10AM

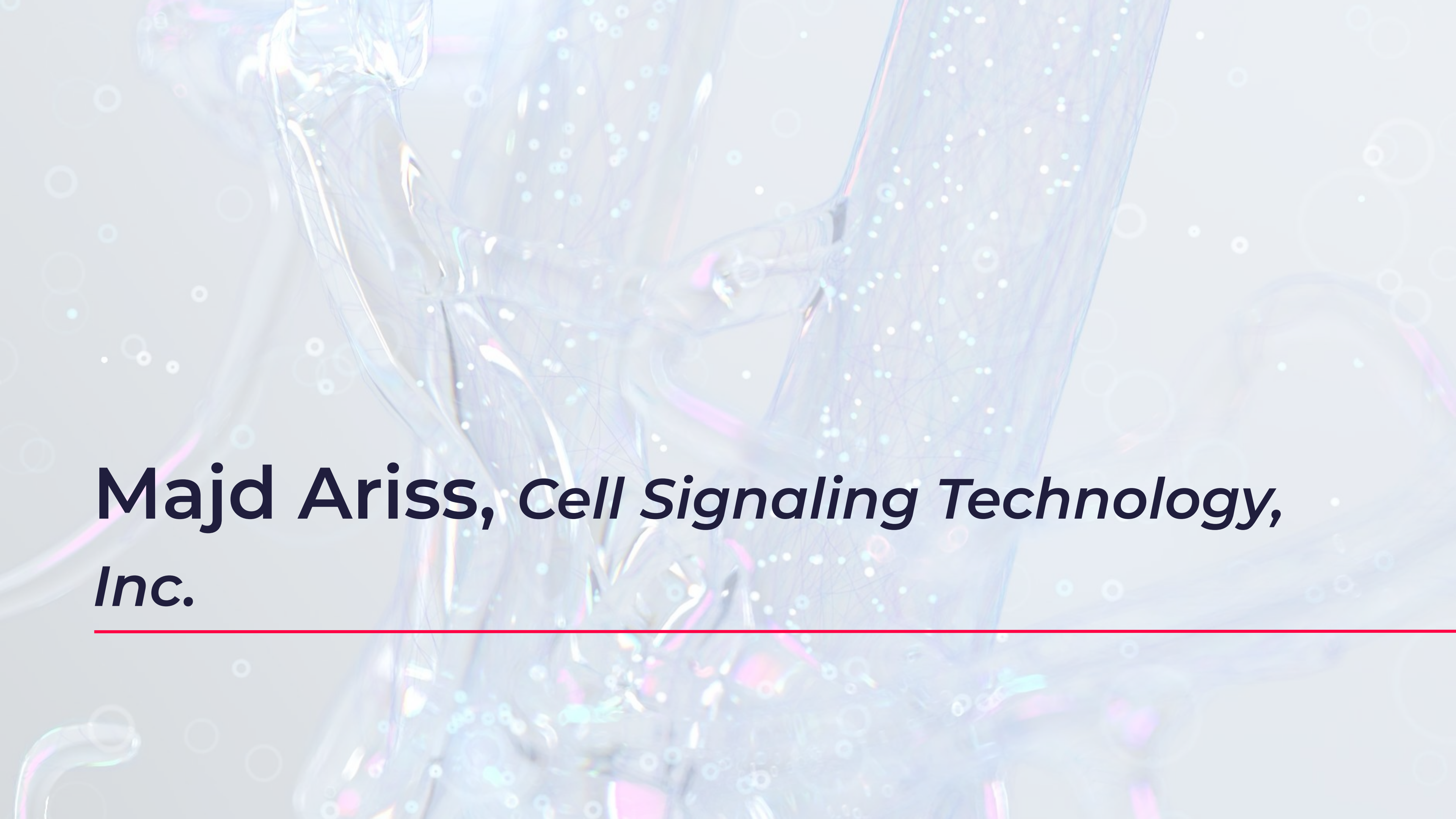
3PM in London (GMT), 12AM in Tokyo (GMT+9)

Novel Methods and Technologies

Moderator: Katy Börner, *Indiana University*

Presenters:

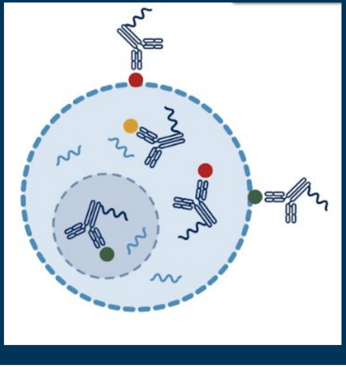
- Majd Ariss, *Single Cell Technologies*
- Jiang He, *Vizgen, Inc*
- Colles Price, *Takeda*
- Daniel Moline, *10x Genomics*
- Sarah Teichmann, *Cambridge Stem Cell Institute, UK (CIFAR co-director)*
- Tobias Wenzel, *Pontificia Universidad Católica de Chile, Chile*



Majd Ariss, *Cell Signaling Technology, Inc.*

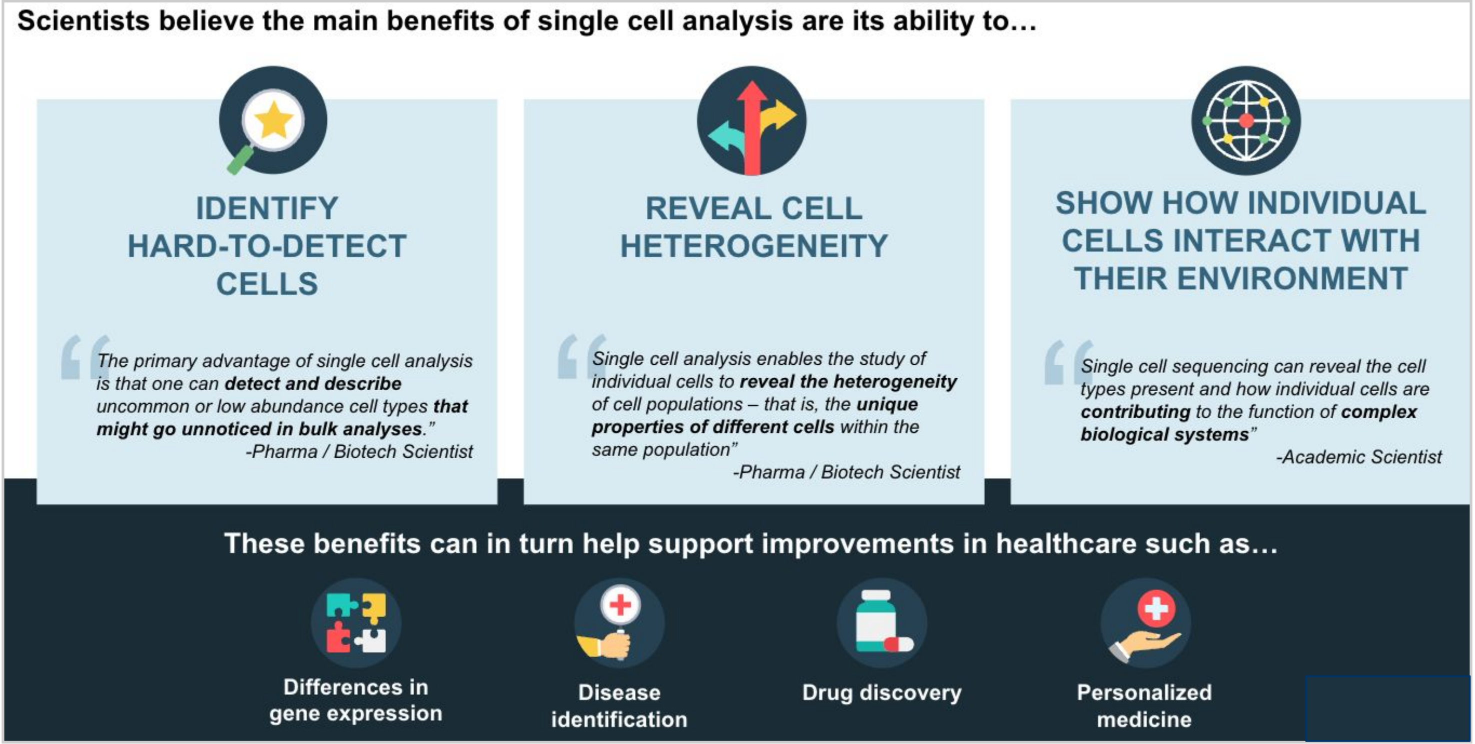
Uncovering Signaling Pathways in Single-Cell RNA sequencing using the CST® InTraSeq™ Technology

Majd Ariss, Ph.D. M.S
Senior Scientist
R&D - Single Cell Technologies



InTraSeq™ Technology
Intracellular Proteins & **Tra**nscriptomic **Seq**uencing

Main Benefits of Single Cell Analysis



Scientists believe the main benefits of single cell analysis are its ability to…

IDENTIFY HARD-TO-DETECT CELLS

> *The primary advantage of single cell analysis is that one can* ***detect and describe*** *uncommon or low abundance cell types* ***that might go unnoticed in bulk analyses****."*
>
> *-Pharma / Biotech Scientist*

REVEAL CELL HETEROGENEITY

> *Single cell analysis enables the study of individual cells to* ***reveal the heterogeneity*** *of cell populations – that is, the* ***unique properties of different cells*** *within the same population"*
>
> *-Pharma / Biotech Scientist*

SHOW HOW INDIVIDUAL CELLS INTERACT WITH THEIR ENVIRONMENT

> *Single cell sequencing can reveal the cell types present and how individual cells are* ***contributing*** *to the function of* ***complex biological systems****"*
>
> *-Academic Scientist*

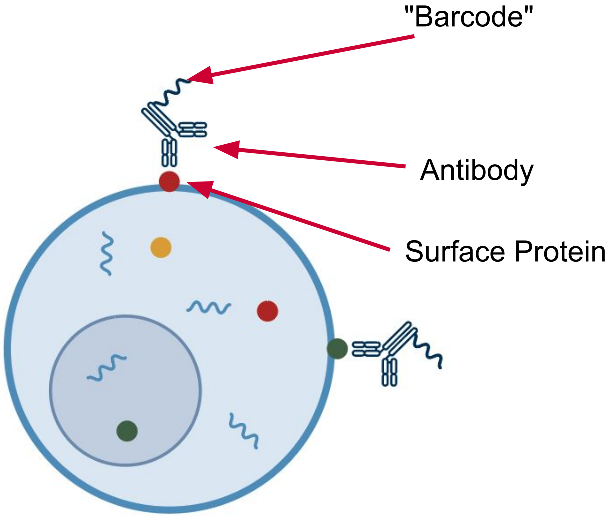
These benefits can in turn help support improvements in healthcare such as…

- **Differences in gene expression**
- **Disease identification**
- **Drug discovery**
- **Personalized medicine**

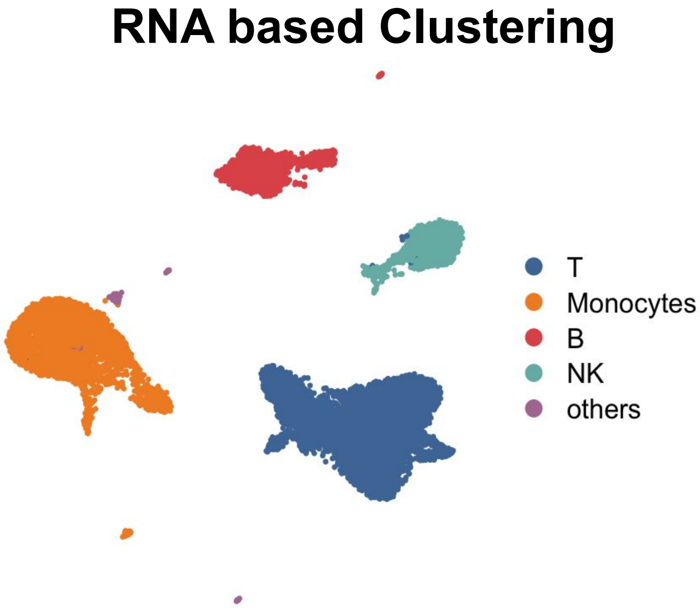
Single Cell RNA-sequencing uncovers the heterogeneity of the sample

RNA based Clustering

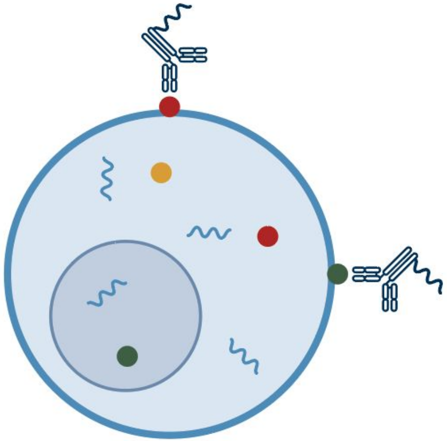
CITE-seq
Cellular Indexing of Transcriptomes and Epitopes by Sequencing

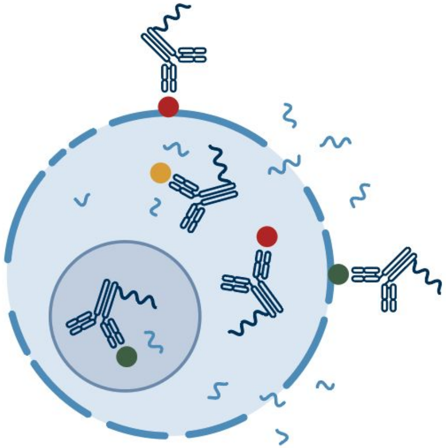


CITE-seq

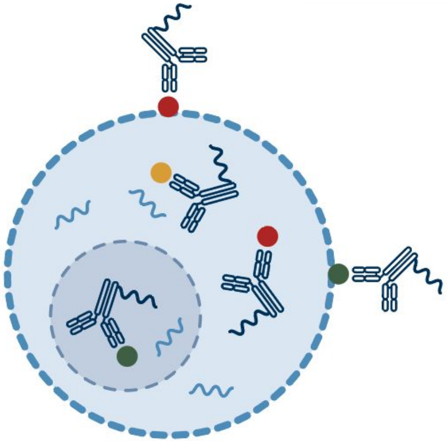


What Is the InTraSeq™ Technology?





Challenge of staining intracellular proteins: RNA degradation & loss

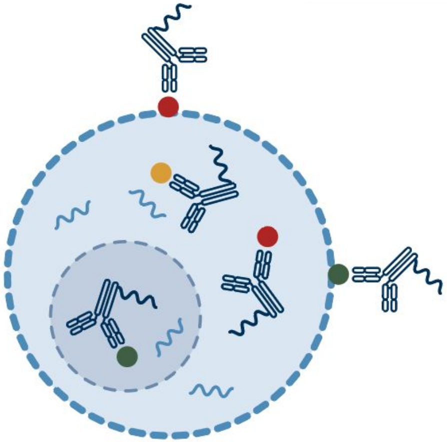


InTraSeq™ Technology

Intracellular Proteins & **Tra**nscriptomic **Seq**uencing

What Is the CST® InTraSeq™ Technology?

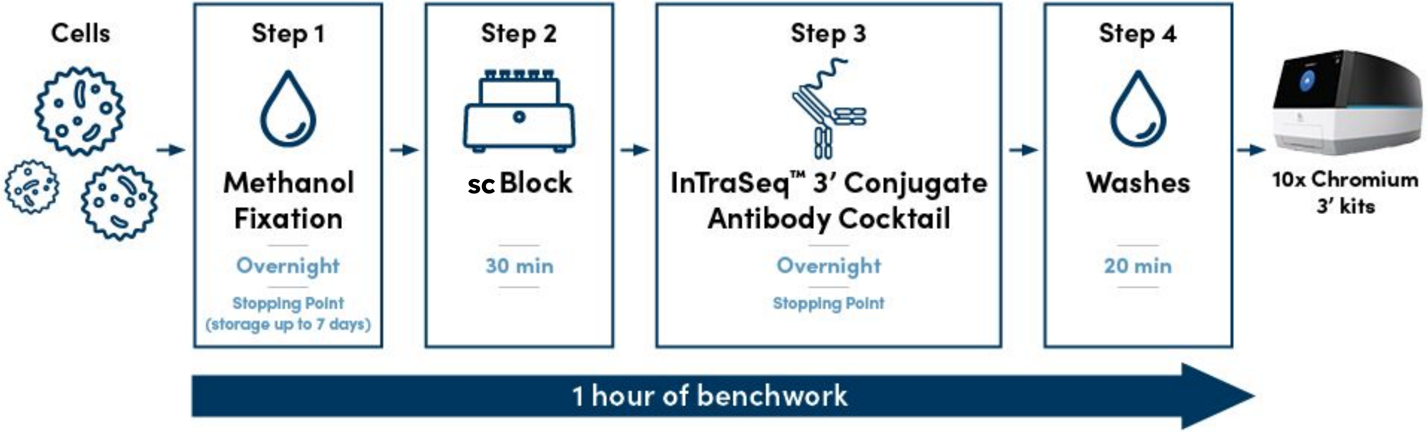
- Developed and validated by CST, using the 10x Genomic Chromium Single Cell 3' Reagent Kits with Feature Barcoding Technology
- To be used on 10x Genomic Chromium instruments



InTraSeq™ Technology

Intracellular Proteins & **Tra**nscriptomic **Seq**uencing

A 4-step Straightforward Immunostaining Protocol



Step 1: Fix the cells overnight. *(~5 min benchwork)*

- Cells can be stored in the freezer for up to 7 days

Step 2: Incubate with scBlock. *(~10 min benchwork, ~30 min incubation)*

- This step is optimized to obtain great quality single cell readout of **both** RNA and proteins

Step 3: Add CST InTraSeq™ 3’ Conjugate Antibody Cocktail overnight. *(~5 min benchwork)*

Step 4: Wash the cells. *(~20 min benchwork)*

- At this point the cells are ready for a single cell 10x Genomics 3’ kit experiment

~1h of benchwork!!

InTraSeq - What can I learn using InTraSeq ?

InTraSeq™ Single Cell Analysis.

Seq What You’ve Been Missing.

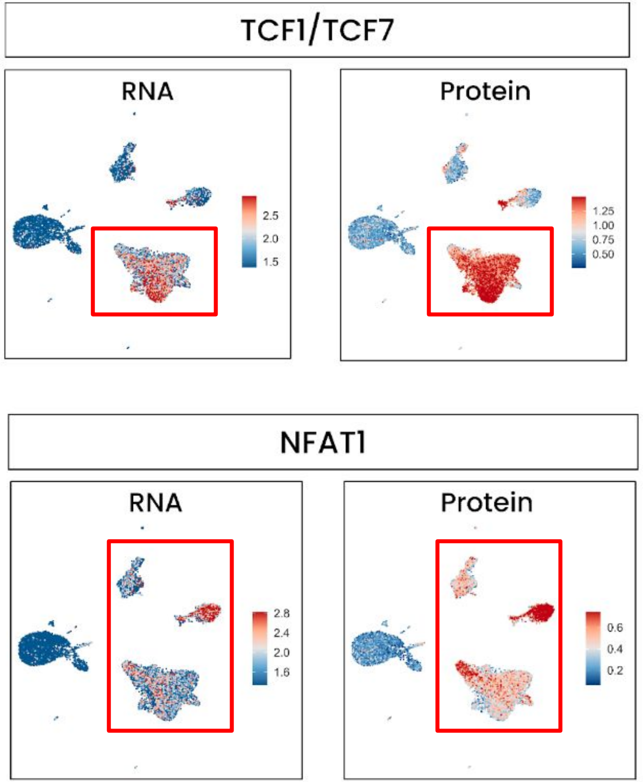
InTraSeq™ Technology - Benefits (and Proofs)

Without InTraSeq

- RNA is unstable, prone to degradation

InTraSeq Benefit

- While RNA expression is well detected, protein expression is **more uniform** than RNA expression
- A more **accurate representation of the target expression** at the protein level



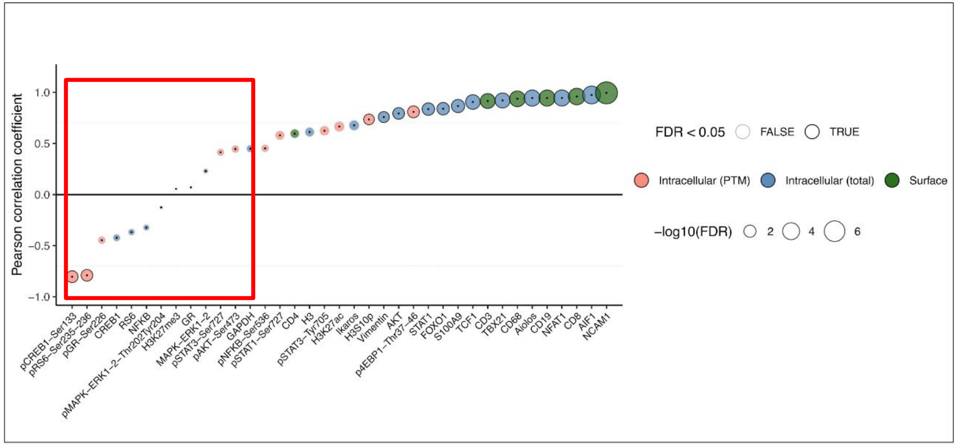
InTraSeq™ Technology - Benefits (and Proofs)

Without InTraSeq

- RNA does not always correlate with protein level, esp for PTM targets (which was expected, as PTM happens in the protein level, and cannot be inferred by RNA alone)

InTraSeq Benefit

- InTraSeq can be used to **uncover missing information** in a scRNA-seq experiment
- Offers **new biological insights** at the post translational modification level



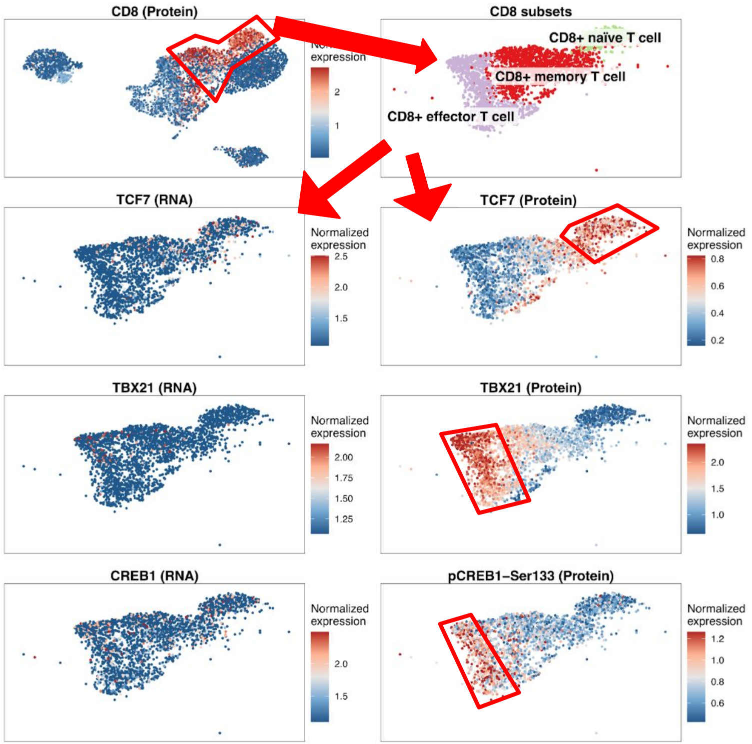
InTraSeq™ Technology - Benefits (and Proofs)

Without InTraSeq

- Difficult to identify cell states by analyzing RNA alone

InTraSeq Benefit

- Enables the categorization of **cell subpopulations** and **cell states** based on intracellular protein and PTM readout



Measuring Post-Translational Modifications in Your single Cell Data using InTraSeq™

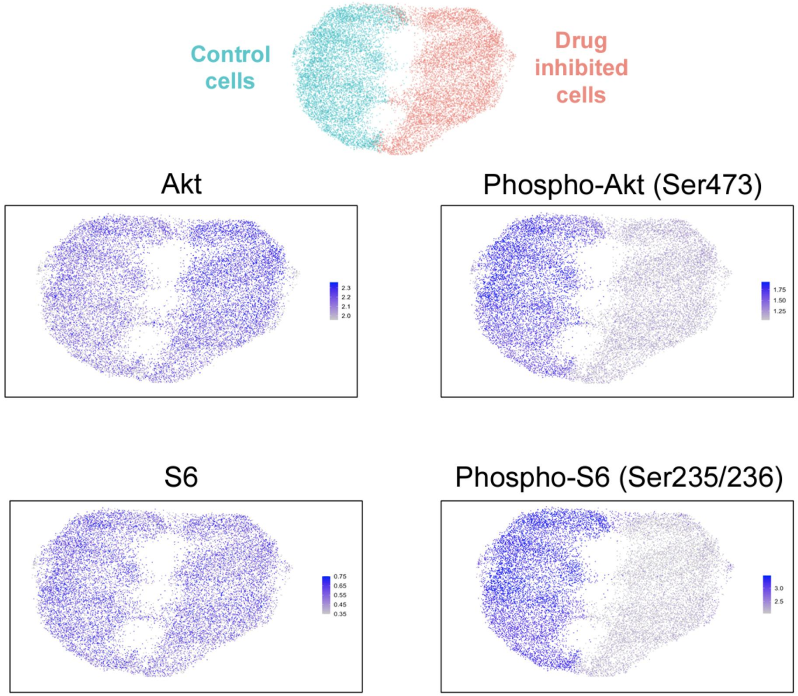
Without InTraSeq

- Inability to obtain functional information about the protein state

InTraSeq Benefit

- InTraSeq measures Post-Translational Modifications (PTMs) in a single cell assay and determines whether the **protein is in an active or inactive state**
- Offers **functional proteomics insights**

Acute PI3K inhibition in Jurkat cells using Wortmannin shows a decrease in p-Akt and p-S6 and **not** total Akt and S6 protein level



Akt

Phospho-Akt (Ser473)

S6

Phospho-S6 (Ser235/236)

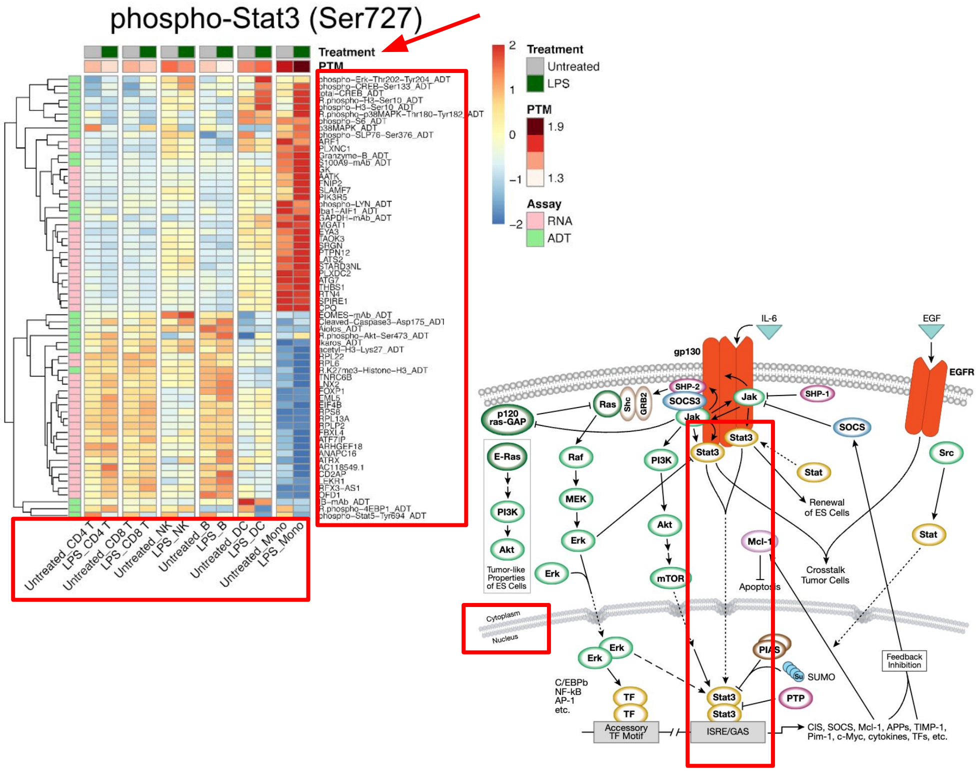
InTraSeq™ Technology - Benefits (and Proofs)

Without InTraSeq

- Difficult (if not impossible) to determine if the targets along the signaling pathway are affected, esp. for transcription factors, using only RNA data

InTraSeq Benefit

- Gaining a comprehensive understanding of **signaling pathways at the single cell resolution**



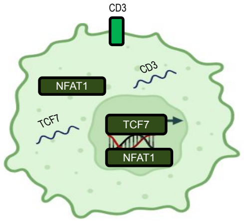
InTraSeq™ Technology - Benefits (and Proofs)

