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# Unmasking the many faces of Menin: translating basic discovery to clinical insights

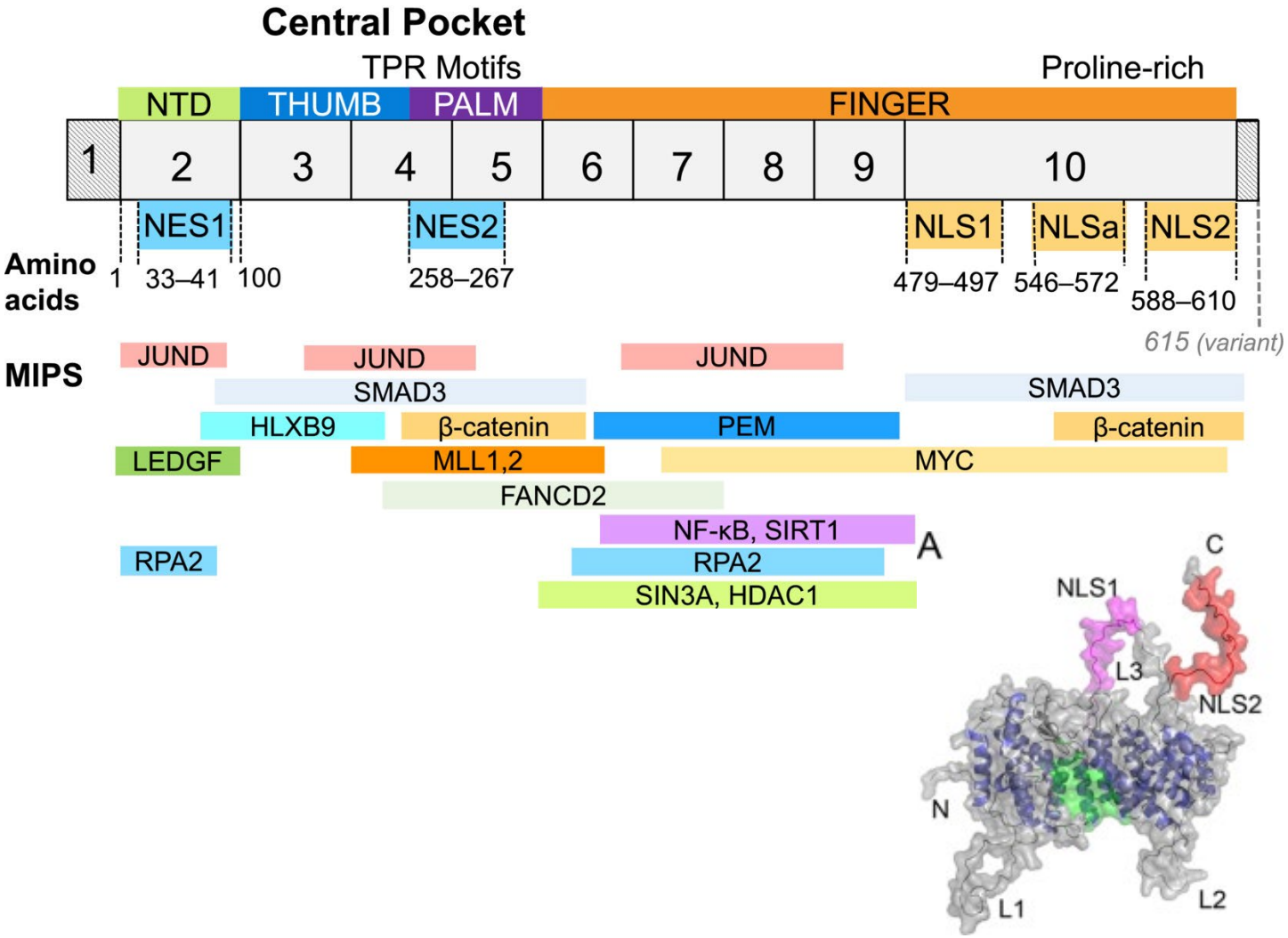
**Suzann Duan, PhD**

**2026 Scientific Retreat**

November 5, 2026

# Decoding Menin structure and function

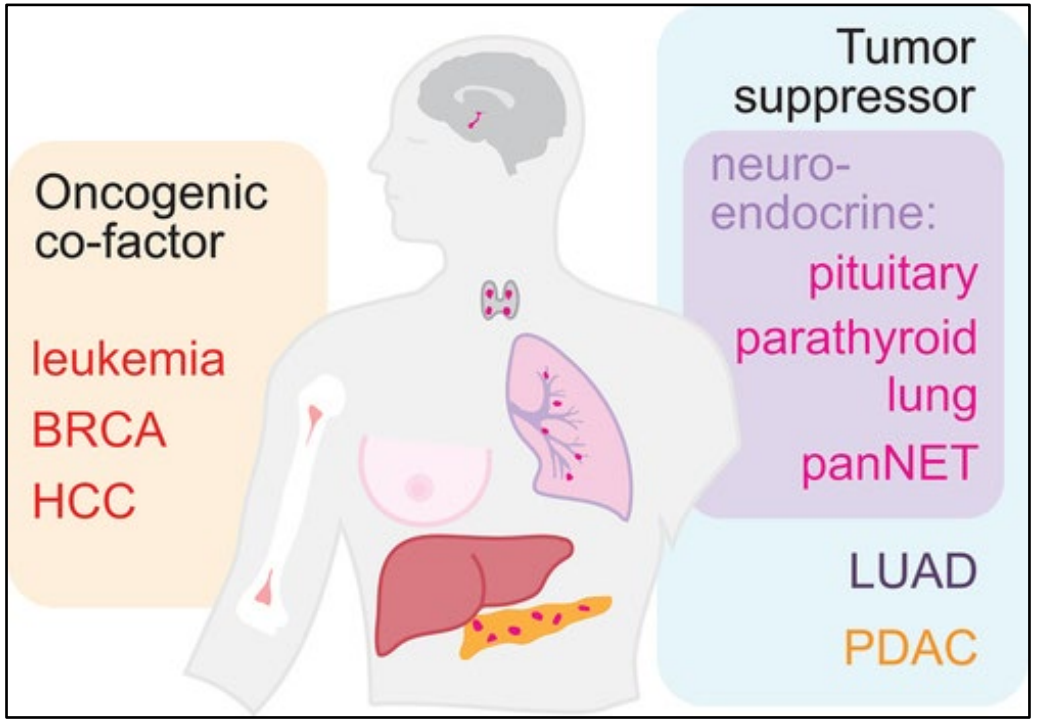
- Menin is a ubiquitously expressed nuclear scaffold protein
- Turnover is mediated by **nuclear export** and degradation
- Truncating mutations accelerate protein turnover
- Interacts with several **epigenetic** factors: **EZH2**, PRMT5, HDAC, SIRT1, **MLL**
- **Up to 55-80%** of duodenal pancreatic neuroendocrine tumors (NETs) show aberrant Menin localization




*Duan et al. Molecular Cancer 2026; Duan et al. Cancer Res Comm 2023; Elvis-Offiah, Duan, & Merchant FASEB J 2023*

PMID: 40152985; PMID: 21757704

# Decoding Menin structure and function




Menin's function and regulation in these cancers remain poorly understood

*Duan et al. Molecular Cancer 2026; Duan et al. Cancer Res Comm 2023; Elvis-Offiah, Duan, & Merchant FASEB J 2023*

