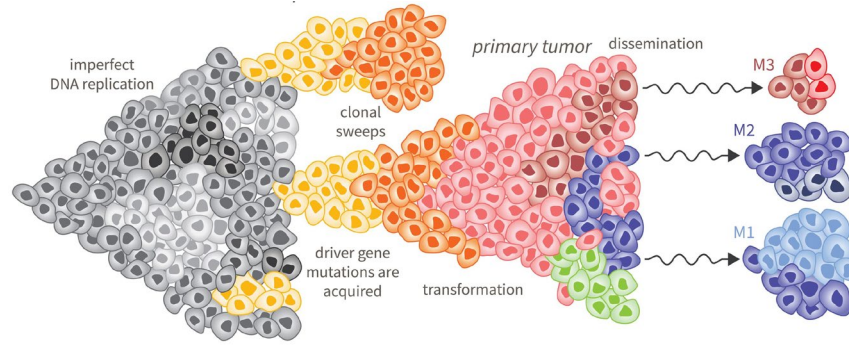
Luiz Machado



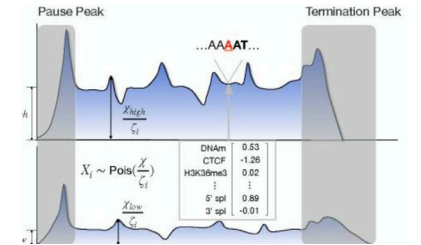
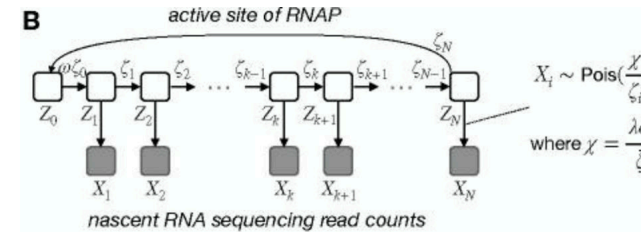
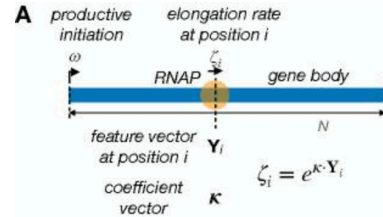
Cold
Spring
Harbor
Laboratory



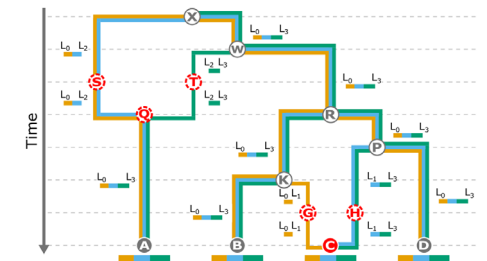
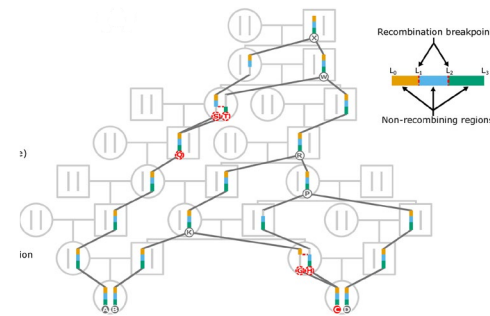
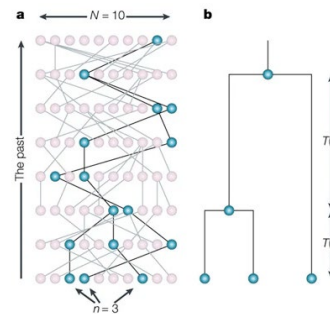
Cancer Evolution



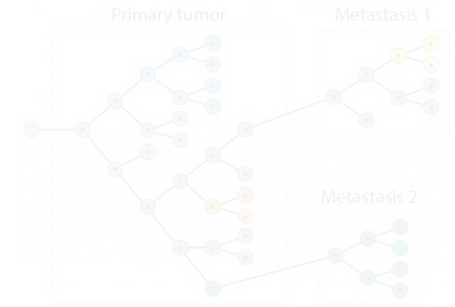
Gene expression



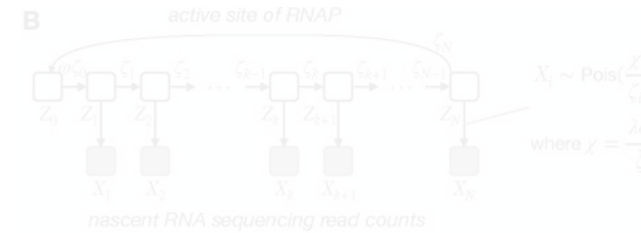
Population Genetics



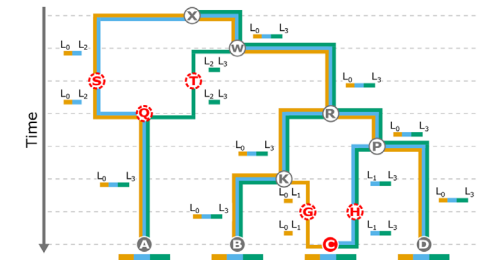
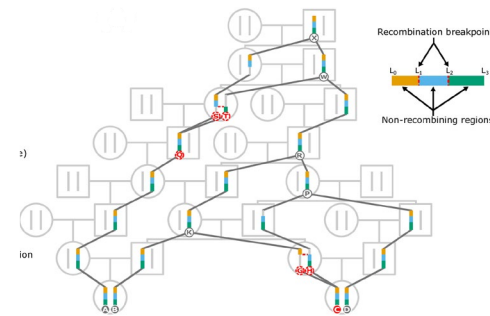
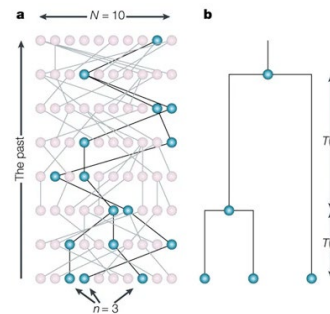
Cancer Evolution



Gene expression



Population Genetics

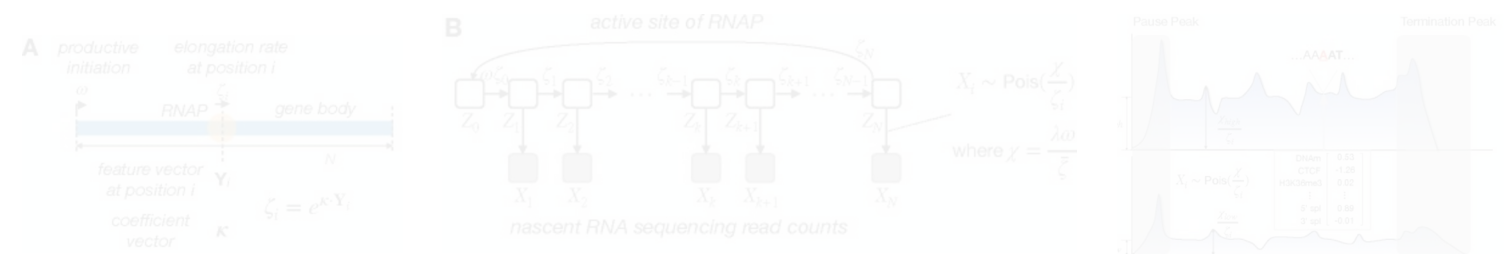


Cancer Evolution

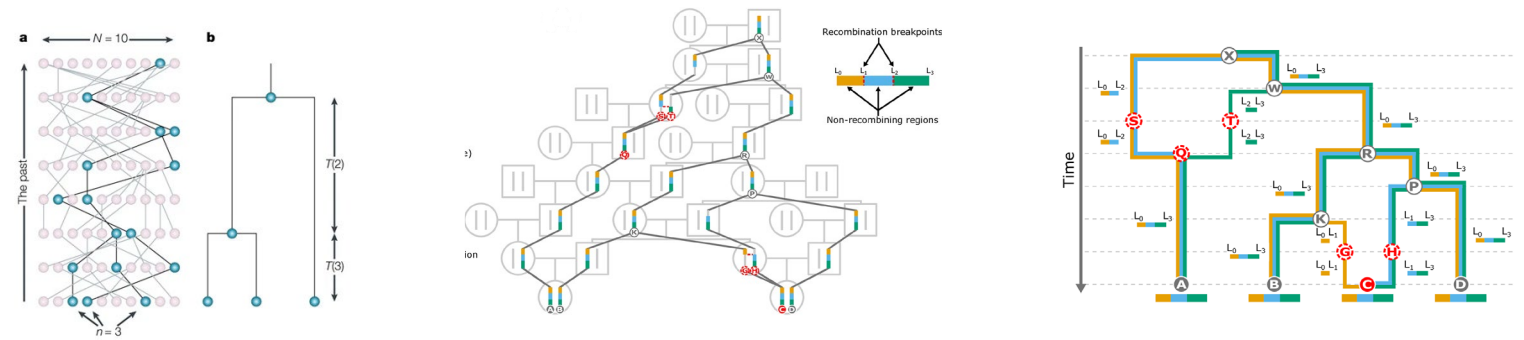


Development of neural network-based methods to infer Adaptive introgression in Ancestral Recombination Graphs

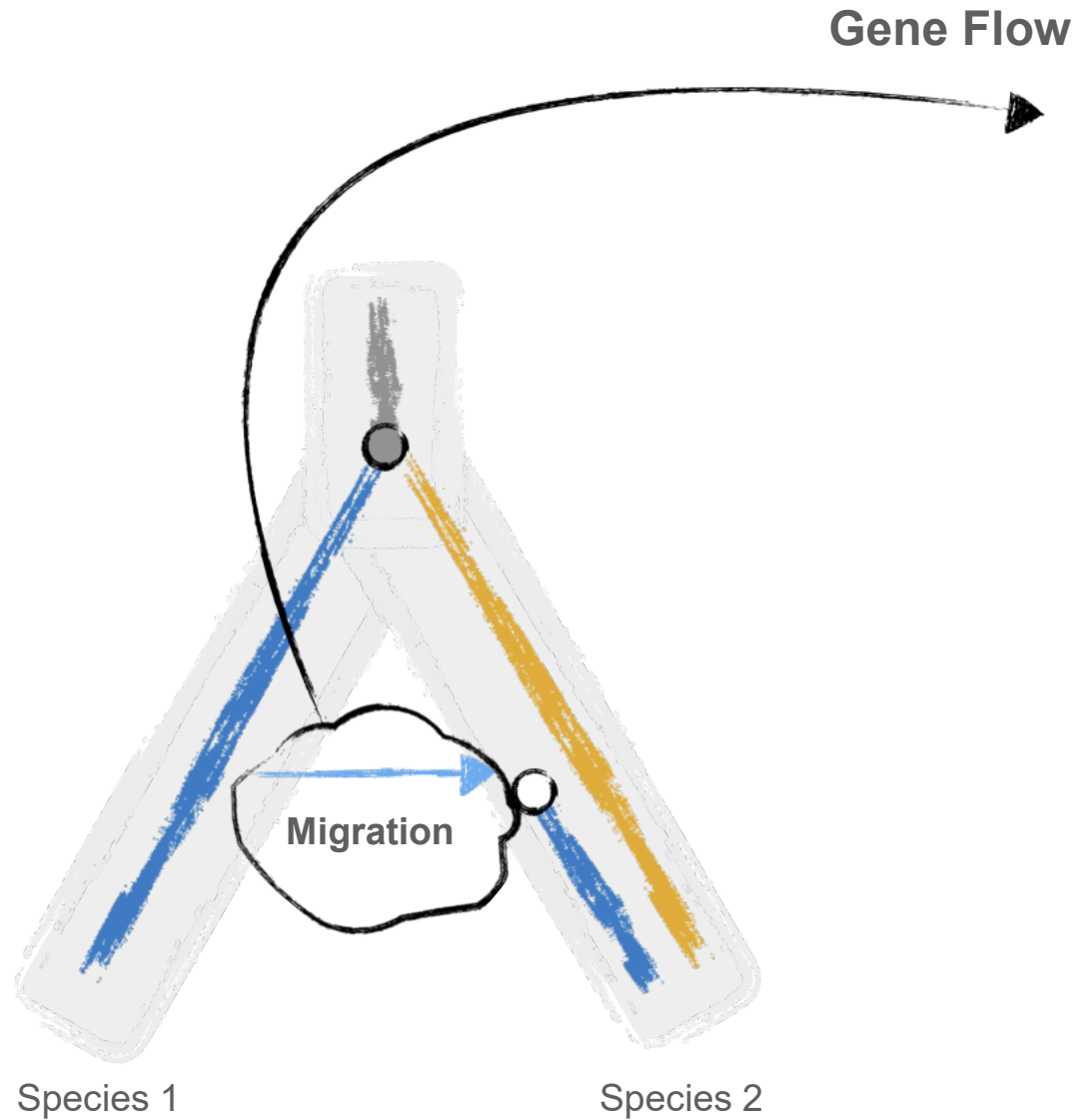
Gene expression



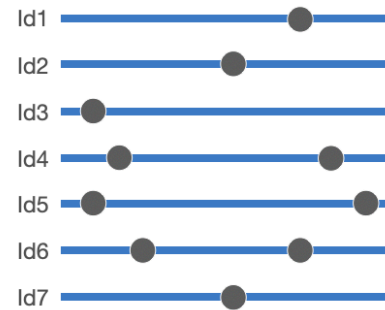
Population Genetics



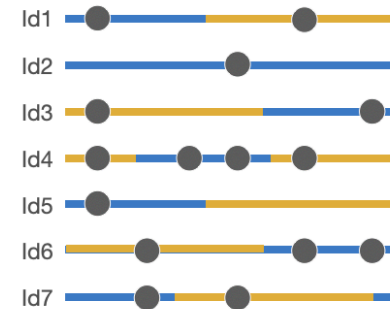
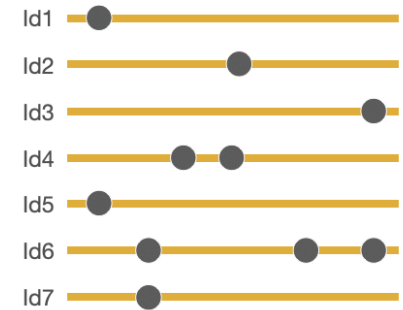
Adaptive Introgression



Species 1

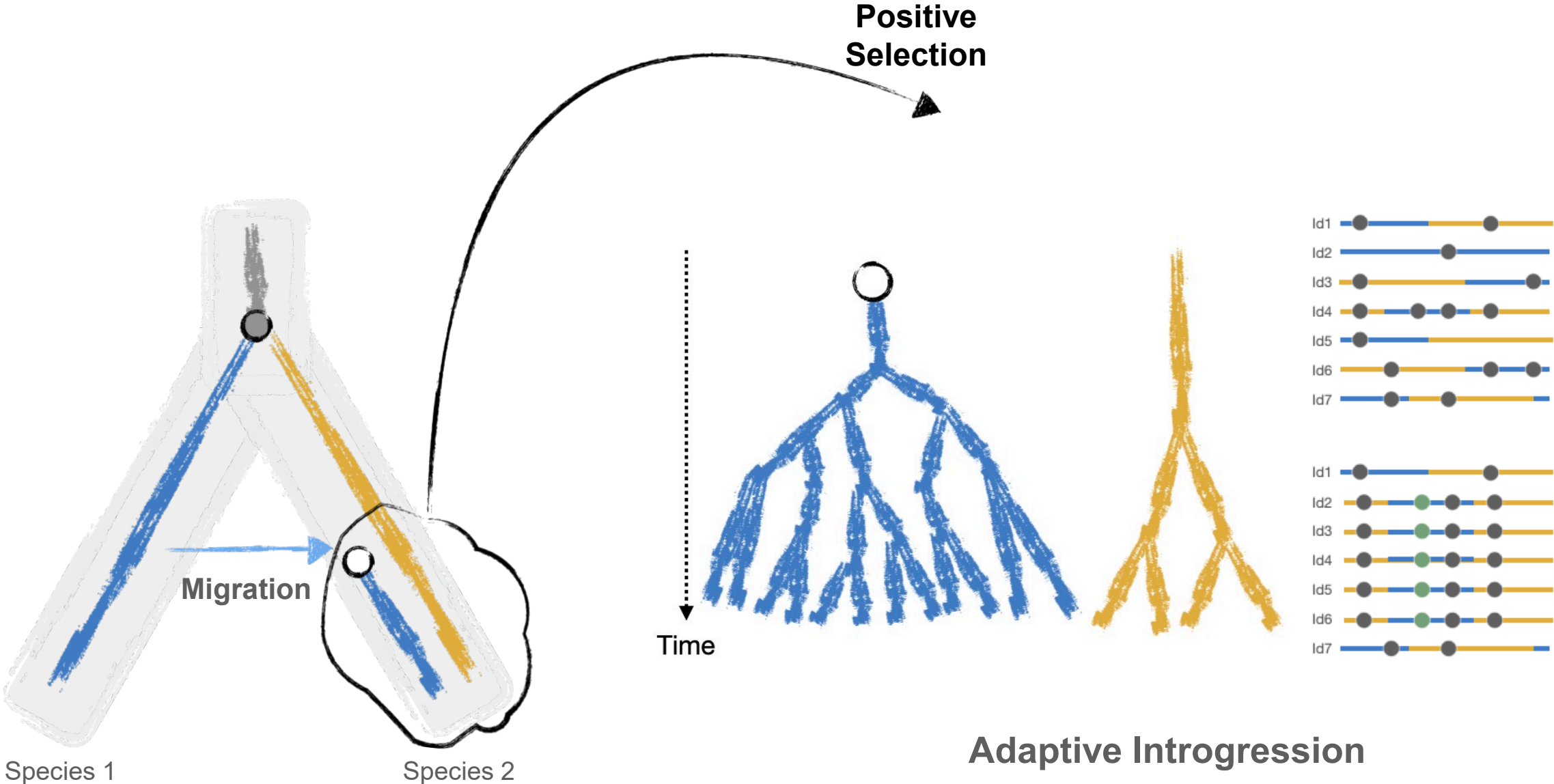


Species 2



Introgression

Adaptive Introgression



Mechanisms of human regeneration?