Without InTraSeq

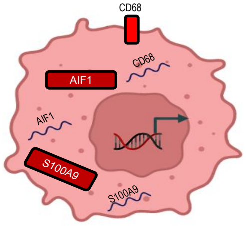
- Cannot gain a full picture by using RNA data alone

InTraSeq Benefit

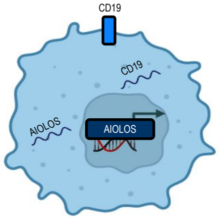
- Comprehensive analysis by **integrating RNA, surface markers, cytoplasmic proteins and nuclear proteins data** at single cell resolution



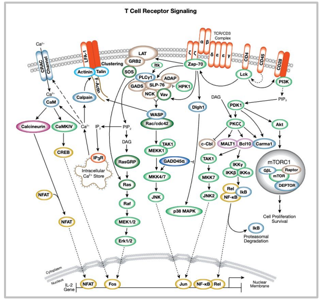
T cells



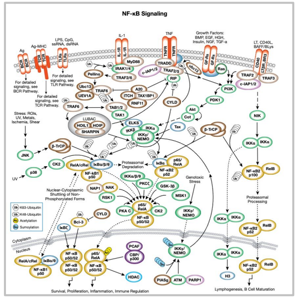
Monocytes



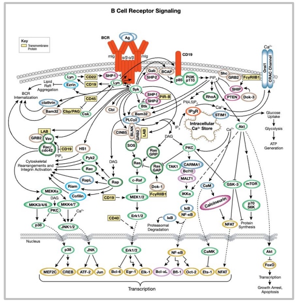
B cells



https://www.cellsignal.com/pathways/t-cell-receptor-signaling

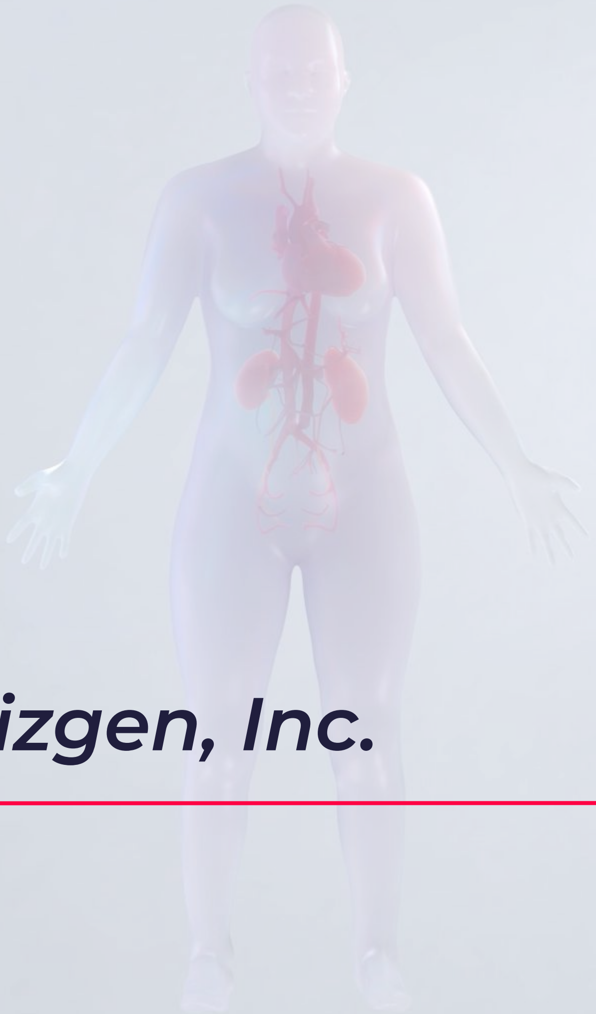


https://www.cellsignal.com/pathways/nfkb-signaling-pathway



https://www.cellsignal.com/pathways/b-cell-receptor-signaling

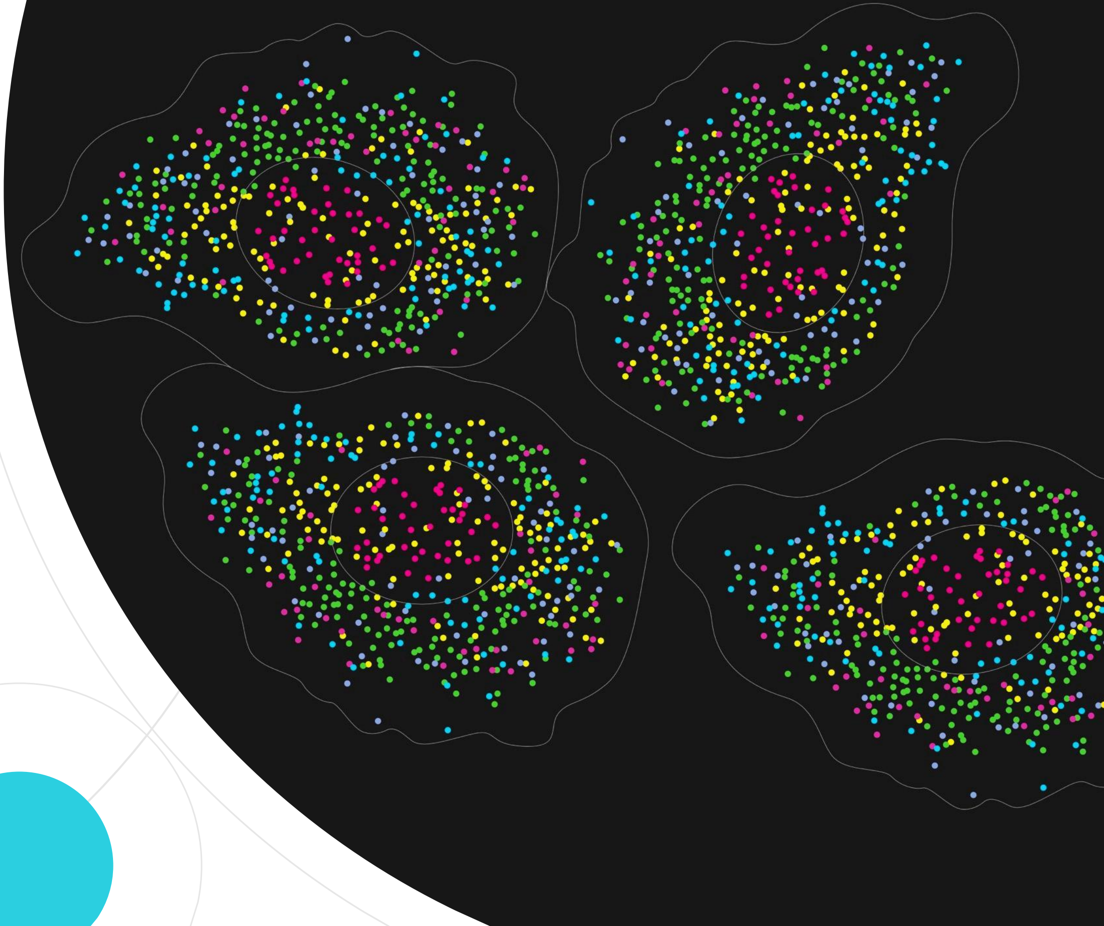
Thank you !



Jiang He, *Vizgen, Inc.*

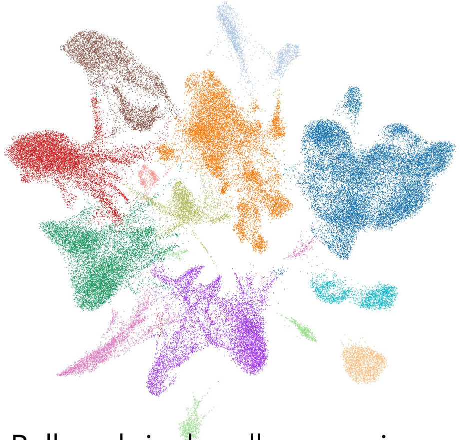
Mapping the Future of Spatial Genomics with MERSCOPE Ultra Platform

Jiang He, Co-founder and VP of R&D, Reagents

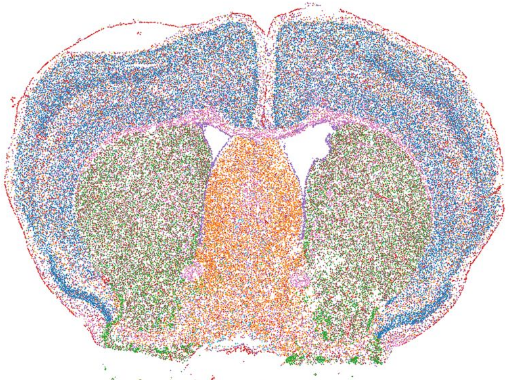


Bulk and single cell sequencing are fundamentally limited

Biological systems are intricately spatially organized



Bulk and single cell sequencing can show us parts



Spatial genomics with true single cell resolution offers highly multiplexed direct in situ detection and valuable insight into the bigger picture

Vizgen brings spatial genomics to labs with the MERSCOPE™ platform

COMPREHENSIVE

100s-1000s of genes in a single run

High sensitivity and accuracy

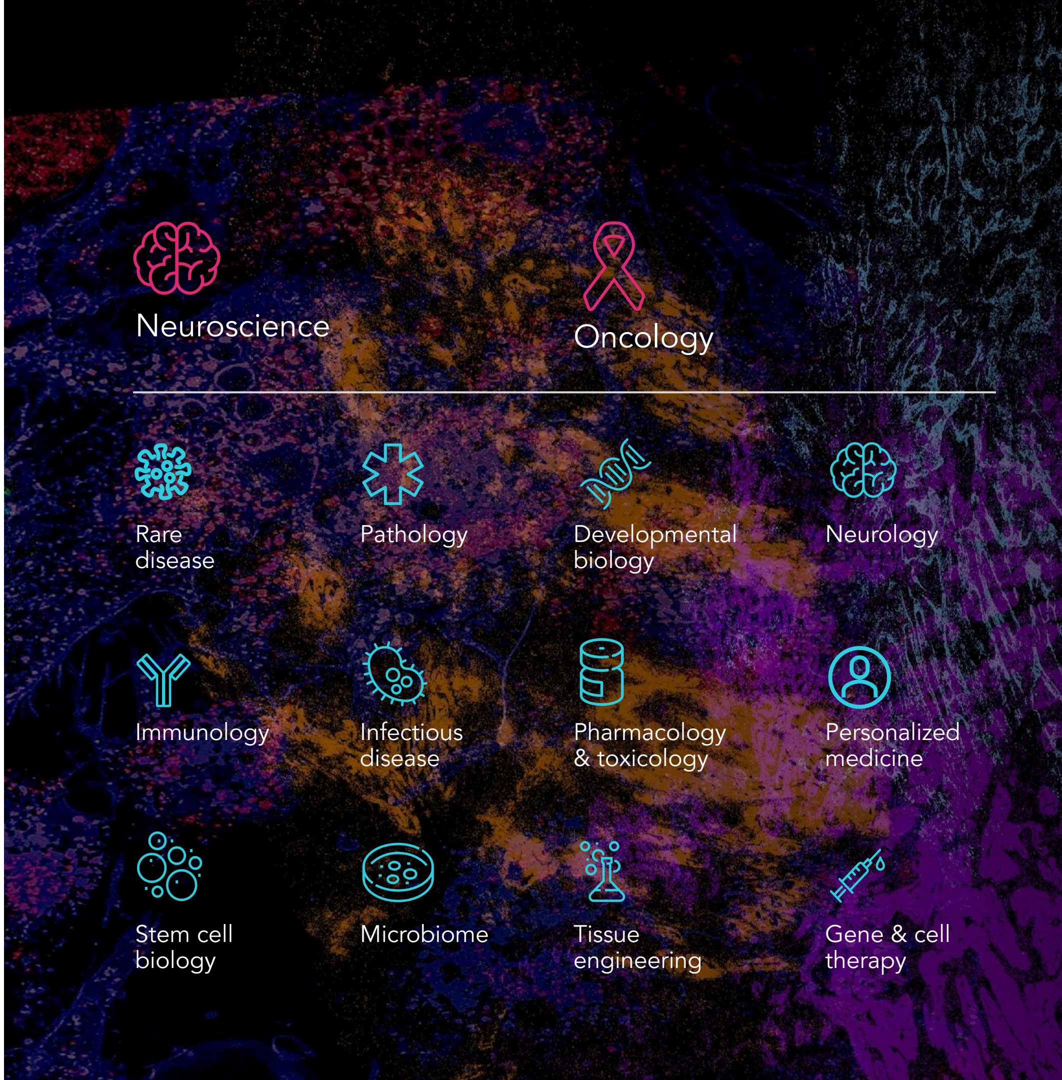
Large imaging area of 3 cm^2 and 100nm resolution

No need for sequencing

USER-FRIENDLY

Instrument and visualization software

Web-based gene panel application



Neuroscience

Oncology

Rare disease

Pathology

Developmental biology

Neurology

Immunology

Infectious disease

Pharmacology & toxicology

Personalized medicine

Stem cell biology

Microbiome

Tissue engineering

Gene & cell therapy

MERSCOPE

smFISH ×

Direct in situ RNA quantification

Proprietary Barcoding System =

Custom gene panels of up to 1000 targets

MERFISH

Highly multiplexed RNA detection enabling single cell analysis

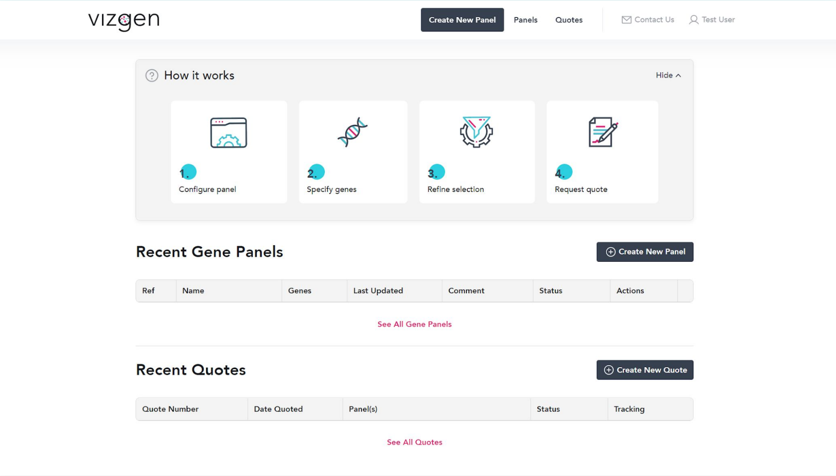
High accuracy and consistency due to error robustness

\+

An easy-to-use, fully automated platform

MERSCOPE is an end-to-end platform solution

Upstream



How it works

1. Configure panel
2. Specify genes
3. Refine selection
4. Request quote

Recent Gene Panels

Ref	Name	Genes	Last Updated	Comment	Status	Actions

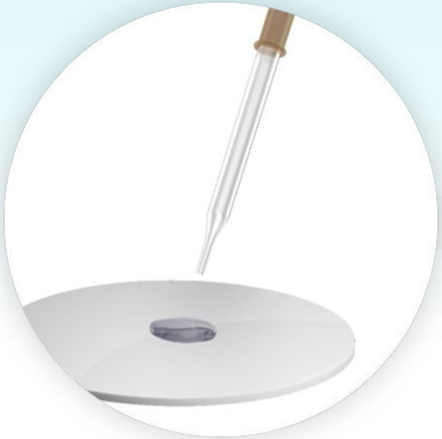
See All Gene Panels

Recent Quotes

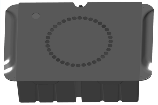
Quote Number	Date Quoted	Panel(s)	Status	Tracking

See All Quotes

Custom Gene Panel Design



Flow chamber

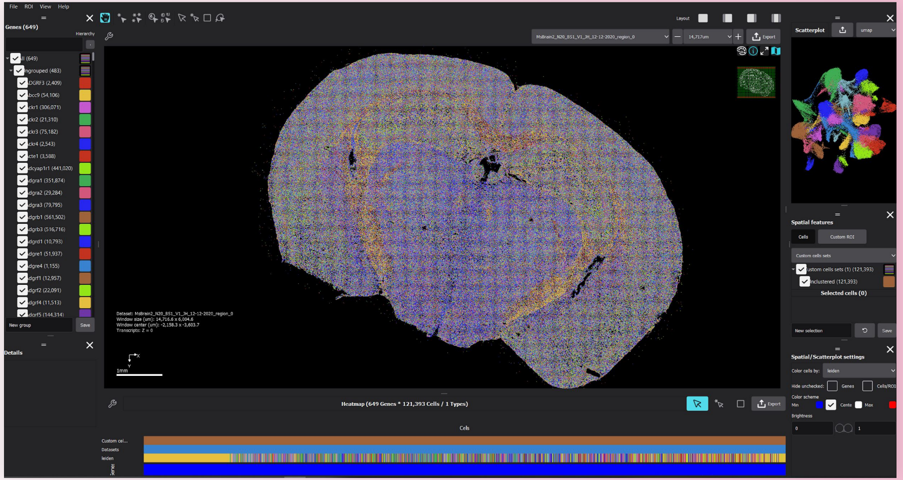


Reagent pack

Sample Preparation

MERSCOPE is an end-to-end platform solution

Downstream



Dataset: MsBrain2_N20_BS1_V1_JH_12-12-2020_region_0
Window size (um): 14,716.6 x 6,004.6
Window center (um): -2,158.3 x -3,603.7
Transcripts: Z = 0

Color cells by: leiden

Hide unchecked: ☐ Genes ☐ Cells/ROI

Min ☑ Cente Max

0 1

Visualization software

Working with MERFISH involves three key stages

STAGE 1

Hybridization

Embedding 10,000s of unique encoding probe onto the sample.

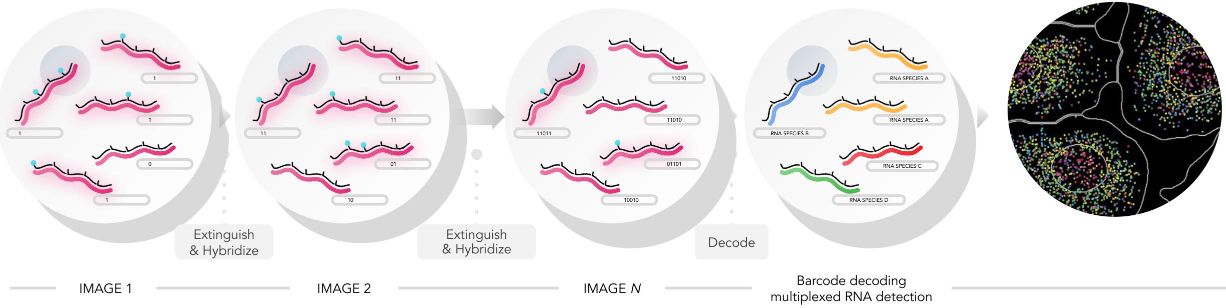
STAGE 2

Clearing

Utilizing a gel to remove unnecessary components of tissue that could interfere with measurement.

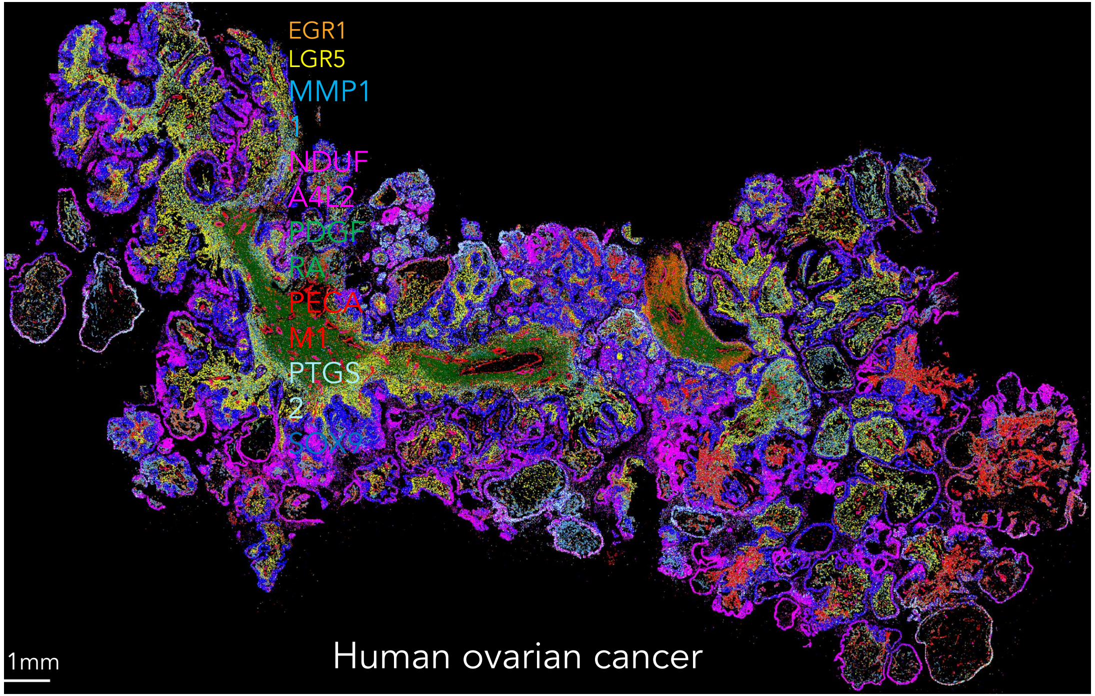
STAGE 3

Imaging

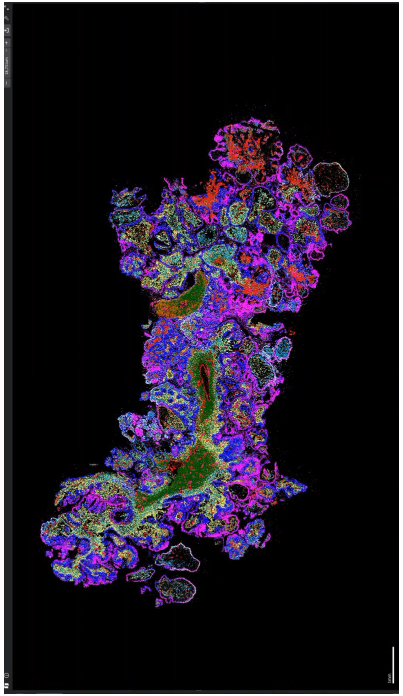


Chen et al, Science, 2015; Moffitt et al, PNAS, 2016; Emanuel et al, Nature Methods, 2017; Moffitt et al, Science, 2018; Wang et al, Sci. Rep, 2018; Wang et al, PNAS, 2019; Xia et al, PNAS, 2019; Xia et al, Sci. Rep, 2019; Favuzzi et al, Cell, 2021; Hara et al, Cancer Cell, 2021; Lu et al, Cell Discov, 2021; Miller et al, CVPR, 2021; Park et al, Nat Commun, 2021; Su et al, Cell, 2020; Wang et al, BioRxiv, 2020; Zhang et el, Nature, 2021

Profile gene expression *in situ*, from whole tissue, to sub-cellular



Human ovarian cancer

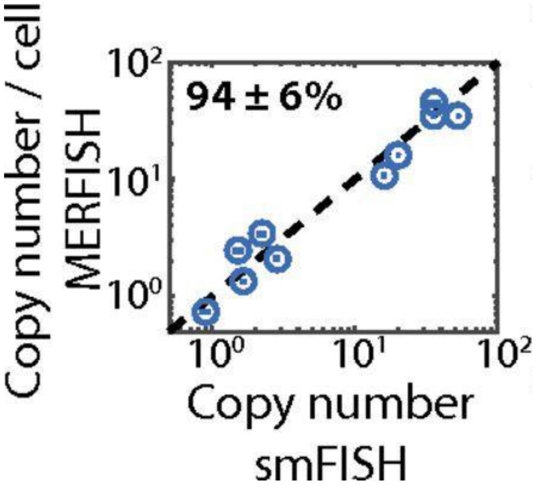


500 gene panel, 174 million RNA transcripts detected

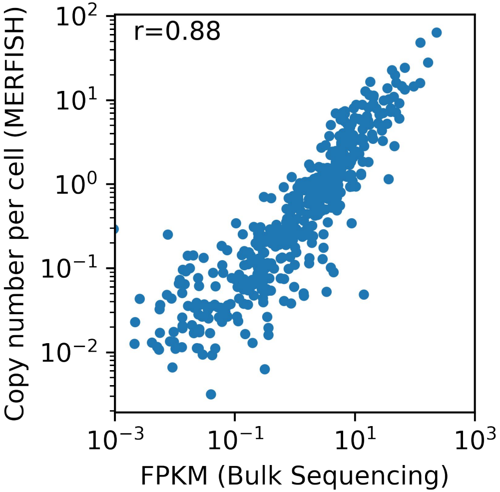
vizgen

MERSCOPE Advantages

Highly quantitative and accurate measurement



Moffitt et al, PNAS, 2016

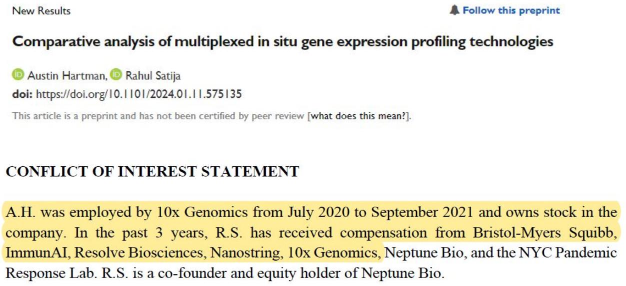


Allows large dynamic range of expression for profiled genes (4 orders of magnitude)

vizgen

Comparison of 6 spatial transcriptomics technologies shows MERSCOPE has the best performance

Independent evaluation



New Results

Follow this preprint

Comparative analysis of multiplexed in situ gene expression profiling technologies

Austin Hartman, Rahul Satija

doi: https://doi.org/10.1101/2024.01.11.575135

This article is a preprint and has not been certified by peer review [what does this mean?].

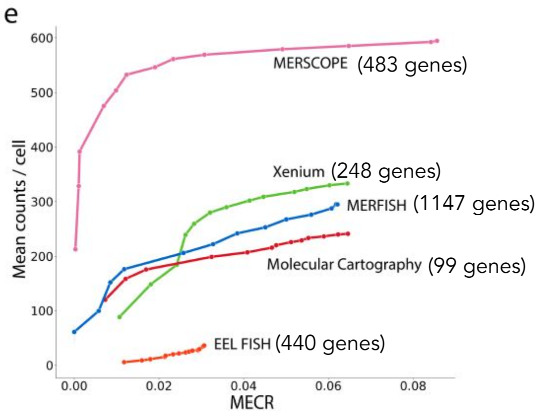
CONFLICT OF INTEREST STATEMENT

A.H. was employed by 10x Genomics from July 2020 to September 2021 and owns stock in the company. In the past 3 years, R.S. has received compensation from Bristol-Myers Squibb, ImmunAI, Resolve Biosciences, Nanostring, 10x Genomics, Neptune Bio, and the NYC Pandemic Response Lab. R.S. is a co-founder and equity holder of Neptune Bio.

