8PM

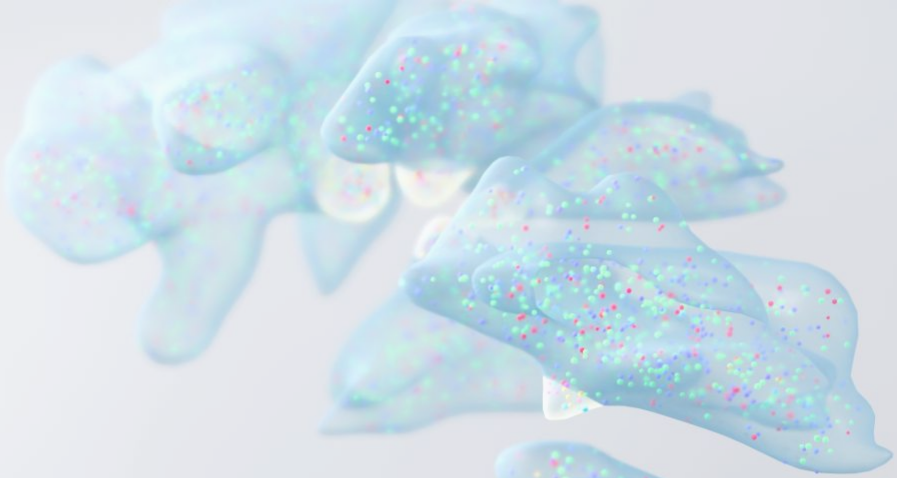
1AM in London (GMT), 10AM in Tokyo (GMT+9)

Multiscale Maps

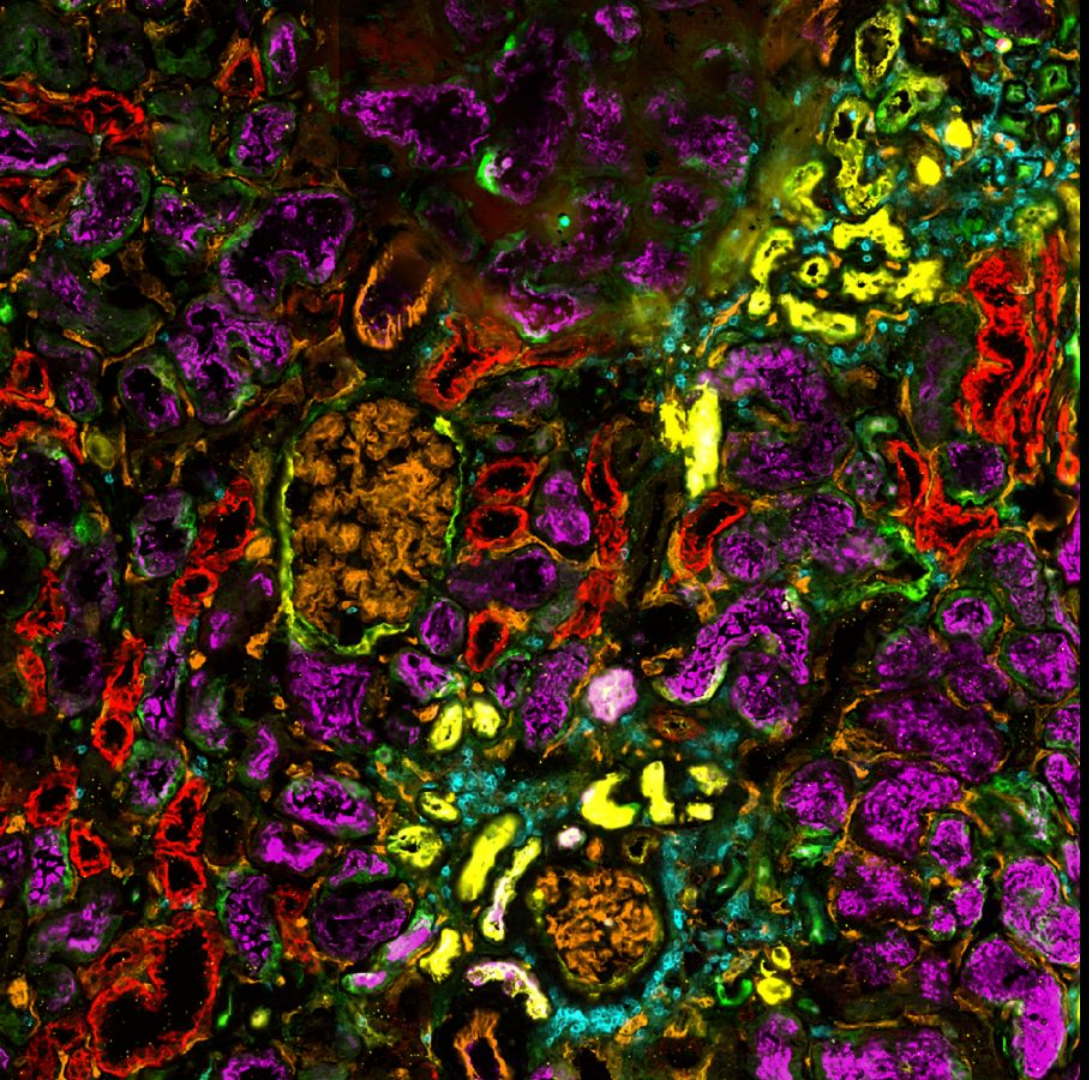
Moderator: Katy Börner, *Indiana University*

Presenters:

- Tarek M. Ashkar, *Indiana University*
- Daria Barwinska, *Indiana University*



Tarek M. Ashkar, *Indiana University*
Daria Barwinska, *Indiana University*



Multiscale mapping of the kidney in health and disease

Tarek M. Ashkar, MD
Daria Barwinska, PhD

12/14/2024

Acknowledgements

Ashkar Lab

Tarek Ashkar
Mahla Asghari
Bill Bowen
Michael Ferkowicz
Shehnaz Khan
Azuma Nanamatsu
George Rhodes
Angela Sabo
Seth Winfree*

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Michael Eadon
Ricardo Melo-Ferreira
Debora Gish
Yinghua Cheng

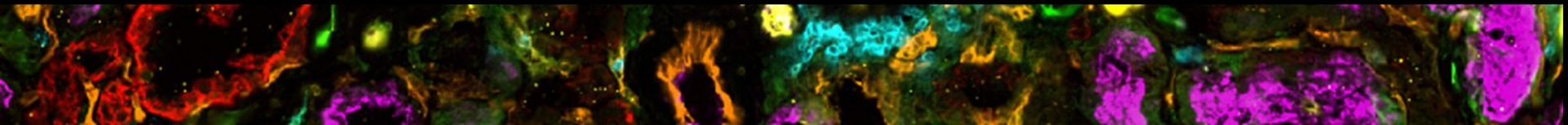
Sharon Moe

Sanjay Jain

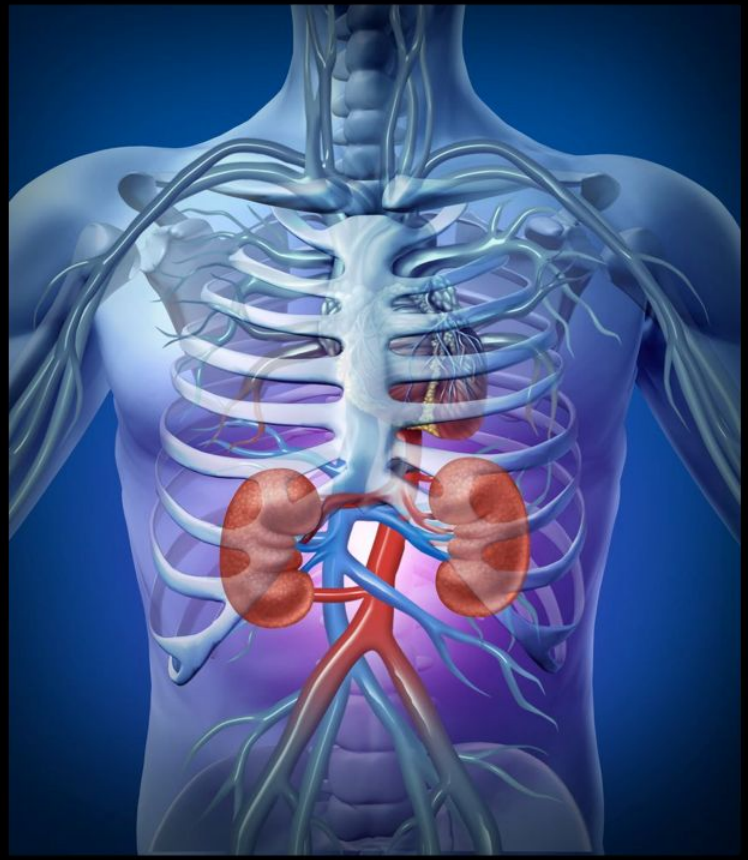
Katy Borner

Indiana Center for Biological Microscopy/
O'Brien Center for Advanced
Microscopic Analysis

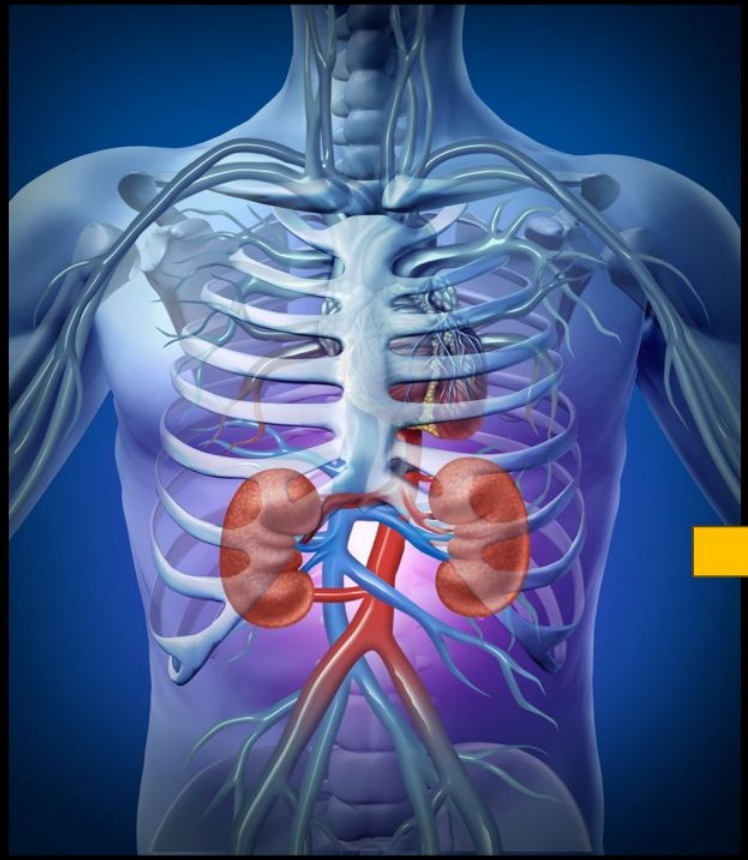
Center for Medical Genomics
IU Showalter Fund

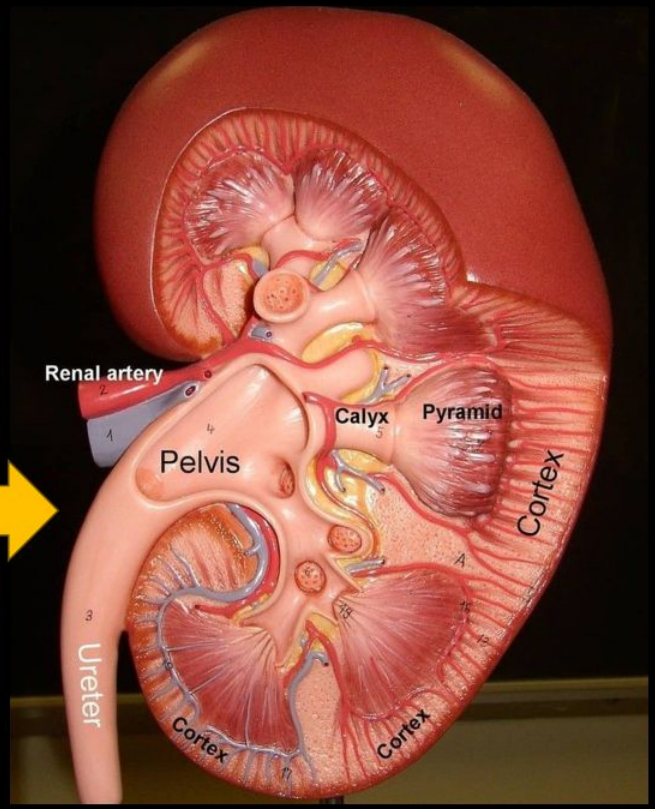


Kidneys

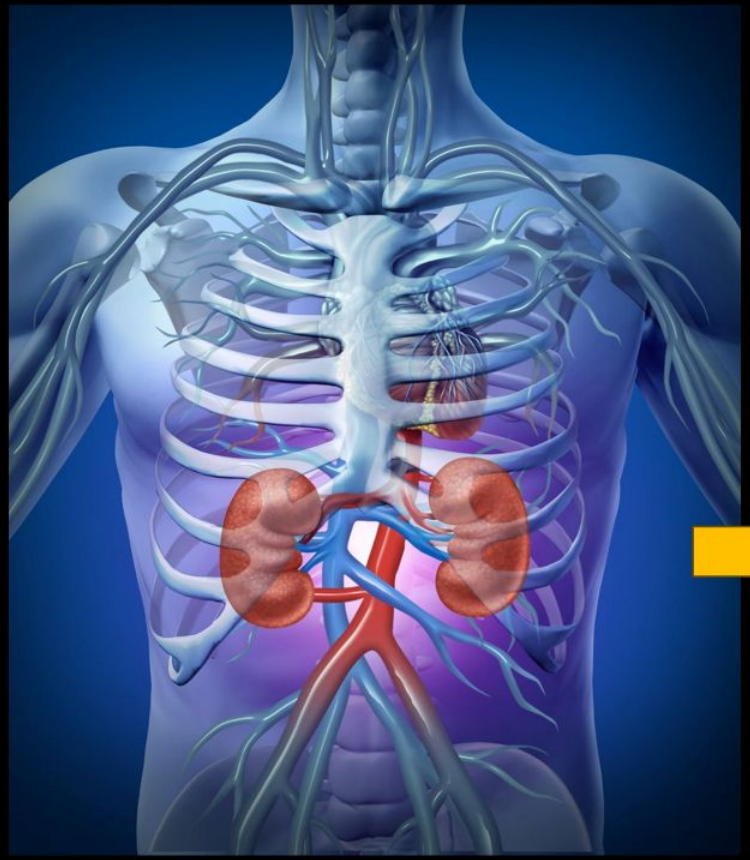


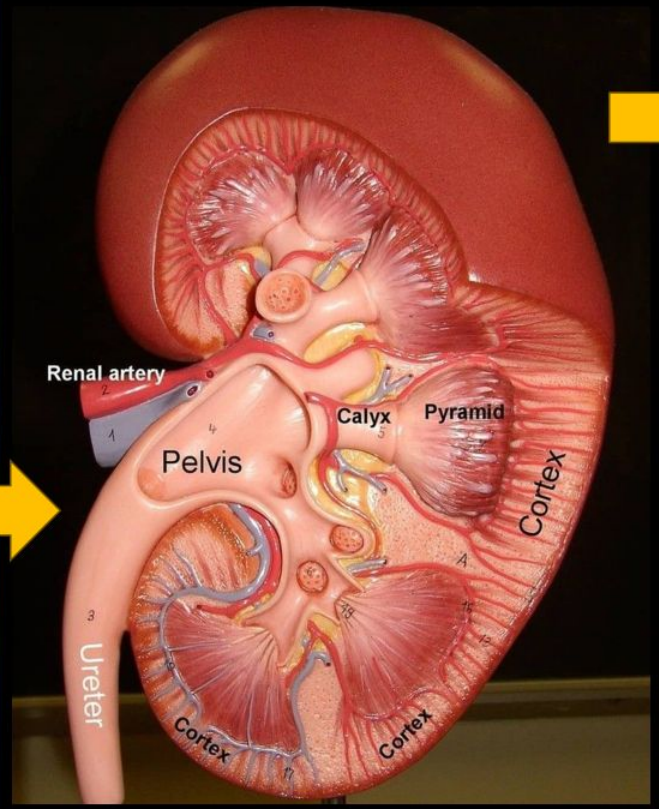
Kidneys




Renal artery
Calyx
Pyramid
Pelvis
Cortex
Ureter
Cortex
Cortex

Kidneys




Renal artery
Calyx
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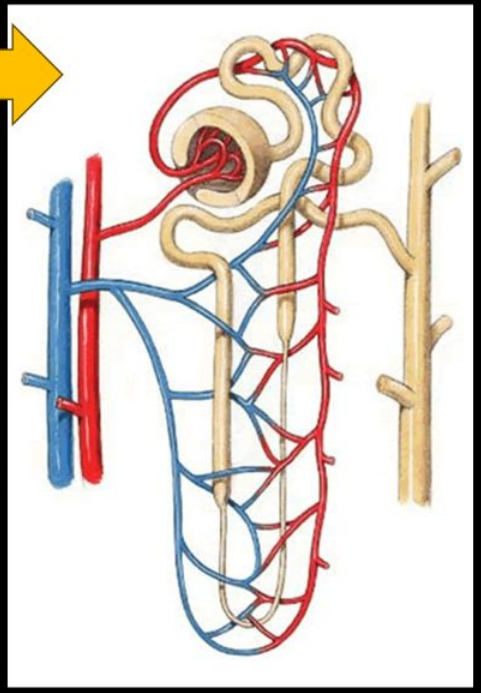
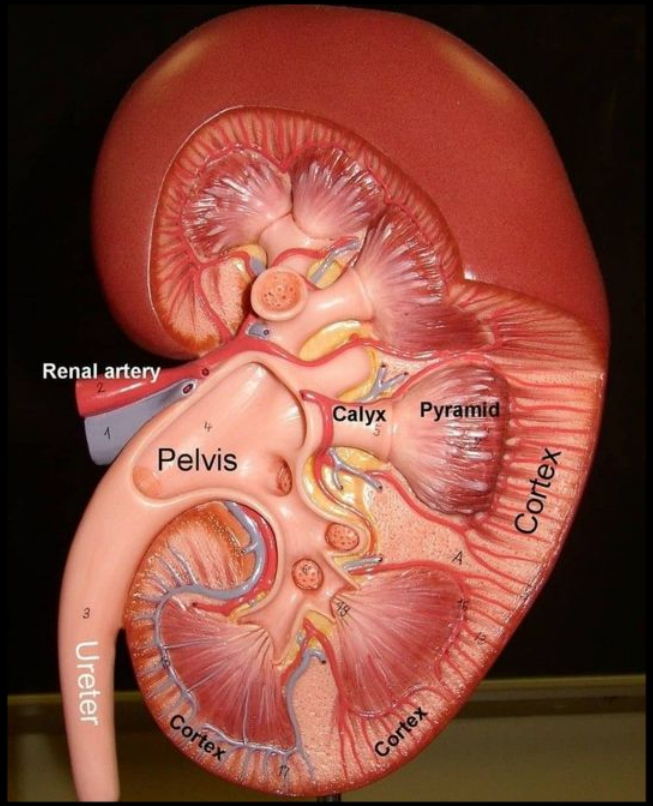


