SPEED SCIENCE 2024

Session One

Alex Cicala

Background:

- Undergrad at UW-Madison
- Post-grad research at UCSD
- Current SBU MSTP

Research Interests:

- Genetics
- Tumor microenvironment and evolution
- Immunology

Clinical Interests:

- Oncology

Thesis Lab:

Peter Westcott (CSHL)

Personal Interests:

- Coffee
- Sports
- Nature

EMORY

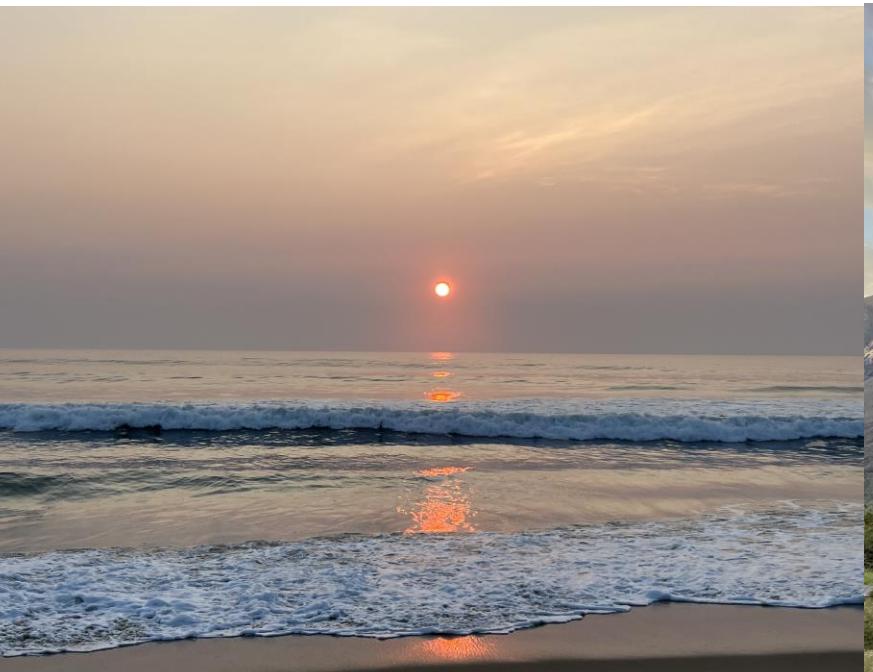
NIH

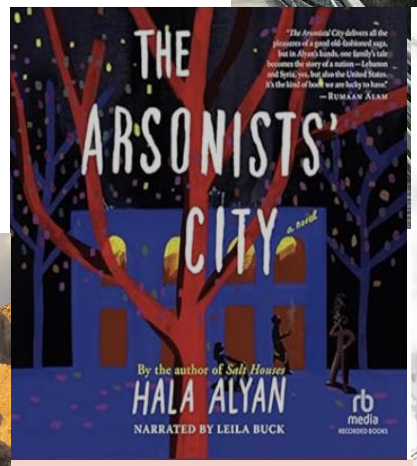
JSPG
Journal of Science Policy & Governance

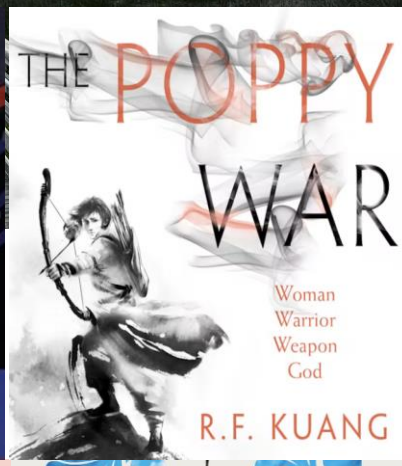
NATIONAL CANCER INSTITUTE

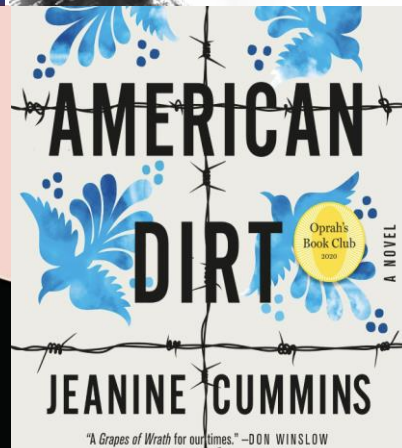
AMA

Rohini Guin









Jason Harper

B.S. – Stony Brook University, Class of ‘24

Majored in Biochemistry

Fun fact: originally from Stony Brook!

Research Background

SBU Dept. of Biomedical Informatics (June 2022 – August 2023)

PI: Dr. Joel Saltz (with Kenneth Shroyer)

Studied the effects of Keratin 17 on the tumor microenvironment

Work published in *Journal of Translated Medicine*

Stony Brook Cancer Center (June 2023 – July 2024)

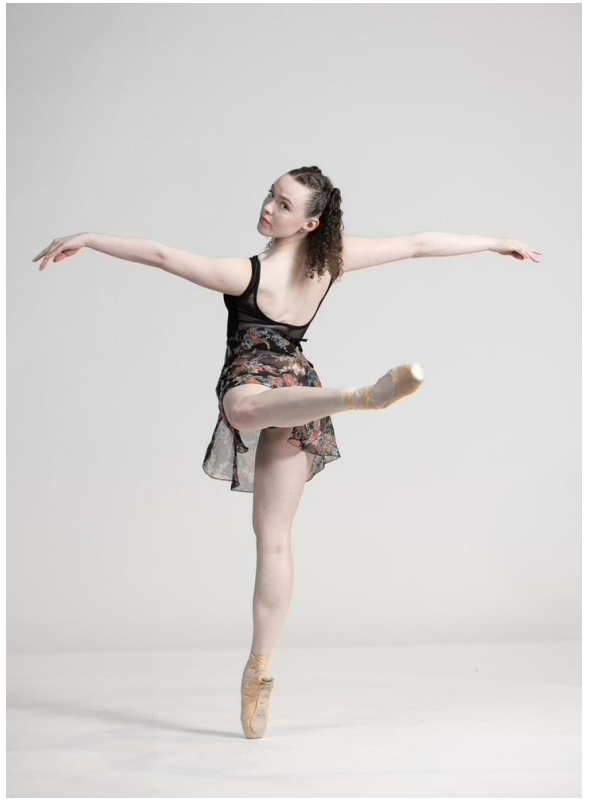
PI: Dr. Yusuf Hannun

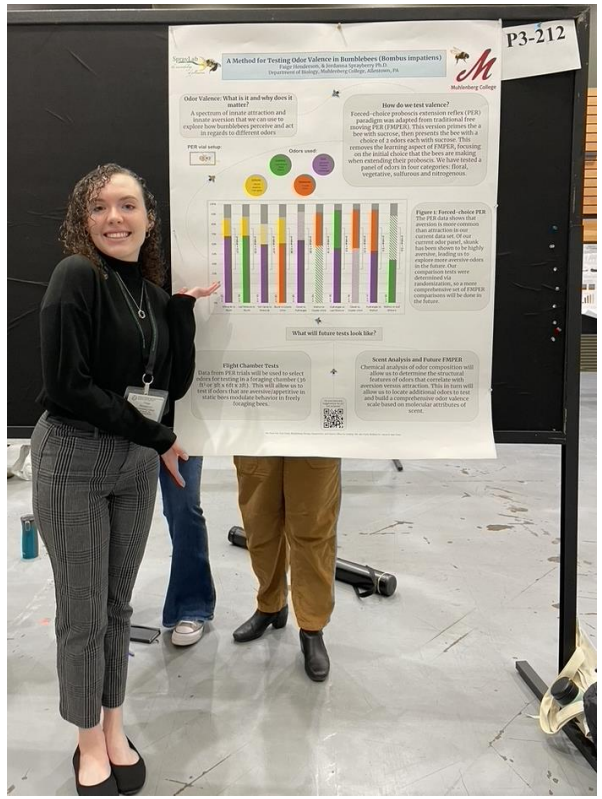
Studied the effects of glucosylceramide on the oncogenicity of KRas-transformed rat intestinal cells

Research Interest: tumor epigenetics

Speed Science: Introduction

Paige Henderson





Introduction – Shareef Khalid

2016	2017	2018 – 2020	2021 – 2024	2024+
Lahore, Pakistan	Atlanta, GA	Tarrytown, NY	NYC	Stony Brook, NY

Research Experience / Interests

- Pre-2018: Cancer Genomics
- Post-2018: Leverage large scale human genetic biobanks to discover mutations which modulate disease risk, identify potential drug targets and perform in-silico screens for potential side effects.
- Interested in **Evolutionary Genetics**: how evolutionary pressures shaped the genomes of various organisms

Research highlights from previous lives

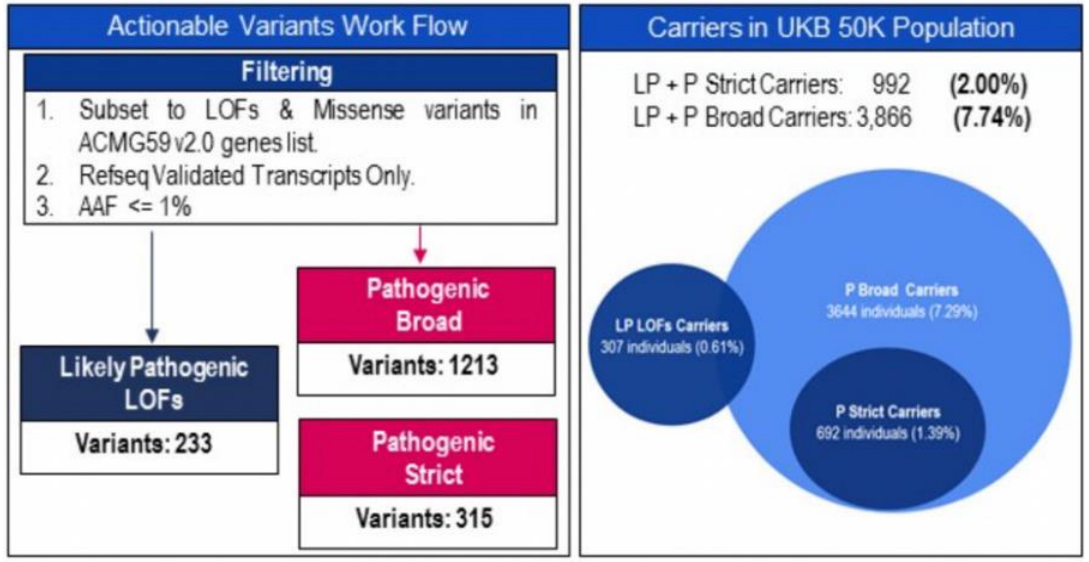
<u>Mutation in 1 in 92 South Asians</u> increases the risk of subcortical stroke by <u>3-fold</u>

Trait	OR (95% CI)	P value
Stroke		4.92E-08
Ischemic stroke		2.49E-03
Intracerebral hemorrhage		1.79E-08
Subcortical intracerebral hemorrhage		3.87E-09
Partial anterior circulation infarcts		4.84E-03

0 1 2 3 4 5 6

Rodriguez-Flores, Khalid et al 2024

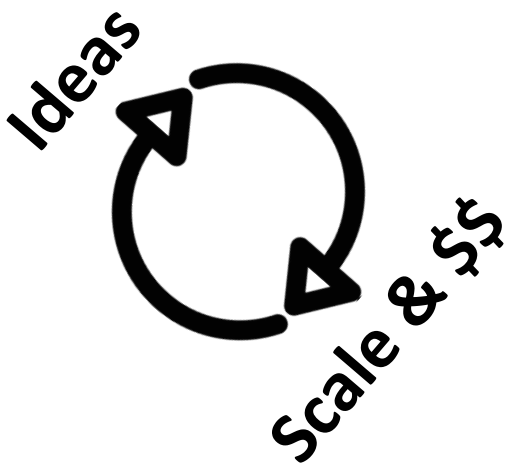
2% of people in a healthy population cohort carry pathogenic mutations that increase risk of preventable diseases



Van Hout et al 2021

FAQ

Why’d you leave industry to come back to Academia and start a PhD?

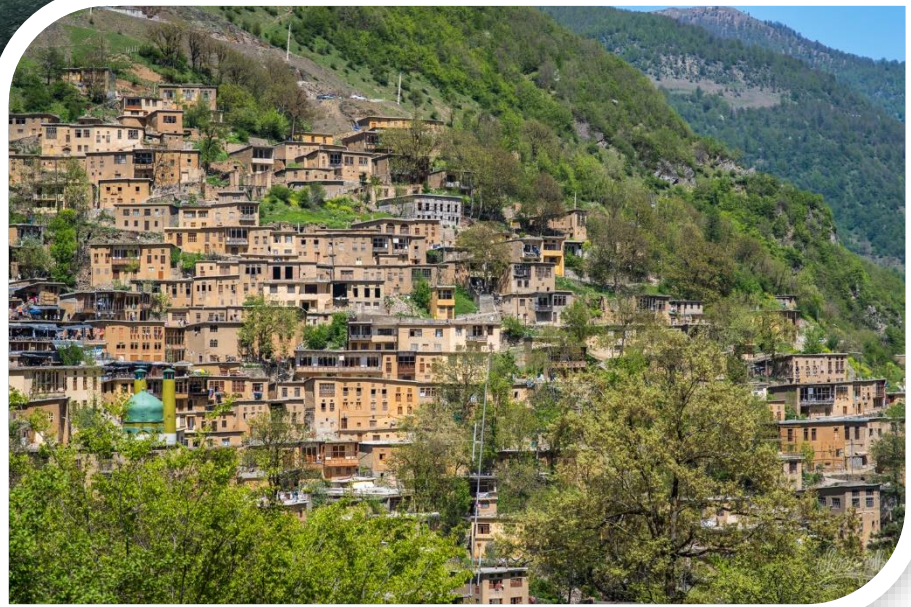


- With cost of sequencing going down, industries are beginning to figure out what can be done with genetics
- Opportunity to work in an Academia/Industrial middle ground with both translational + basic science

Hamidreza Khodajou Masouleh

First-year PhD student in Genetics

Stony Brook University



Masouleh City

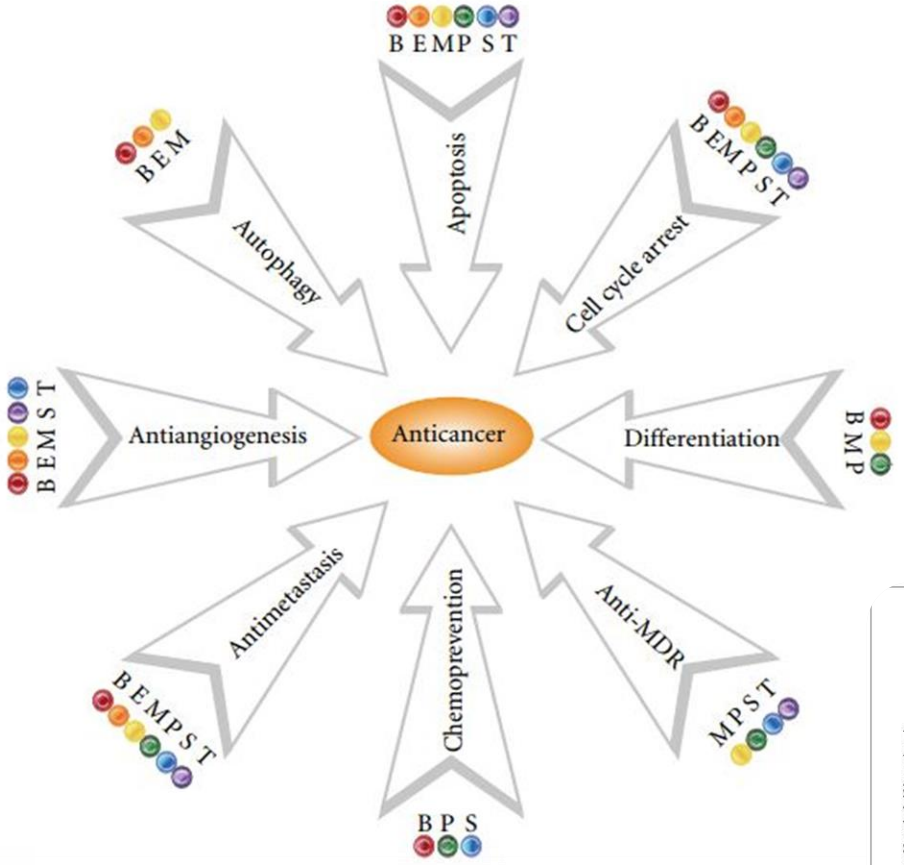
Alkaloids & Cancer Chemoprevention

World Health Organization

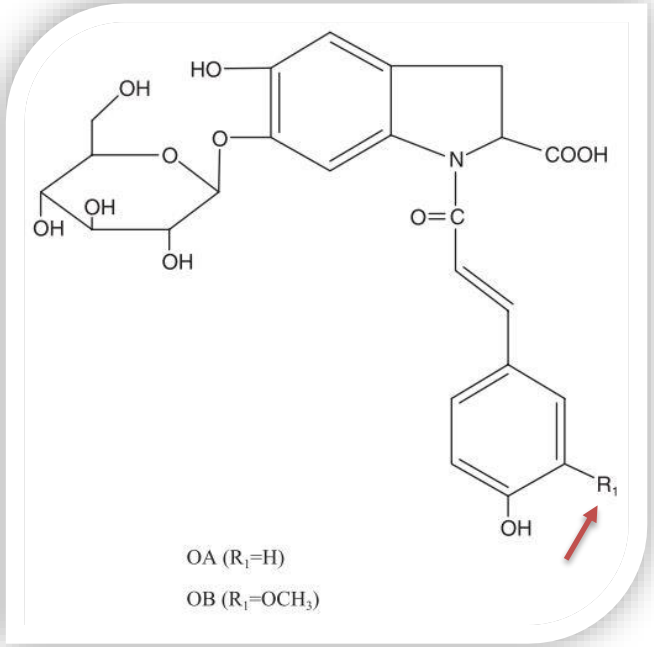
Portulaca oleracea
(Global Panacea)