Rahul Satija Lab in New York Genome Center

No Affiliation with Vizgen

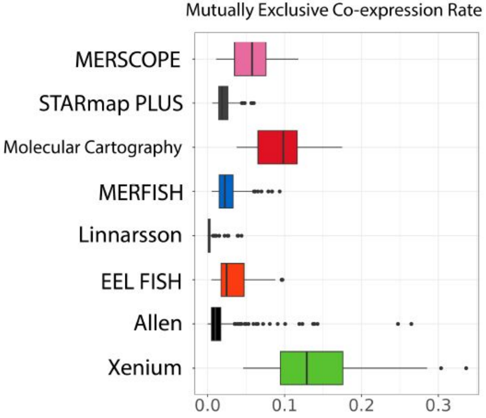
MERSCOPE has highest sensitivity



Highest sensitivity among all

2X more sensitive than Xenium

MERSCOPE has superior specificity



Excellent specificity

Optimal trade-off between sensitivity and specificity

Hartman & Satija, eLife, 2024

MERSCOPE Ultra – a High Throughput Platform for Spatial Genomics

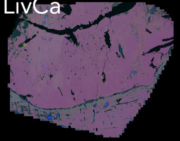
2021

- 3x Larger Imaging Area
- 2x Faster Imaging
- Large and Std Flow Cells
- New Compute, Storage and Analysis

Sep 2024

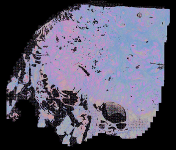
Detect 1,000 Genes in 3cm^2 Tissue

FFPE human LivCa



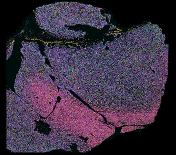
3.0cm^2 area
1 billion trx
321 counts/100um^2
227 trx/cell

FFPE human BrCa



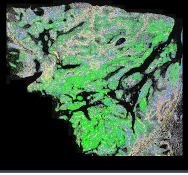
1.63cm^2 area
98 million trx
63 counts/100um^2
220 trx/cell

FF human brain



1.85 cm^2 area
553 million trx
313 counts/100um^2
261 trx/cell

FFPE human LuCa



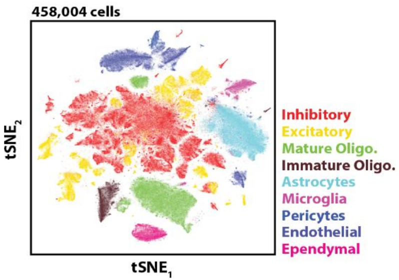
1.26 cm^2 area
194 million trx
162 counts/100um^2
131 trx/cell

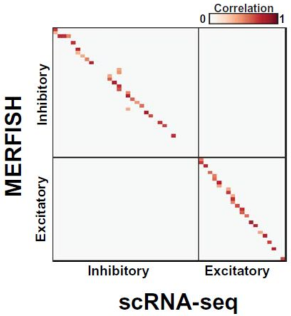
Enables true single cell atlasing

By profiling 155 genes in the preoptic region of the mouse hypothalamus, MERFISH was able to:

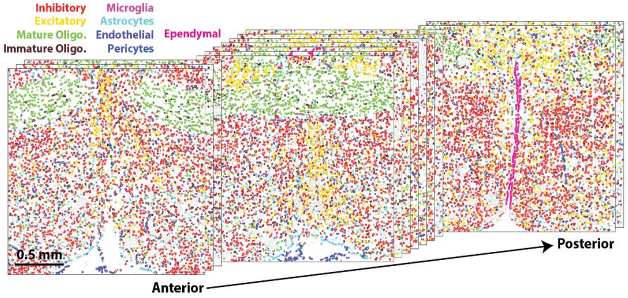
- Identify 75 cell types
- Map their spatial location
- Identify single neuronal types selectively activated during individual behaviors

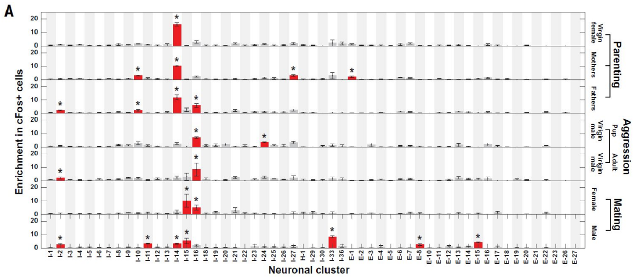
Single cell characterization





Spatial analysis in tissue





Moffit. et al, Science, 2018

Integration of transcriptome-wide single cell data

MERSCOPE data × sc/snRNAseq data = Transcriptome-wide spatial data

ARTICLES

https://doi.org/10.1038/s41592-021-01264-7

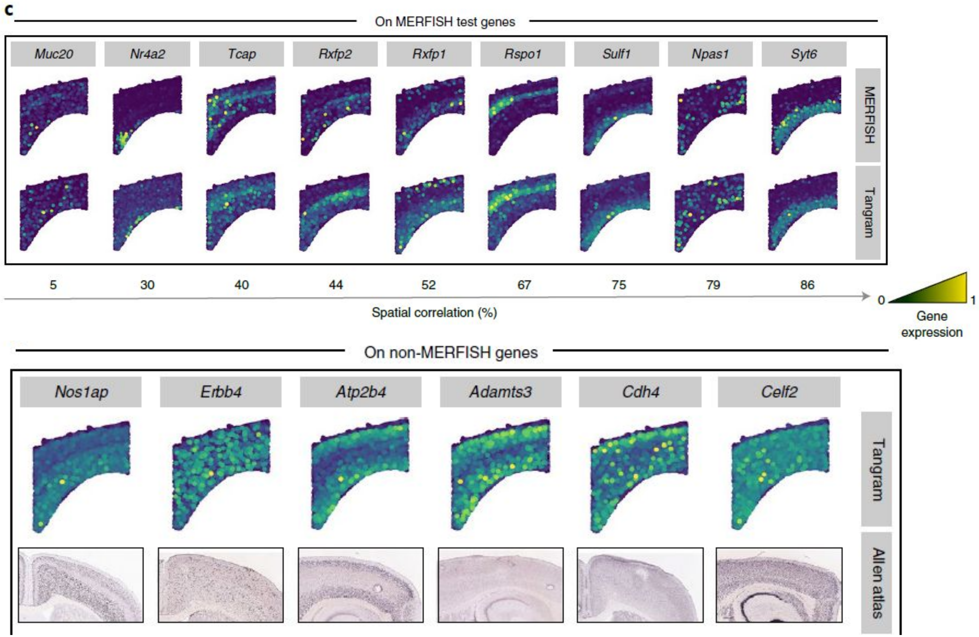
nature methods

Check for updates

OPEN

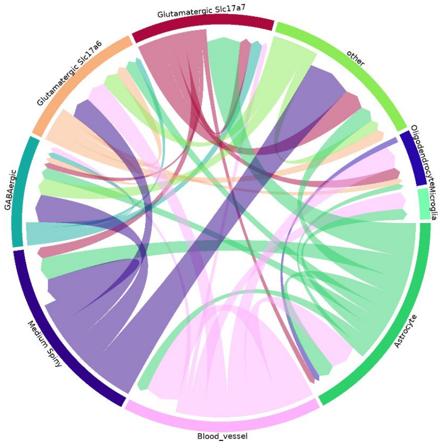
Deep learning and alignment of spatially resolved single-cell transcriptomes with Tangram

- **Tangram**, a method that aligns sc/snRNA-seq data to various forms of spatial data collected from the same region, was developed by **Aviv Regev lab** at Broad Institute
- Tangram maps cells with high-resolution MERFISH measurements and expands them to genome scale

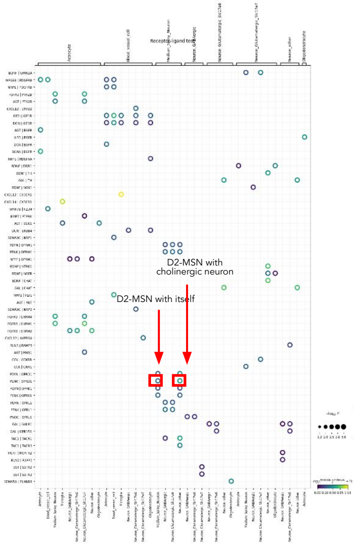


Biancalani et al, Nature Methods, 2021

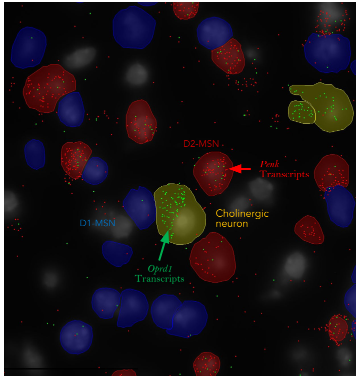
Ligand and receptor interactome analysis, with spatial context



Ligand-receptor interactome

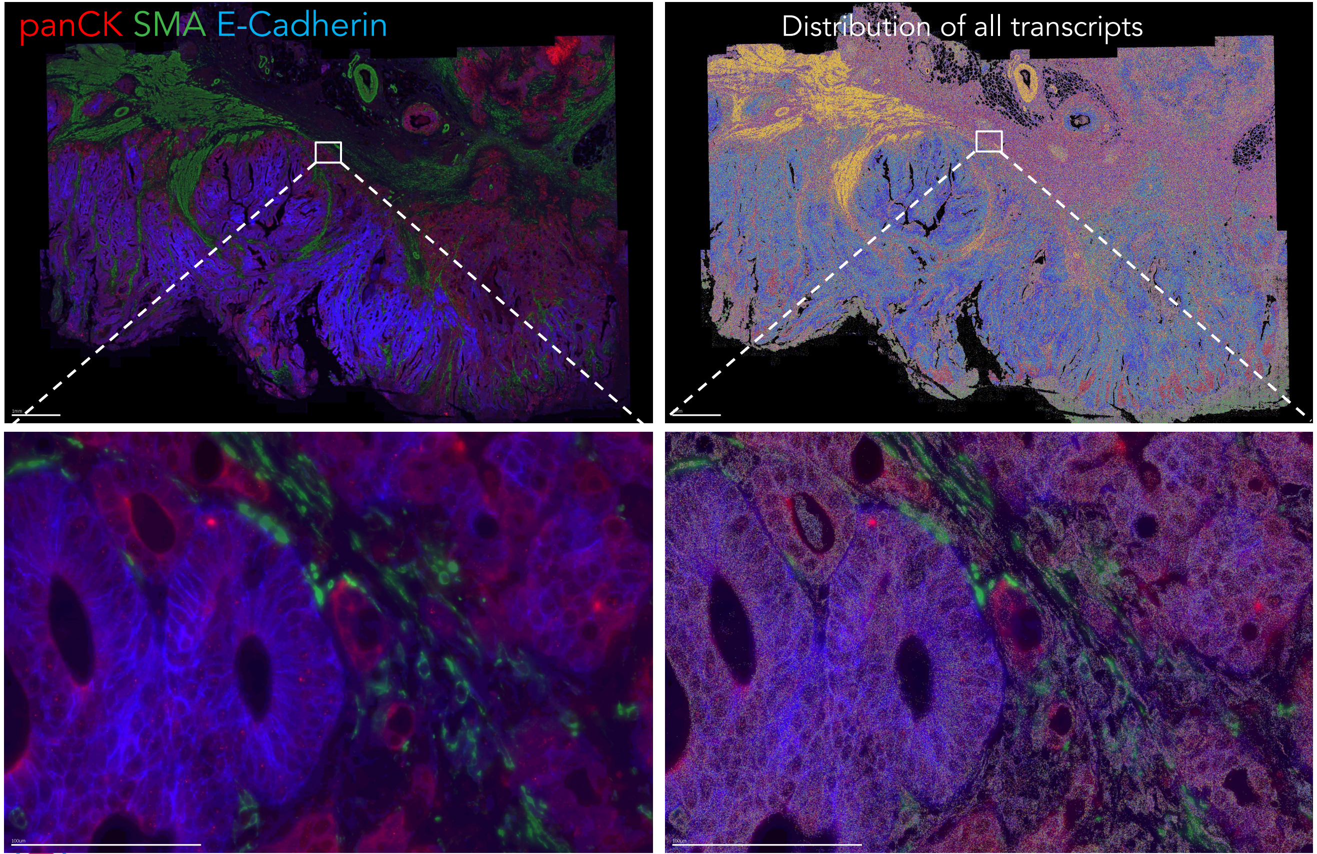


Ligand-receptor pairs



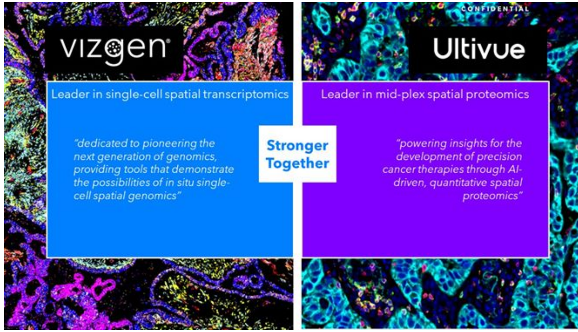
D2-MSN and cholinergic neuron interaction

Compatible with protein co-staining



Human Colon Cancer

- 347 genes
- 3 proteins
- 67,045,210 counts



Leader in single-cell spatial transcriptomics

"dedicated to pioneering the next generation of genomics, providing tools that demonstrate the possibilities of in situ single-cell spatial genomics"

Stronger Together

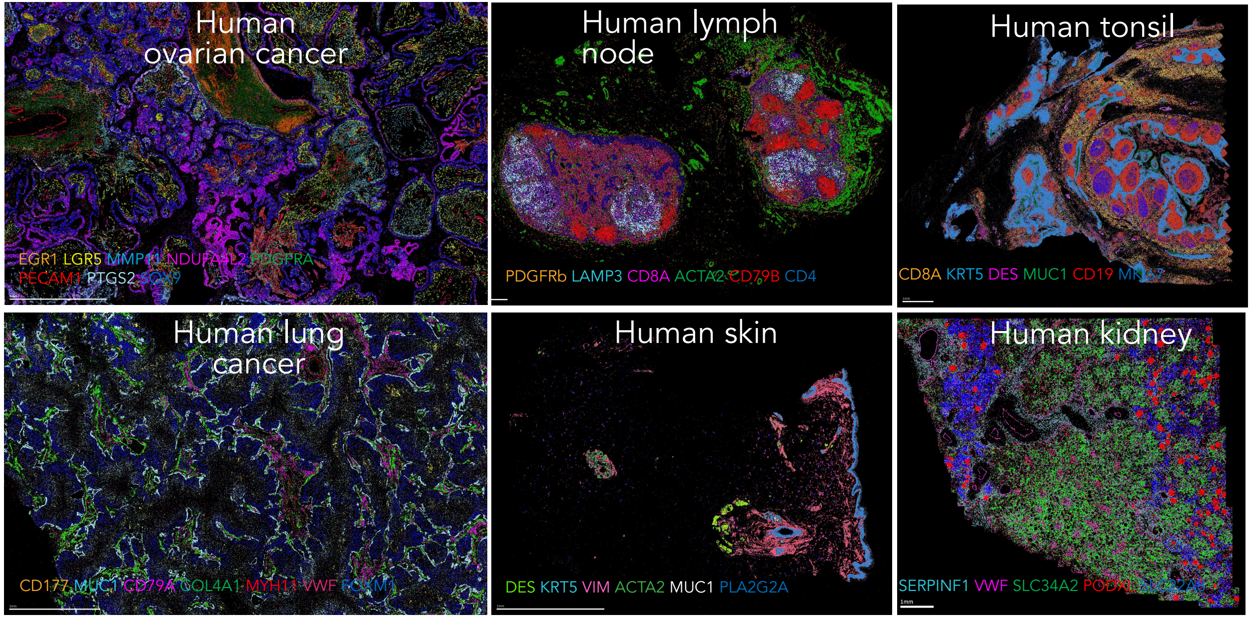
Leader in mid-plex spatial proteomics

"powering insights for the development of precision cancer therapies through AI-driven, quantitative spatial proteomics"

Vizgen merged with Ultivue, a spatial proteomics company

Widely applicable across different sample types, including FFPE samples

Spatial distribution of select genes out of 244-plex gene panel



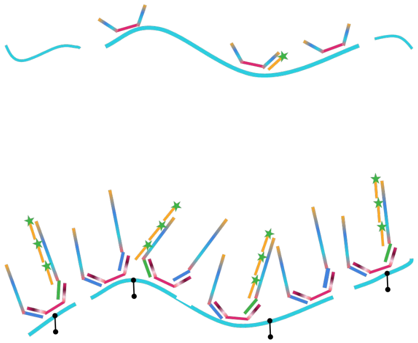
Validated in 60+ tissues, with 270+ peer reviewed publications and preprints
Compatible with cells, fresh/fixed frozen, FFPE tissue blocks

vizgen

Introducing MERFISH 2.0 – Making the Best Better

MERFISH claims the highest RNA detection efficiency for good quality samples

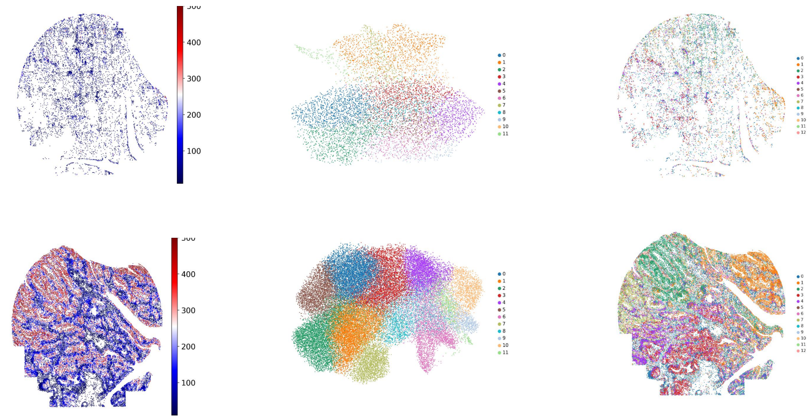
But performance can decrease when detecting degraded RNA or running poor-quality samples



MERFISH 1.0

MERFISH 2.0

FFPE Human Colorectal Cancer



Total transcripts

UMAP

Spatial distribution of cell clusters

Increased sensitivity for degraded RNA

Enables detection in more challenging samples

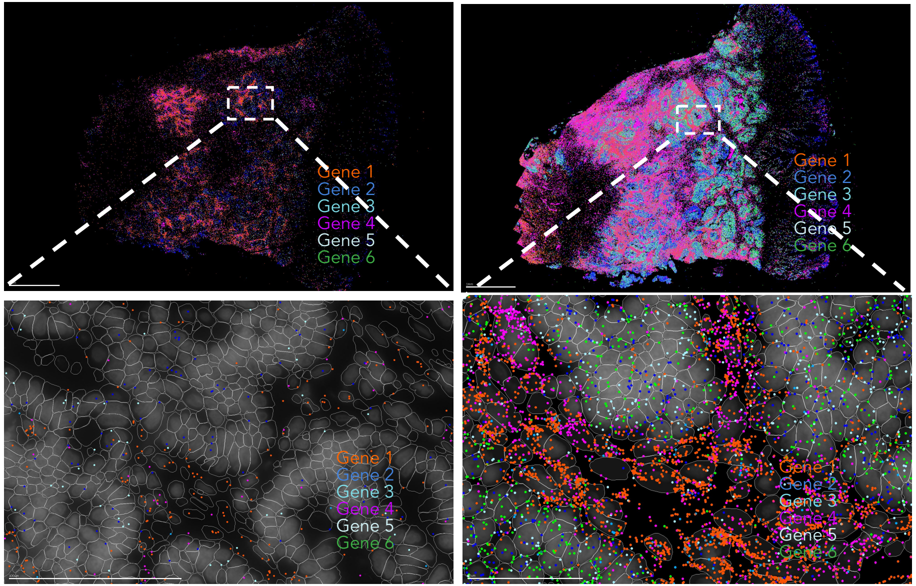
Improves differential gene expression analysis

Reduces cell drop out and improves spatial analysis

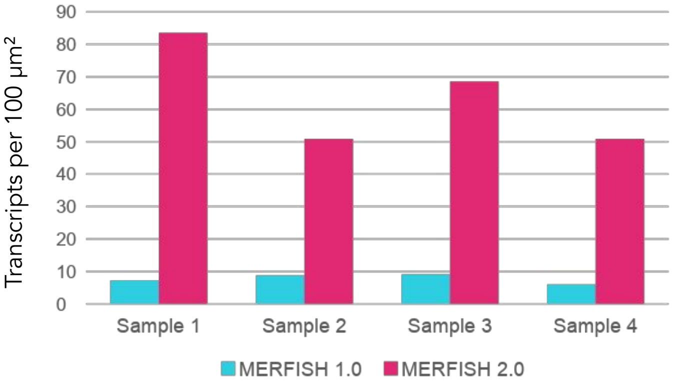
MERFISH 2.0 substantially improves transcript detection efficiency in FFPE human colorectal cancer samples

MERFISH 1.0

MERFISH 2.0



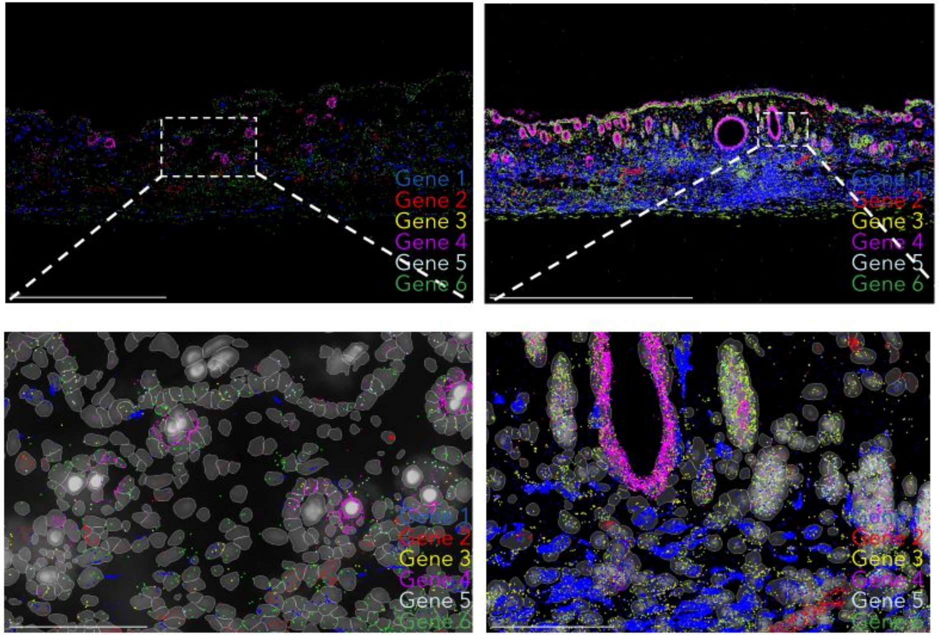
Comparison of detection efficiency



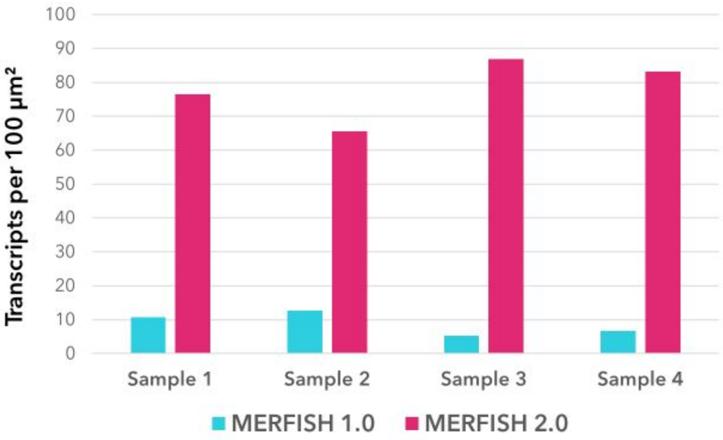
> "We decided on MERFISH due to the high sensitivity and the relatively low requirements for tissue samples. Our expectations were greatly surpassed by the astonishing (subcellular) resolution of MERFISH 2.0, especially when compared to MERFISH 1.0. This will allow us to mechanistically test the main hypothesis of the project using this data alone, Thank you very much!!!”
>
> University Hospital Tübingen, Germany

MERFISH 2.0 substantially improves transcript detection efficiency in FFPE mouse skin

MERFISH 1.0 **MERFISH 2.0**



Comparison of detection efficiency



Biotech Customer, USA

MERSCOPE enables ground-breaking research

PROFILE

Gene expression in situ across large tissue areas

Clinically relevant samples

CHARACTERIZE

Cell function and state

ANALYZE

Intracellular organization of the transcriptome

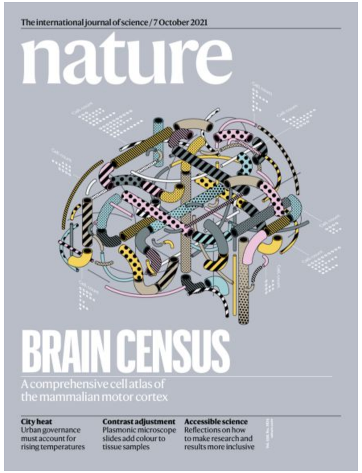
DISCOVER

and map cell types in complex tissues

No Follow-Up Sequencing Needed

Cell atlasing in mouse, non-human primate, and the human brain

Brain Census, *Nature*, 2021 Brain Cell Census, *Science*, *Science Advances*, 2023 Brain Maps, *Nature*, 2023


The international journal of science / 7 October 2021

nature

BRAIN CENSUS

A comprehensive cell atlas of the mammalian motor cortex

City heat
Urban governance must account for rising temperatures

Contrast adjustment
Plasmonic microscope slides add colour to tissue samples

Accessible science
Reflections on how to make research and results more inclusive


A naturalist goes to bat for Mexico's biodiversity p. 144

Adapting COVID-19 booster vaccines to variants p. 157

Spin selectivity across a chiral bridge pp. 160 & 197

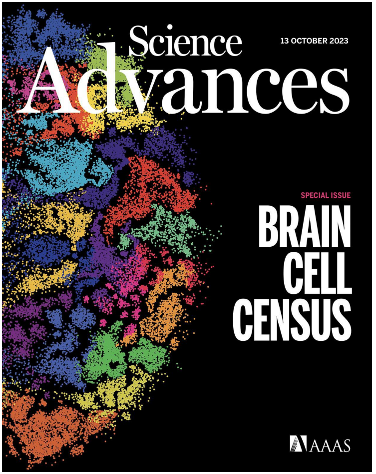
Science

$15
13 OCTOBER 2023
science.org

AAAS

SPECIAL ISSUE

BRAIN CELL CENSUS

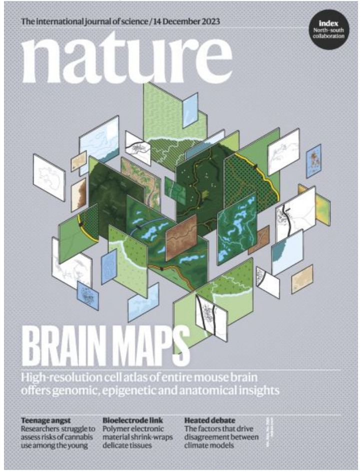

Science Advances

13 OCTOBER 2023

SPECIAL ISSUE

BRAIN CELL CENSUS

AAAS


The international journal of science / 14 December 2023

index
North-south collaboration

nature

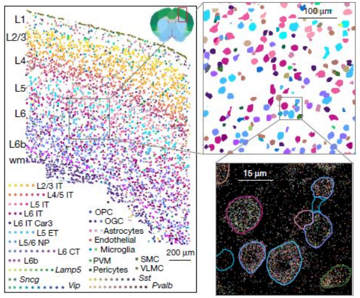
BRAIN MAPS

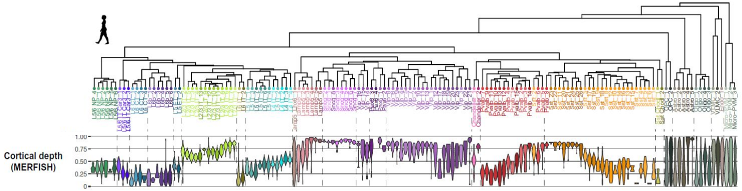
High-resolution cell atlas of entire mouse brain offers genomic, epigenetic and anatomical insights

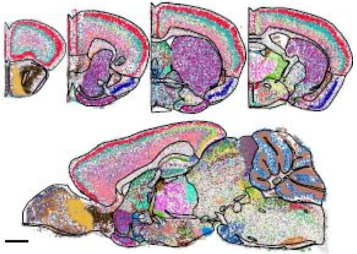
Teenage angst
Researchers struggle to assess risks of cannabis use among the young

Bioelectrode link
Polymer electronic material shrink-wraps delicate tissues

Heated debate
The factors that drive disagreement between climate models





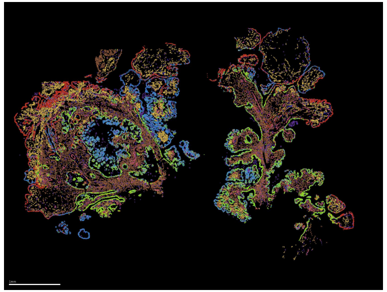


A total of 7 *Nature* papers, 6 *Science* papers, and 1 *Nature Methods* paper used MERFISH and MERSCOPE

BRAIN Initiative Cell Census Network (BICCN), *Nature* 2021, *Science*, *Science Advances*, *Science Translational Medicine*, 2023, *Nature* 2023