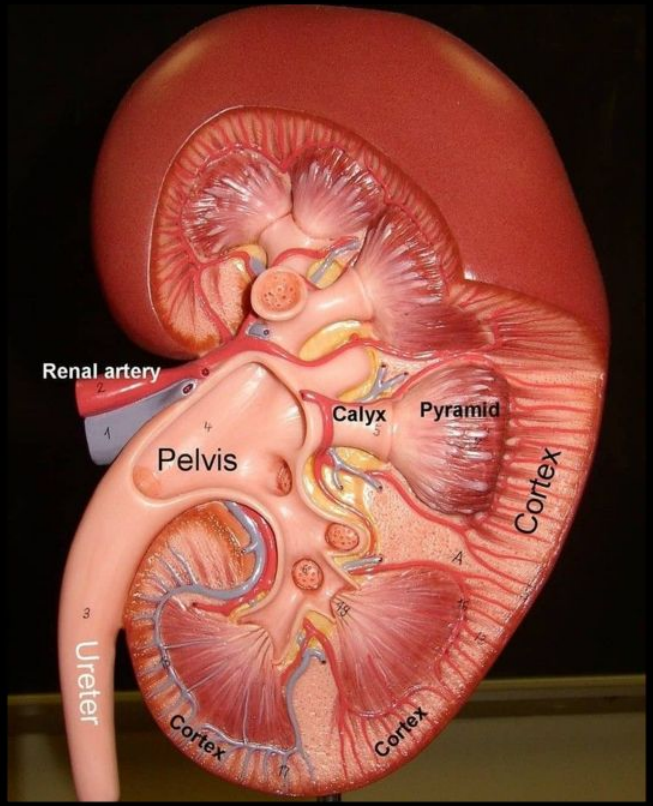
Kidneys - Function



"Saying the product of the kidneys is urine is like saying the product of a factory is pollution. Urine is a by-product.
The product is homeostasis"