B: Berberine
E: Evodiamine
M: Matrine

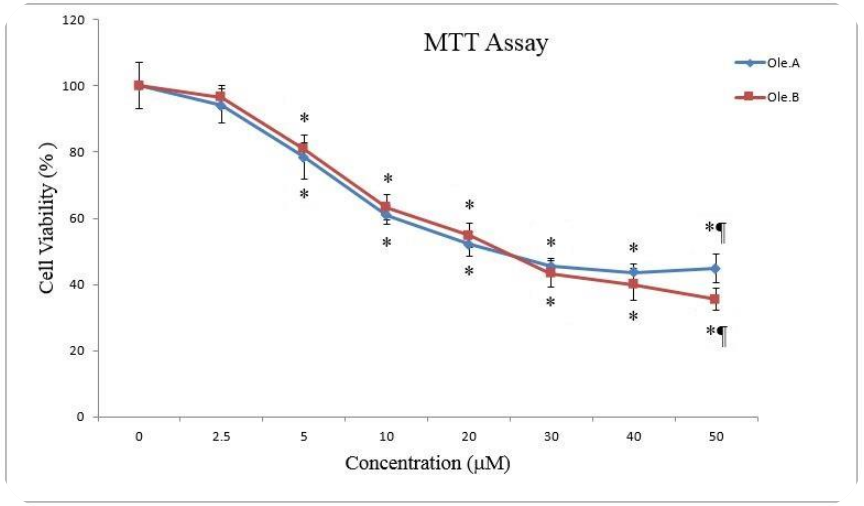
P: Piperine
S: Sanguinarine
T: Tetrandrine



Mechanisms of Action



Oleracein A & B



Trace (Thy) Le

Hometown: Vietnam
Knox College, IL
Class of 2024
Research interest:
RNA biology, cancer

Hobbies

Outdoor activities

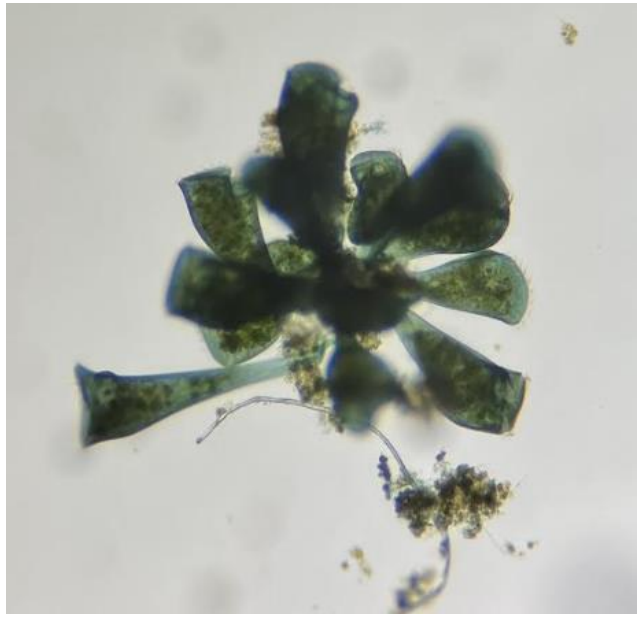
Hangout with friends

Documentaries - Nature, True Crime

Previous research

Regeneration in *Stentor coeruleus*

- Screened for genes responsible for the oral apparatus regeneration



Functions of microRNAs in Cnidaria - Corals, Anemones, Hydras, Jellyfish

- Predicted and analysed conserved gene targets of cnidaria miRNAs

Xiao Han | Egeblad Lab

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xhan@cshl.edu;
xiao.han.1@stonybrook.edu
Linkedin: xiao-han-jhu/
Twitter: @XiaoHan_JHU

Mikala Egeblad Lab @ JHU

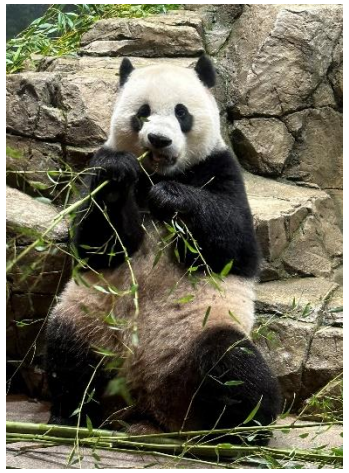
Stony Brook University

Mario Shields Lab @ SBU

Peter Westcott Lab @ CSHL

Cold Spring Harbor Laboratory

Fun facts about Xiao



A Chinese student from Chengdu, China
= Giant Panda + Hot Pot

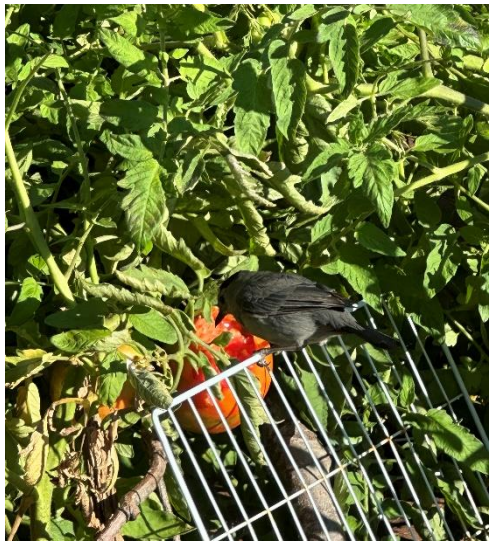
A mother of identical twin boys Sven & Ryan

Department of Health and Human Services
National Institutes of Health
NATIONAL CANCER INSTITUTE

Notice of Award
FAIN# F99CA284292
Federal Award Date
02/13/2024

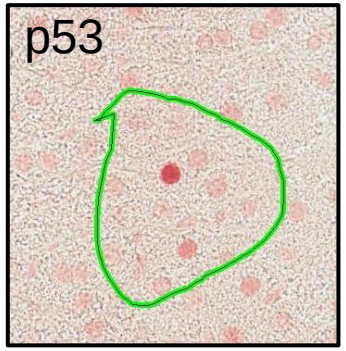
Recipient Information	Federal Award Information
1. Recipient Name THE RESEARCH FOUNDATION FOR THE STATE UNIVERSITY OF NEW YORK W5510 FRANKS MELVILLE MEMORIAL LIBRARY STONY BROOK, NY 11794	**11. Award Number** 1F99CA284292-01
2. Congressional District of Recipient 01	**12. Unique Federal Award Identification Number (FAIN)** F99CA284292
3. Payment System Identifier (ID) 1146013200F7	**13. Statutory Authority** 284(b)(1)(C) 42 CFR Part 63a
4. Employer Identification Number (EIN) 146013200	**14. Federal Award Project Title** Immune Regulation of Dormancy at the Metastatic Site
5. Data Universal Numbering System (DUNS) 804878247	**15. Assistance Listing Number** 93.398
6. Recipient's Unique Entity Identifier M746VC6XMNH9	**16. Assistance Listing Program Title** Cancer Research Manpower
7. Project Director or Principal Investigator Xiao Han, BS	**17. Award Action Type** New Competing (REVISED)
	18. Is the Award R&D? Yes

An NCI Predoctoral to Postdoctoral Fellow Transition Awardee (F99/K00 fellowship)



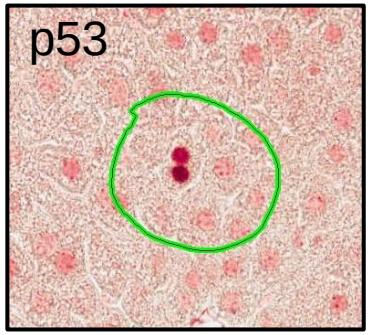
I grow vegetables in the backyard

Immune Regulation of Cancer Dormancy



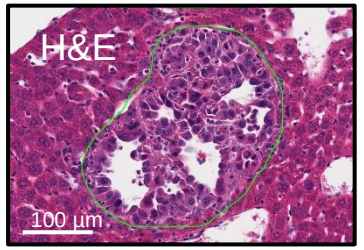
Single dormant cancer cell

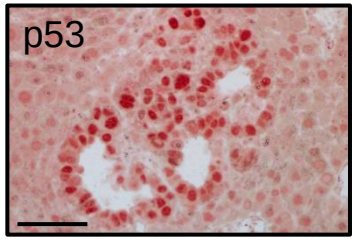
Inflammation(LPS)
Physical stress
Corticosterone



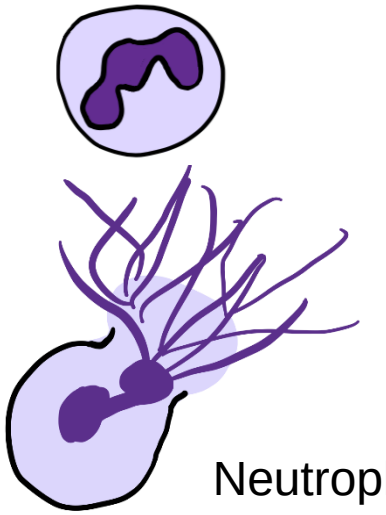
Double proliferative cancer cell

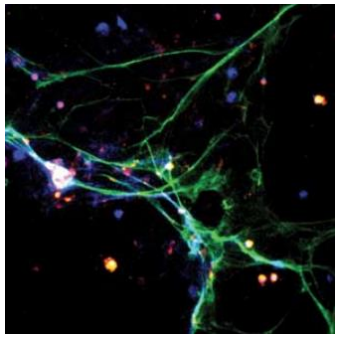
Immune suppression



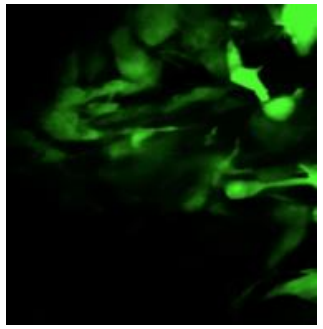


Metastasis

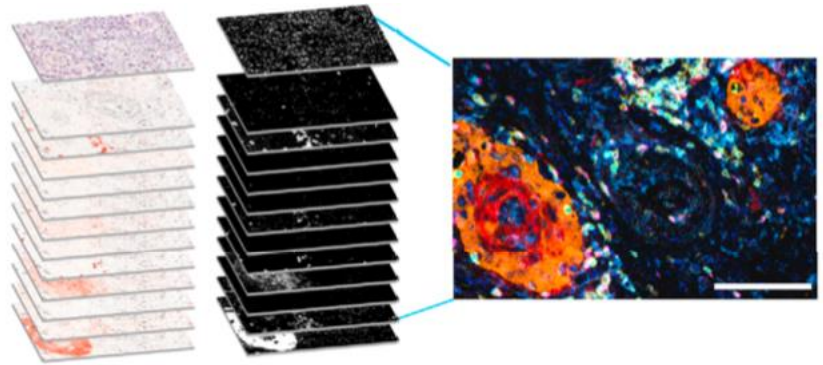




Neutrophil Extracellular Traps



Intravital imaging



Multiplex IHC

Name: Fatima Ejaz

From Brooklyn, NY

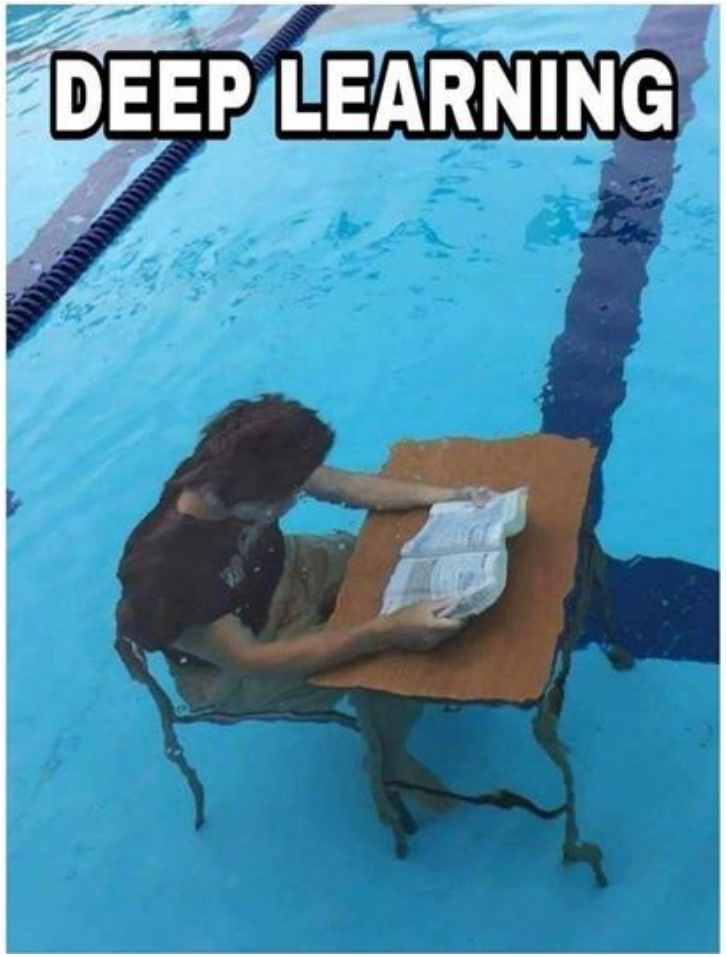
Hobbies: walking, learning languages (Duolingo)

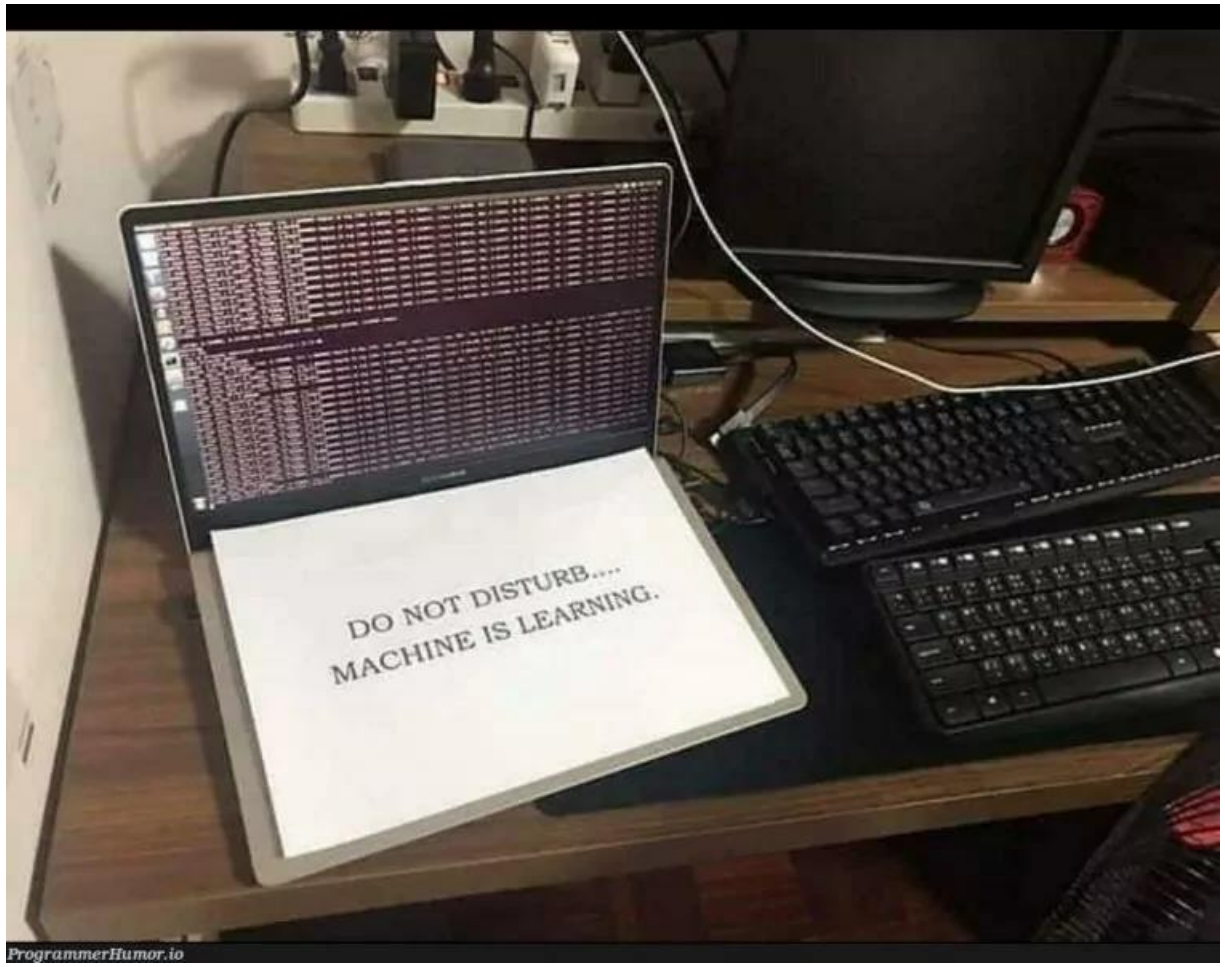
Second year Genetics PhD student in the Talos Lab

- Project: exploring age, lineage plasticity, and intratumor heterogeneity in Prostate Cancer
  - clonal dynamics in aging prostate
  - role of intermediate cell state (LumI) in aging and cancer models


