



# Animal Model Workshop

Ex vivo tumor slices as an immune-intact human model to study tumor and immune responses in renal cell

**Allison May**

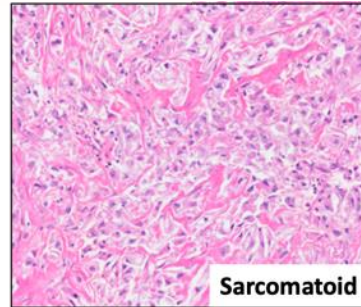
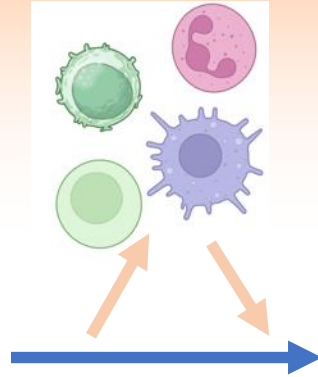
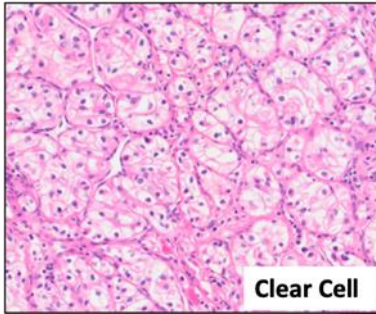
Assistant Professor  
Department of Urology  
University of Virginia

**September 11-13, 2025**



# Ex vivo tumor slices –What and Why?

Our question:



- Replicate human biology
- Intact immune cells and tumor/immune interactions

- GEMMs
- PDX
- Humanized?
- Organoids
- Tumor explants

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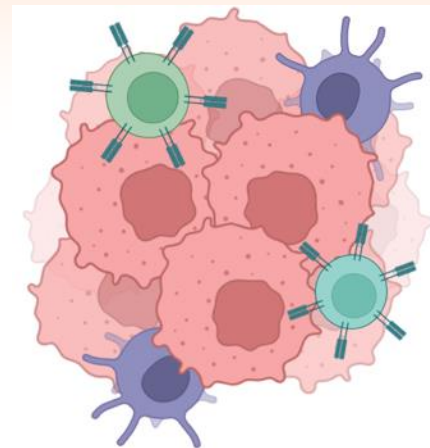


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# Ex vivo tumor slices –What and Why?

- Maintains human biology and heterogeneity
- Intact tumor microenvironment, including infiltrating immune cells
- Viable for up to 2 weeks
- Maintains spatial architecture
- Can manipulate to test drugs, study biologic pathways, tumor/immune interactions, etc.
- Adjacent slices serve as nearly identical controls



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Image generated with Biorender



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# Tumor slices in RCC

- Stenzel, et al. Cancers, 2021 – nivolumab treated slices show decreased PD-1 expression on immune cells and variable changes in CD8 proliferation/density
- Roelants et al. Cancers, 2020 – tumor slices show differential responses to TKI's and mTORi