– Joel Topf, MD

Kidneys - Function



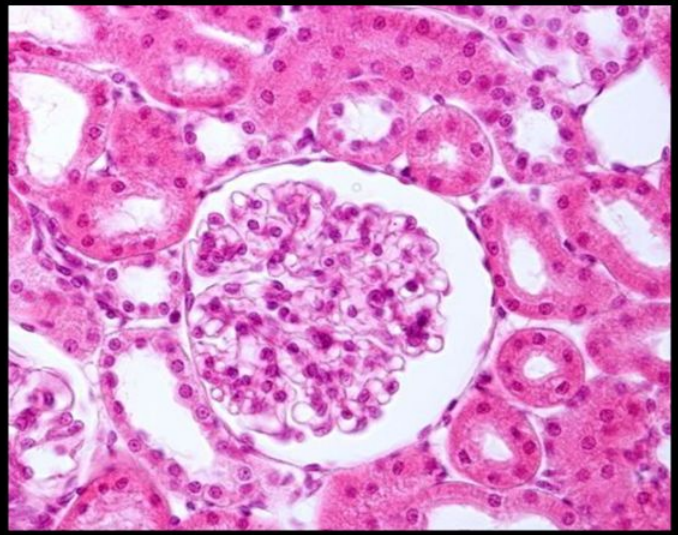
Waste removal

Fluid balance

Blood pressure regulation

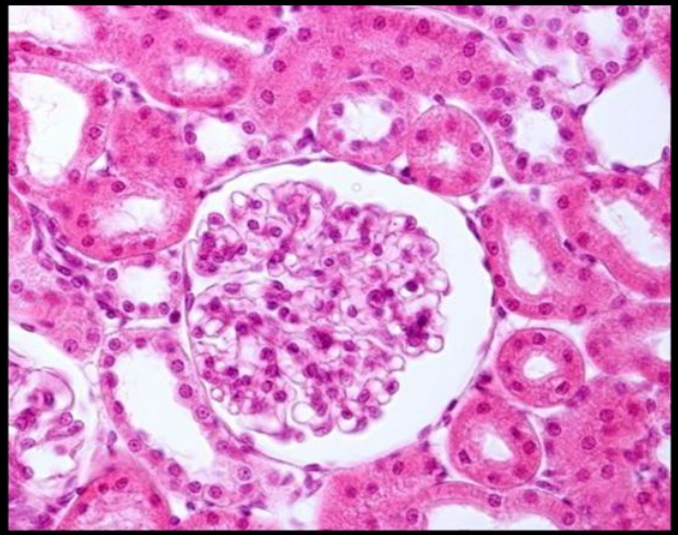
Hormone production

Kidney under the microscope

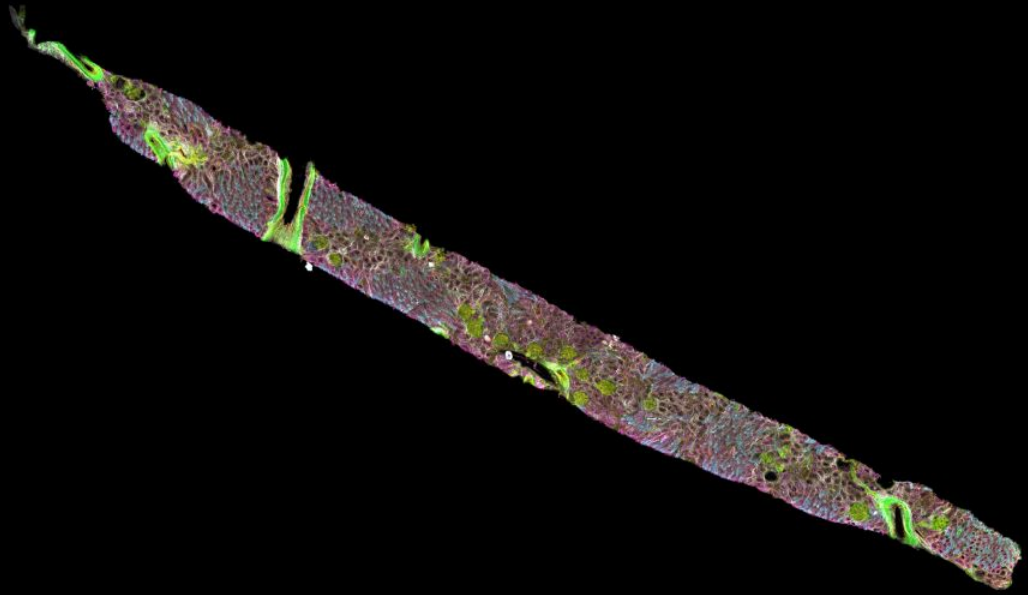


2D Light microscope

Kidney under the microscope

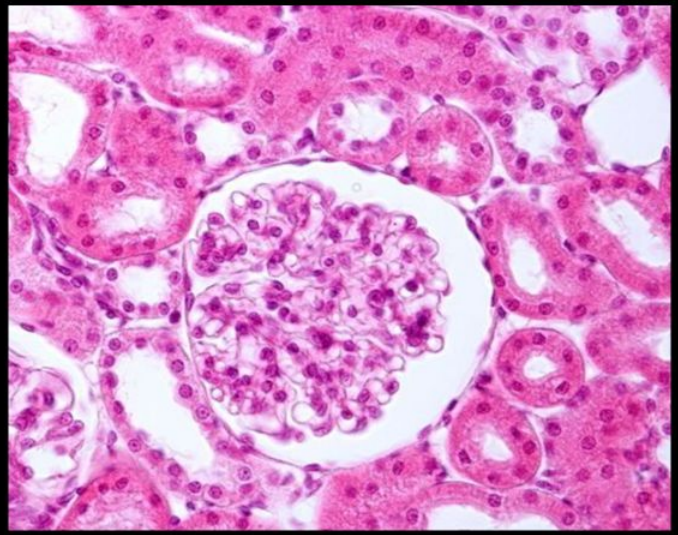


2D Light microscope

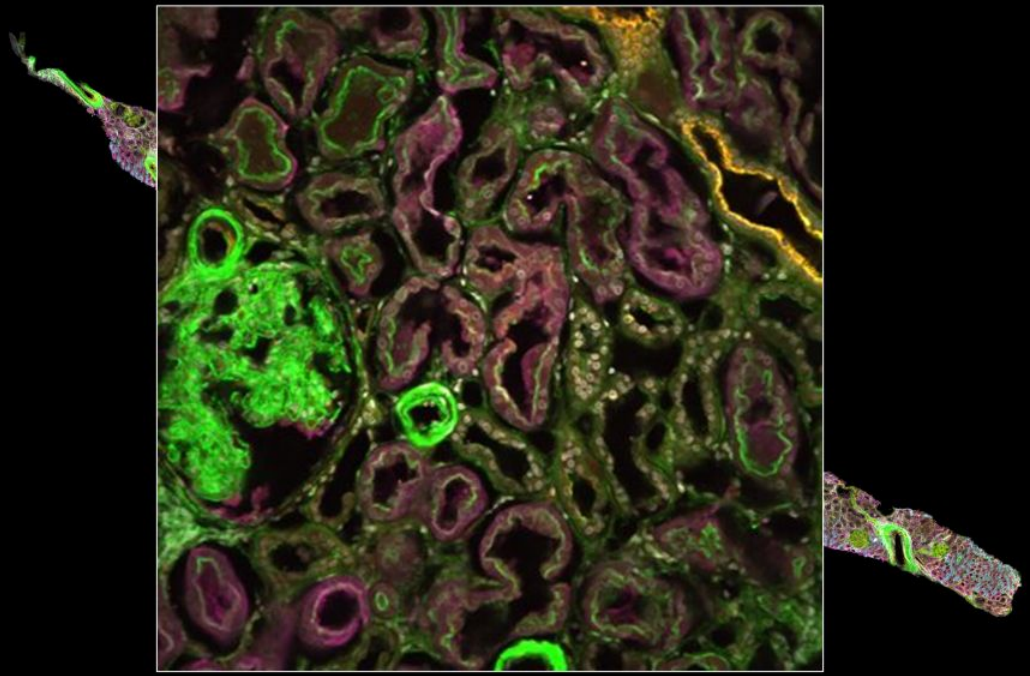


3D Confocal microscope

Kidney under the microscope

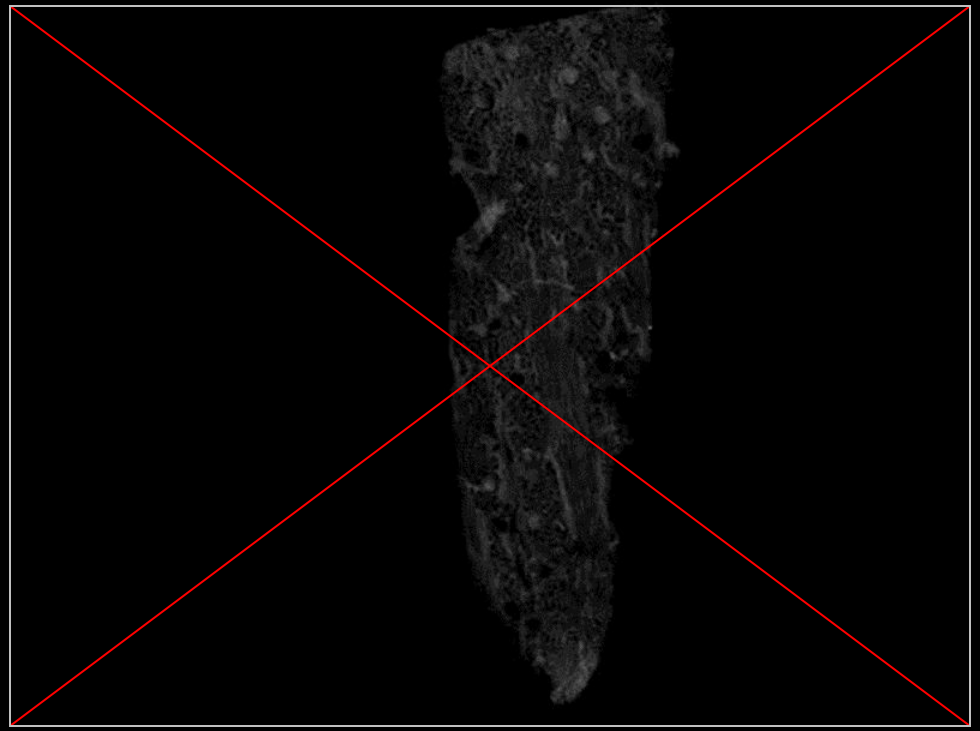


2D Light microscope



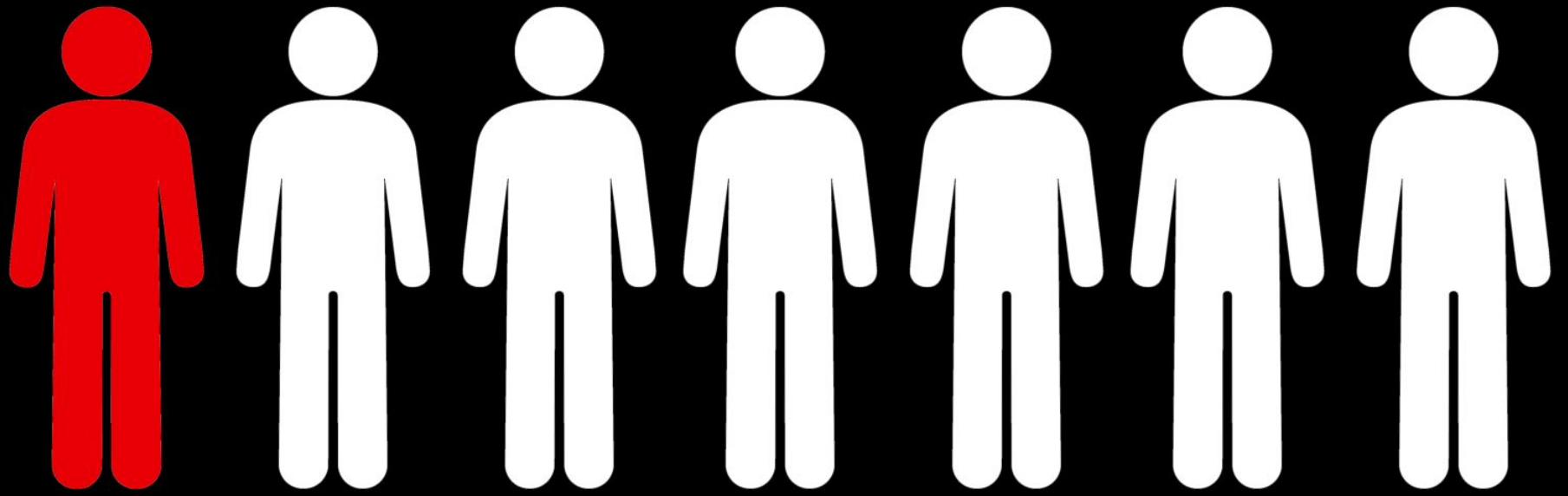
3D Confocal microscope

Kidney under the microscope

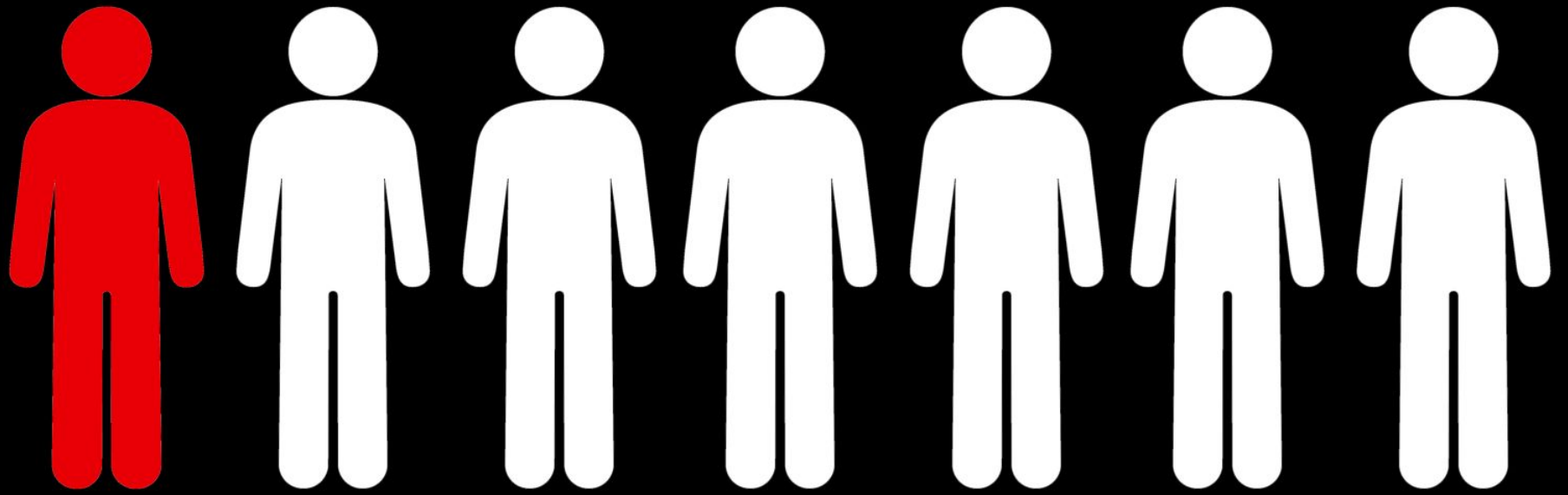


3D Confocal microscope

Chronic Kidney Disease in the US

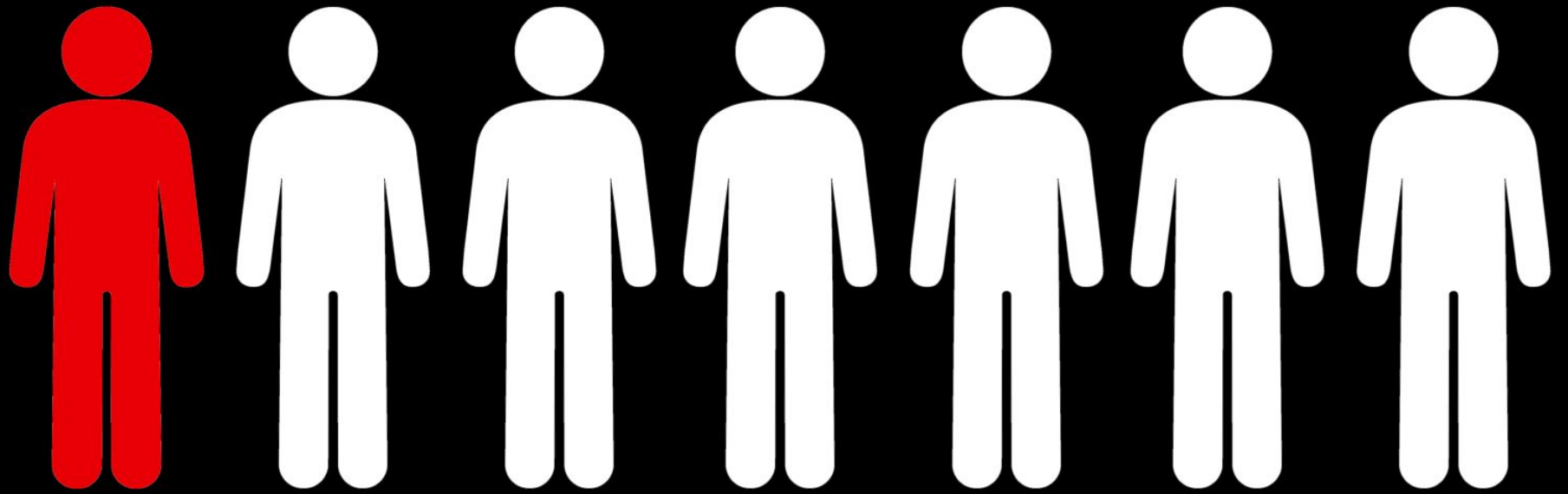


Chronic Kidney Disease in the US



37 million people in the US

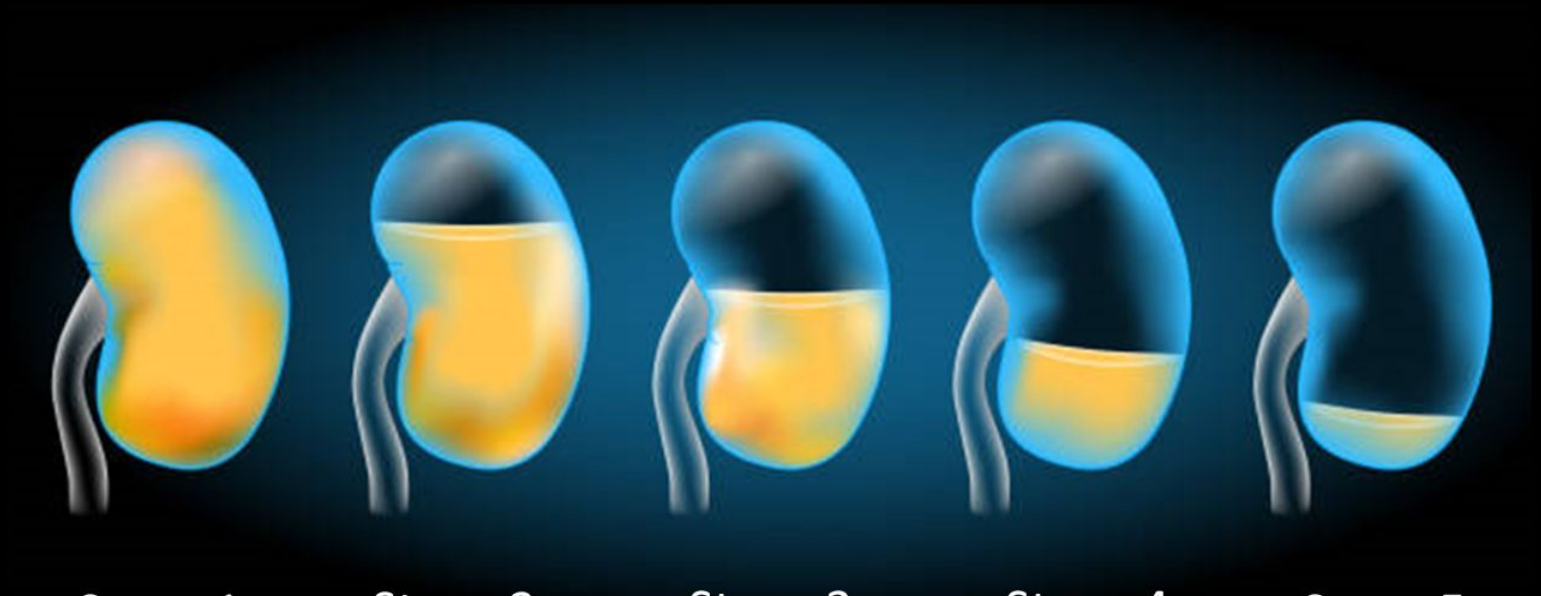
Chronic Kidney Disease in the US



37 million people in the US

9th leading cause of death

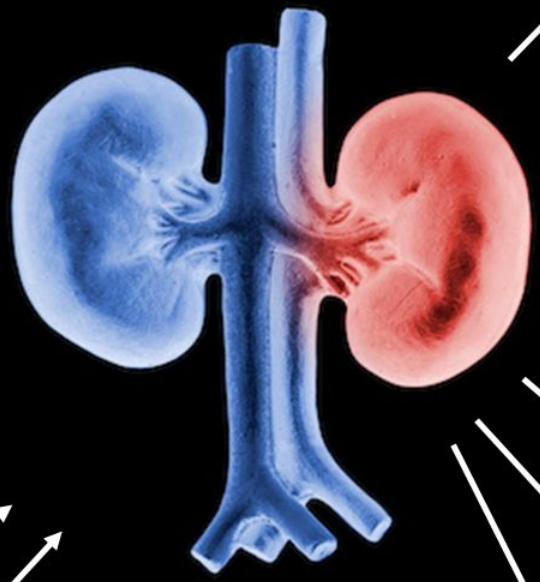
Kidney disease progression



Stage 1	Stage 2	Stage 3	Stage 4	Stage 5
Normal Function	Mild Impairment	Moderate Impairment	Severe Impairment	Kidney Failure

Kidney disease - causes and types

Obesity
Diabetes
Alcohol
Uncontrolled blood pressure
Infections
Advanced age
Genetics
Heart disease
Medications
Smoking



Focal Segmental Glomerulosclerosis
Kidney stones
Acute kidney injury
Diabetic kidney disease
Lupus nephritis
IgA nephropathy
Kidney infections
Polycystic kidney disease

Spatial Technologies

Spatial Technologies

CODEX
CO-Detection by indeXing

IBEX
Iterative Bleaching Extends Multiplexity

cycIF
Cyclic Immunofluorescence

ST
Spatial Transcriptomics

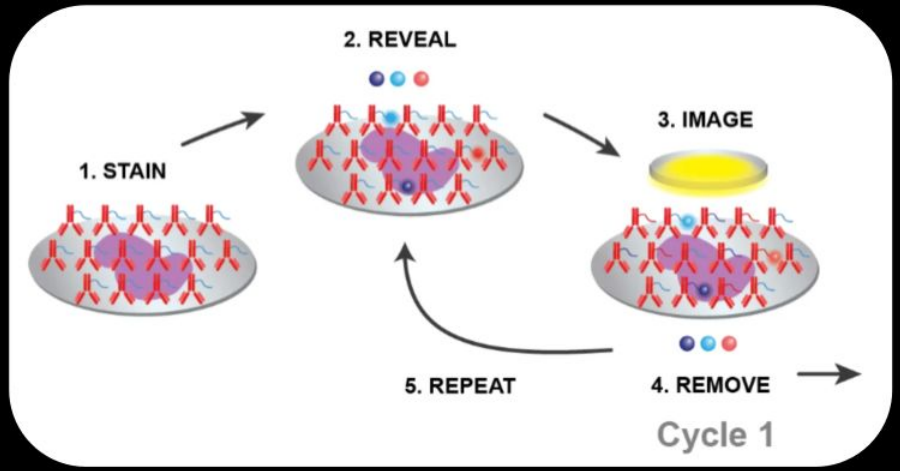
IMC
Imaging Mass Cytometry

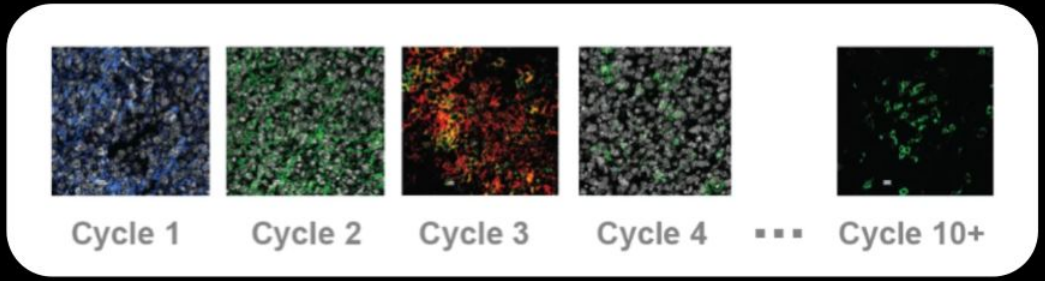
IMS
Imaging Mass Spectrometry

MIBI
Multiplexed Ion Beam Imaging

Spatial Technologies

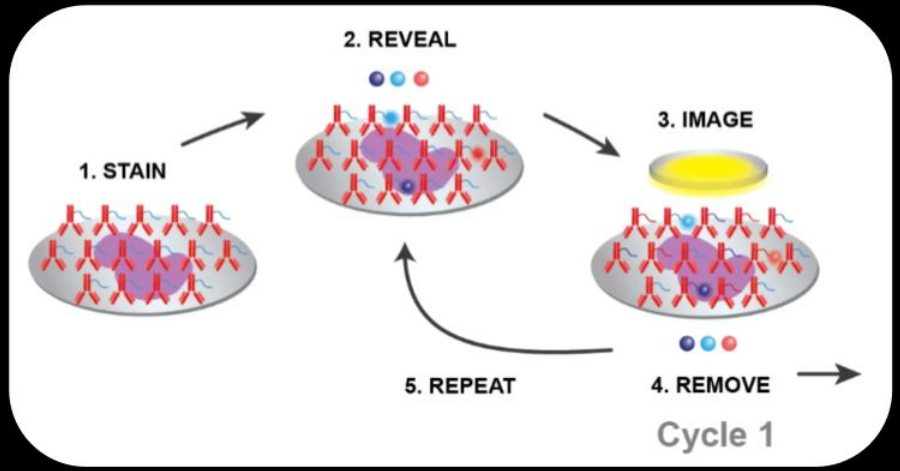
CODEX Imaging

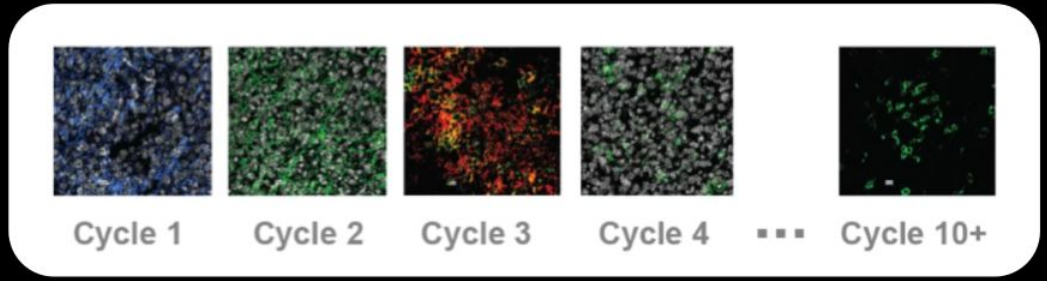




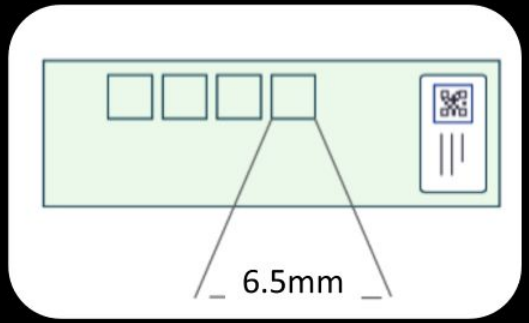
Spatial Technologies

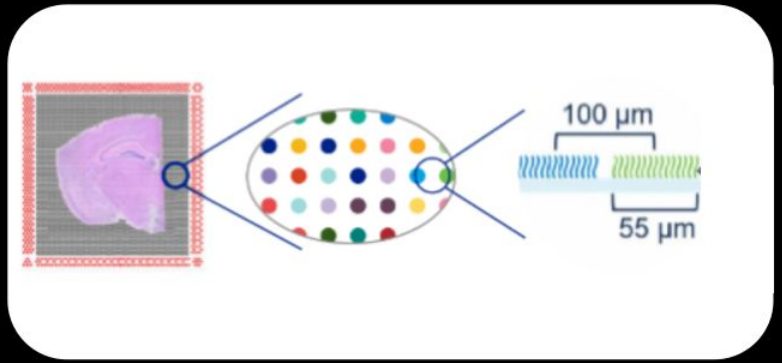
CODEX Imaging





Visium Spatial Transcriptomics





nature methods

Editorial | Published: 06 December 2024

Method of the Year 2024: spatial proteomics

Spatial Proteomics

nature methods

Editorial | Published: 06 December 2024

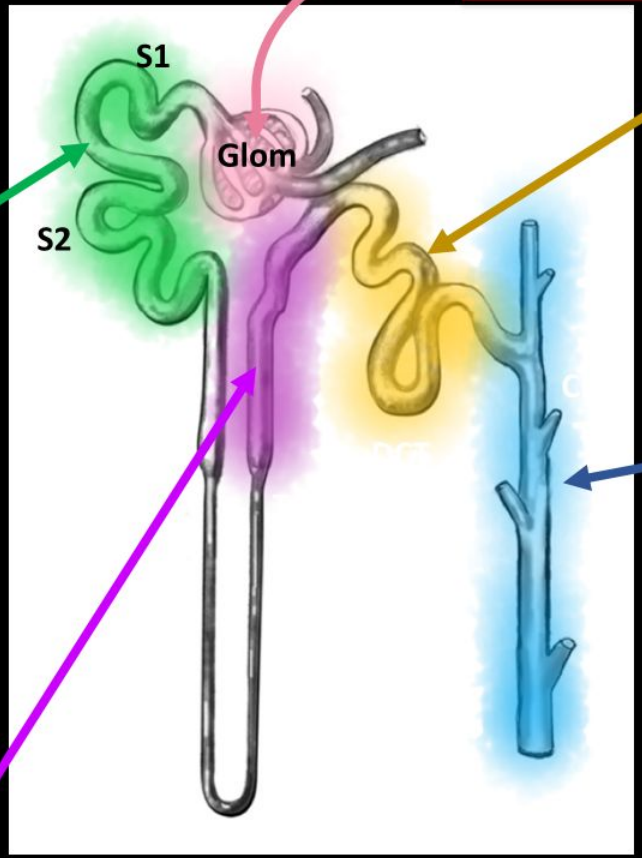
Method of the Year 2024: spatial proteomics