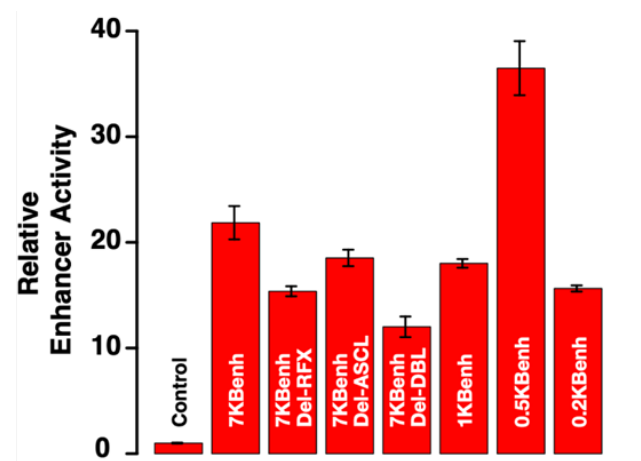
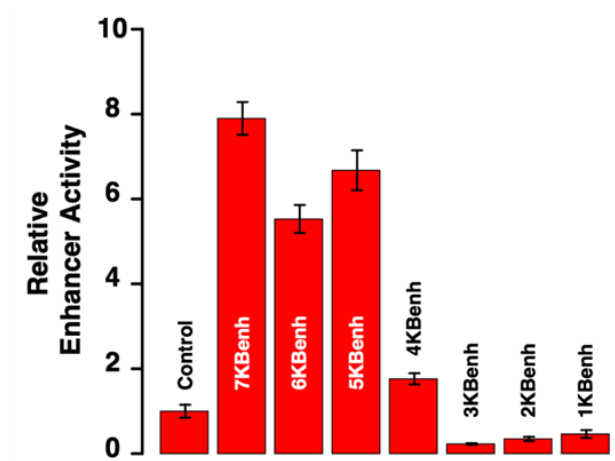
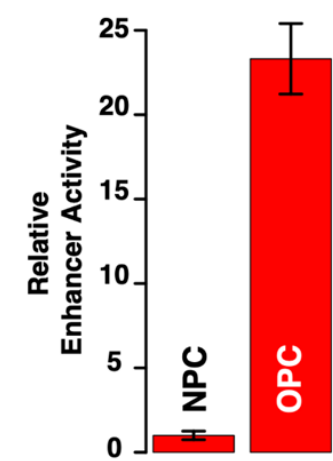
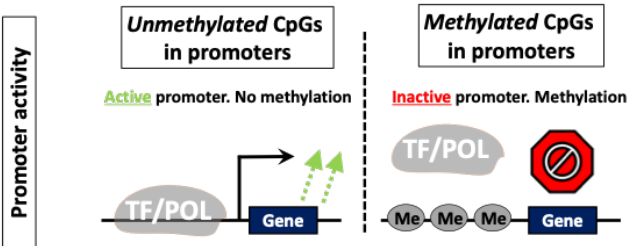
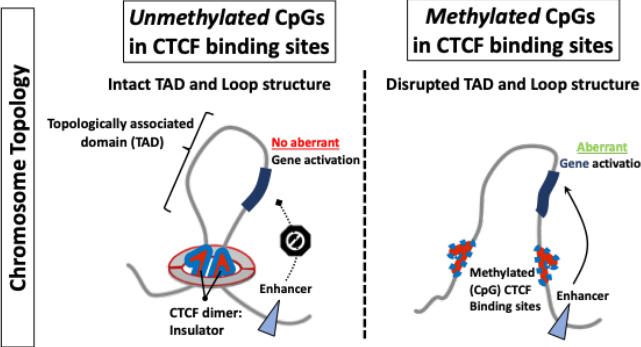


Harriet Wu X)



Rahme Lab
CANCER EPIGENETICS



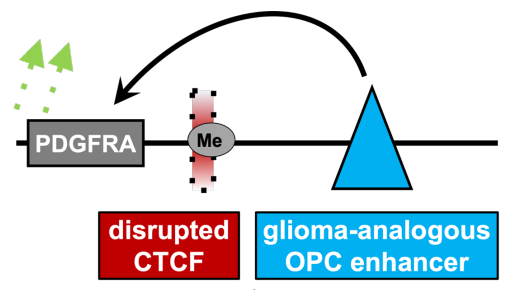


Approach

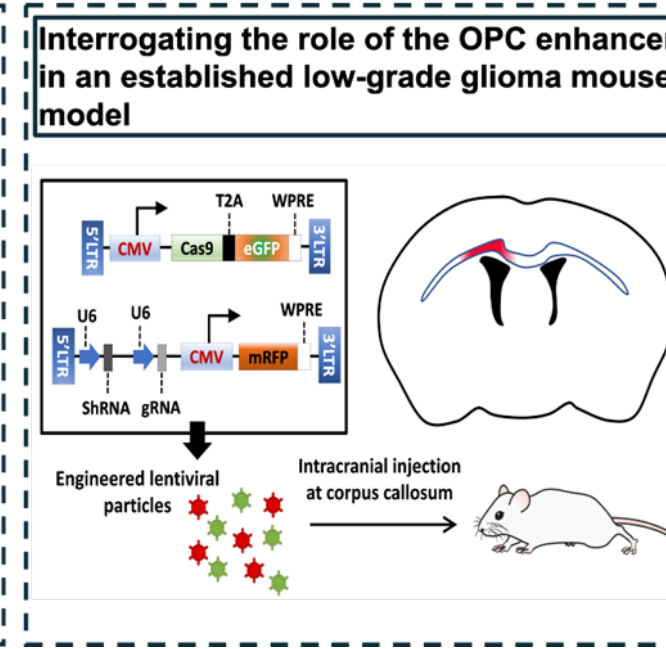
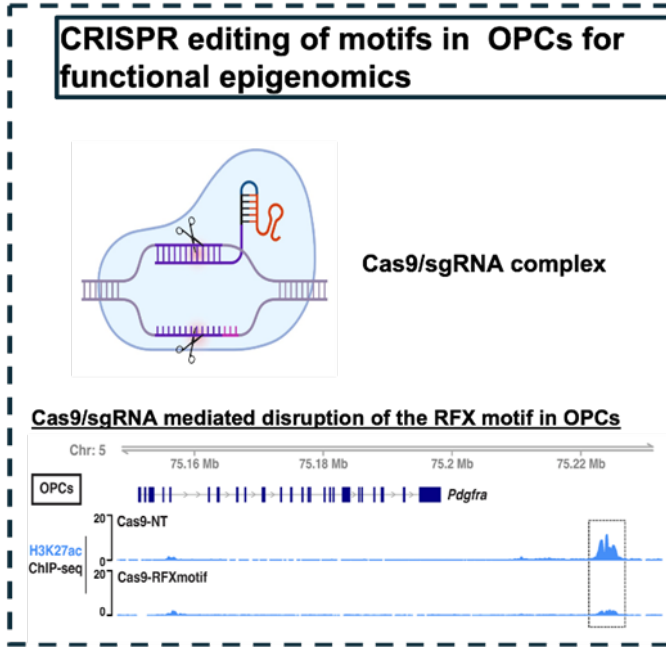
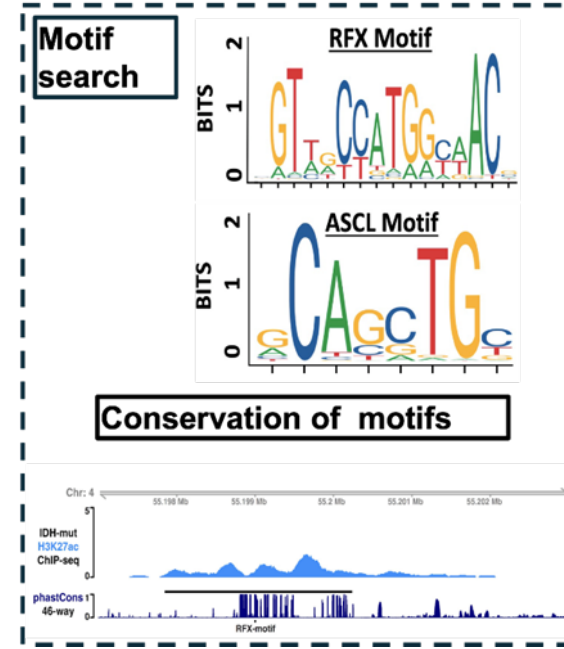
Motif Discovery

Functional epigenomics in vitro

Functional epigenomics in vivo



Aim 1: Determine the regulatory network that drives the critical enhancer
Aim 2: Examine the role of the critical enhancer in an established mouse model of diffuse glioma



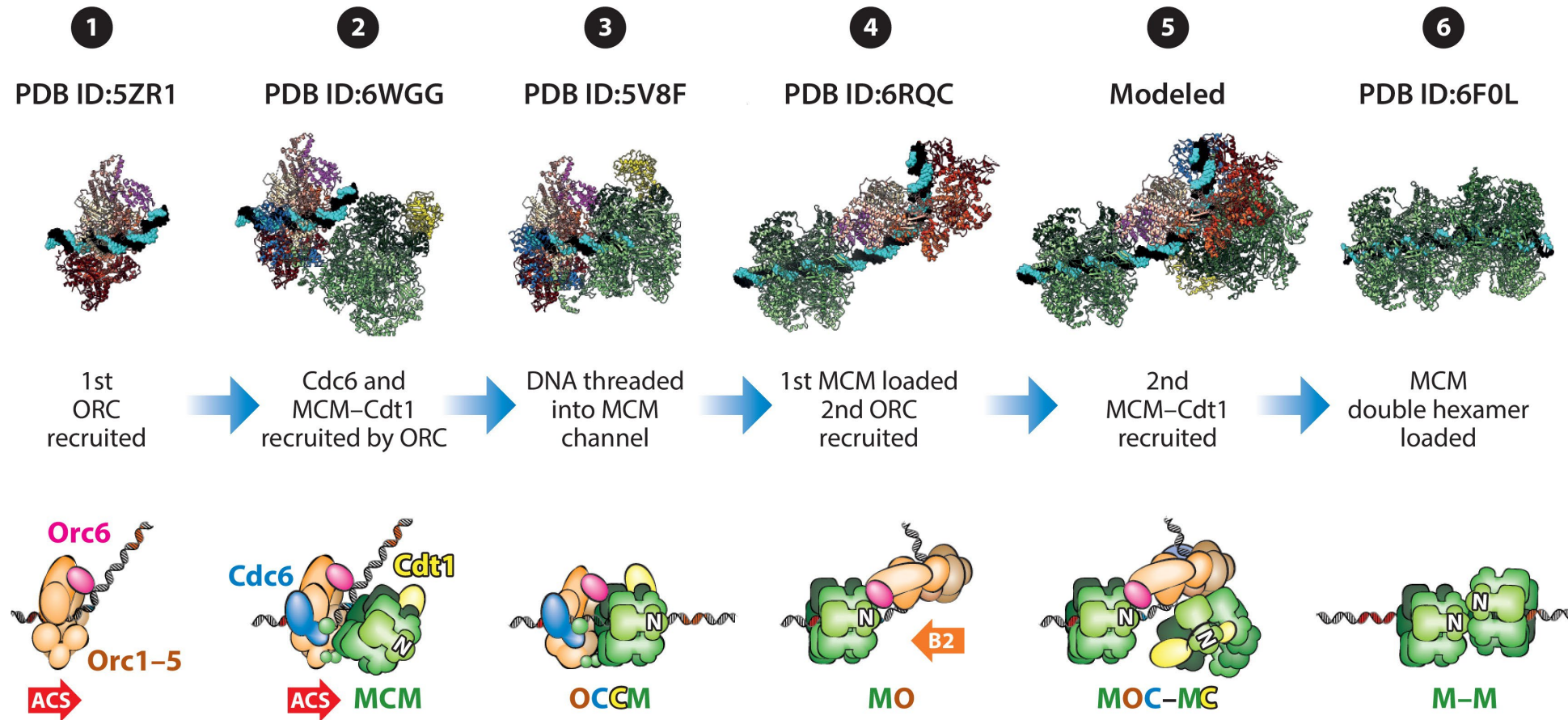


Dynamics of DNA Replication in *Yarrowia lipolytica*

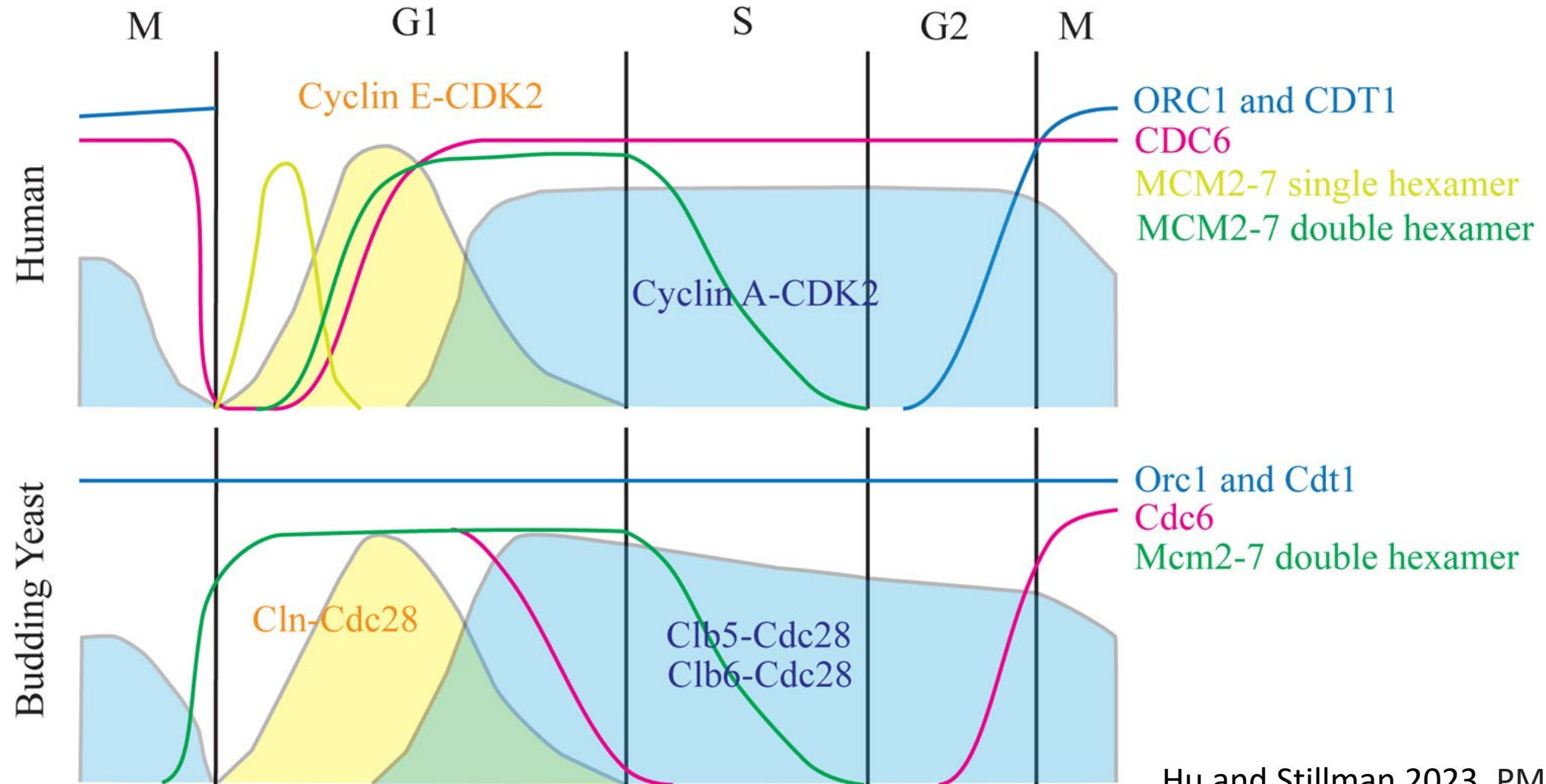
Kim Hane
Speed Science 2024
Stillman Laboratory



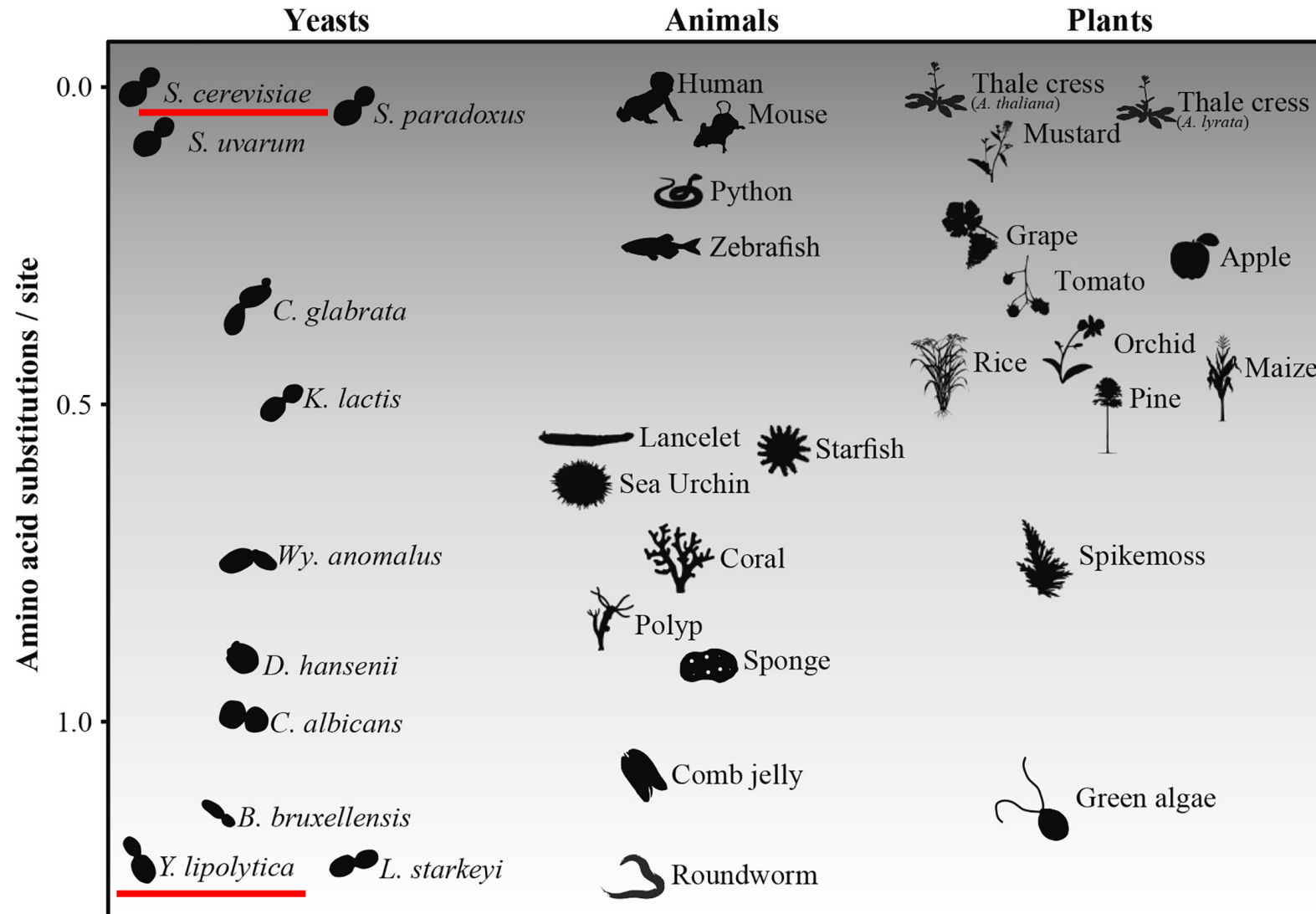
Initiation of DNA Replication in Eukaryotes

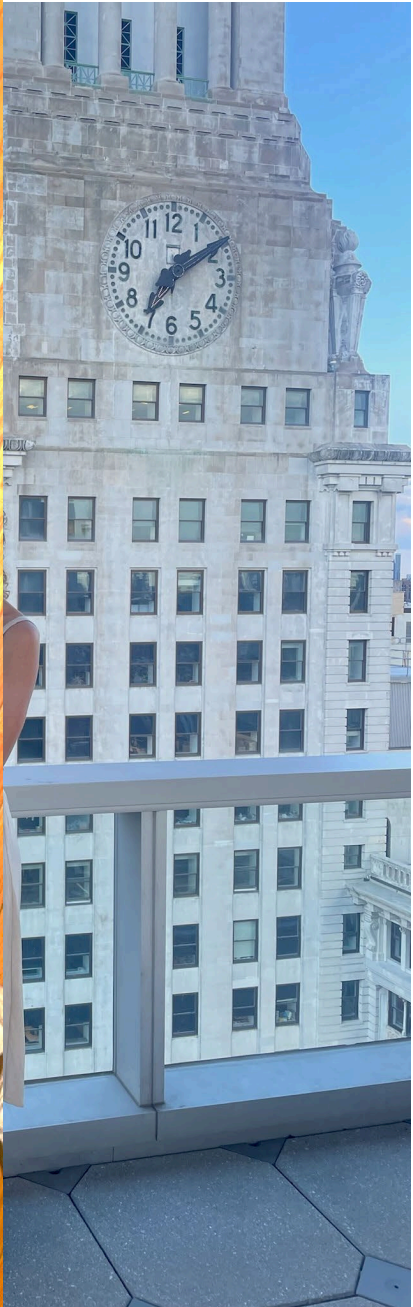
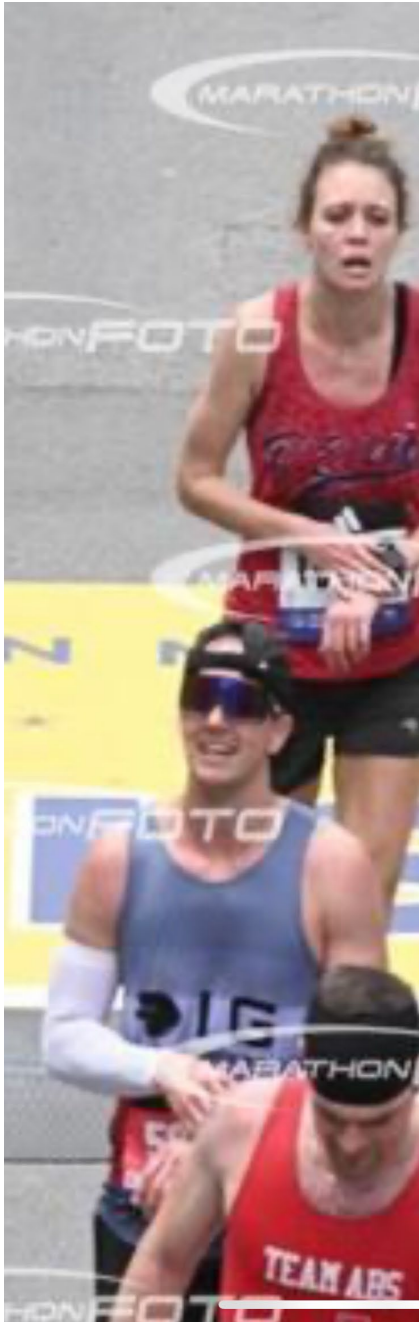