Yijie Kang
Ph.D. student, Graduate Program in Genetics, SBU
Koo Lab at CSHL

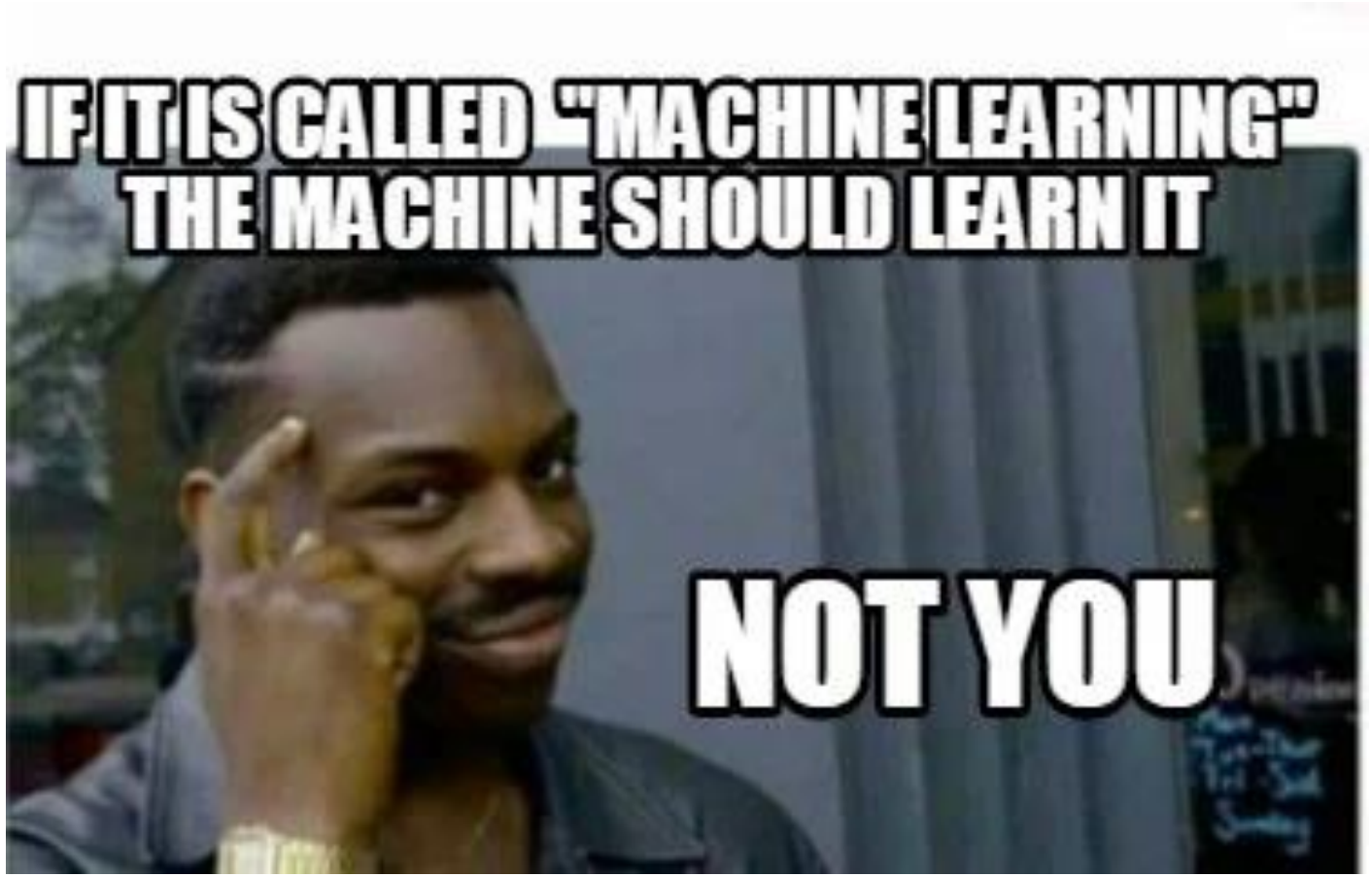
Deep Learning for Regulatory Genomics





Source: programmerhumor.io

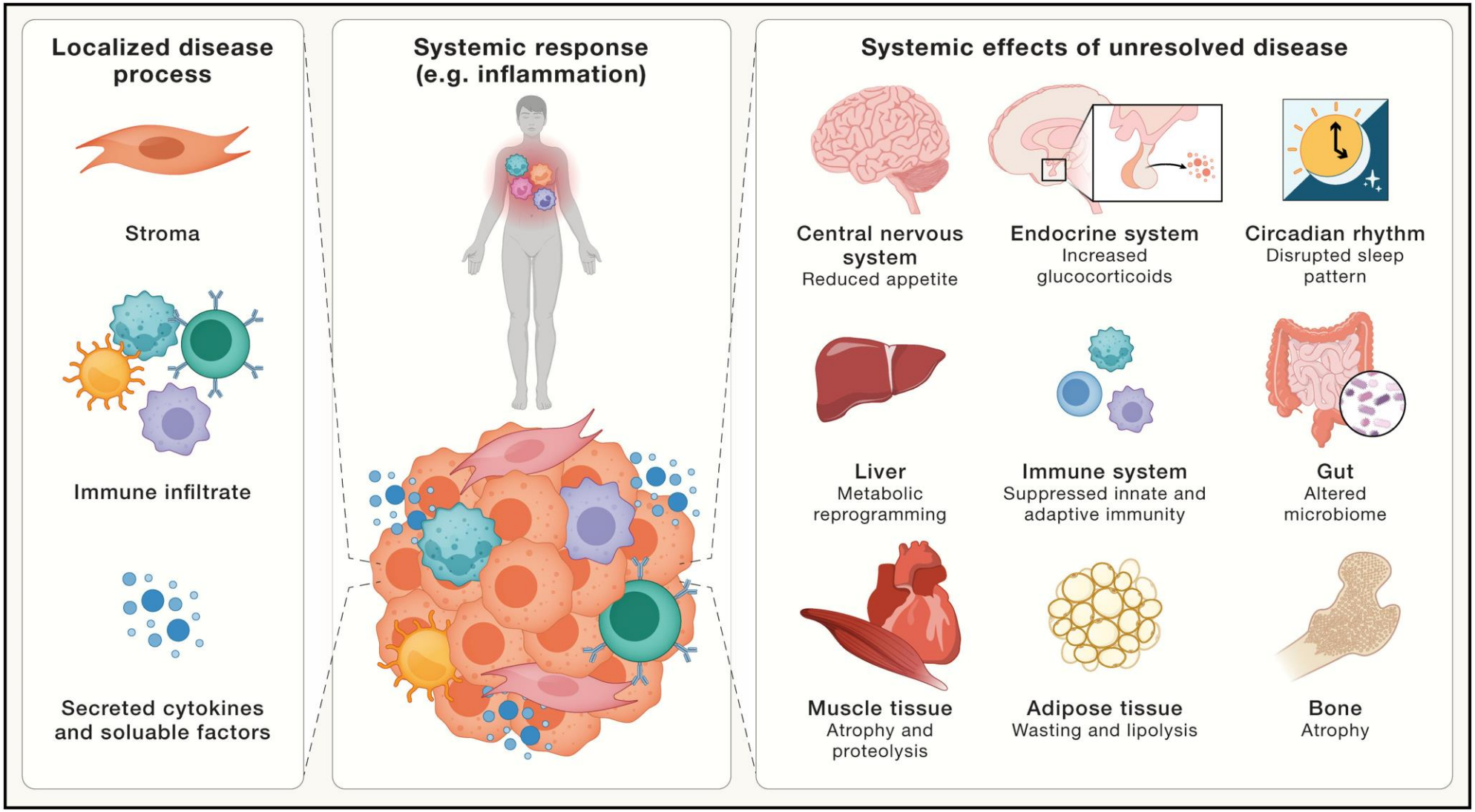
Deep Learning for Regulatory Genomics, **Interpretable!**



K	L	M	N
	DEC	December	
	NOV	November	
	OCT	October	
	APR	Aprember	
	AUG	Augember	
	FEB	Febember	
	JAN	Janember	
	JUL	Julember	
	JUN	Junember	
	MAR	Marember	
	MAY	Mayember	
	SEP	Sepember	

Source: programmerhumor.io

Cancer cachexia

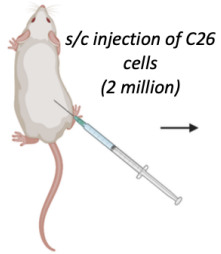


Ferrer et al. Cell (2023)

Alice Wang
(Tobias Janowitz lab at CSHL)

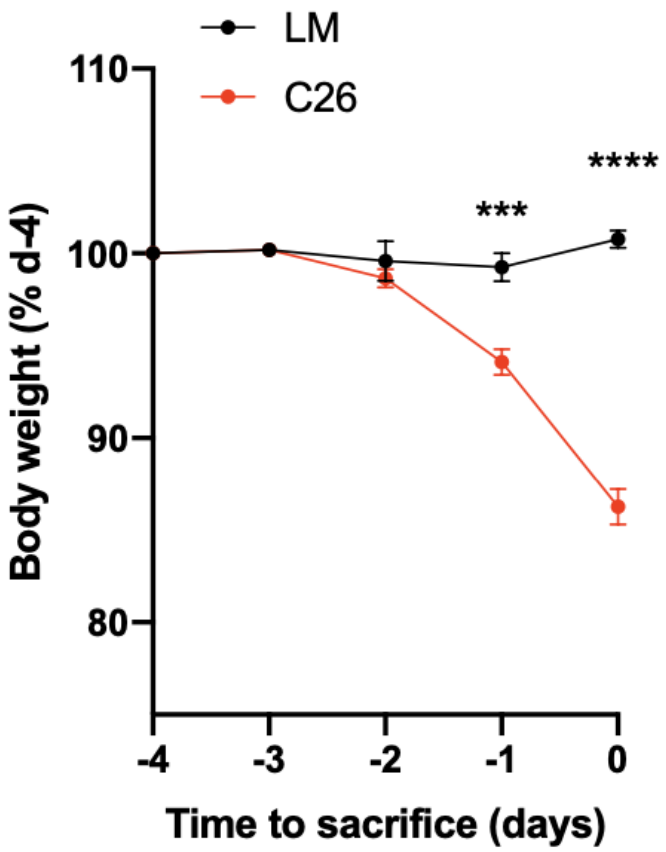
Cancer cachexia mouse model

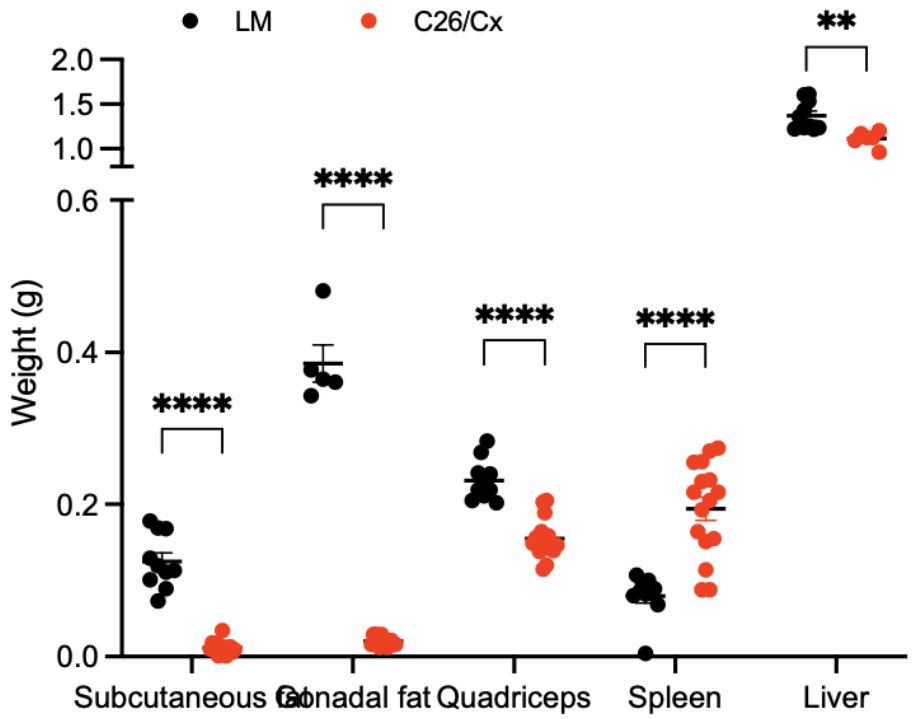
Male, Balb/C, 8 weeks old



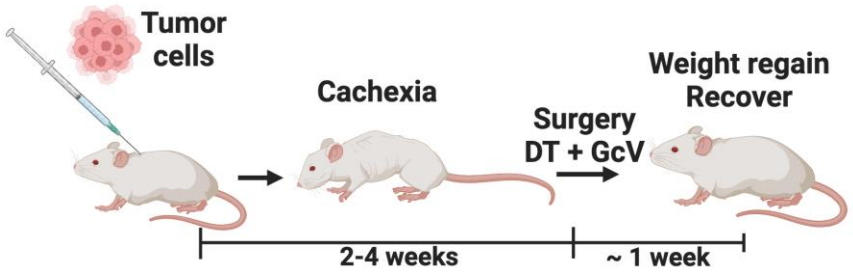
Pre-cachexia
Weight-stable tumor-bearers

Cachexia (endpoint)
Weight loss of >15% peak weight

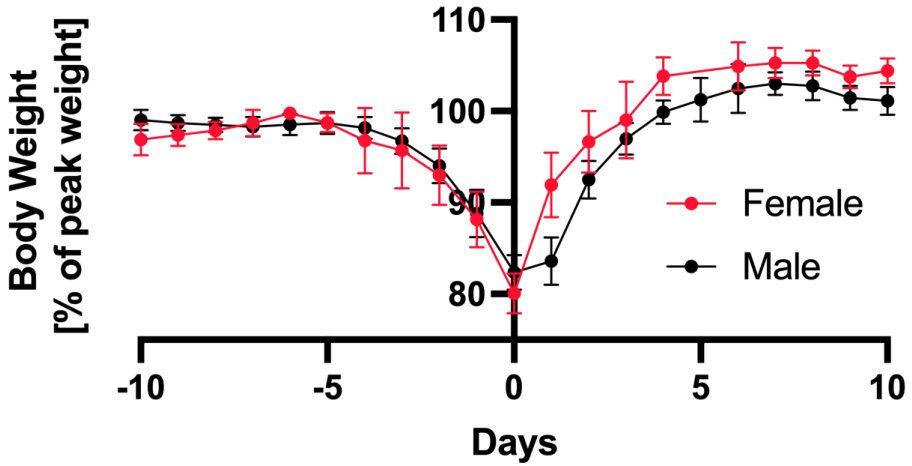


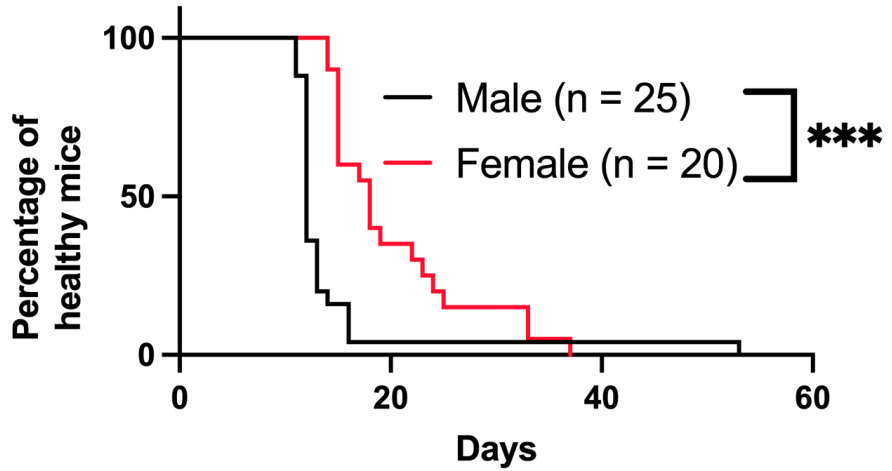


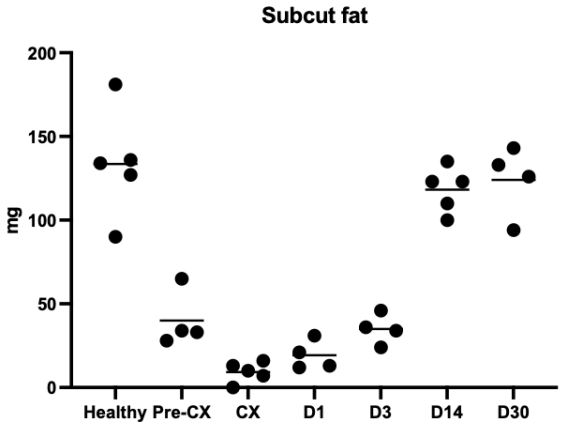
Cancer cachexia induction/recovery mouse model