CODEX Targets

Structural/ Pan tubular/ Stromal
Collagen IV
Vimentin
Cytokeratin8
Fibronectin
B-catenin
aSMA

Podocytes
Podocalyxin

Cell state/ injury
Ki67
p- c-Jun
LC3
PLSCR1
KIM-1
pMLKL
Cystatin3
PROM1
IGFBP7
OPN
VCAM1
CD90
MCP1

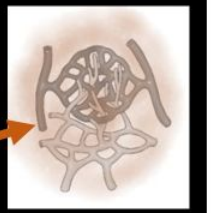


Distal Tubule
SLC12A3
NaK ATPase

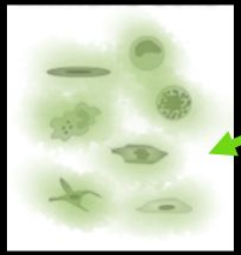
Proximal Tubule
LRP2
AQP1

Collecting ducts
AQP2
GATA3

Vasculature



Immune Cells



Immune
CD45
CD3
CD8
CD4
CD45RO
FOXP3
GATA3
CD20
CD11c
CD68
CD206
HLA-DR
MPO

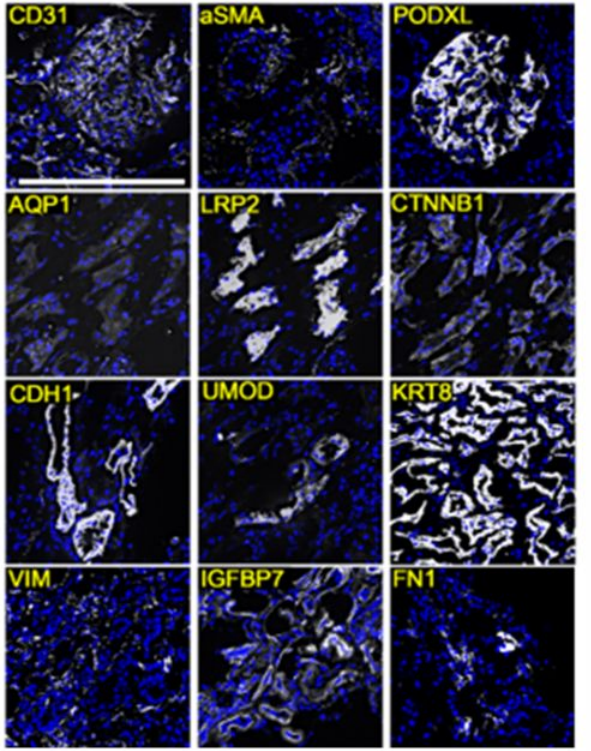
Endothelium/ VSM
CD31
aSMA

Thick Ascending Limb
Uromodulin
NaK ATPase

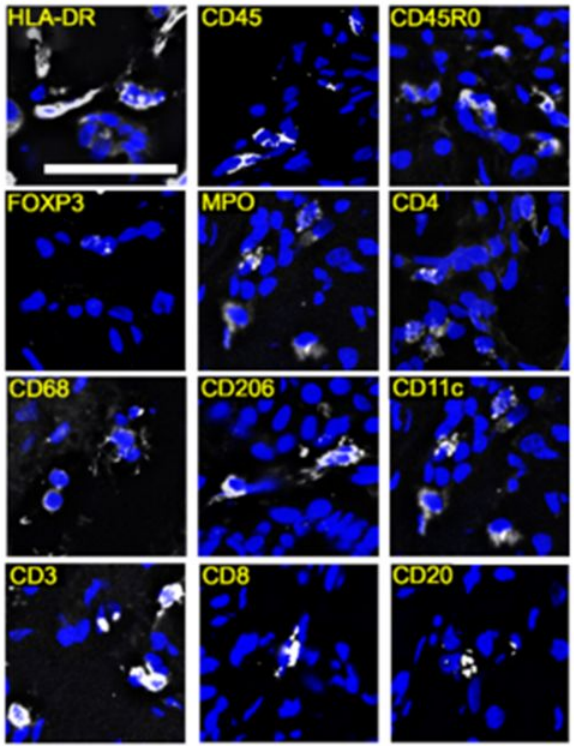
CODEX Marker Panel

EXAMPLES

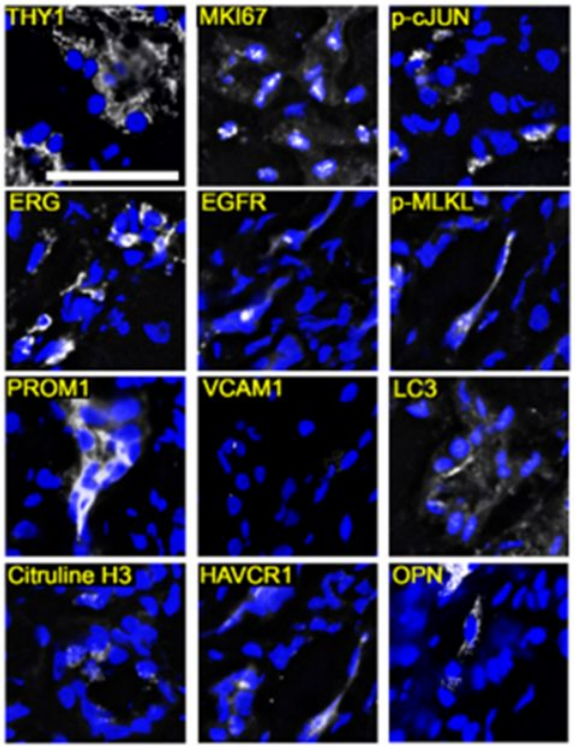
Structural markers



Immune markers

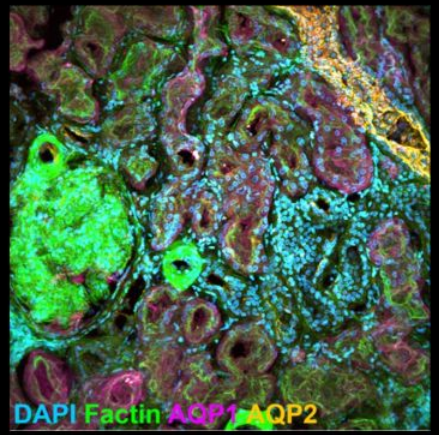


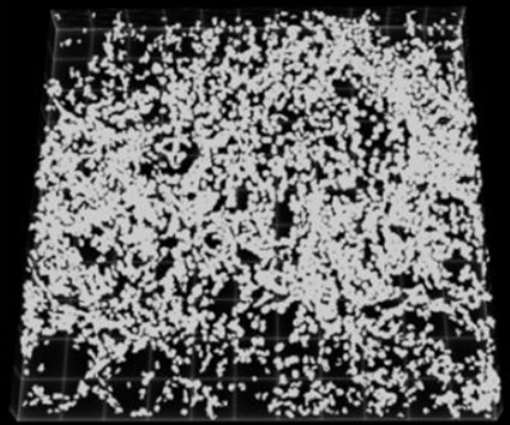
Injury markers

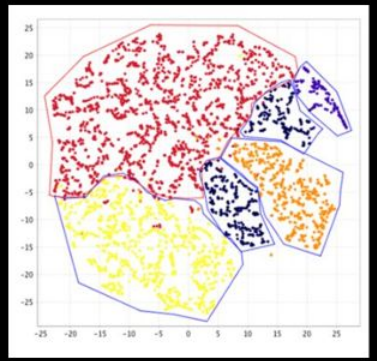


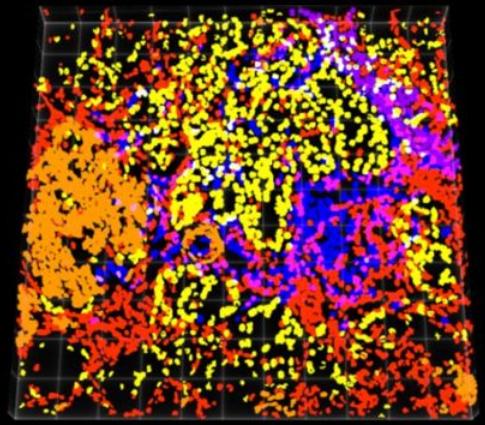
Integration of spatial multiplexed protein imaging and transcriptomics in the human kidney tracks the regenerative potential timeline of proximal tubules. bioRxiv, November 2024, https://doi.org/10.1101/2024.11.26.625544

Volumetric Tissue Exploration and Analysis (VTEA)







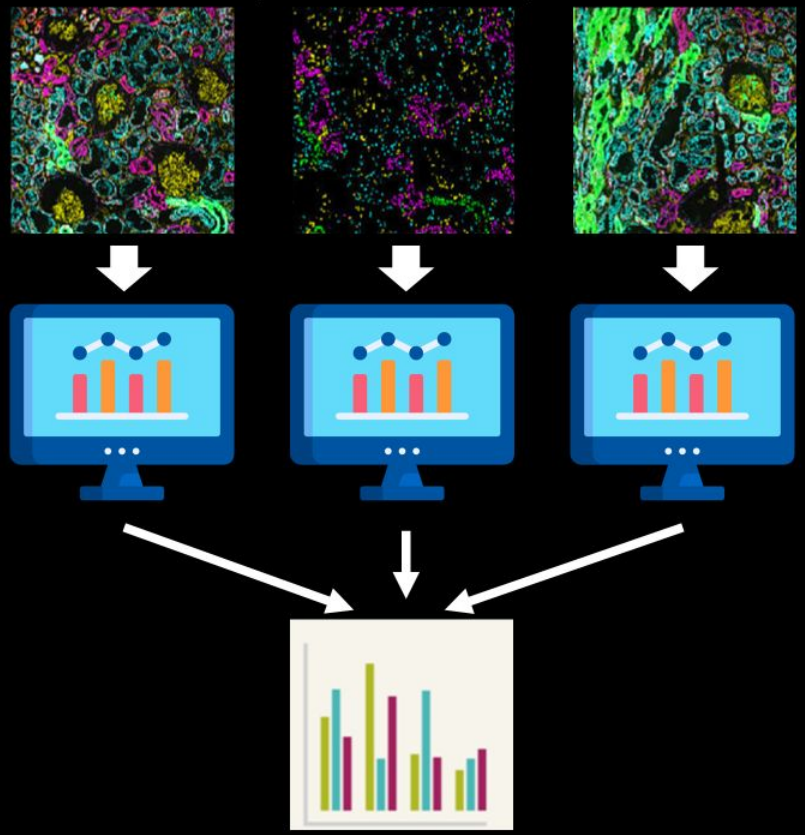


https://vtea.wiki/

Winfree S, et. al.. Integrated Cytometry With Machine Learning Applied to High-Content Imaging of Human Kidney Tissue for In Situ Cell Classification and Neighborhood Analysis. Lab Invest. 2023 Jun;103(6):100104. doi: 10.1016/j.labinv.2023.100104. Epub 2023 Feb 4. PMID: 36867975; PMCID: PMC10293106.

