SPEED SCIENCE 2025

Session Two

Cancer Ecology & Evolution Lab
Stony Brook Cancer Center

Sogol Ghanbari
Mehdi Damaghi's Lab - Cancer Center

Stony Brook University

About Me:

- I was born and raised in Iran.
- I received both my Bachelor's and Master's degrees in Genetics.
- During my Master's, I focused on the role of non-coding RNAs as internal controls in breast cancer.
- After graduation, I worked for two years as an R&D Manager at HANIFA Genetics.
- I'm passionate about translating cellular and molecular findings into insights that can inform better diagnostics and therapies.

Outside the Lab, I Enjoy:

- Traveling and exploring new places 🌎
- Gardening and spending time in nature 🌱
- Painting and creative expression 🎨
- Taking long walks to clear my mind 🚶
- Quality time with my family ❤️

- Cancer is a complex evolving ecosystem, where a single cell escapes normal controls and disrupts tissue homeostasis.
- We study how changes in tumor microenvironment apply selective pressure on cancer cells, influencing their evolution and adaptation.
- This interplay between tumor cells and the microenvironment drives tumor heterogeneity and phenotypic plasticity.
- We use the integration of spatial single-cell omics (transcriptomics, proteomics, metabolomics, lipidomics) and machine learning to analyze cancer cell adaptation within their native microenvironments.

Tumor-Associated Macrophages (TAMs): A Double-Edged Sword in Ovarian Cancer Progression and Immunosuppression

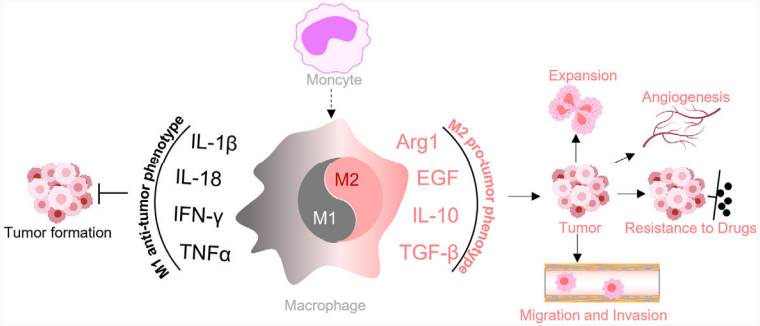
- TAMs Exhibit high plasticity:
  - **M1 phenotype:** pro-inflammatory, anti-tumor
  - **M2 phenotype:** anti-inflammatory, pro-tumor

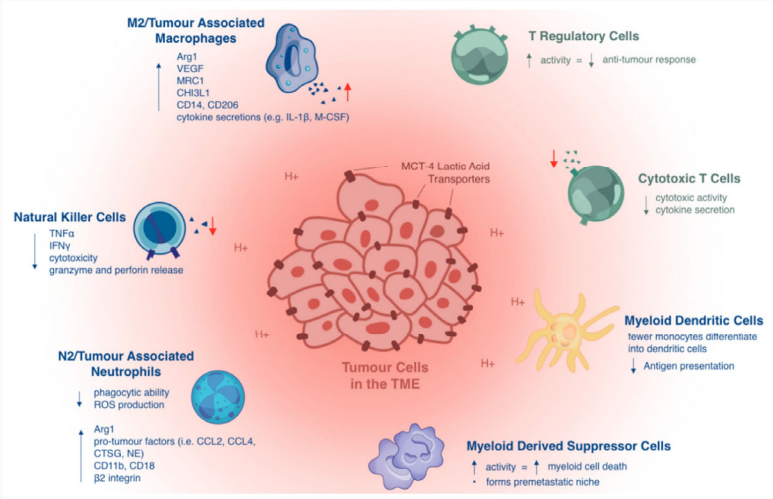
- Frequently localize at the tumor–stromal interface in ovarian lesions.

- Associated with:
  - Tumor cell invasion into stroma
  - Promotion of angiogenesis
  - Immune suppression through checkpoint signaling and cytokine release

- Tumor microenvironmental stressors:
  - **Acidosis** (low extracellular pH)
  - **Glucose deprivation** from high metabolic demand

- Effects on TAMs:
  - **Promote M2-like polarization** → immune suppression and tumor promotion
  - **Reduce antigen presentation capacity** (e.g., MHC-II downregulation)
  - **Increase extracellular vesicle (EV)** secretion carrying immunosuppressive cargo



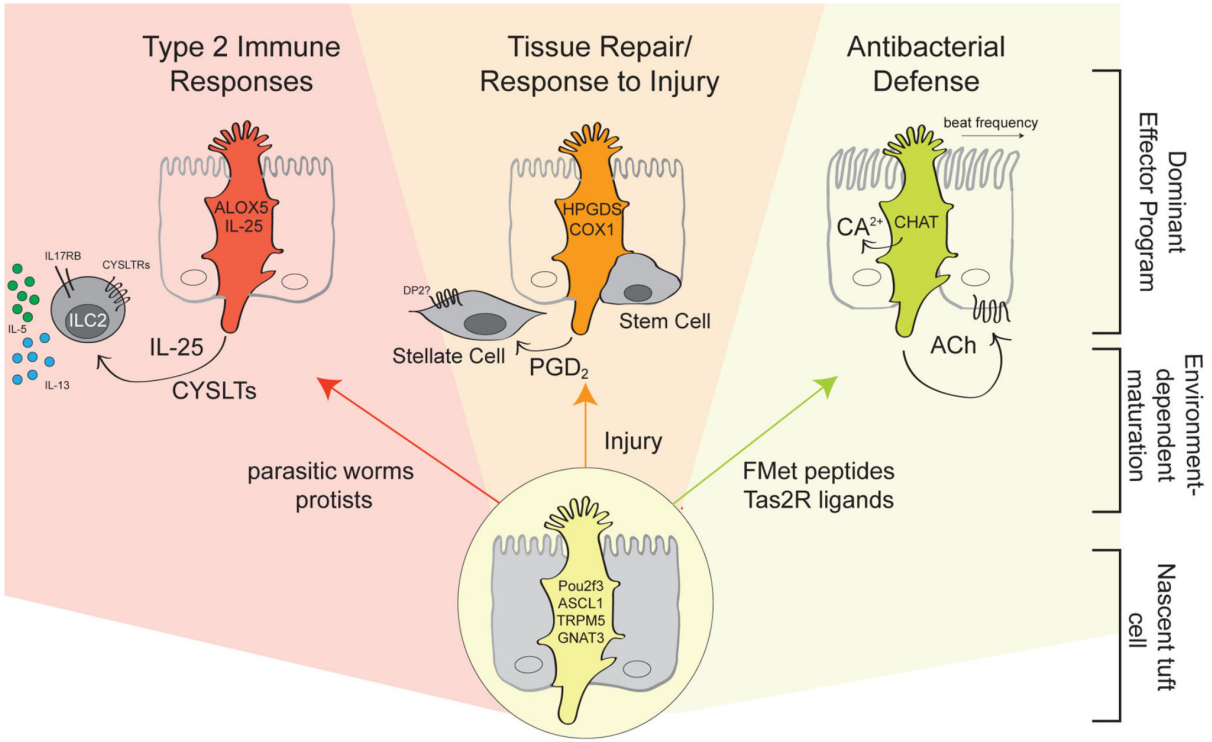


Wang, Joy X., et al. "Lactic acid and an acidic tumor microenvironment suppress anticancer immunity." *International journal of molecular sciences* 21.21 (2020): 8363.

POU2F3 Co-Activator OCA-T2 is Essential for Tuft Cell Lineage Development

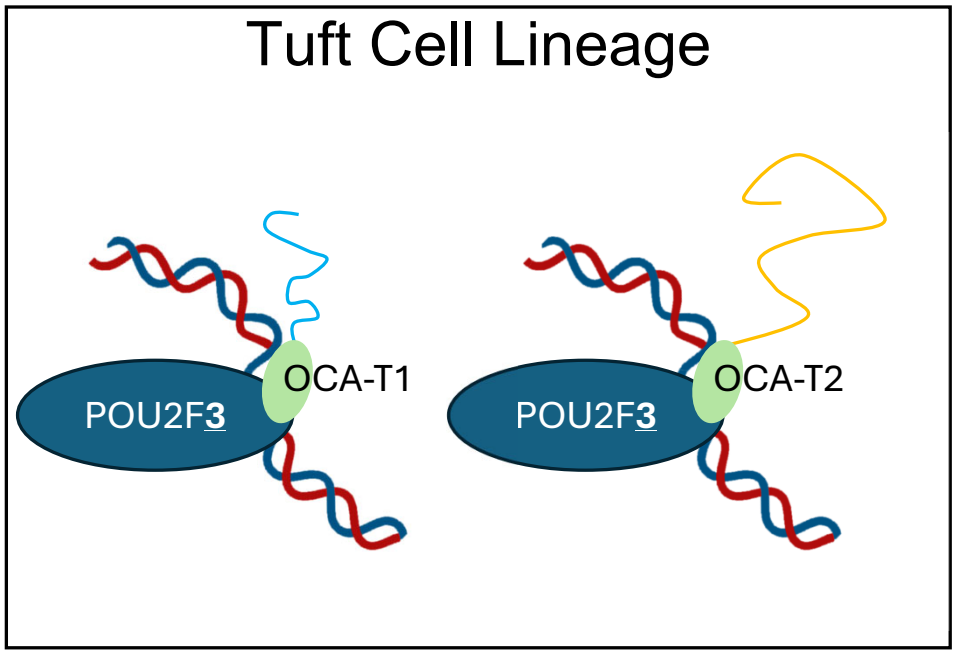
Liam Shanley
Fourth Year PhD Student
Vakoc Lab
Speed Science, 9/10/25

Tuft cells are rare chemosensory cells found in the epithelium in mucosal tissues



Kotas, et al *Annu Rev Pathol* (2023)

The Vakoc lab studies transcription factors, their co-activators, and the ways they cooperate to drive cell lineage



TC loss	TC reduction	No TC loss

		trachea	small intestine	colon	thymus	stomach
Various publications	*Pou2f3*$^{-/-}$	X	X	X	X	X
Wu...Vakoc, et al (2022)	OCA-T1$^{-/-}$	X	X	↓	✓	✓
	OCA-T2$^{-/-}$	X	X	X	X	X

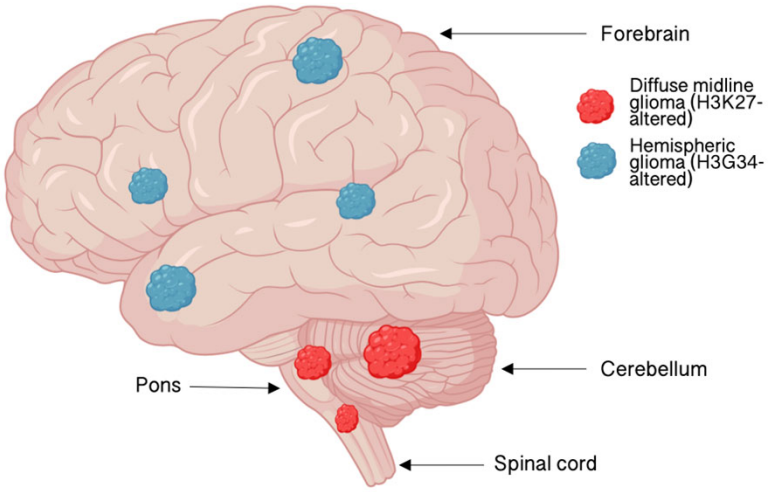
Wu... Vakoc *Nature* (2022)

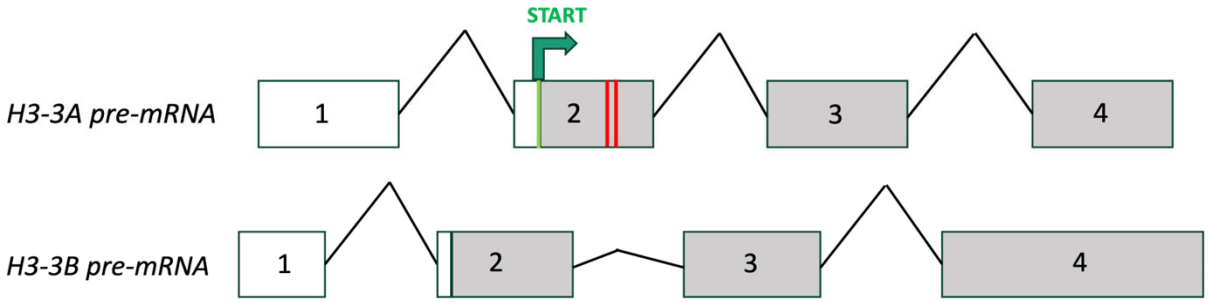
Targeting *H3-3A* using antisense oligonucleotides as a therapy for pediatric high-grade glioma

Shivani Deshpande

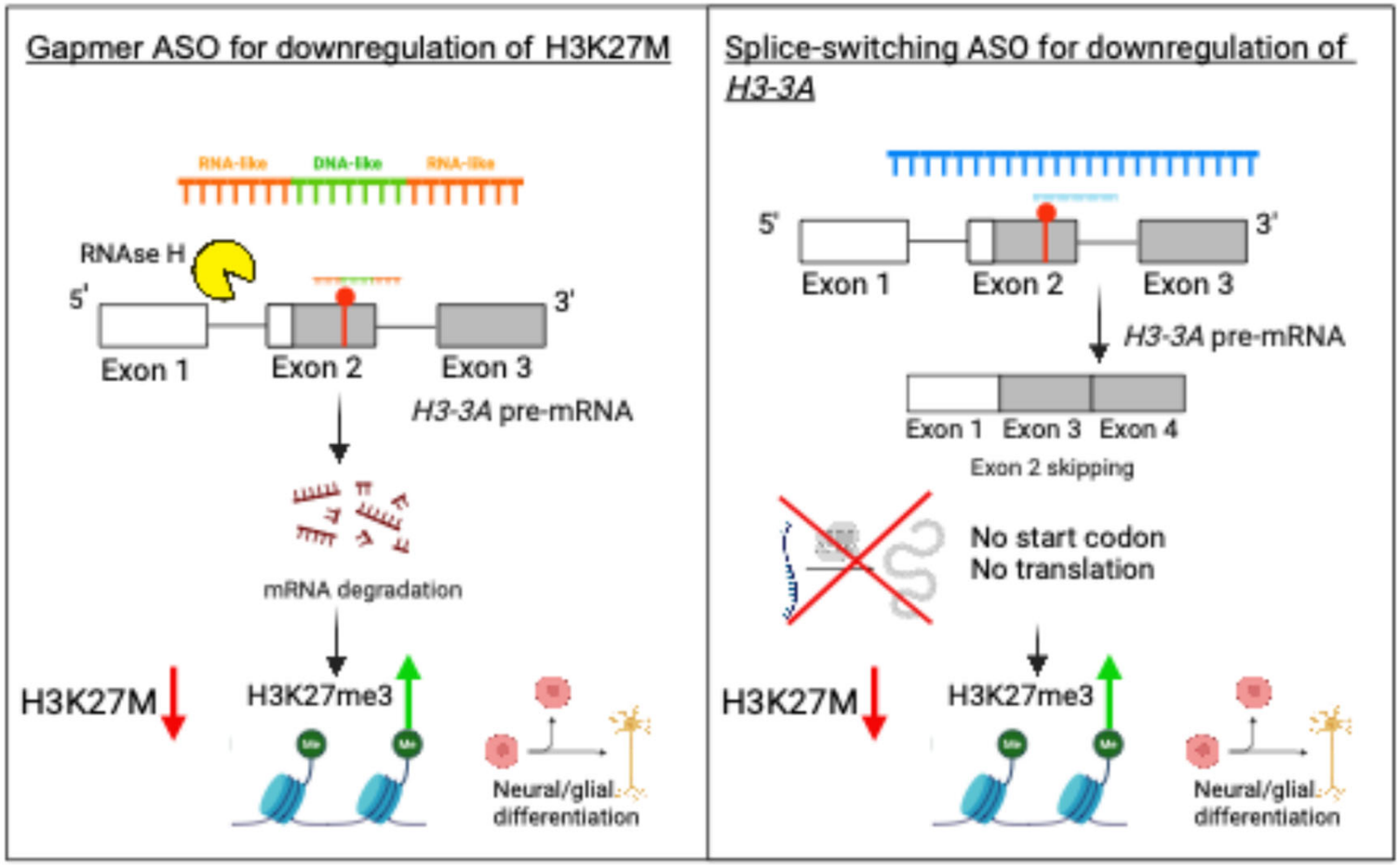
3rd year graduate student

Krainer Lab at CSHL





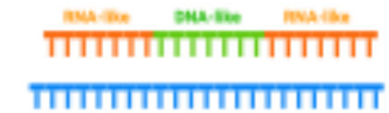
ASO Targeting of *H3-3A*



Qian Zhang

Lucia Yang

Broad aims of my project

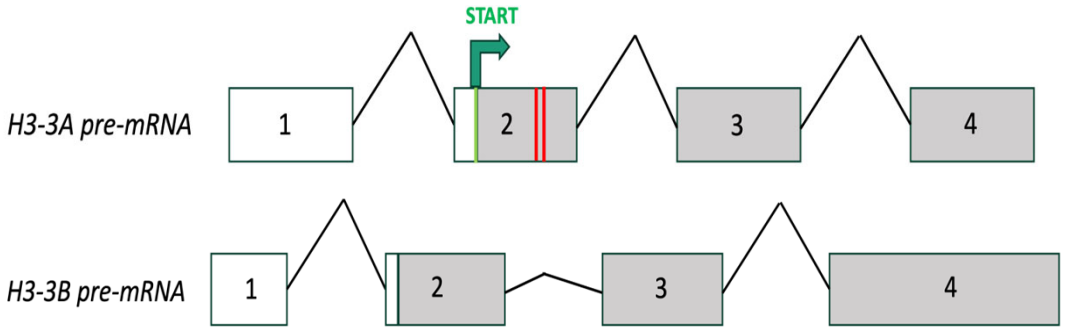


+

Focal irradiation

HDAC inhibition

- Combination therapy protocols for H3.3K27M DMG
- Using the splice-switching ASOs to target a second mutation in the same exon: G34R/V