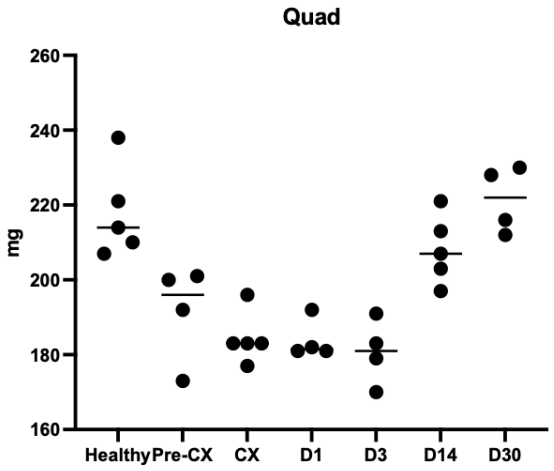


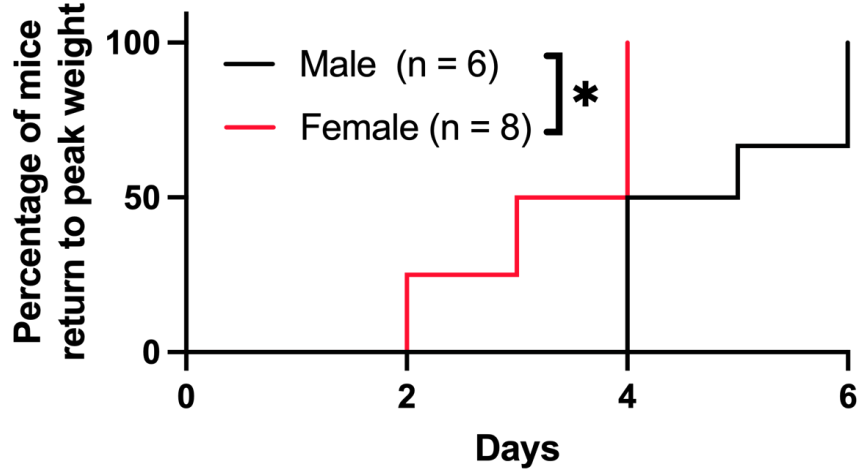
DT: diphtheria toxin
GcV: ganciclovir







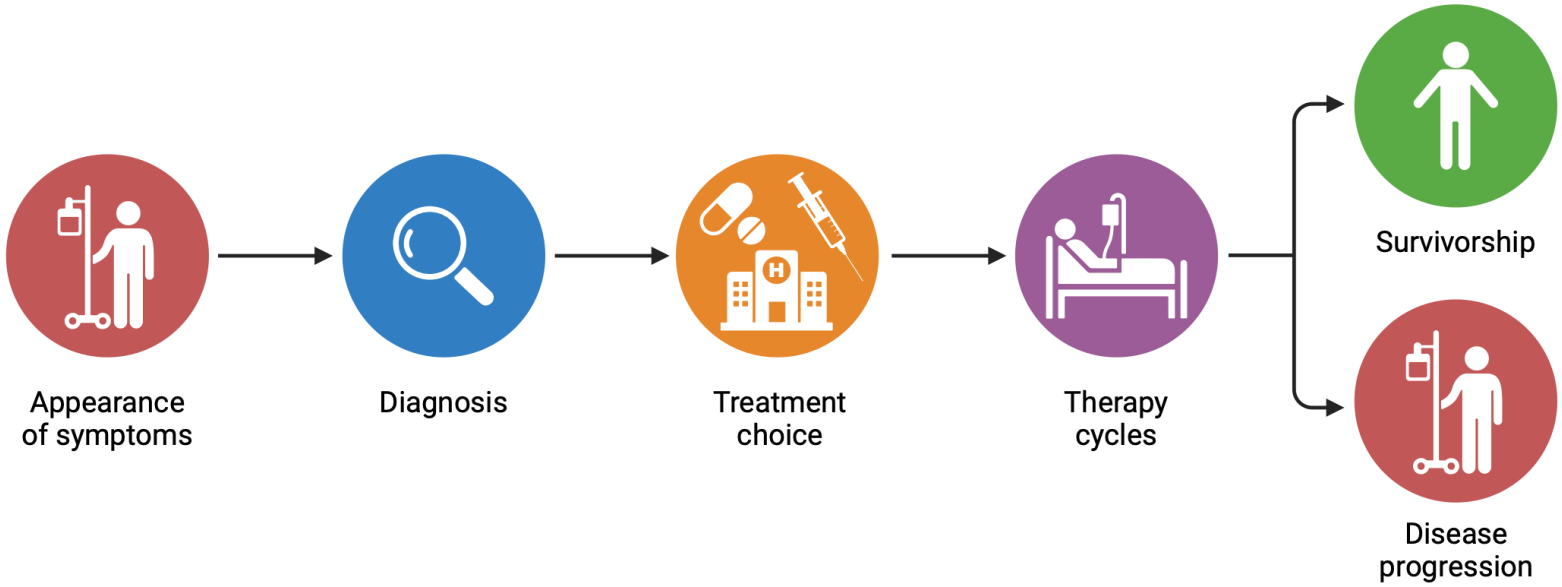


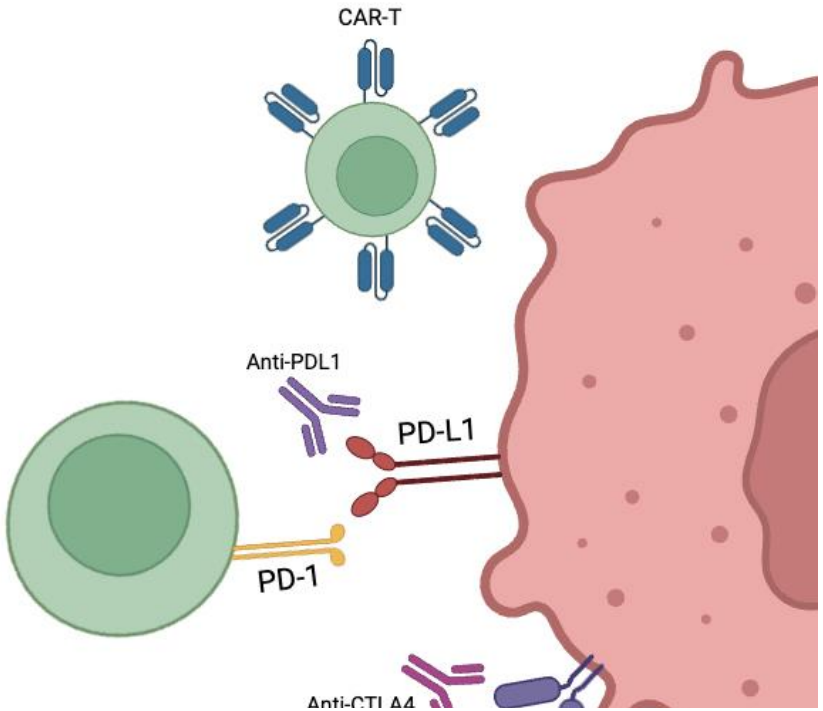


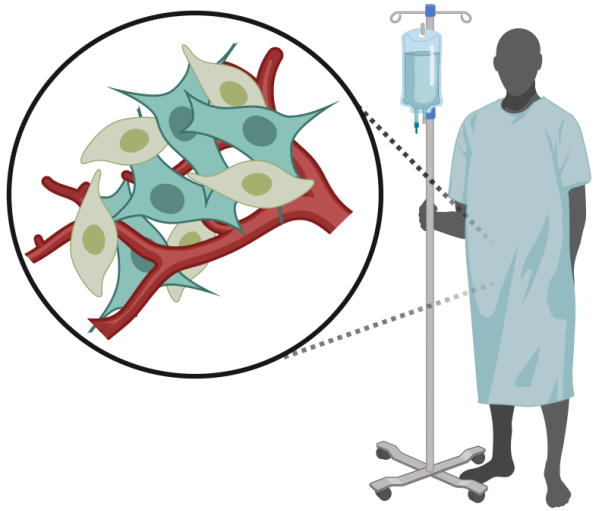
Metabolic reprogramming in immune cells enhances anti-tumor immunity

Tim Maher
Dr. Semir Beyaz Lab
08/28/24

Cancer treatment has advanced, but challenges remain





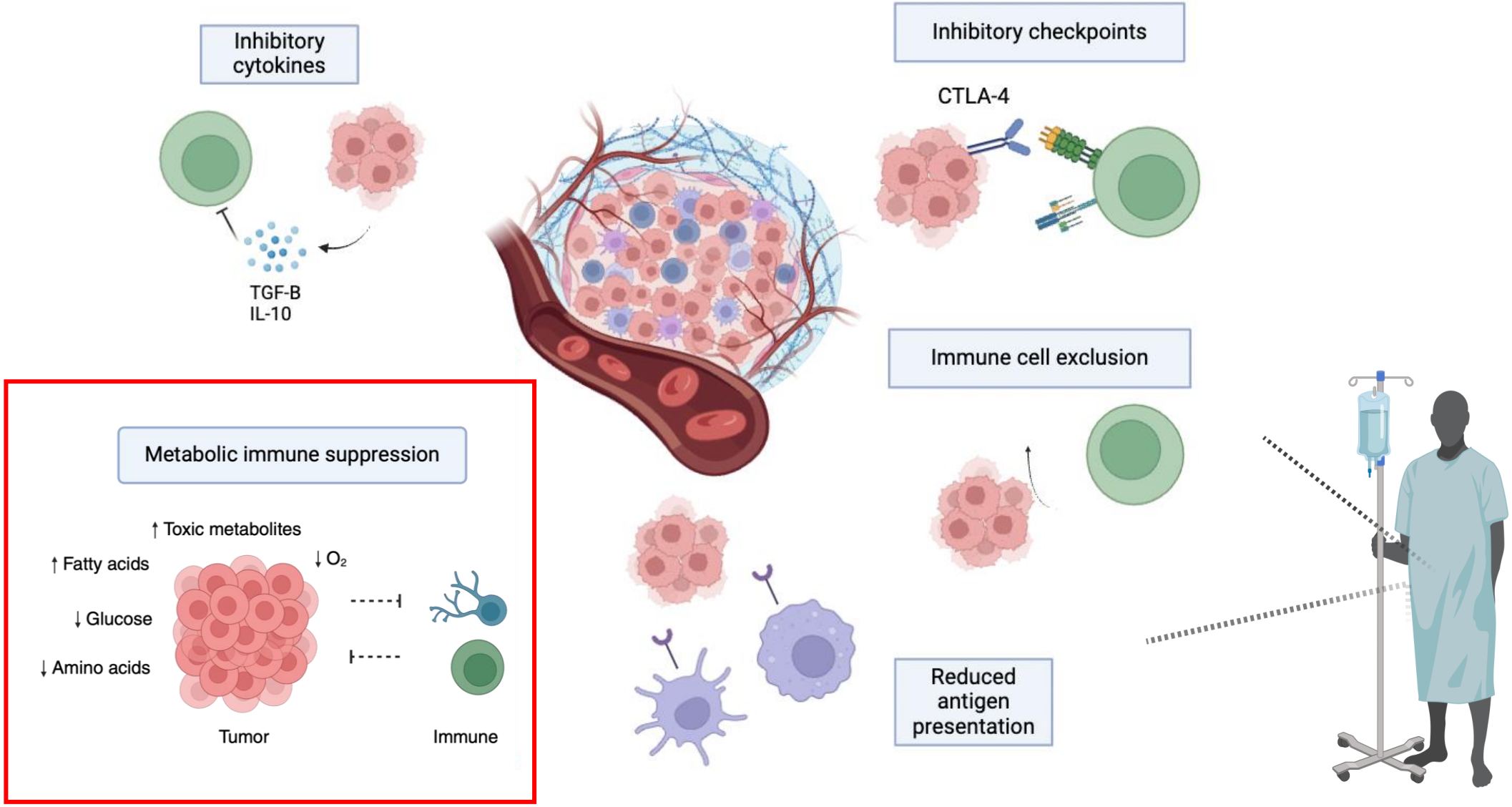


Primary, Adaptive, and Acquired Resistance to Cancer Immunotherapy

Padmanee Sharma,[1,*] Siwen Hu-Lieskovan,[2] Jennifer A. Wargo,[3] and Antoni Ribas[2,*]
[1]Department of Genitourinary Medical Oncology and Immunology,The University of Texas MD Anderson Cancer Center, Houston, TX 77030, USA
[2]Department of Medicine, Division of Hematology-Oncology, University of California, Los Angeles and the Jonsson Comprehensive Cancer Center, Los Angeles, CA 90095, USA
[3]Department of Melanoma Medical Oncology, The University of Texas MD Anderson Cancer Center, Houston, TX 77030, USA
*Correspondence: padsharma@mdanderson.org (P.S.), aribas@mednet.ucla.edu (A.R.)
http://dx.doi.org/10.1016/j.cell.2017.01.017

Biorender

Tumor microenvironment (TME) hinders immune response



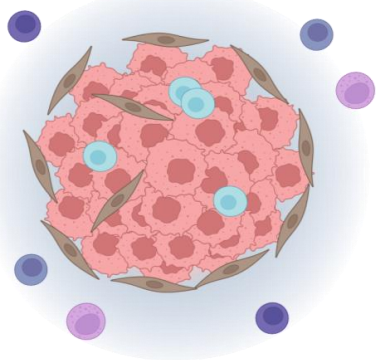
- ***Majority of patients with solid tumors, including colorectal cancers, either do not respond to immunotherapy or develop resistance over time***

Rebalance the metabolic tug-of-war to boost immune cell fitness and function in the TME

Nutrient consumption and metabolic fitness

Cancer cell

Immune cell



Immunosuppressive TME

Nutrient consumption and ~~metabolic fitness~~

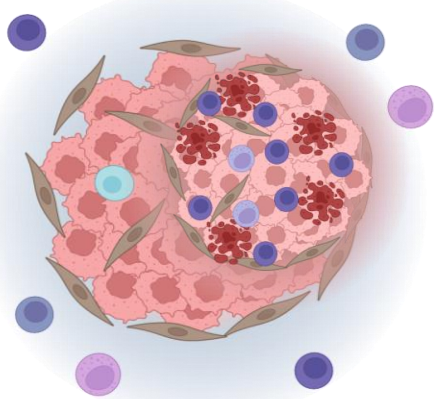
Nutrient consumption and metabolic fitness

Cancer cell

Cancer cell

Immune cell

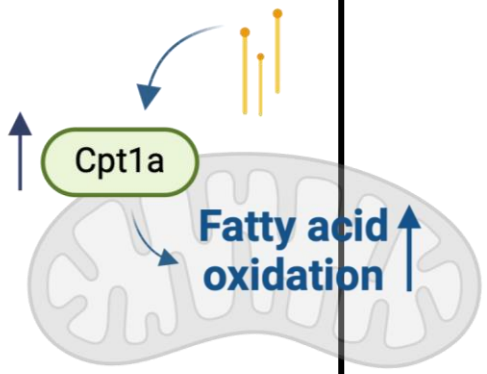
Immune cell



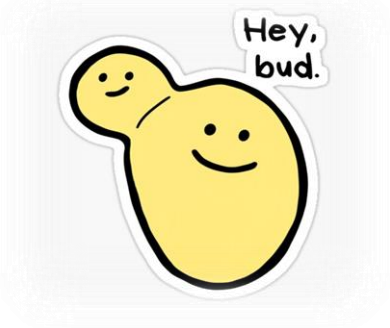
Pro-inflammatory TME reprogramming

Immunosuppressive TME

Peroxisome proliferator activated receptor δ (PPARδ) is a metabolic switch to enhance anti-tumor immunity

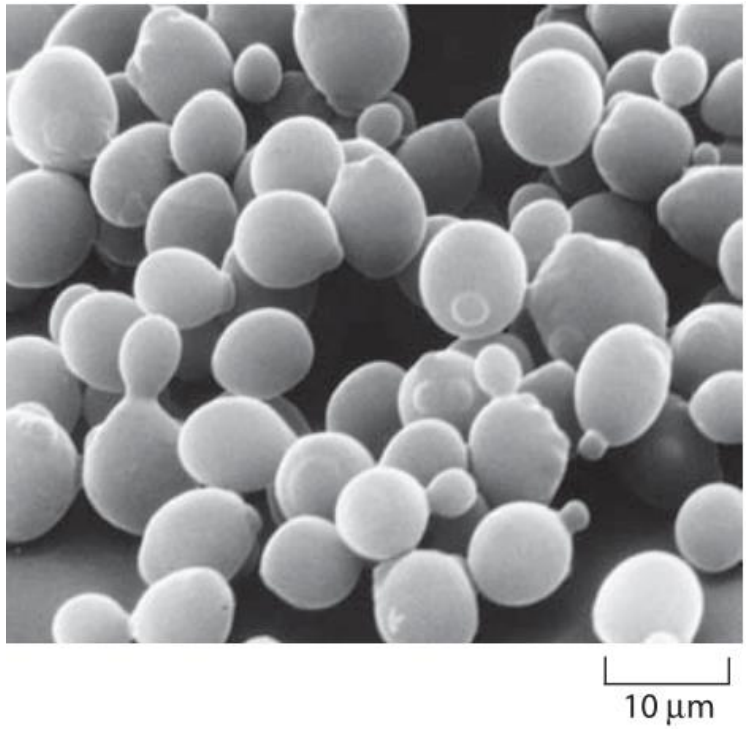


Tumor control



Chenjun (June) He

from Bruce Futcher Lab



Electron Micrograph of Budding Yeast Cells

Topics:

Cell Cycle (Mitosis and Meiosis)

Cell Size Control

RNA Degradation

……

Methods:

Yeast Molecular Genetics

Omics (RNA, Protein)