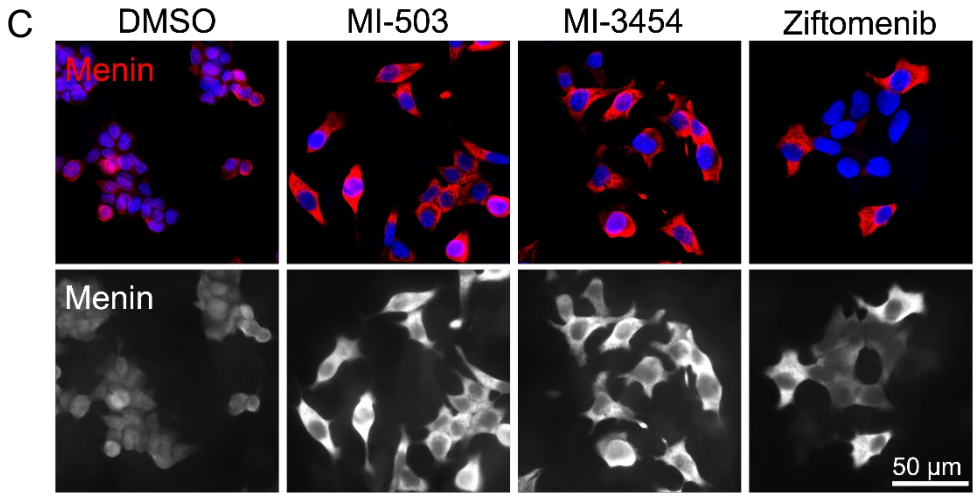
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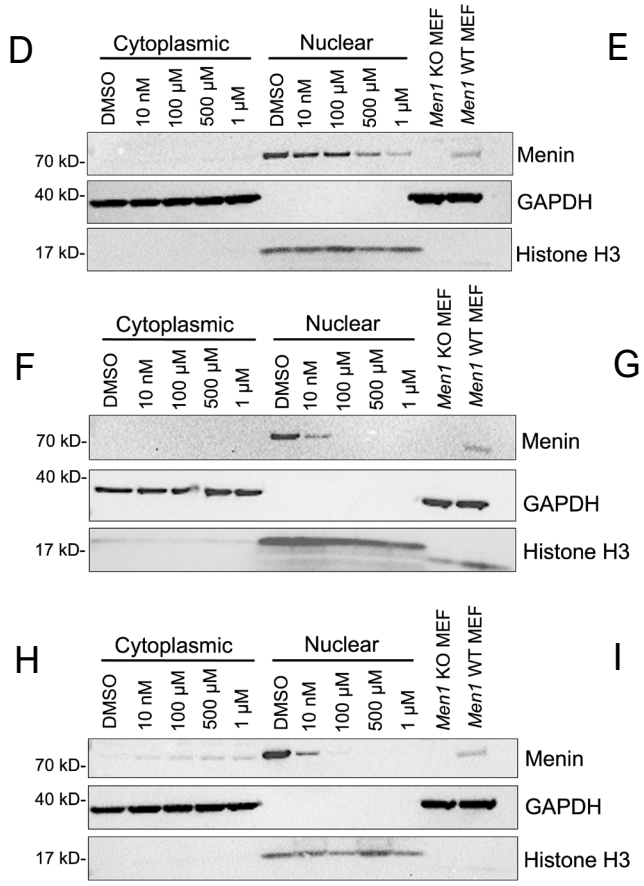
# Menin inhibitors (MIs) induce nuclear export and degradation of Menin protein in PanNET cells

Can we leverage a new class of Menin-targeting drugs (Mis) to model the events following Menin loss?



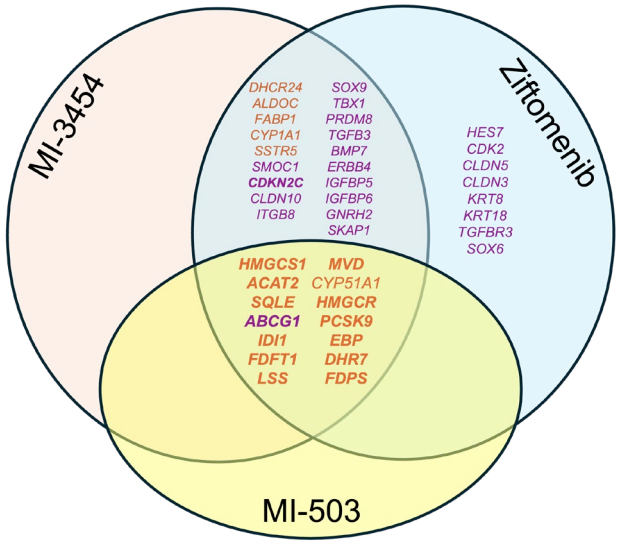

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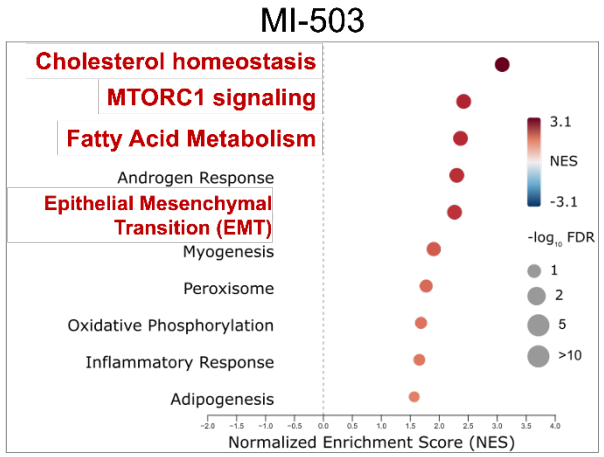


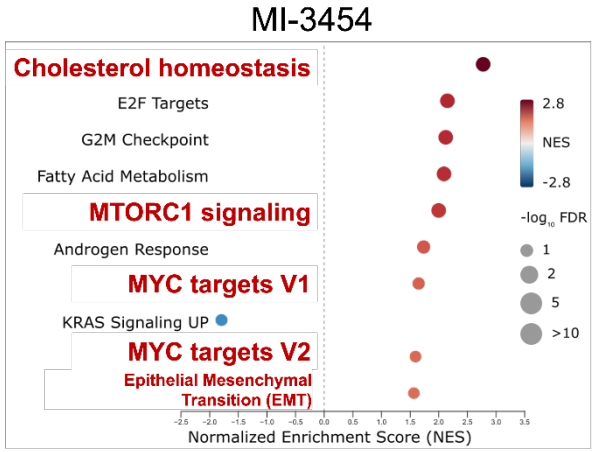



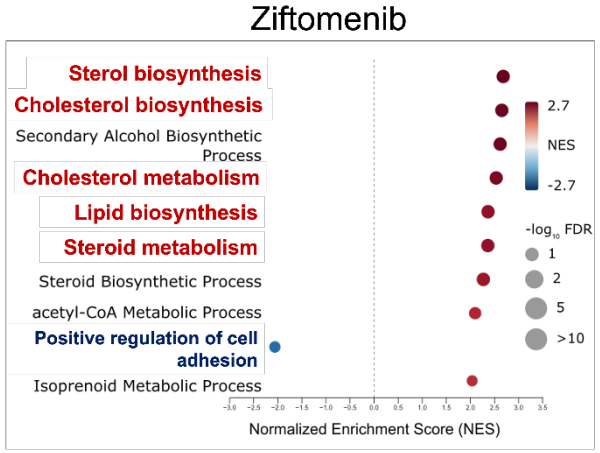

What are the downstream consequences of nuclear Menin loss?