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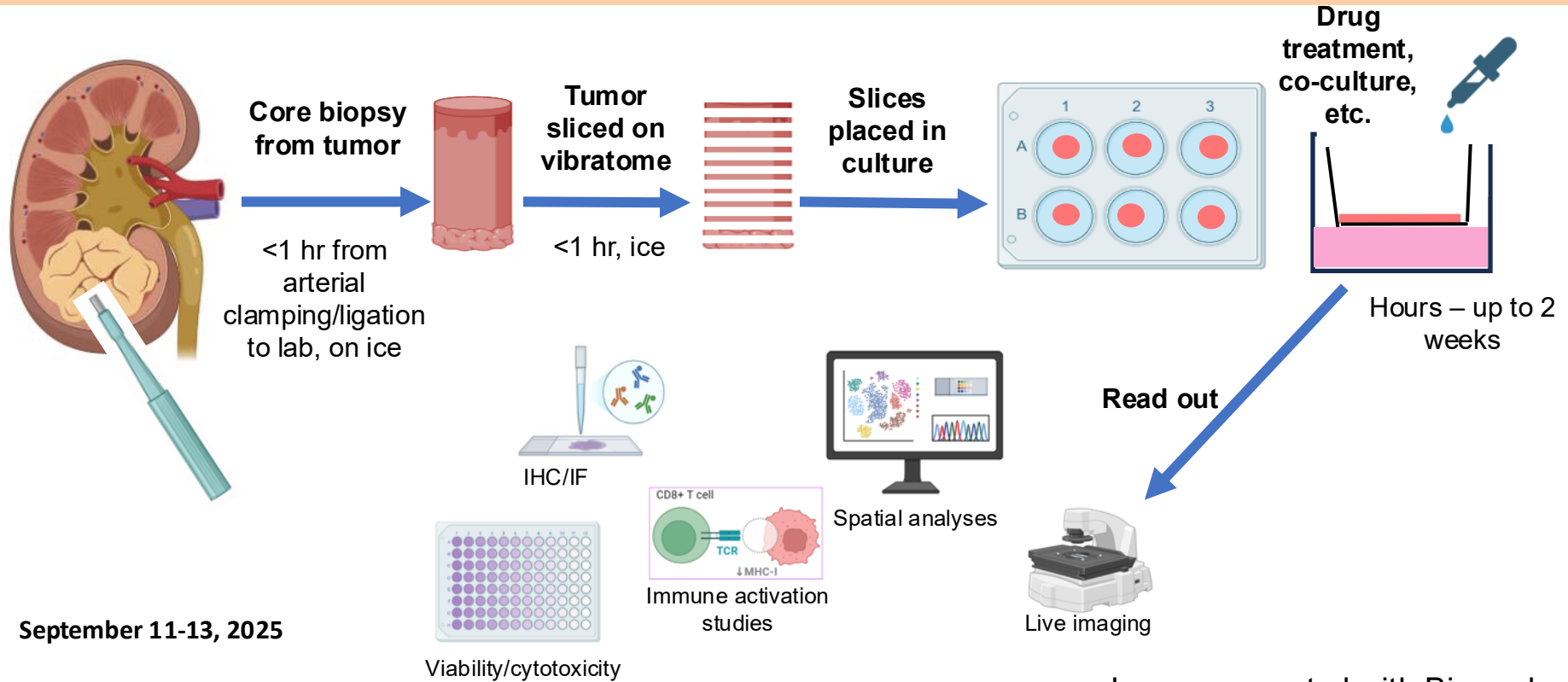
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# Workflow



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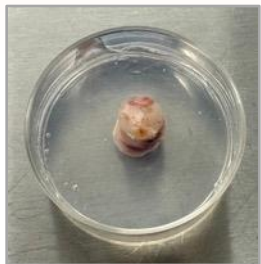


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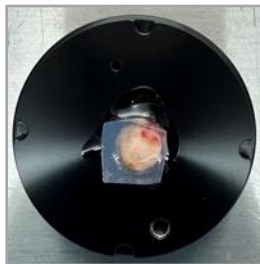
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# Workflow

Biopsy Punch –  
LMA Mold



Biopsy Punch –  
LMA Mold  
on specimen tray



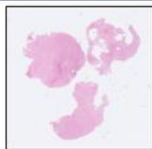
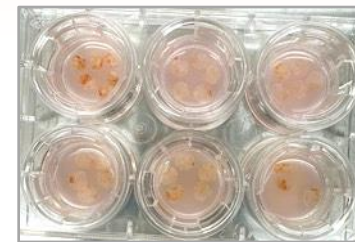
Specimen tray  
fixed on buffer  
tray



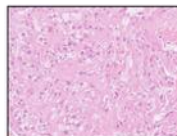
Buffer tray  
with sliced  
tumor biopsy  
specimen



Slices in 6-well  
plate



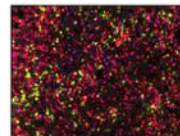
Tumor slices embedded, cut  
on slide, and H&E stained