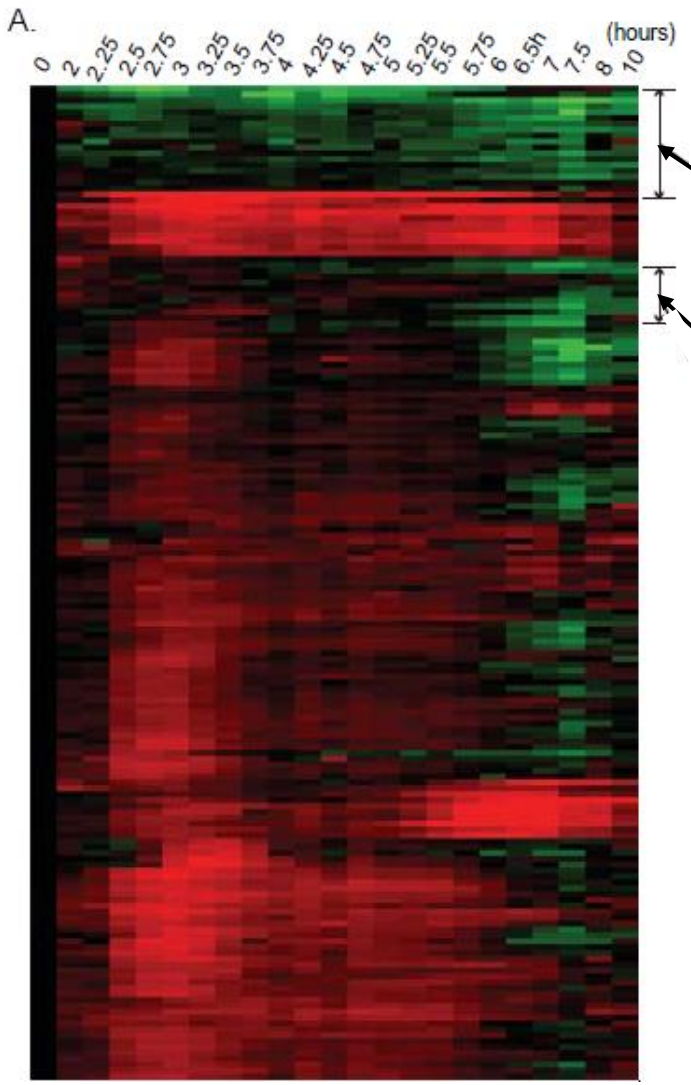
Microscopic

Bioinformatics

Systems Biology

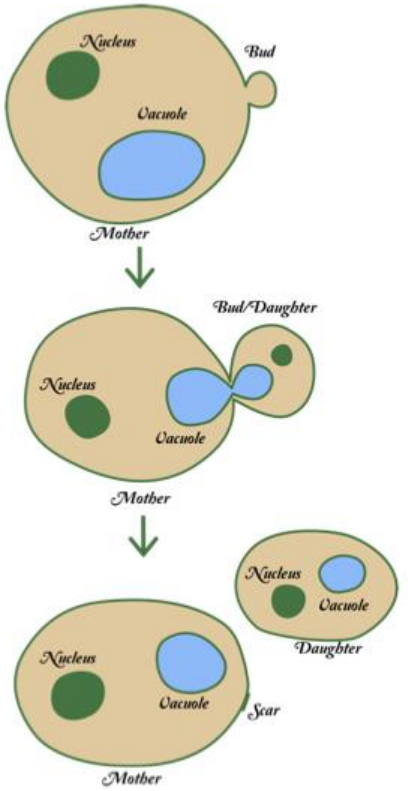
……

What I am doing now: How *SSD1* affect **meiosis (sporulation)** ability.

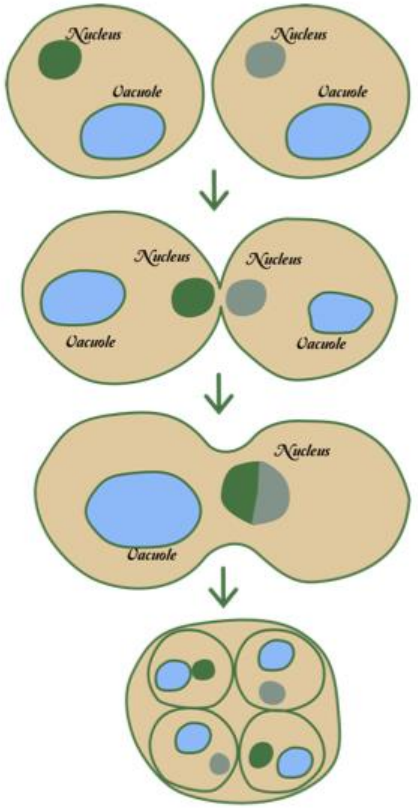


≈30 Genes
Downregulated
in Meiosis
(including important
cyclins: CLN1, CLN2)

Expression of 169 reported SBF and MBF targets during Meiosis



Asexual: Budding

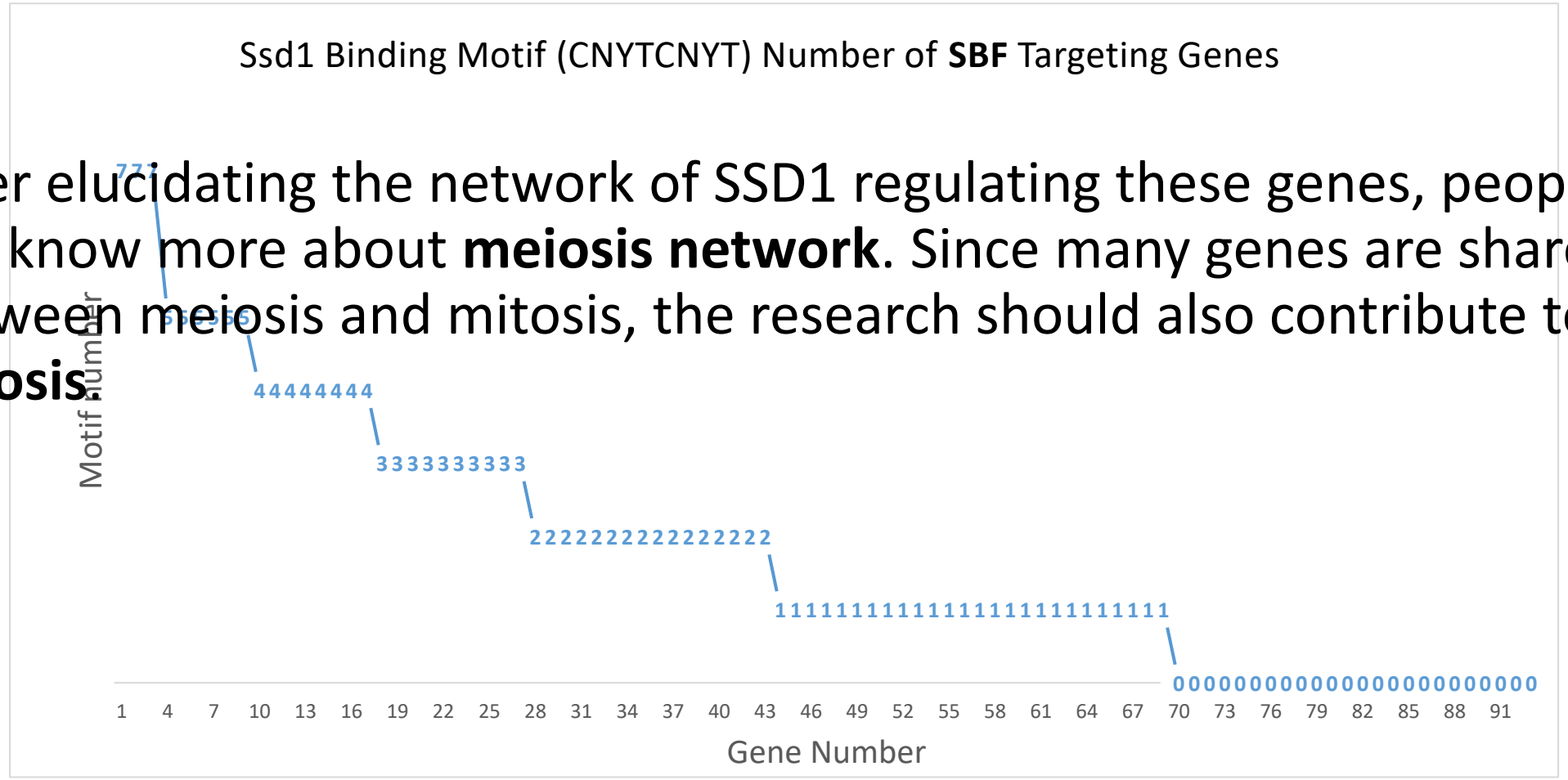


Sexual: Sporulative

Budding Yeast Reproduction

- Not know the mechanism of mRNA abundance regulation of these cell cycle related genes.
- *SSD1* maybe important; because lots of the downregulated genes including *Ssd1*-binding-site.

e.g.



- After elucidating the network of SSD1 regulating these genes, people can know more about **meiosis network**. Since many genes are shared between meiosis and mitosis, the research should also contribute to **mitosis**.

Determining the role of pregnancy-induced alterations to mammary B cells in breast oncoprotection

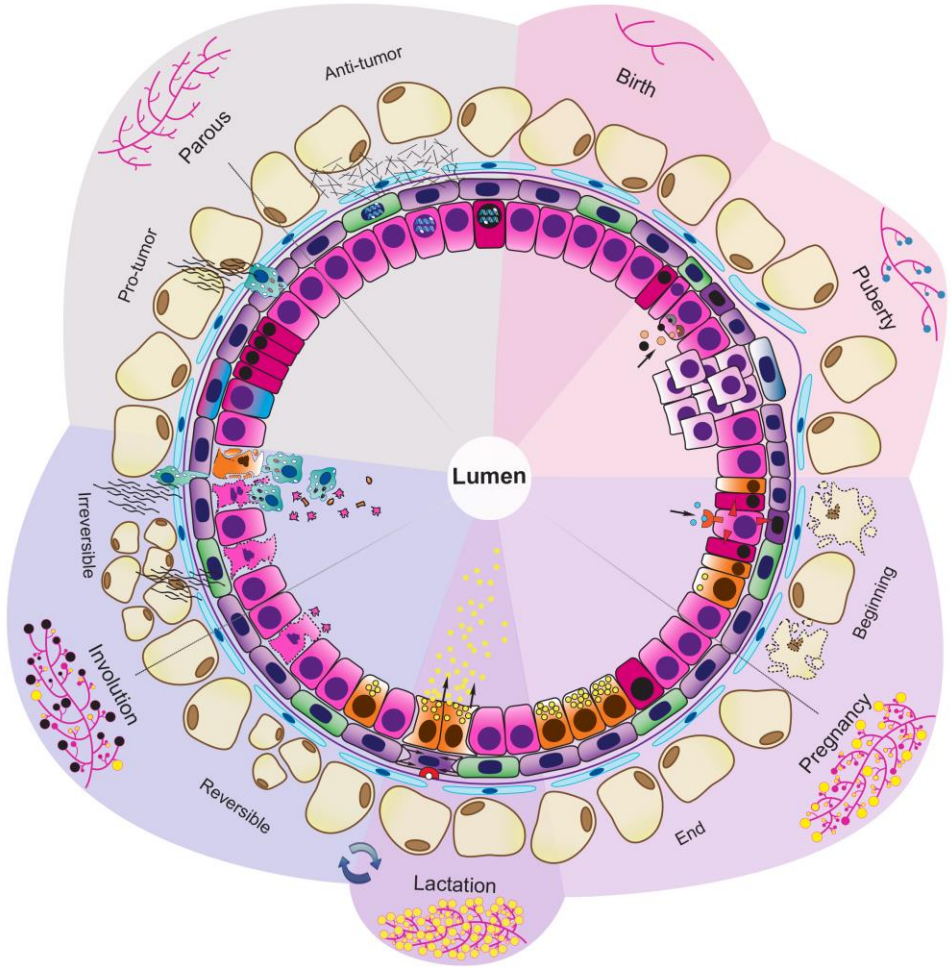
Dhivyaa Anandan

dos Santos Lab at CSHL

Genetics Speed Science

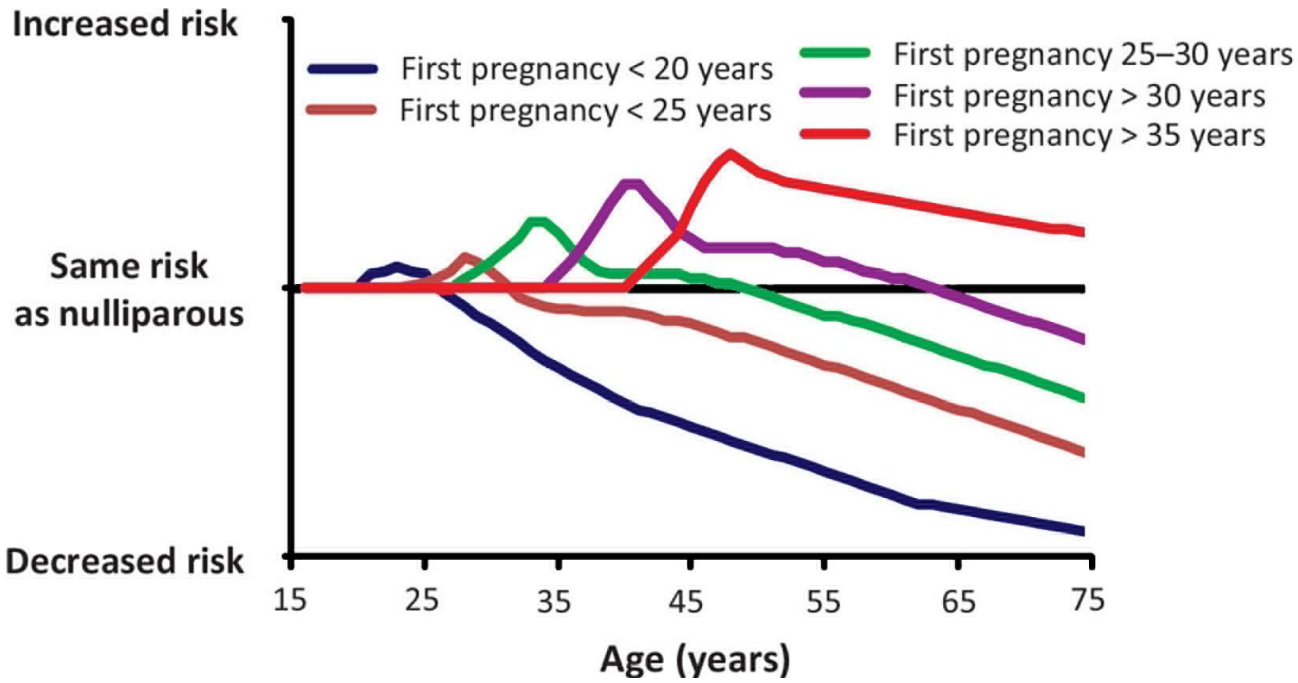
August 28, 2024

Understanding mechanisms of mammary oncoprotection through the lens of mammary gland development



Slepicka et al., *Trends Mol Med* 2019

An early age of first pregnancy decreases lifelong risk for breast cancer by ~30%.



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

Pregnancy-associated mammary gland development shares hallmarks with breast cancer development.

Rapid proliferation of the ducts and alveoli

Growth factor signaling necessary for morphogenesis

Epithelial plasticity that enables ductal branching and gland maturation

Pregnancy-induced epigenetic changes

Regulatory T cells and immunosuppression

Increased glucose utilization for milk synthesis

Apoptosis of milk-secreting cells is tightly regulated and only enabled during involution

Mammary stem cells with self-renewal capacity

Immune cell infiltration and inflammatory signature

Replicative stress
Binucleated cells during lactation

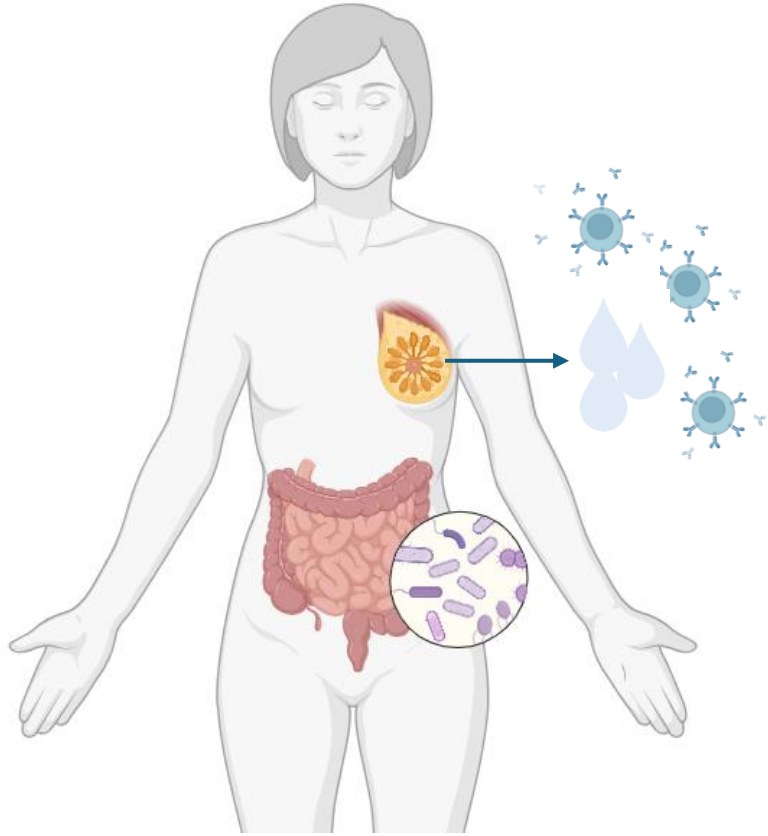
Pregnancy-associated oncogene-induced senescence

Polymorphic microbiomes
Breastmilk microbiome

Angiogenesis during pregnancy and lactation
Release of angiogenic factors

Ductal branching morphogenesis that activates EMT pathways

Pregnancy-associated changes to the maternal gut microbiome alter mammary B cell composition.