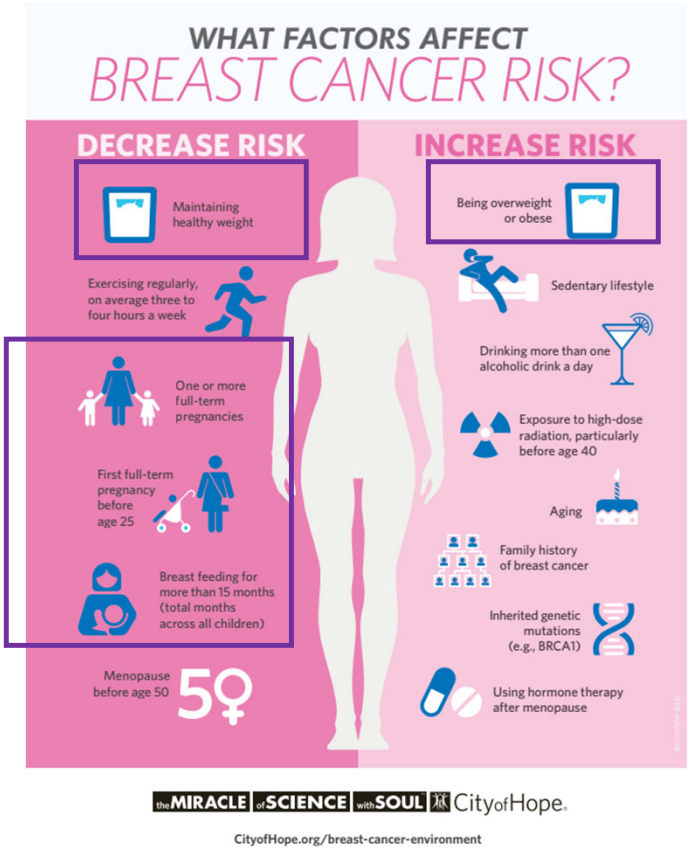
Investigating strategies for decreasing the risk of mammary tumorigenesis in young women

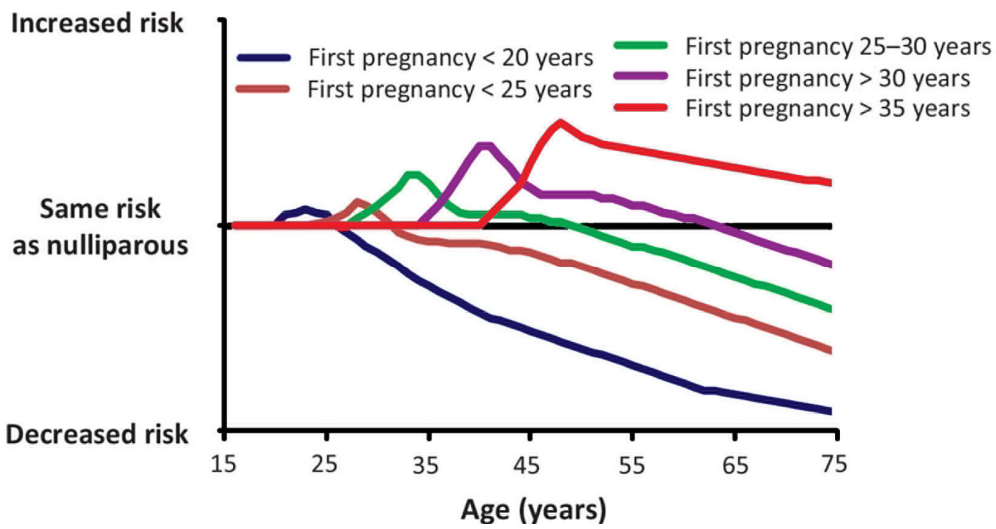
Dhivyaa Anandan
dos Santos Lab, CSHL
Genetics Speed Science
September 10, 2025

Stony Brook MSTP

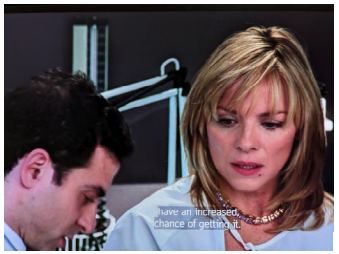
CSH Cold Spring Harbor Laboratory

Lifestyle factors and environmental exposures play a role in risk for breast cancer





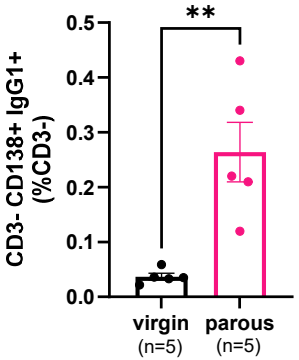
Meier-Abt & Bentires-Alj, *Trends Mol Med* 2014

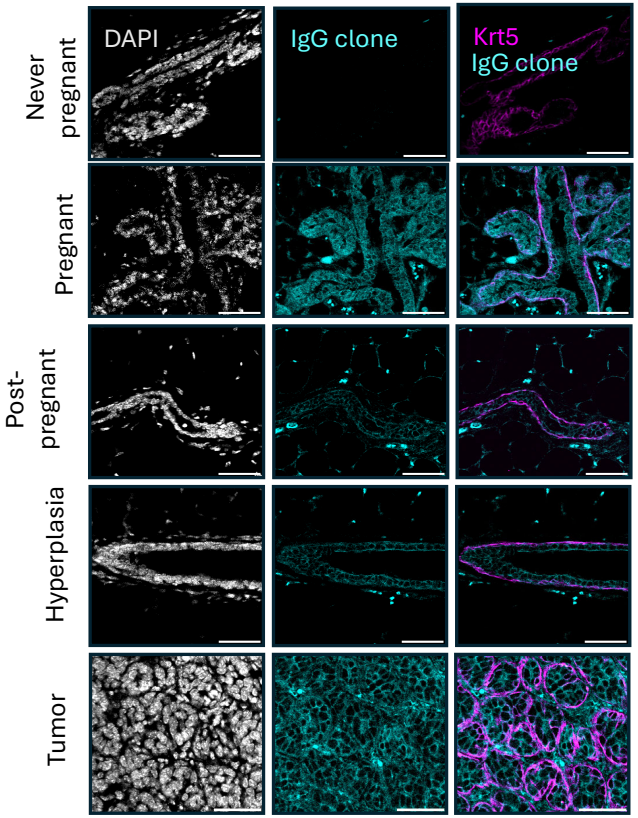


1. **What is the underlying mechanism behind the protective effect of an early first pregnancy?**
2. **Looking beyond pregnancy – can dietary interventions mediate risk for breast cancer?**

Mimicking pregnancy-induced changes to mammary immunity

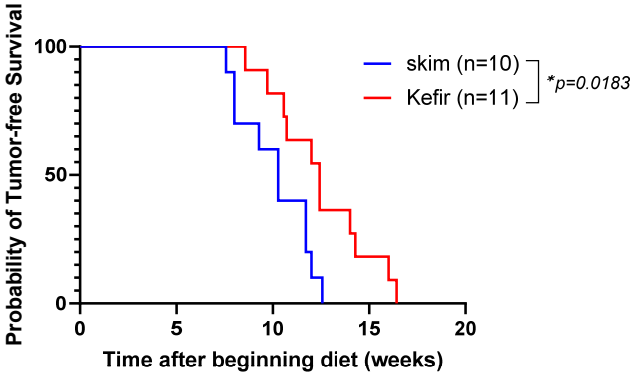
IgG plasma cells are elevated in post-pregnancy mammary glands and recognize antigens associated with pregnancy and mammary tumorigenesis.

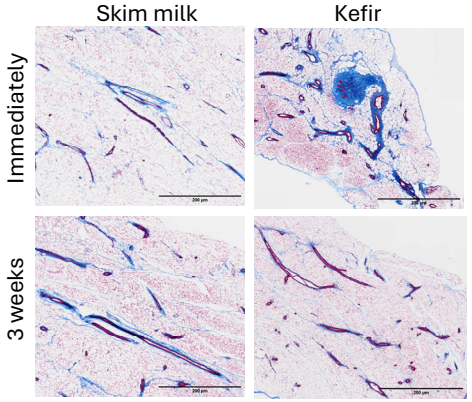


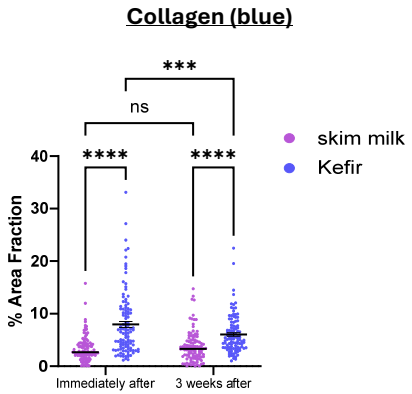


Investigating the effect of probiotics on mammary tumor development

Probiotic diet delays mammary tumor development and alters the collagen composition of the gland.

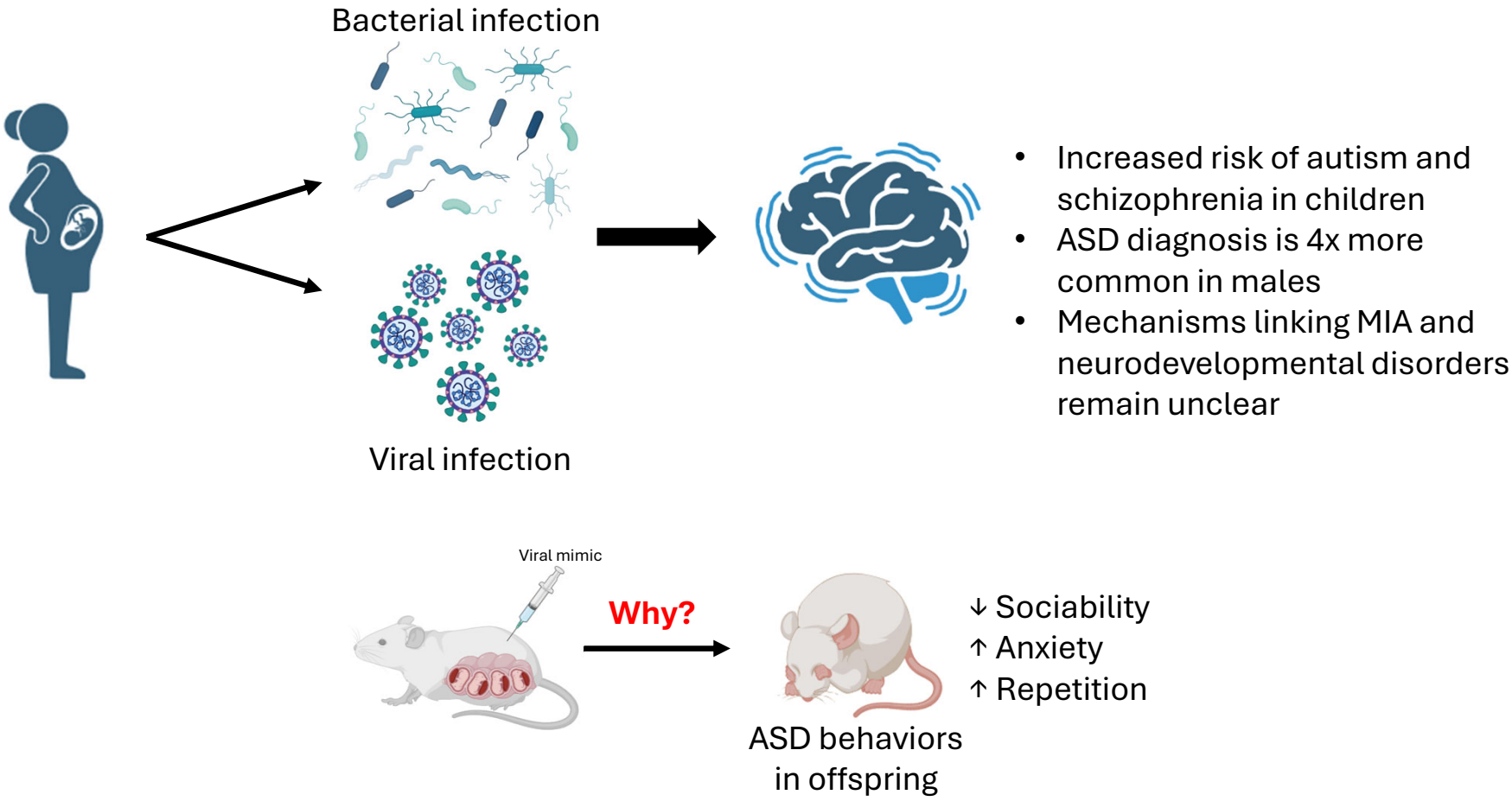


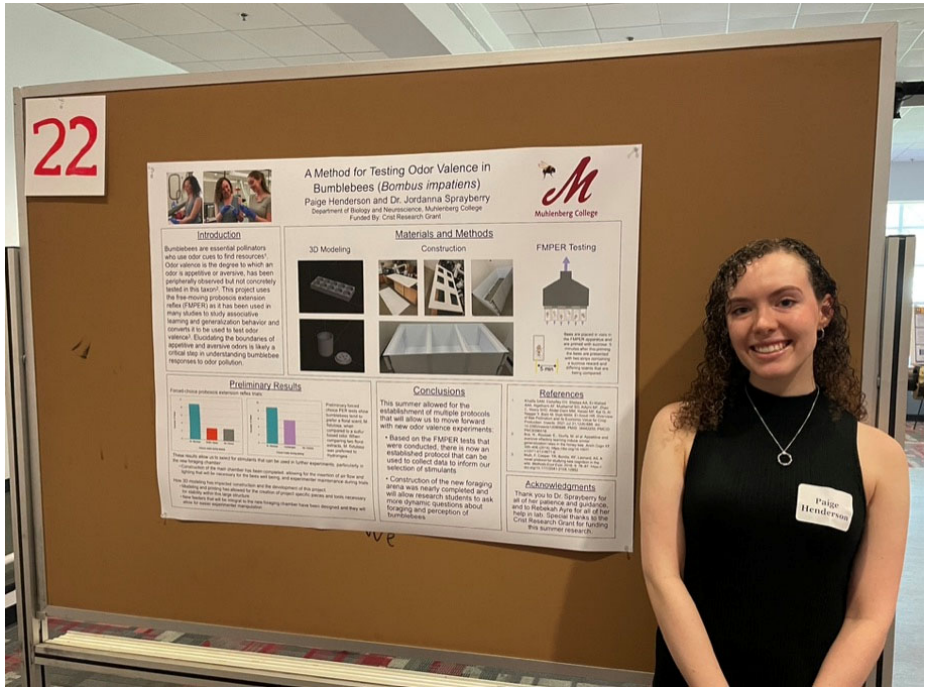


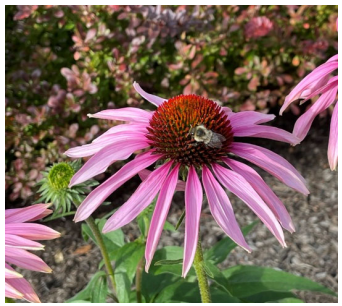


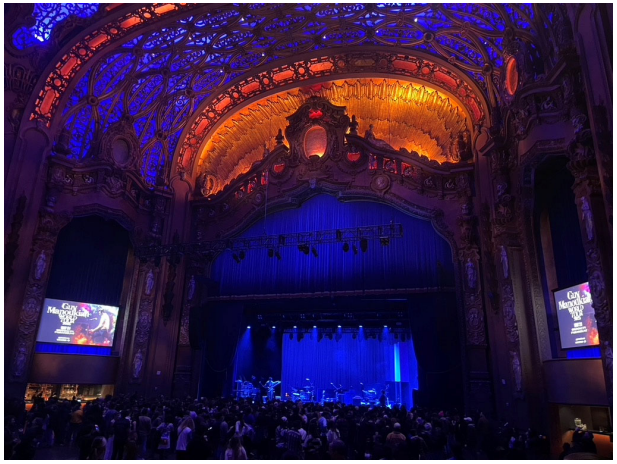
Role of maternal immune activation in neurodevelopmental disorders

Paige Henderson


Bacterial infection
Viral infection
Increased risk of autism and schizophrenia in children
ASD diagnosis is 4x more common in males
Mechanisms linking MIA and neurodevelopmental disorders remain unclear
Viral mimic
Why?
↓ Sociability
↑ Anxiety
↑ Repetition
ASD behaviors in offspring


22
A Method for Testing Odor Valence in Bumblebees (Bombus impatiens)
Paige Henderson and Dr. Jordanna Sprayberry
Department of Biology and Neuroscience, Muhlenberg College
Funded By: Crist Research Grant
Muhlenberg College
Introduction
Materials and Methods
3D Modeling
Construction
FMPER Testing
Preliminary Results
Conclusions
References
Acknowledgments
Paige Henderson






85
AMERICAN BALLET THEATRE
YEARS
SUSAN JAFFE, ARTISTIC DIRECTOR





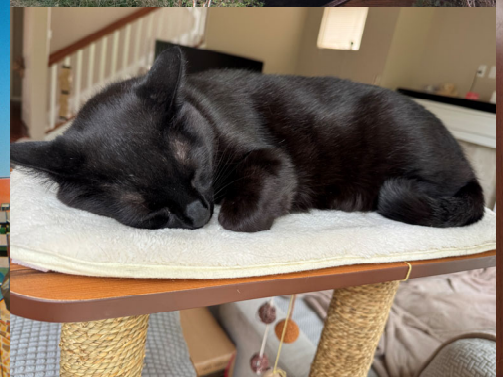




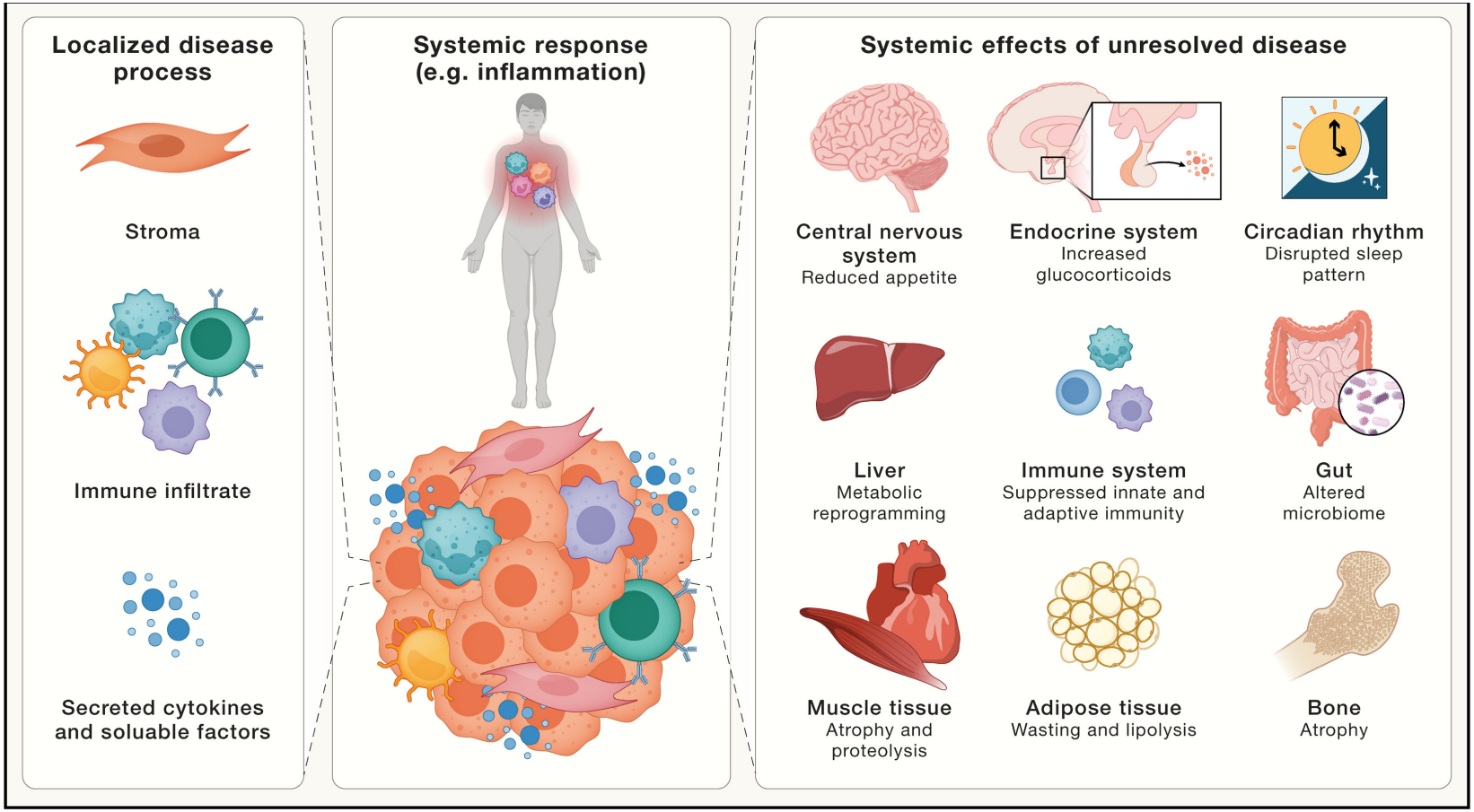









Cancer cachexia



Ferrer et al. Cell (2023)