Spatially Resolved Single-Cell Transcriptomic Imaging in Oncology

Cancer cell atlasing

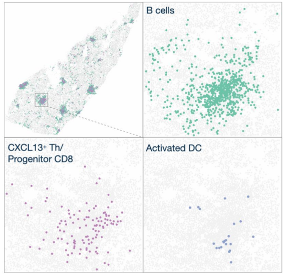


- https://info.vizgen.com/merscope-ffpe-solution

Mechanism of action for PD1 treatment in human liver and lung cancer

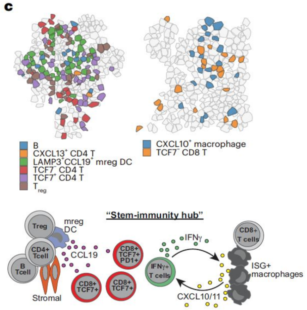
Mt. Sinai

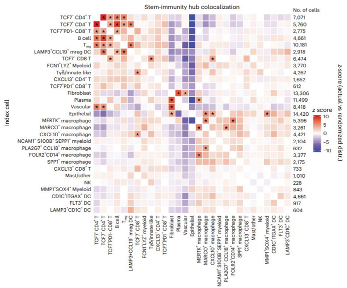
In-situ map of responder's tumor



Magen. et al, Nature Medicine, 2023

MGH

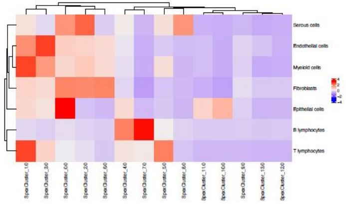


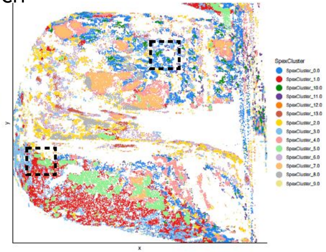


Chen et al, Nature Immunology, 2024

Cancer signaling pathway profiling and biomarker discovery

Genentech

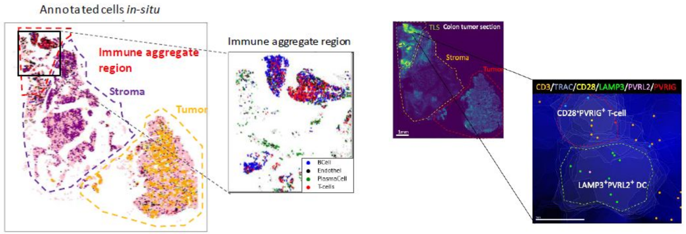




Pechuan-Jorge, et al, BioRxiv, 2022

Mechanism of action for novel therapeutic target

Compugen



Alteber et al, Cancer Immunology Research 2024

MERSCOPE Advantages

Pushing the boundaries of spatial transcriptomics

Effective Multiplexing

Cover 100's or even 1,000's of genes in a single sample, custom gene panel, protein co-detection

Cell Throughput

Up to millions of cells in a single sample and greatly reduced cost per cell

Resolution

From whole tissue section to single cell and sub-cellular imaging

Flexibility

Ability to run on many sample or tissue types

Sensitivity and Specificity

Highest detection efficiency for identifying RNA

For More Information

Website

www.vizgen.com

Email

info@vizgen.com

LinkedIn

linkedin.com/company/vizgen

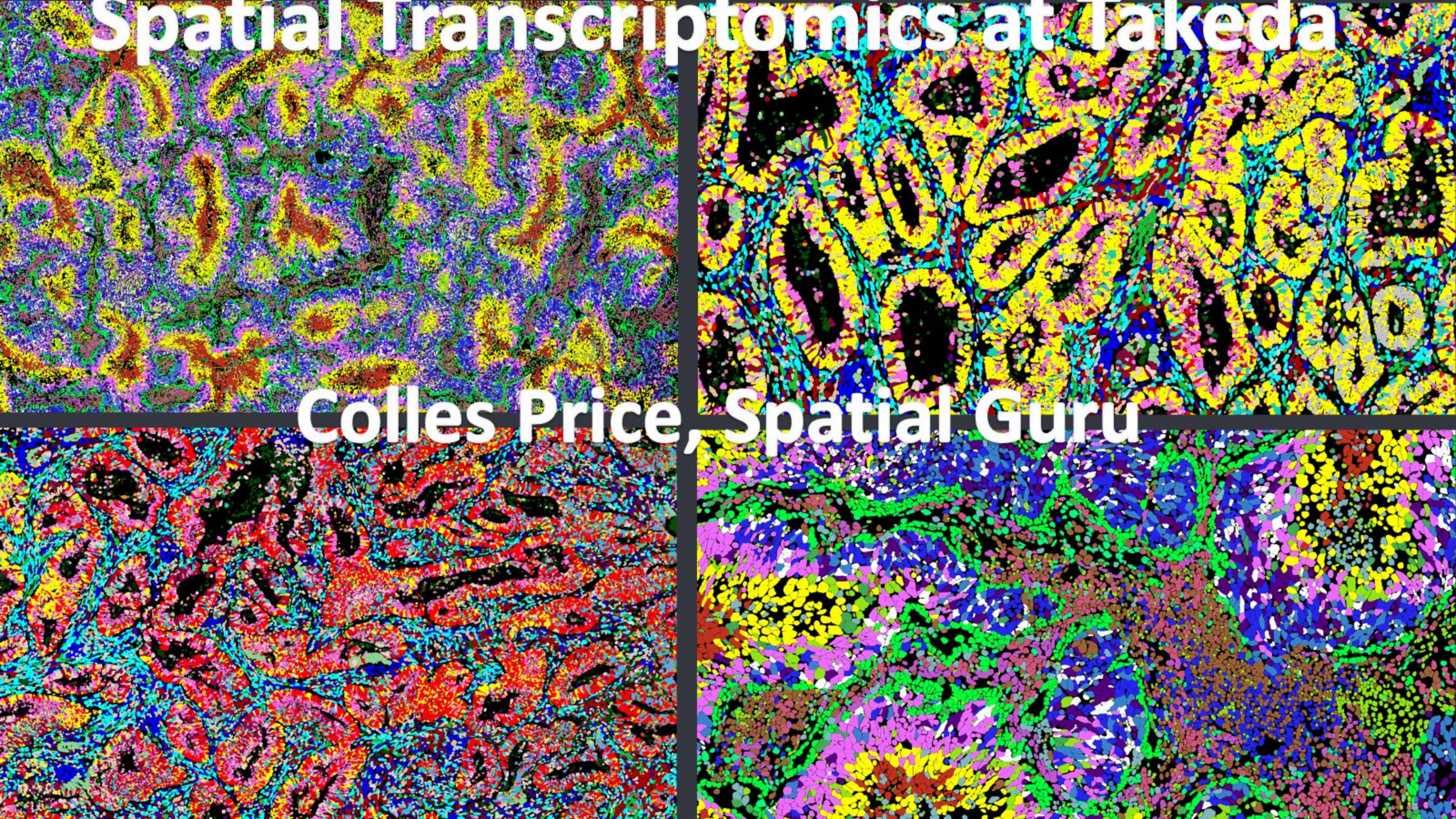
Twitter

@vizgen_inc

vizgen

Price Colles, *Takeda*

Spatial Transcriptomics at Takeda



Colles Price, Spatial Guru

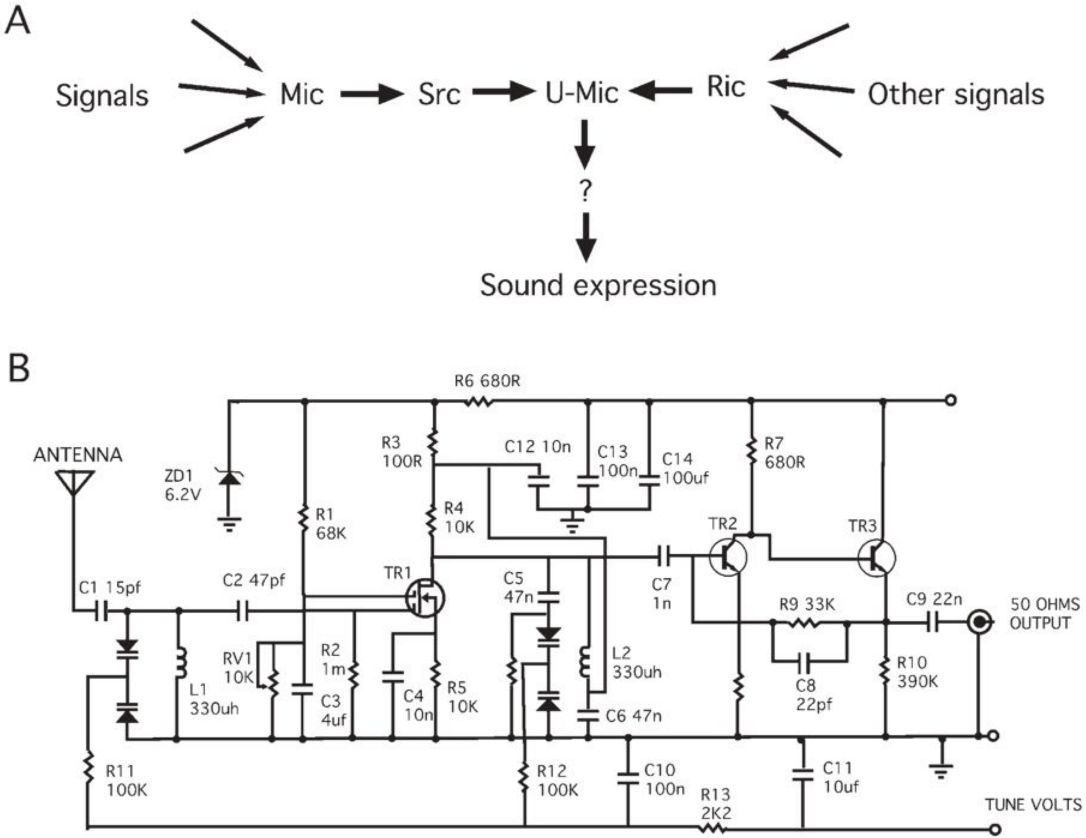


Figure 3. The tools used by biologists and engineers to describe processes of interest

Lazebnik 2002

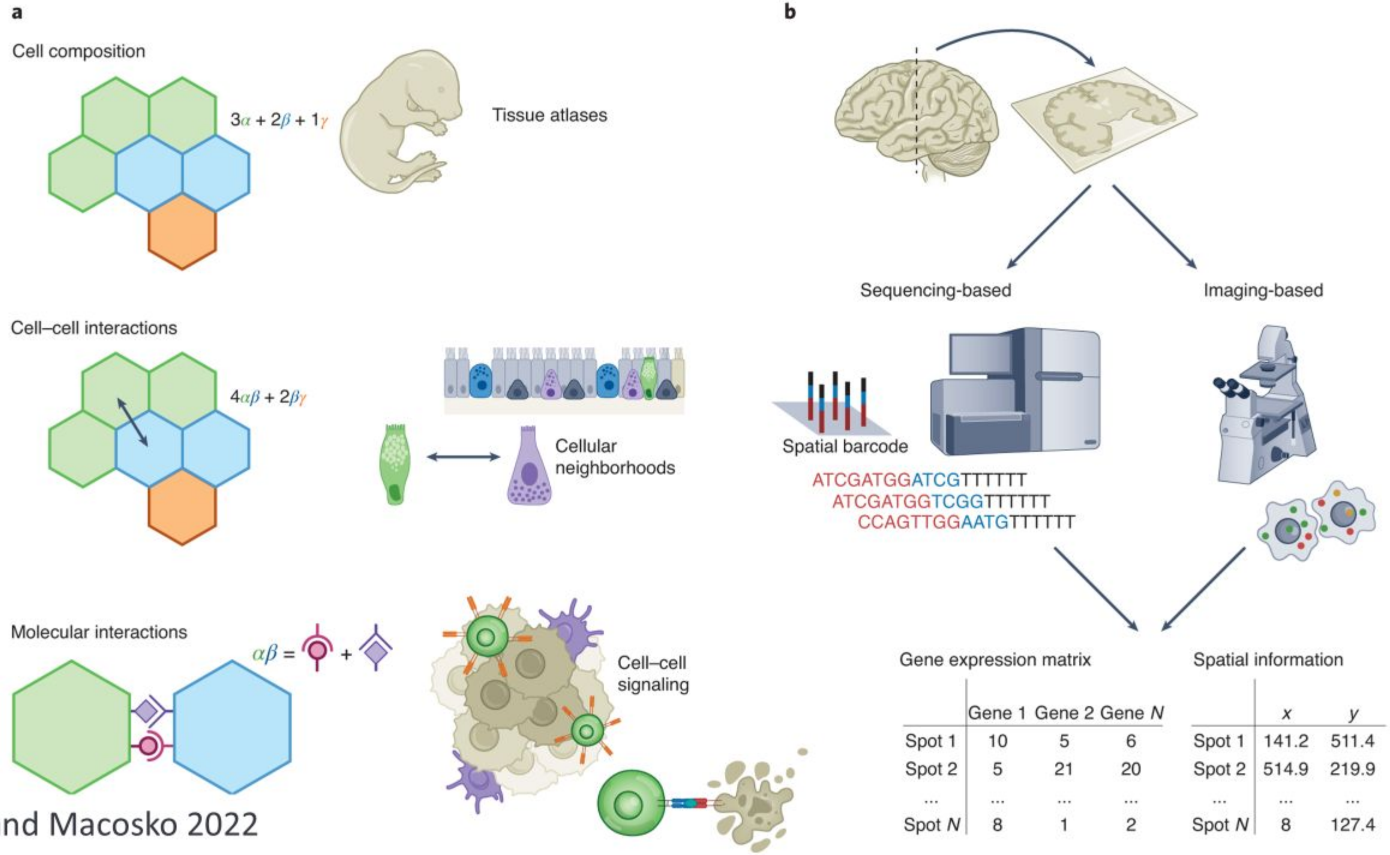
As technologies and methods have evolved throughout the years we discovered how important context is to understanding human biology

Bulk

Single Cell

Spatial

Spatial Transcriptomics, broken into either sequencing or imaging based technologies, have been used for tissue atlases, cell-interactions and complex signaling



Gene expression matrix

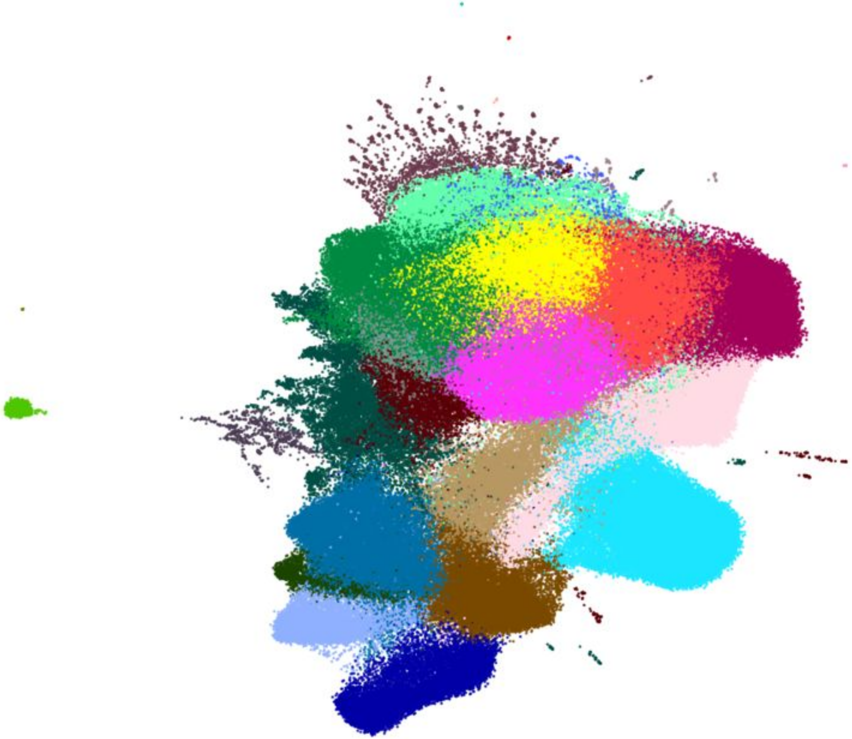
	Gene 1	Gene 2	Gene *N*
Spot 1	10	5	6
Spot 2	5	21	20
...	...	...	...
Spot *N*	8	1	2

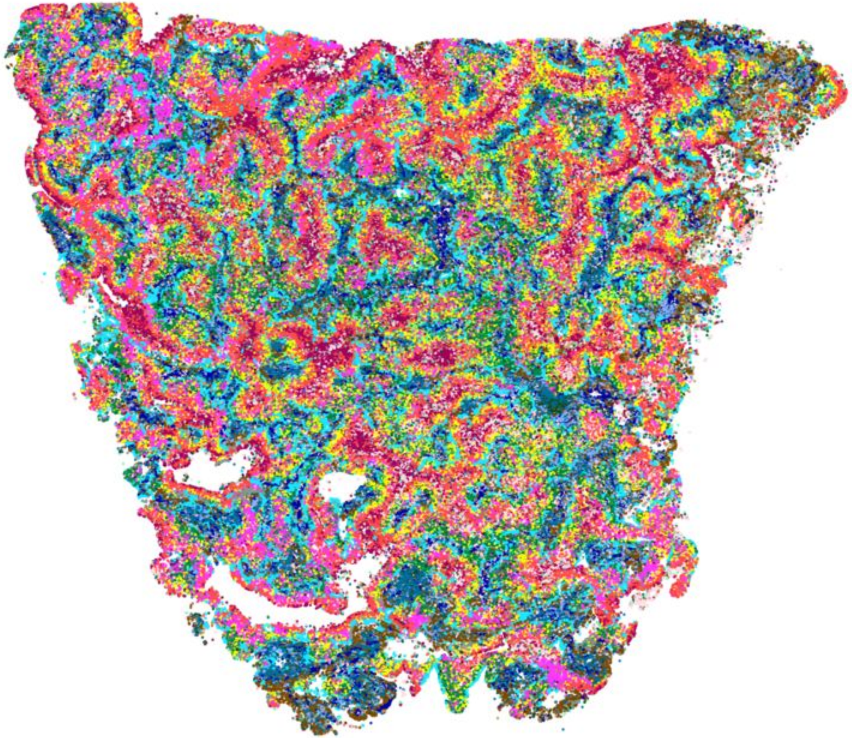
Spatial information

	x	*y*
Spot 1	141.2	511.4
Spot 2	514.9	219.9
...	...	...
Spot *N*	8	127.4

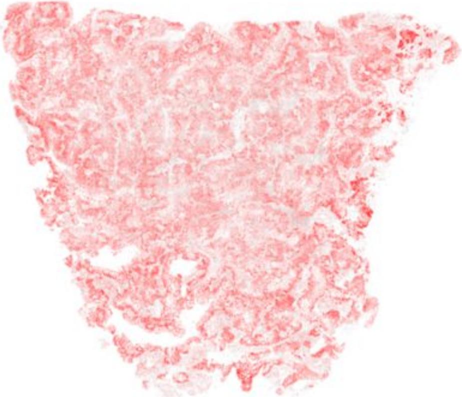
Tien, Chen and Macosko 2022

We can do generate UMAPs from spatial data and map those clusters onto the tissue

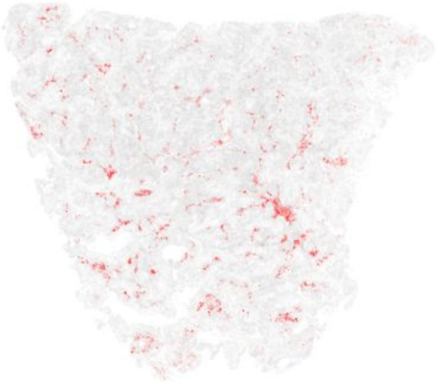




Spatial transcriptomics can visualize numerous genes individually or together on a tissue

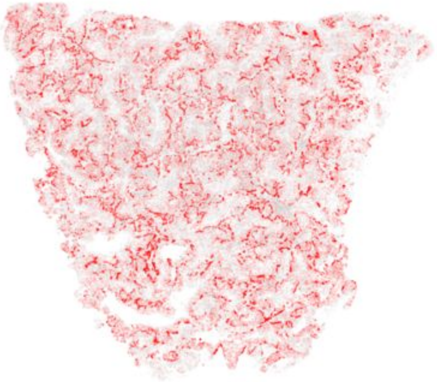


AKT1

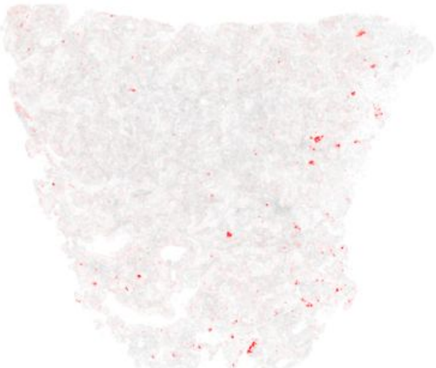


CD79A

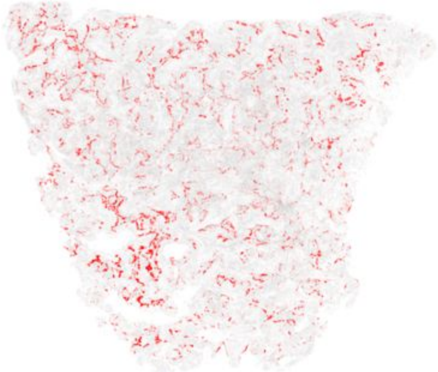
COL1A1



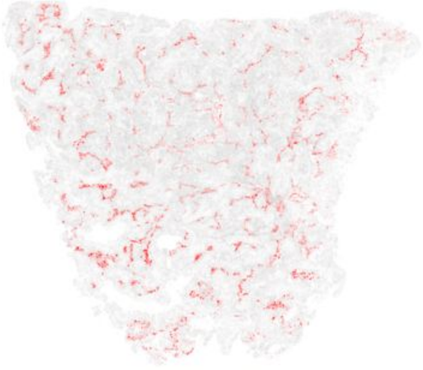
ERBB2



IOD1



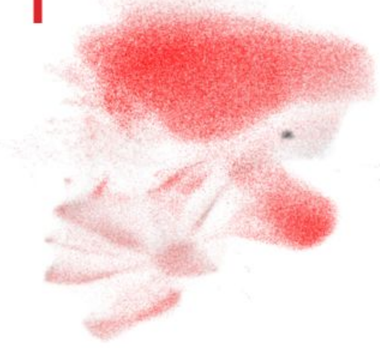
LAG3



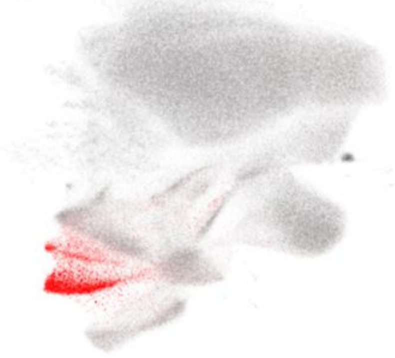
PECAM1

VEGFA

Spatial transcriptomics can visualize genes in their UMAP cluster



AKT1

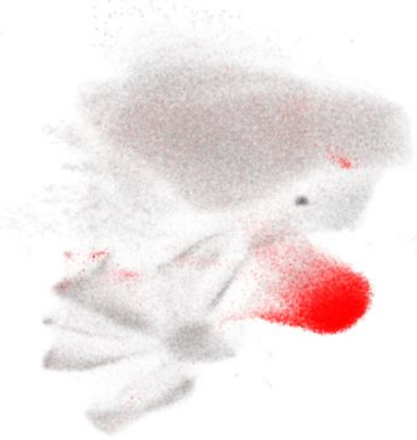


CD79A

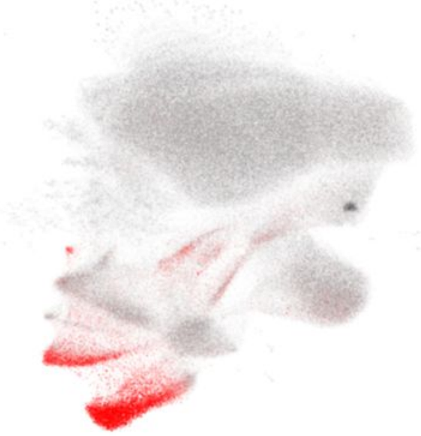
COL1A1

ERBB2

IOD1



LAG3

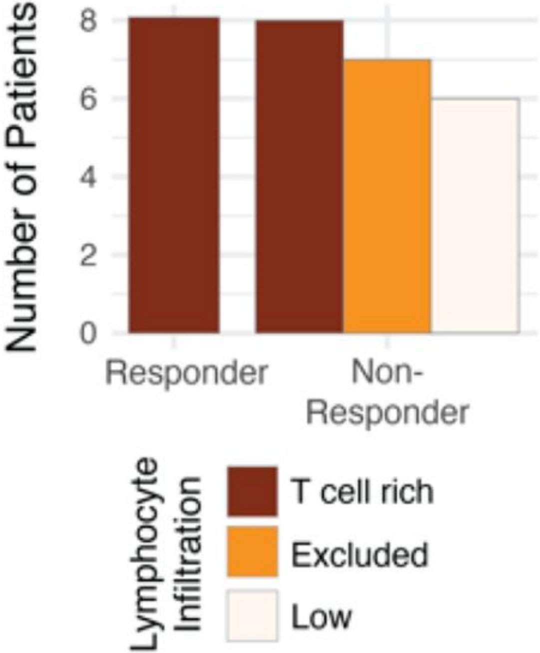


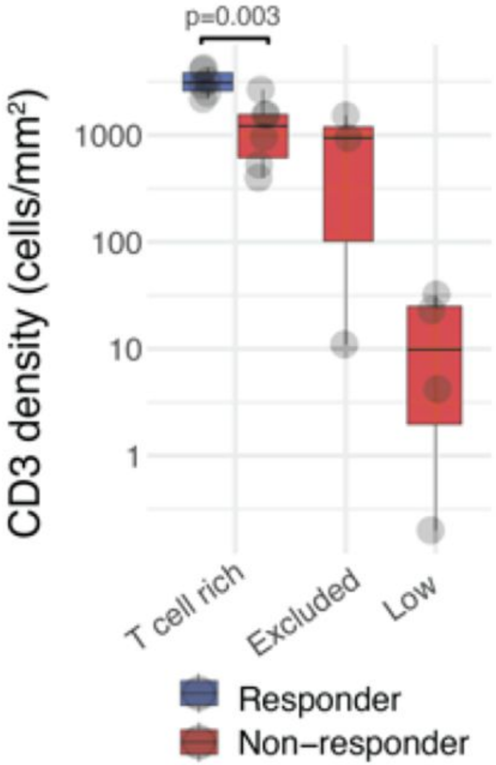
PECAM1

VEGFA

Spatial transcriptomics can be used clinically to identify patients who would best benefit from therapy

Despite presenting with a large amount of T cells some patients don't respond to immune checkpoint blockade (ICB)

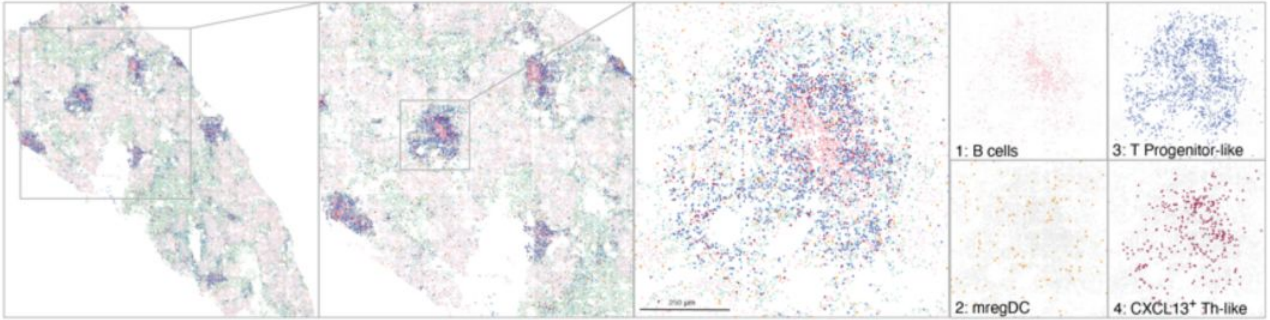




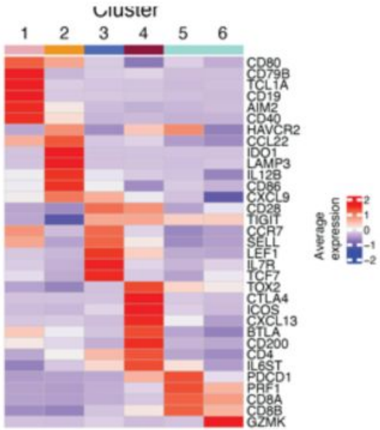
Identify and profile the T-cell population within responders and nonresponders following immune checkpoint blockage in a clinical trial

This study was able to reduce prediction of response to a single IHC marker which is now being used to help stratify patients in a new clinical trial (new manuscript pending)