The Regulation of ORC in the Cell Cycle Differs Between Eukaryotes



Yarrowia lipolytica is Evolutionarily Far from *cerevisiae*

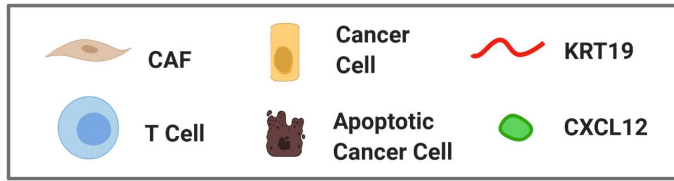




T Cell Exclusion in Pancreatic Ductal Adenocarcinoma (PDA)

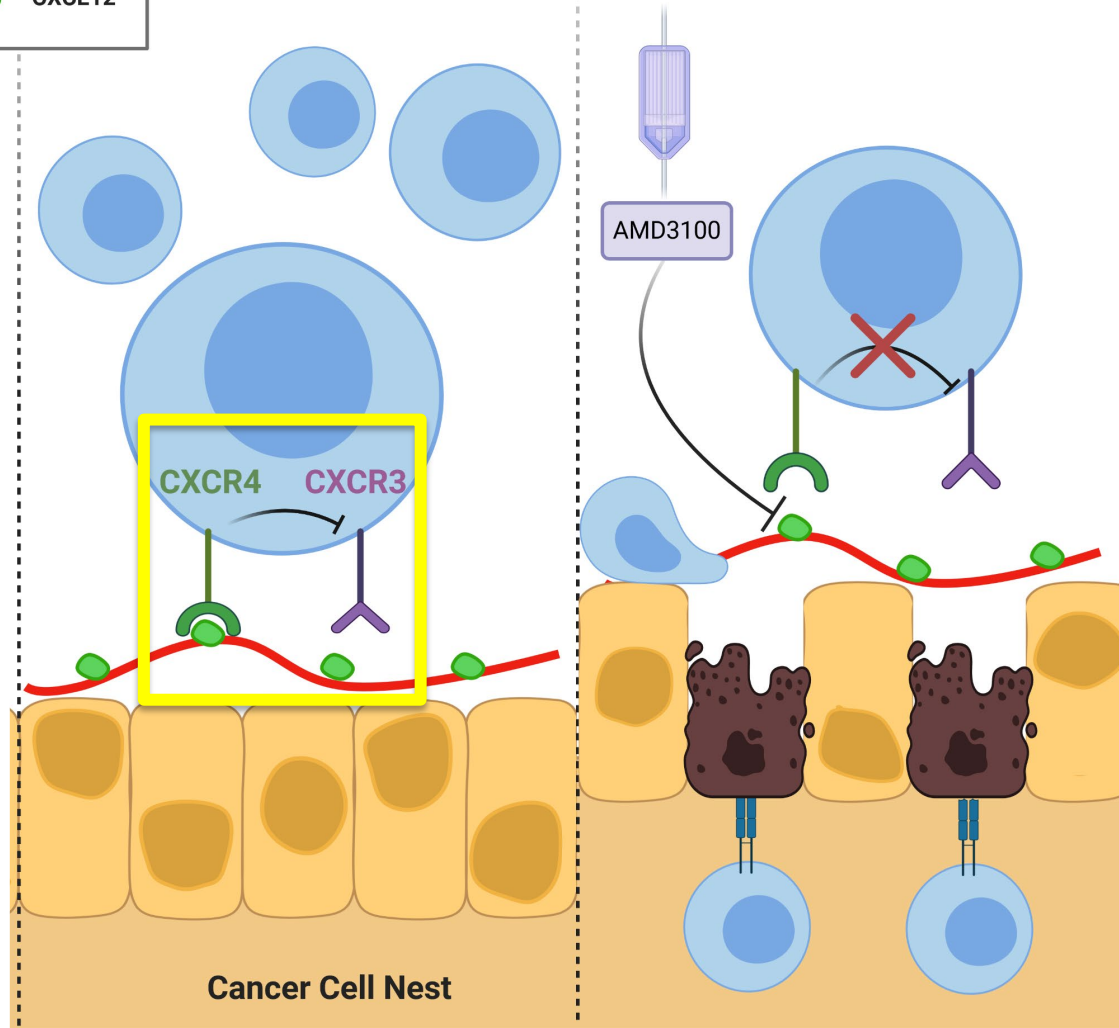
1. T cells are unable to enter cancer cell nests
2. The cancer is able to grow and thrive

How?



Tumor Periphery

- PDA is coated with CXCL12 and Keratin 19
- CXCL12 interacts with T cells by binding to their CXCR4 receptors
- This interaction inhibits CXCR3, blocking migration into the cancer nest



Gene-Specific Antisense Oligonucleotide Therapy for Diffuse Midline Glioma



Lucia Yang
Speed Science 2024
PI: Adrian Krainer



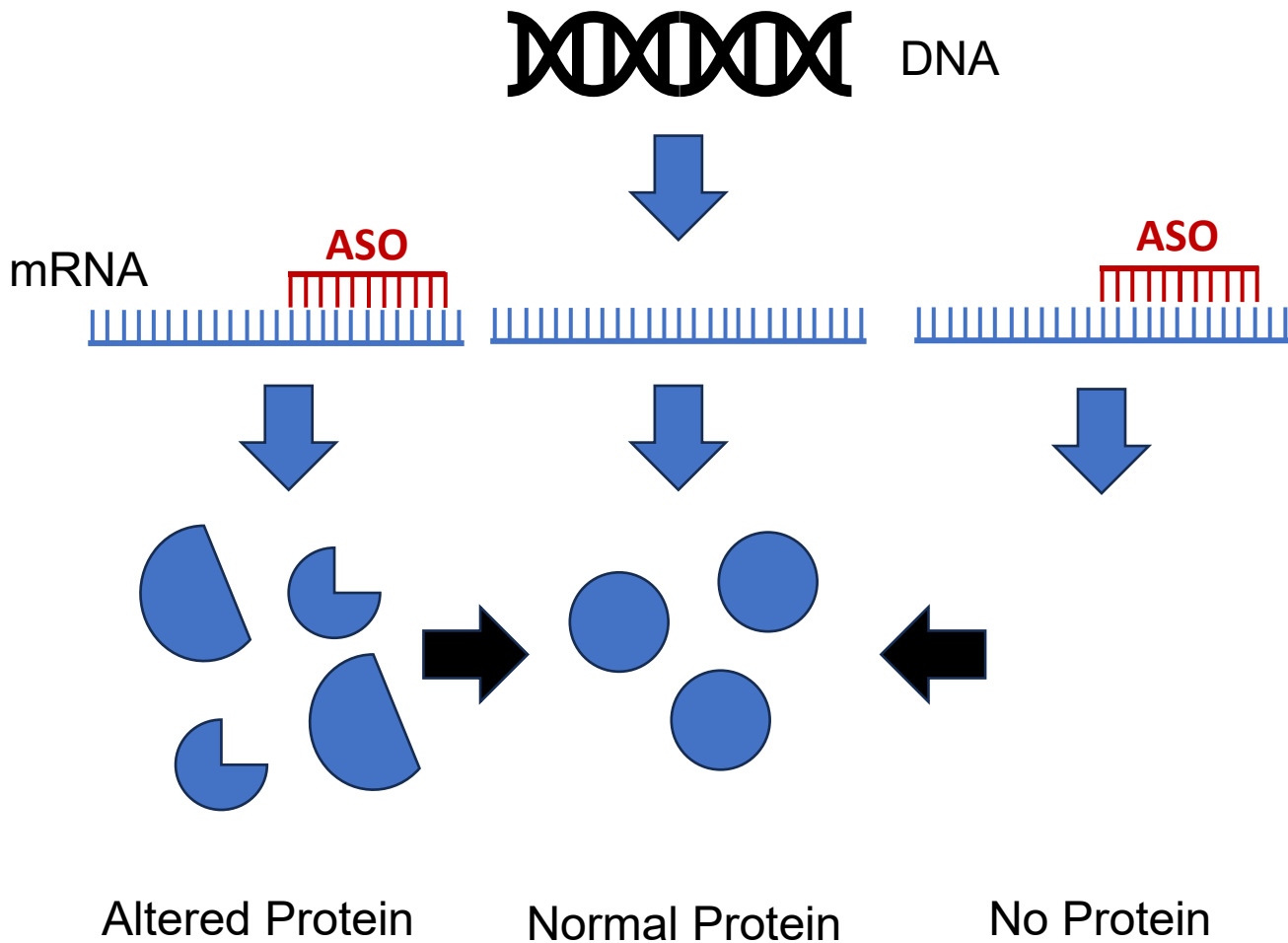
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Laboratory

The **Krainer Lab** is interested in:

1. Mechanisms of RNA processing, including splicing
2. Applying the above to therapy development for genetic diseases



Antisense Oligonucleotides (ASOs)



...as potential therapies for different diseases

- ASOs have shown potential in many diseases (e.g. spinal muscular atrophy, cystic fibrosis, and now a variety of cancer types)

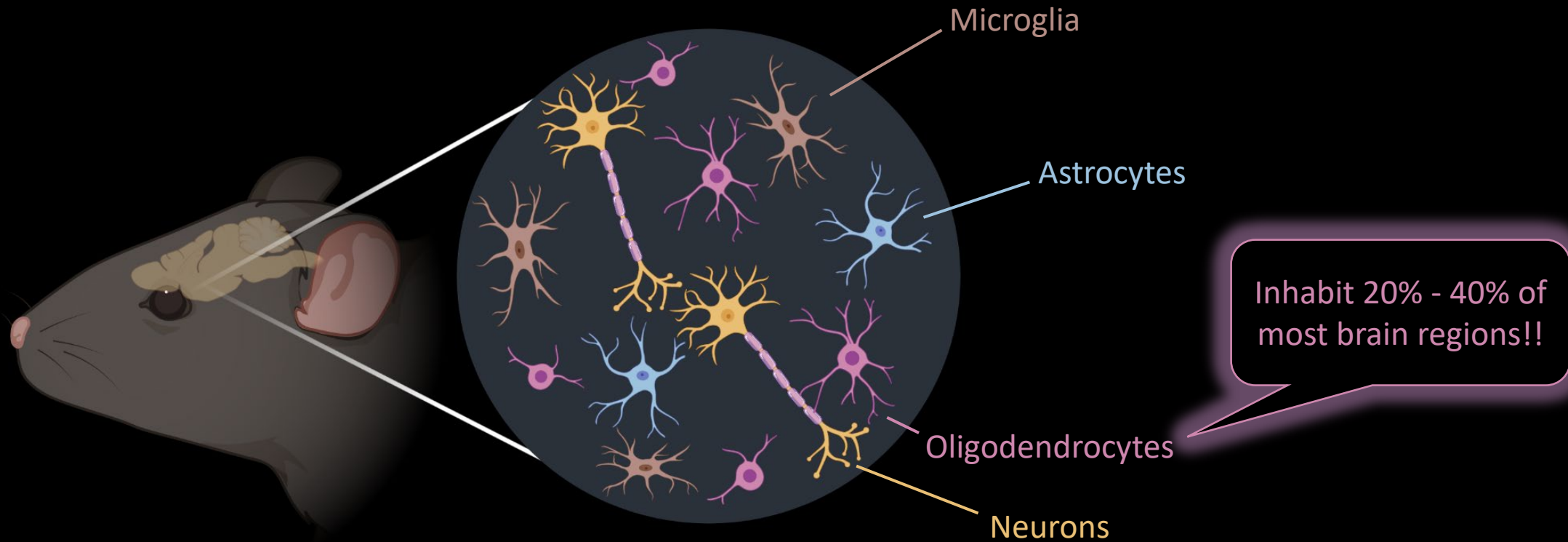
My project then aims to...

- Design and apply ASOs to target the causative mutation for a class of pediatric high-grade gliomas

krainerlab.cshl.edu

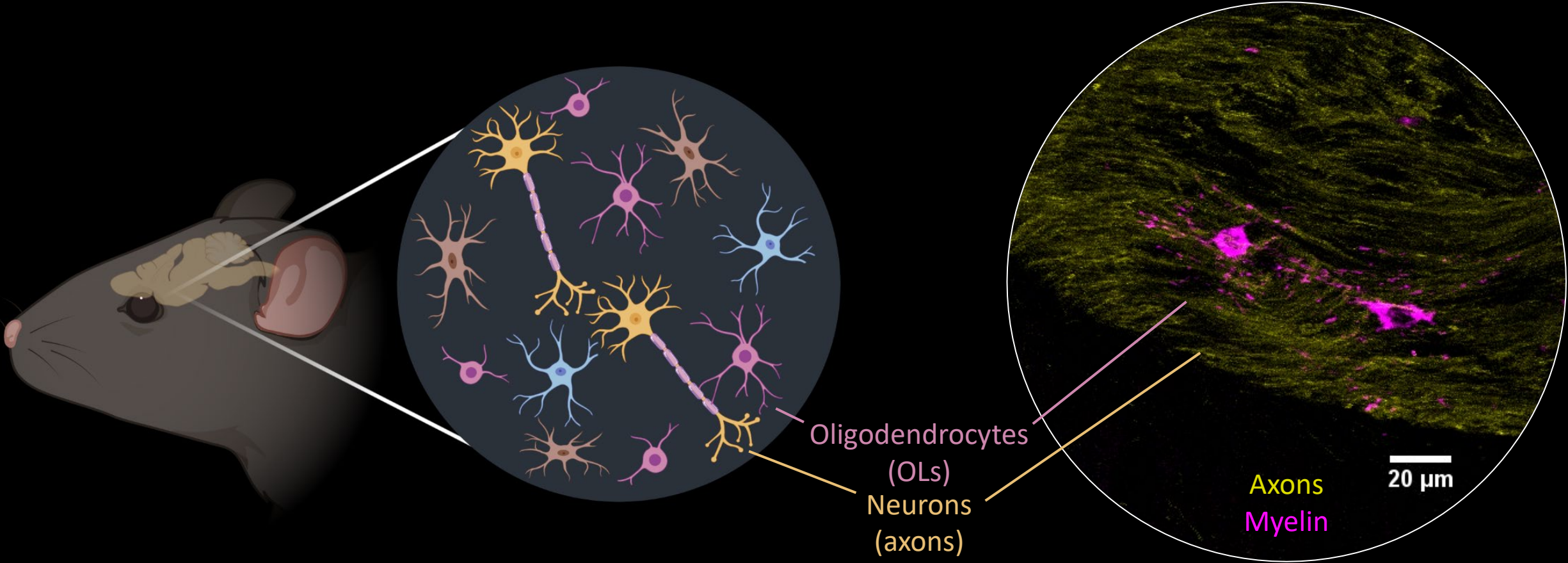


Colognato Lab Oligodendrocytes

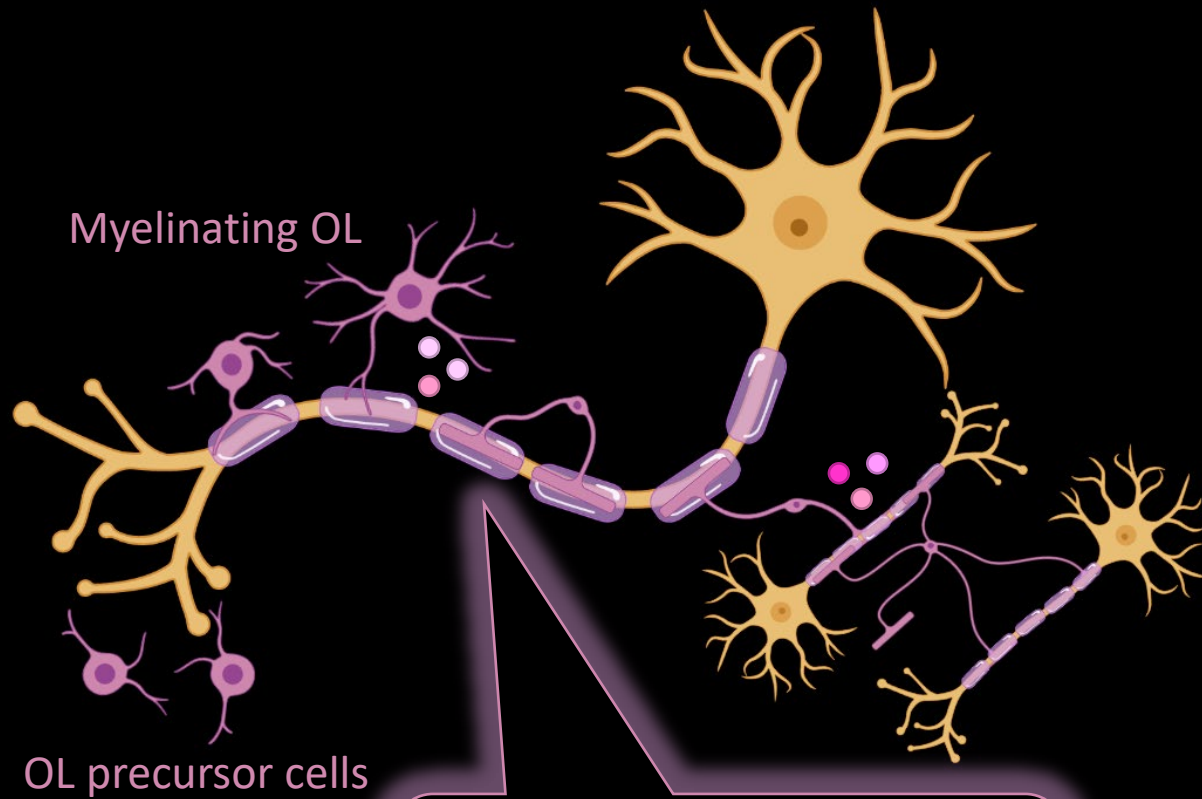


Maryam (Minnie) Azmi
5th year candidate
Advisor: Dr. Holly Colognato

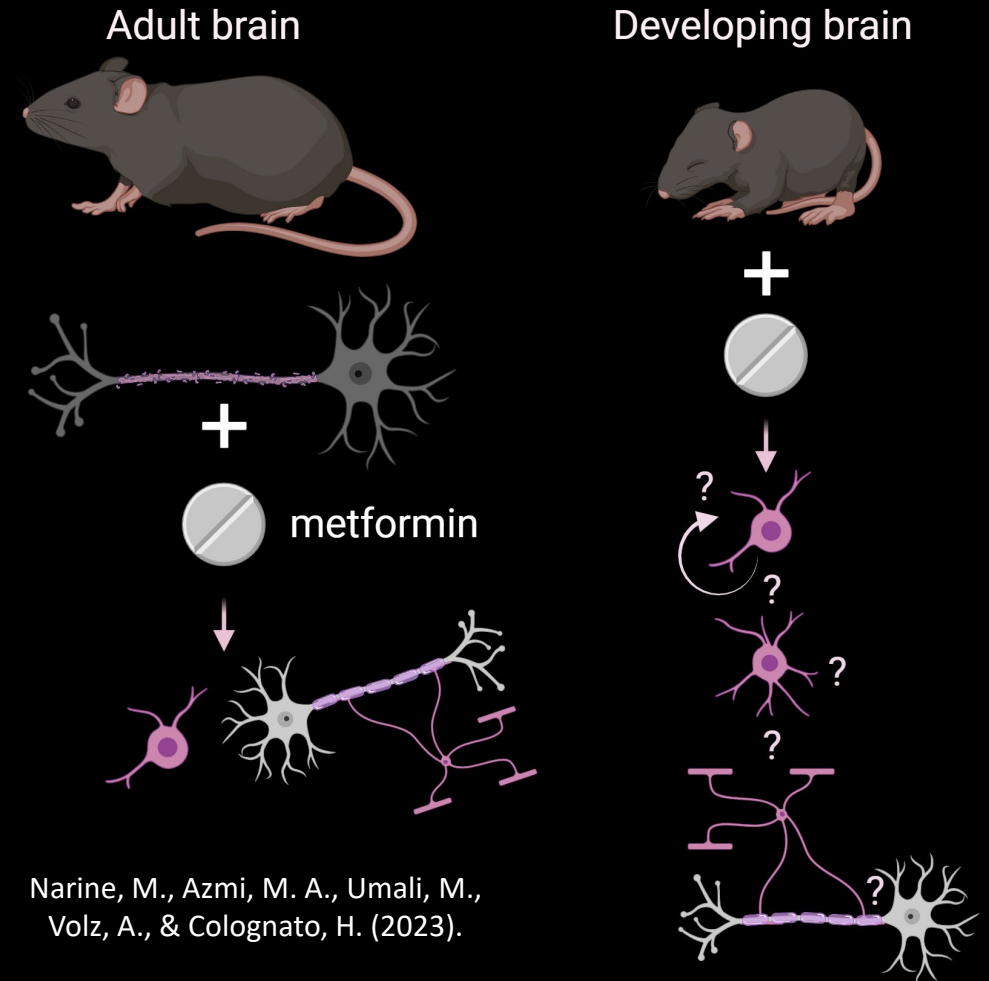
Oligodendrocytes (OLs) extend and wrap their processes (arms) around multiple axons



OLs myelinate axons and aid neuronal survival, differentiation, and plasticity (refinement of neurites)



Myelinated nerve cell can transmit electrical signals 100x faster than an uncoated nerve!