H&E



IHC stains



Immunofluorescence

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# Tips for optimization

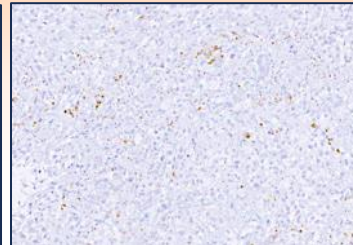
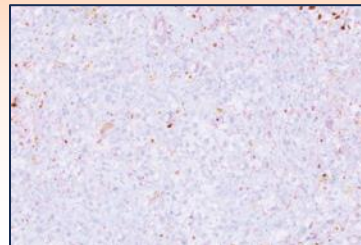
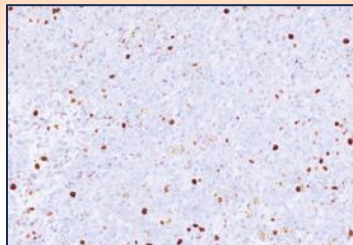
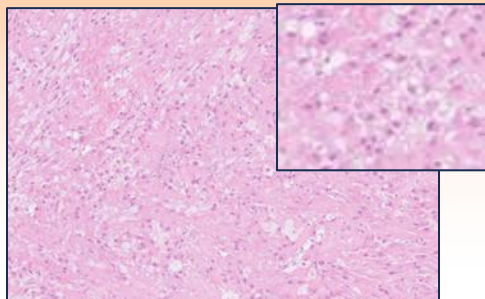
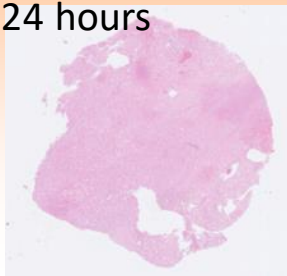
- Patient selection: RN>PN; large mass; no IVC thrombus; clear cell
- Close collaboration between surgeon, OR team, pathology, lab
- Optimization of slicing settings
  - Softer tissue/sticking to blade -> increase speed
  - Softer tissue -> lower frequency/amplitude
  - Blade angle
  - Slice thickness
- Everything on ice

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# Tumor slices remain viable for at least 5 days

24 hours



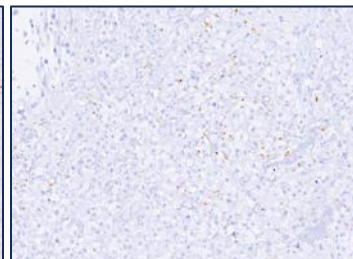
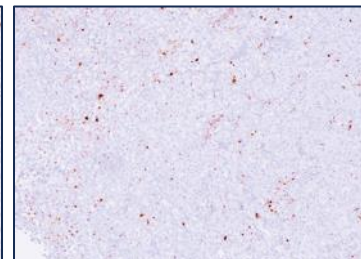
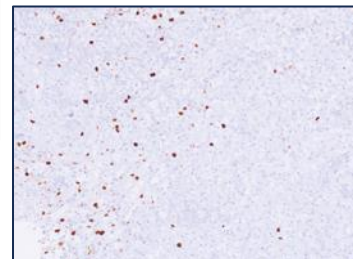
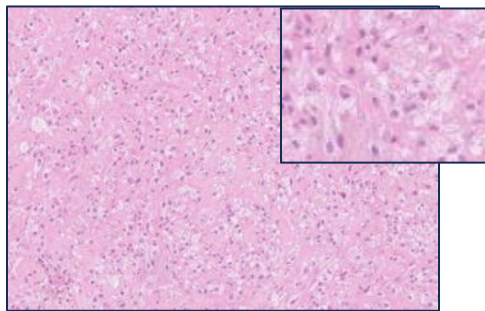
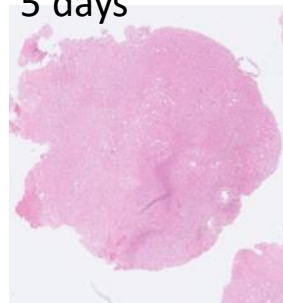
H&E