C



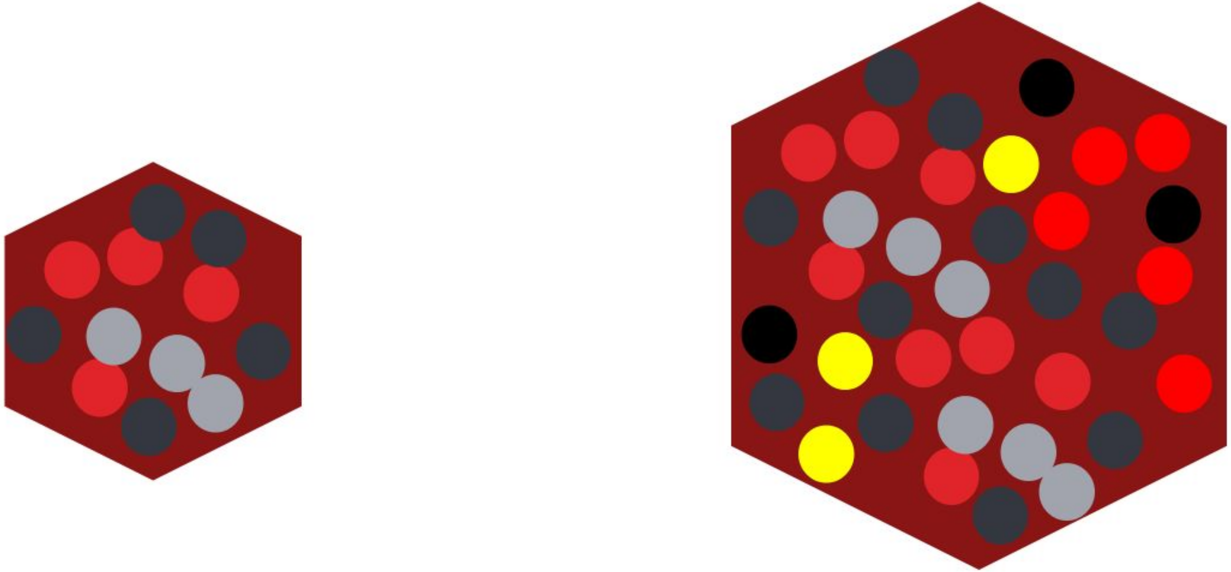
D



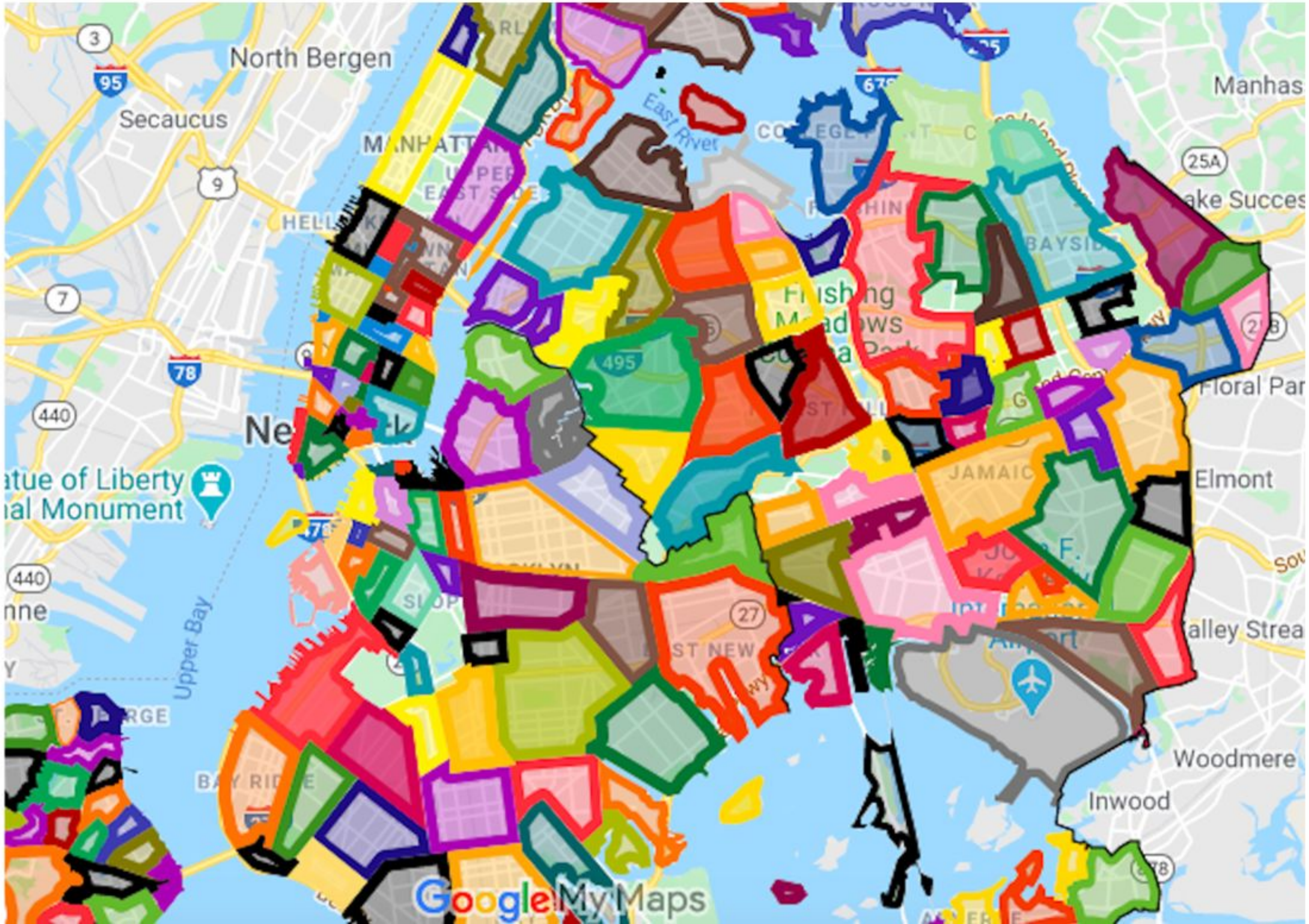
Magen et al 2023 *Nat Med*

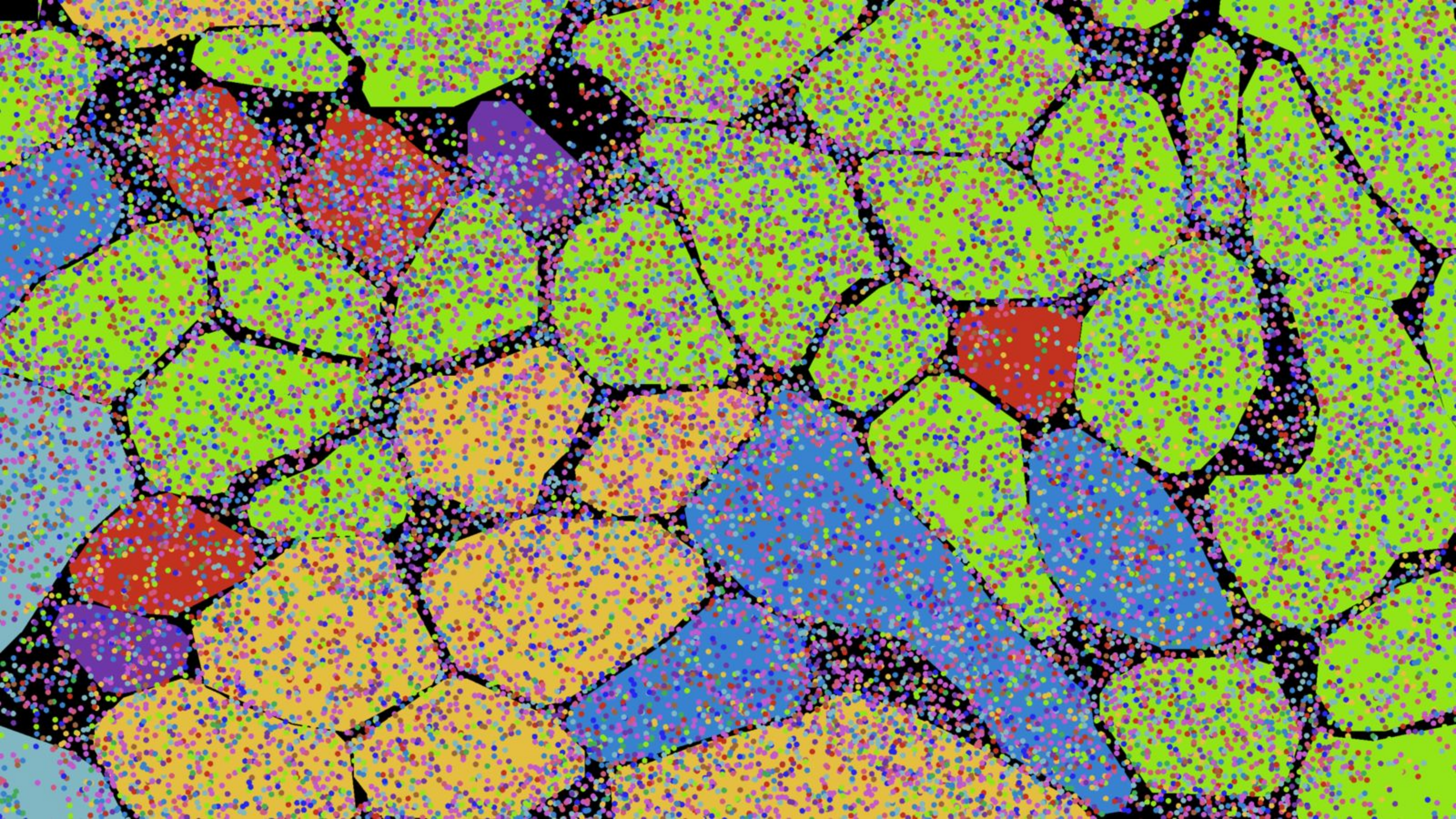
Different approaches to defining neighborhoods provides insight into human biology and human atlases

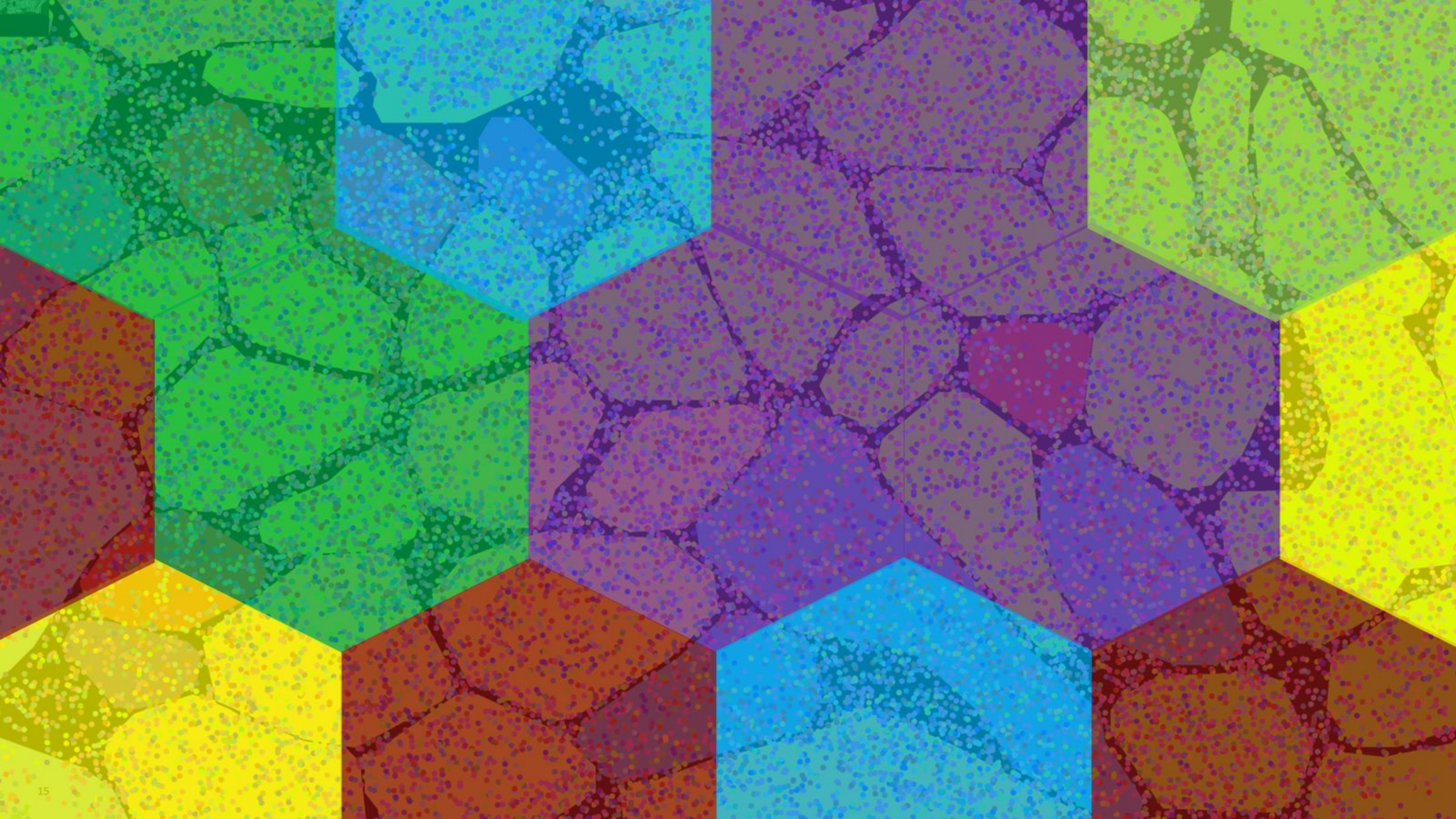
By defining a neighborhood of diverse cells and cell types we can look at how these communities interact with other communities or how communities interact within communities

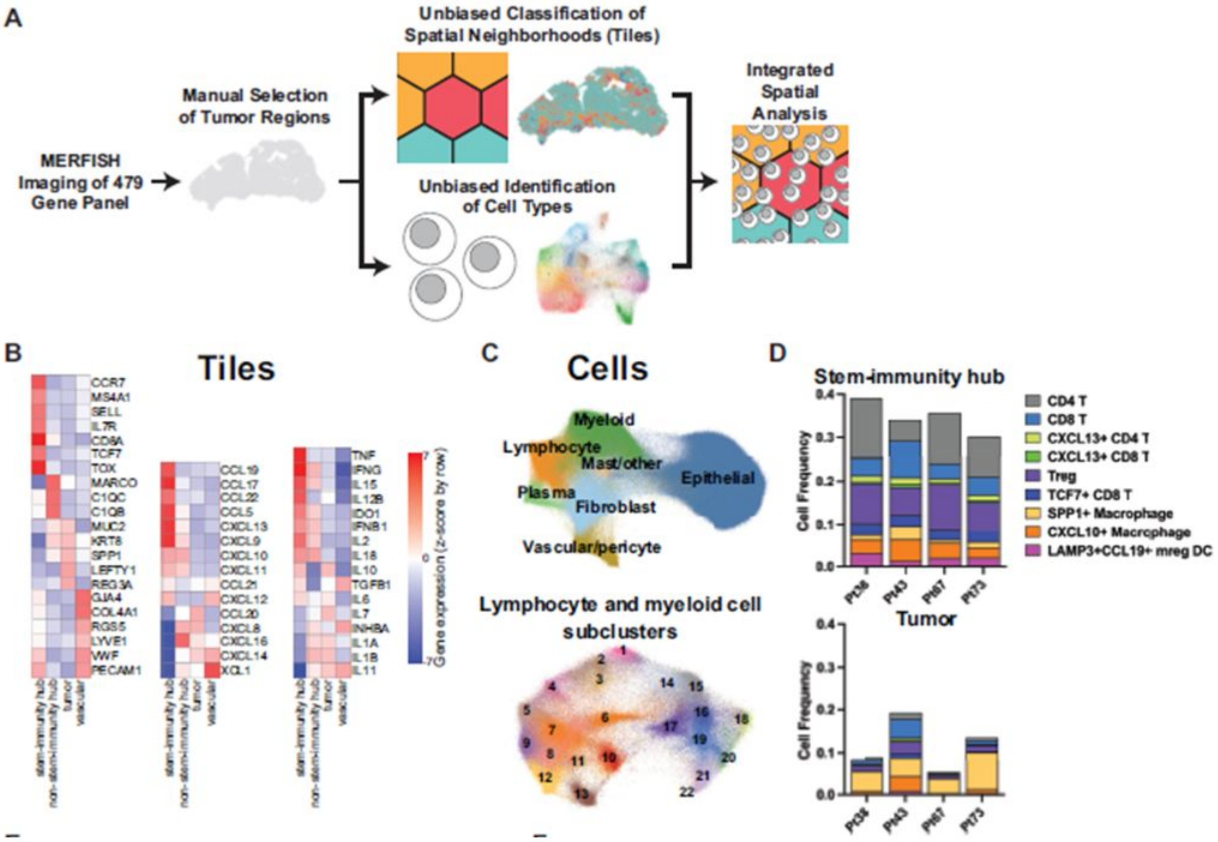


Similar concept – looking at the defined regions (neighborhoods) in NYC and identifying the populations within those regions



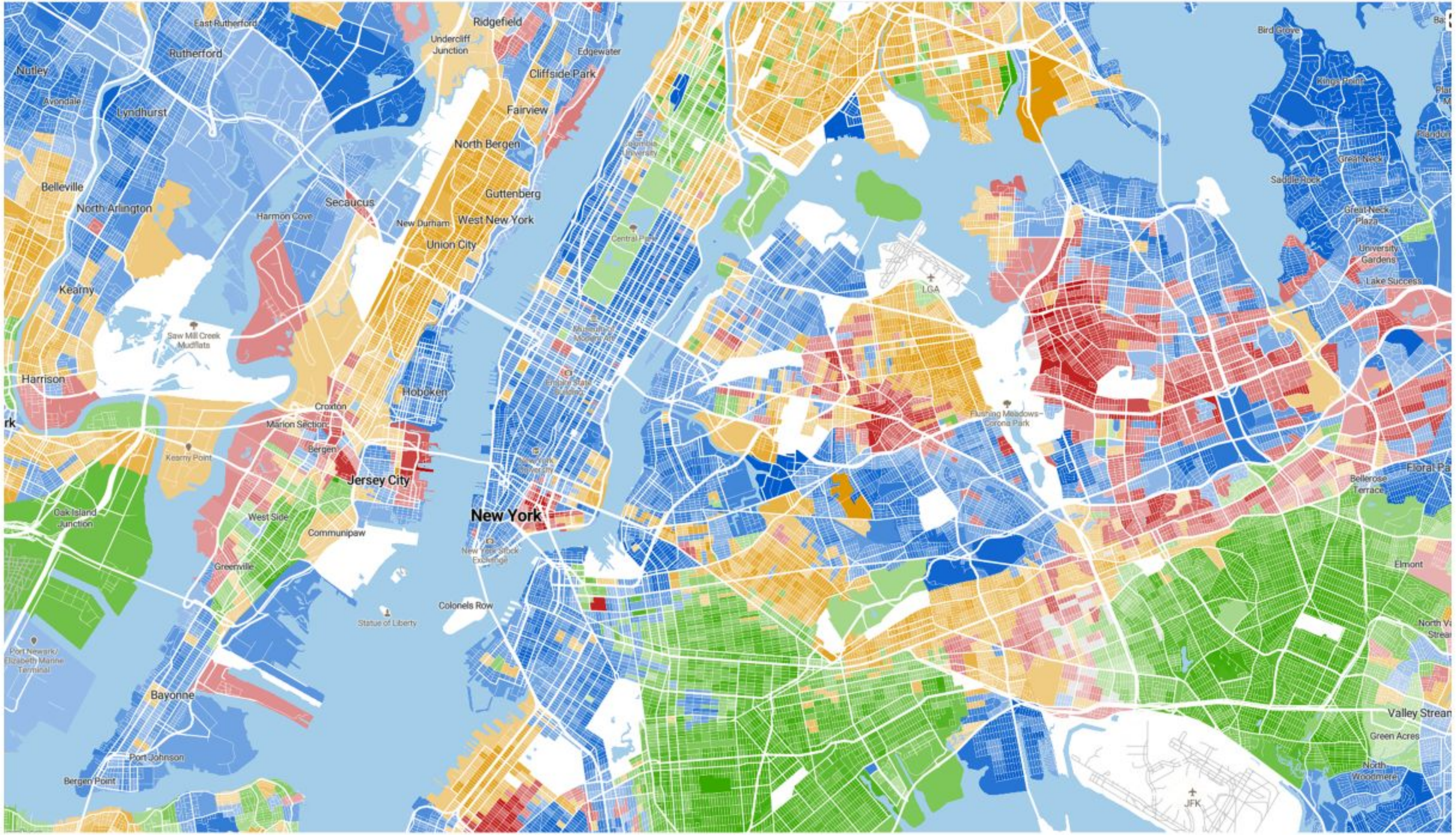






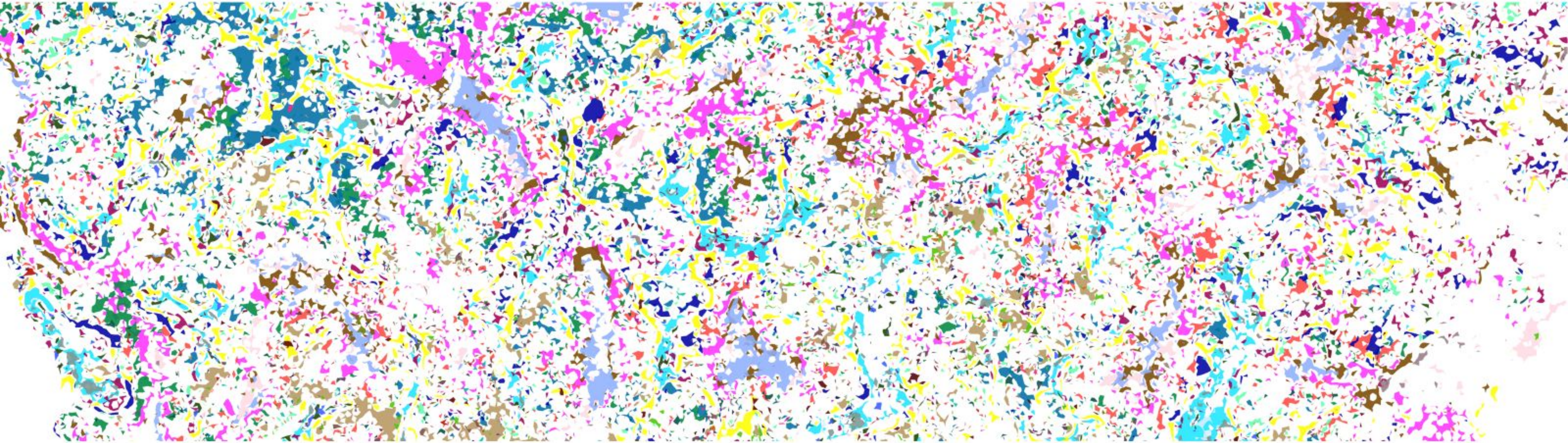
Chen et al 2024 *Nat Immunity* 2024

Similar approach is defining neighborhoods, not by regions but by demographics



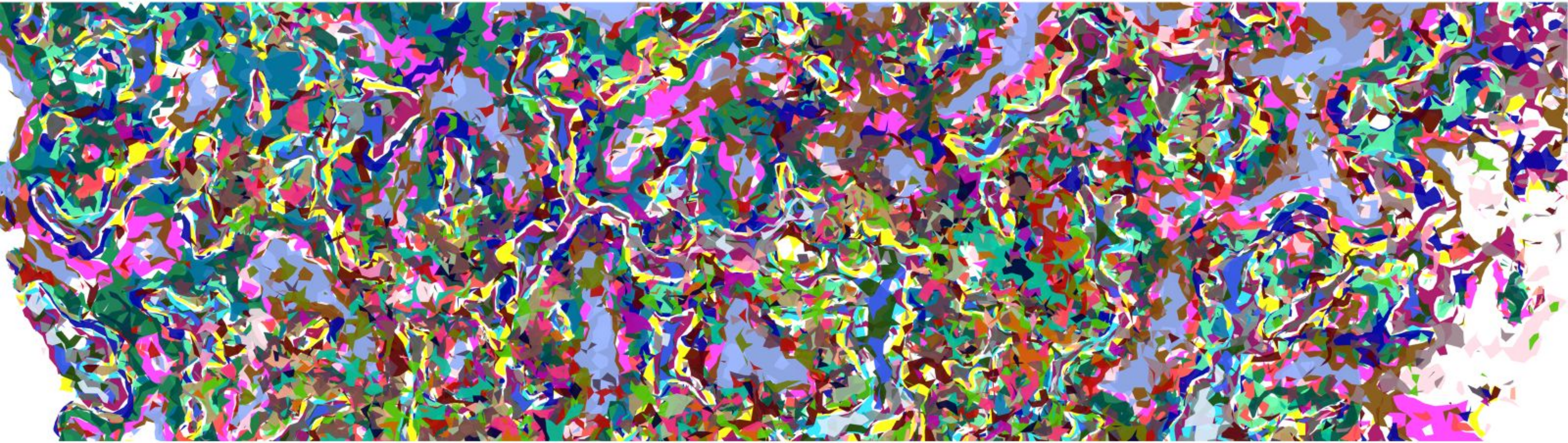
How to build a neighborhood based on cellular demographics - alpha shape

Ideally need to choose the right size threshold to choose – too little



Ideally need to choose the right size threshold to choose – too big

Ideally need to choose the right size threshold to choose – just right

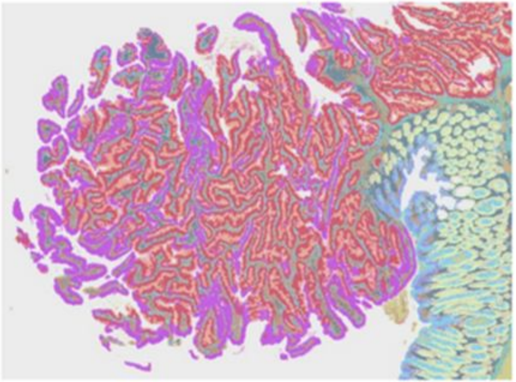


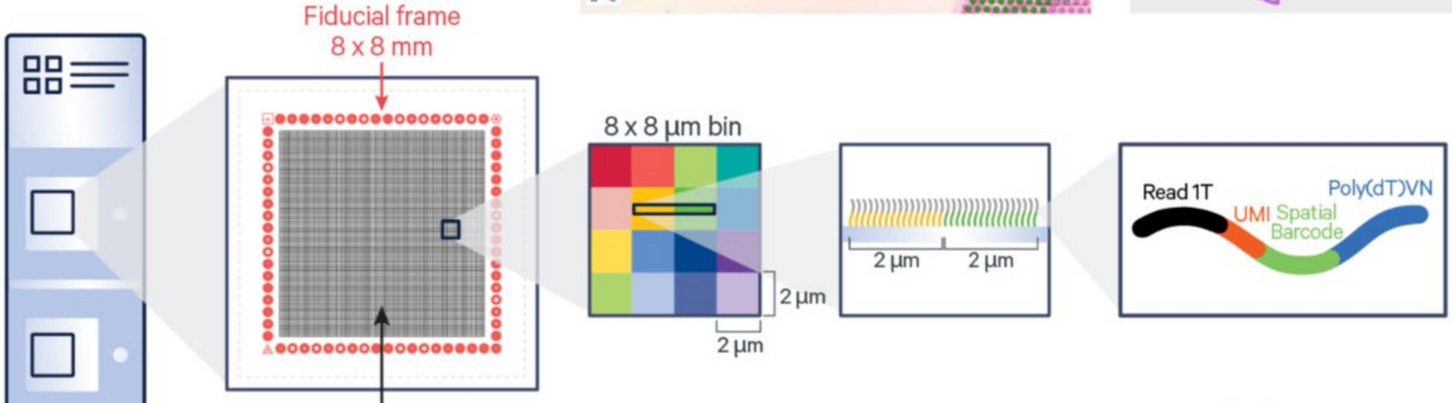
Imaging based spatial methods are incredibly powerful and provide a high resolution view in biology across an entire tissue but require previous knowledge to choose genes of interest. Sequencing based methods have significantly improved over the past few years

Visium HD is a dramatic increase in resolution compared to Visium (sequencing based assays)