Adaptive myelination continues throughout life!



Nail art on me and my friends 🖌️



Legend of Zelda 🎮💖



Improving cognition



Embarrassing amount of anime





The Veeramah Lab

Contemporary evolution in three-spined stickleback in Alaska

*(How does **rapid** local adaptation happen?)*

Alexander Kwakye

Advisor: Krishna Veeramah

Veeramah Lab

- Analyses of temporal genomic data to answer specific evolutionary questions

PNAS

RESEARCH ARTICLE | GENETICS

OPEN ACCESS

The role of emerging elites in the formation and development of communities after the fall of the Roman Empire

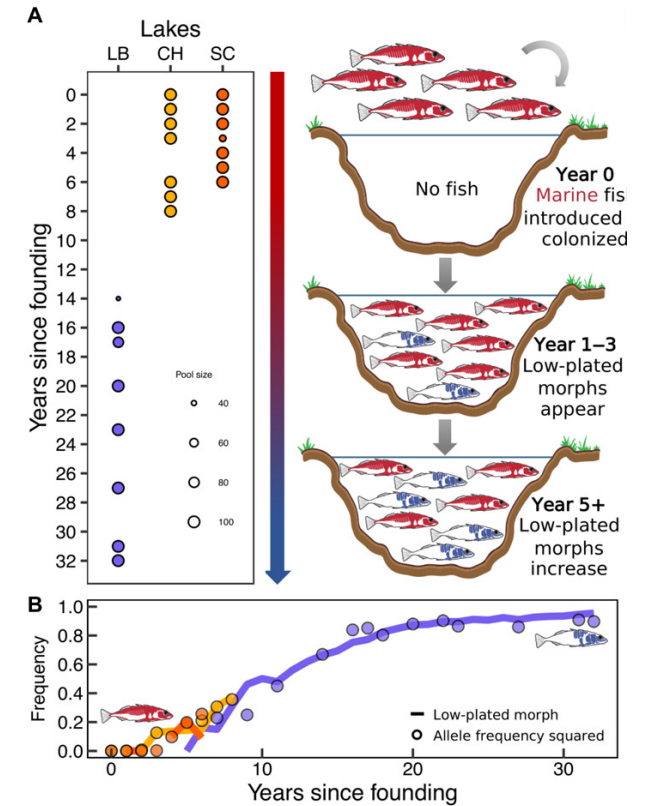
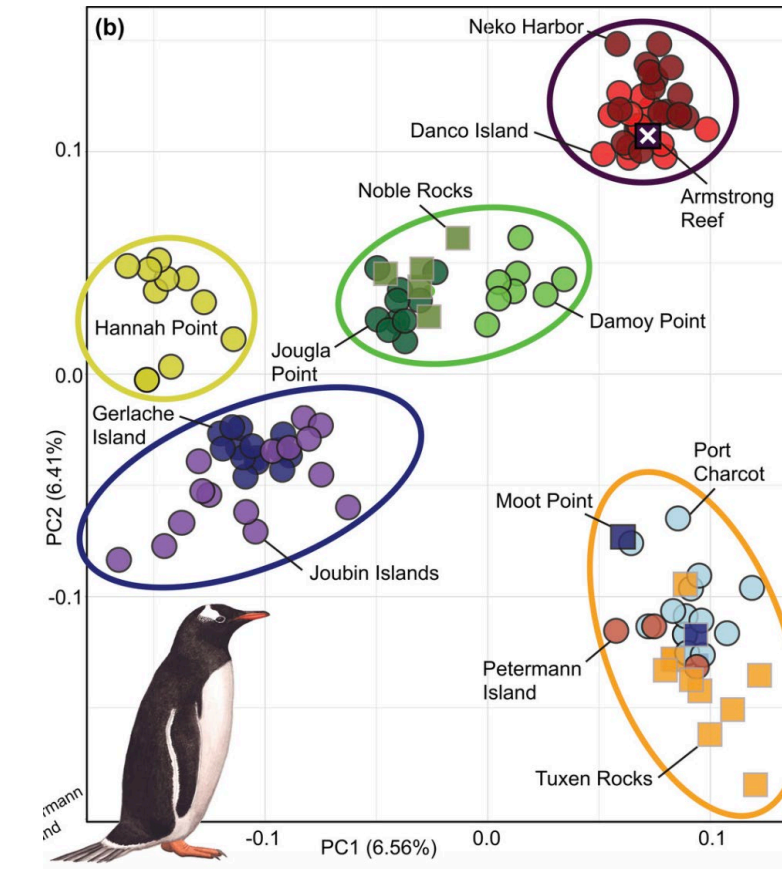
ORIGINAL ARTICLE

MOLECULAR ECOLOGY | WILEY

SCIENCE ADVANCES | RESEARCH ARTICLE

EVOLUTIONARY BIOLOGY

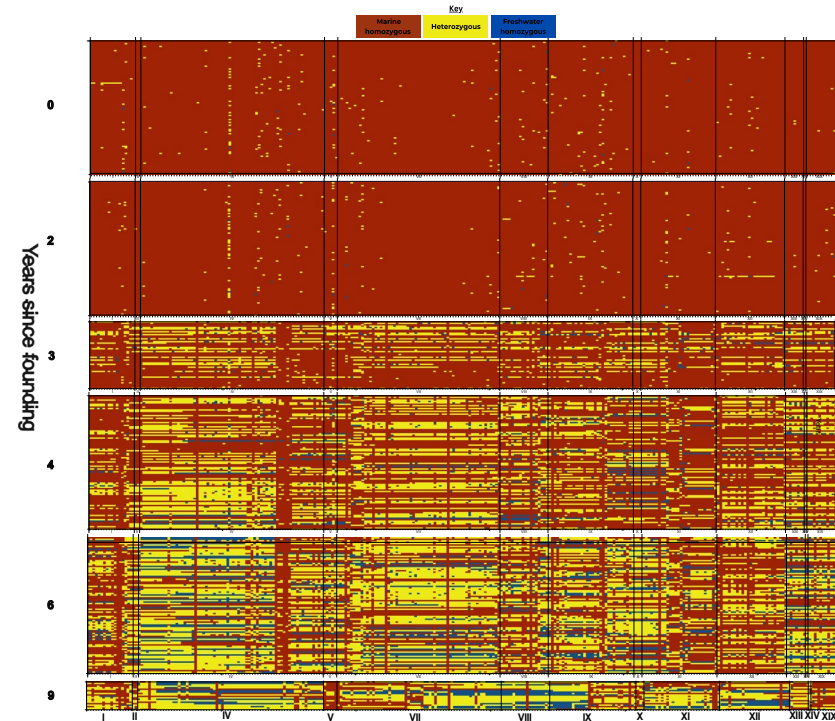
Predicting future from past: The genomic basis of recurrent and rapid stickleback evolution



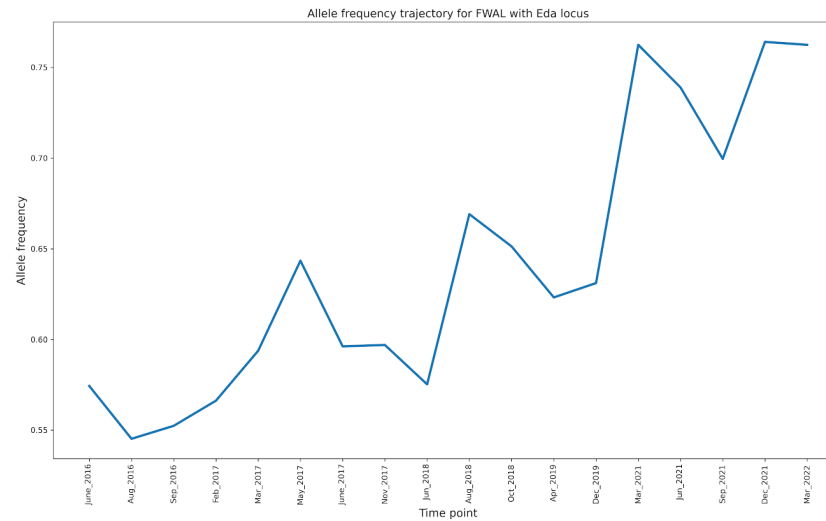
How does *rapid* local adaptation happen?

- Understand rapid adaptation in a forward-in-time manner

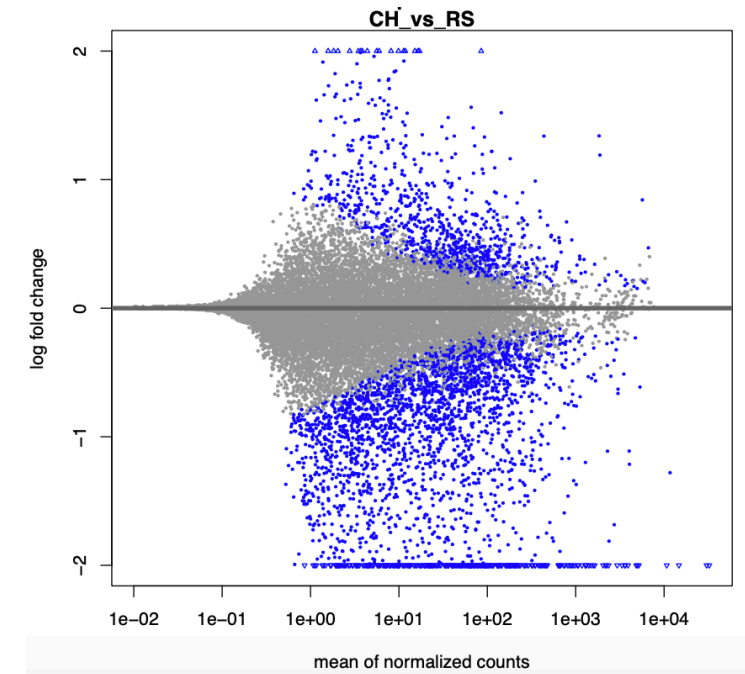
AIM 1



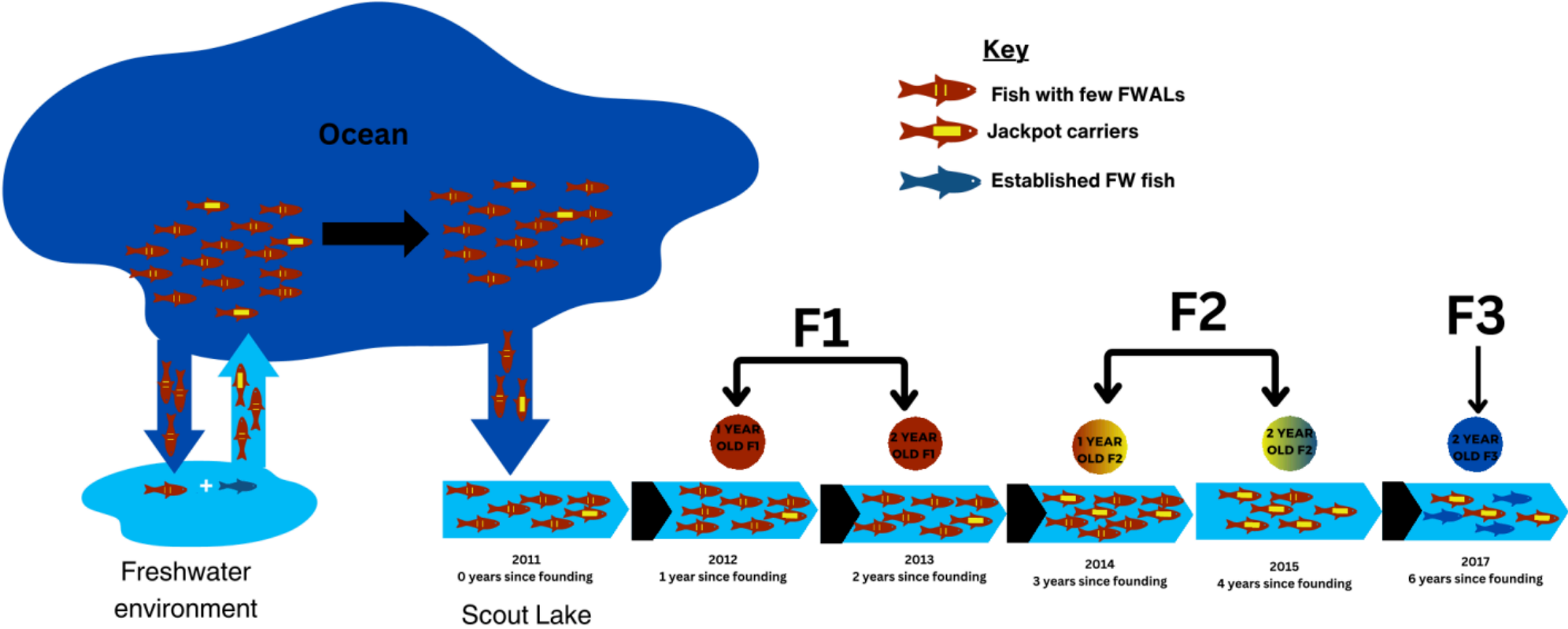
AIM 2



AIM 3



Model of rapid freshwater adaptation

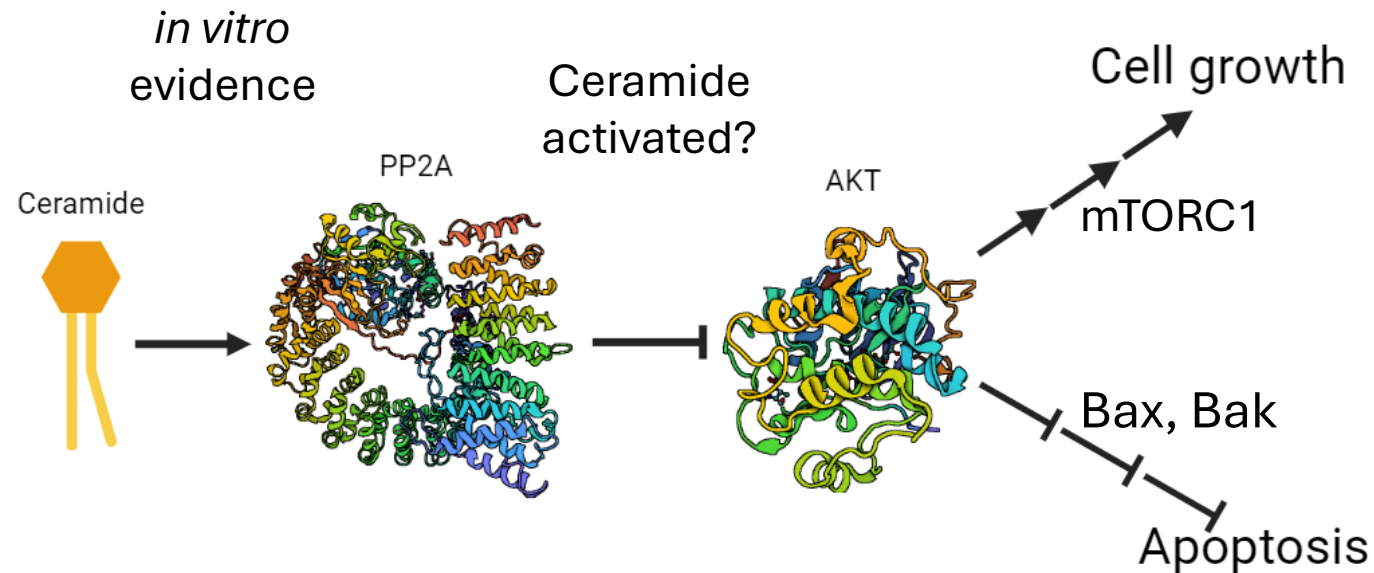


Speed Science

Sam Chiappone

9/4/24

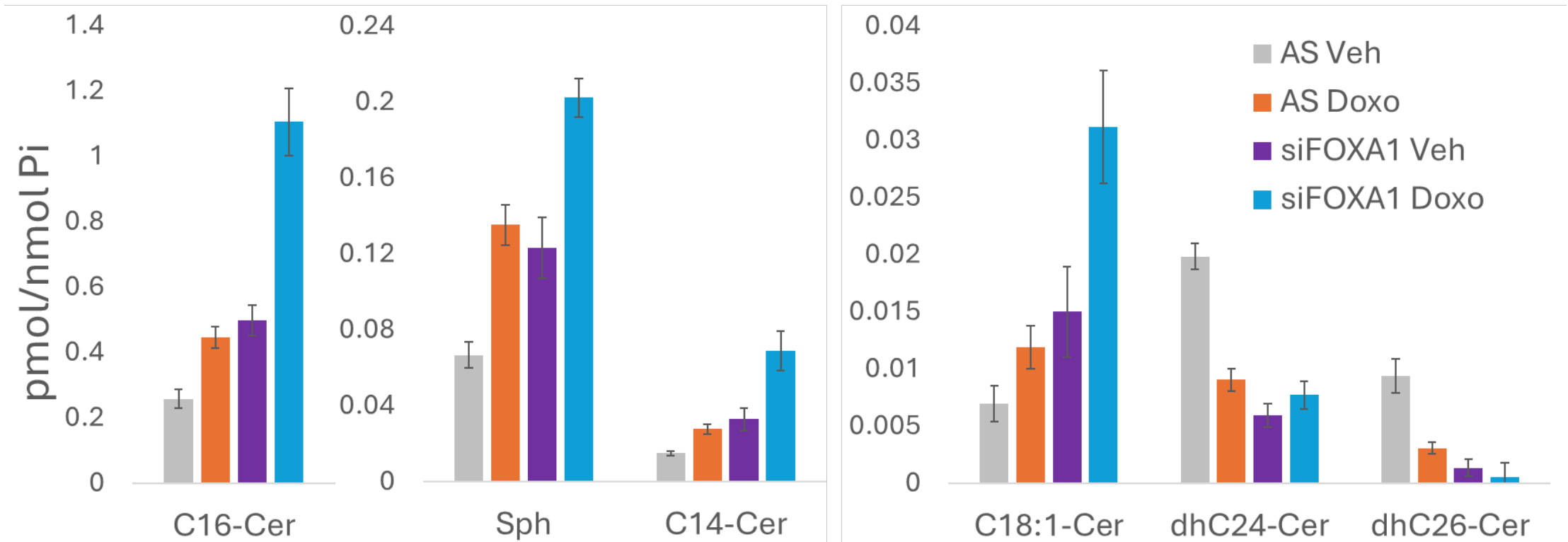
Ceramide, a bioactive sphingolipid (SL), is known to cause apoptosis, but the particulars of how such ceramide-induced apoptosis is mediated remain elusive