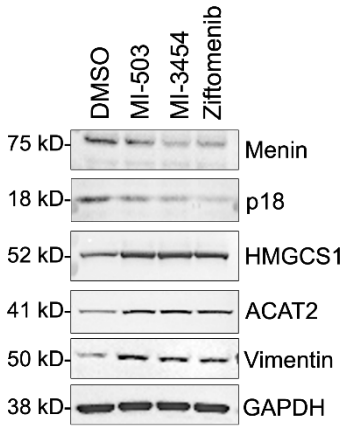
# Menin inhibition upregulates cholesterol biosynthesis and a pro-oncogenic program in PanNET cells

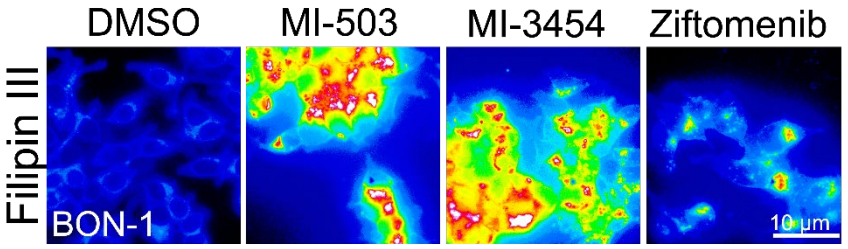


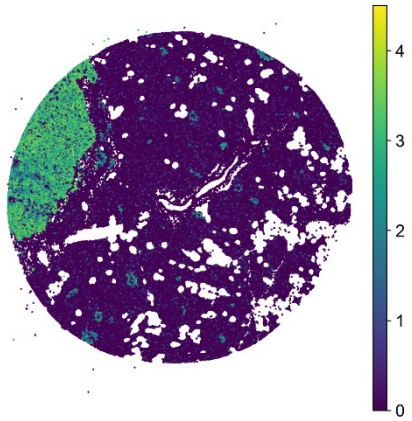



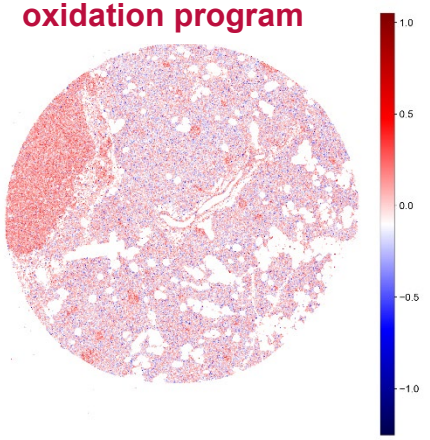




***CHGA* (tumor marker)**

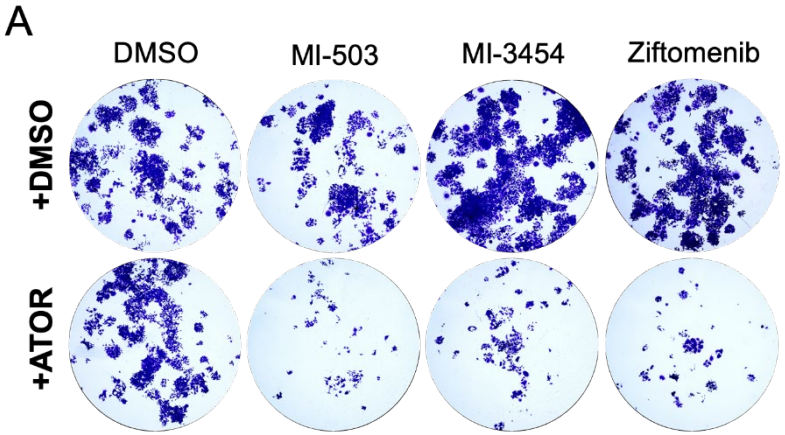


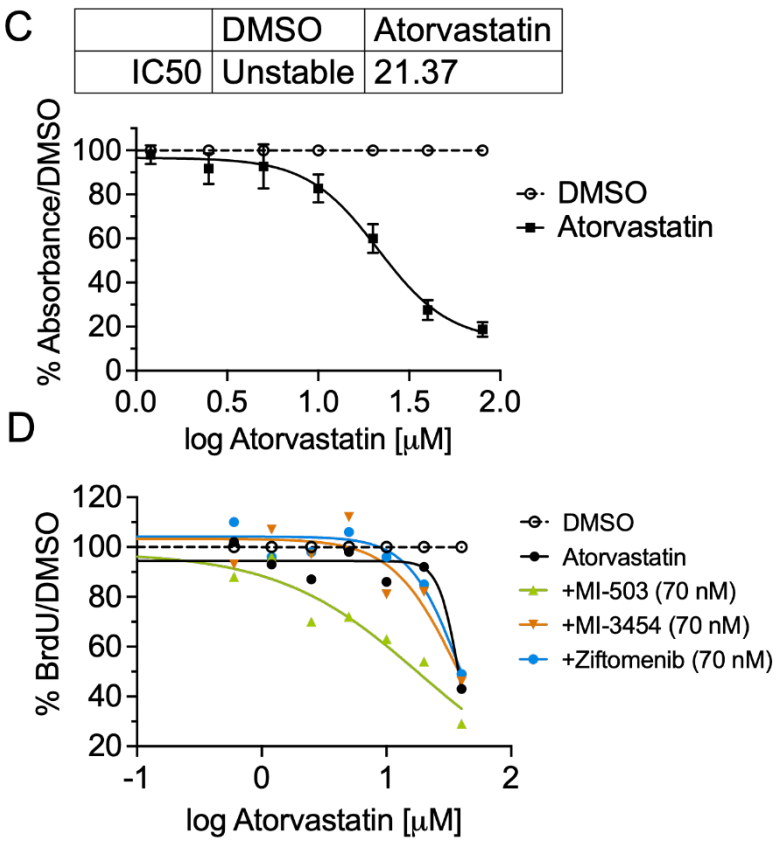

**Lipid synthesis/ oxidation program**

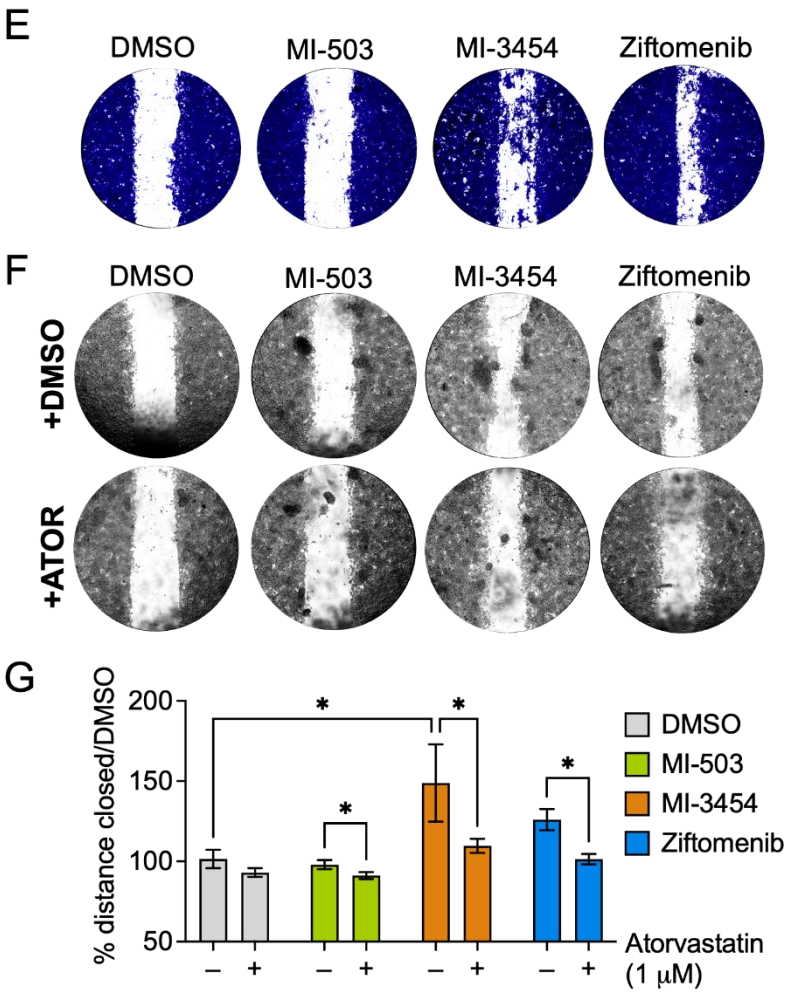



**Does Menin-induced lipid reprogramming confer a functional benefit to tumor cells?**

# Inhibition of cholesterol synthesis blocks a Menin-dependent malignant phenotype in vitro




Ongoing work: diving deeper into targeting lipid-dependent signaling

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# Is there a role for Menin in other solid malignancies beyond NETs?