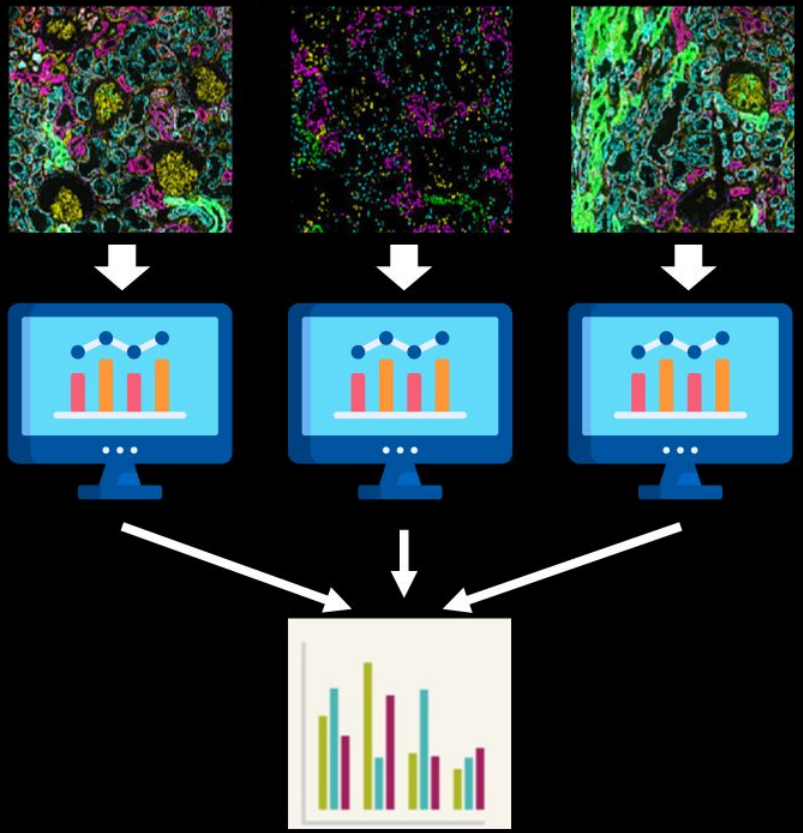
Integrated Image Analysis

Separate Analytical Space

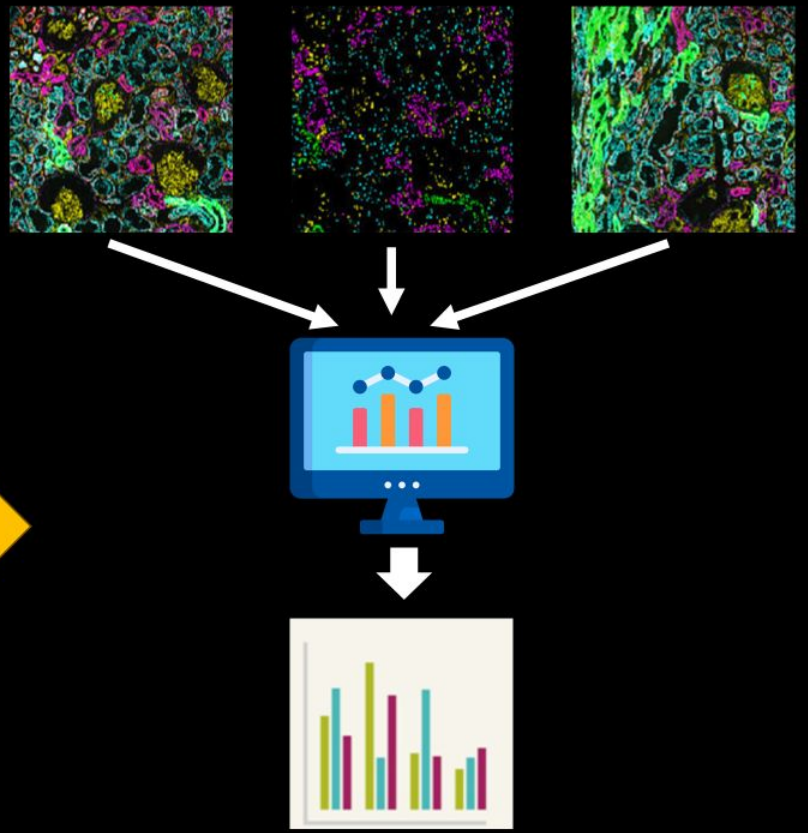


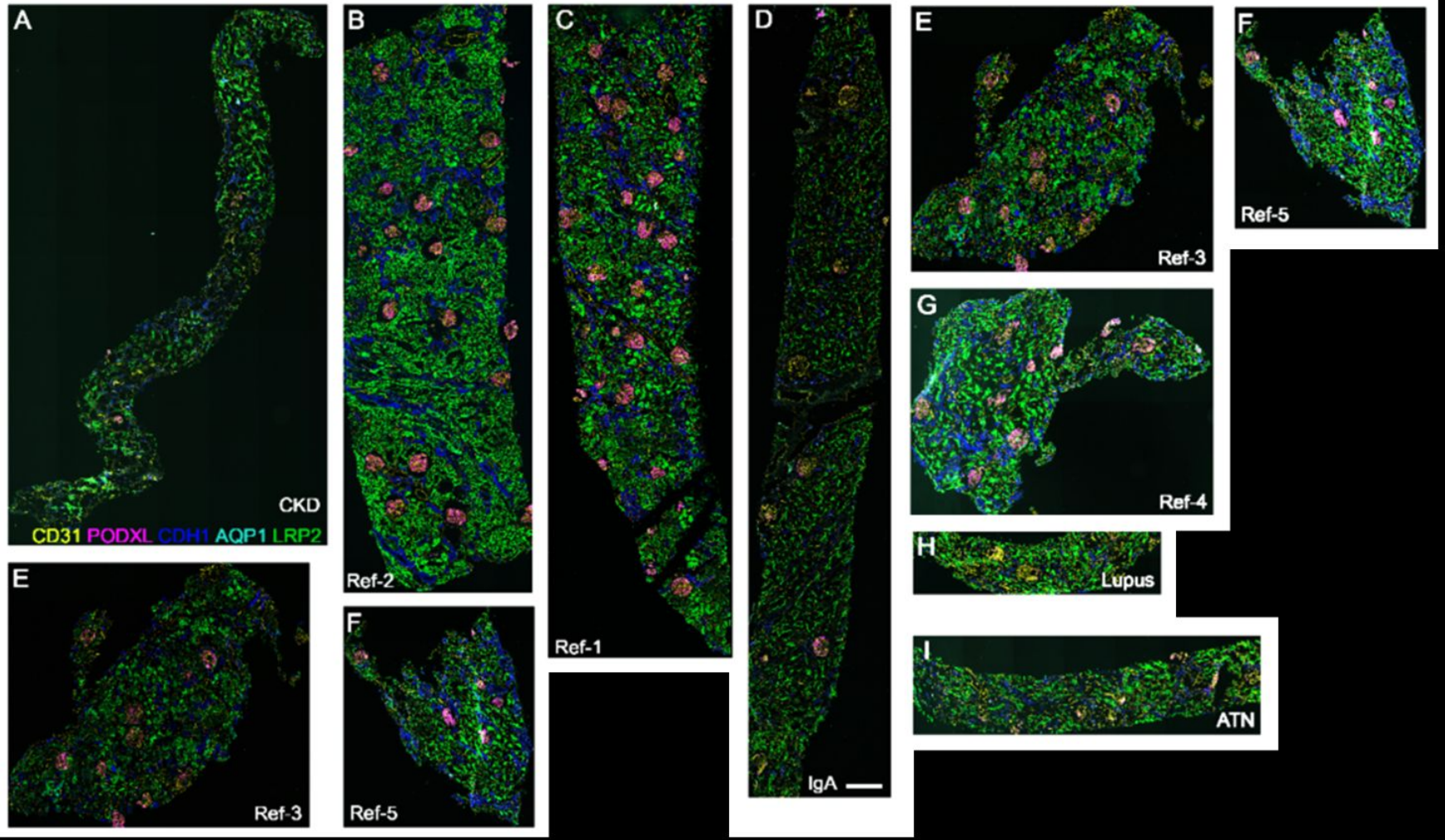
Integrated Image Analysis

Separate Analytical Space

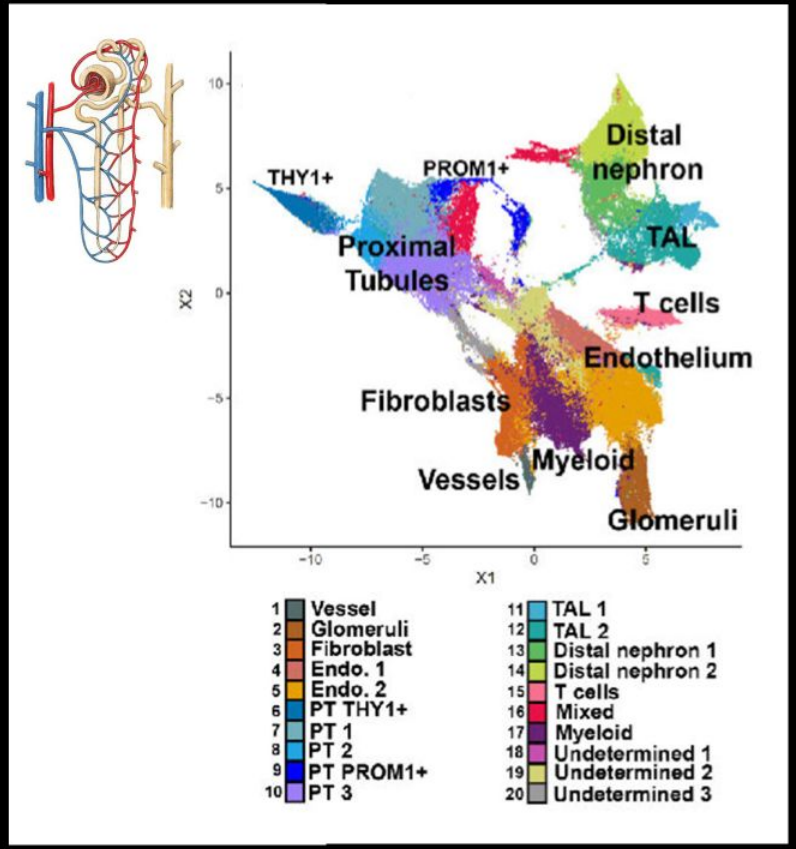


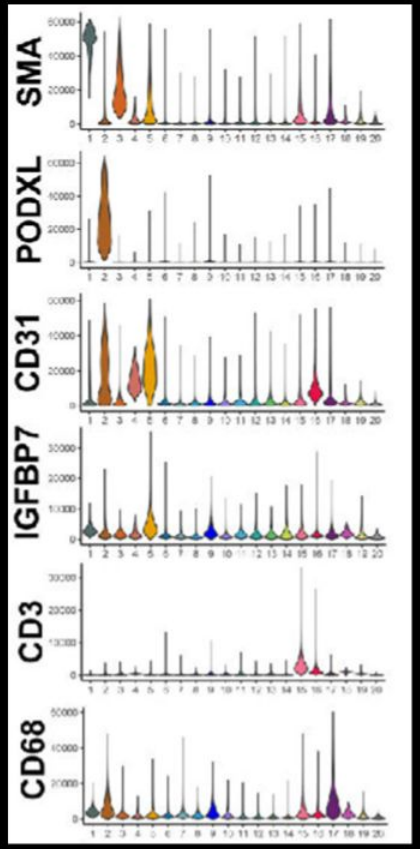
Combined Analytical Space

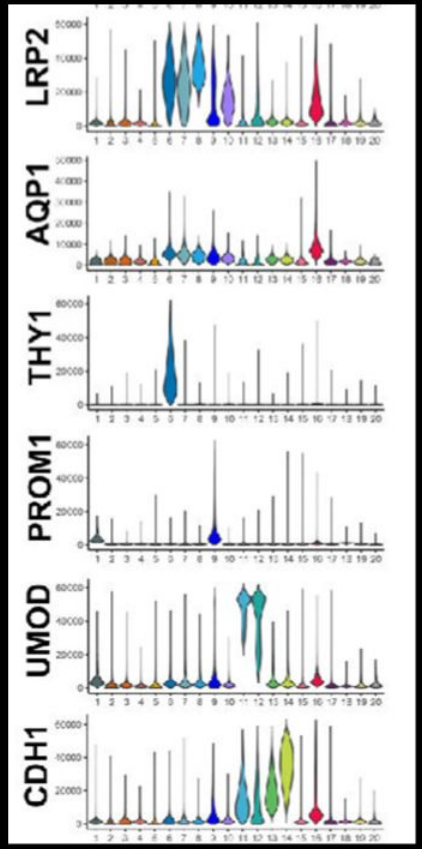



A
CKD
CD31 PODXL CDH1 AQP1 LRP2
B
Ref-2
C
Ref-1
D
IgA
E
Ref-3
F
Ref-5
E
Ref-3
F
Ref-5
G
Ref-4
H
Lupus
I
ATN

Cell Classification based on CODEX







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THY1

CD90, Cell surface protein

Expressed on:

Stem cells (HSC, MSC, CSC)
Neurons
Endothelial cells
Fibroblasts
T-cells (1964, first T-cell marker)

Role:

Cell migration
Adhesion,
Signaling
Stem cell marker
Nerve cell function

PROM1

CD133, Cell surface protein

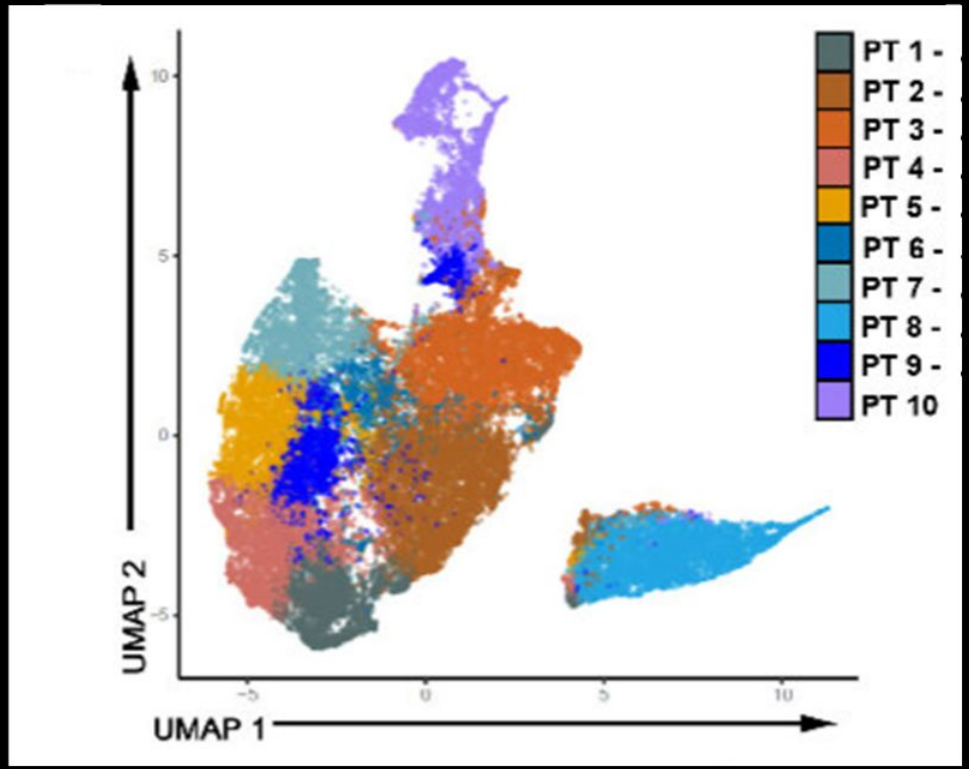
Expressed on:

Stem cells (HSC, MSC, CSC)
Neurons
Endothelial cells

Role:

Cell migration
Cell proliferation
Cell differentiation
Signaling
Stem cell marker
Structure and function of cilia

Subclustering Proximal Tubule cell populations



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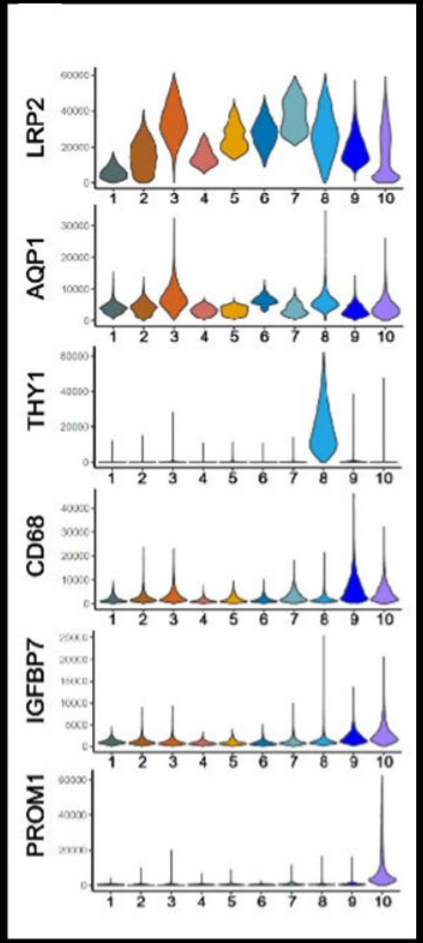
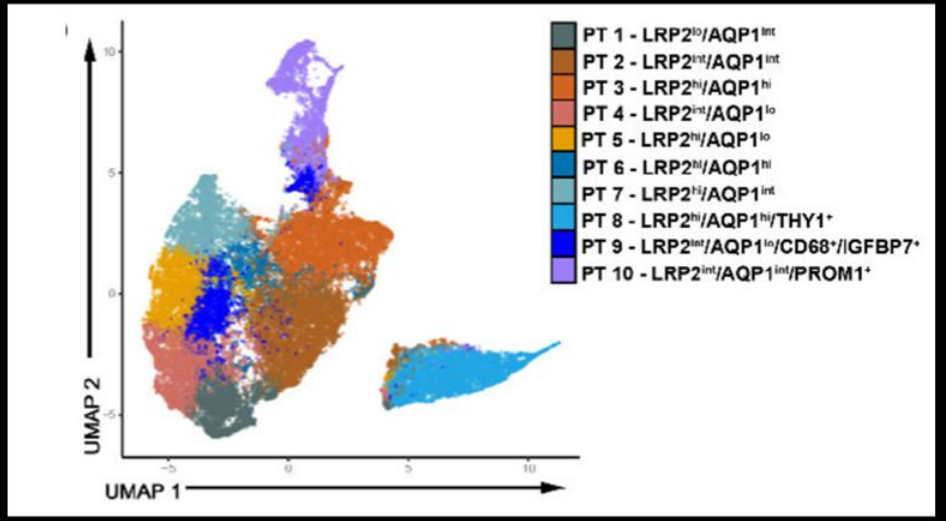
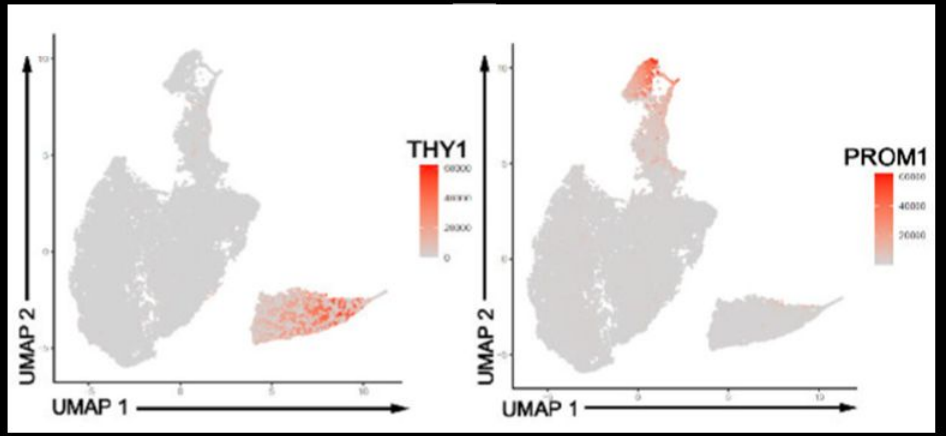
Subclustering Proximal Tubule cell populations