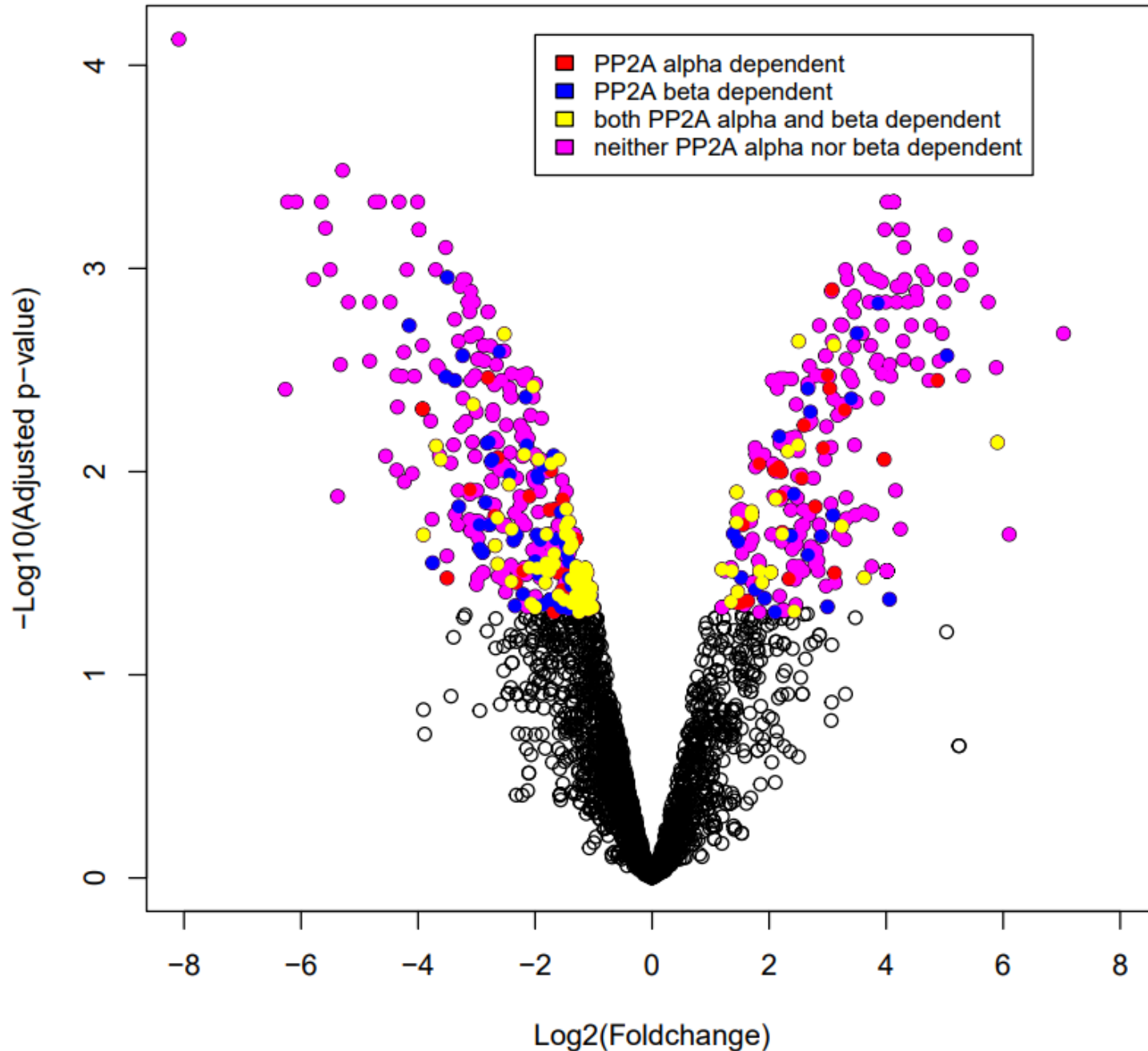


Two major questions about sphingolipids (SL):

- What regulates SL levels?
- What does ceramide regulate in order to cause cell cycle arrest and/or apoptosis?

So far, I have discovered that FOXA1 controls the steady-state levels of SL in breast cancer





What does ceramide regulate?

Preliminary results indicate that there are a number of PP2A-dependent dephosphorylation events in response to ceramide, including cell-cycle and apoptosis related ones

Nelson Gautier van der Velden Lab



I scream... You scream



+ Follow



ABC News

CDC warns not to 'kiss or cuddle your turtle' as salmonella outbreak hits 11 states

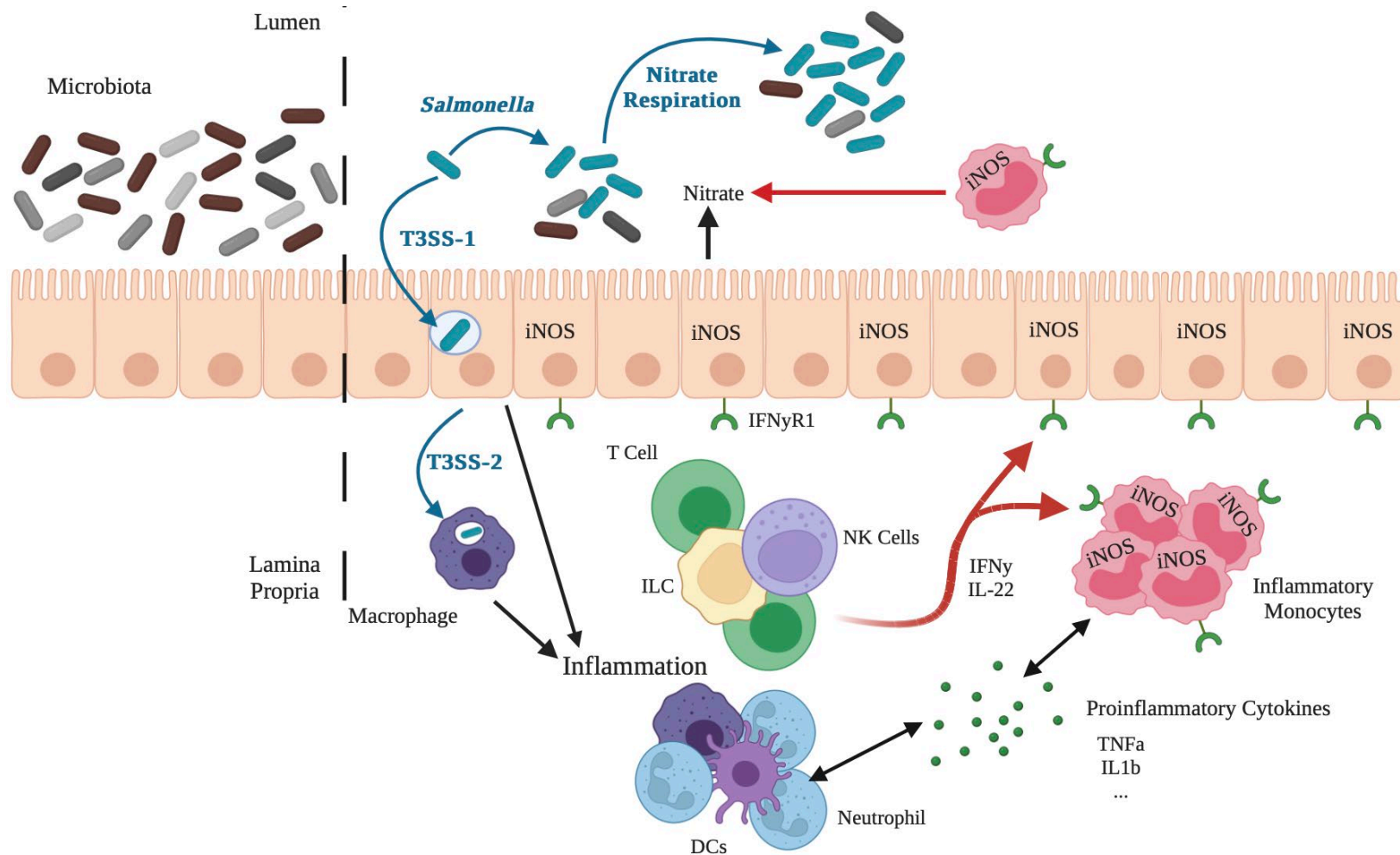
breaks in: Ground beef, onions, chicken

Salmonella enterica serovars are responsible for a combined global toll of approximately 1 million deaths annually.

Recalled cucumbers in salmonella outbreak sickened 449, CDC says



Model of how Inflammatory Monocytes may promote nitrate-dependent STm growth

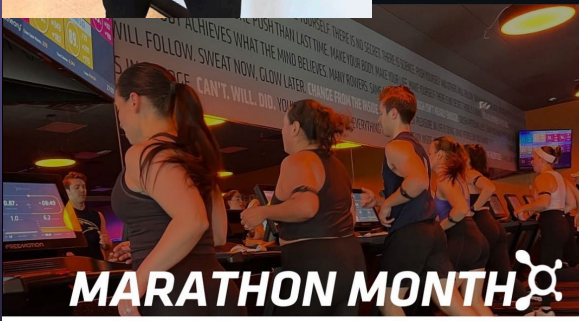


- Specifically, I am interested in how IMs contribute both **directly** and **indirectly** to the generation of host-derived nitrate and the subsequent expansion of salmonella in the lumen of the inflamed intestine.

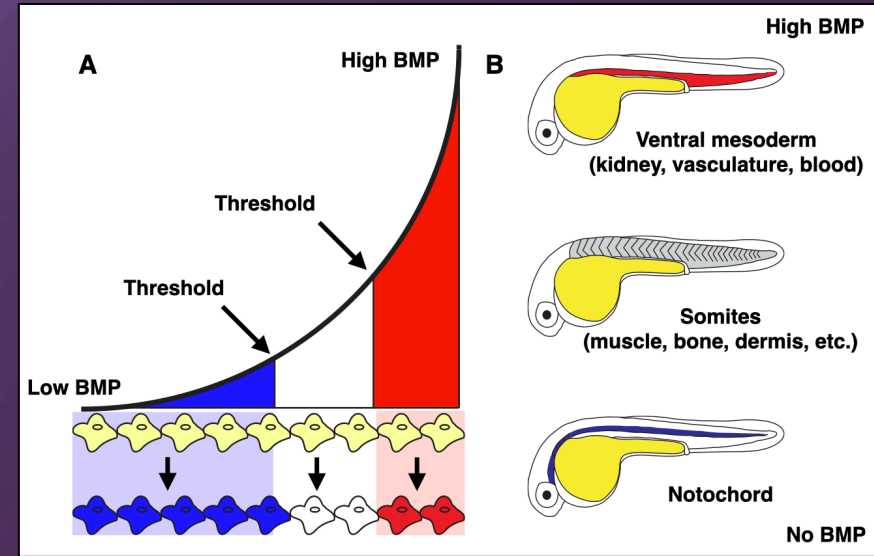
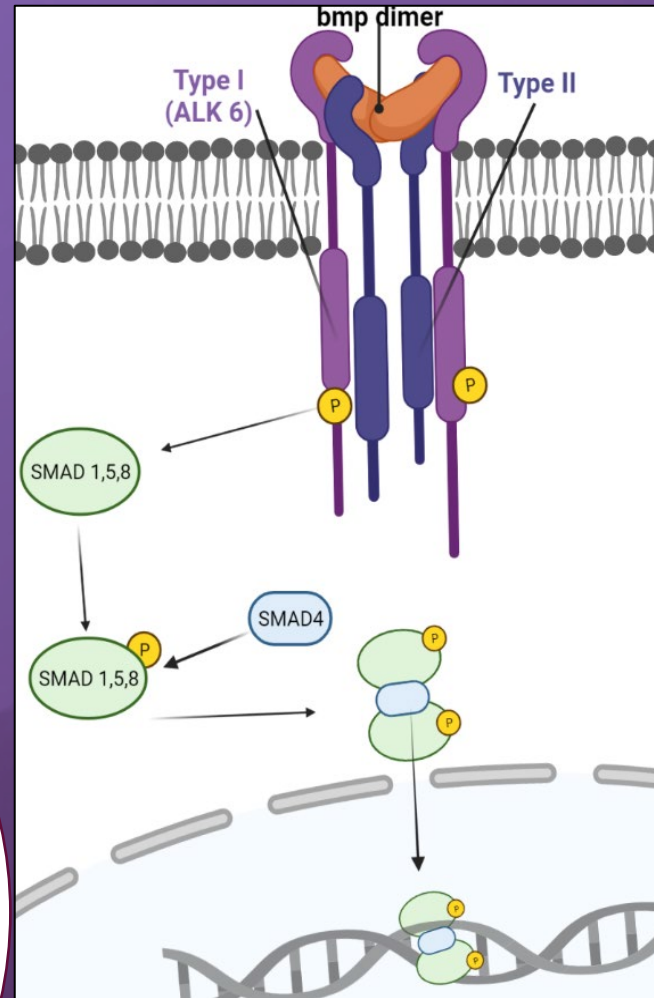
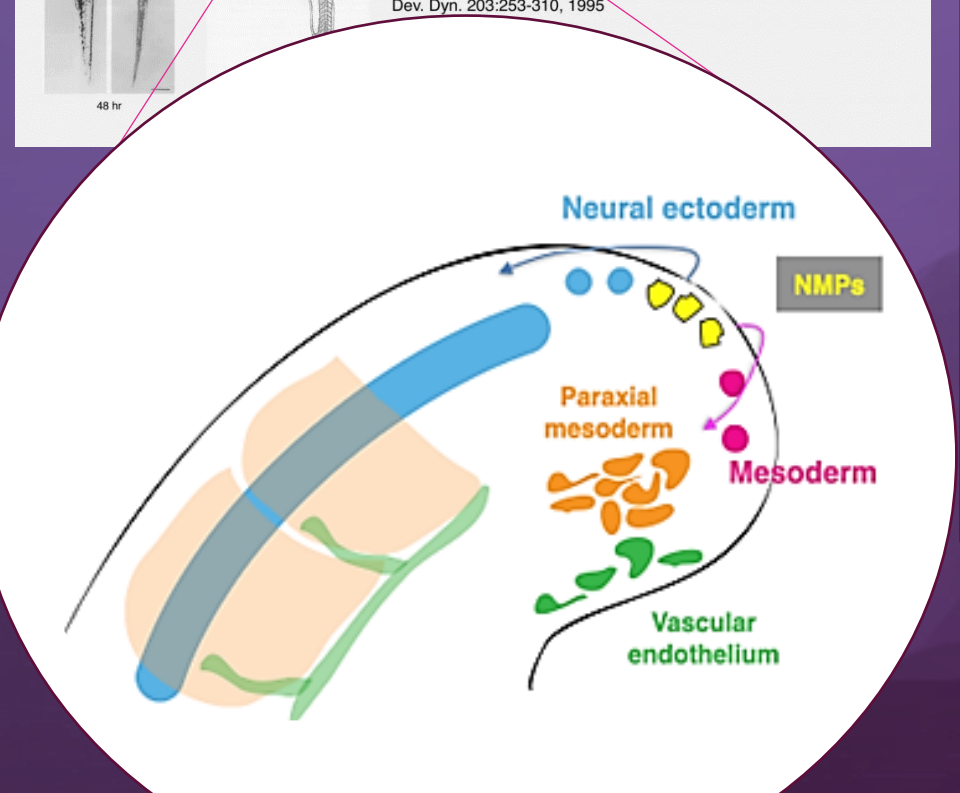
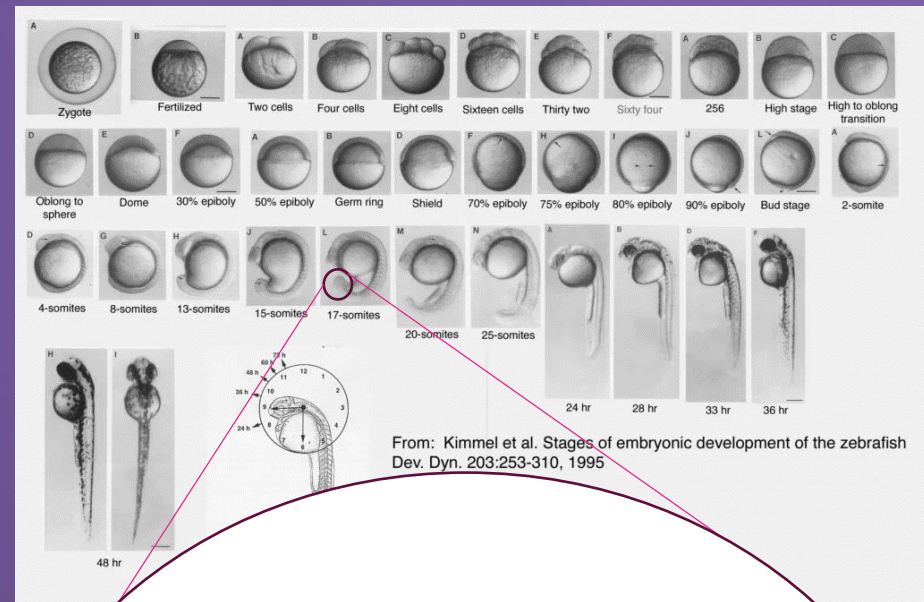
Interpreting Bone Morphogenetic Protein Gradients in Vertebrate Development