Ki-67

Cleaved PARP

CD8

5 days



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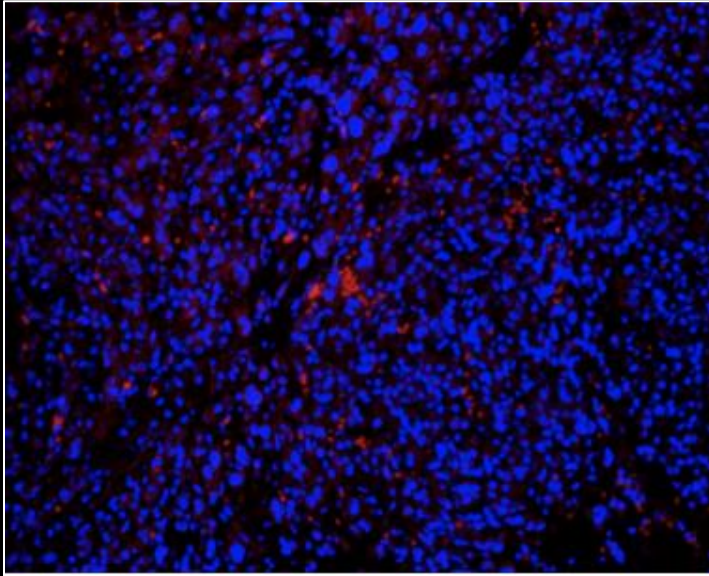
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# Tumor cell features can be altered

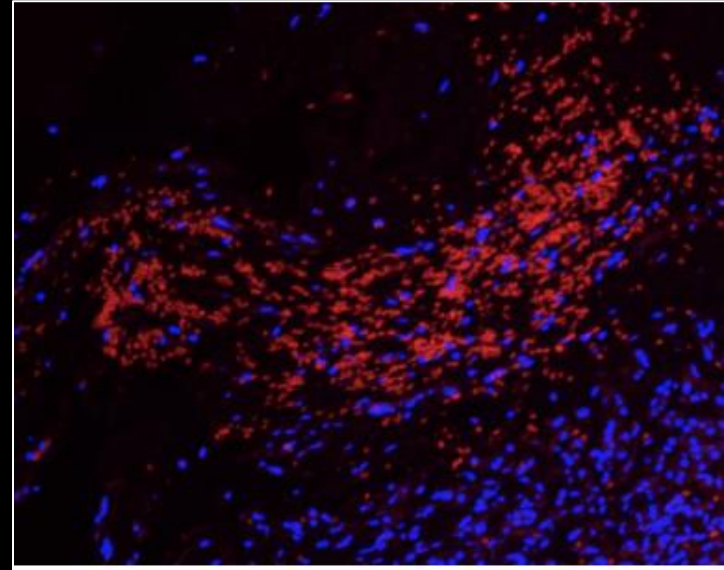
Protein markers:

**DAPI (nuclear)**

**N-cadherin**



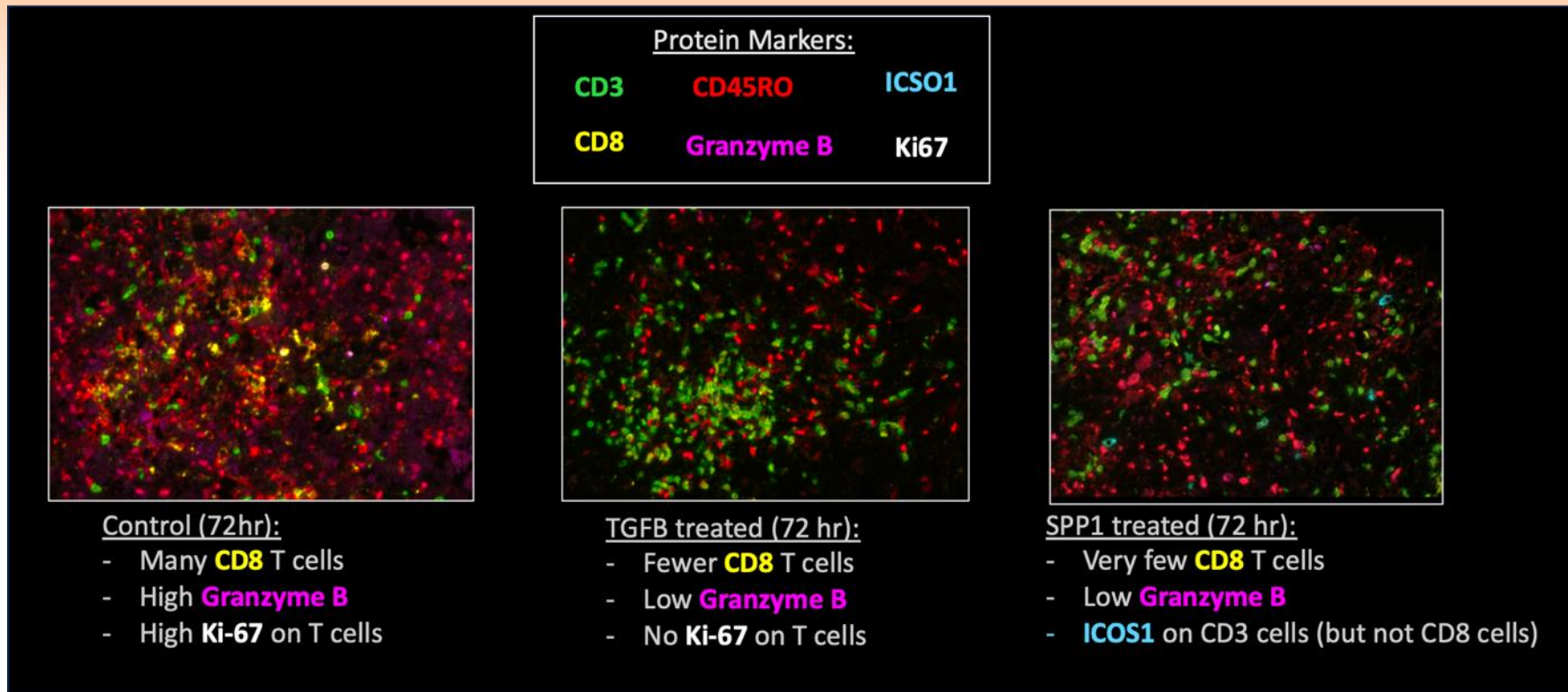
Control (12 hr)



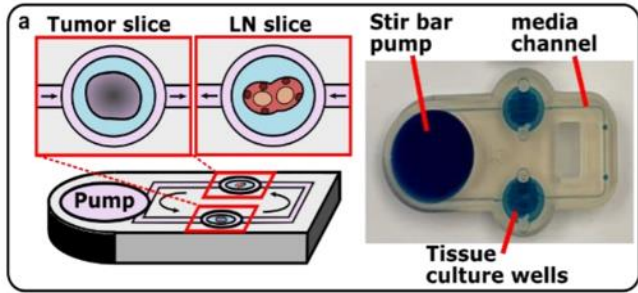
TGFB treated (12 hr)



# Tumor immune microenvironment can be altered



# Future directions – endless possibilities



Rebecca Pompano; Melanie Rutkowski

Introduce circulation and additional tissues

- Lymph nodes – ICI response
- Lymph node/benign kidney/adrenal - metastasis

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Live imaging

- Macrophage infiltration
- Sarcomatoid cells



Drug testing for precision medicine



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# Limitations

- Finite length of culture
- Requires timing
  - Freeze/thaw?
- Transcriptomic and other changes from ischemia/environmental change
- No systemic circulation/complexity
- May not be able to measure full therapy effect, particularly for immunotherapy
- Requires coordination with OR and pathology
- No standardized protocols
- Unclear yet whether ex vivo responses predict true clinical outcomes

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# Summary

- Ex vivo tumor slices provide an immune-intact model that replicates human RCC biology, TME, and heterogeneity
- Tumor slices can be manipulated with biologic changes seen in short time periods
- Good option for studying drug effects, tumor/immune interactions, details of complex biologic processes
- Tumor slices provide an important model to complement in vivo and other in vitro models

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# THANK YOU

## May Lab

Ratnakar Bynigeri  
Xinghua Liao  
Campbell Johnston  
Gabe Alencar

## Mentors and collaborators at UVA

Rebecca Pompano  
Melanie Rutkowski  
Matt Lazzara  
Dan Gioeli  
Stephen Culp

## University of Michigan

Evan Keller  
Suguru Kadomoto

## Patients and their families

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