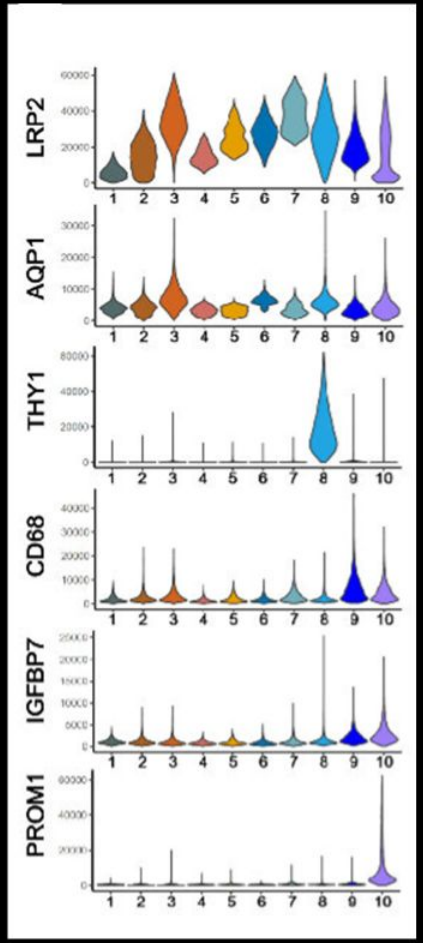


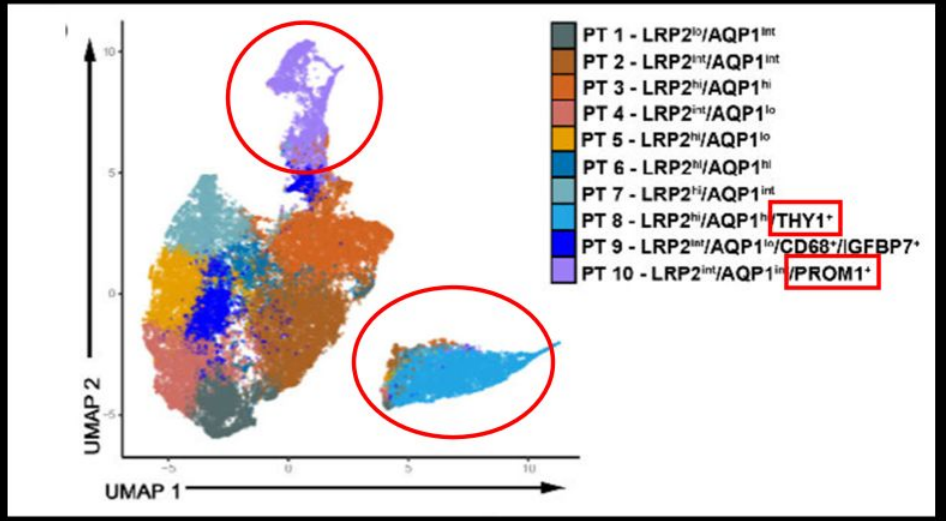


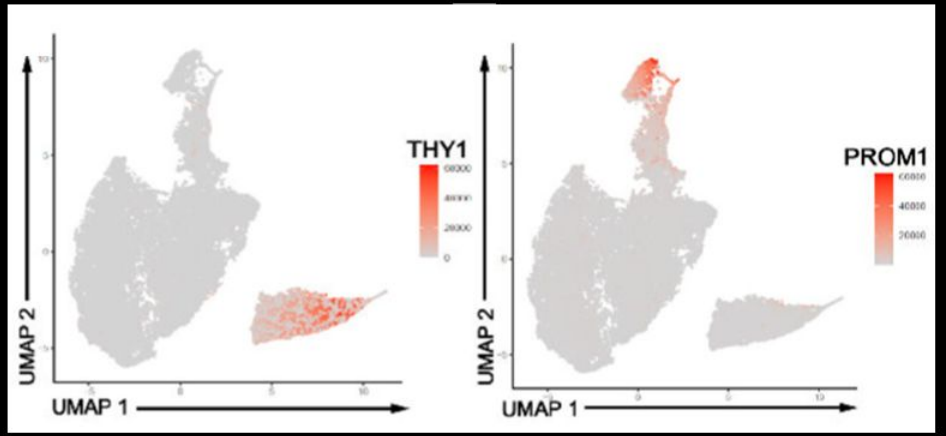


Integration of spatial multiplexed protein imaging and transcriptomics in the human kidney tracks the regenerative potential timeline of proximal tubules. bioRxiv, November 2024, https://doi.org/10.1101/2024.11.26.625544

Subclustering Proximal Tubule cell populations







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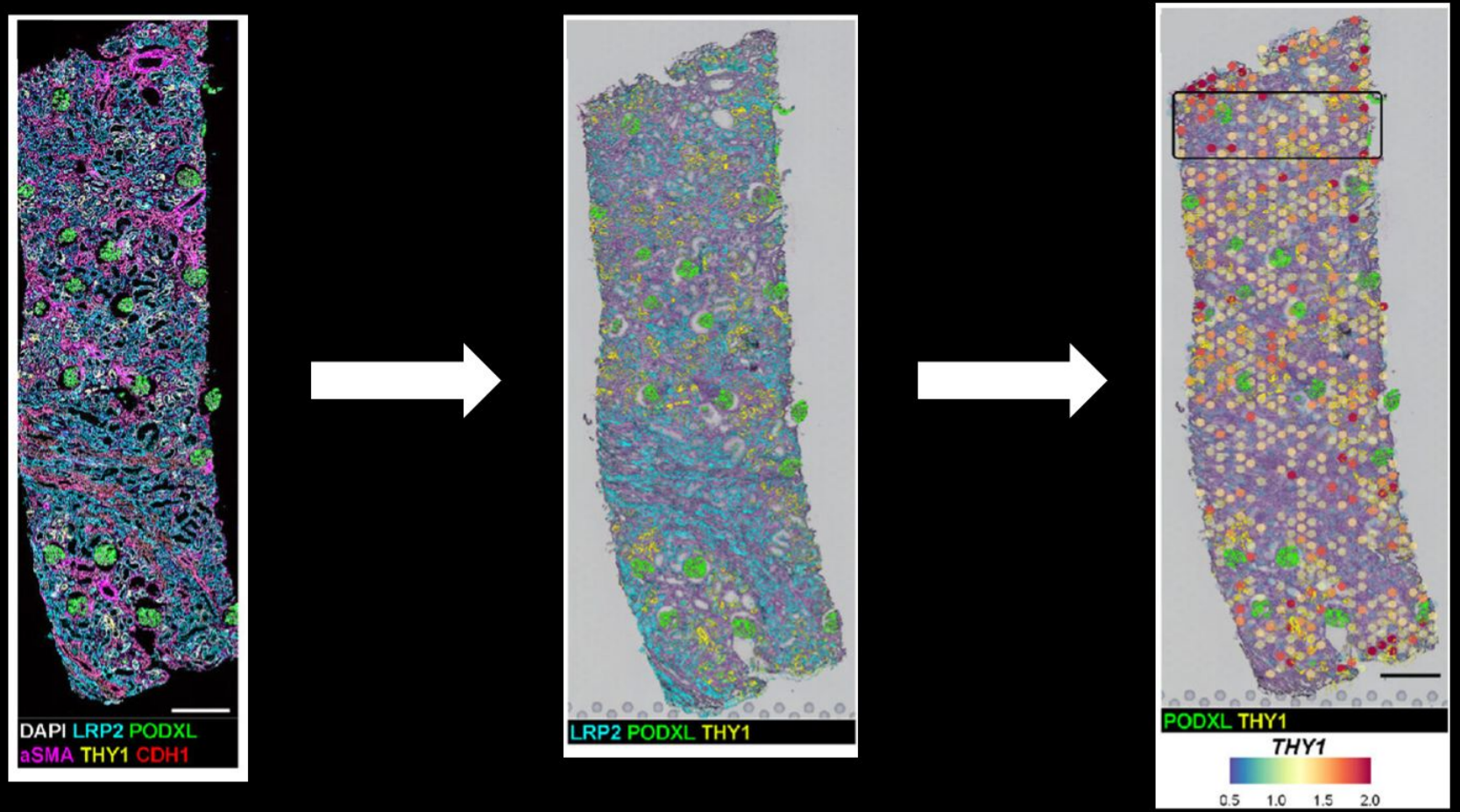
From protein to RNA: THY1 expression



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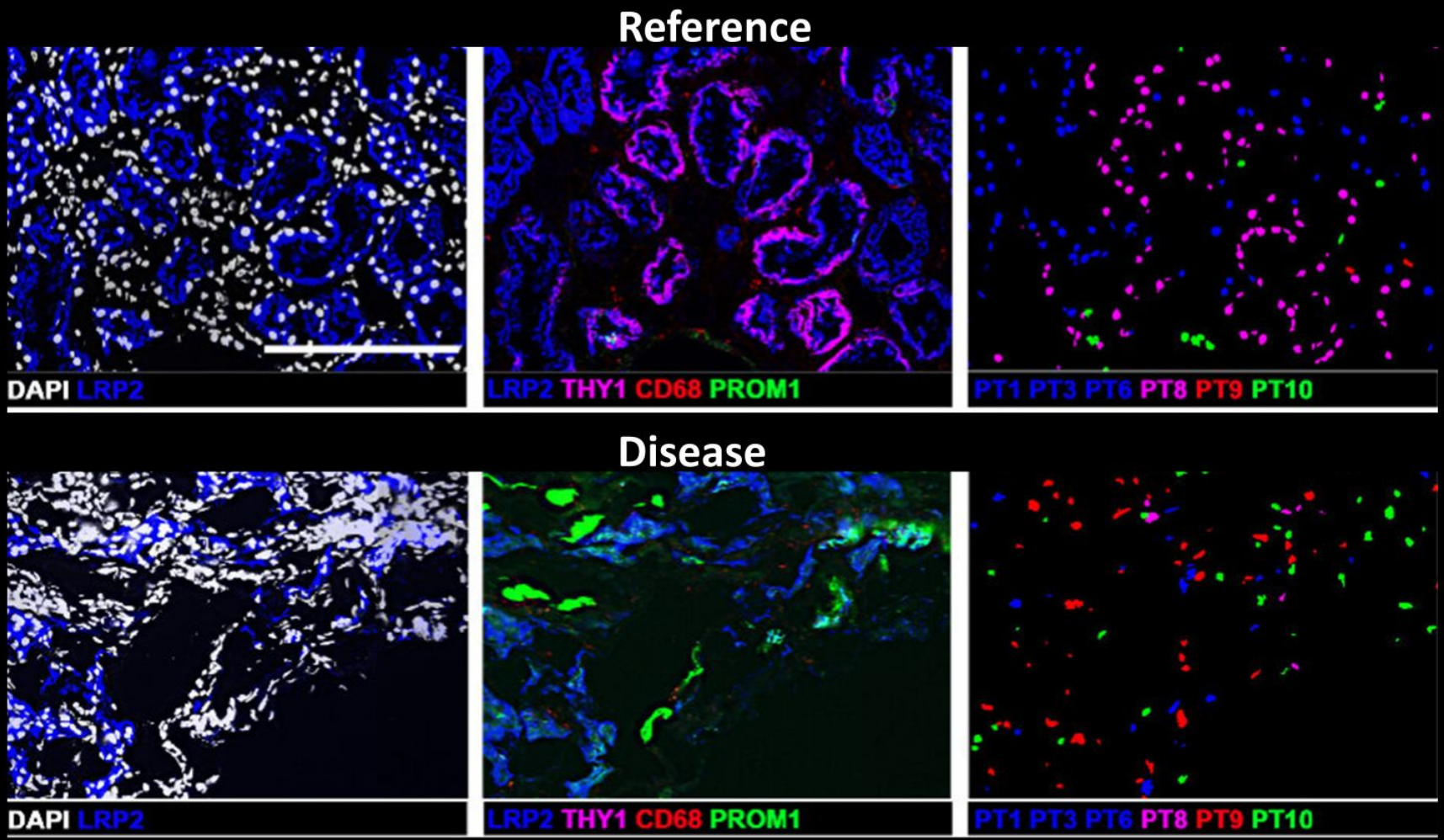

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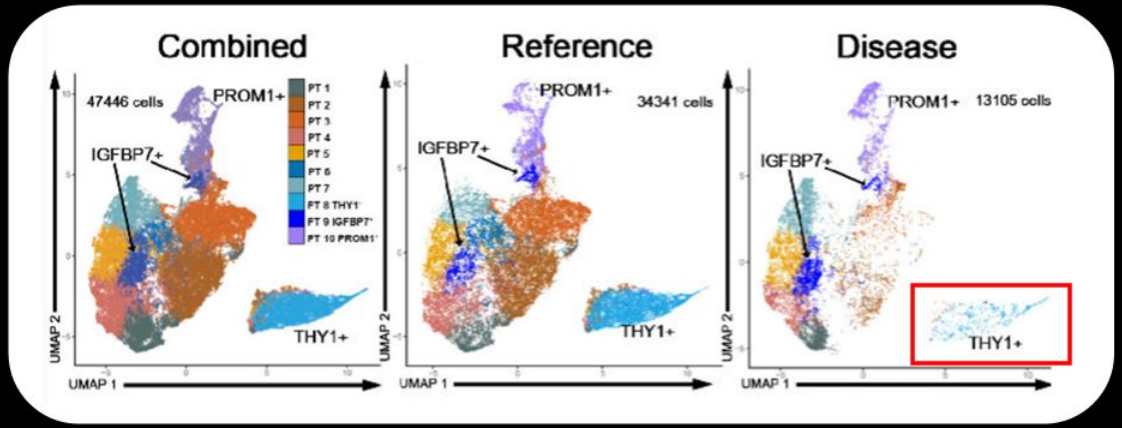
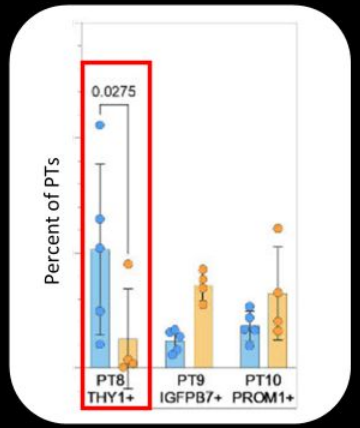
Expression of CD90 in Reference and Disease





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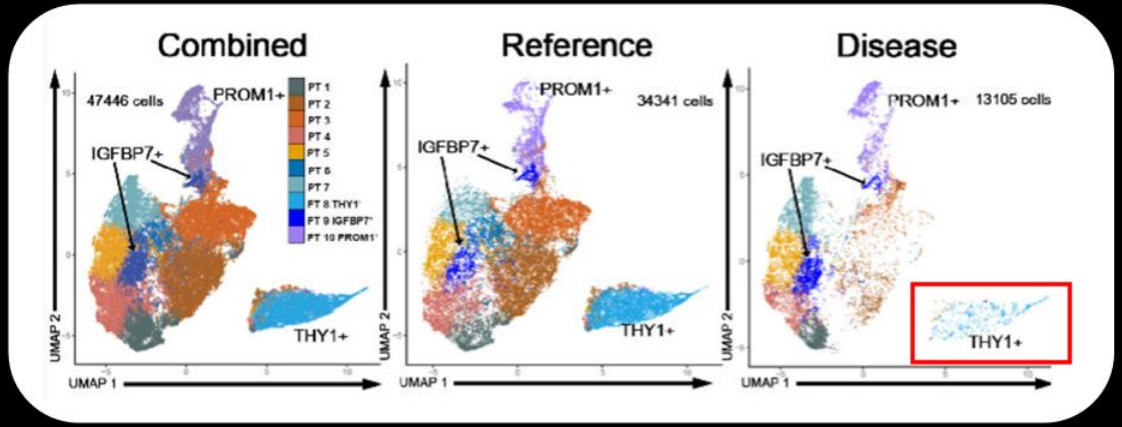
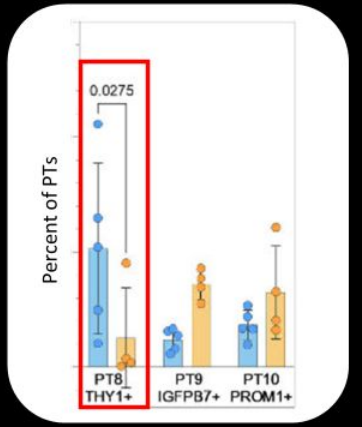
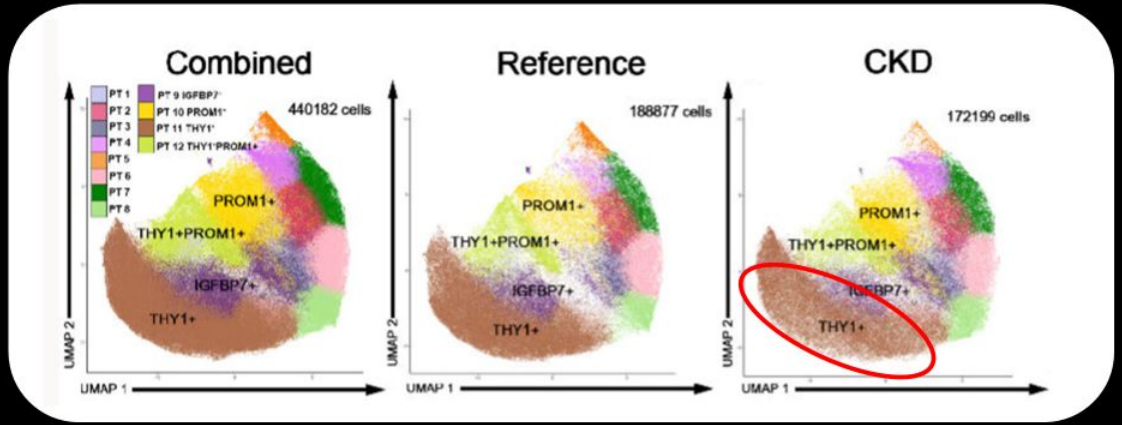
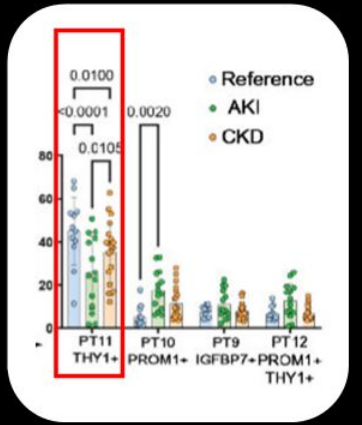
Expression of CD90 in Reference and Disease