Alice Wang
(Tobias Janowitz lab at CSHL)

Speed Science 2025

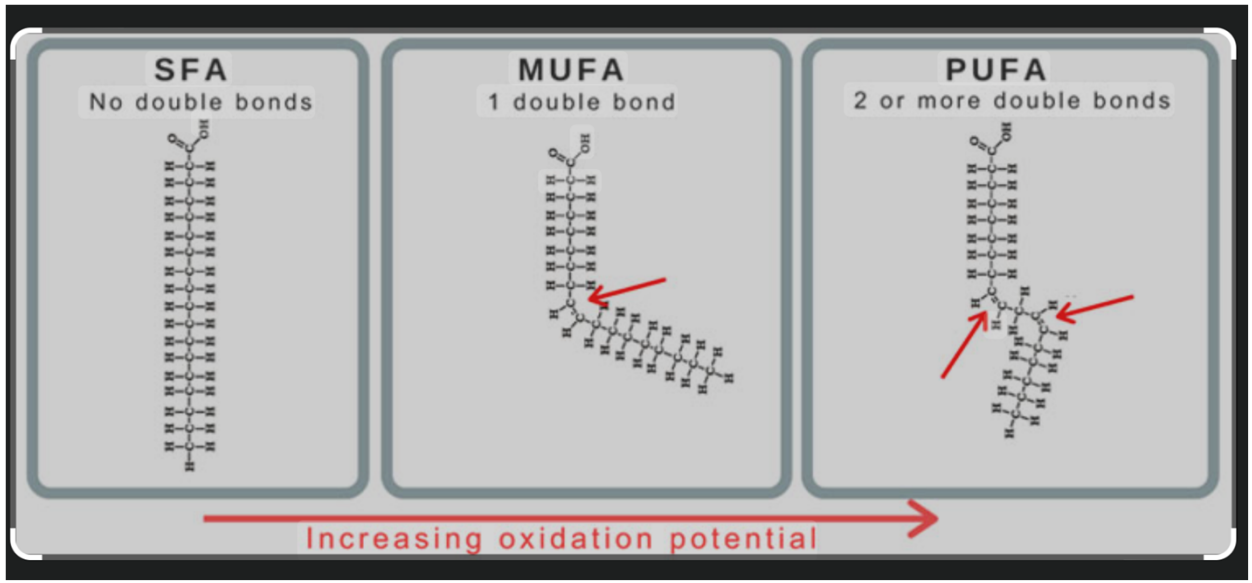
---YUJIA JI

MICHAEL LUKEY' LAB AT CSHL

4TH YEAR PH.D. IN GENETICS PROGRAM

STONY BROOK UNIVERSITY

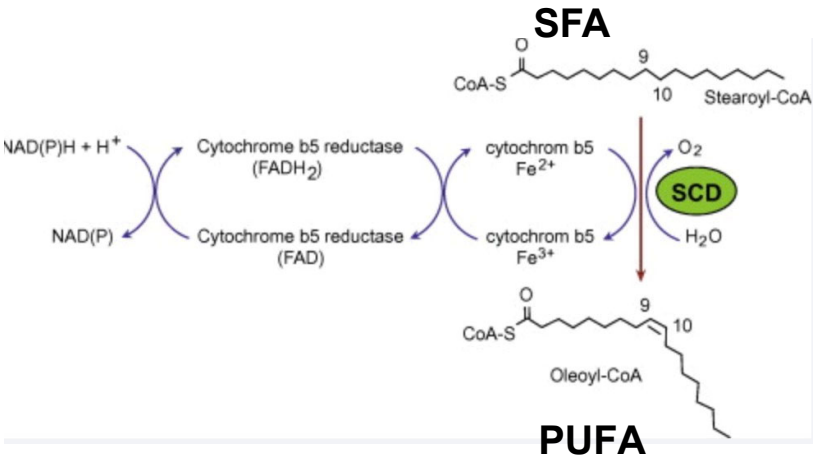
Deciphering the role of stearoyl-CoA desaturase 1 (SCD) in breast cancer



Lipotoxicity — Ferroptosis

Cell membrane

SCD is a key player in populating this balance



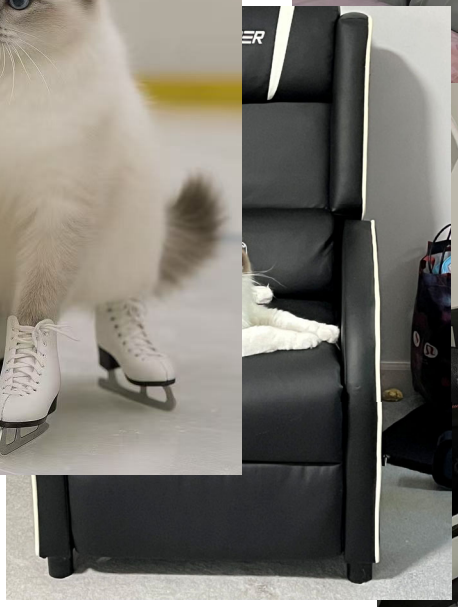
SFA: Saturate fatty acid

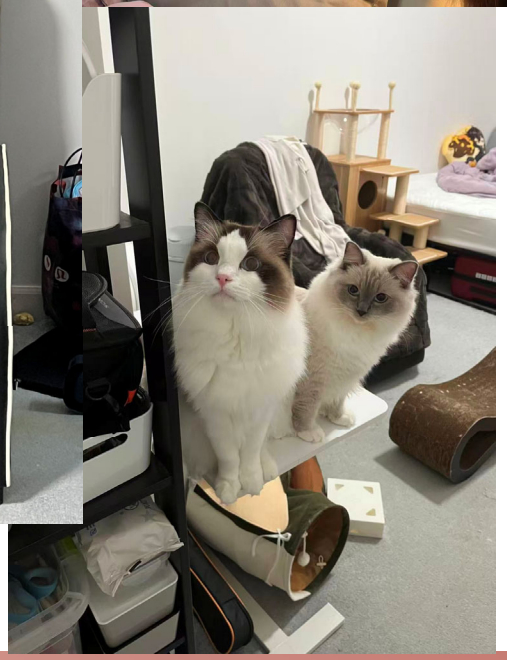
MUFA: Mono-unsaturate fatty acid

PUFA: Poly-unsaturate fatty acid

Something About Me…

Skate an





Kimble and Miffy!

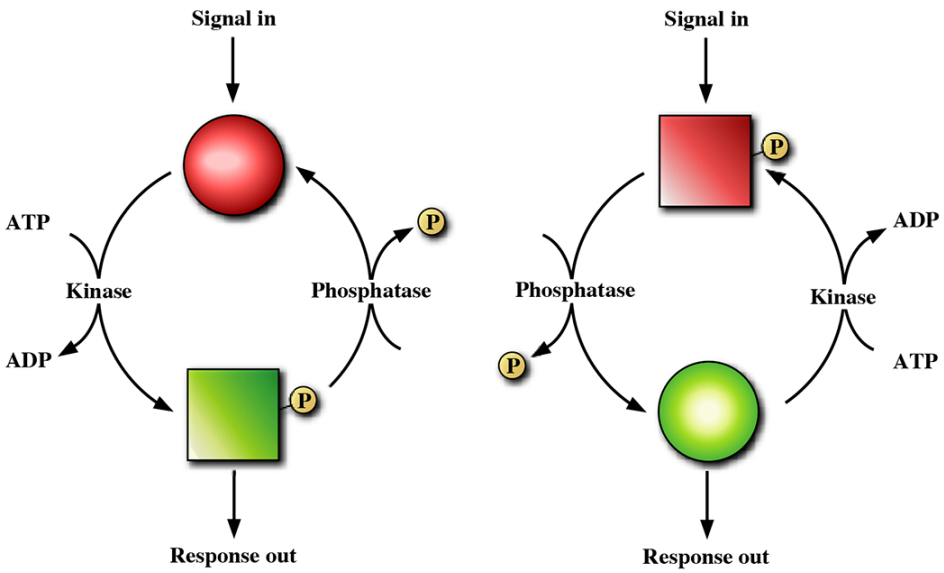
Reversible Redox Regulation of T-Cell Protein Tyrosine Phosphatase (PTPN2)

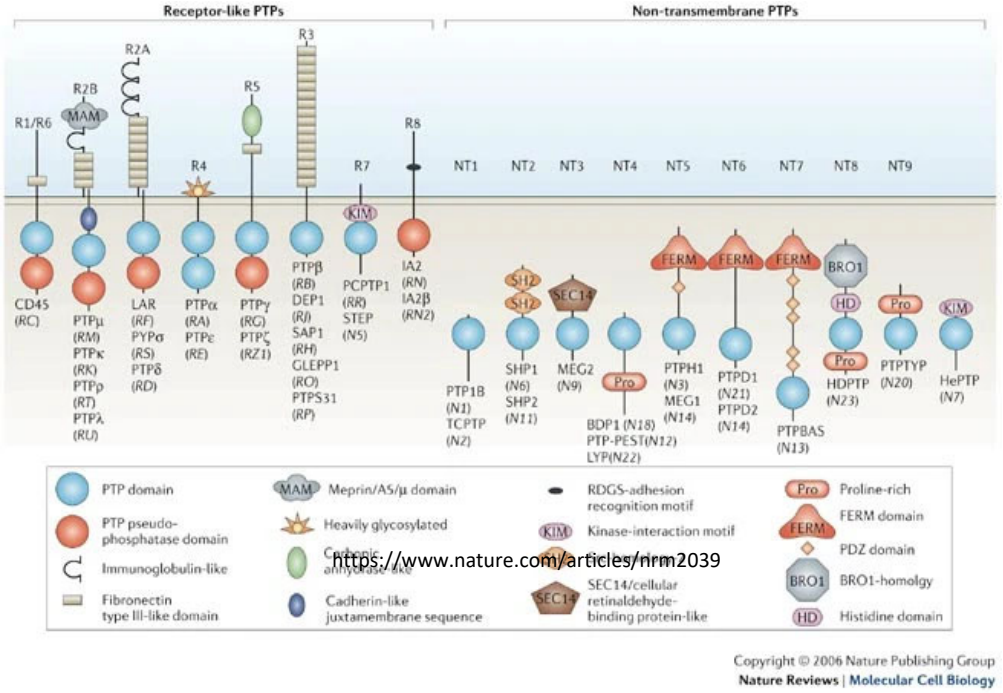
TanChun Kuo
Tonks Lab

CSH Cold Spring Harbor Laboratory

Stony Brook University

Reversible Redox Regulation of PTPN2 (TCPTP)

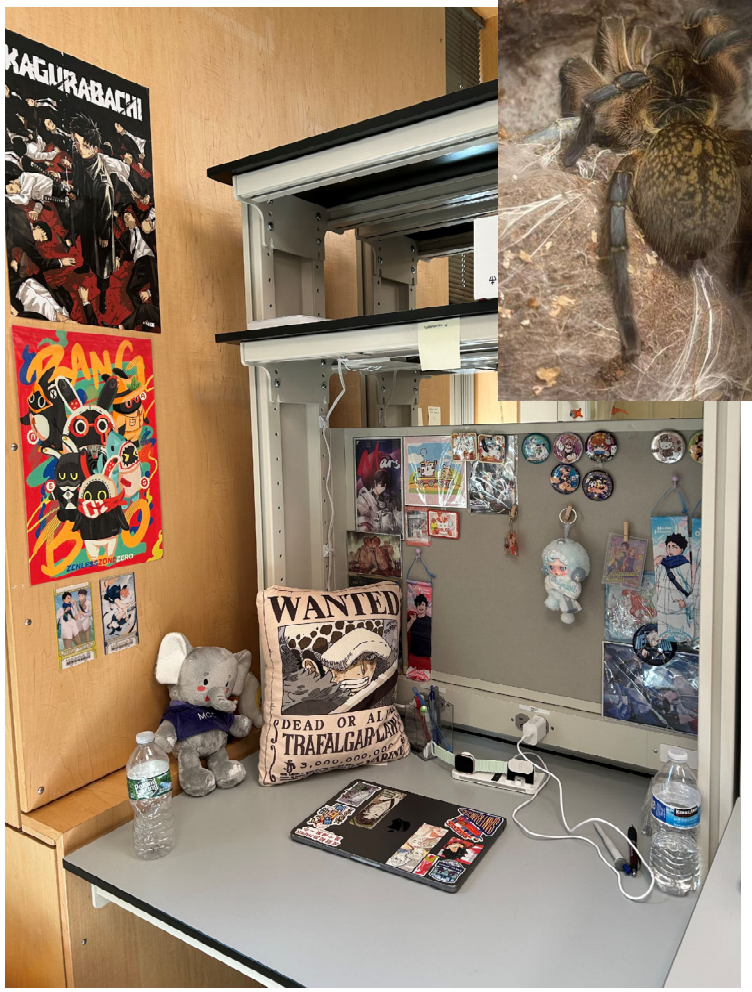


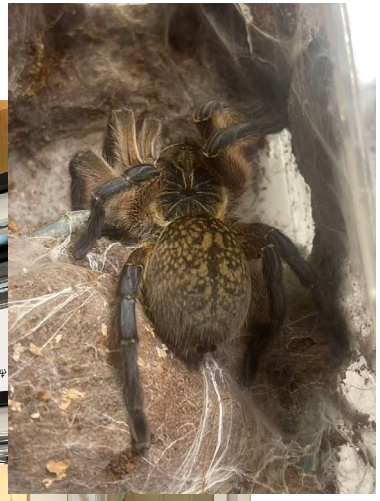


https://www.nature.com/articles/nrm2039

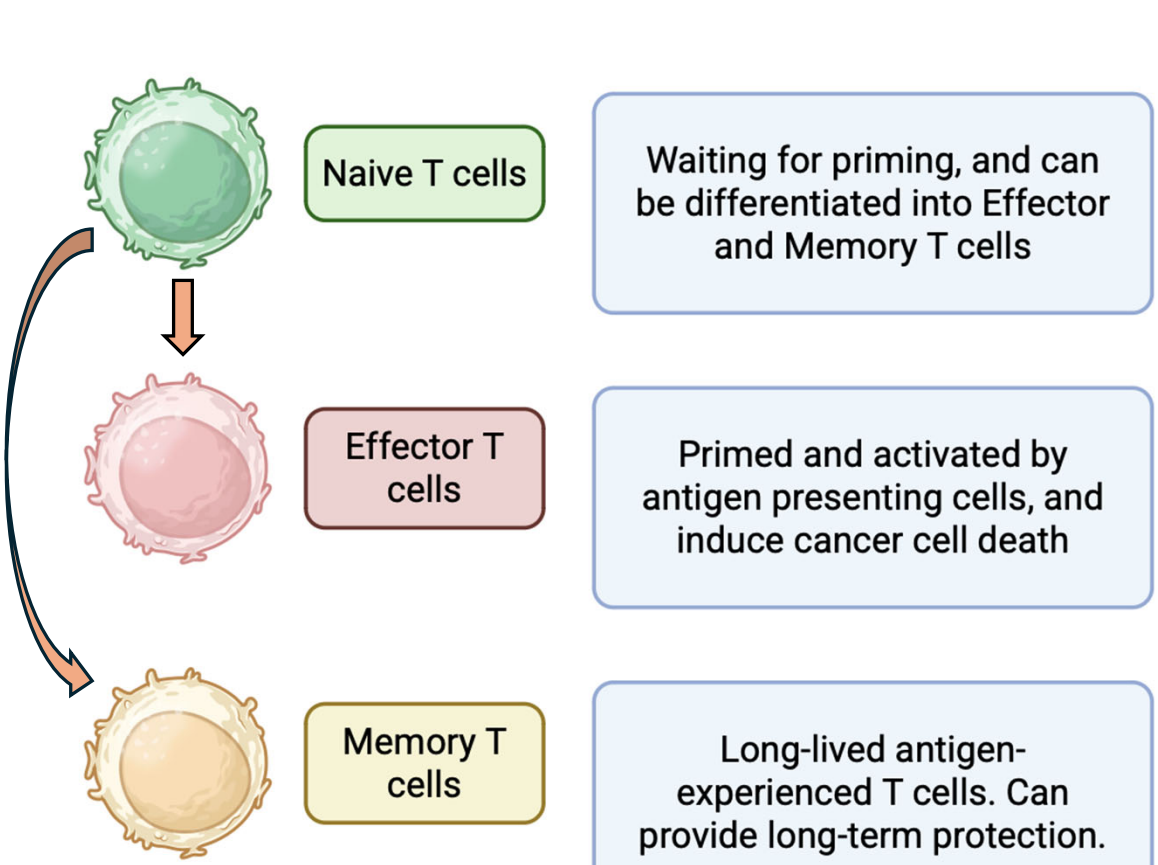
- pTyr-Specific Classical protein tyrosine phosphatases (PTPs)
  - Receptor – like PTPs
  - Non-transmembrane PTPs
    - PTP1B
    - TCPTP