Visium

Visium HD





Visium HD Slide, 6.5 mm

Capture Area with continuous lawn of oligos, 6.5 x 6.5 mm

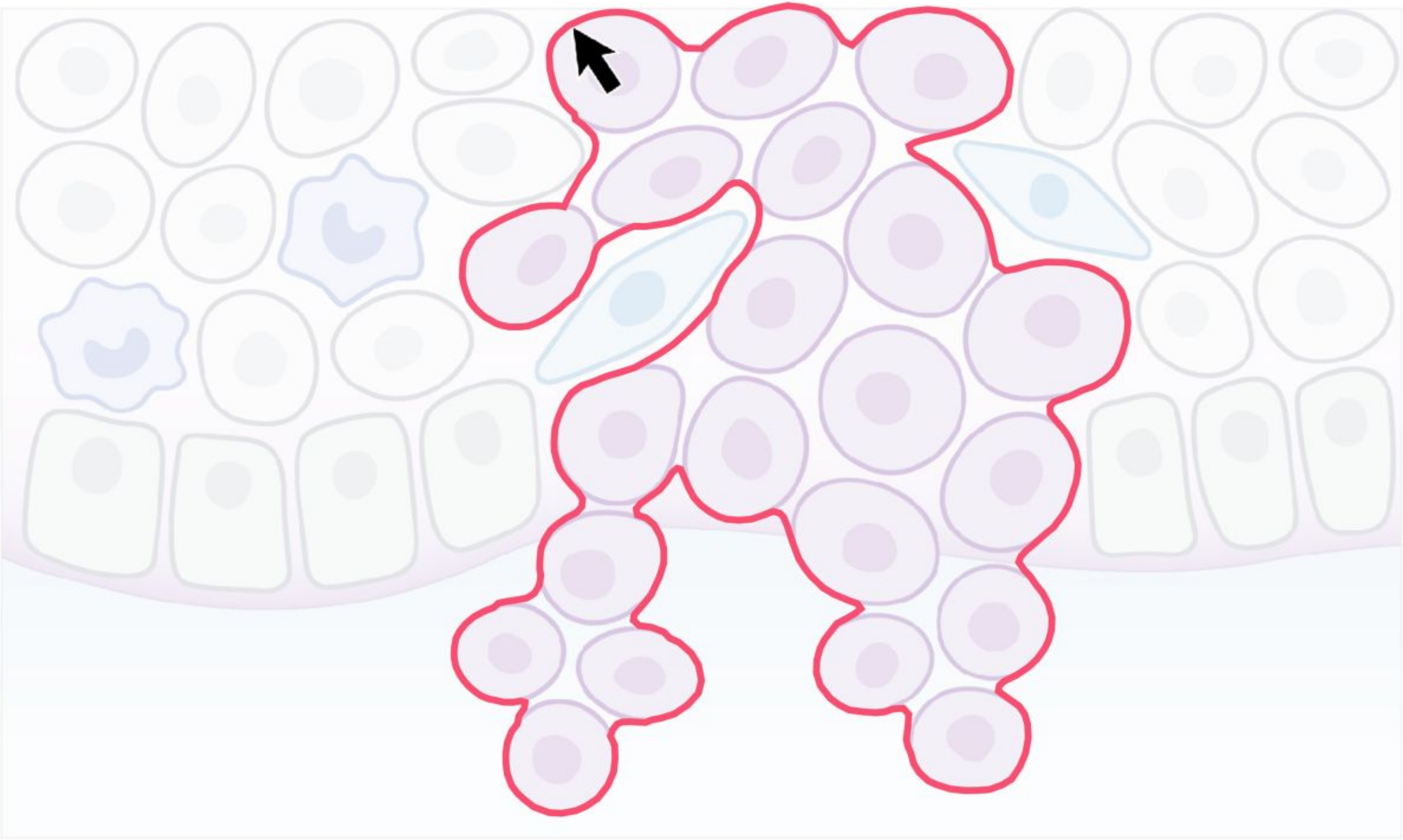
Grid of 2 x 2 µm barcoded squares, binned to 8 x 8 µm

Oligo with Spatial Barcode

10X Genomics

Sequencing based approaches can isolate different cellular populations on a tissue

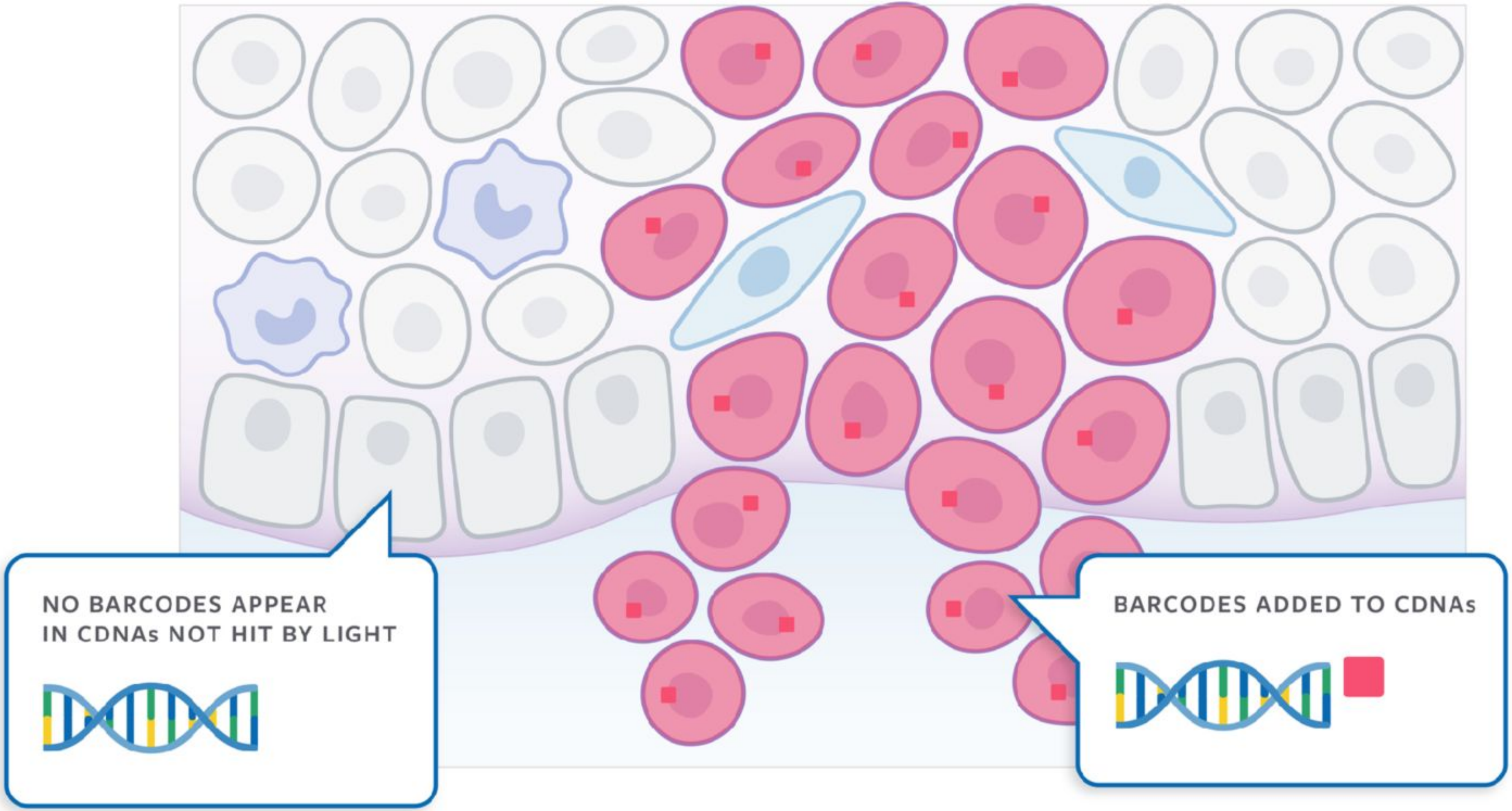
BARCODE 1 🟥



BARCODE 1 🟥

Digital Biology

BARCODE 1 🟥

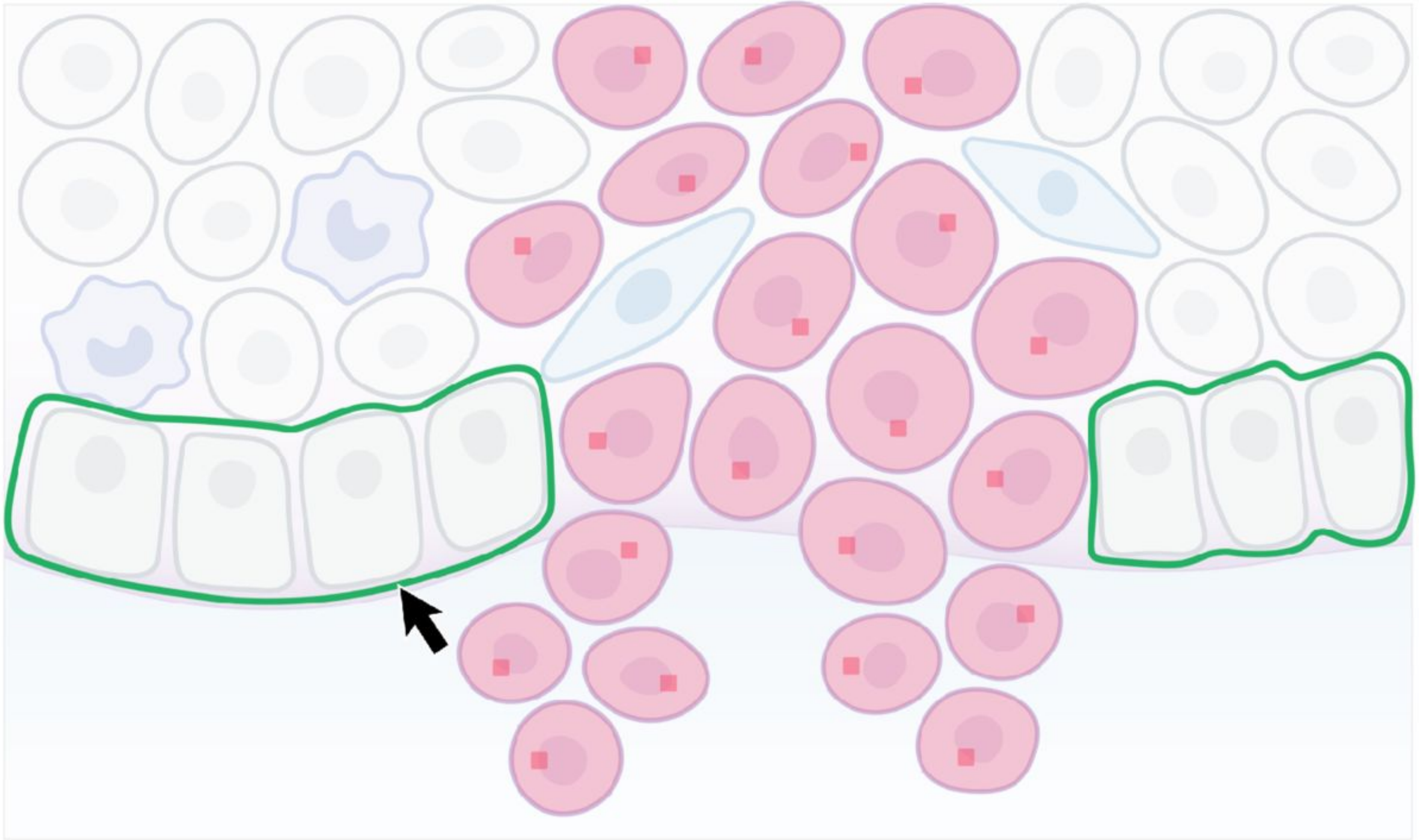


NO BARCODES APPEAR IN CDNAs NOT HIT BY LIGHT

BARCODES ADDED TO CDNAs

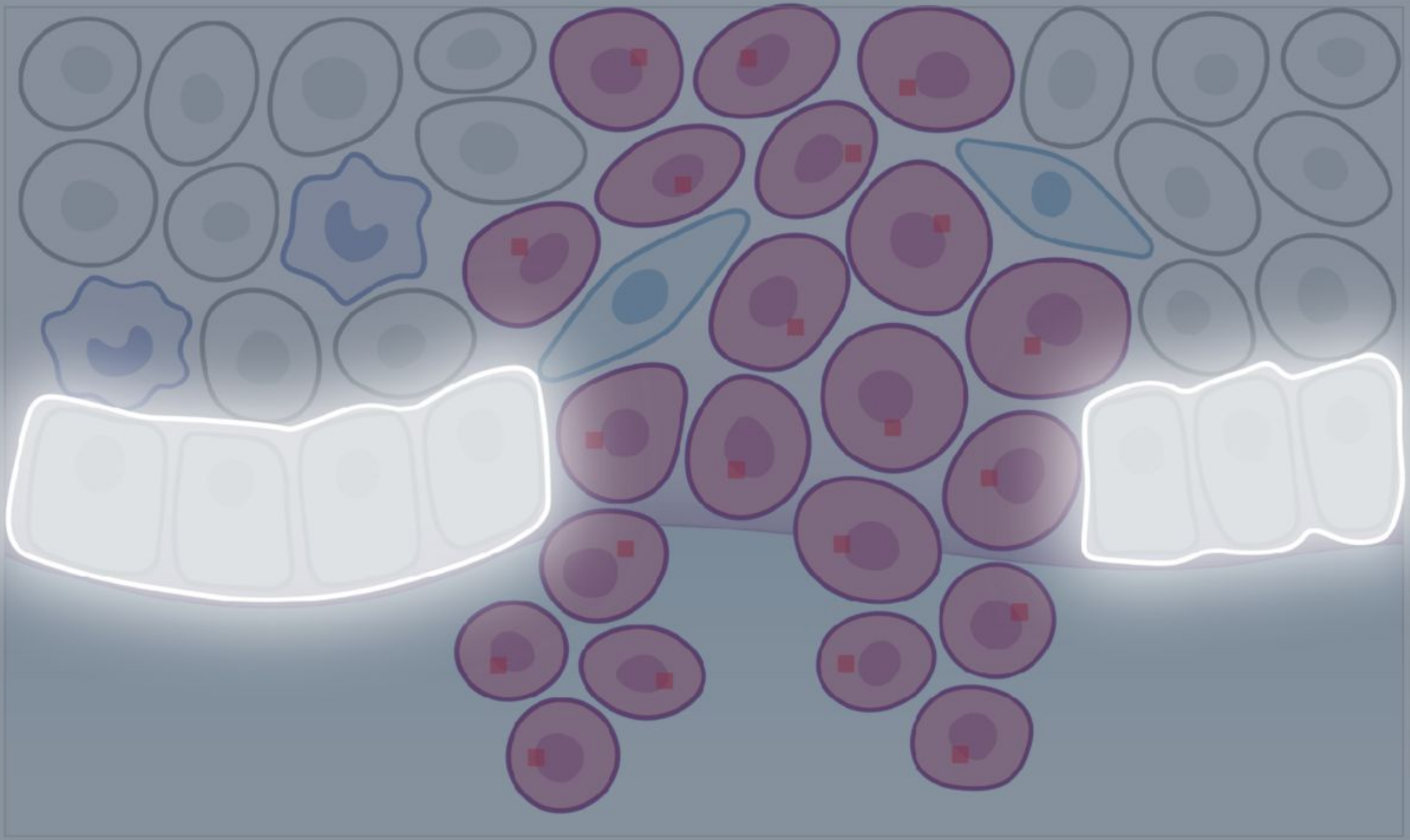
Digital Biology

BARCODE 2 🟩

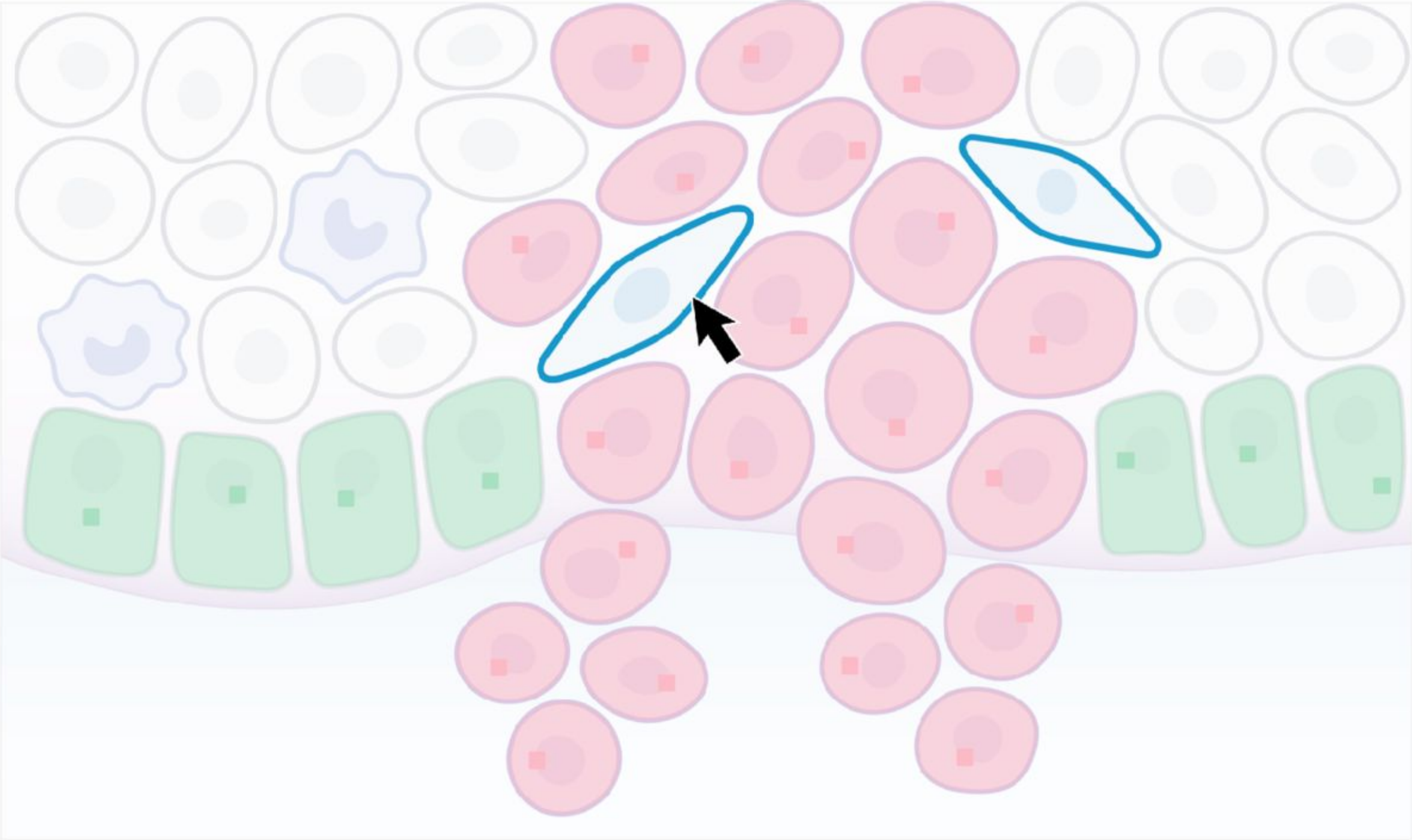


Digital Biology

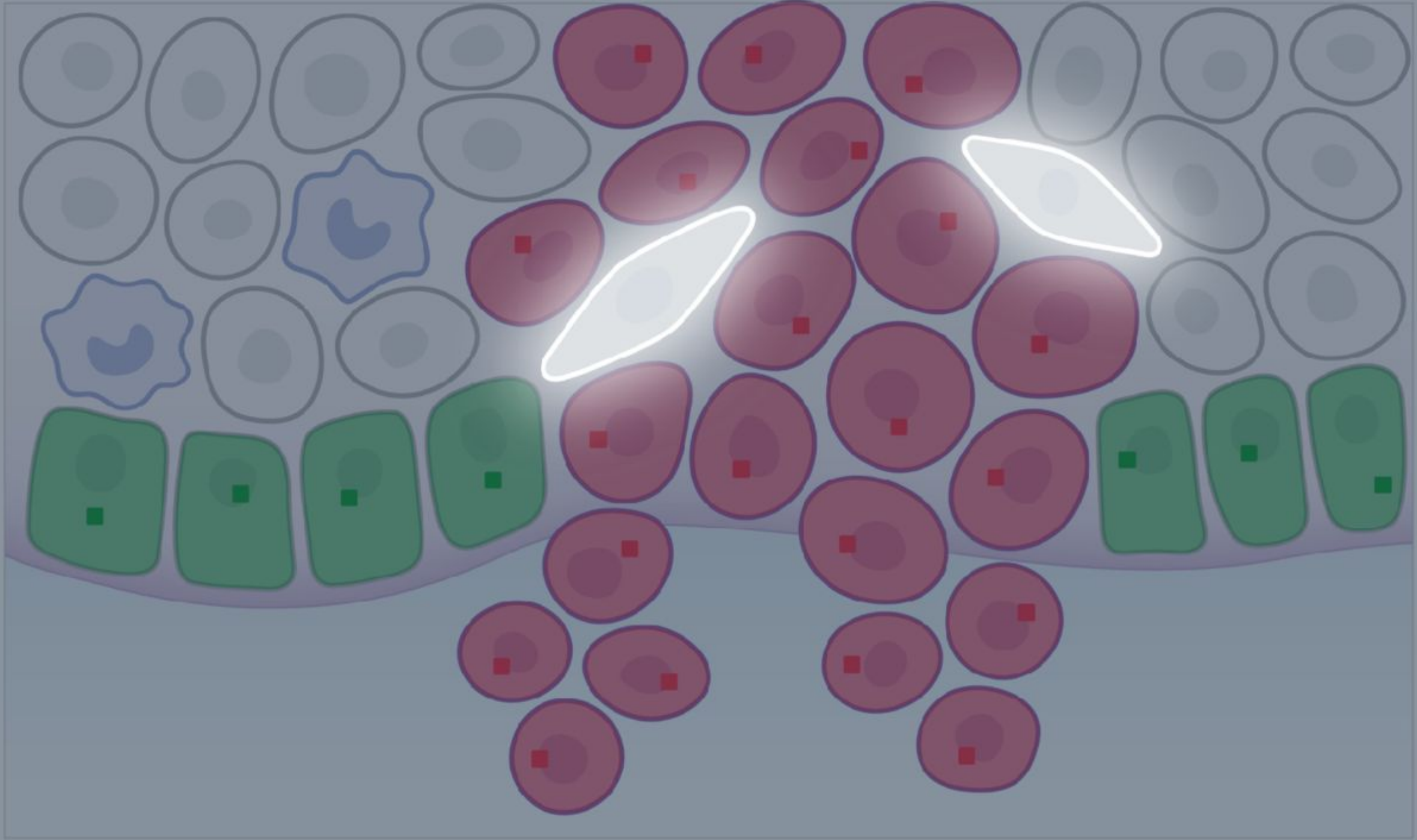
BARCODE 2 🟩

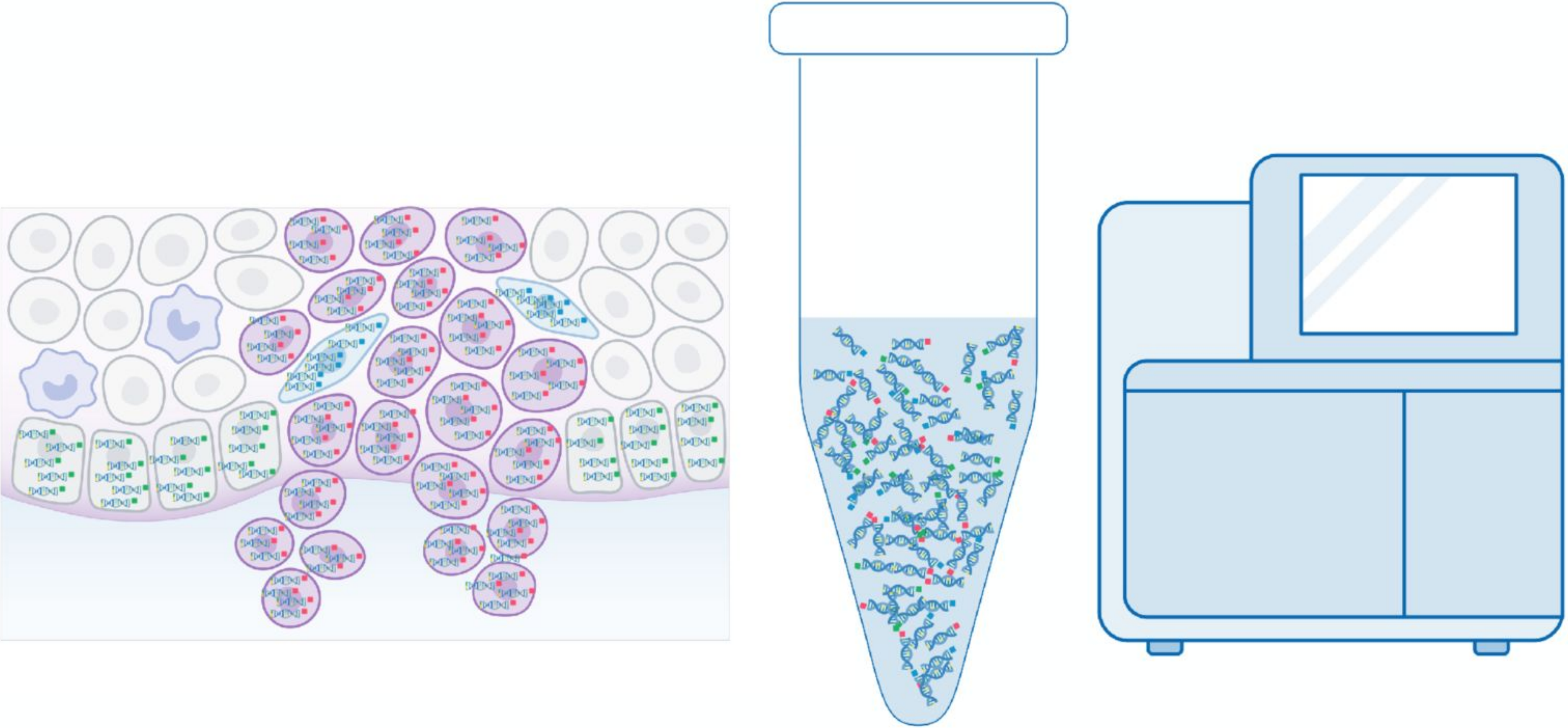


BARCODE 3 🟦

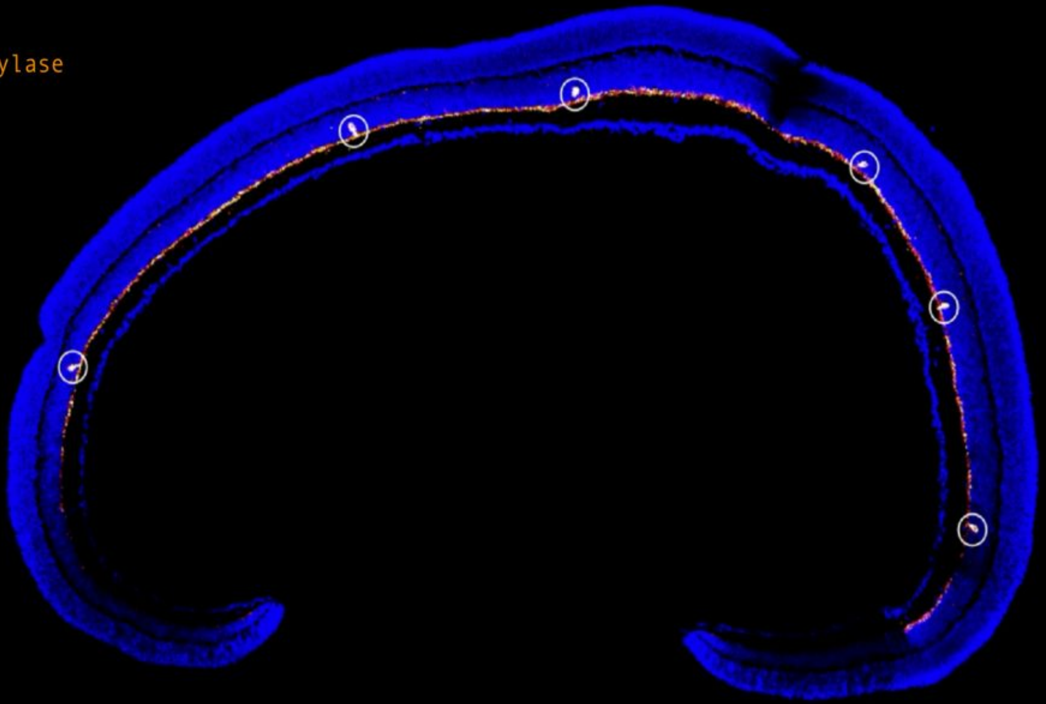


BARCODE 3

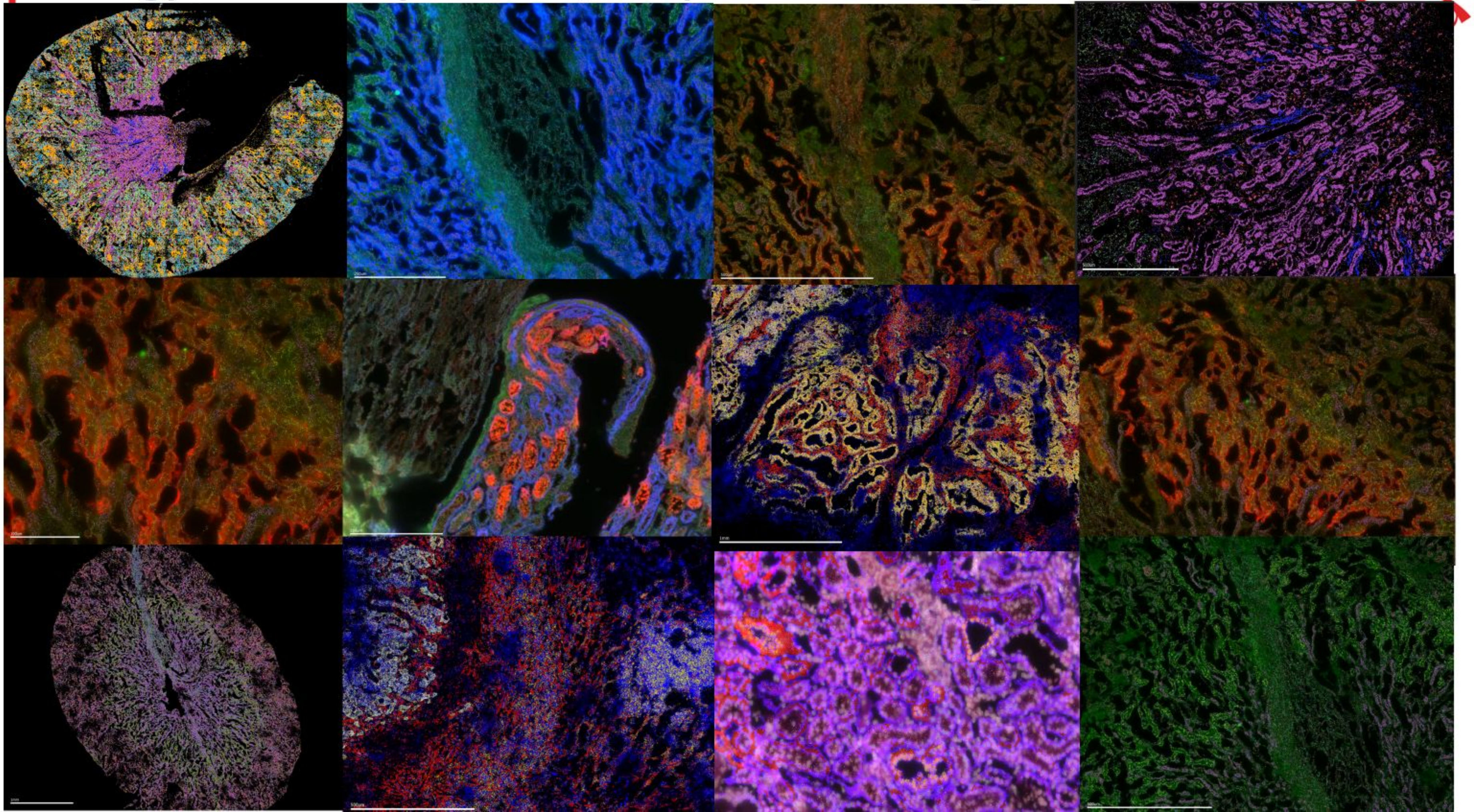




Dopaminergic amacrine cells represent 0.005% of all cells in the mouse retina, with only 4-8 cells per 18 μm tissue section.