Speed Science

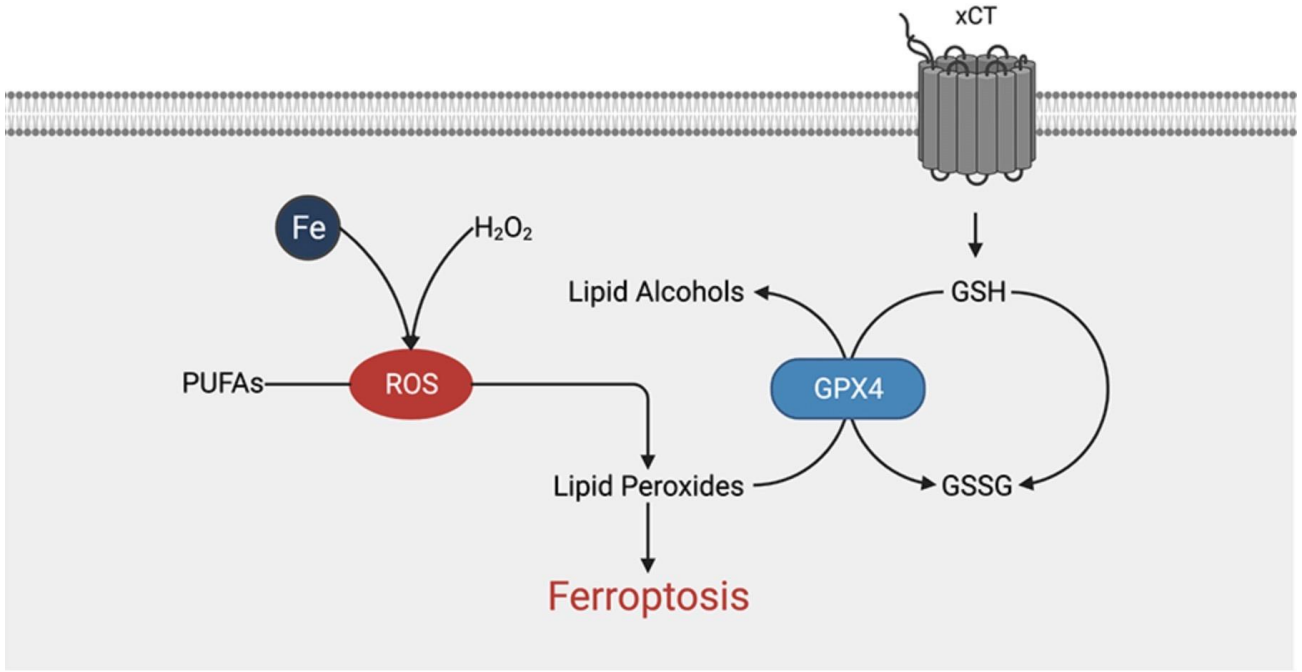
---YUJIA JI

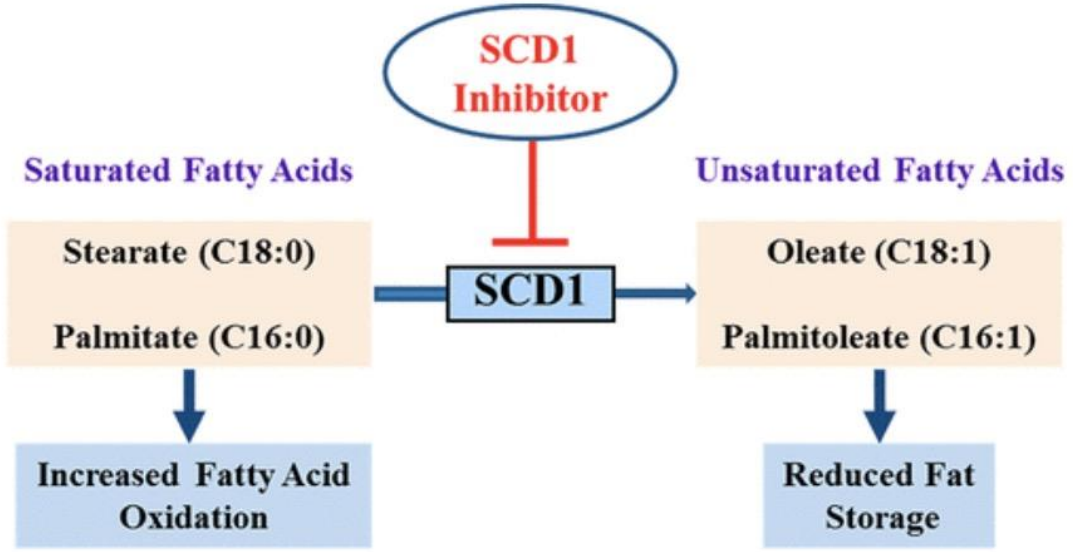
LUKEY LAB AT CSHL

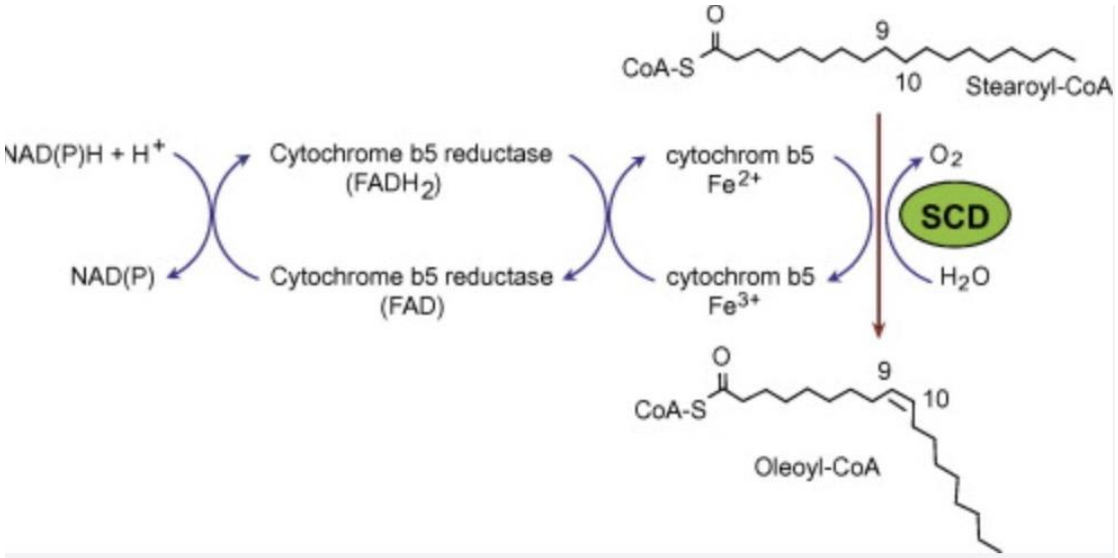
PH.D. STUDENT IN GENETICS PROGRAM

STONY BROOK UNIVERSITY

Ferroptosis with SCD1








SWEETEST KENKEN! (MY DREAM LIFE)

OCA-T1 and OCA-T2 as essential transcriptional co-activators in tuft cell development

LIAM SHANLEY | SPEED SCIENCE 2024

VAKOC LAB, CSHL

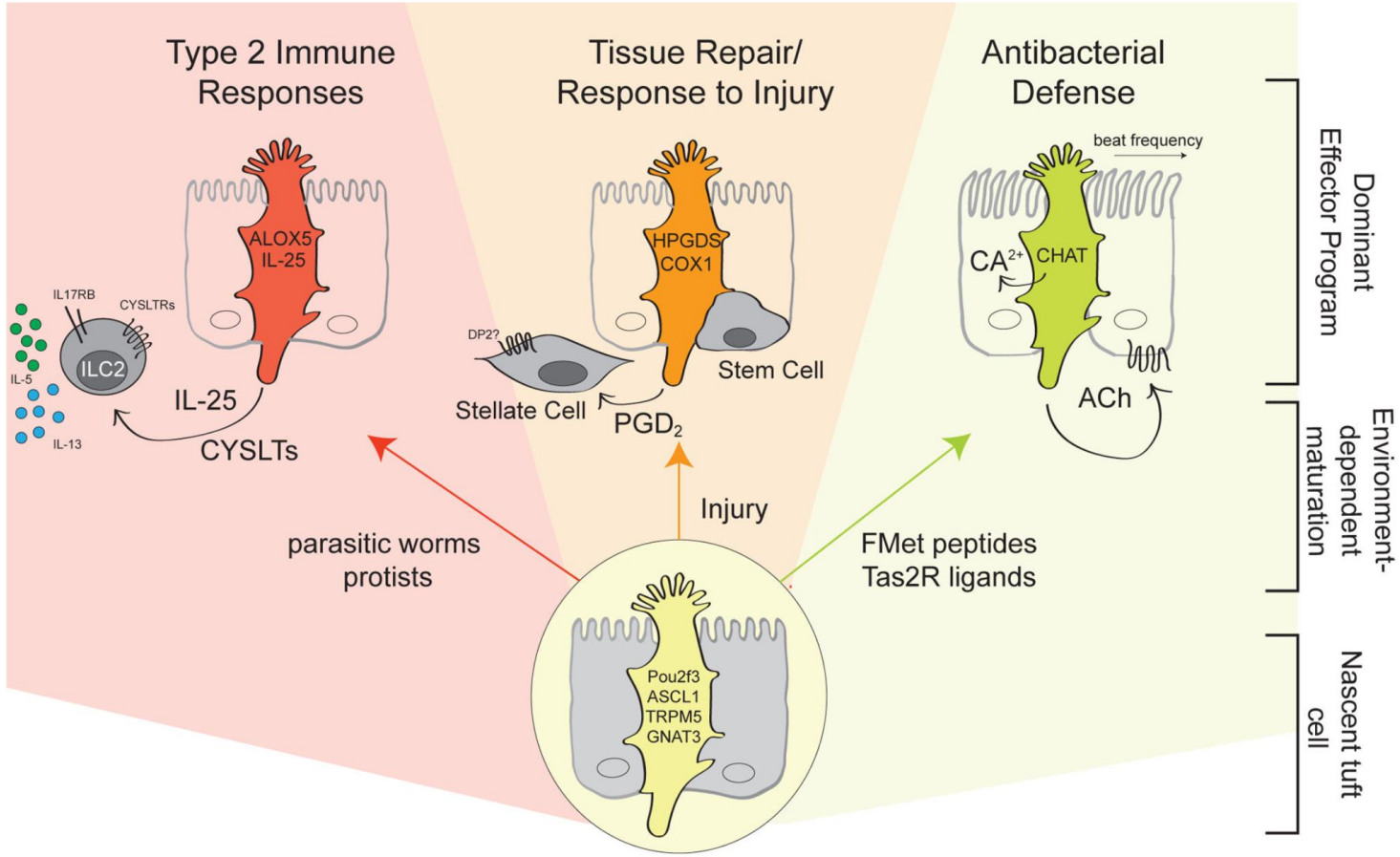
8/28/24

Tuft Cells are Rare Chemosensory Cells in Mucosal Membranes

POU2F3 is the lineage-defining transcription factor

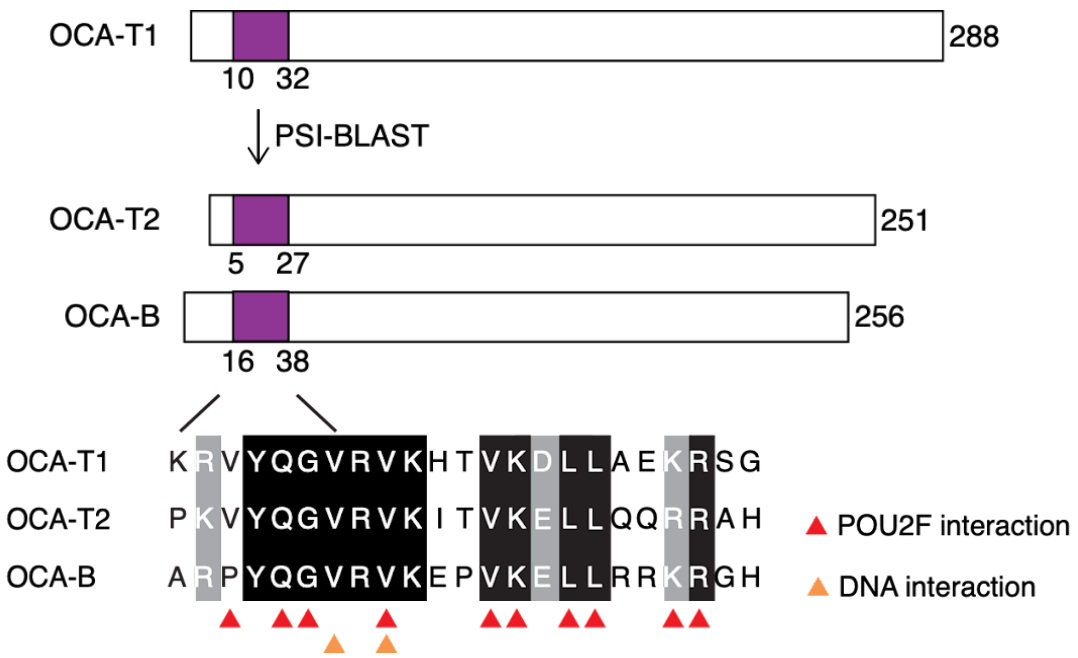
Express taste-specific signaling pathways

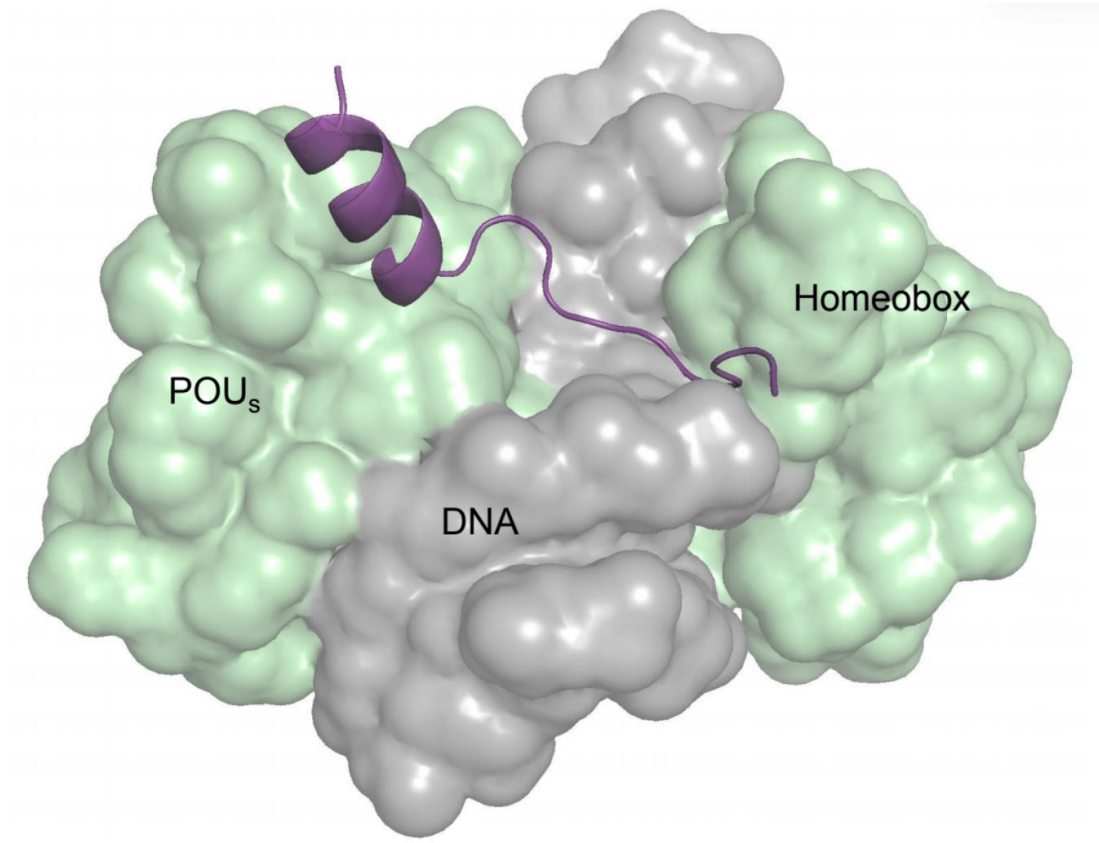
Well characterized tuft-ILC2 circuit in the small intestine, which modulates immune response to protists and helminths



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

OCA-T1 and OCA-T2 are co-activators of POU2F3





Wu, et al *Nature* (2022)

What features and functions make OCA-T1 and OCA-T2 different?

Specific Aim 1: Profile and compare the expression of OCA-T1 and OCA-T2 across tissues and cell types.

Specific Aim 2: Generate and compare phenotypes associated with OCA-T1- and OCA-T2-deficient mice.

Specific Aim 3: Define differences in gene regulation by OCA-T1 and OCA-T2 and the molecular basis for these differences.