Courtney Tello

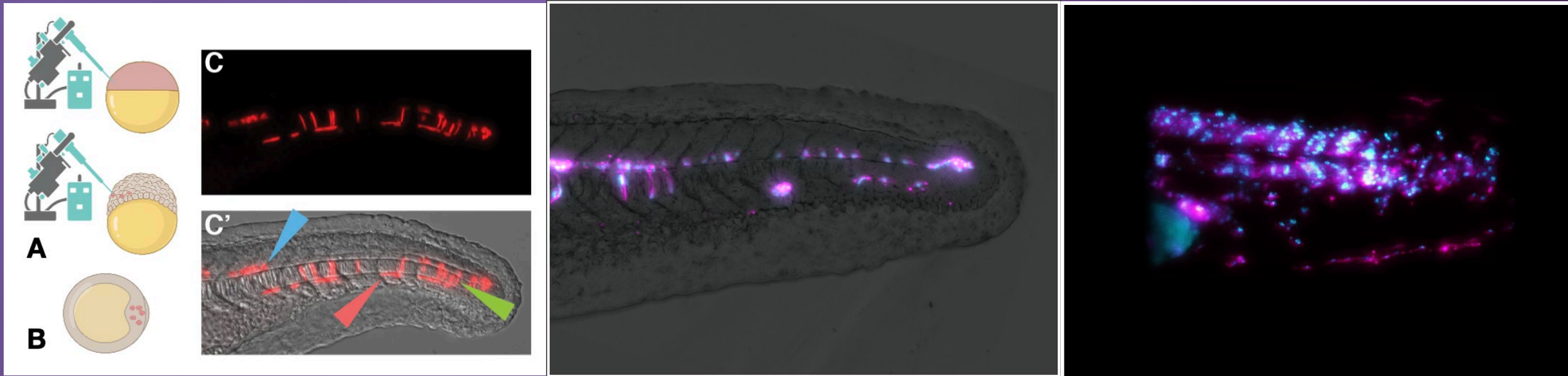
Martin Lab



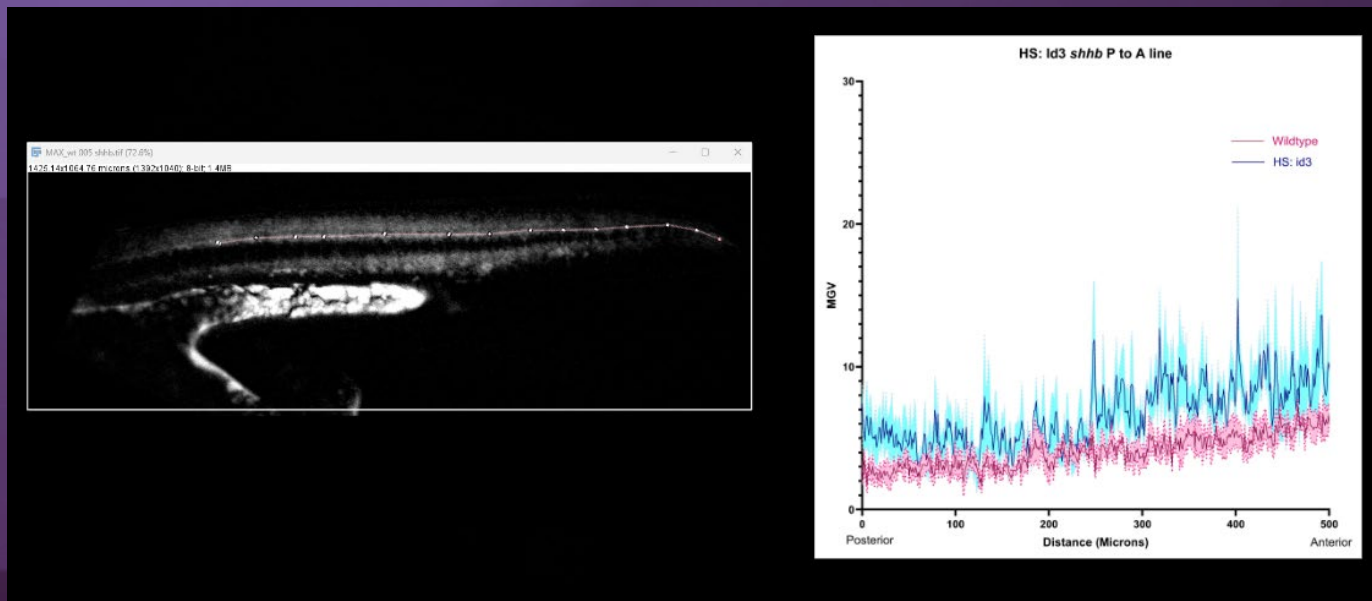
Vertebrate development consists of complex cell signal coordination



Utilizing transplantation techniques we can get a better understanding of how progenitor cells interpret Bone Morphogenetic Protein signal gradients *in vivo*



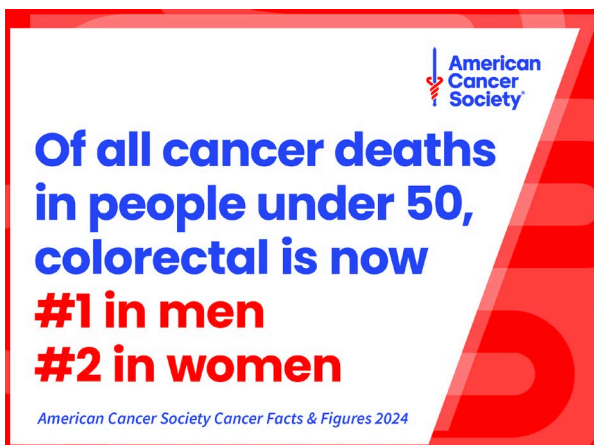
Row, R., et al., 2016



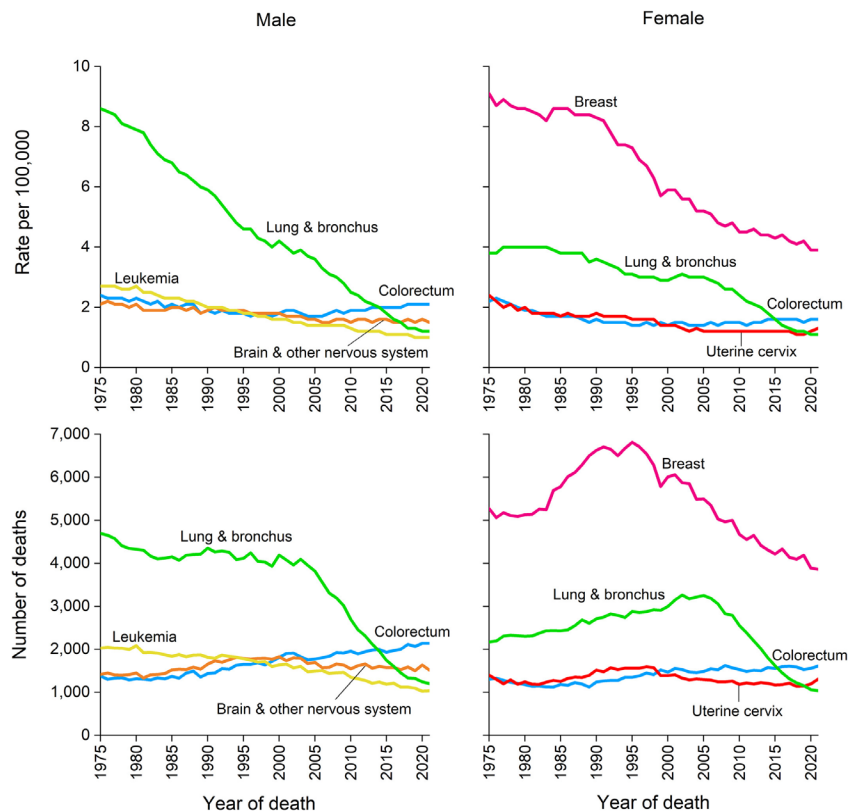
Microbial Regulation of Anti-tumor Immunity in Metastatic Colorectal Cancer

Charlie Chung
Beyaz lab

Concerning facts about colorectal cancer (CRC)



SEER stage	5-year relative survival rate
Localized	91%
Regional	73%
Distant	13%



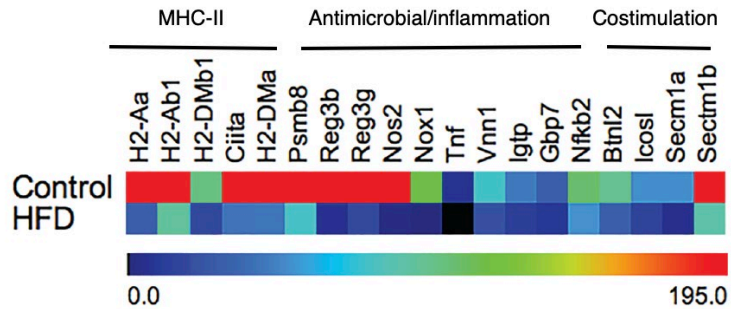
Knowledge gaps:

- *What makes metastatic CRC an incurable disease?*
- Immune evasion?*
- Lack of models that recapitulate human disease?*

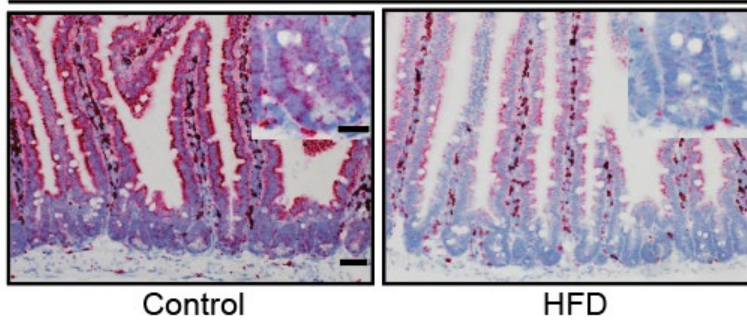
- *What causes the rise of CRC in young adults?*
- Diet?*
- Obesity?*
- Stress? Pollution? Microbiome dysbiosis?*

Microbial regulation of anti-tumor immunity in metastatic CRC

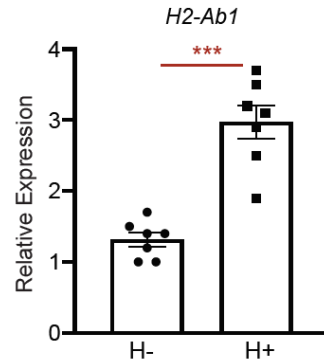
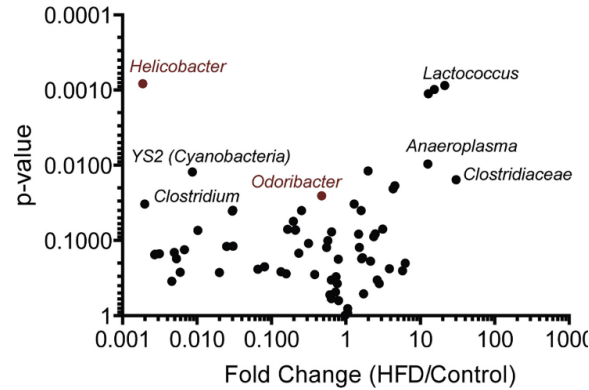
A pro-obesity HFD dampens MHC-II expression in ISCs



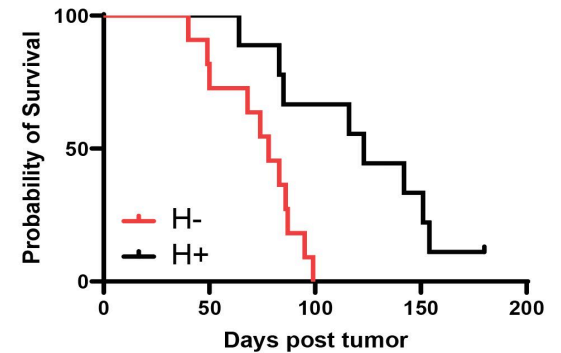
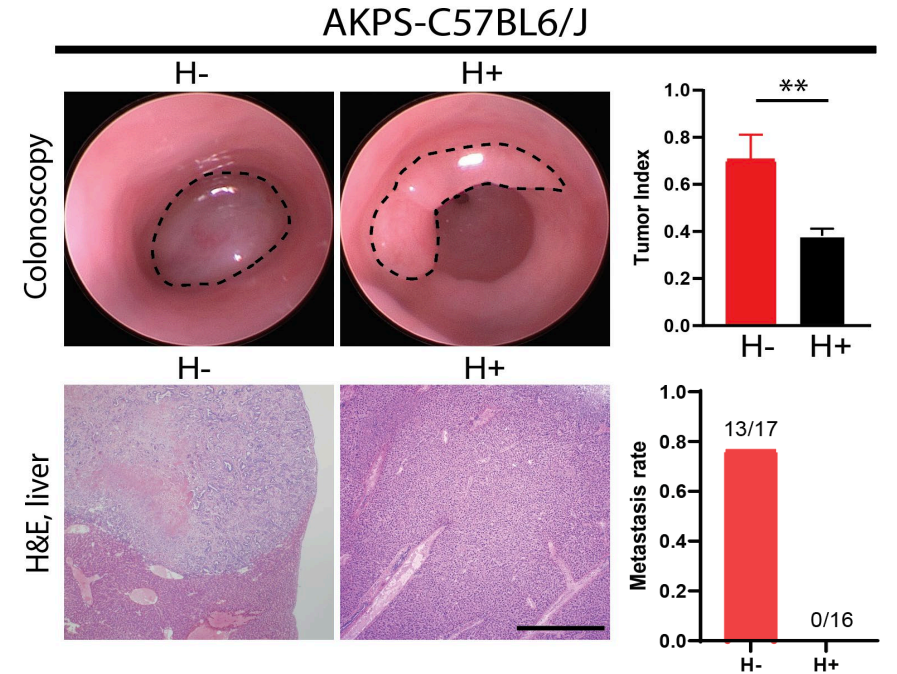
H2-Ab1 in situ hybridization



A pro-obesity HFD depletes helicobacter species in the gut



Helicobacter species in the gut restricts tumorigenesis



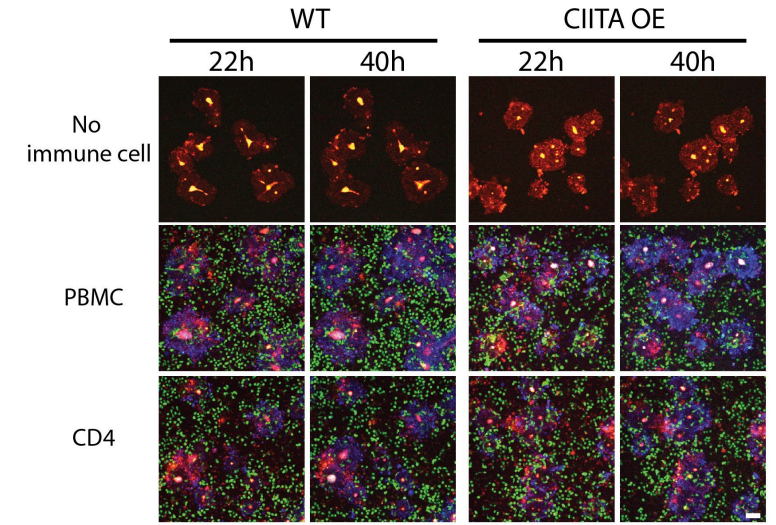
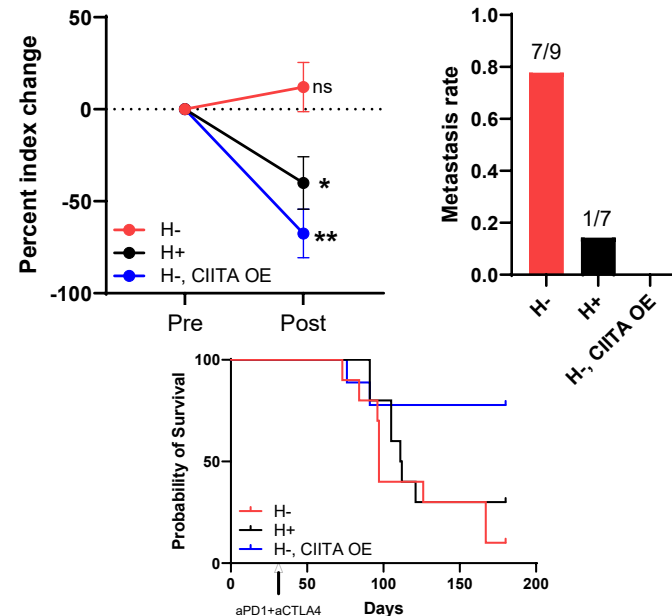
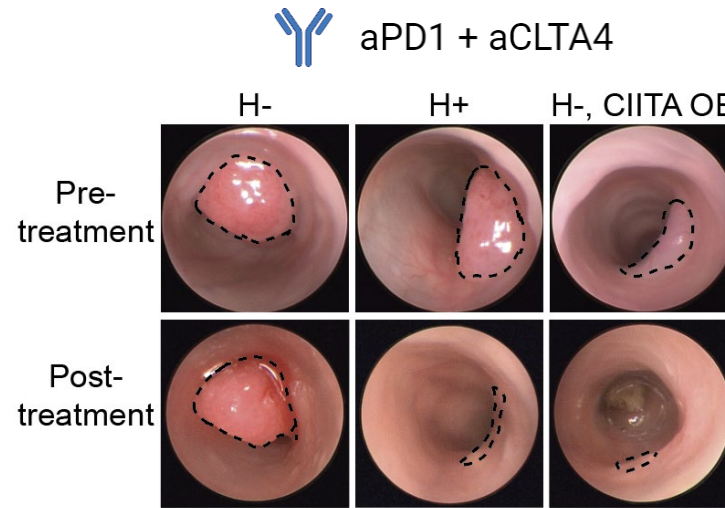
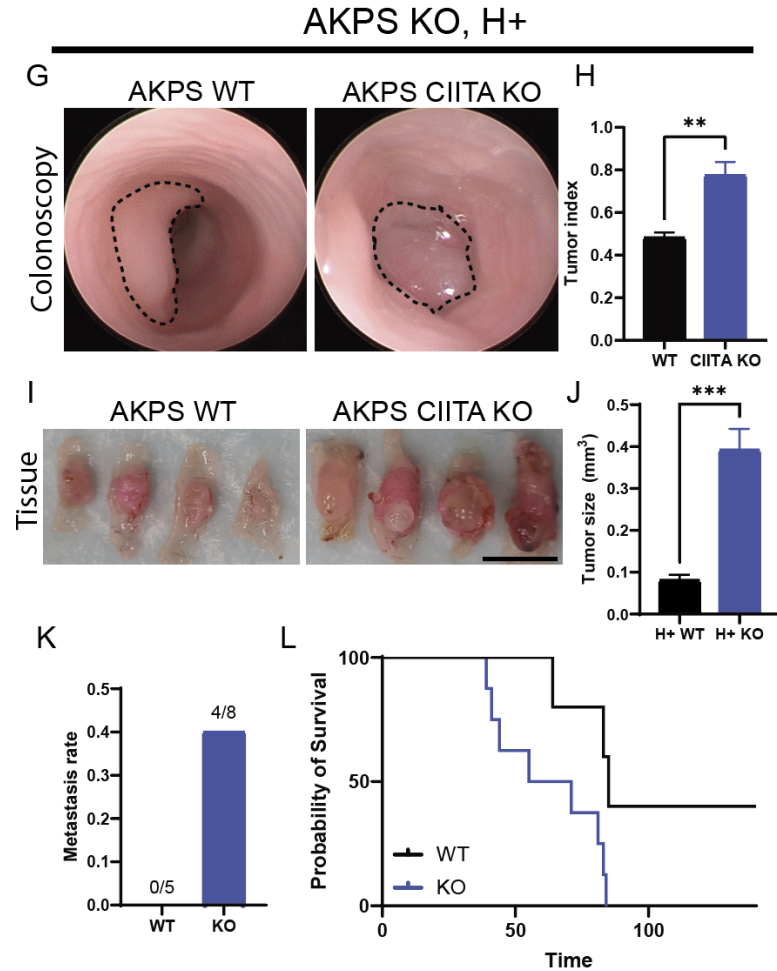
- ✓ HFD leads to depletion of *Helicobacter* species (*H. mastomyrinus* or *H. typhlonius*)
- ✓ *Helicobacter* colonization correlates with MHC-II expression

Cancer MHC-II expression is critical for regulating immune response against CRC

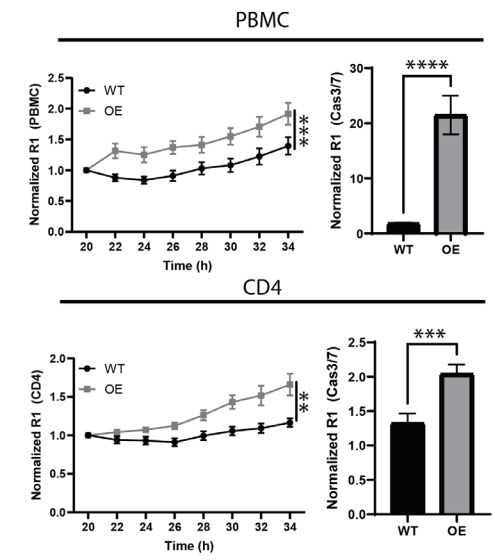
Cancer MHC-II is necessary for microbial anti-tumor effects