Biology is incredibly intricate, complex and striking



The application of spatial technology to human biology is only limited by your mind and your question.

Tissue annotation

Cell Annotation

Nearest Neighbor Analysis

Cell Mobility and Chemokine signaling

Clustering of cells (and cellular deviation)

Subcellular quantification

Identification of cell states

Drug response (and other functional disruption)

Integration with other omic data

Three dimensional reconstruction

Generate beautiful images

> “You want your technology limited by the question you ask, not the question you ask limited by your technology”

> “You want your technology limited by the question you ask, not the question you ask limited by your technology”
>
> -Colles Price

Acknowledgements -

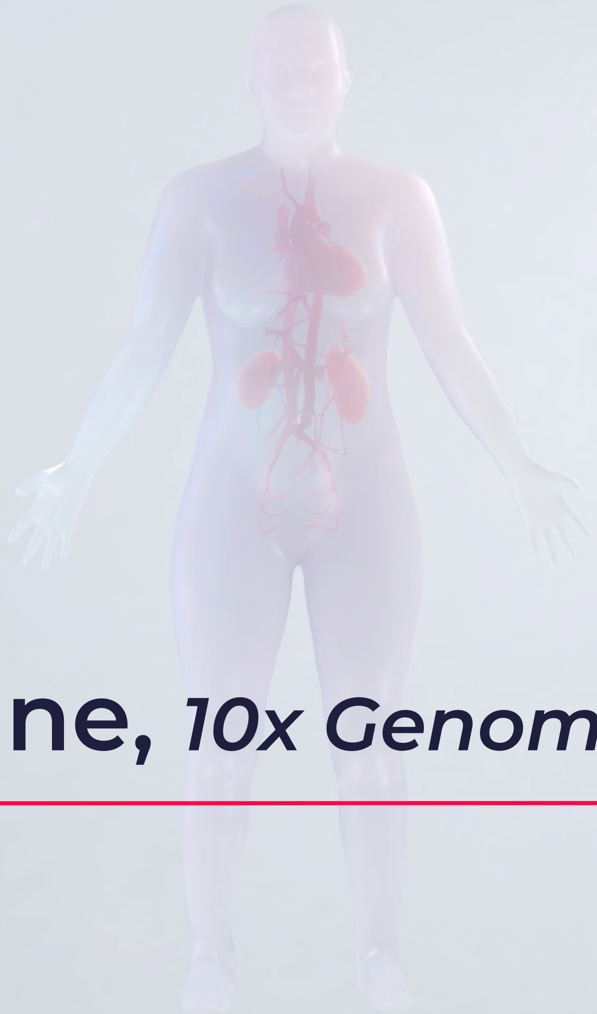
- Experimental and Molecular Pathology
  - Russell Weiner
  - Darrell Borger
  - Alina Ainbender
  - Joao Costa
  - Brad Stringer
  - Stefan Collins
  - Chris Gallego Lazo
  - Jacqueline Cerbone
  - Sarah Fortin
  - Cassandra Kilsolvsky
  - Hank Reinhart
  - Kenny Trieu
  - Brittany Scott
  - Yury Sheykin

Organizers of 24HR of amazing biology and talks!!!!!

- Takeda
- Several Takeda departments
- ***Broad Institute***
- Mt. Sinai
- MGH
- Harvard Medical School
- Dana Farber Cancer Institute
- Howard University
- Columbia University
- Northwestern University
- Harvard University
- MIT
- PathAI
- Aspect Analytics
- Vizgen
- 10x
- Nanostring
- Digital Biology

Takeda

Better Health, Brighter Future

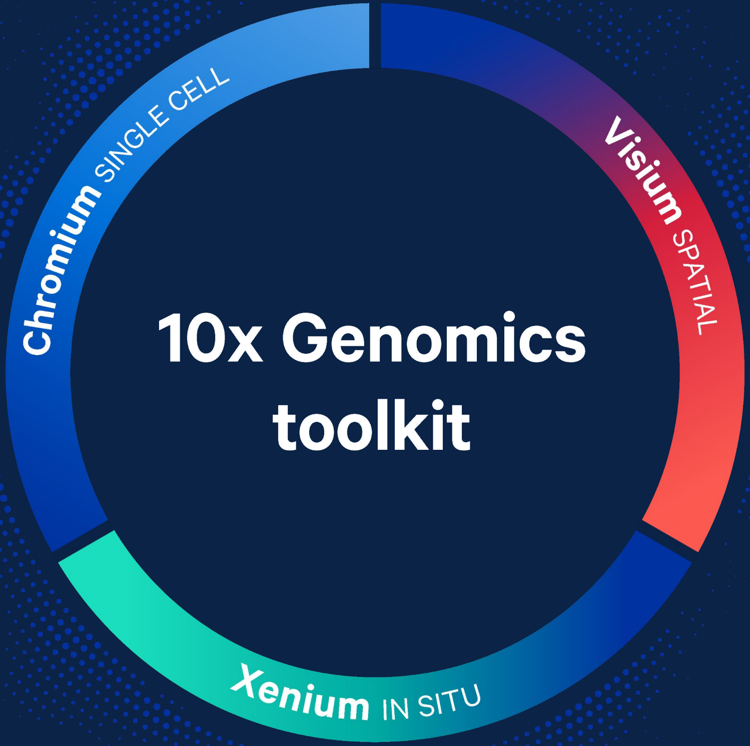


Daniel Moline, *10x Genomics*

In-Depth Cell Profiling with the 10x Toolkit

Dan Moline, PhD
Science and Technology Advisor

Three platforms to **resolve biology's complexity**

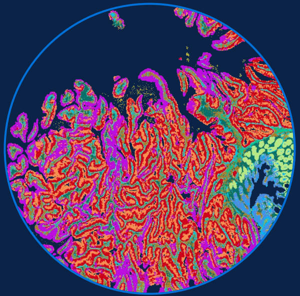


10x Genomics toolkit

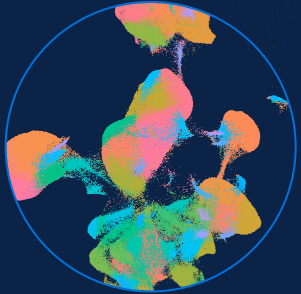
Chromium SINGLE CELL

Visium SPATIAL

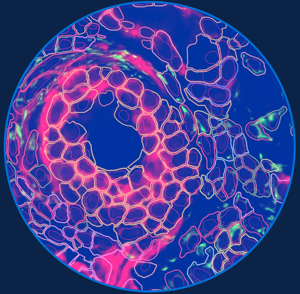
Xenium IN SITU



Visium Spatial



Chromium Single Cell



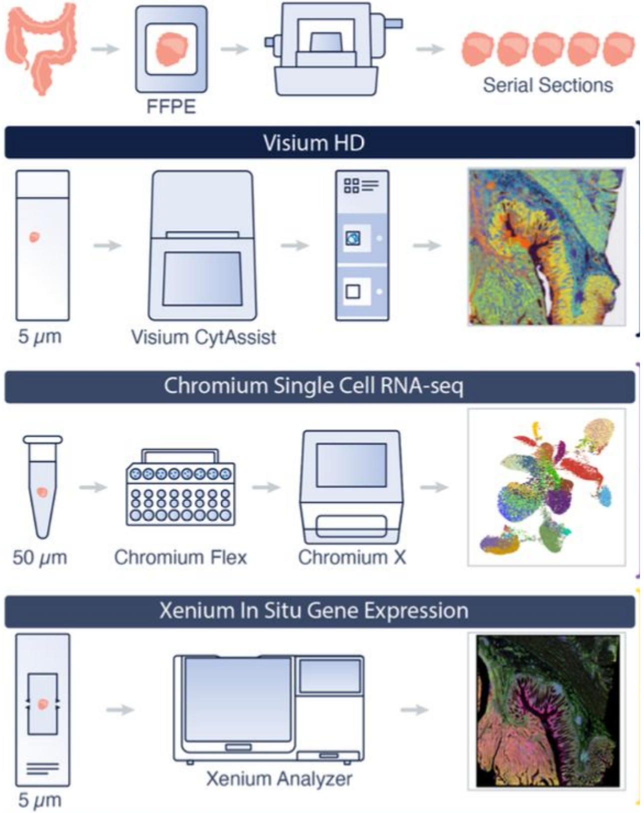
Xenium In Situ

Using Visium HD to investigate the tumor microenvironment in colorectal cancer

Characterization of immune cell populations in the tumor microenvironment of colorectal cancer using high definition spatial profiling

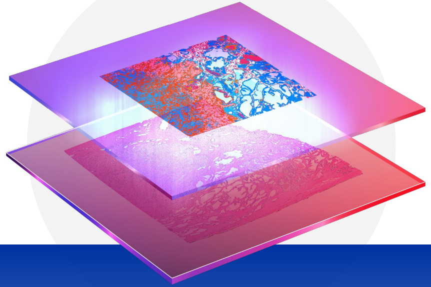
Michelli F. Oliveira, Juan P. Romero, Meii Chung, Stephen Williams, Andrew D. Gottscho, Anushka Gupta, Susan E. Pilipauskas, Syrus Mohabbat, Nandhini Raman, David Sukovich, David Patterson, Visium HD Development Team, Sarah E. B. Taylor

doi: https://doi.org/10.1101/2024.06.04.597233



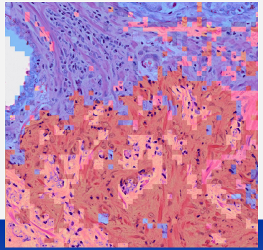
Introducing Visium HD

The spatial discovery power you want with the resolution and data quality you need



Unparalleled Spatial Discovery

Whole transcriptome gene expression analysis



Resolved at Single Cell Scale

Capture Area with continuous lawn of 2 x 2 µm barcoded squares

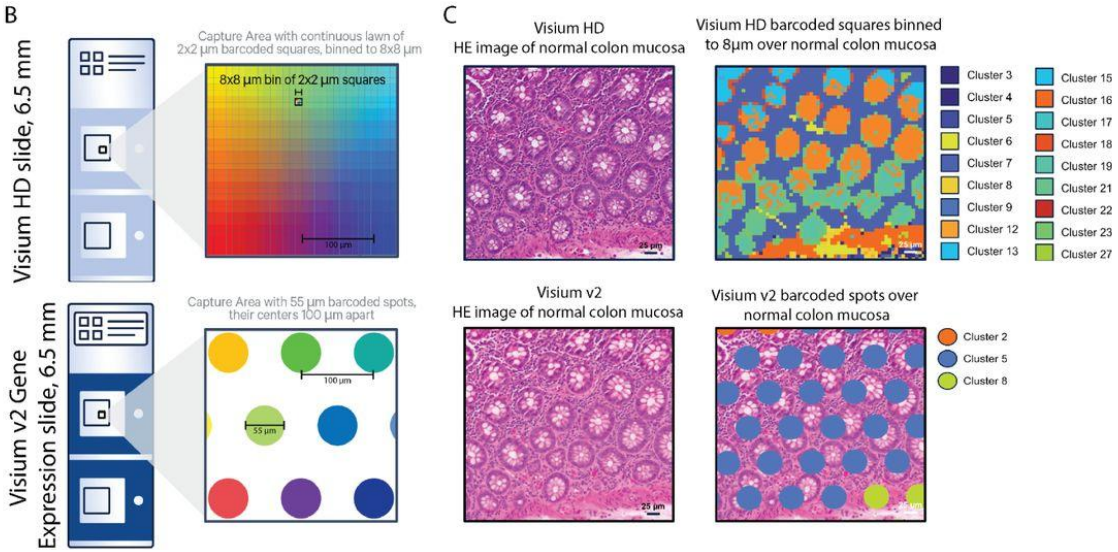
Data Quality You Can Trust

Accurate transcript localization enabled by Visium CytAssist

Visium HD spatially maps gene expression at high resolution

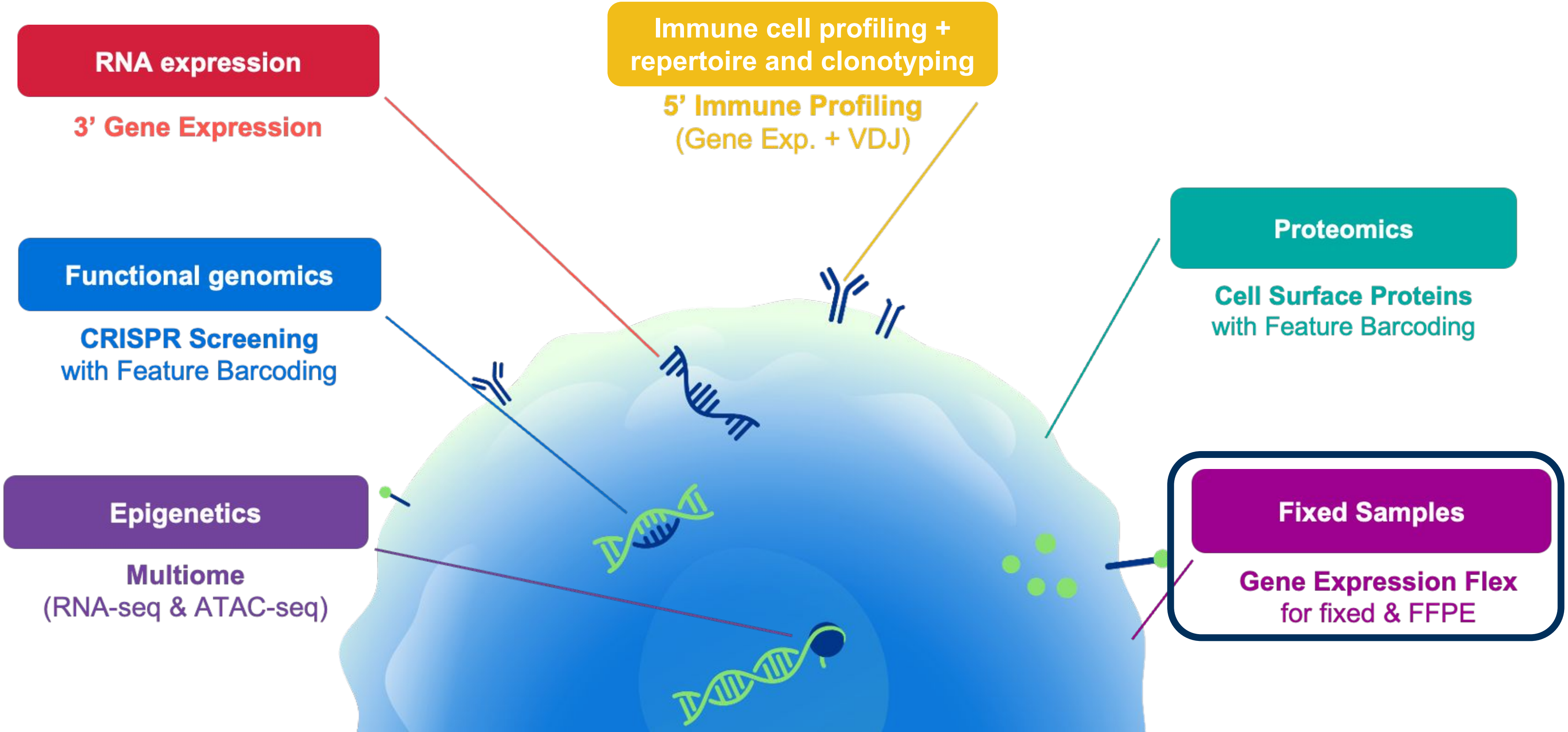
-Unbroken lawn of oligos avoids lost information

-Better conforms to tissue morphology



Comprehensive Toolkit for Single Cell Multiomics

Enabling the Broadest Range of Applications and Analytes



RNA expression

3’ Gene Expression

Functional genomics

CRISPR Screening
with Feature Barcoding

Epigenetics

Multiome
(RNA-seq & ATAC-seq)

Immune cell profiling + repertoire and clonotyping

5’ Immune Profiling
(Gene Exp. + VDJ)

Proteomics

Cell Surface Proteins
with Feature Barcoding

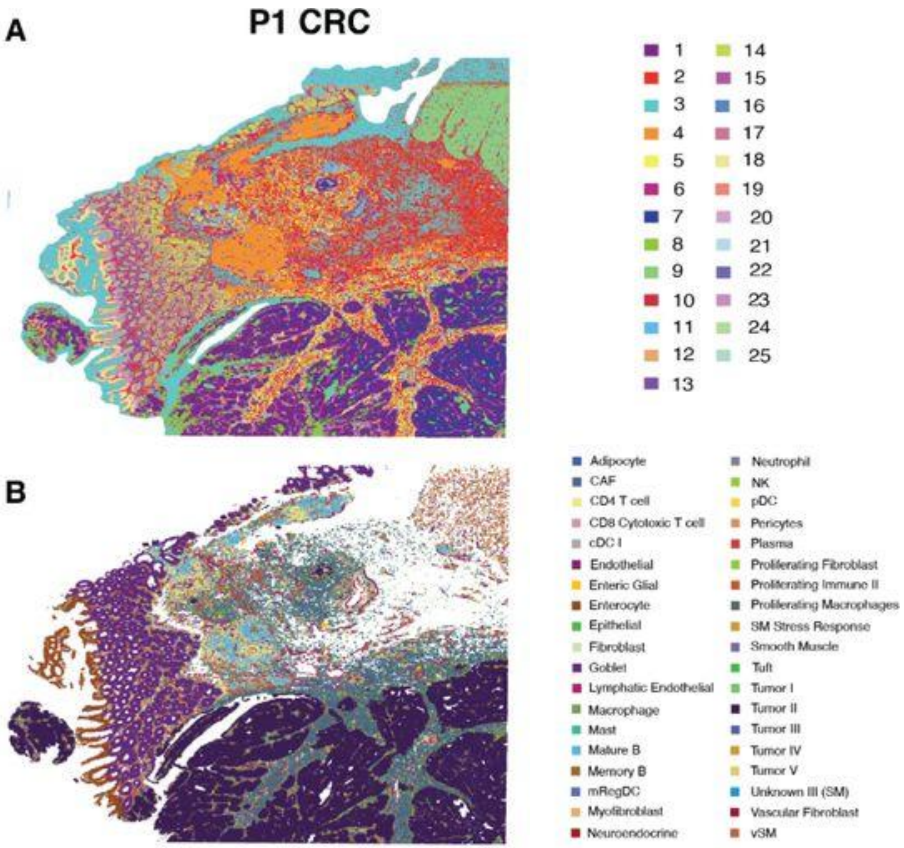
Fixed Samples

Gene Expression Flex
for fixed & FFPE

Identification of cell types aided by single cell data

-Single cell data provides ground truth for identification

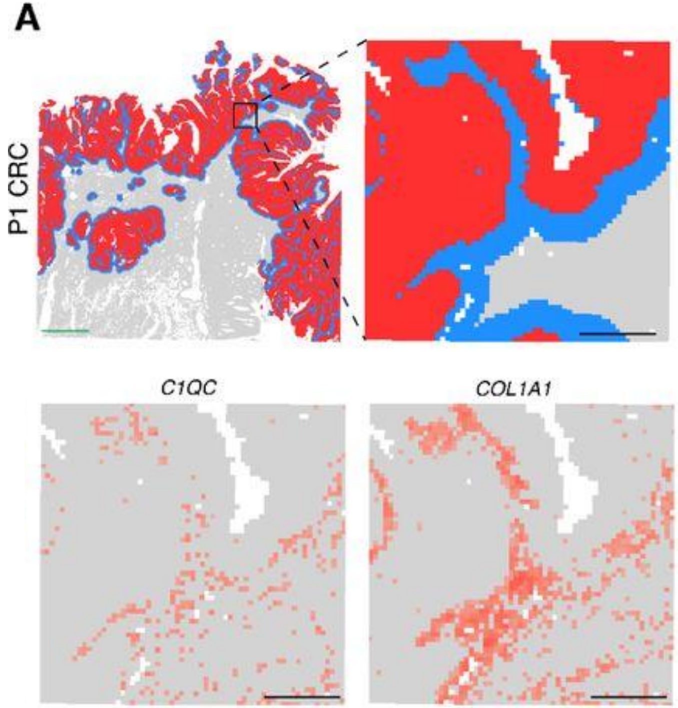
-Also allows for removal of bins that sit under multiple cells



Macrophages and CAFs are prominent at tumor periphery

-After cell identification, wanted to focus on tumor periphery

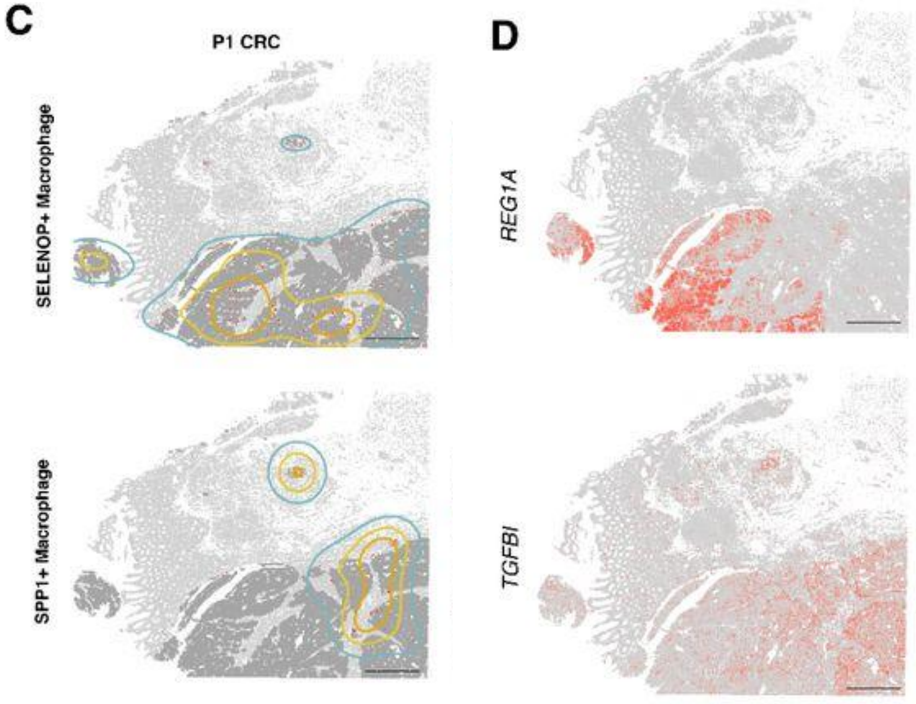
-Is there diversity among the macrophages at the periphery?