Speed Science 2024

Katie Donnelly-Sharon

4th year, van der Velden Lab

When I am not in lab, you will most likely find me…

Hanging out with some kind of animal

Near the ocean

Screaming at a hockey game

Typhoid fever is a cause of high morbidity and mortality in humans worldwide

- Infection with ***Salmonella typhi*** **(STy)** is estimated to cause 11-21 million cases of typhoid fever with 200,000 deaths annually

- **1-6% of typhoid patients become chronic carriers who are oftentimes asymptomatic**

Determining the role of inflammatory monocytes in the granulomatous response to *Salmonella* infection

- **Granulomatous lesions** are organized aggregates of immune cells that surround a pathogen to help control its growth and spread throughout the tissue

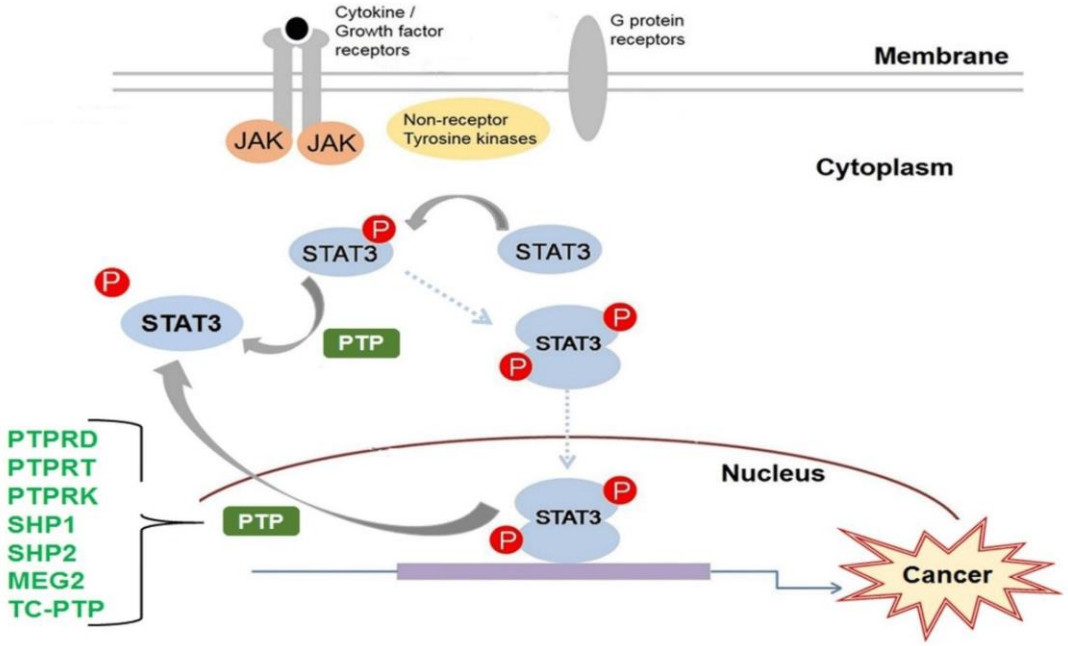
Failure of initial immune response

Development of granulomatous lesions

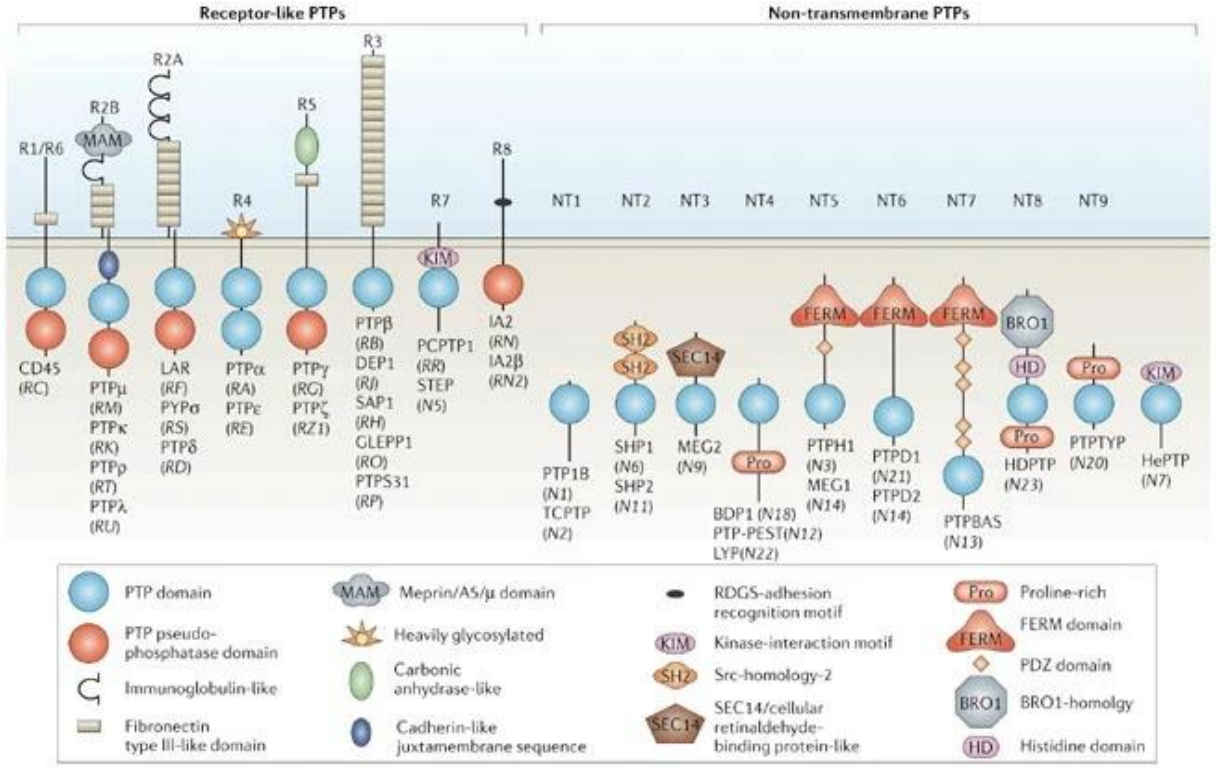
- My project is specifically focused on elucidating the mechanisms inflammatory monocytes (type of cell found in granulomatous lesions) use to contribute to the formation and maintenance of these granulomatous lesions.

Reversible Redox Regulation of PTPN2 (TCPTP)

- Tan-Chun Kuo
  - aka: John
  - 3rd year Student
  - Tonks Lab @ CSHL



https://www.mdpi.com/1422-0067/19/9/2708



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

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

Cold Spring Harbor Laboratory

Stony Brook University

Antisense repression of *H3-3A* for G34R-mutant pediatric high-grade gliomas

Shivani Deshpande- Graduate Program in Genetics, SBU

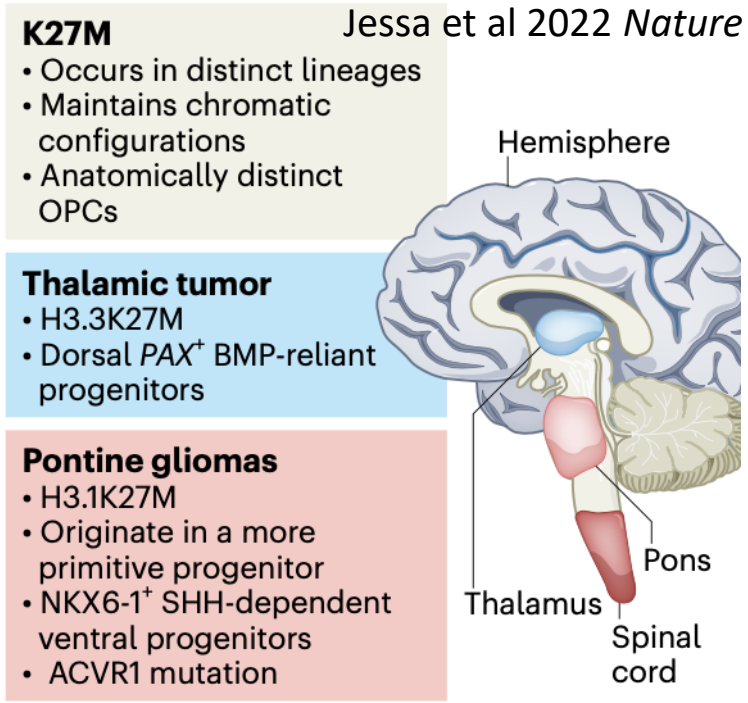
2nd year graduate student

Krainer Lab at CSHL

Histone mutations drive the development of pediatric high-grade gliomas

- Pediatric high-grade gliomas: 10-15% of pediatric brain tumors
- Mean survival 9 months- death for most patients within 2 years of diagnosis

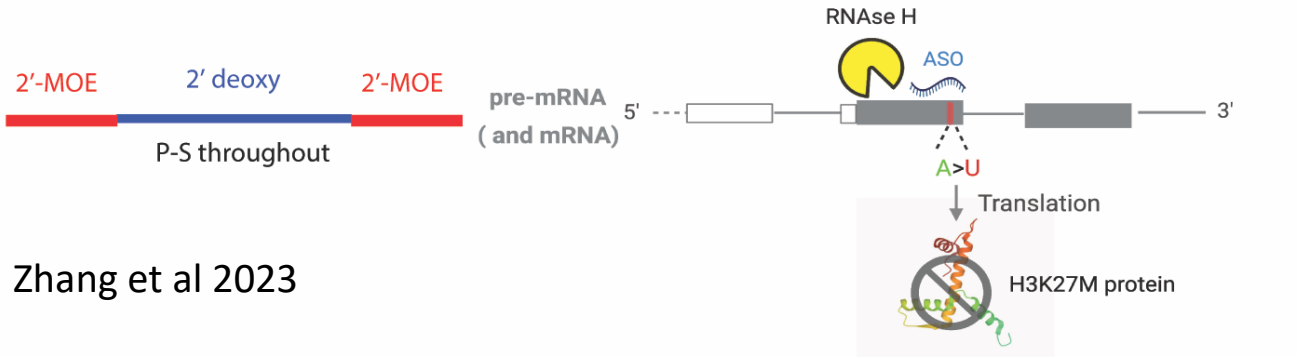
Jessa et al 2022 *Nature Genetics*



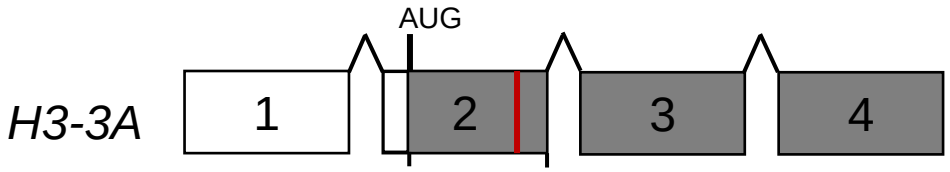
- Pathogenic oncogenic mutation in H3.3 (K27M)~ 80%
- H3G34V and H3G34R mutations that result in gliomas exclusively affect histone variant H3.3 on the *H3-3A* gene (~16%)
- Mutually exclusive with the K27M mutation

Almouzni et al 2011

Repression of *H3-3A* via antisense oligonucleotides (ASOs)



Zhang et al 2023



Antisense oligonucleotides (ASOs)

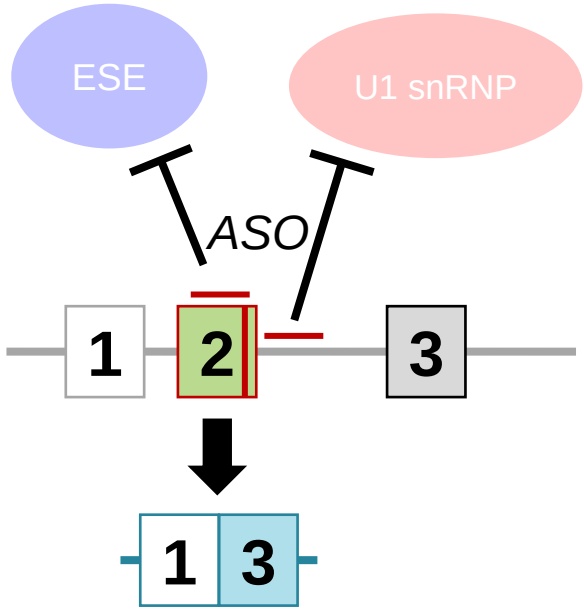
mechanism

RNAse H-active

Promote degradation of mRNA via RNAse H

Splice-switching

Bind and interfere with splicing machinery to induce exon skipping



From Lucia Yang

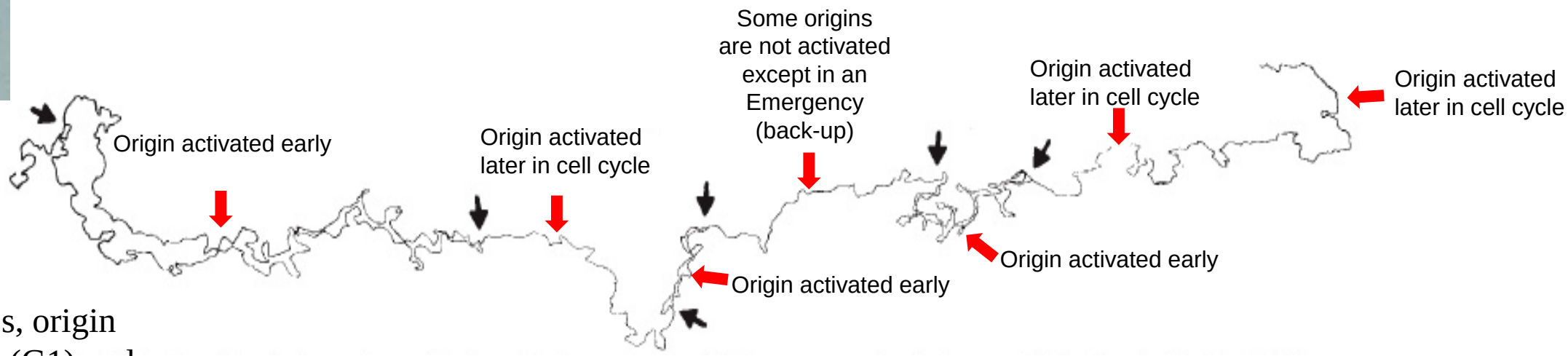
Narges Zali

Advisor: Dr. Stillman CSHL

Genetics 2018

Marking of Origins of DNA Replication Across the Genome

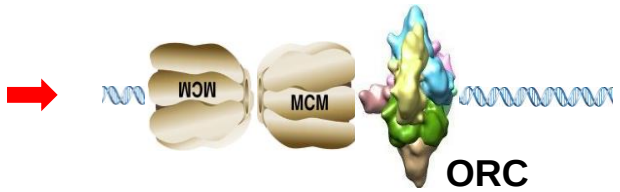
Budding yeast



- Two steps, origin licensing (G1) and origin firing (S-phase)

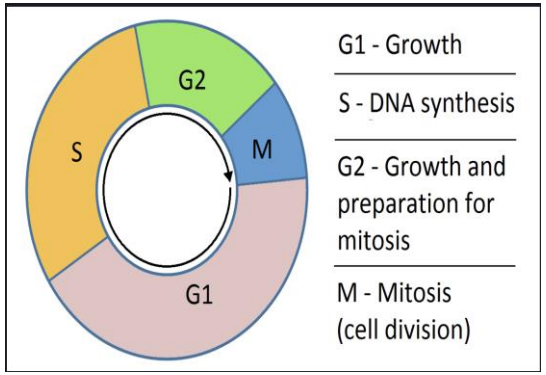
➡ DNA replication fork

➡ Potential origin



Pre-Replicative Complex

~500 origins of DNA replication in *S.cerevisiae*
in G1 phase
~ 50,000 in mammalian genome



Newlon, Petes, Hereford and Fangman (1974) *Nature*

Why studying replication initiation in budding yeast *Yarrowia lipolytica* ?

- Are there any currently unknown origin sequences in *Yarrowia* that provide a basis for ORC recognition?

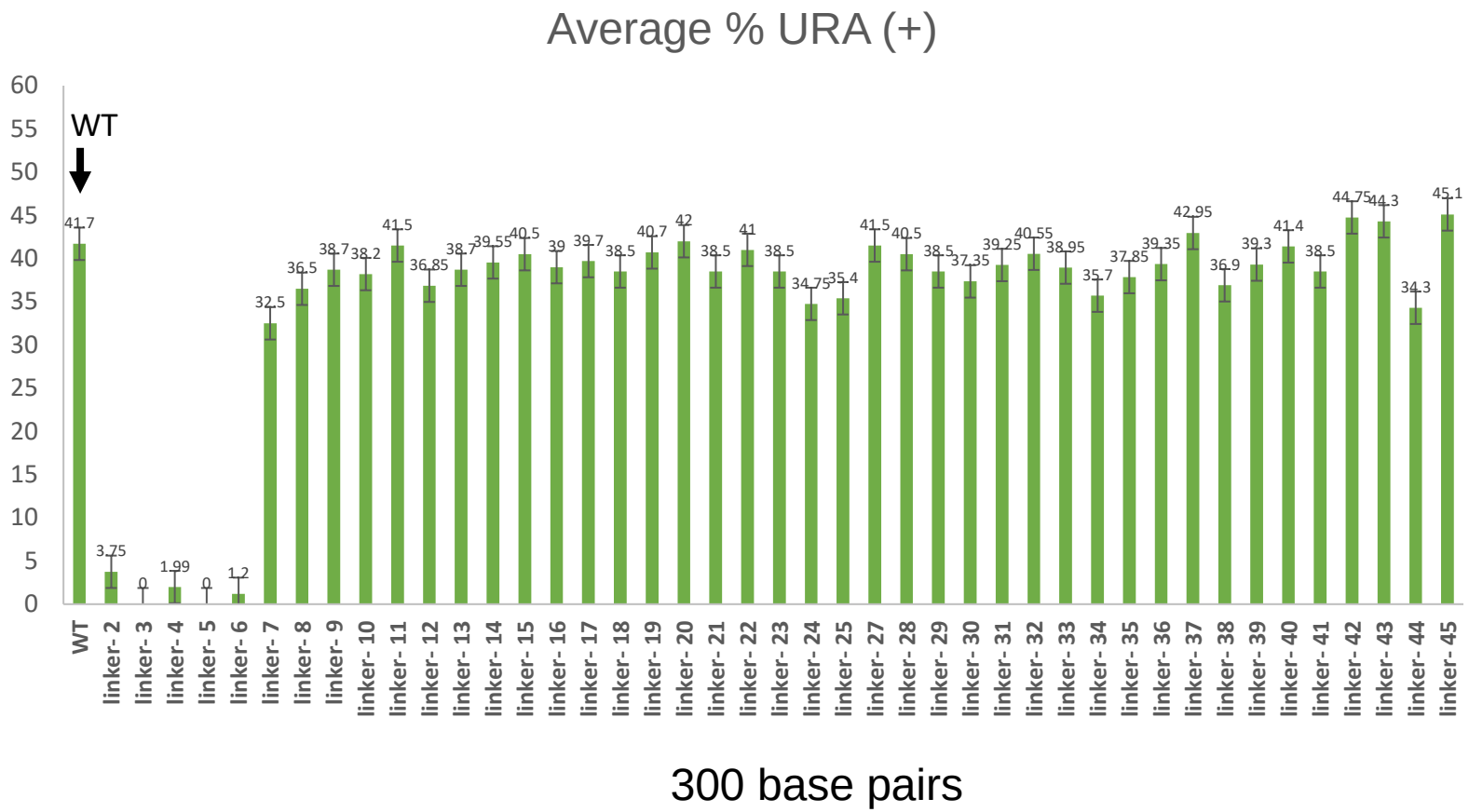
- How is **ORC** recruited to origins in *Yarrowia, if Yarrowia l*acks (origin specificity)?