Cancer MHC-II synergize with immunotherapy

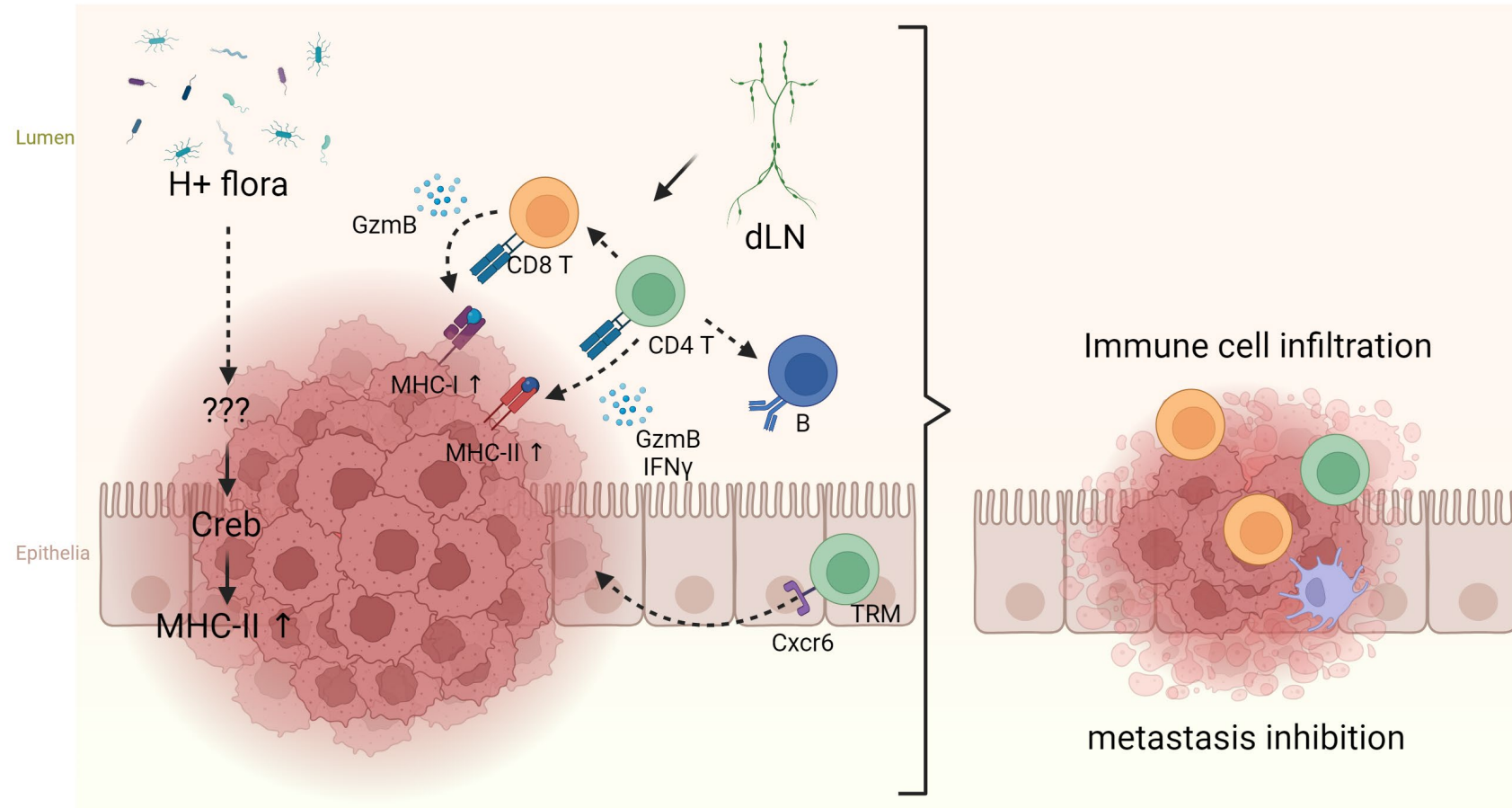
Cancer MHC-II is critical for immune response in human



Caspase 3/7 Immune cells Organoid



How does helicobacter species in the gut enhance cancer MHC expression?





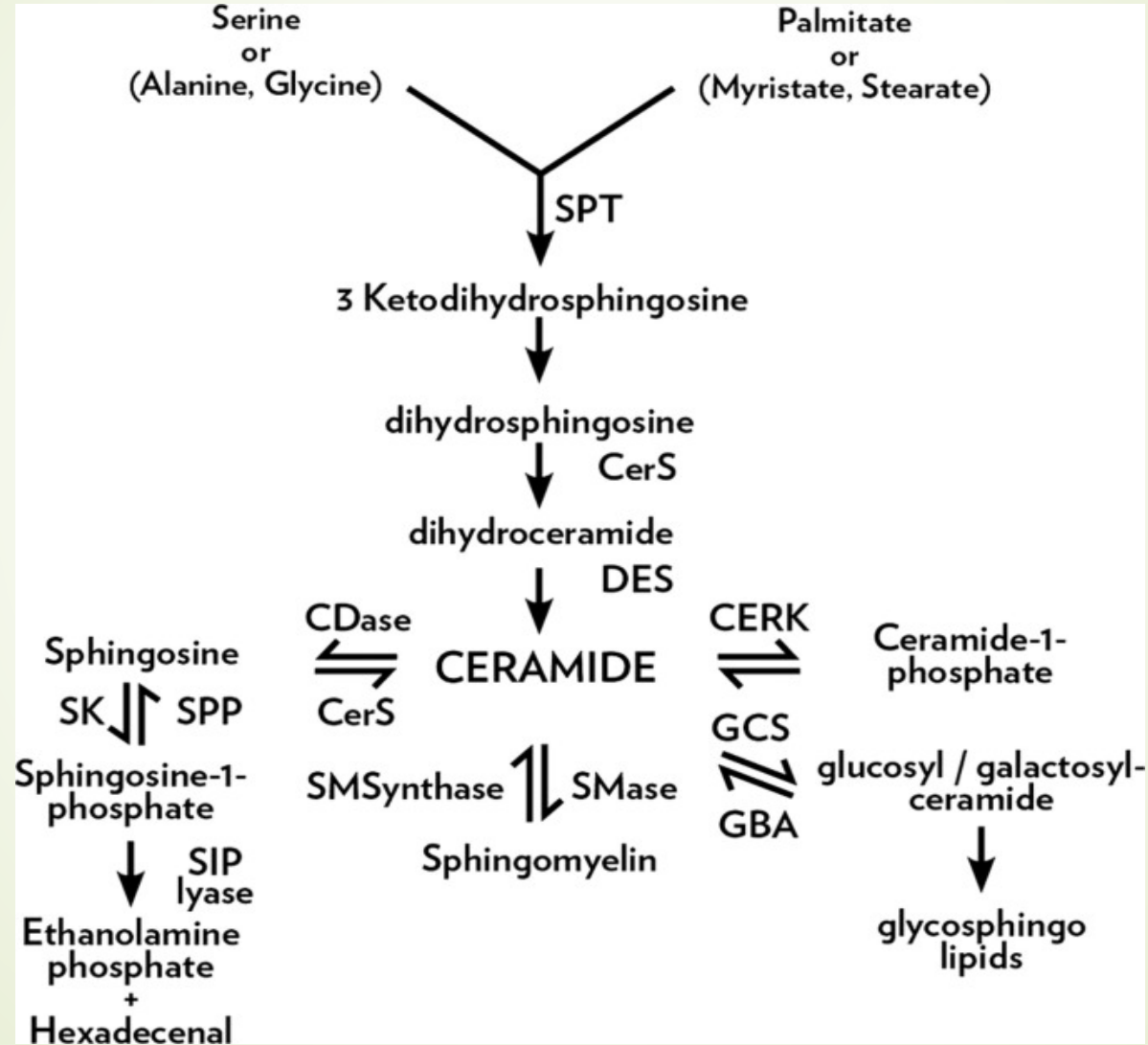
Speed Science

Abhay Kanodia

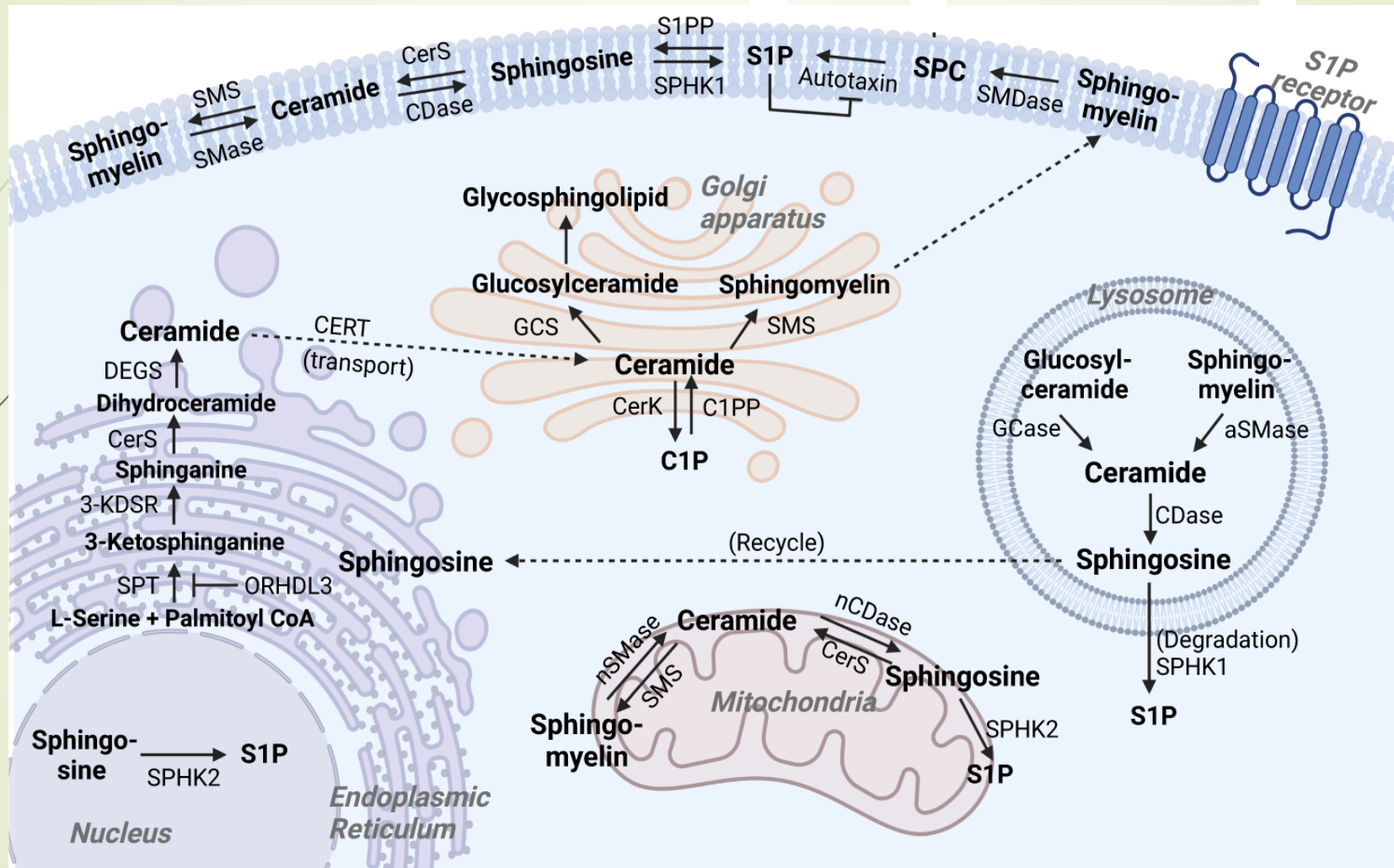
Canals Lab

09/04/2024

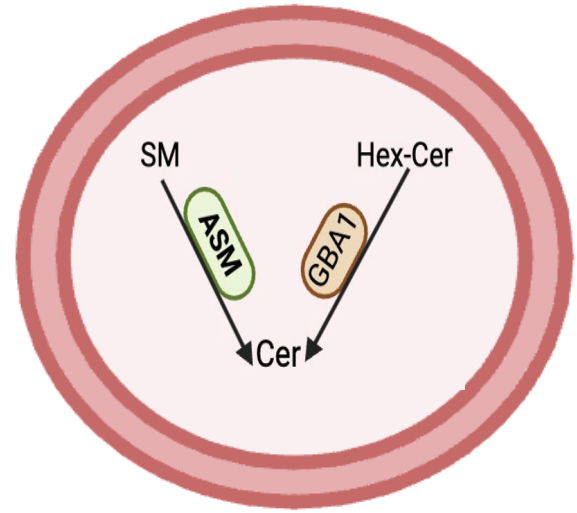
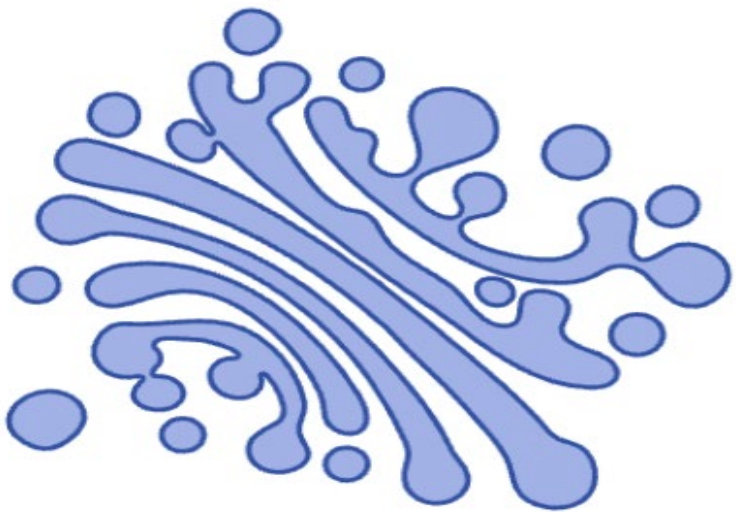
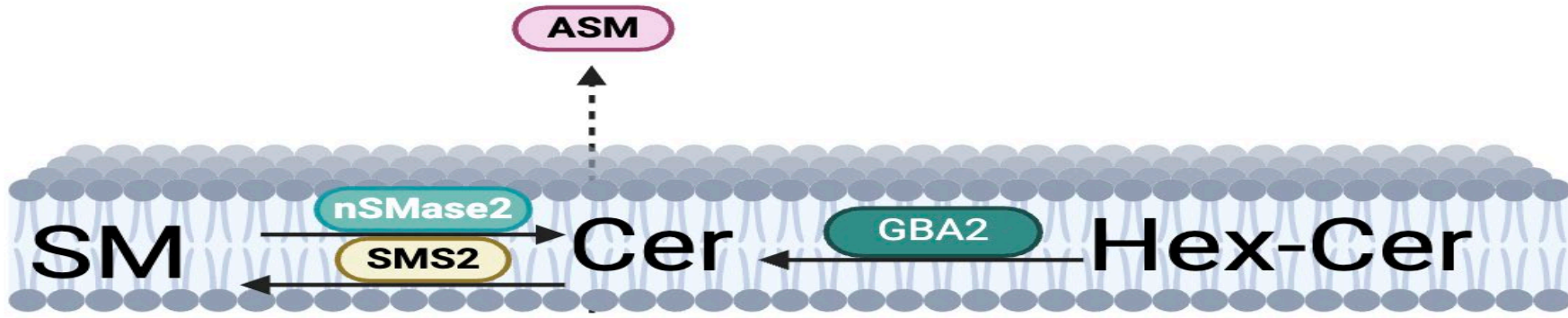
Cancer Lipidomics lab



Compartmentalization of Ceramide: Many Ceramide Hypothesis



Enzymes in PM-Ceramide metabolism

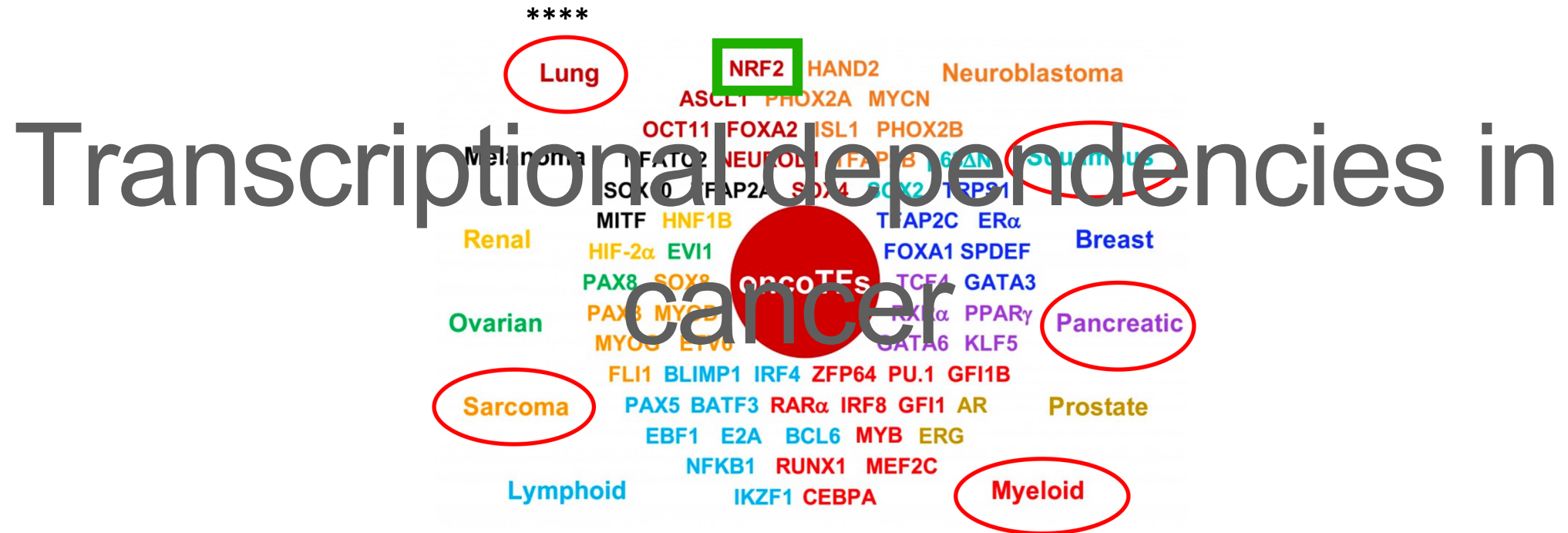


Identifying novel NRF2 functional binding partners in NSCLC

Speed Science session 2024
Santiago Espinosa | Vakoc Lab

09/5/23

The Vakoc Laboratory



Select Key Publications:

RNAi screen identifies Brd4 as a therapeutic target in acute myeloid leukemia. *Nature* 478, 524-528 (2011).