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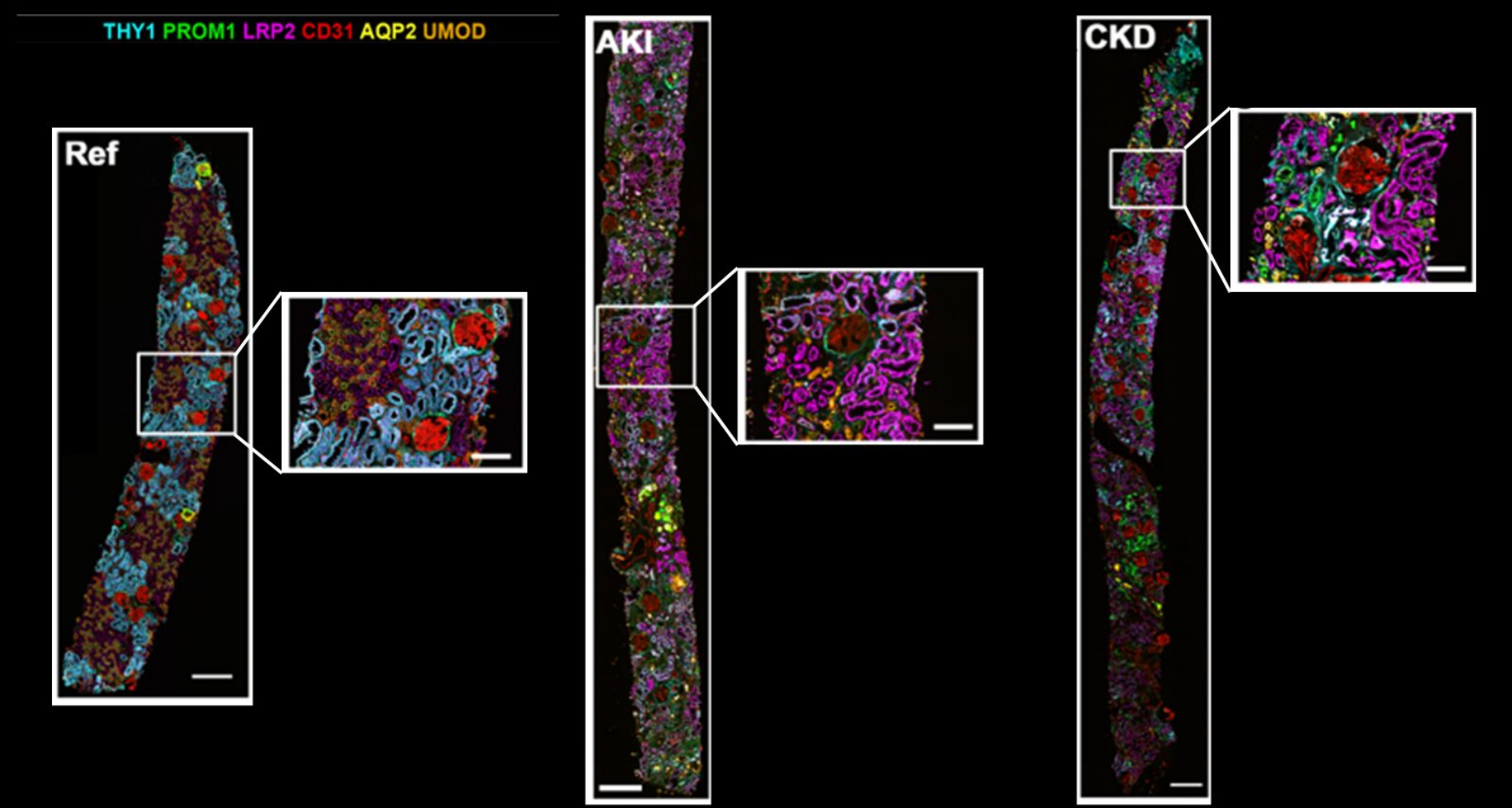

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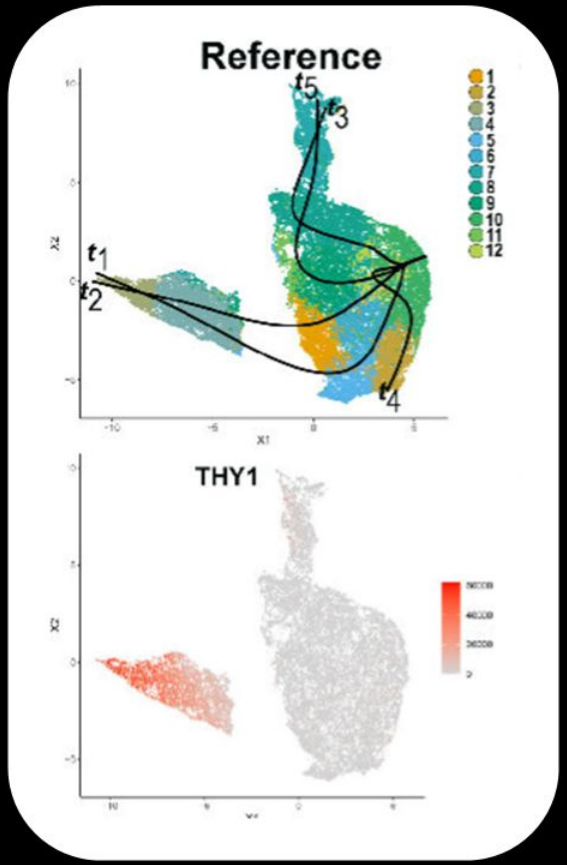
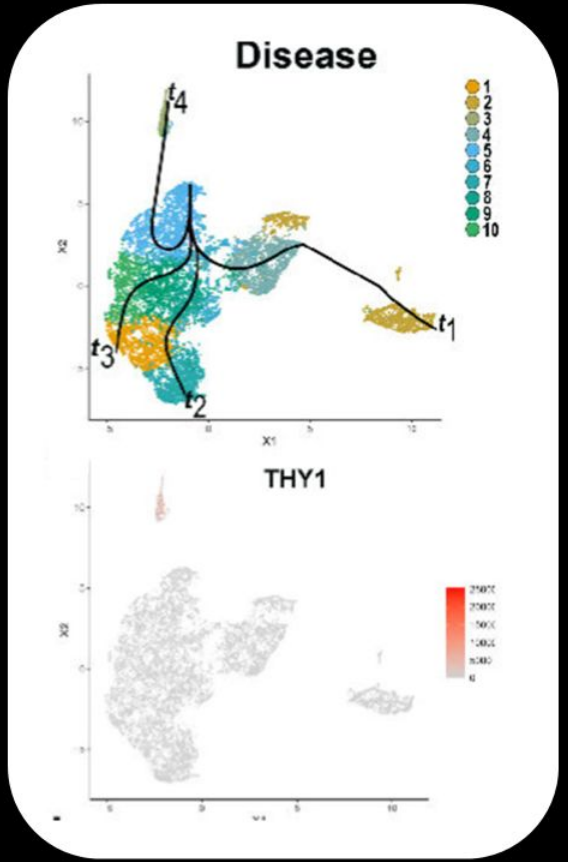
Trajectories on CODEX data





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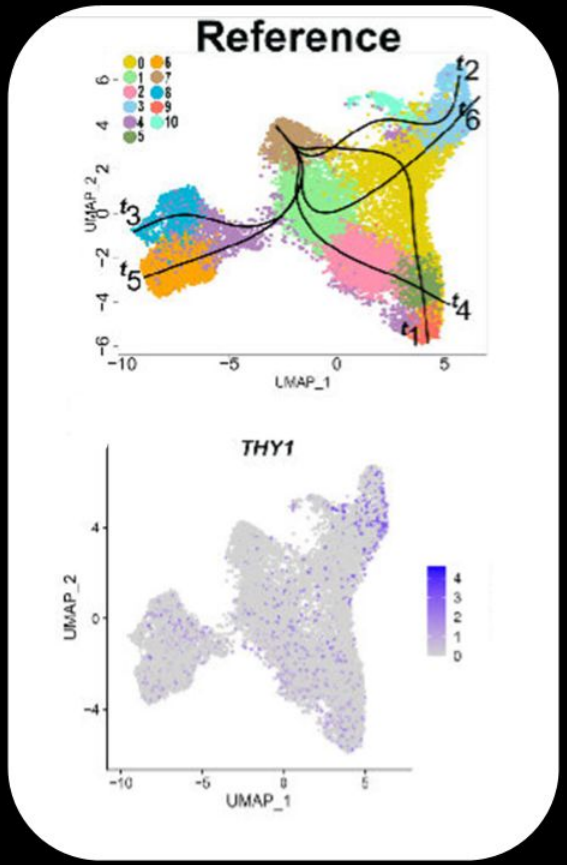
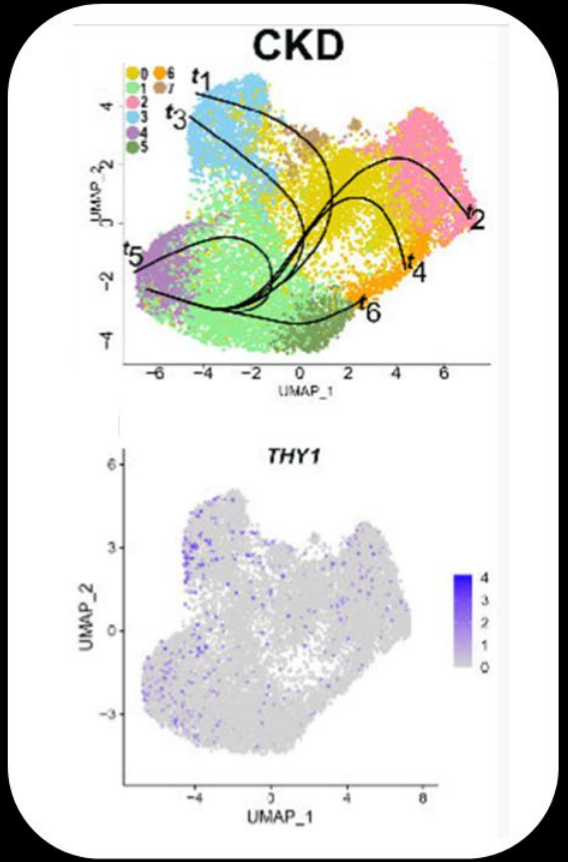
Trajectories on RNA data





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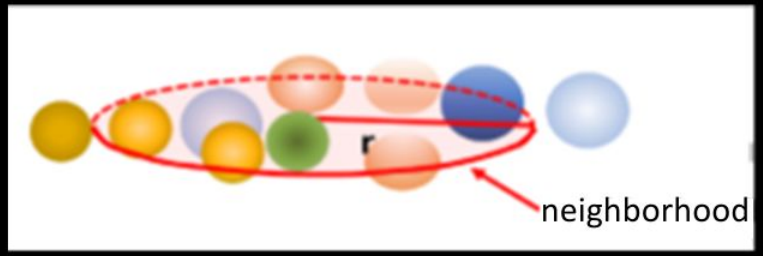
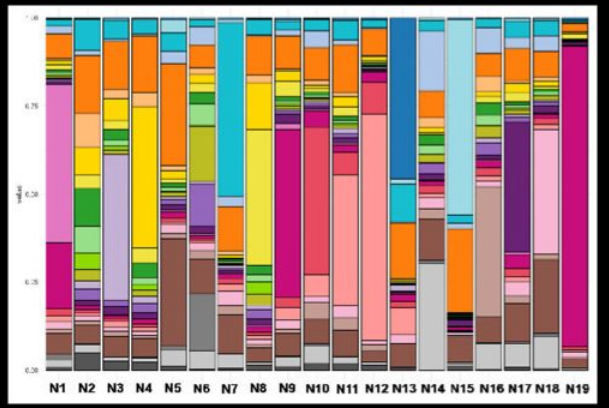
Neighborhood analysis



Cell-centric neighborhood



Tissue neighborhood visualization

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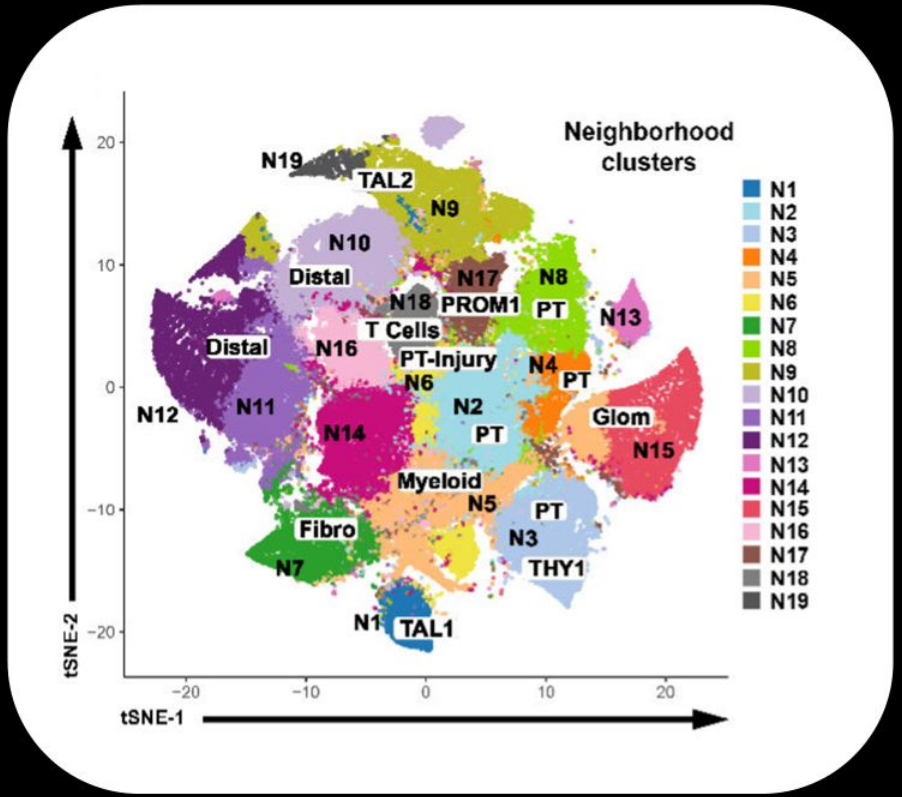
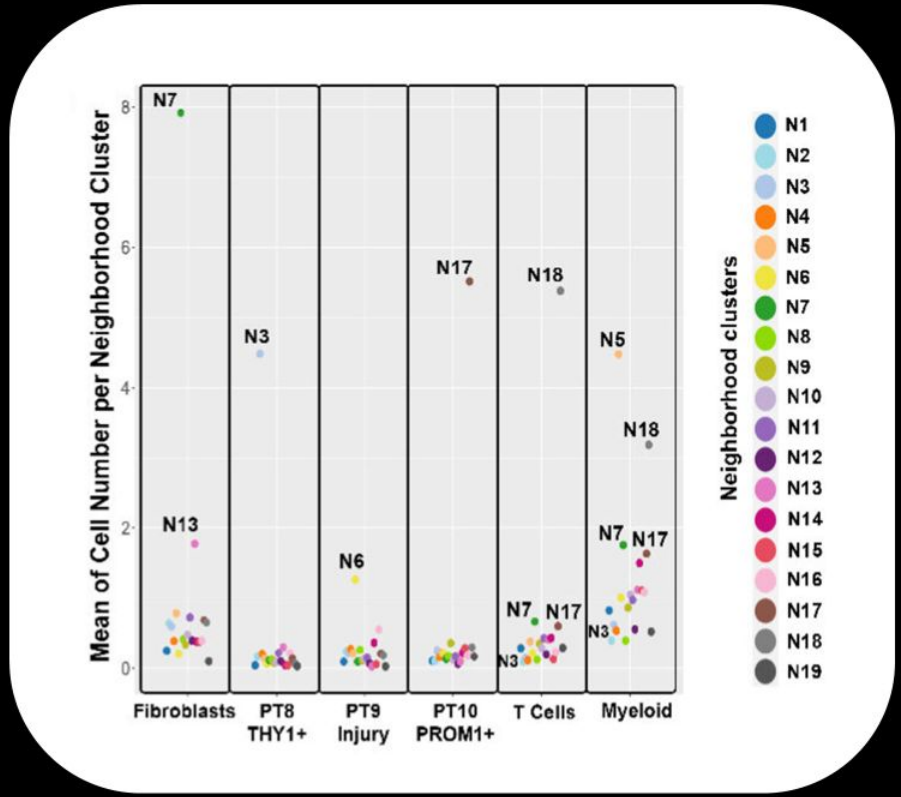
Neighborhood analysis