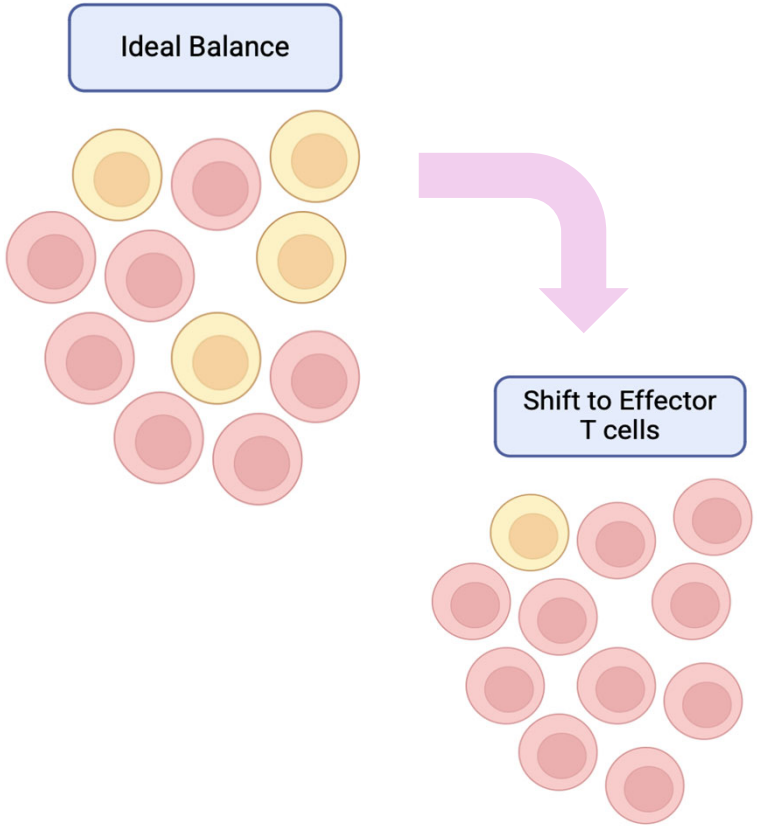
Silvia Shui @ Westcott Lab in CSHL



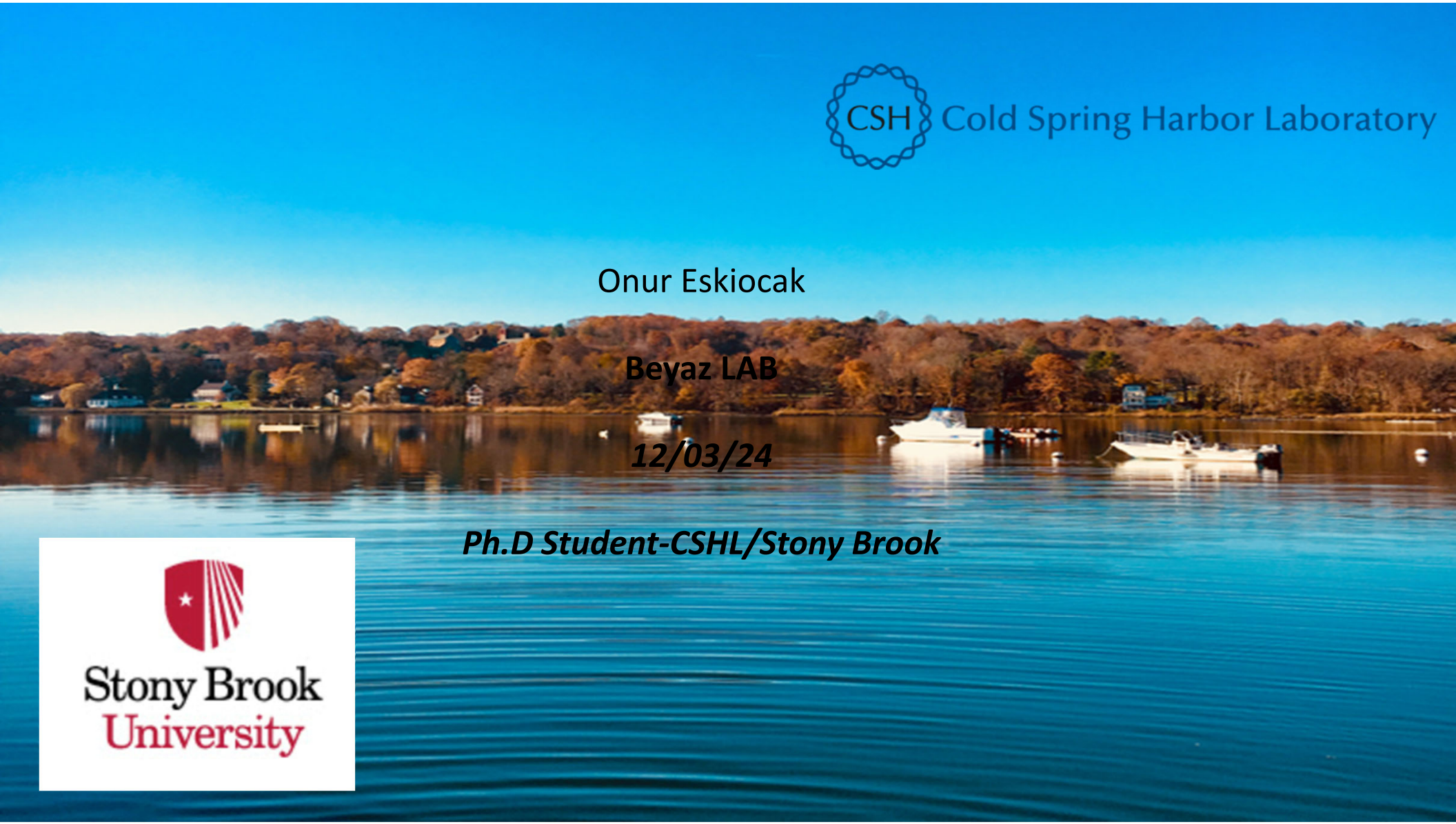


T Cell Immunity Is Important in Cancer Immunology

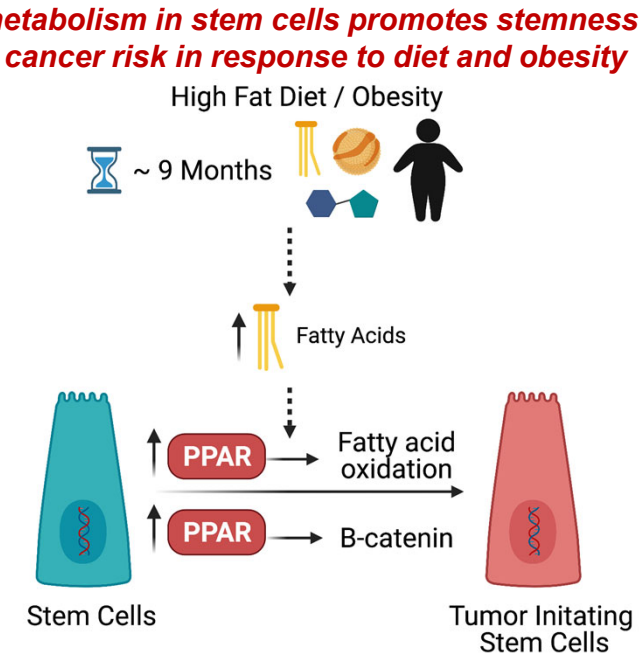




Ahmed et al., *Cancer Pathogenesis and Therapy* (2023)


CSH
Cold Spring Harbor Laboratory
Onur Eskiocak
Beyaz LAB
12/03/24
Ph.D Student-CSHL/Stony Brook
Stony Brook
University

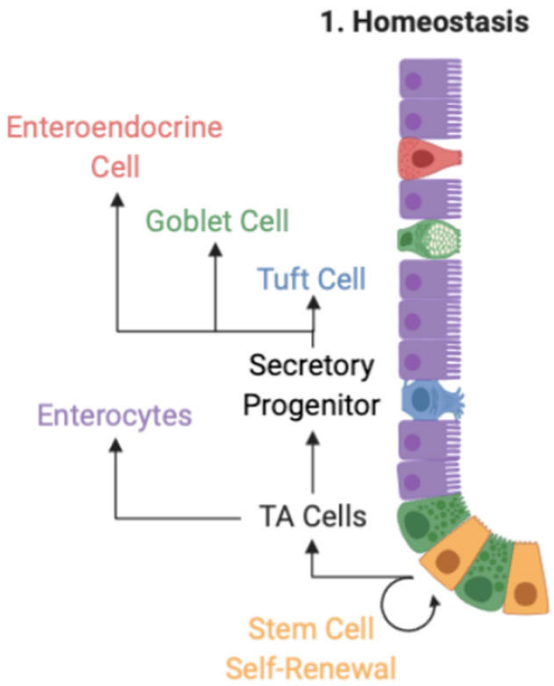
Dietary fatty acid (FA)-induced PPARd activation in stem cells is a causal mechanism that links HFD/obesity to increased intestinal cancer risk



How do distinct dietary fatty acids influence stem cell activity and regeneration in the intestine?

Beyaz et al. 2016, Beyaz et al. 2021a

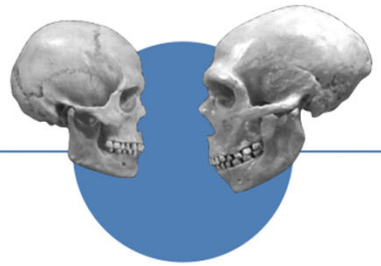
Intestinal epithelium as a model to study stem cell regeneration and plasticity?



- *What are the signals?*
- *Plasticity in physiological contexts?*
- *The influence of nutrient metabolism?*

Cheng and Leblond 1974, Potten et al. 1977, Barker et al. 2007, Buczacki et al. 2013, Nusse et al. 2018, Ayyaz et al. 2019, Murata et al. 2020, Cheng et al. 2019, Beyaz et al. 2016