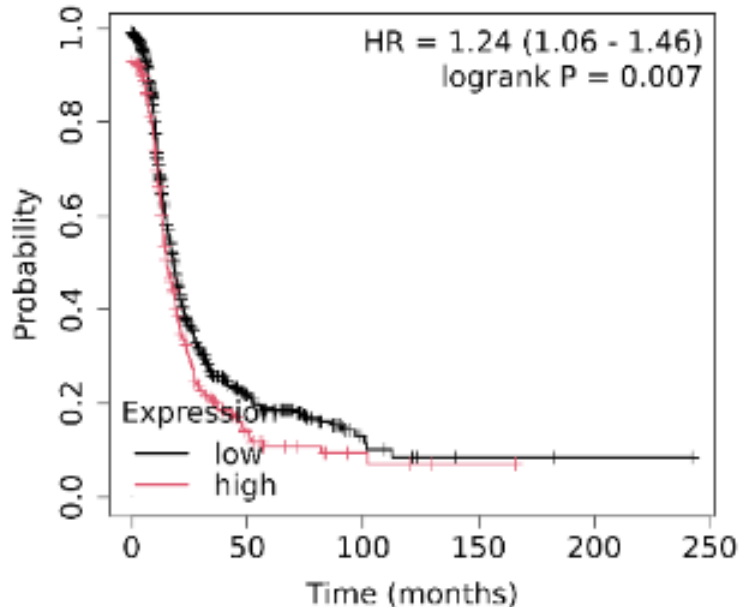
# MEN1 is overexpressed in high-grade serous ovarian cancer (HGSOC)

Correlates with increased tumor grade, lower PFS

A

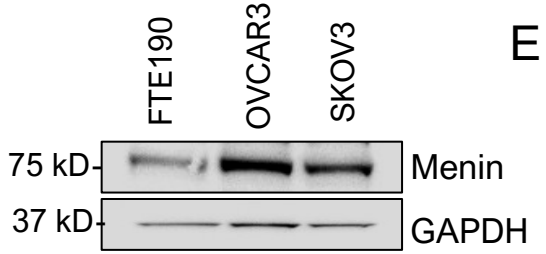
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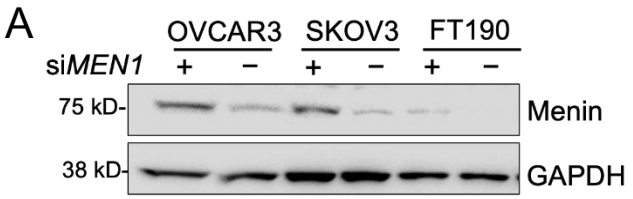


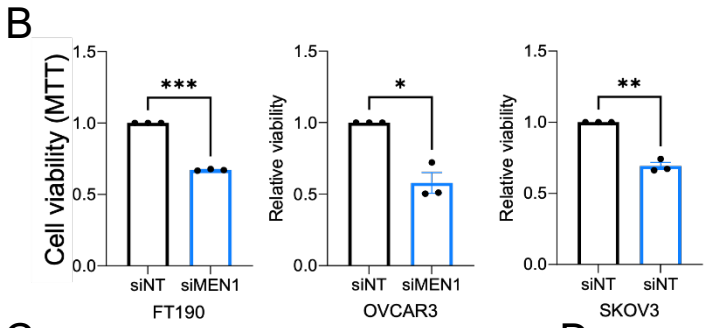

Ongoing analyses of patient tumors collected as UCI Health will evaluate the function of *MEN1*/Menin in organoid cultures

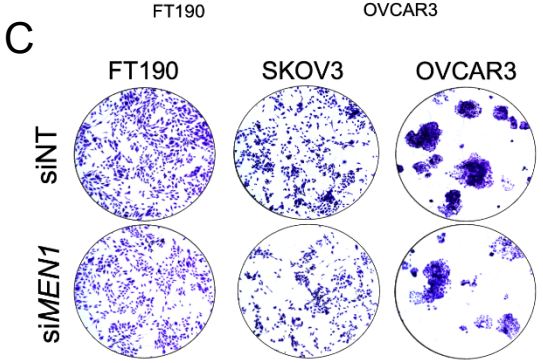
What role does increased *MEN1*/Menin expression play in HGSOC?

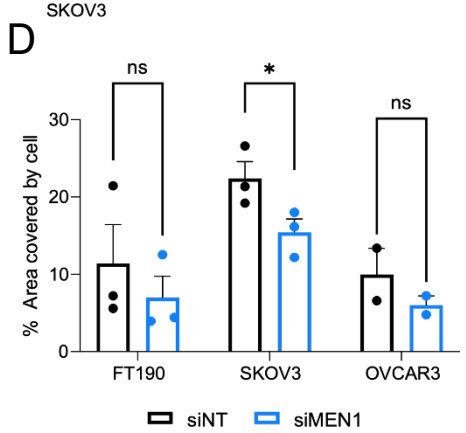
# MEN1/Menin depletion in ovarian cancer cells

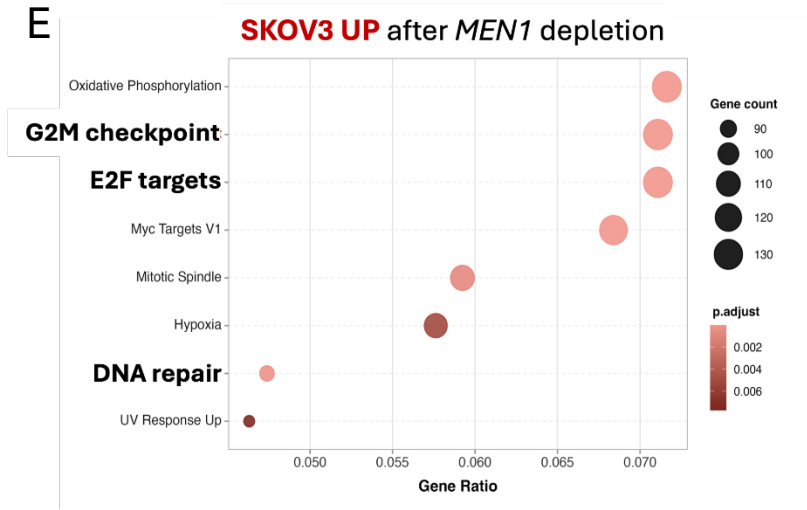
## Reduces viability and activates checkpoint and DNA repair pathways