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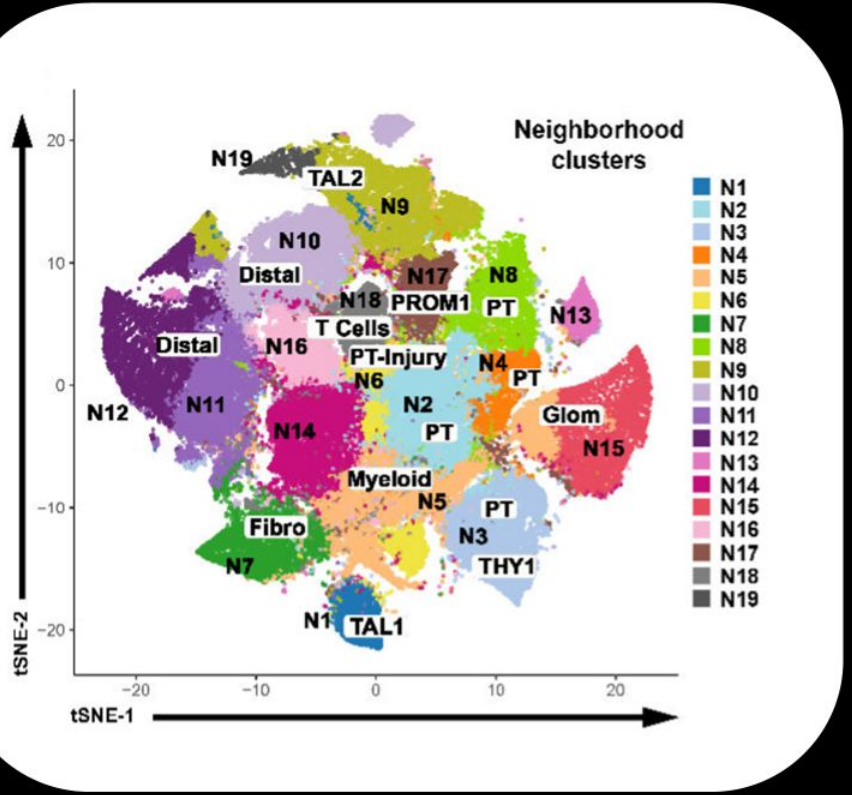

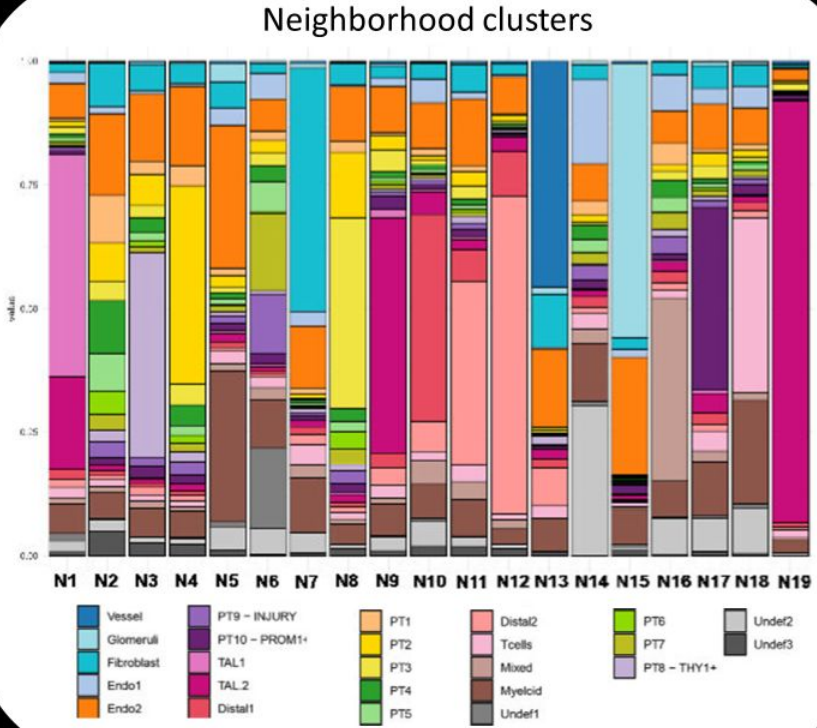

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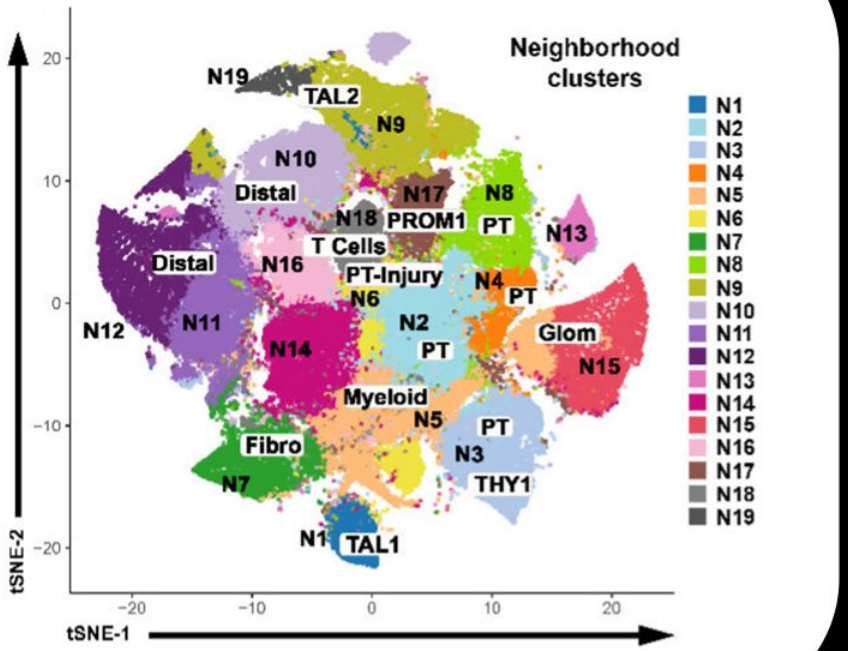
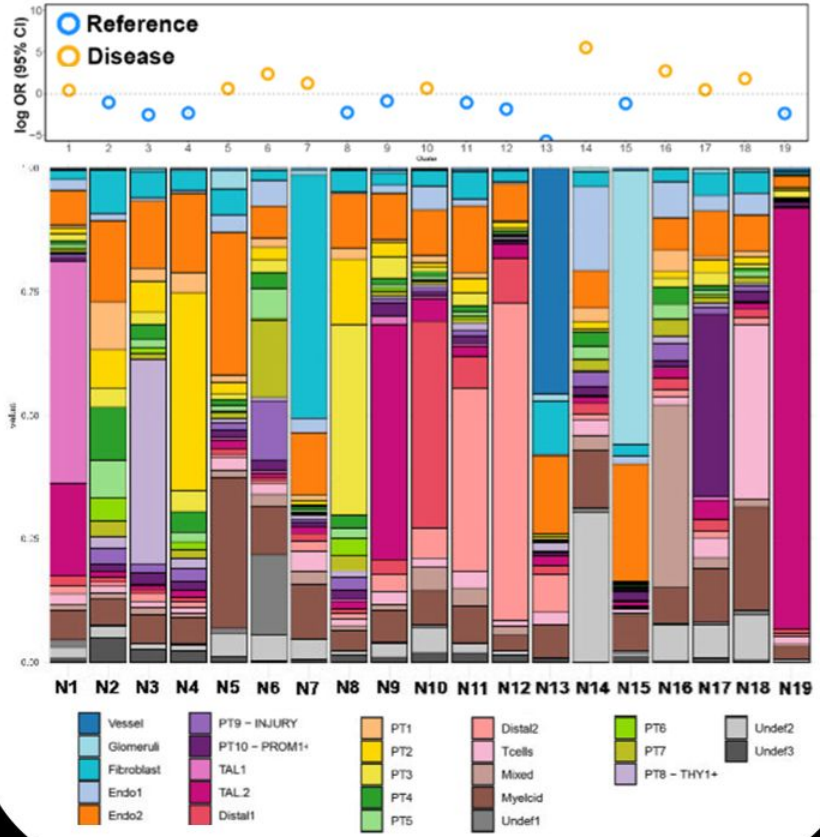


Neighborhood clusters



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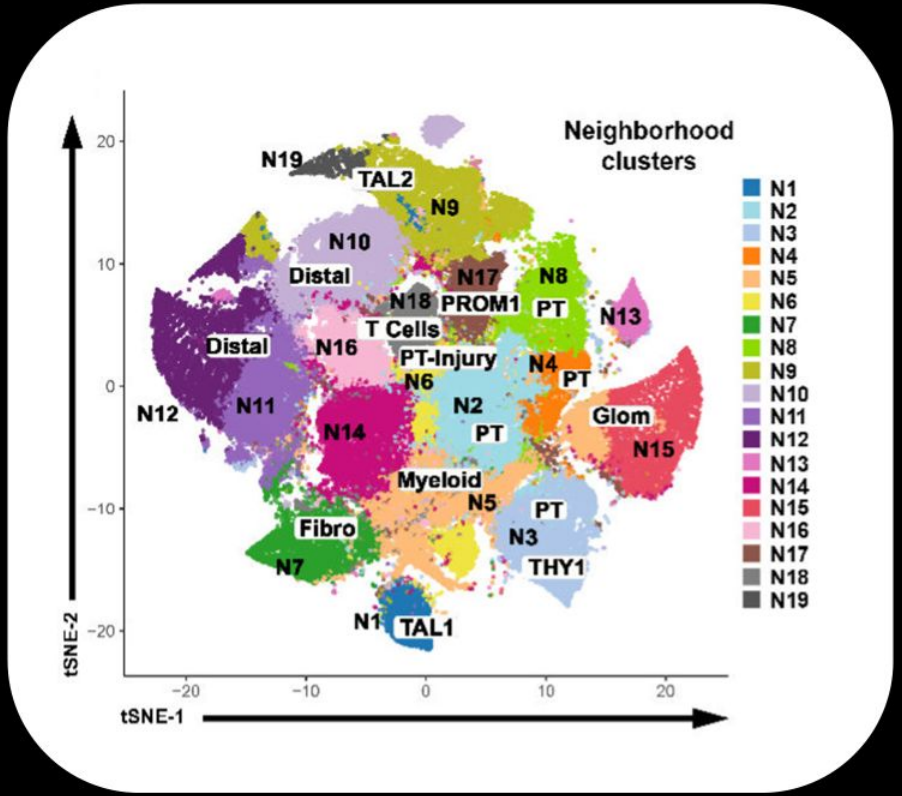
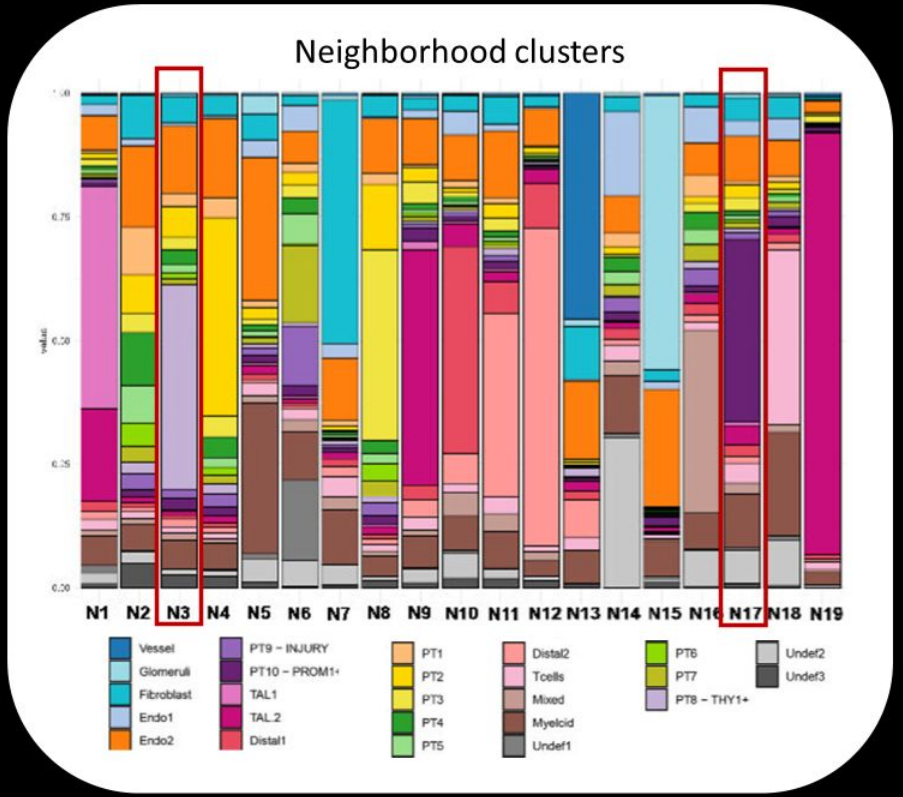
Neighborhood analysis





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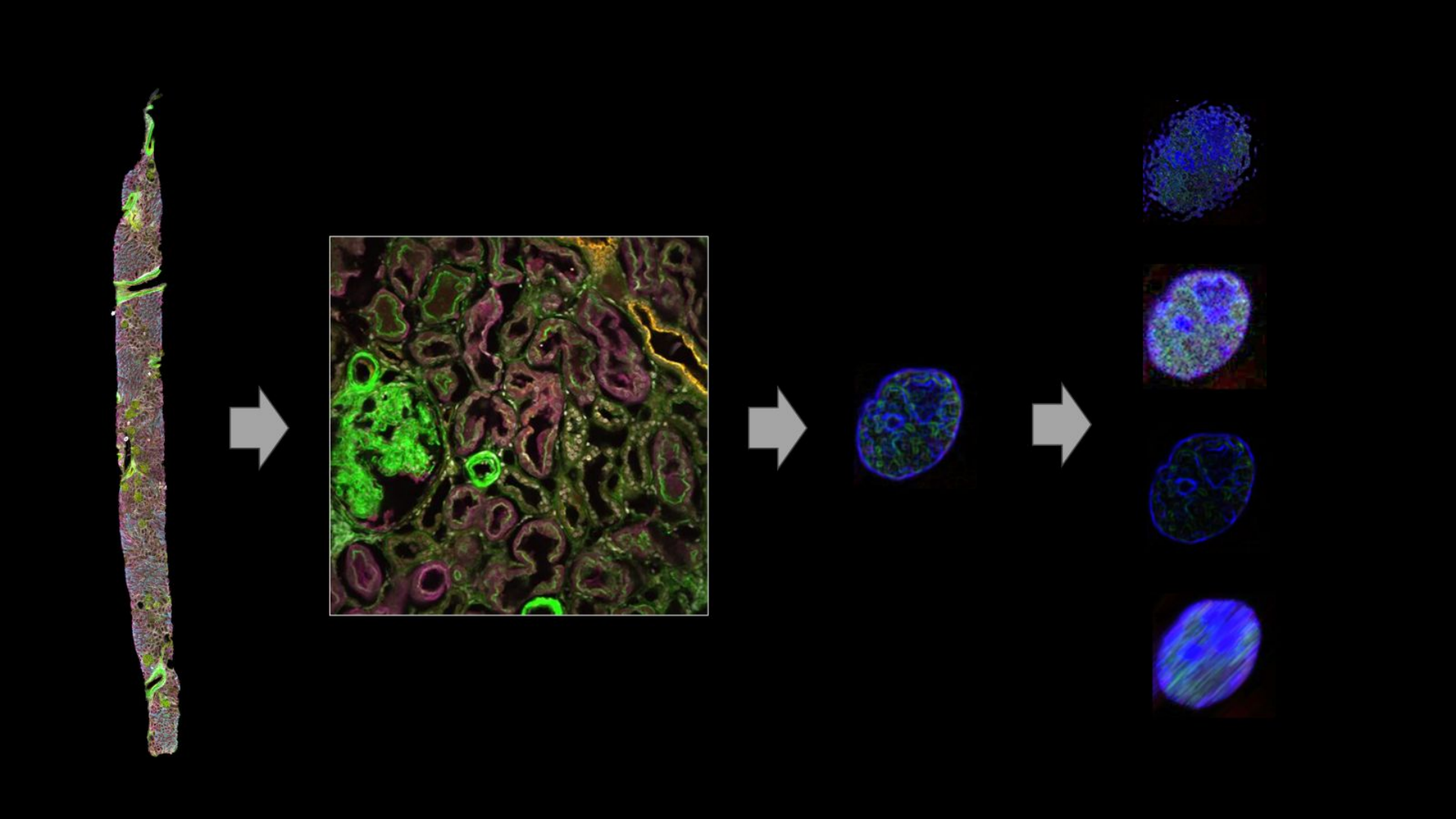
Spatial Technologies

It’s important where you sit



Q&A

https://humanatlas.io/events/2024-24h

Thank you