Tracing modern human-specific adaptations with Ancestral Recombination Graphs

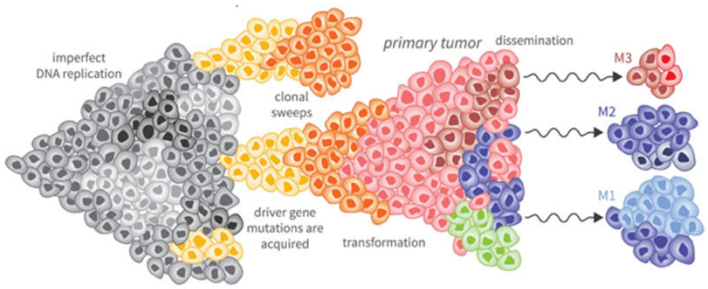


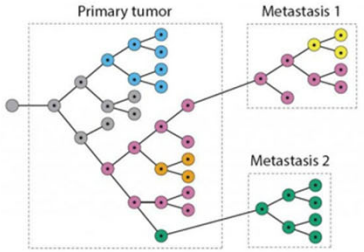
Luiz Machado

Cold Spring Harbor Laboratory

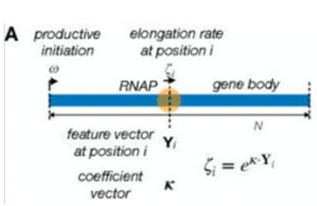
Stony Brook University

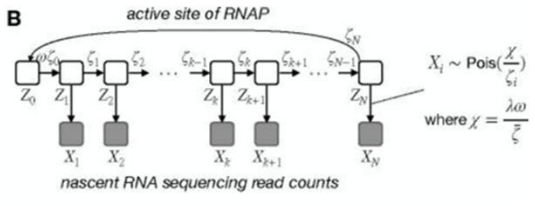
Cancer Evolution

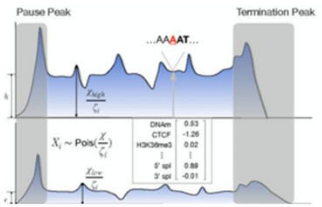




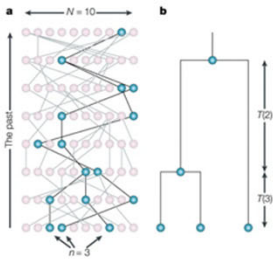
Transcriptional Regulation

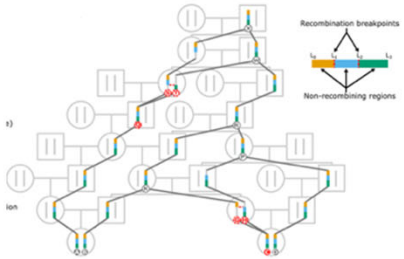


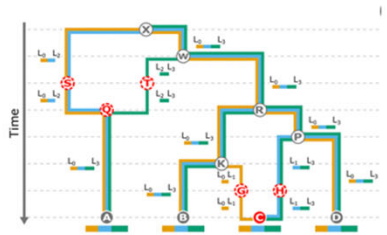




Quant/Pop Genetics

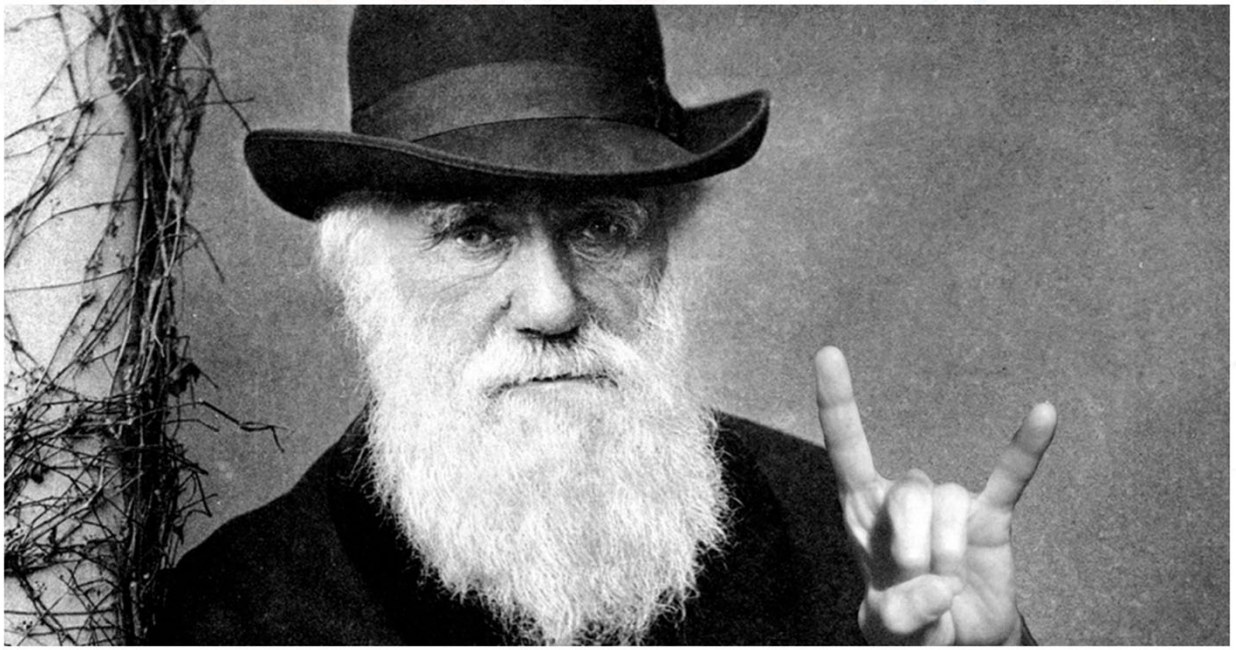




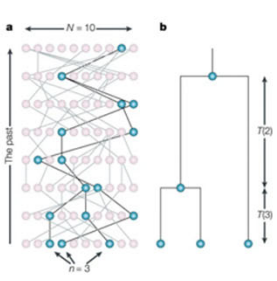


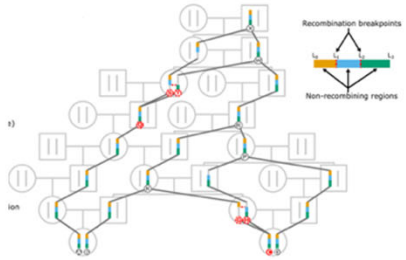
Cancer Evolution

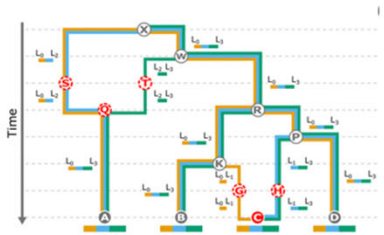
Transcriptional Regulation



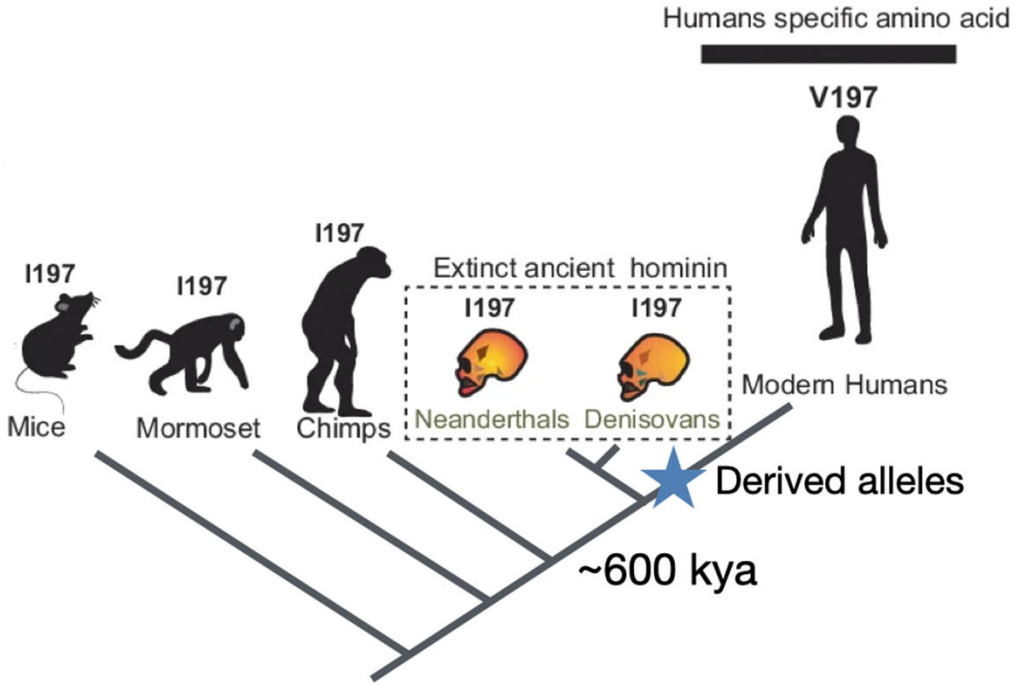
Quant/Pop Genetics

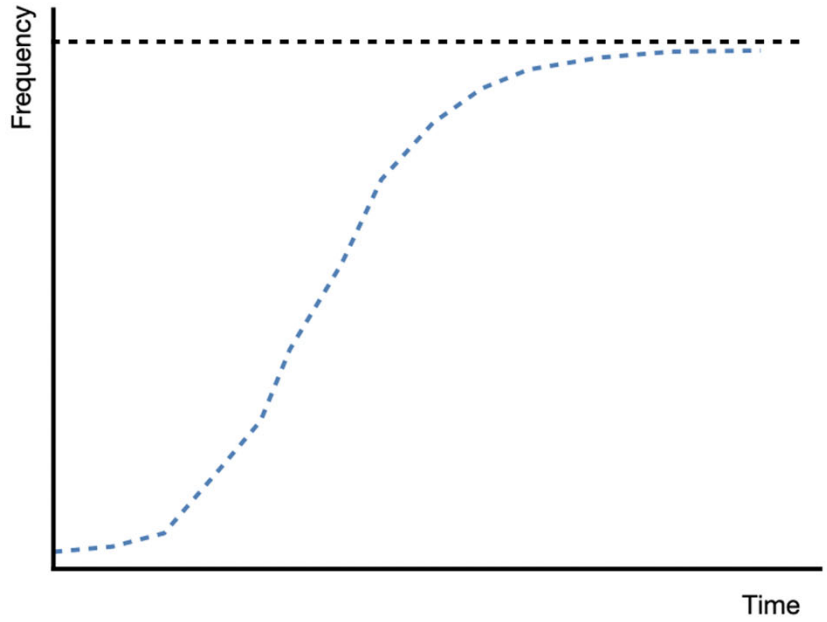






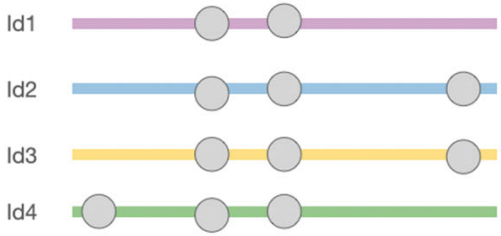
Modern Human–Specific Genetic Variants





What We Observe and What We Want to Know

Observed

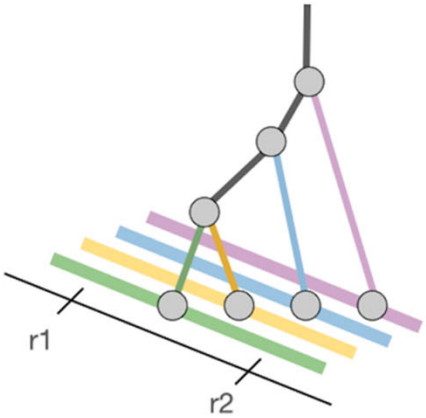


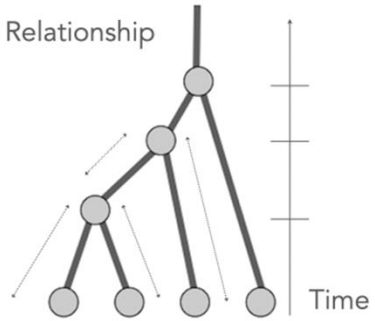
Present-day haplotypes

Patterns of shared variants

No time or ancestry information

Unobserved



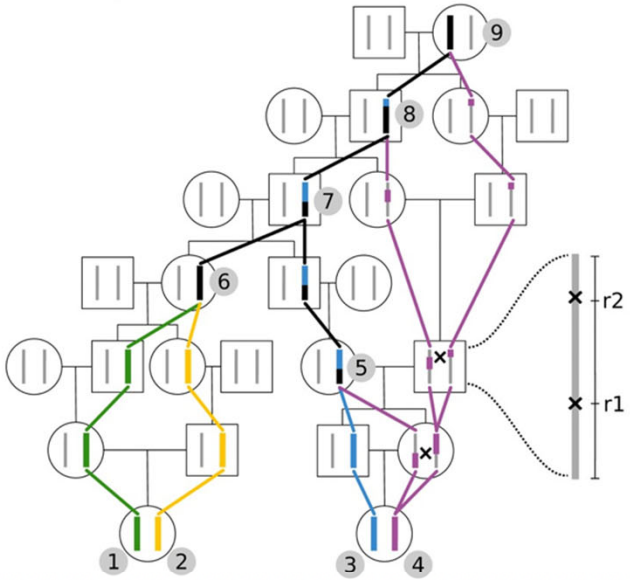


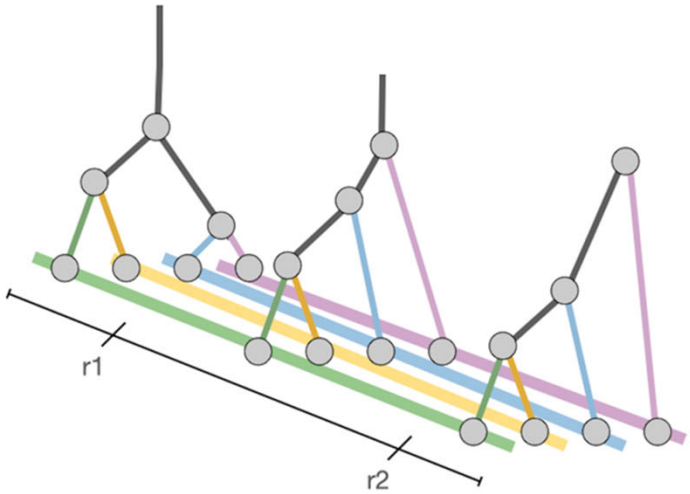
Genealogical relationships

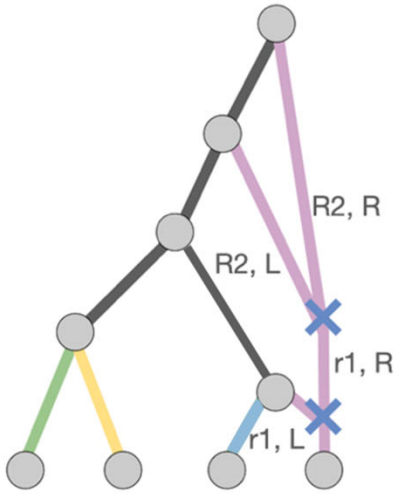
When lineages coalesce

How variants spread through time

What is Ancestral Recombination Graph?

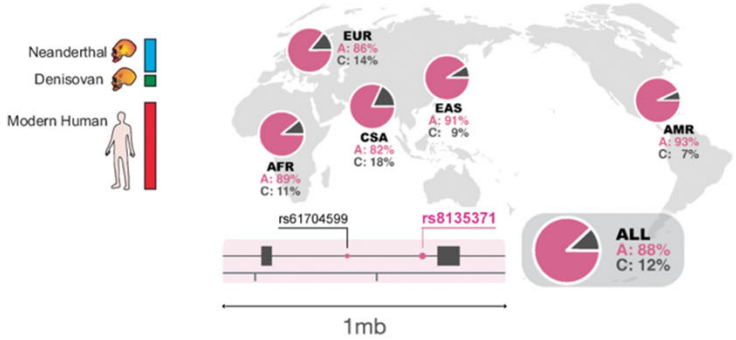






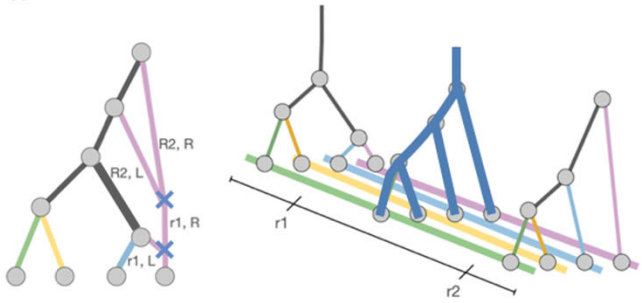
Workflow

I

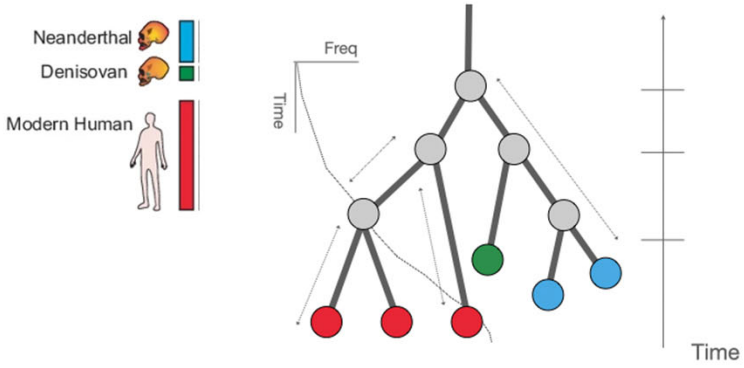


ARG Inference

II

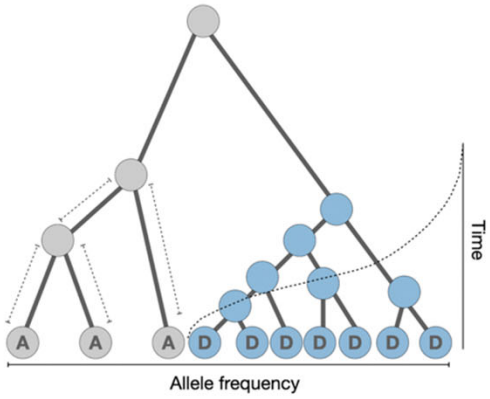


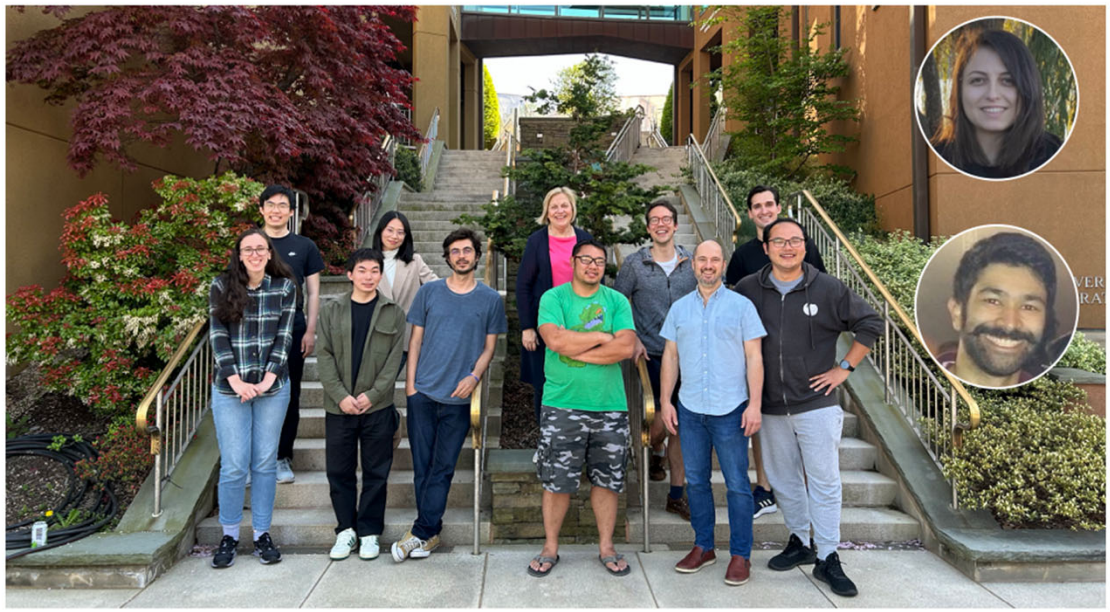
III

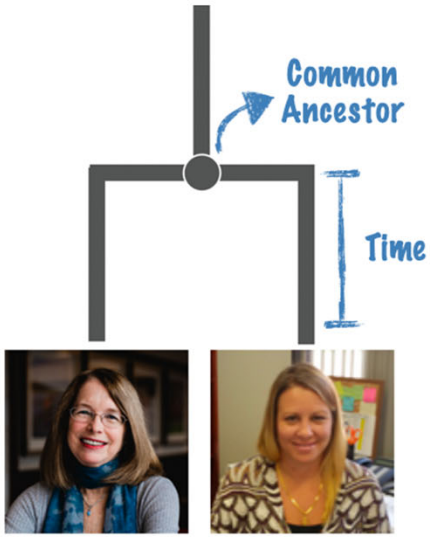


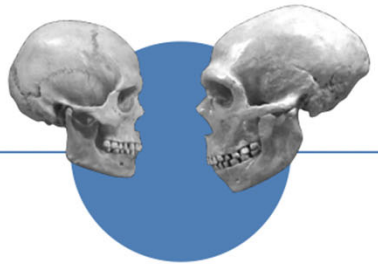
Test Selection

IV









Siepel Lab

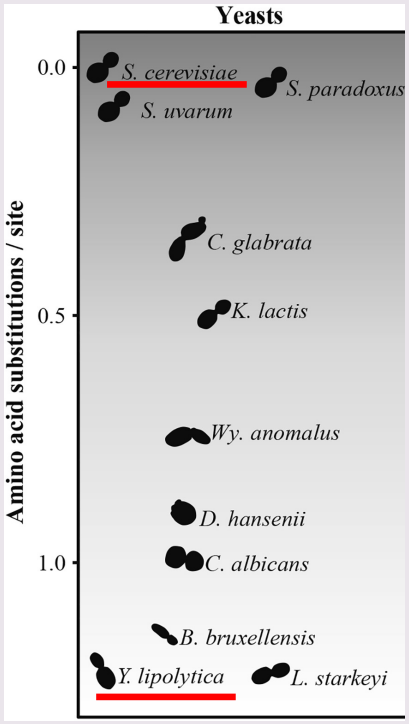
Cold Spring Harbor Laboratory

Stony Brook University

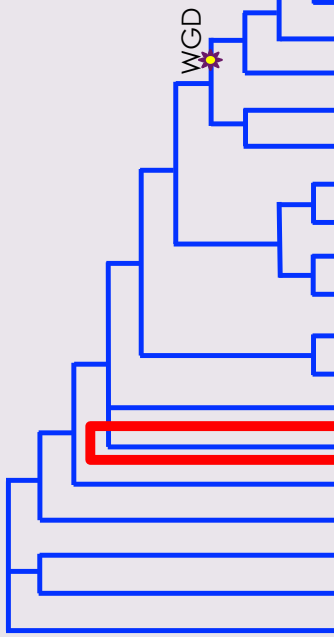
Dynamics of DNA Replication in *Yarrowia lipolytica*

Kimberly Hane
Speed Science 2025
Stillman Lab

Using *Y. lipolytica* as a Hybrid Model for DNA Replication

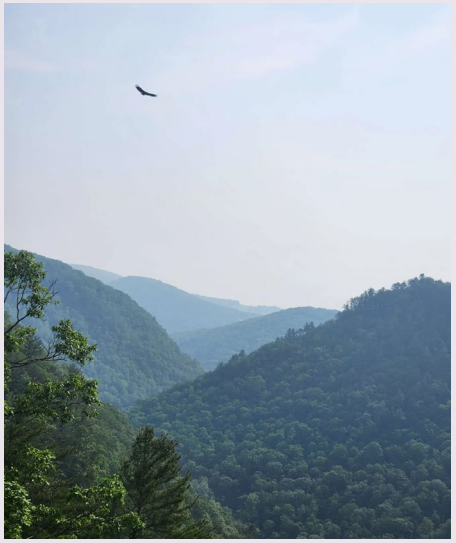


Shen, *et al.* 2018. PMID: 30415838



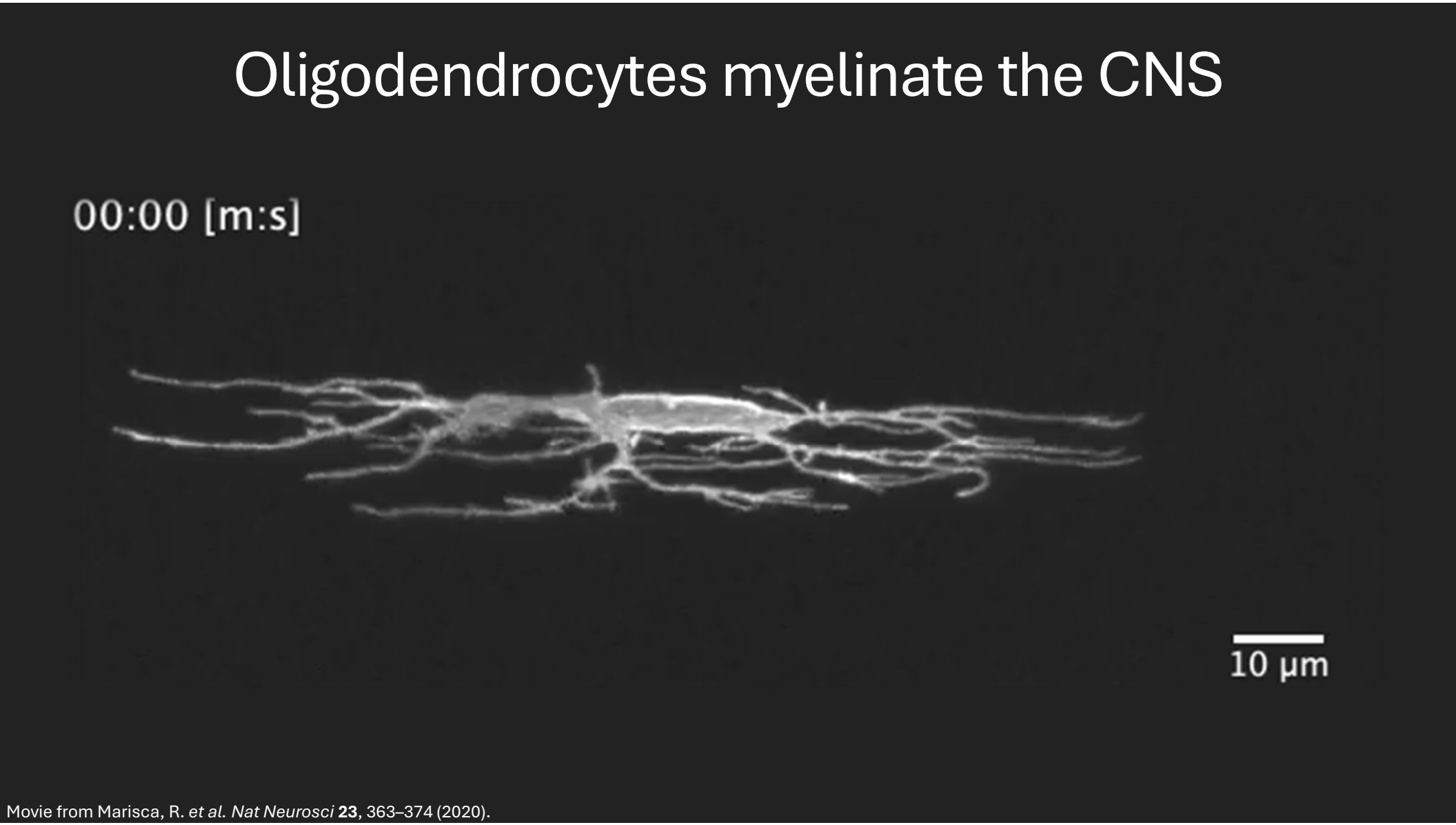
	Orc4 a-helix	Orc2 loop	Defined Origin
Saccharomyces cerevisiae	+	+	+
Saccharomyces bayanus	+	+	+
Candida glabrata	+	+	+
Naumovozyma castellii	+	+	+
Torulaspora delbrueckii	+	+	+
Zygosaccharomyces rouxii	+	+	+
Lachancea kluyveri	+	+	+
Lachancea waltii	+	+	+
Ashbya gossypii	+	+	+
Kluyveromyces lactis	+	+	+
Candida albicans	-	-	-
Debaryomyces hansenii	-	-	-
Pichia pastoris	-	-	-
Yarrowia lipolytica	-	-	-
Neurospora crassa	-	-	-
Schizosaccharomyces pombe	-	-	-
Drosophila melanogaster	-	-	-
Homo sapiens	-	-	-
Arabidopsis thaliana	-	-	-

Hu, *et al.* 2020. PMID: 33056978



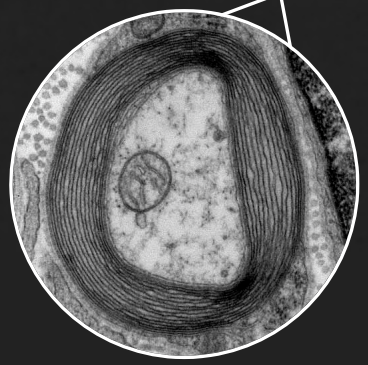
Give yourselves a pat on the back!