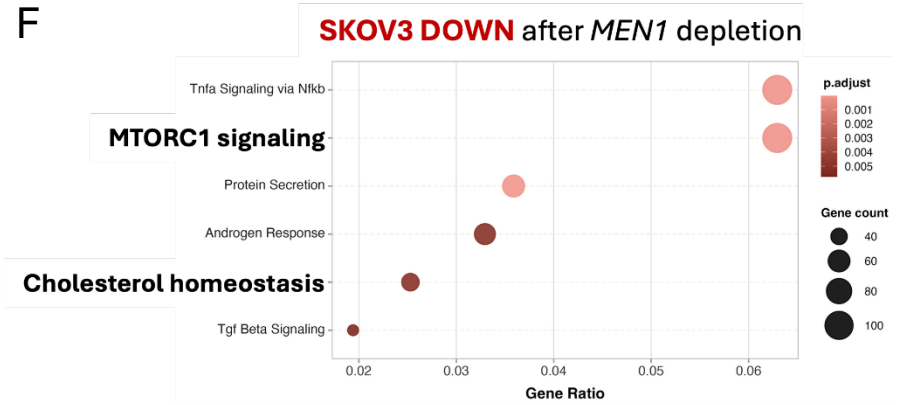


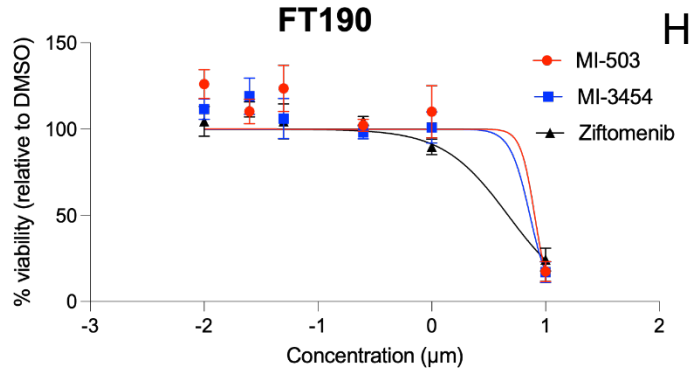



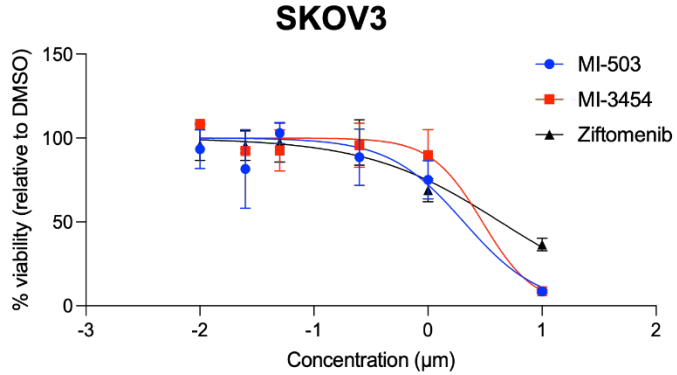




| | MI-503 | MI-3454 | Ziftomenib |
|---|---|---|---|
| IC50 | 8.014 | 7.282 | 4.680 |




| | MI-503 | MI-3454 | Ziftomenib |
|---|---|---|---|
| IC50 | 2.058 | 3.002 | 4.318 |

**Can Menin inhibitors sensitize ovarian cancer cells to first-line chemotherapies (PARPi)?**

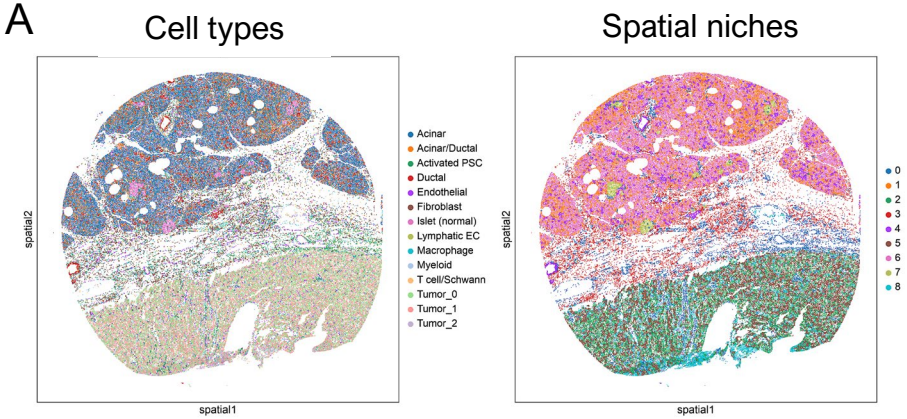
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# Is there a role for Menin in the Tumor Microenvironment?

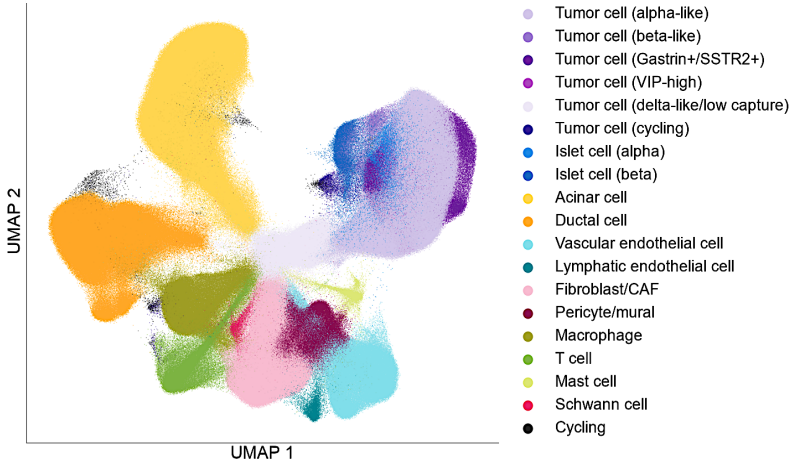
# Single cell spatial transcriptomics of patient PanNETs

## Identifies a **myofibroblast**-like signature associated with **immune exclusion**

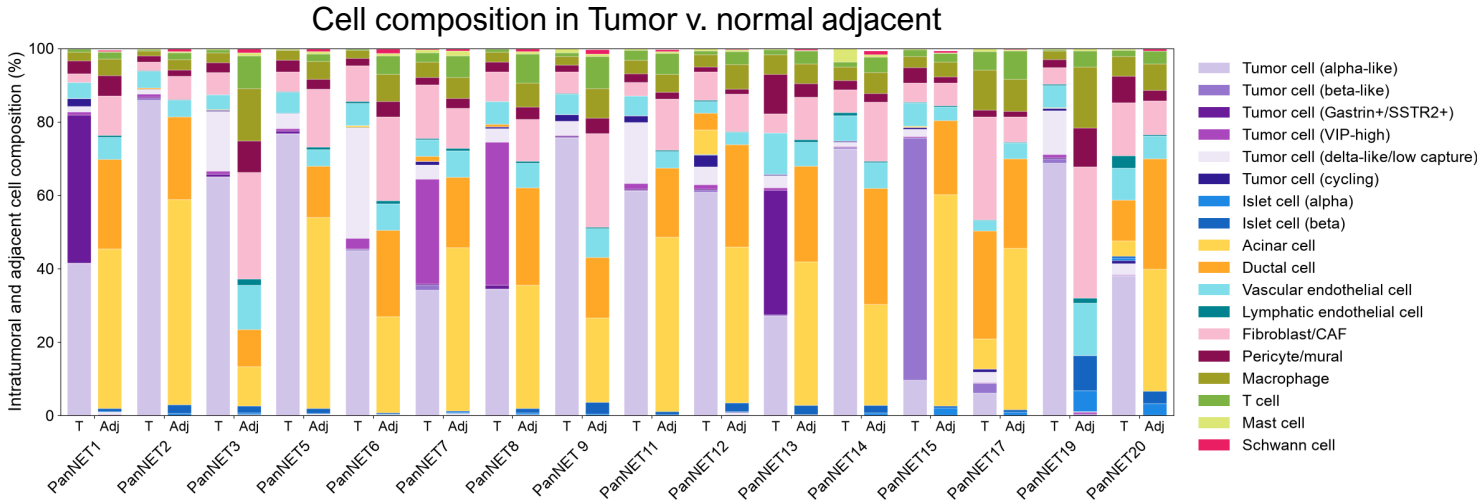
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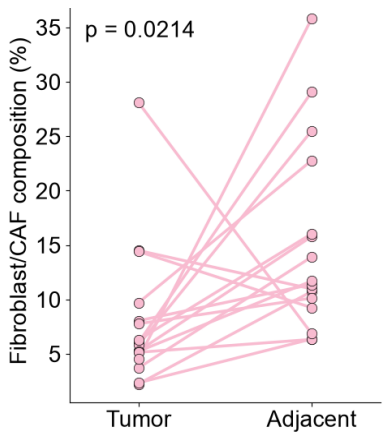



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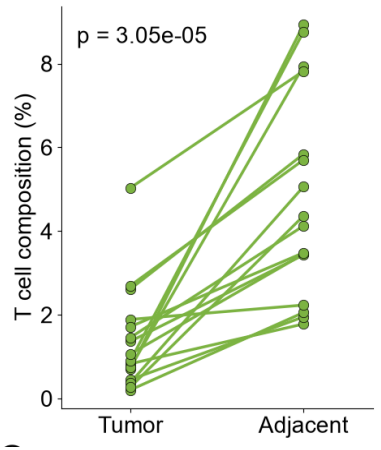