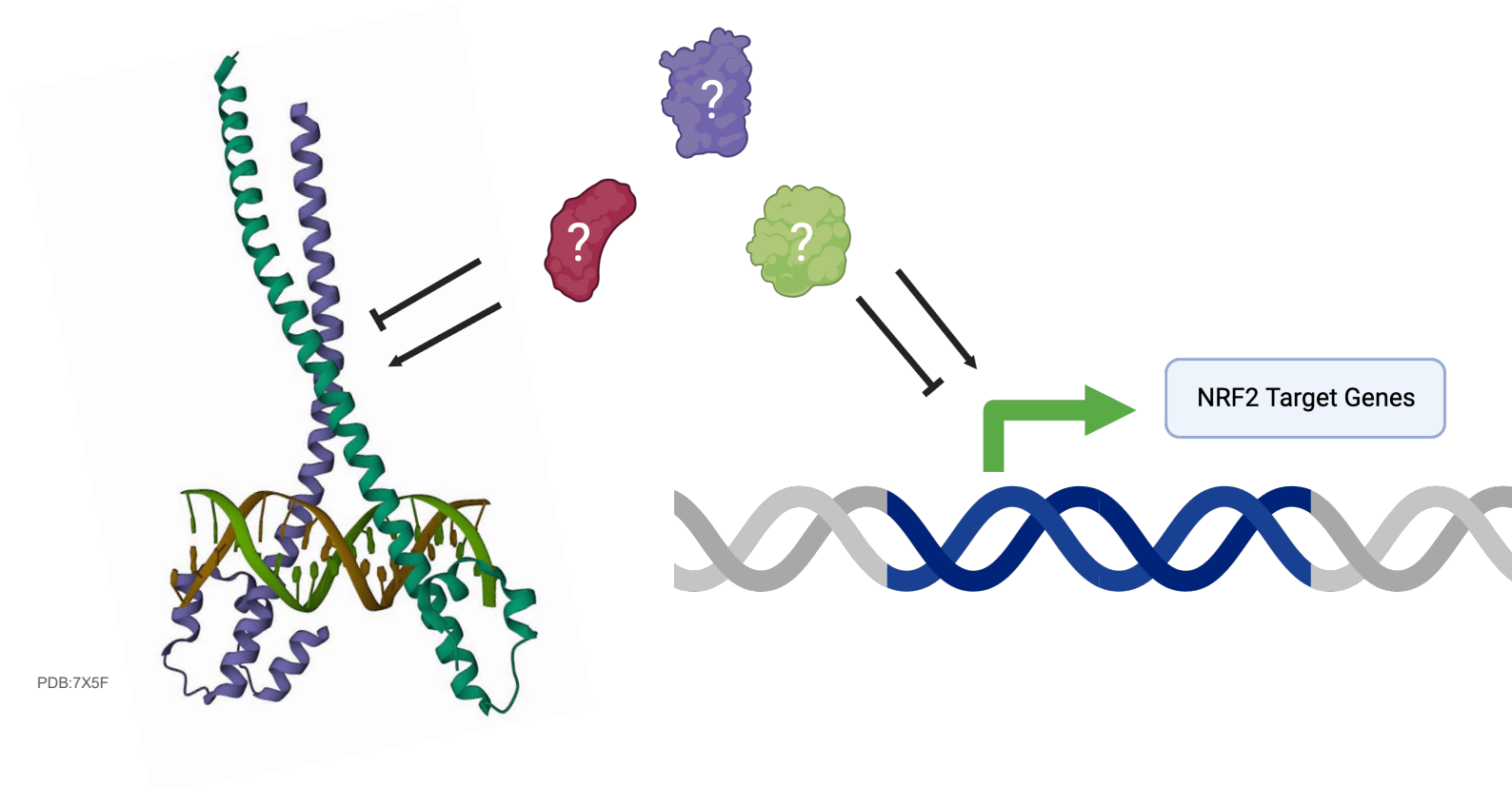
Discovery of cancer drug targets by CRISPR-Cas9 screening of protein domains. *Nature Biotechnology*. 33(6):661-7 (2015).

Enhancer Reprogramming Promotes Pancreatic Cancer Metastasis. *Cell*. 170(5):875-888 (2017).

A TFIID-SAGA Perturbation that Targets MYB and Suppresses Acute Myeloid Leukemia. *Cancer Cell*. 33(1):13-28 (2018).

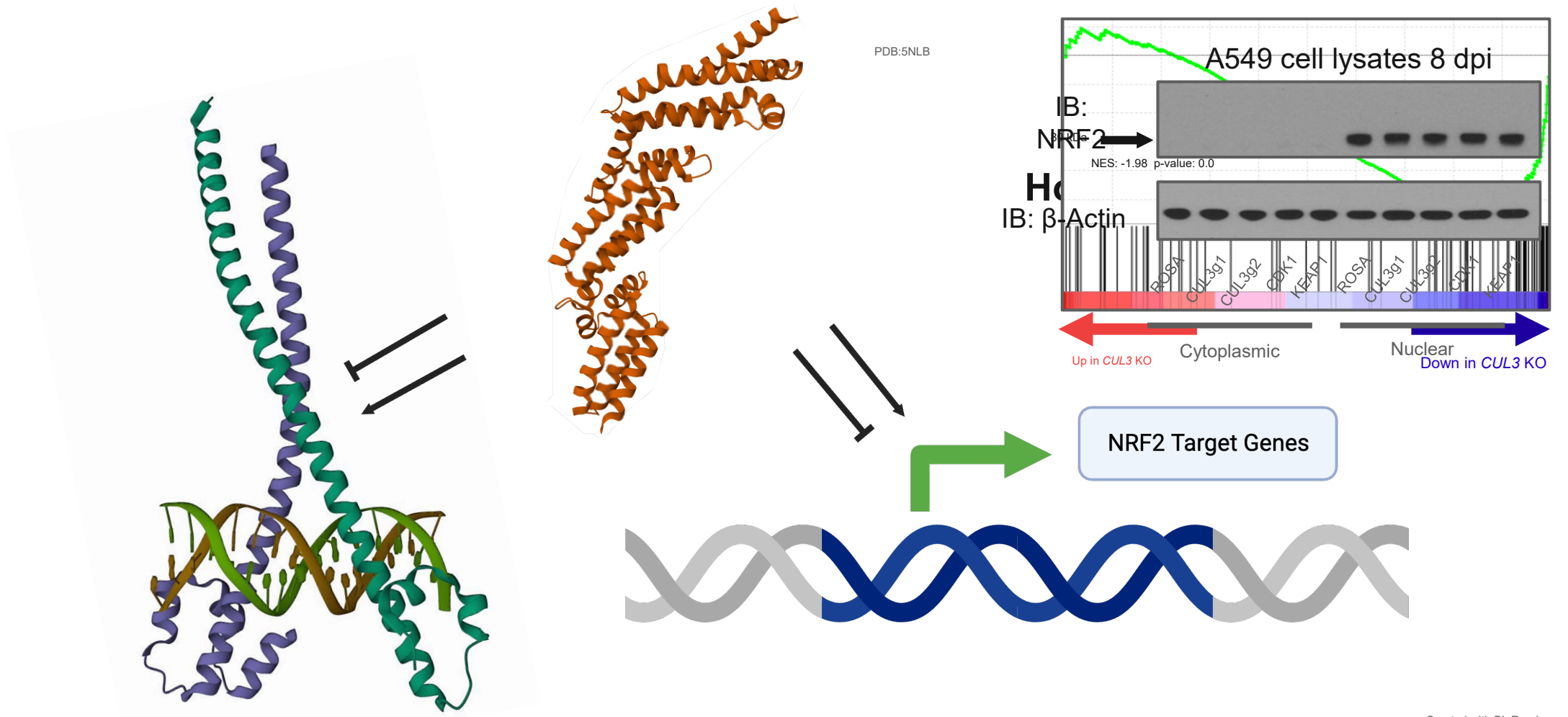
POU2F3 is a master regulator of a tuft cell-like variant of small cell lung cancer. *Genes Dev*. 32(13-14):915-928 (2018).

Our goal: to reveal novel mechanisms of NRF2 function in *KEAP1*-mutant NSCLC



1. Mapping of cancer-relevant domains of NRF2
2. To identify and biochemically characterize cancer-related NRF2 regulators

CUL3 is a putative coregulator of NRF2 activity in *KEAP1*-mutant LC



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School of Medicine**

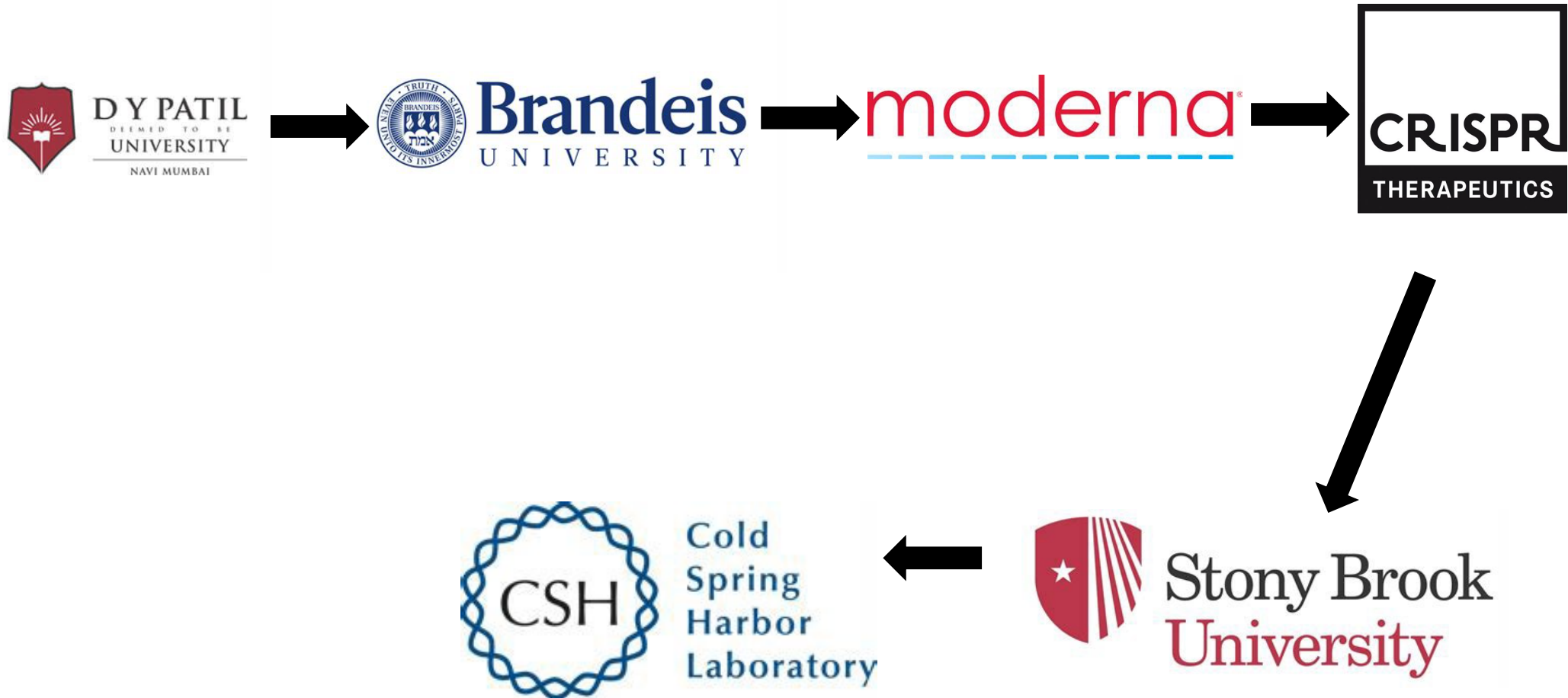
Stony Brook University

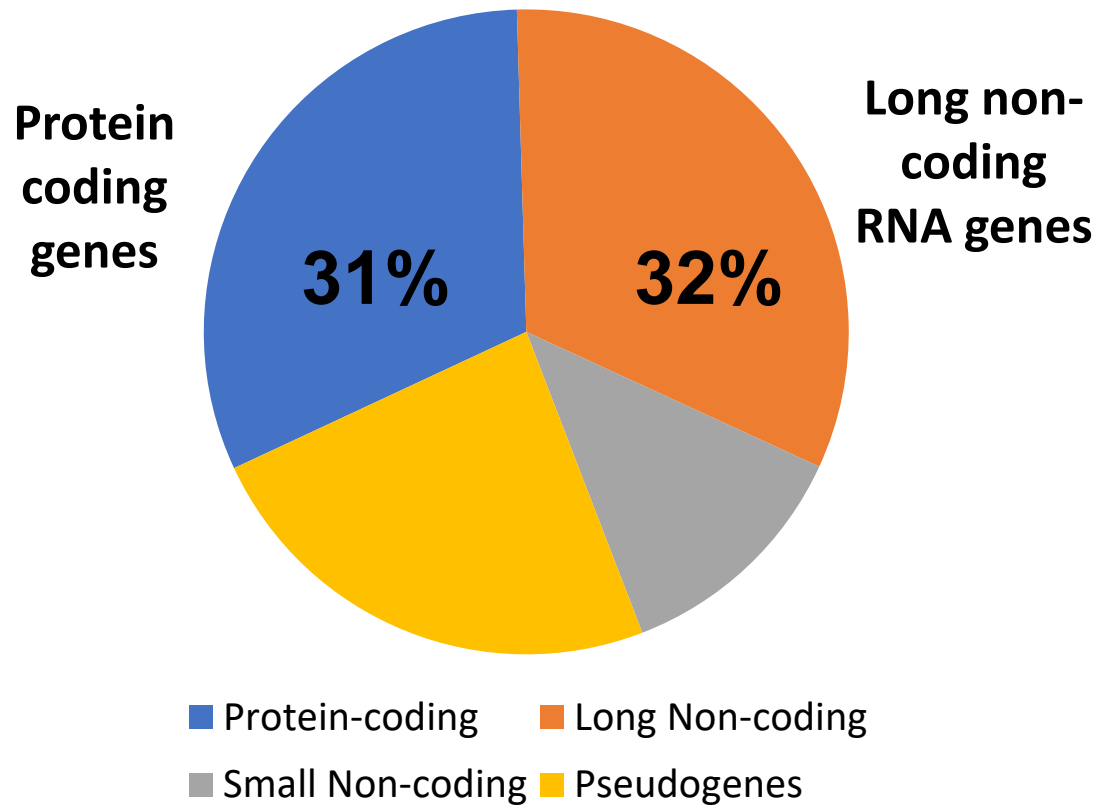
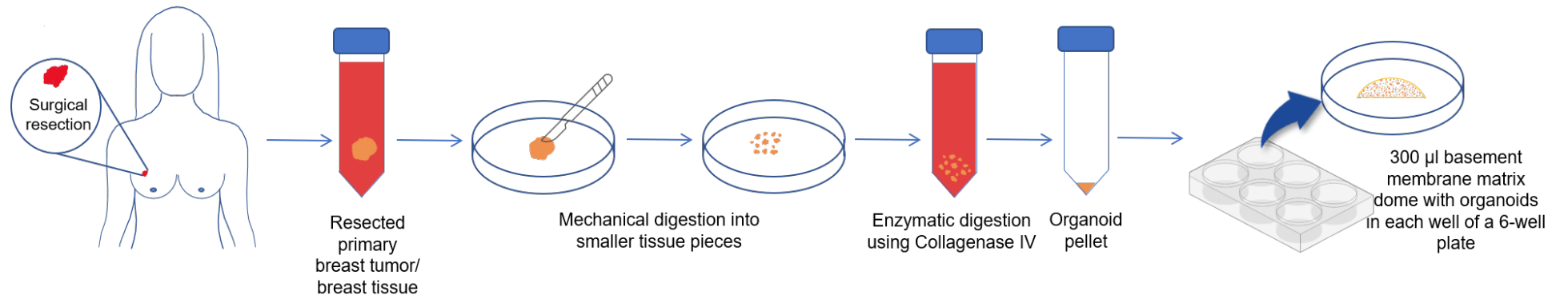


Disha Aggarwal

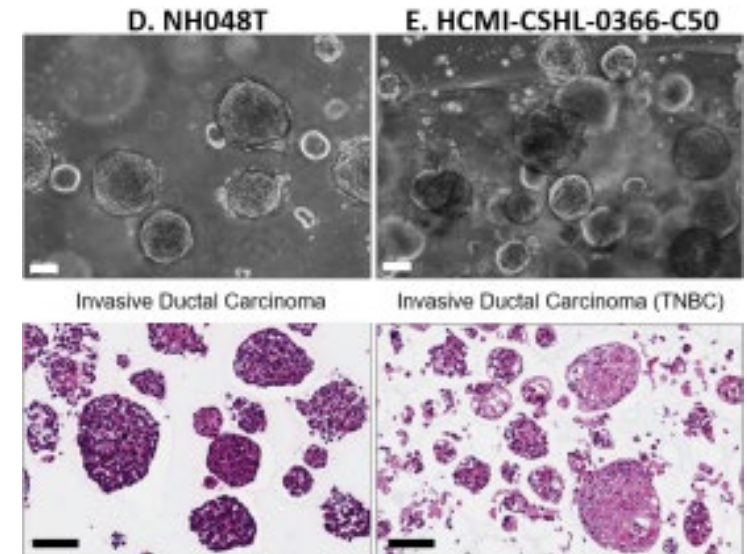
Spector Lab, CSHL

Speed Science 2024



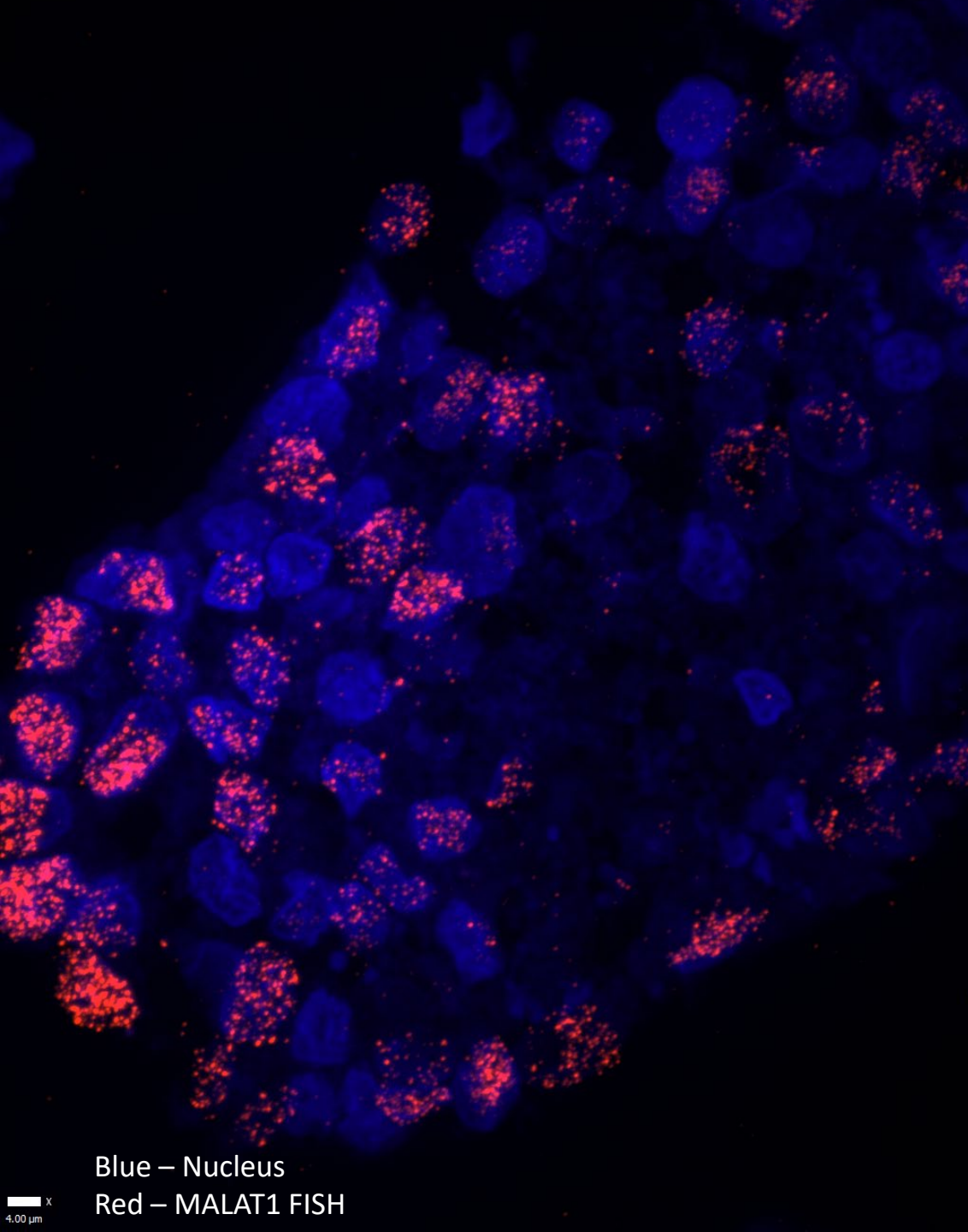


Patient-derived breast tumor ORGANOIDs



Aggarwal et. al., 2023. JoVE.
 ([PMC10193304](https://pubmed.ncbi.nlm.nih.gov/41111111/))

Based on GENCODE Data from Release 44



Blue – Nucleus
Red – MALAT1 FISH

Role of lncRNA *MALAT1* in breast cancer

- Overexpressed in 20 cancer types
- Important in metastases of breast cancer