Oligodendrocytes myelinate the CNS



Movie from Marisca, R. *et al. Nat Neurosci* **23**, 363–374 (2020).

Oligodendrocytes myelinate the CNS



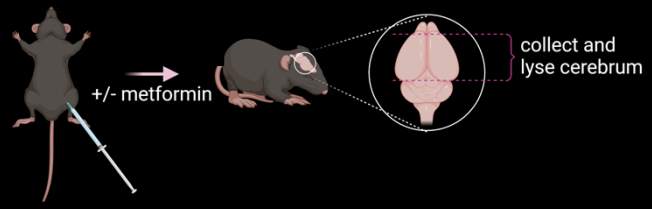
- Provide neural network stability
- Increase action potential speed
- Metabolically support neurons

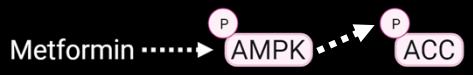
10 µm

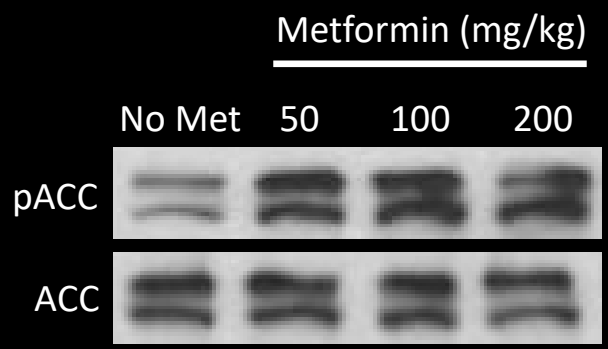
Image from EM facility at Trinity College

Movie from Marisca, R. *et al. Nat Neurosci* **23**, 363–374 (2020).

Metformin accelerates myelin repair in adult rodents







Myelin Repair

Age-matched Control | Myelin Loss | No Metformin | + Metformin

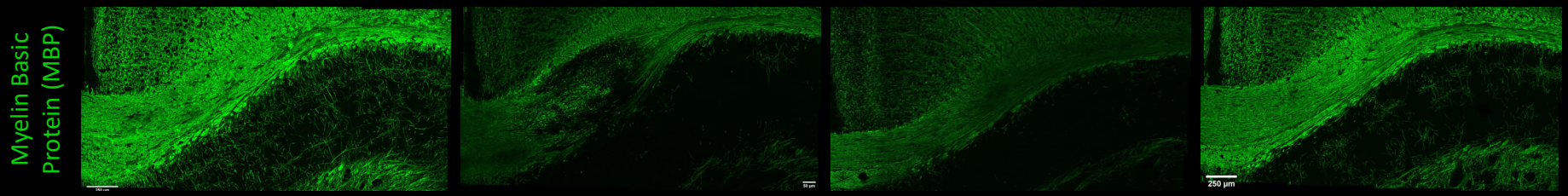


Figure adapted from Narine, M., Azmi, M. A., et al. Front Cell Neurosci. 2023.

Myelination is a prolonged process

Developmental myelination take place in waves during:

- Infancy
- Childhood
- Late teen/Early adulthood

Adaptive myelination continues throughout life.

Does metformin affect developmental myelination?

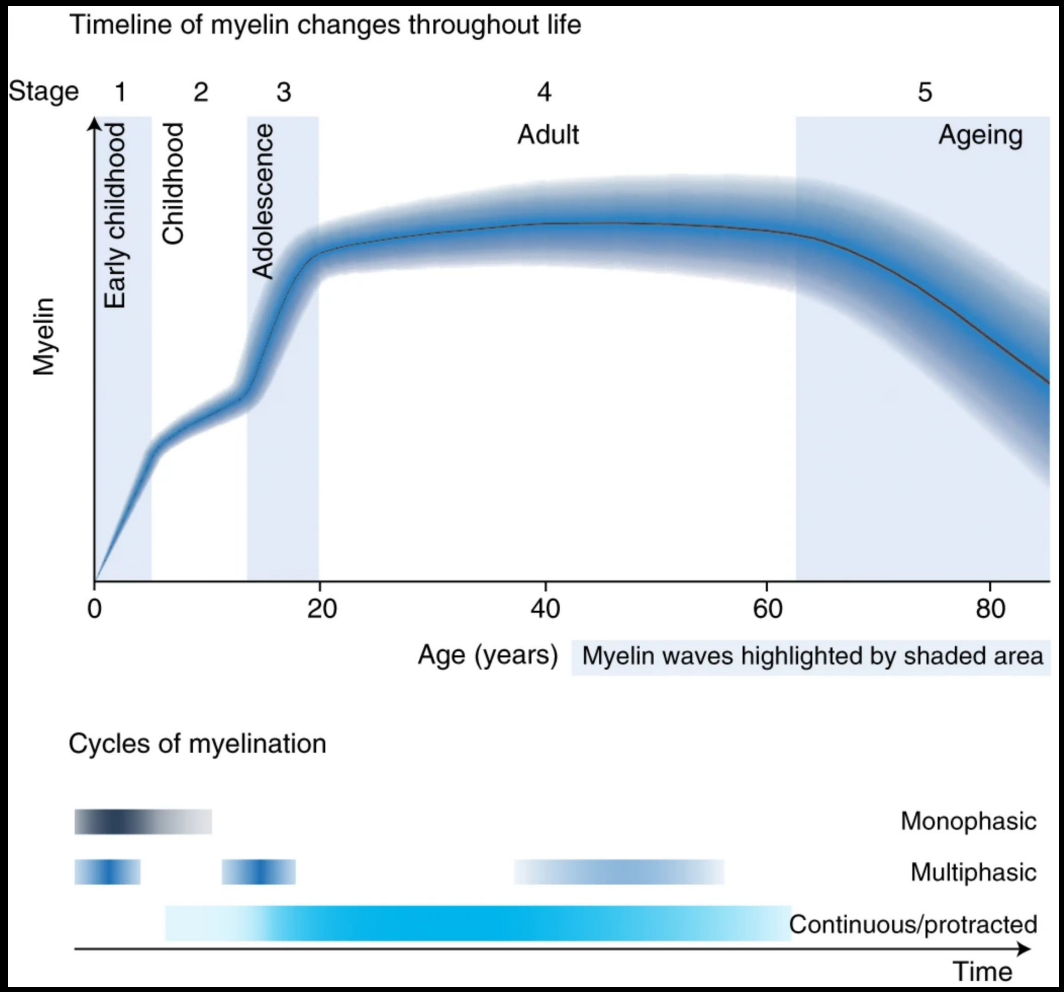
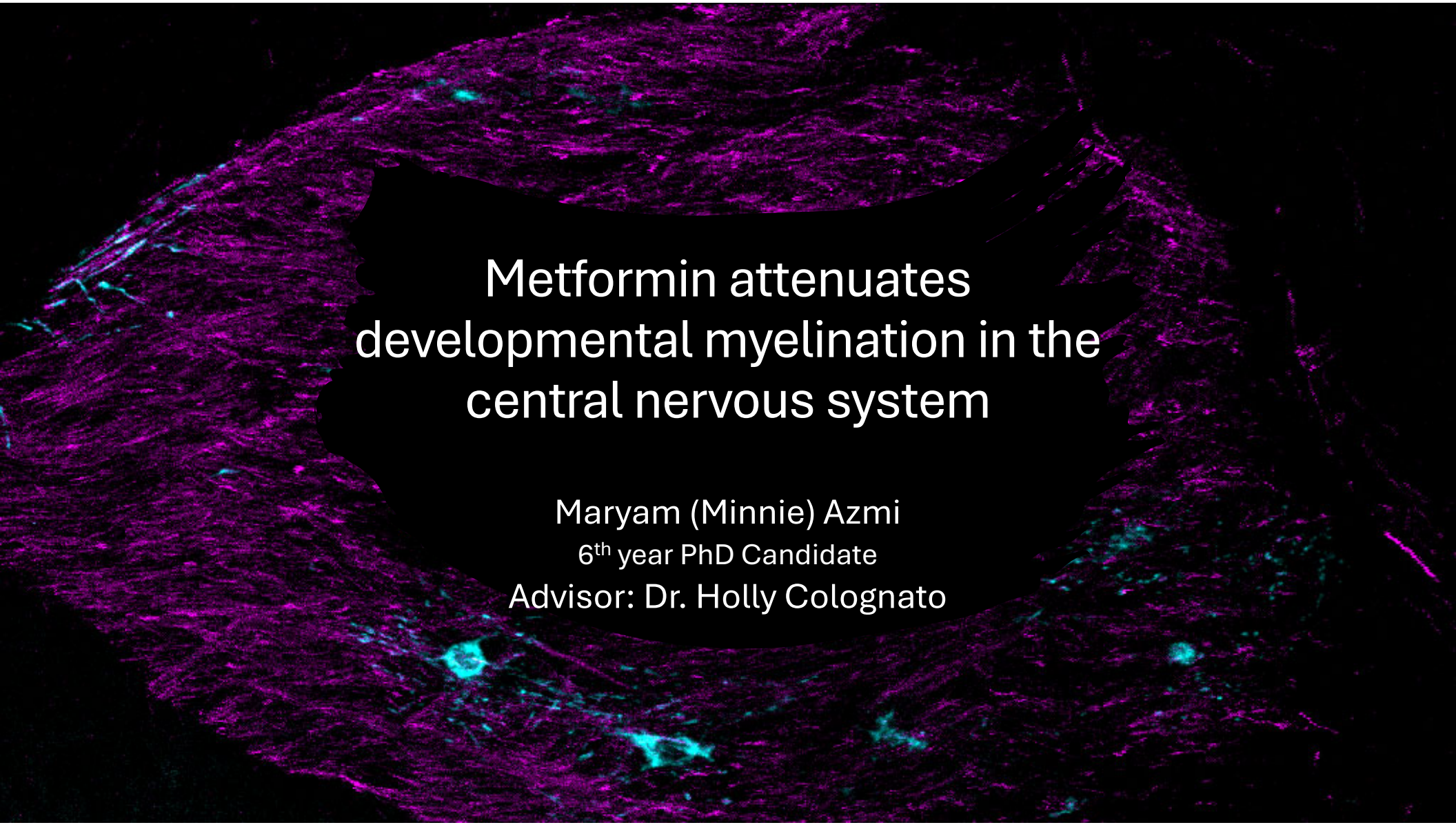


Figure adapted from de Faria, O. *et al. Nat Neurosci* **24**, 1508–1521 (2021).



Metformin attenuates developmental myelination in the central nervous system

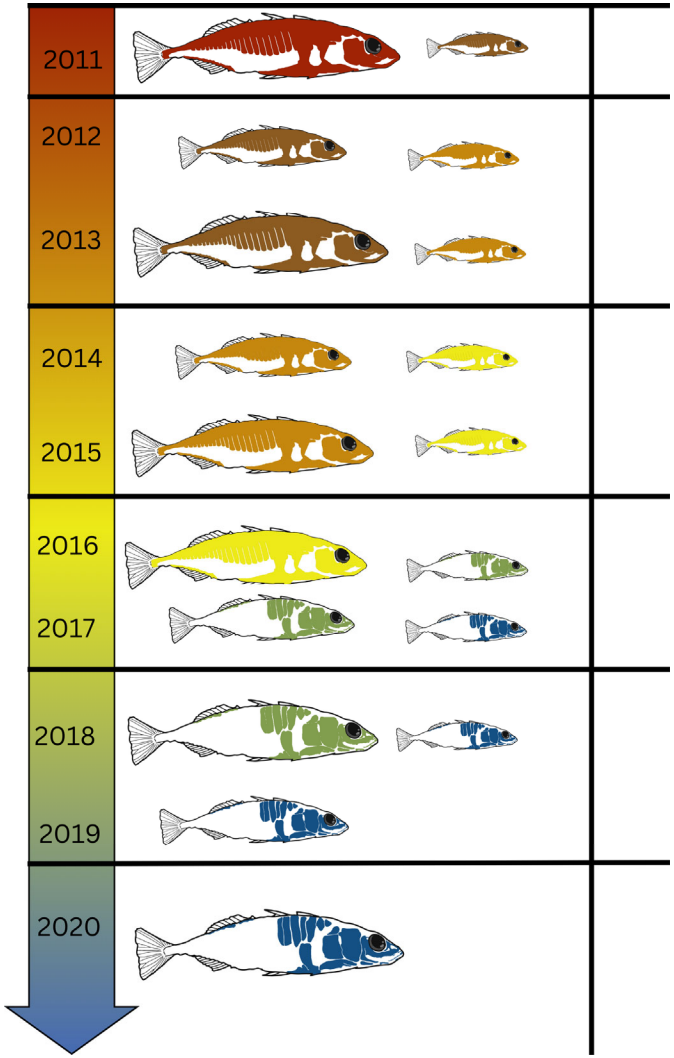
Maryam (Minnie) Azmi
6th year PhD Candidate
Advisor: Dr. Holly Colognato