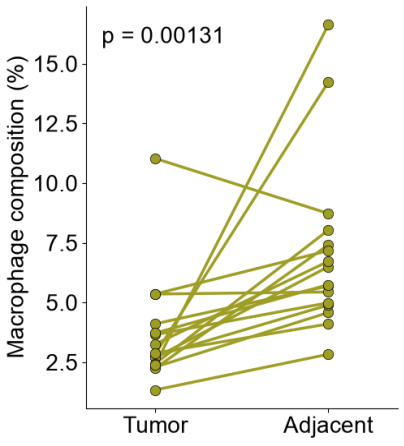

D

CAFs form spatial niche around Tumors




T cells and Macrophages **excluded** from Tumor niche

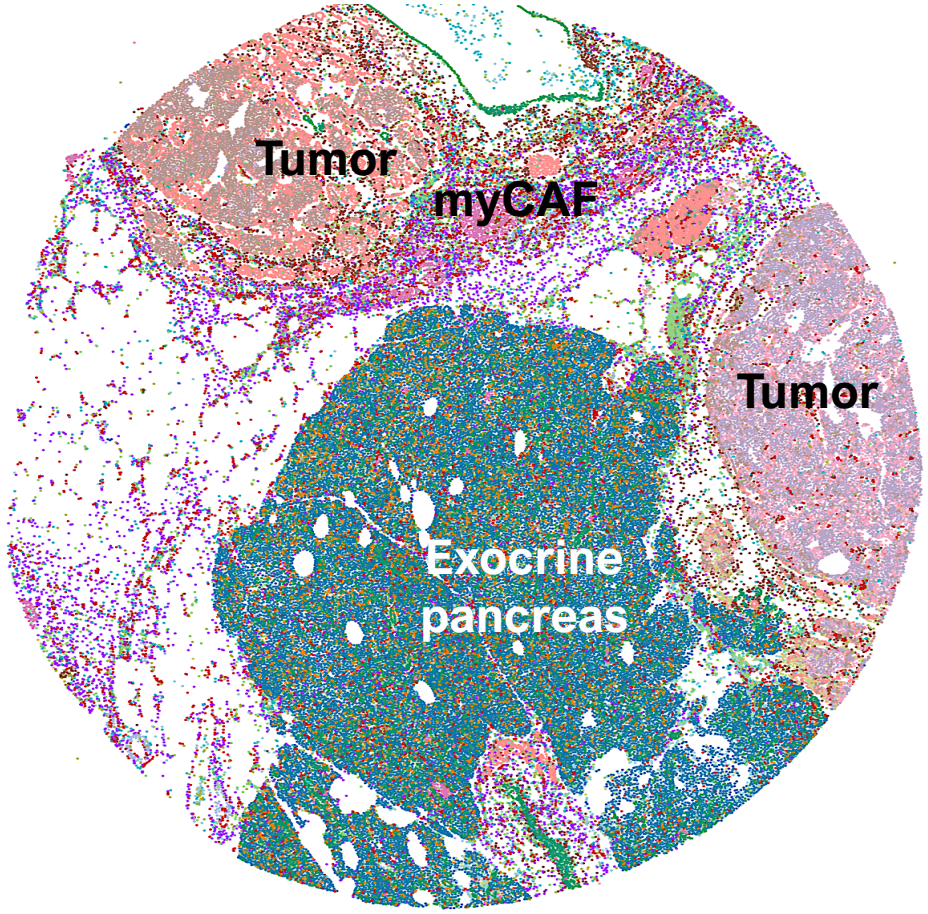


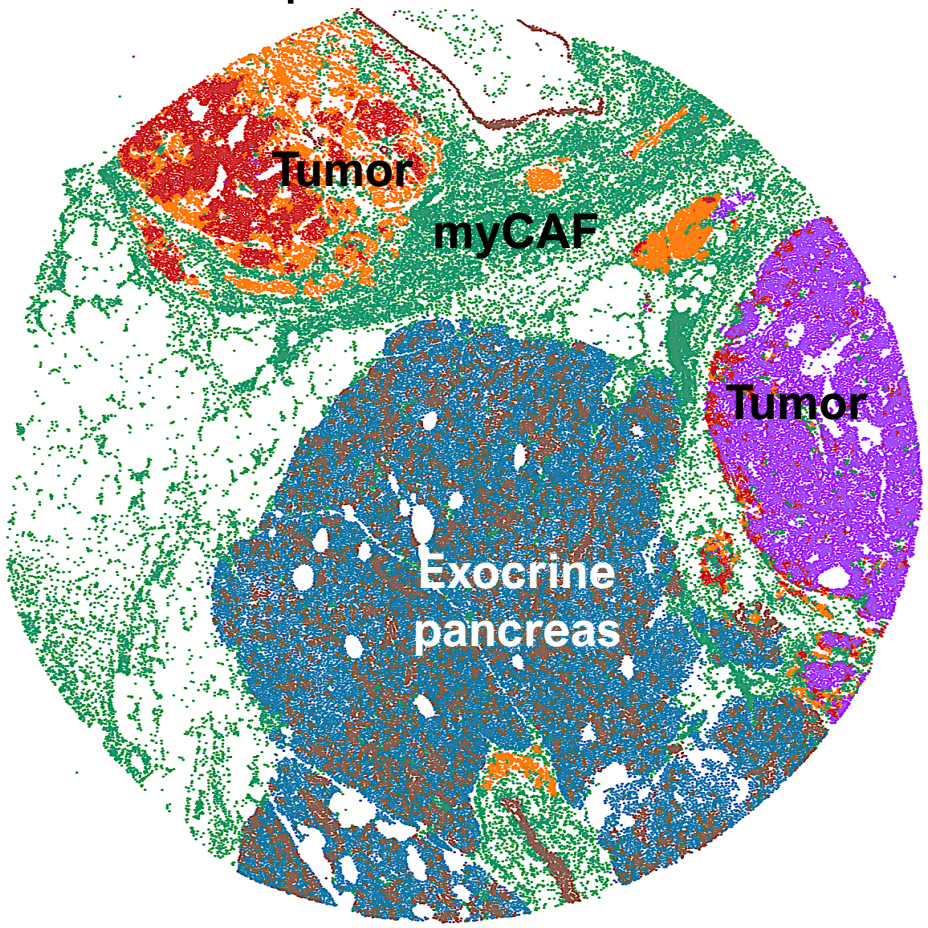
# Single cell spatial transcriptomics of patient PanNETs

Identifies a **myofibroblast**-like signature associated with **immune exclusion**

Cell types




Spatial niches

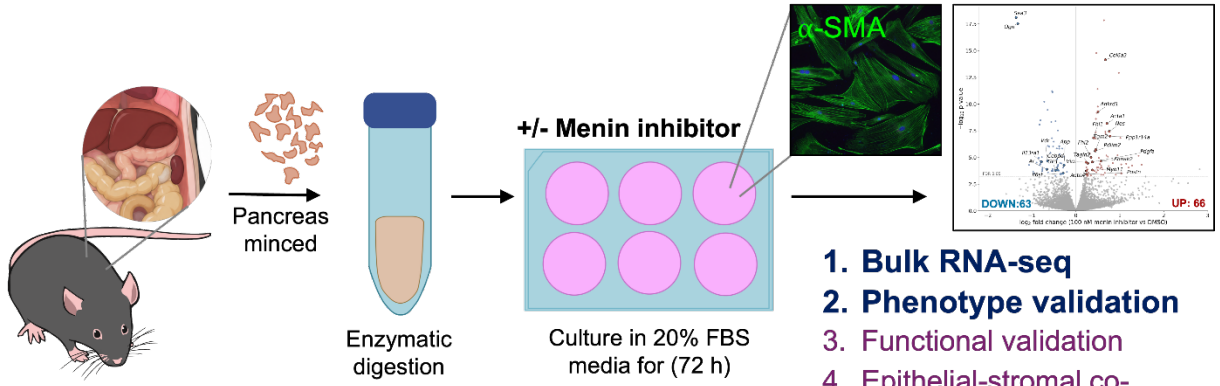



Is there a potential role for Menin signaling in regulating CAF/myCAF identity?