1. EdU-sequencing
2. ARS assays and linker scan along with structural studies
3. MPOS assay (mutant ARS library to find Motif)

Genetic analysis of *Y. lipolytica* Ori-C using linker scan mutagenesis showed an essential region for ARS activity

High Frequency Transformation

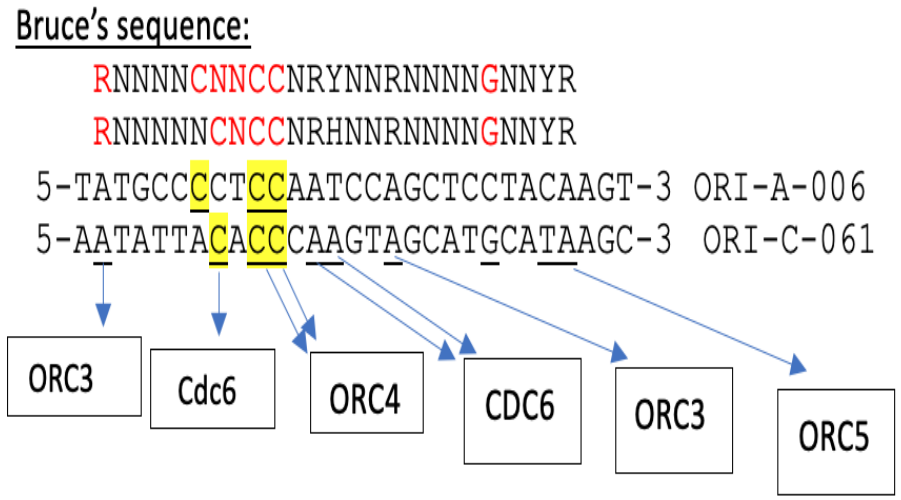
Ori + CEN	+
Ori (no CEN)	–
CEN (no Ori)	–

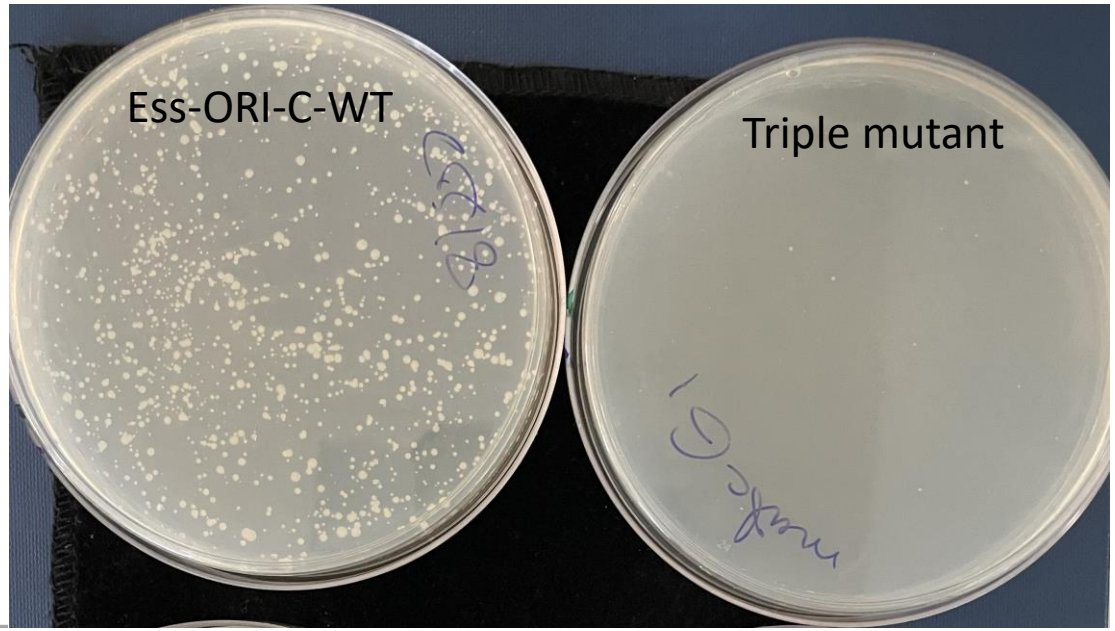



```
GATCCC AATATT ACACCC AAGTCG CATGCA TAAGCT AAAAGT AACTCG CAGCGC
CTAGGG TTATAA TGTGGG TTCAGC GTACGT ATTCGA TTTTCA TTGAGC GTCGCG
  1      2      3      4      5      6      7      8      9
```

Linker scan along with structural studies showed a common motif in Origins of replication in *Y. lipolytica*

ARS activity abolished when ORI motif was mutated





Collaboration with Leemor's lab-Jack Buer- ORC binding assays

Studying the impact of life events on breast cancer risk and progression

Steven Lewis
MD/PhD student
Camila dos Santos lab, CSHL

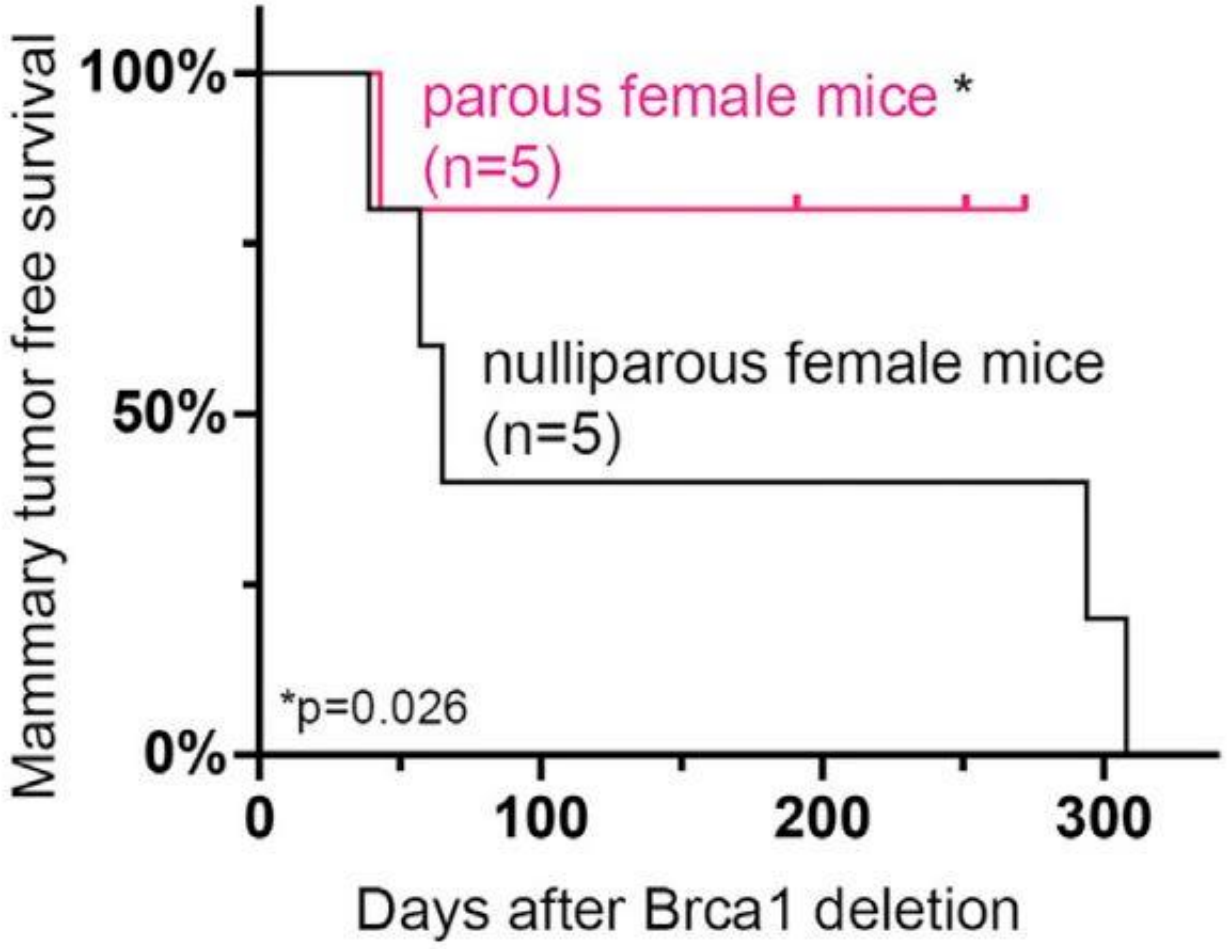
4th year PhD student (6th year MSTP)
Graduate Program in Genetics, SBU

Speed Science
8/27/24

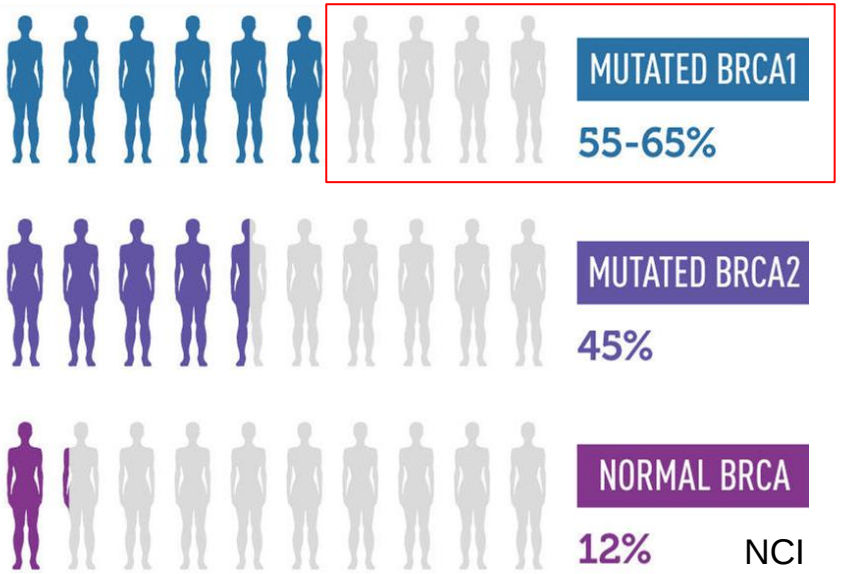
Cold Spring Harbor Laboratory
Cancer Center

Stony Brook MSTP

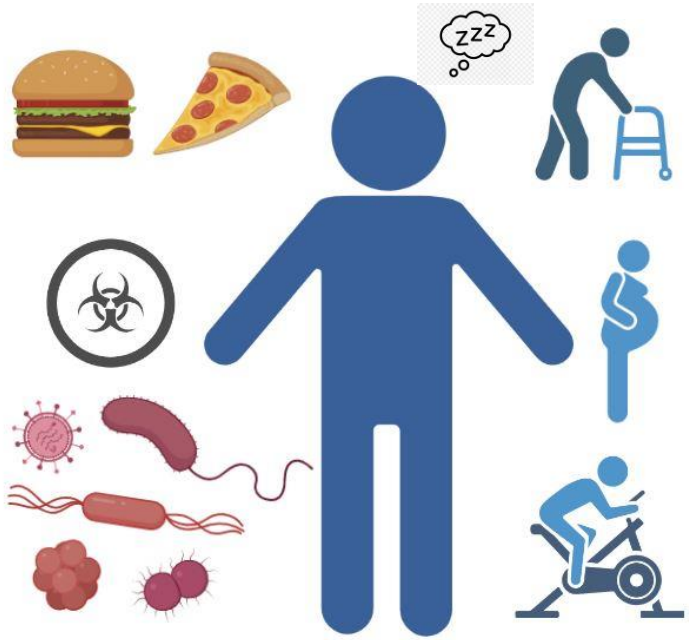
Life events impact mammary tumor incidence in *Brca1* KO model of breast cancer



Hanasoge Somasundara et al. Cell Reports. 2021.

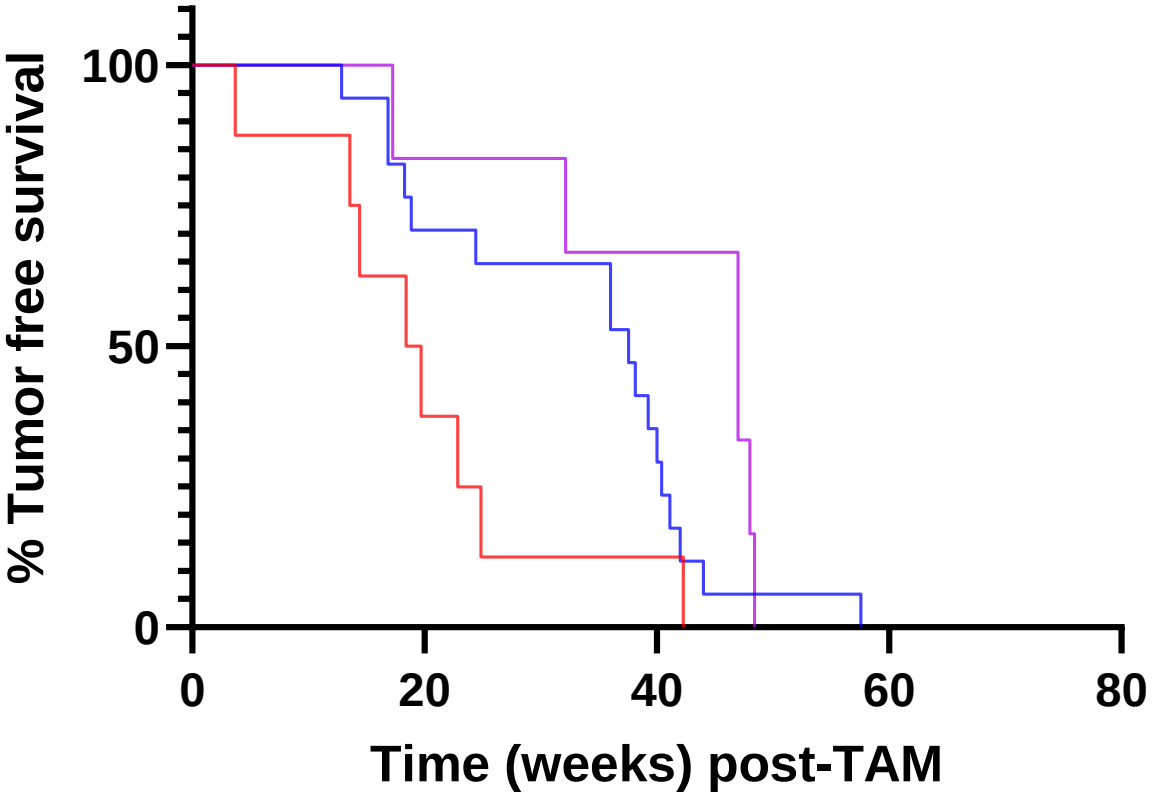


NCI



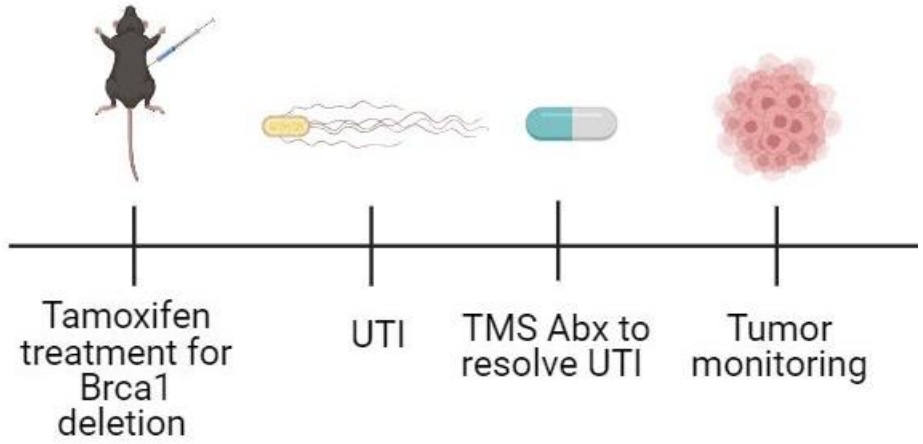
Borniger et al. Cell Metabolism. 2018.
Parhi et al. Nat Comm. 2020.
Li et al. Cell Reports. 2020.

Host response during unresolved UTI accelerates tumor formation



Brca1-UTI
Brca1-PBS
Brca1-TMS

Transient exposure to UTI-host response is not sufficient to accelerate tumors



TAM Tx 2-4 weeks before UTI. TMS administered 1 week *p.*i.

Krt5$^{CRE\text{-}ERT2}$*Brca1*$^{fl/fl}$*p53*$^{+/-}$ UTI (n = 10*/**), PBS (n = 15), UTI-TMS (n = 6 ns)

p < 0.05 Mantel-Cox, p < 0.01 Gehan-Breslow-Wilcoxon test

City Yang, Chen Chen, Samantha Cyrill