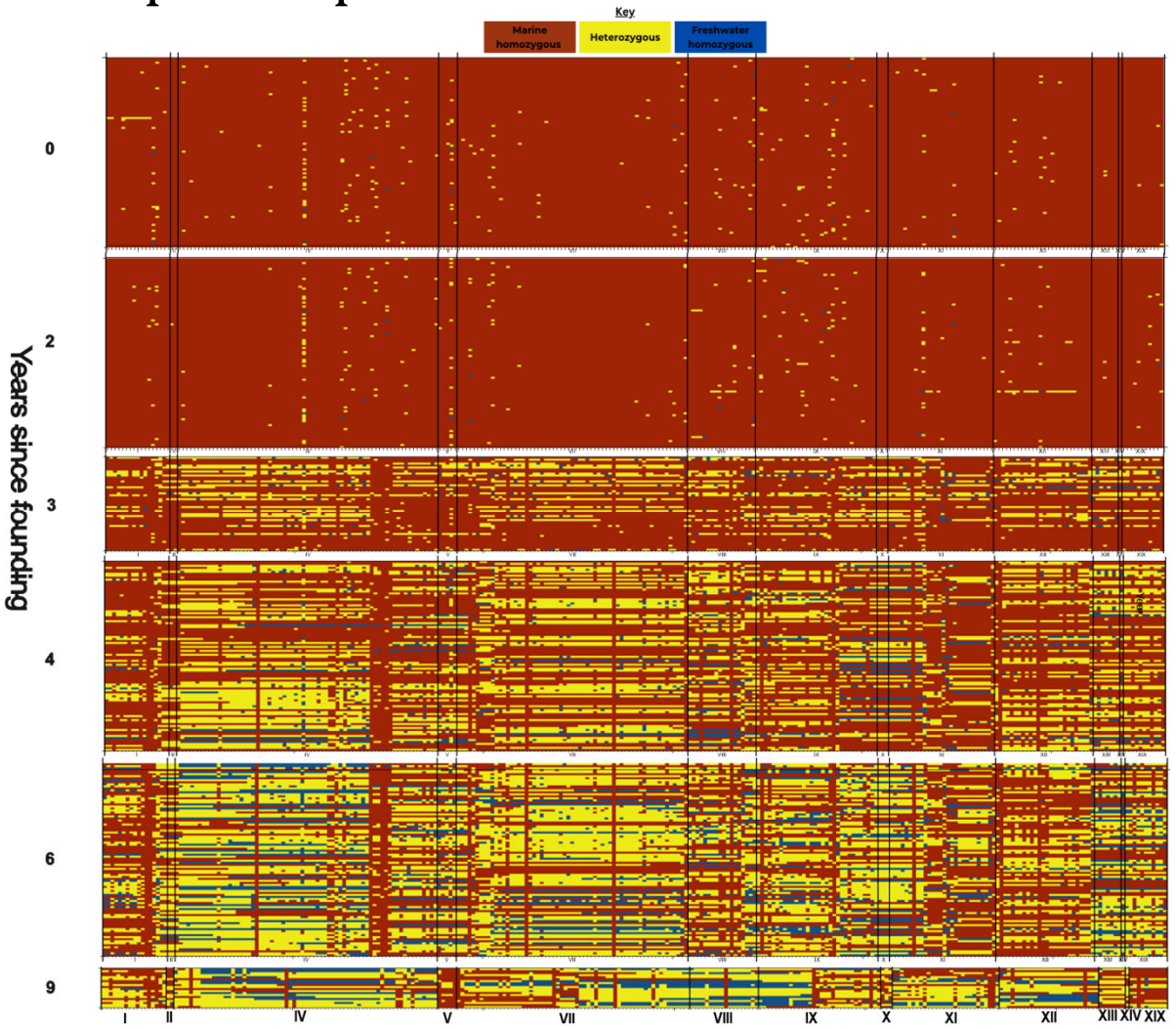
The Veeramah Lab

Molecular evolutionary mechanisms of rapid adaptation

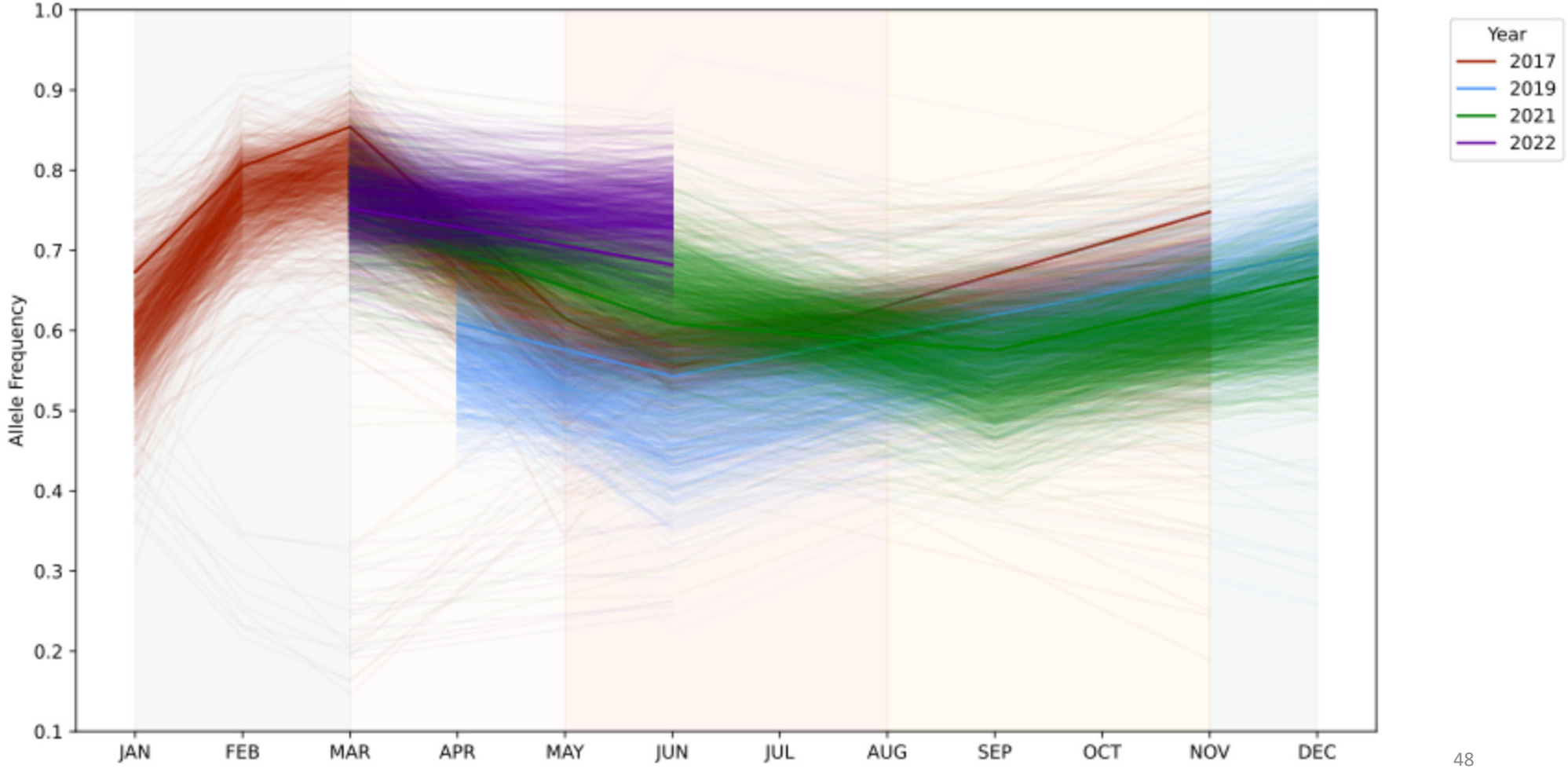
Alexander Kwakye

Jackpot mediated rapid adaptation

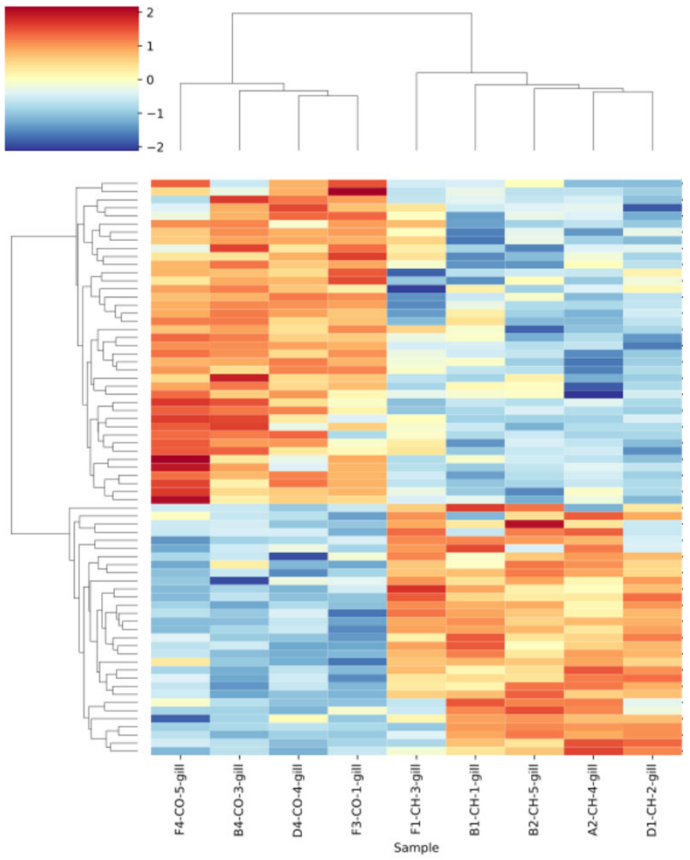


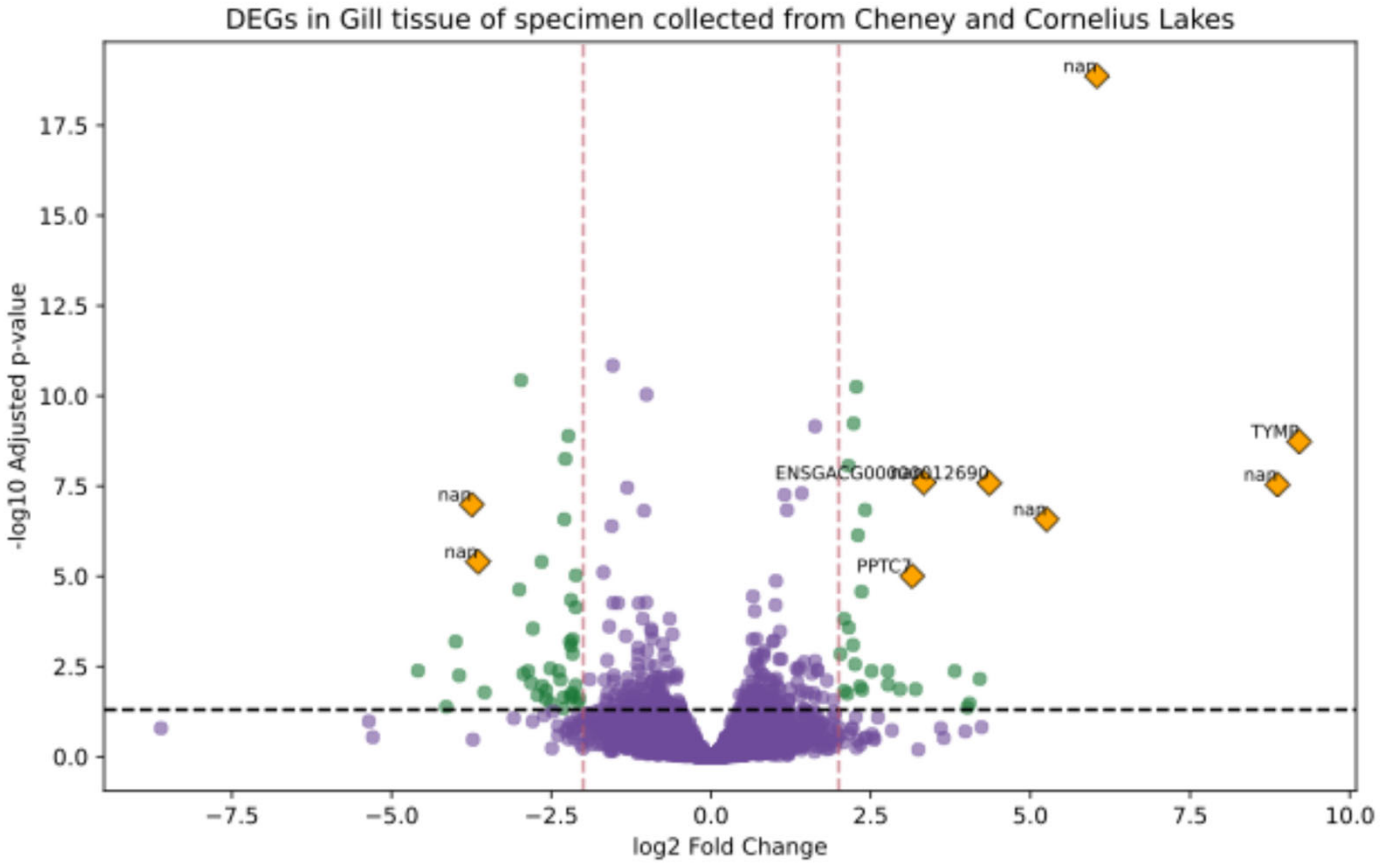


Trajectory of SNPs within a year across multiple years



Differentially expressed genes between Cheney and Cornelius lakes





FOXA1 restrains cytotoxic sphingolipids in breast cancer

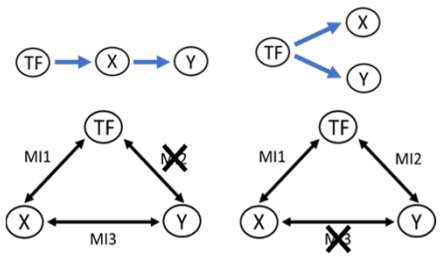
Sam Chiappone

9-10-25

The family of sphingolipids known collectively as ceramide are cytostatic and also cytotoxic at high levels, giving ceramide the status of a putative "tumor suppressor lipid"

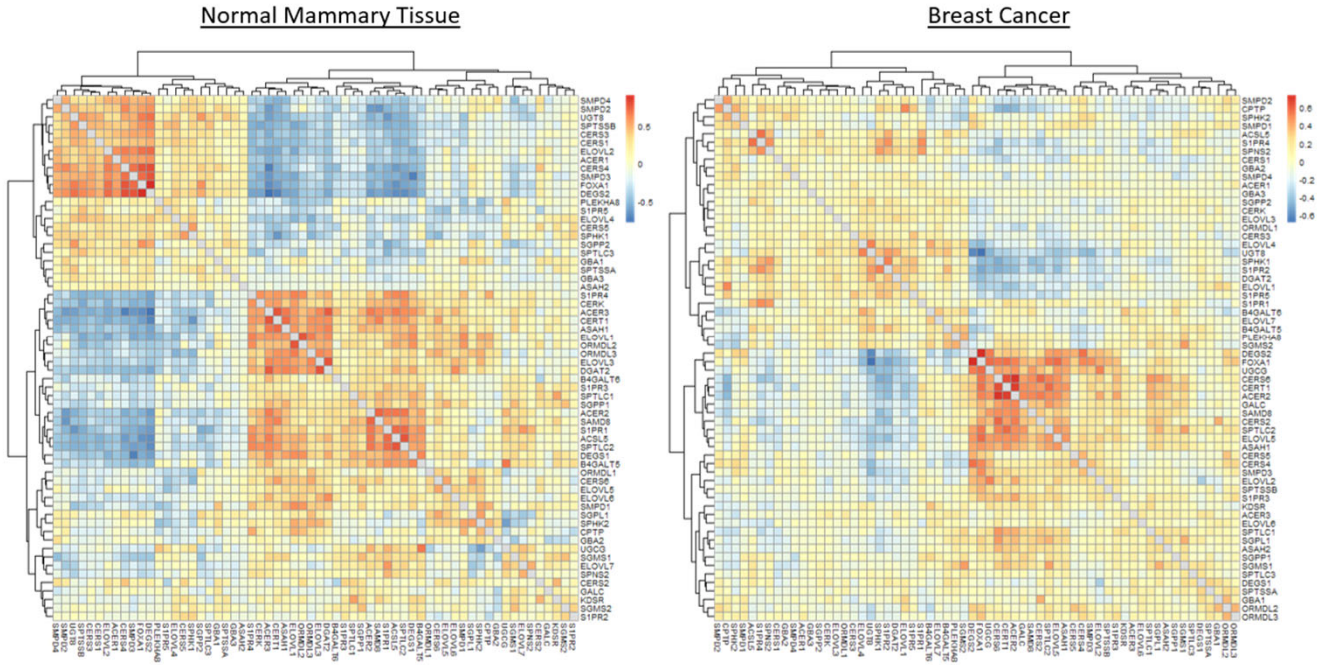
What regulates ceramide levels in cancer?

$$MI_{x,y} = D_{KL}(P_{(x,y)}||P_x \otimes P_y)$$



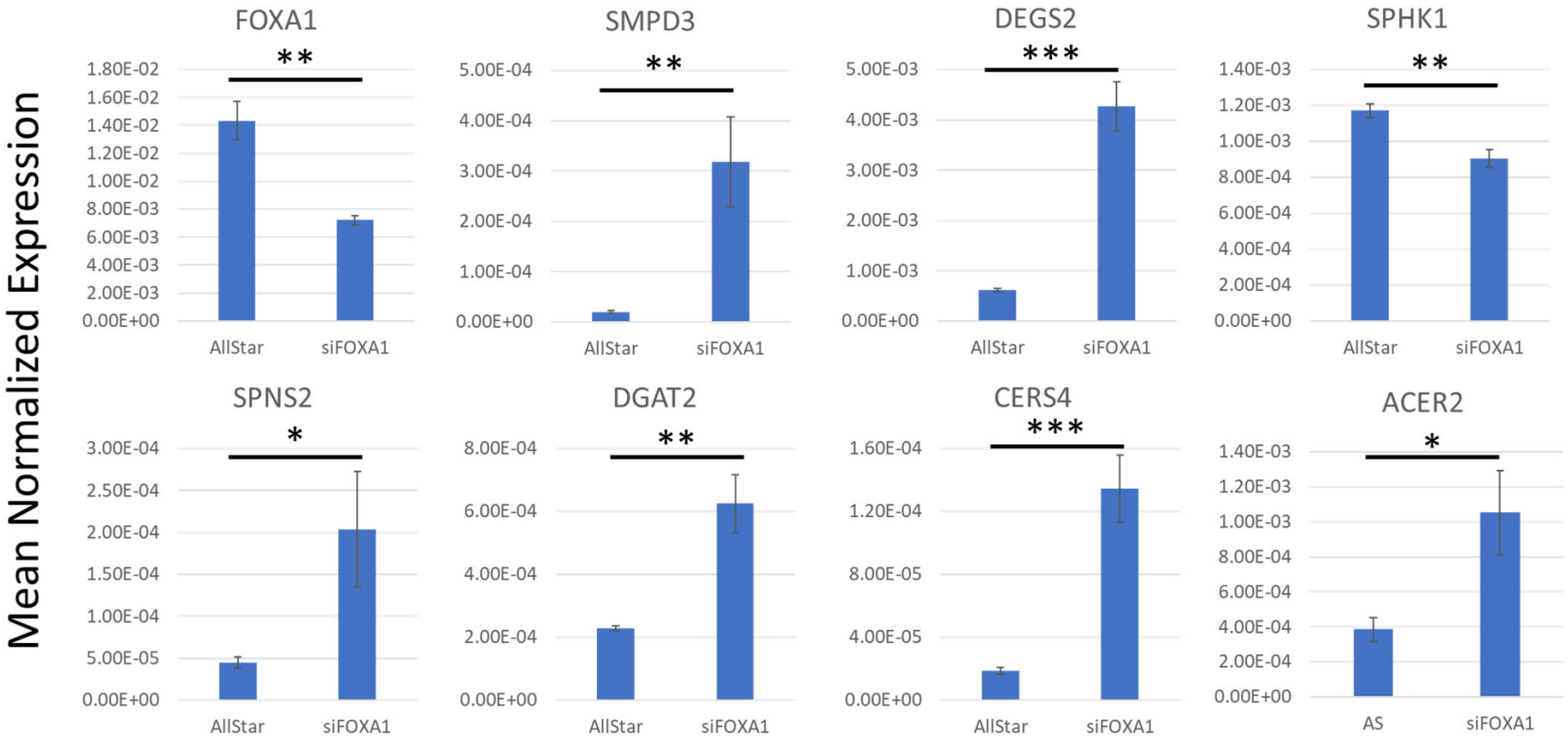
Gene X	Gene Y	MI	Adjusted p-value
FOXA1	SPHK1	0.3808	0 (small)
	SPNS2	0.3116	1.78E-7
	S1PR2	0.4082	0 (small)
	DGAT2	0.2609	0 (small)
	SMPD3	0.2993	0 (small)
	CERS2	0.3221	1.78E-7
	ELOVL5	0.3828	0 (small)

The machine learning algorithm ARACNE predicted FOXA1 to be the most significant regulator of sphingolipid (SL) genes in breast cancer RNA-Seq samples from TCGA



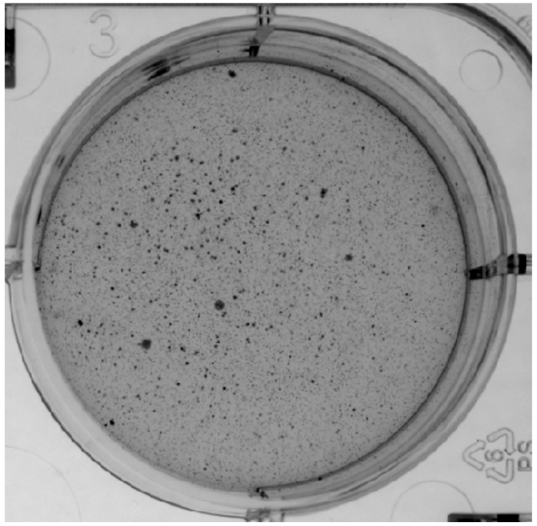
WGCNA also classified FOXA1 as associated with the most significant cluster of SL genes in RNA-Seq from breast cancer in TCGA

Experimental validation of FOXA1 function in breast cancer; control of SL gene expression

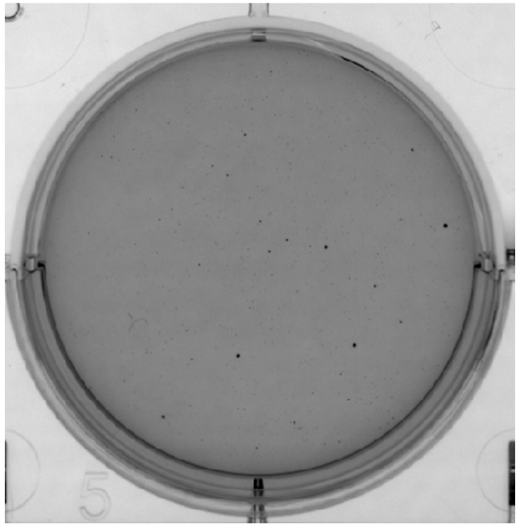


Does the colony growth defect in FOXA1 knockdown cells depend on ceramide?