# Menin depletion in primary murine pancreatic fibroblasts

## Upregulates transcriptional myCAF programs

A

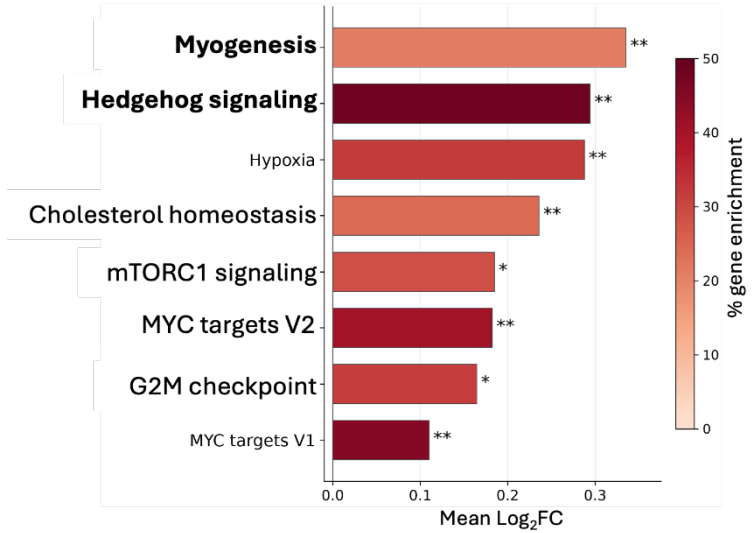



1. **Bulk RNA-seq**
2. **Phenotype validation**
3. Functional validation
4. Epithelial-stromal co-culture

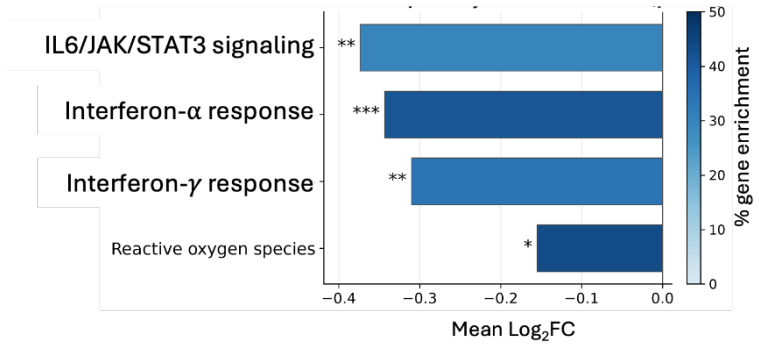
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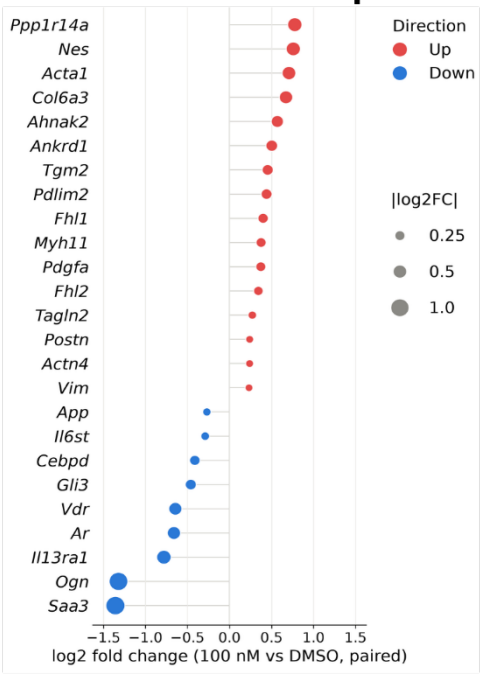

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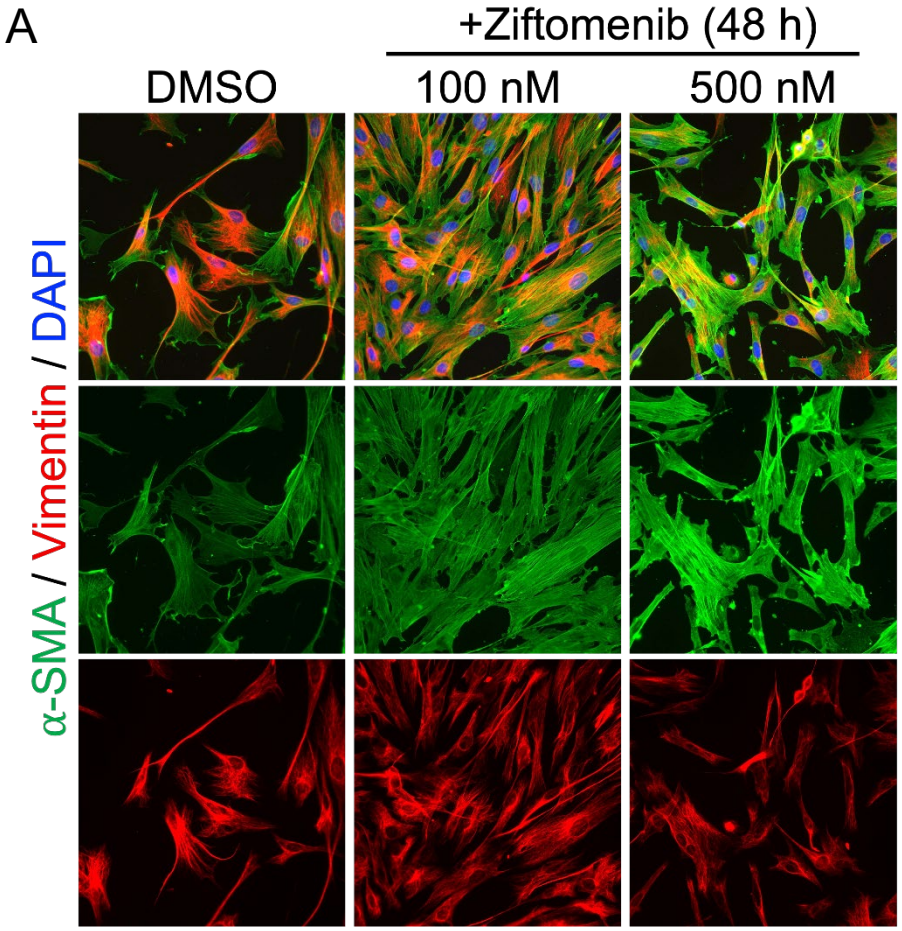

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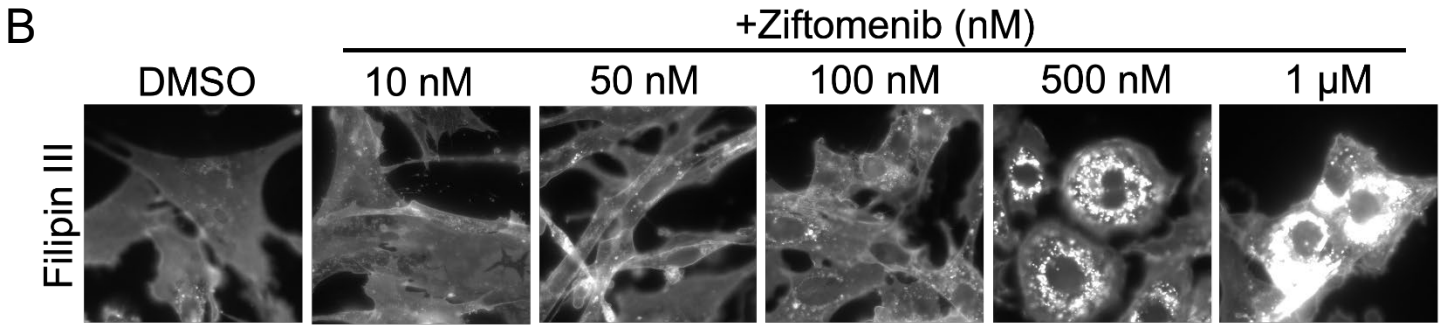


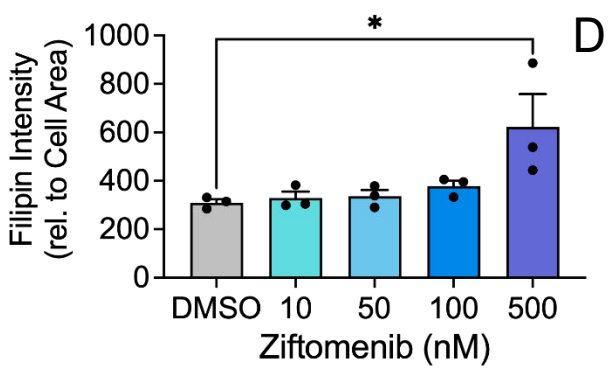

**Can we validate the functional impact of this myCAF conversion in vitro?**

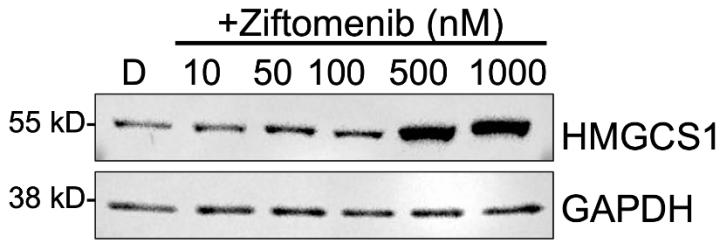
# Menin depletion in primary murine pancreatic fibroblasts

Upregulates the expression of myCAF markers and cholesterol biosynthesis



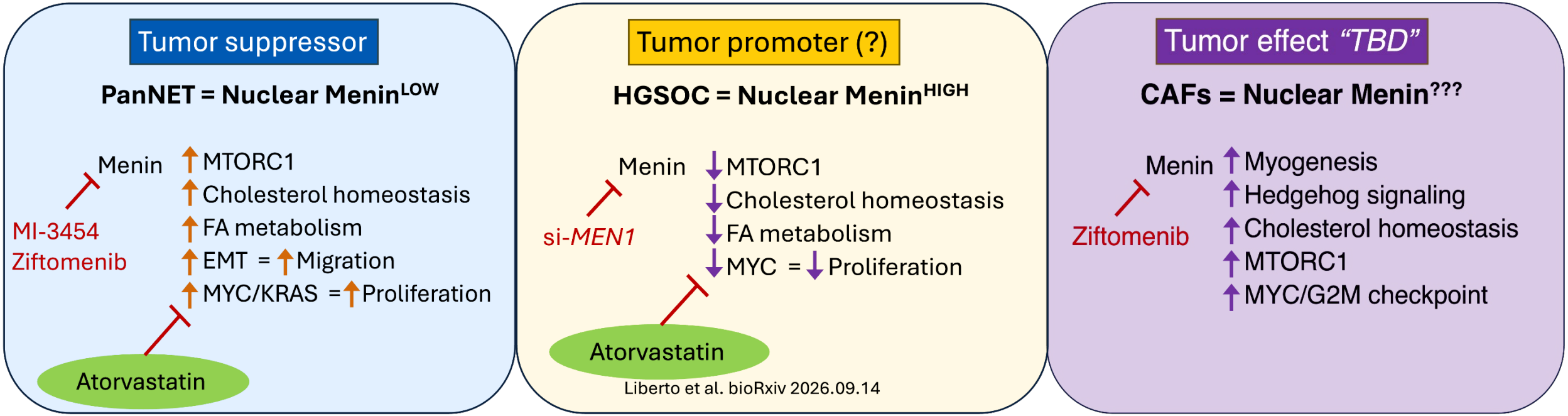

***Seeking collaborators!***

Platforms for evaluating ECM dynamics/stiffening

Future work will evaluate fibroblast/myCAF ECM remodeling and in tumor organoid co-cultures

# The Takeaway: Menin signaling in Solid Tumors

Context-dependent and extends beyond its original identification as a tumor suppressor



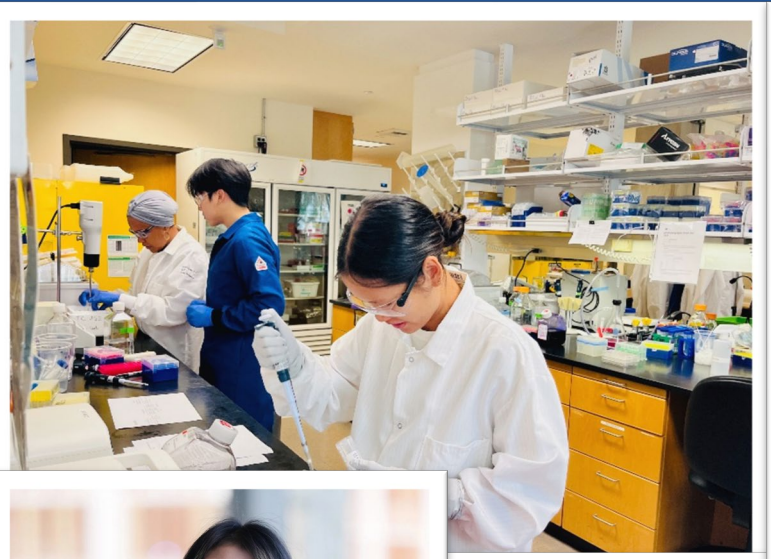
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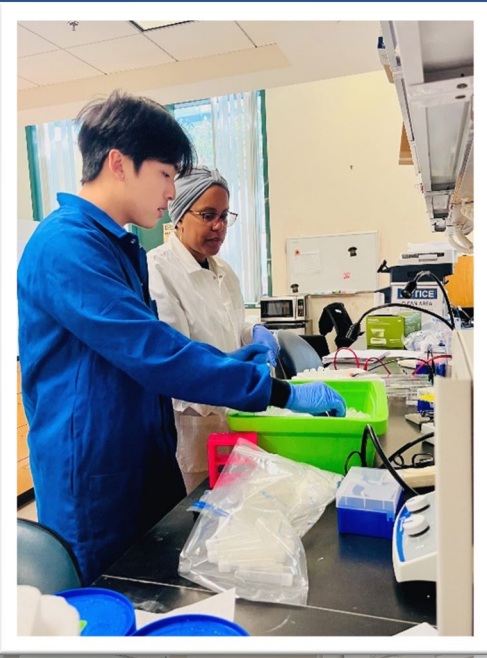

Duan Lab

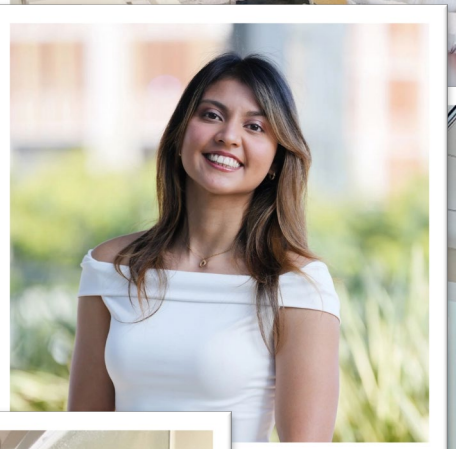
**Dr. Ikrame Naciri, PhD**
**Dr. Christine Nguyen, MD**
**Rebeca Gentry, BS**
**Juliette Moore, BS**
Jayden Luong
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Dr. Cindy Yamamoto, PhD (GRT Hu
Dr. Reed Ayabe, MD
Dr. Jennifer Valerin, MD, PhD
Dr. Zeljka Jutric, PhD
Dr. Chris Halbrook, PhD
Dr. Anjali Hari, MD
Dr. Kiran, Clair, MD
Dr. Jill Tseng, MD











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NIH National Institute of Diabetes and Digestive and Kidney Diseases

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# Questions?