AllStar negative control siRNA



siFOXA1



Conclusions

- In this work, we identify at least one factor controlling ceramide levels in breast cancer, the pioneer transcription factor FOXA1

- We also potentially pin a molecular function on FOXA1's control of aggressiveness in breast cancer, which has been elusive

Nelson Gautier
van der Velden Lab

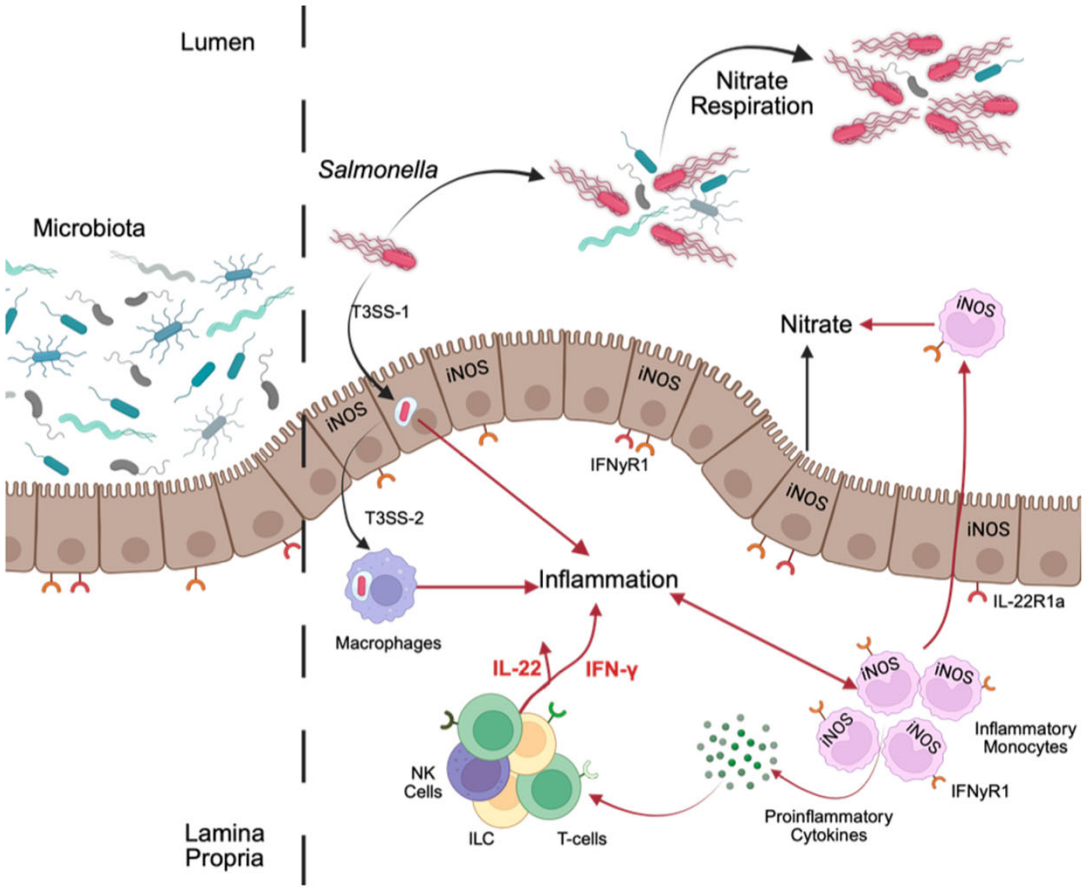






RECALL
Home Delivery Meals Linked to Salmonella Outbreak Across 10 States: What to Know
There have been 16 cases of reported illnesses across the country.
Sept. 9, 2025, 10:00 AM EDT / Source: TODAY
POLITICS
More brands of Dubai chocolate recalled in salmonella outbreak linked to pistachios
More recalls have been issued for a popular type of chocolate after a salmonella outbreak linked to certain brands of pistachios and pistachio-containing products.
Aug. 14, 2025 | 1 min read

Role of Inflammatory Monocytes in Salmonella-Induced Colitis



Adapted from McLaughlin *et al. PLoS Pathogens* 2019

- 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.

Speed Science

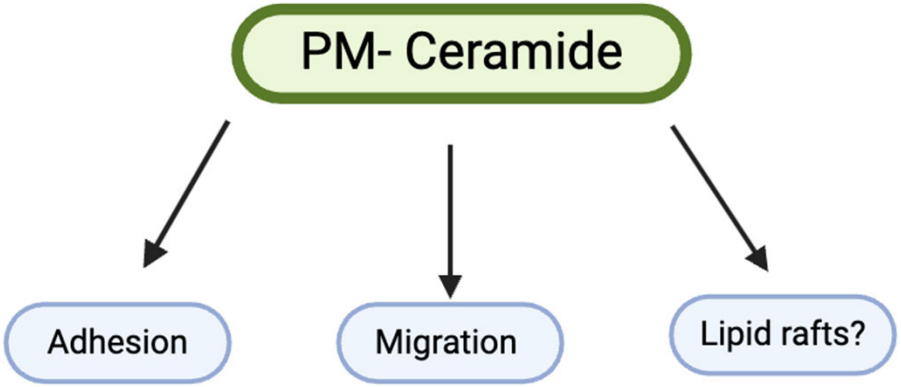
Abhay Kanodia

Canals Lab

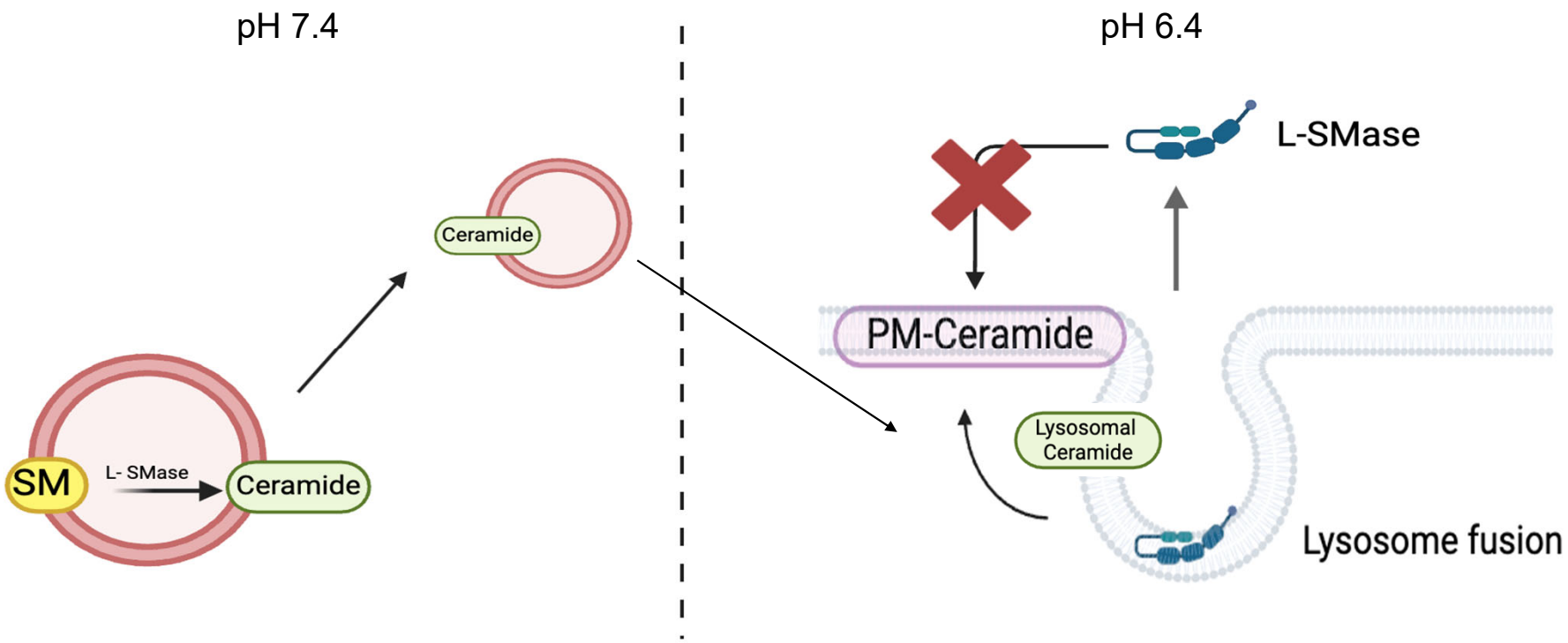
09/10/2025

Lysosomal ceramide-metabolizing enzymes, regulate plasma membrane ceramide in response to acid stress

Functions of Plasma Membrane Ceramide

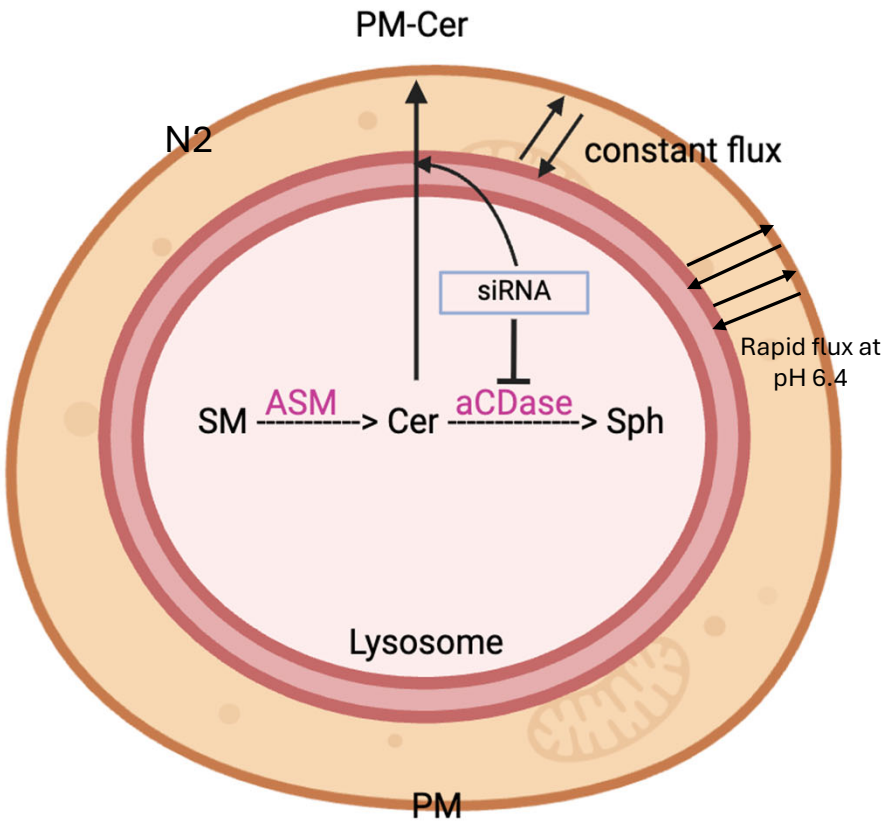


Proposed Model: ASM producing lysosomal ceramide that is transferred to the PM in acidic conditions



Modified model of PMCer generation

pH 7.4



Identifying novel NRF2 functional binding partners in NSCLC

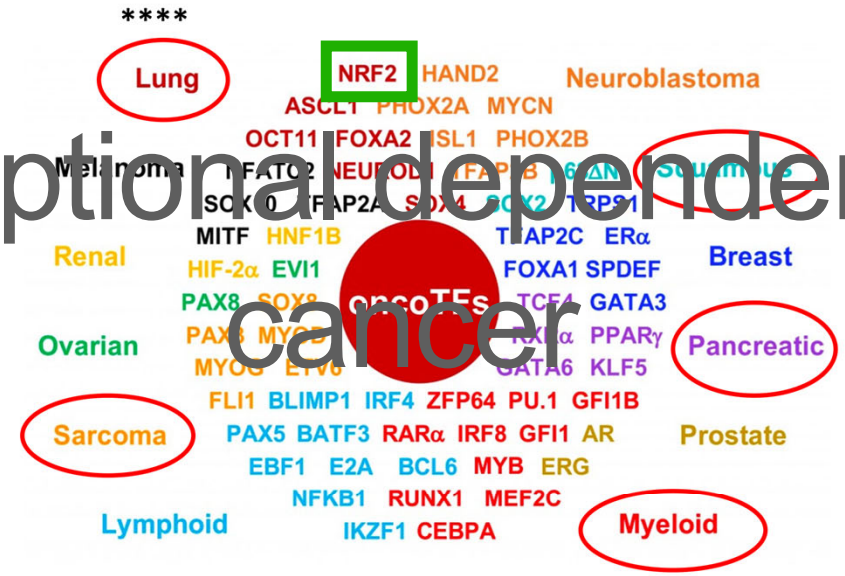
Speed Science session 2025

Santiago Espinosa | Vakoc Lab

09/10/2025

The Vakoc Laboratory

Transcriptional dependencies in cancer



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).

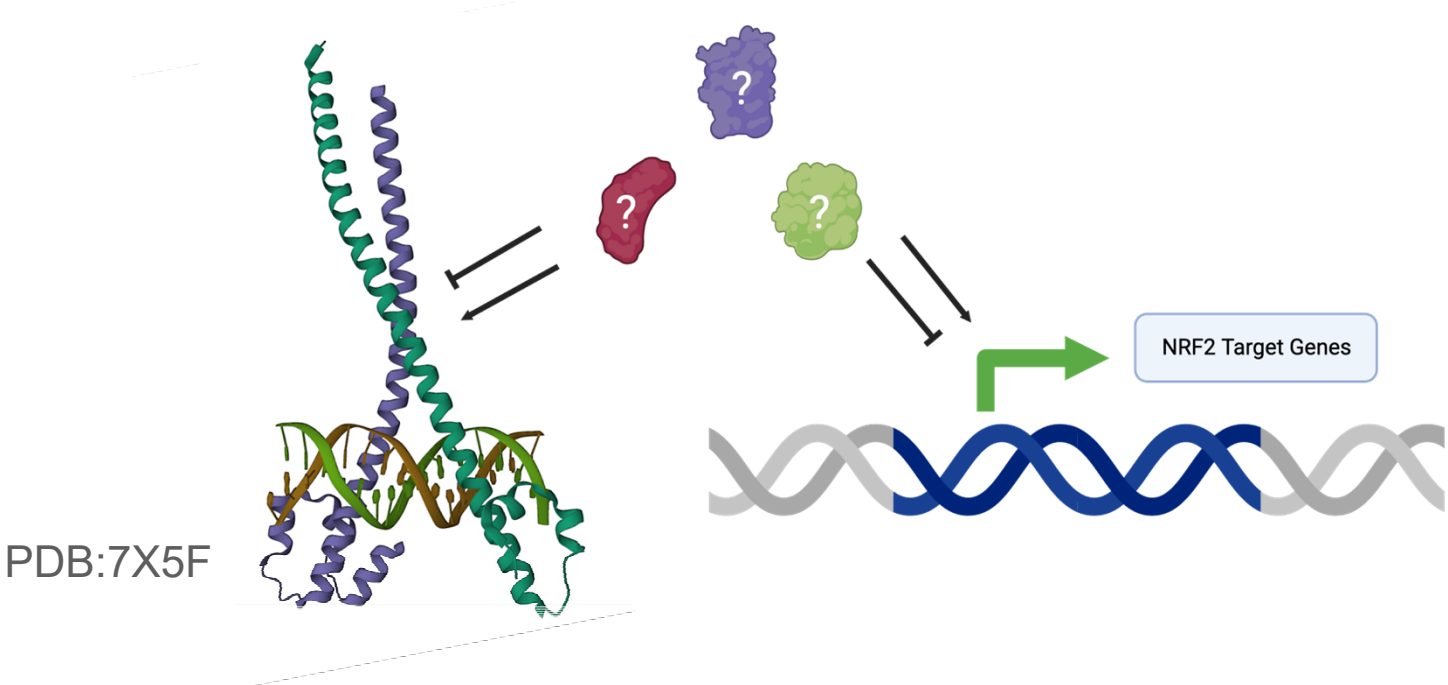
Enhancer Reprogramming Promotes Pancreatic Cancer Metastasis. *Cell.* 170(5):875-888 (2017).

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).

Source: Connor Fitzpatrick

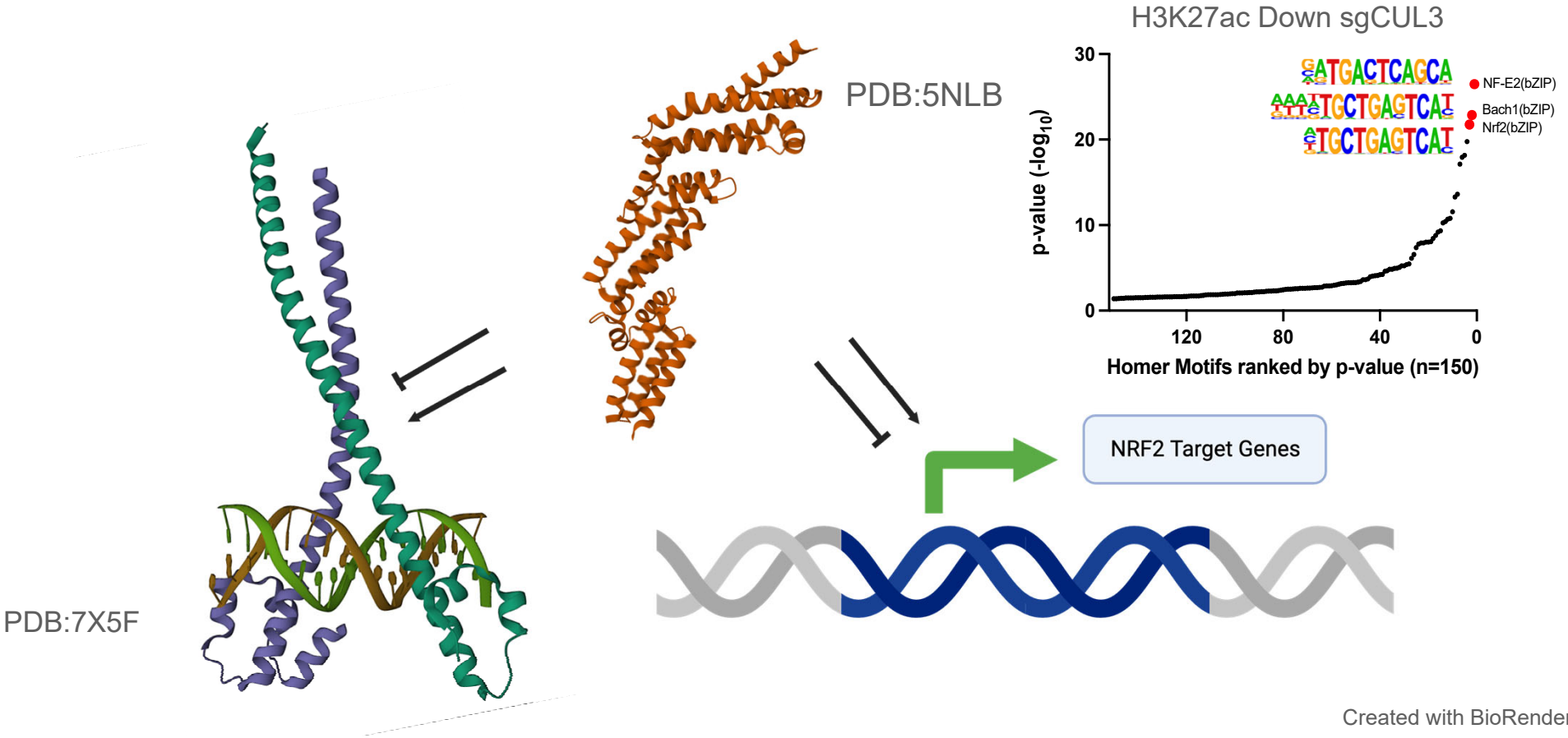
Our goal: to reveal novel mechanisms of NRF2 function in *KEAP1*-mutant NSCLC



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



Created with BioRender.com

Acknowledgements

Vakoc Lab:

Chris Vakoc, MD/PhD
Aktan Alpsoy, PhD
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