Macrophage populations localize independently

-Adjacent tumor cells showed differing expression patterns

-REG1A upgregulated near SELENOP+ cells, TFBI upregulated near SPP1+ cells



Sensitive and **robust** spatial analysis with Xenium In Situ

Highly sensitive and specific padlock chemistry

Integrated multimodal segmentation

Expertly curated and customizable assays

Fast, simple workflow with no tissue optimization

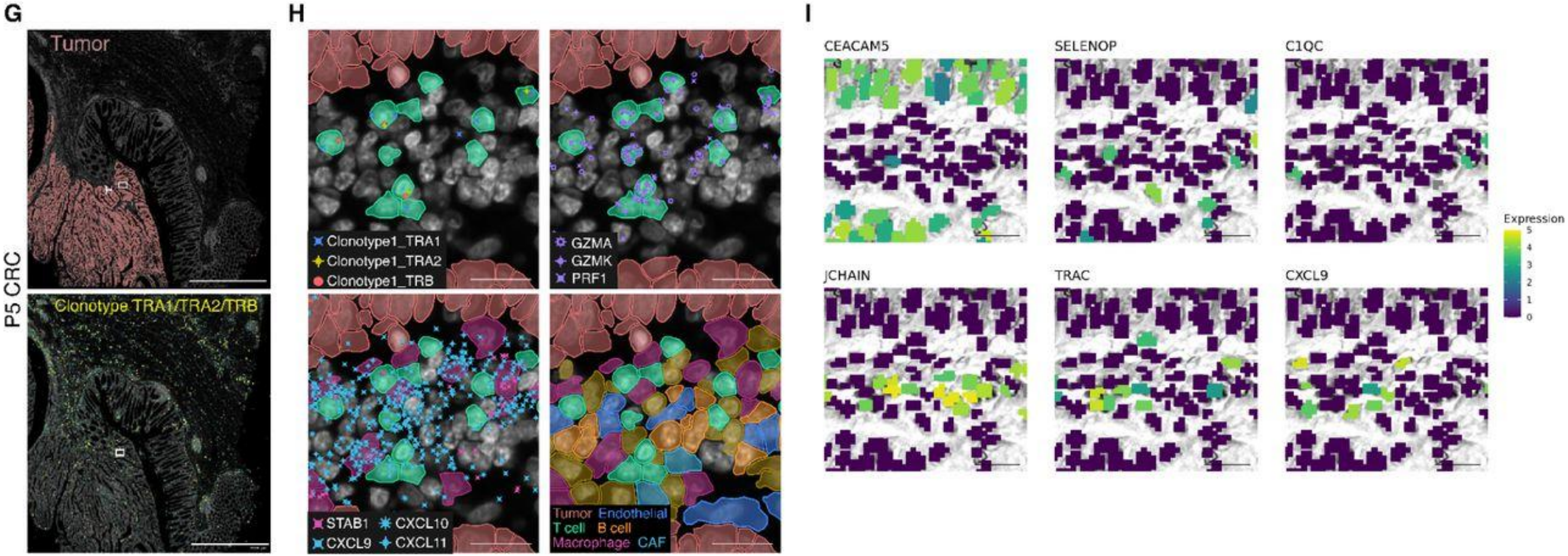
Industry-leading speed and throughput

Post-run section compatibility with IF, H&E, and Visium

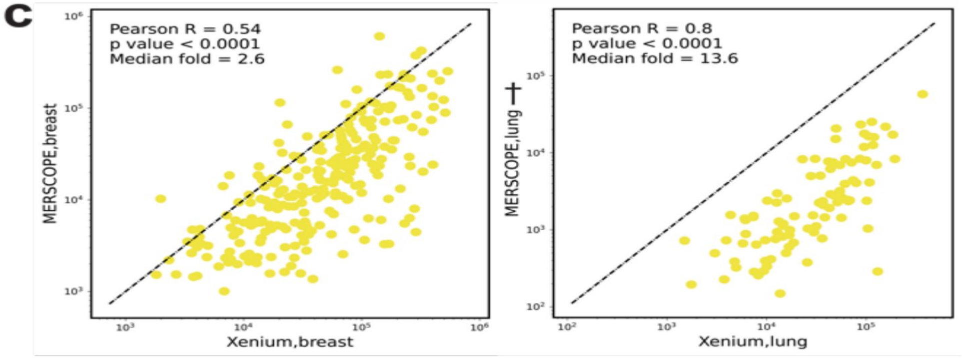
Analysis, data visualization, and exploration

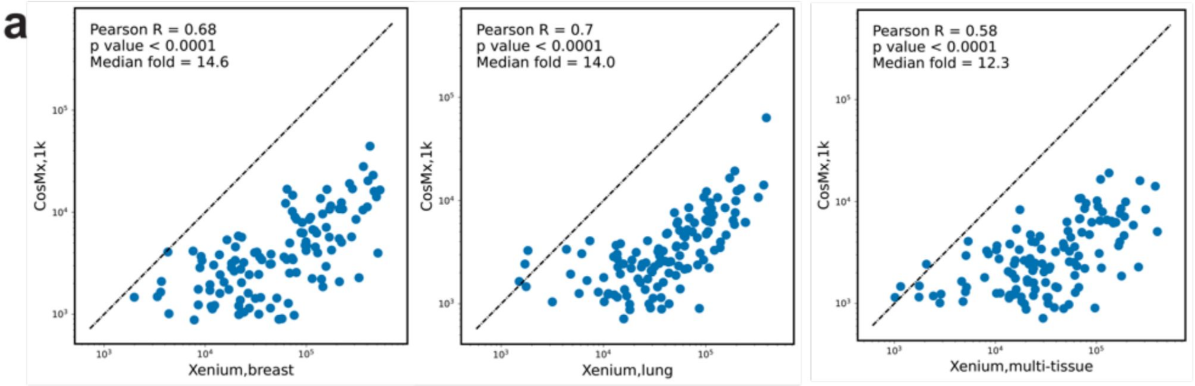
Extensive multi-year roadmap

Xenium and Visium used together to localize peripheral T cells



Xenium Has Class-Leading Sensitivity



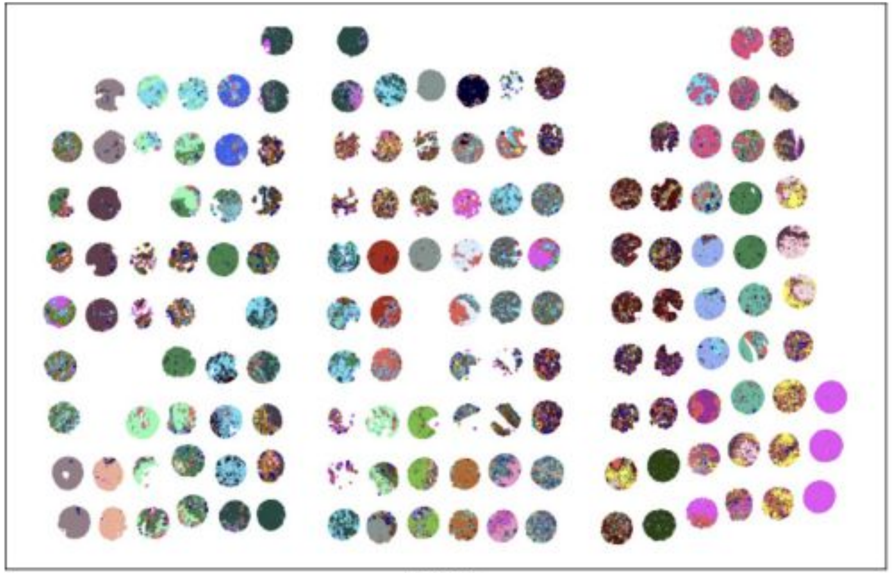


Farhi et al. Systematic benchmarking of imaging spatial transcriptomics platforms in FFPE tissues. *BioRxiv* (2023) (Fig. 2 and underlying data).

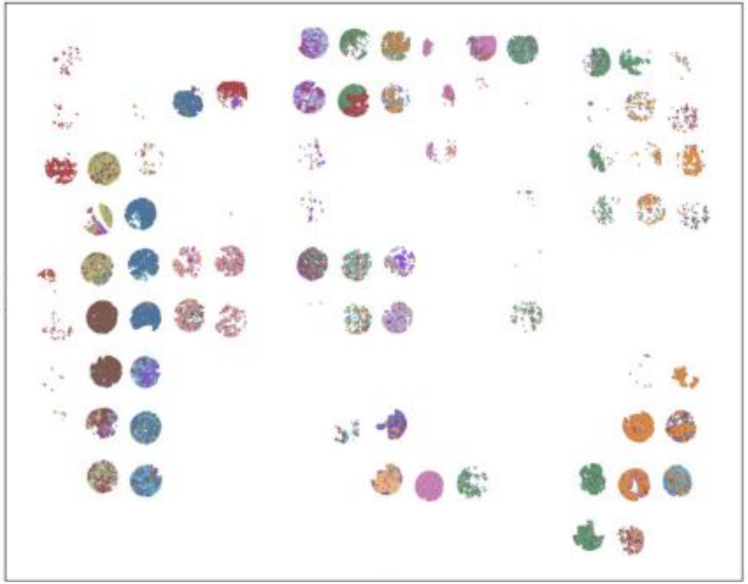
Robustness of Xenium is Revealed in FFPE TMA Images

"We focused on FFPE tissues as the standard method for sample processing and archival in pathology…goal was to determine the compatibility of iST platforms under typical workflows for biobanked FFPE tissues"

Xenium Lung Panel



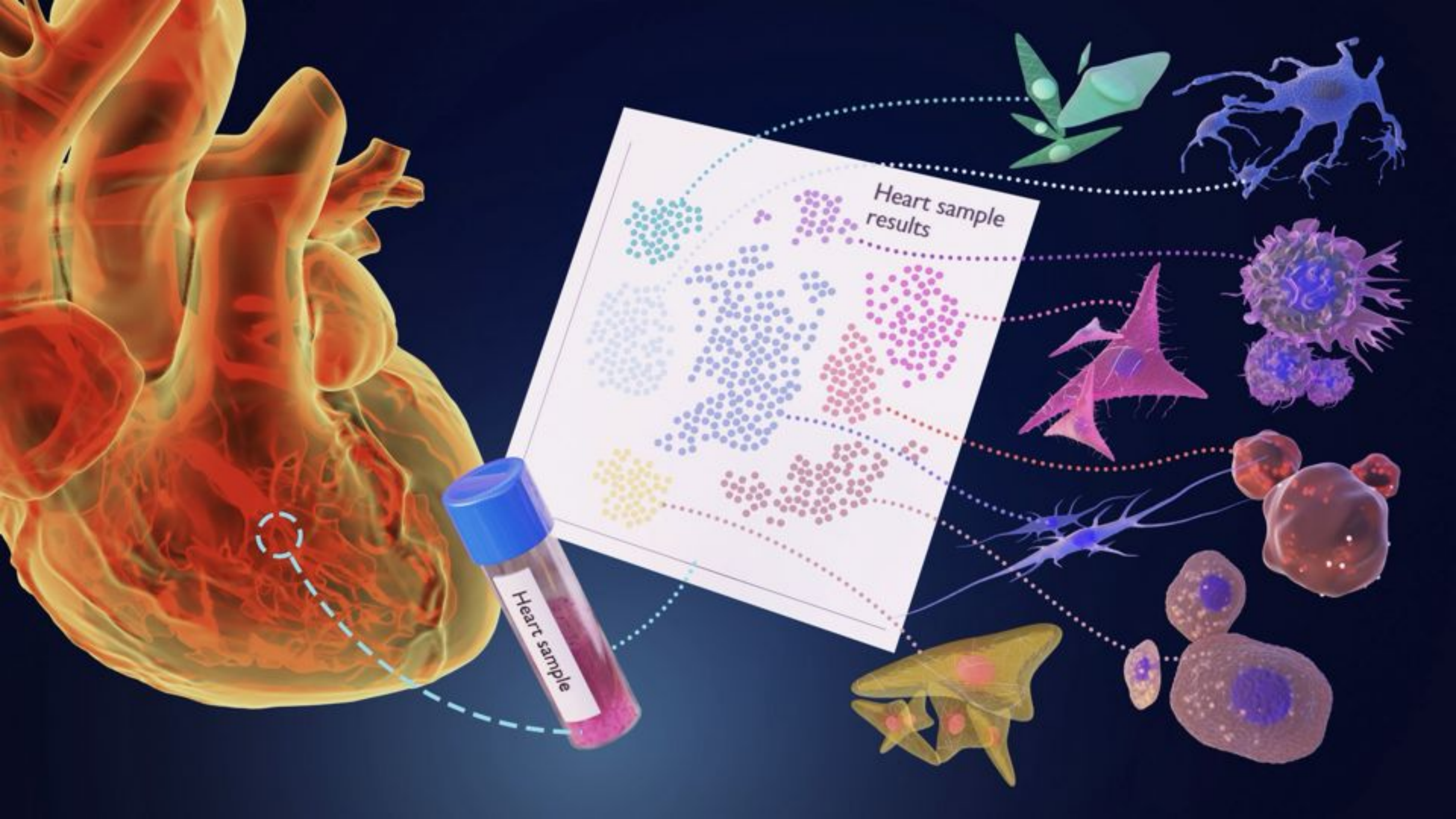
MERSCOPE Lung Panel

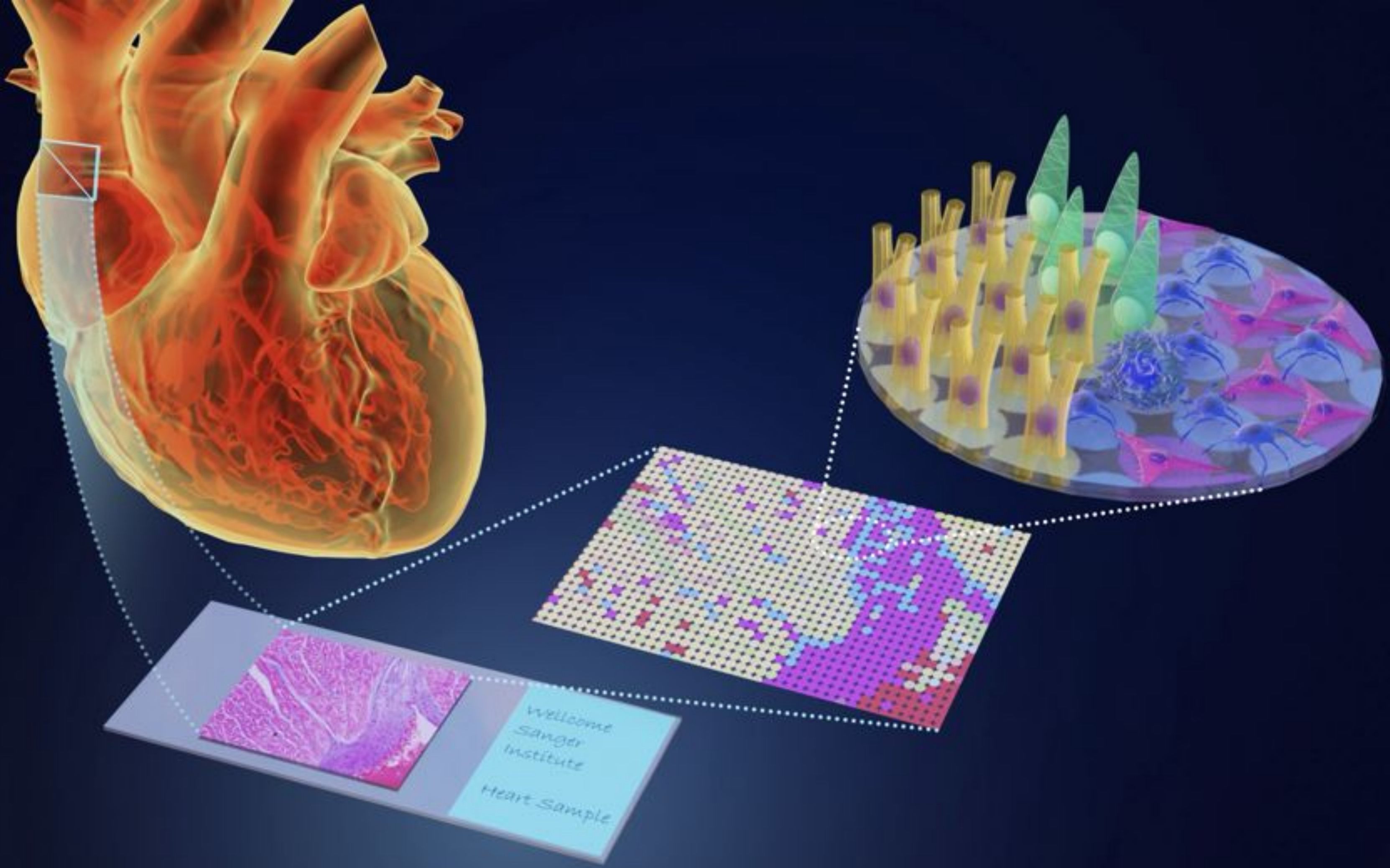


Farhi et al. Systematic benchmarking of imaging spatial transcriptomics platforms in FFPE tissues. *BioRxiv* (2023) (Fig. 2 and underlying data).

Thank you!

Sarah Teichmann, *CIFAR co-director*


Heart sample results
Heart sample

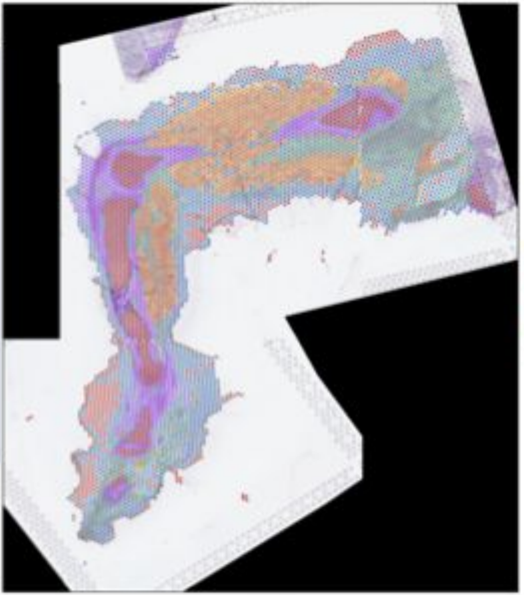

Wellcome Sanger Institute
Heart Sample

Future: Assembling a Molecular Map of the Human Body in 3D

Suspension cell data: 0D

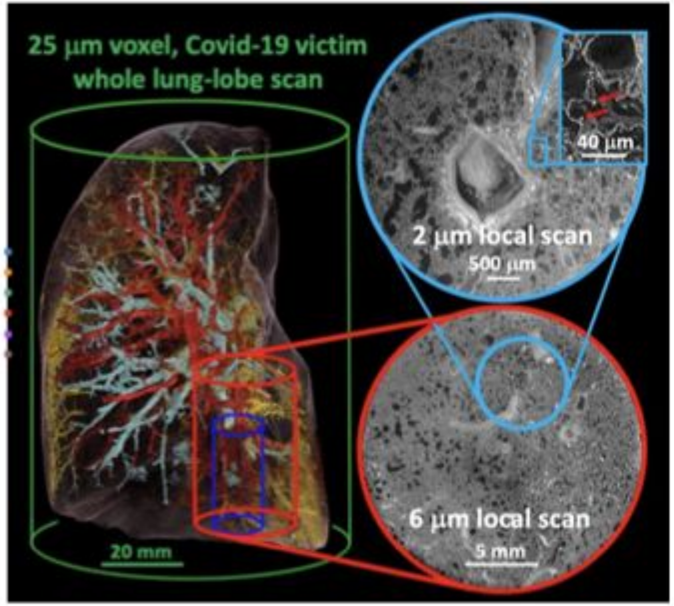
CIFAR

Spatial transcriptomics: 2D



Zhang, He, Lawrence, et al.
Nature 2023

Volumetric reconstructions: 3D

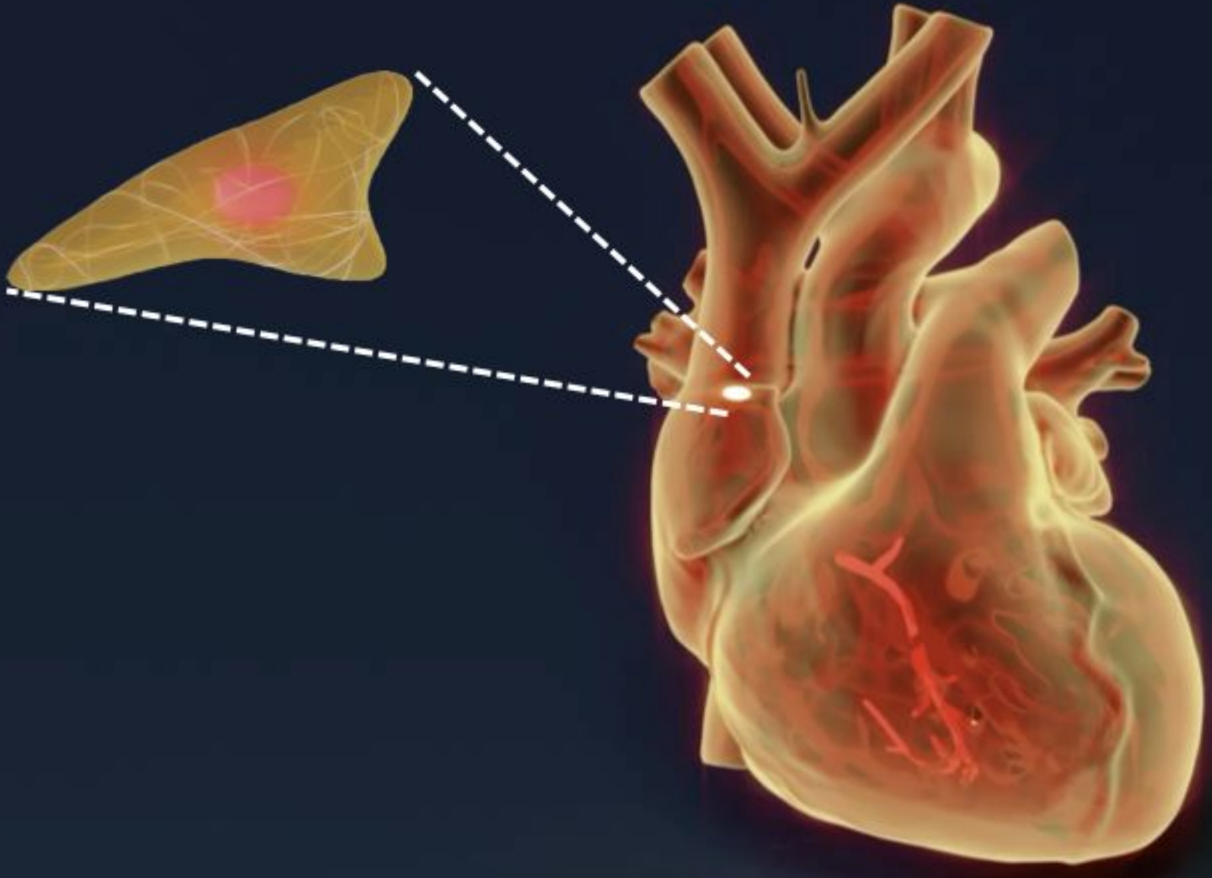


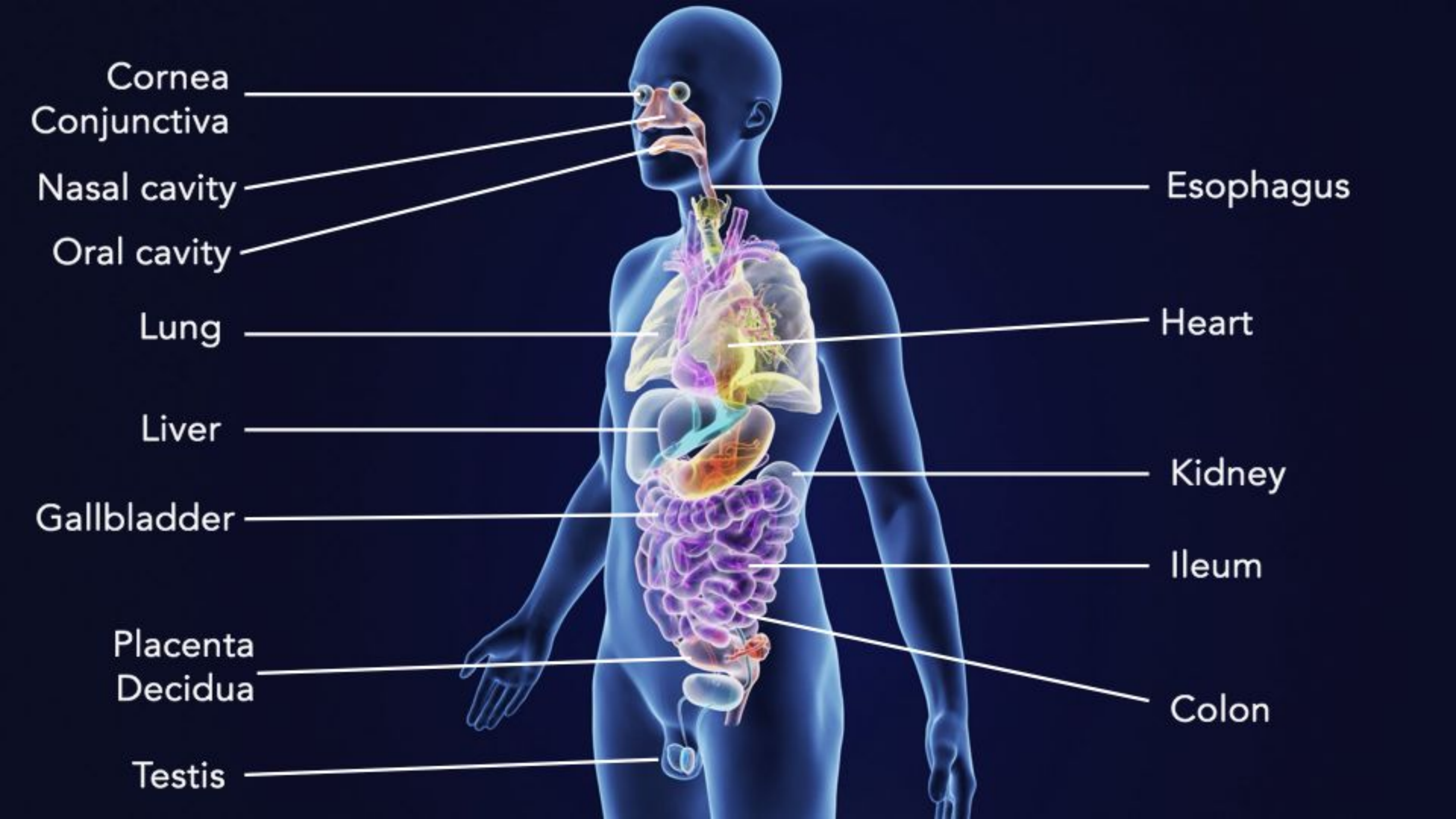
P. Tafforeau/ESRF
P. Lee, C. Walsh/UCL

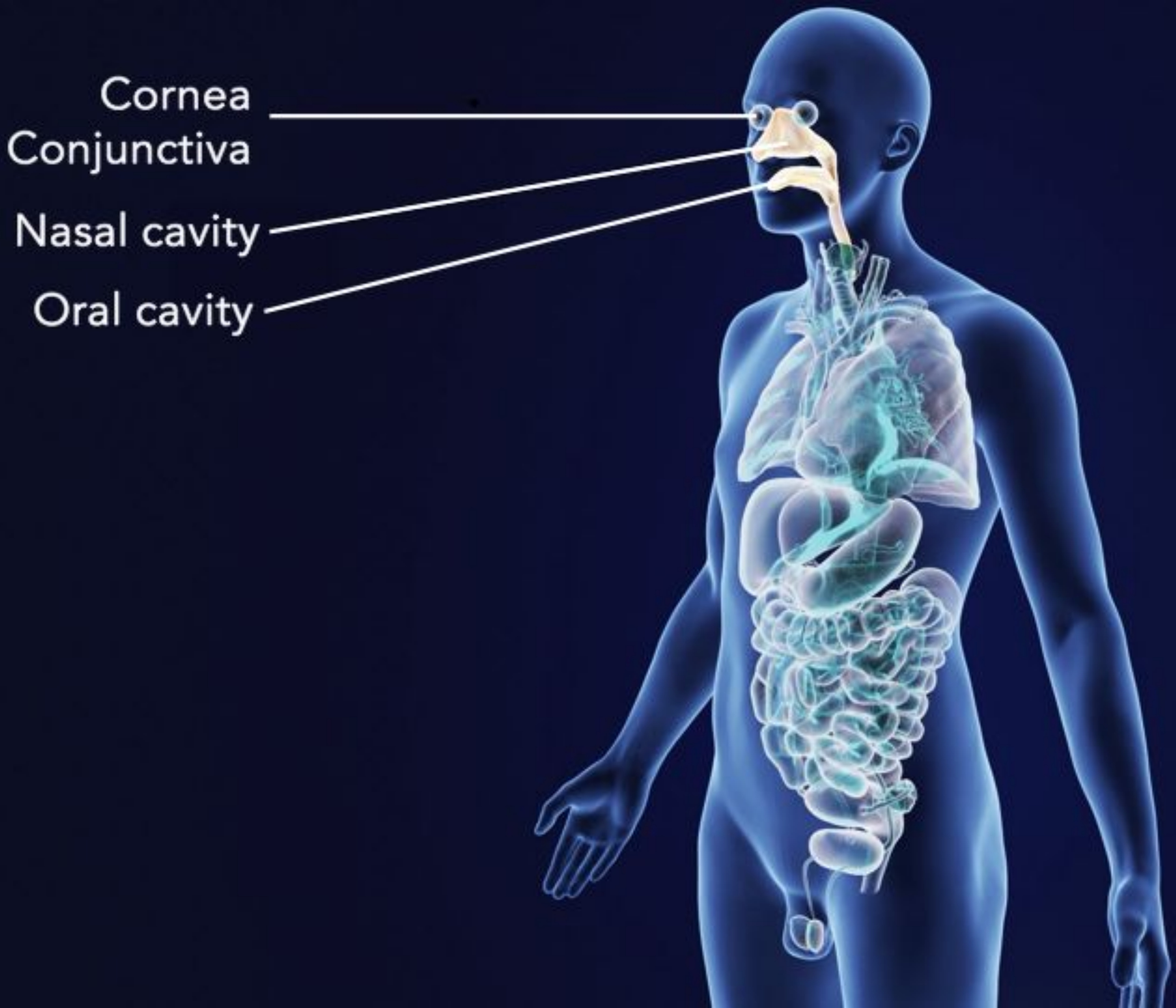
Human Cell Atlas

www.humancellatlas.org

>3000 members




Cornea
Conjunctiva
Nasal cavity
Oral cavity
Lung
Liver
Gallbladder
Placenta
Decidua
Testis
Esophagus
Heart
Kidney
Ileum
Colon


Cornea
Conjunctiva
Nasal cavity
Oral cavity


A
B
C
CELL PROGRAMMING
INCUBATE


SYNTHETIC GENOMICS
INCUBATE

Tobias Wenzel, *Pontificia Universidad Católica de Chile, Chile*

Making organoid interaction studies accessible

Interaction studies in microfluidic droplets

Organoid generation: More control and throughput with microfluidic droplets

Developing accessible open-source research platform to place the new methods in the hand of global bioscientists.

Droplet Microfluidics

- Ultra-high throughput
- Single cell control
- Less contamination
- Versatile
- Reagent efficient

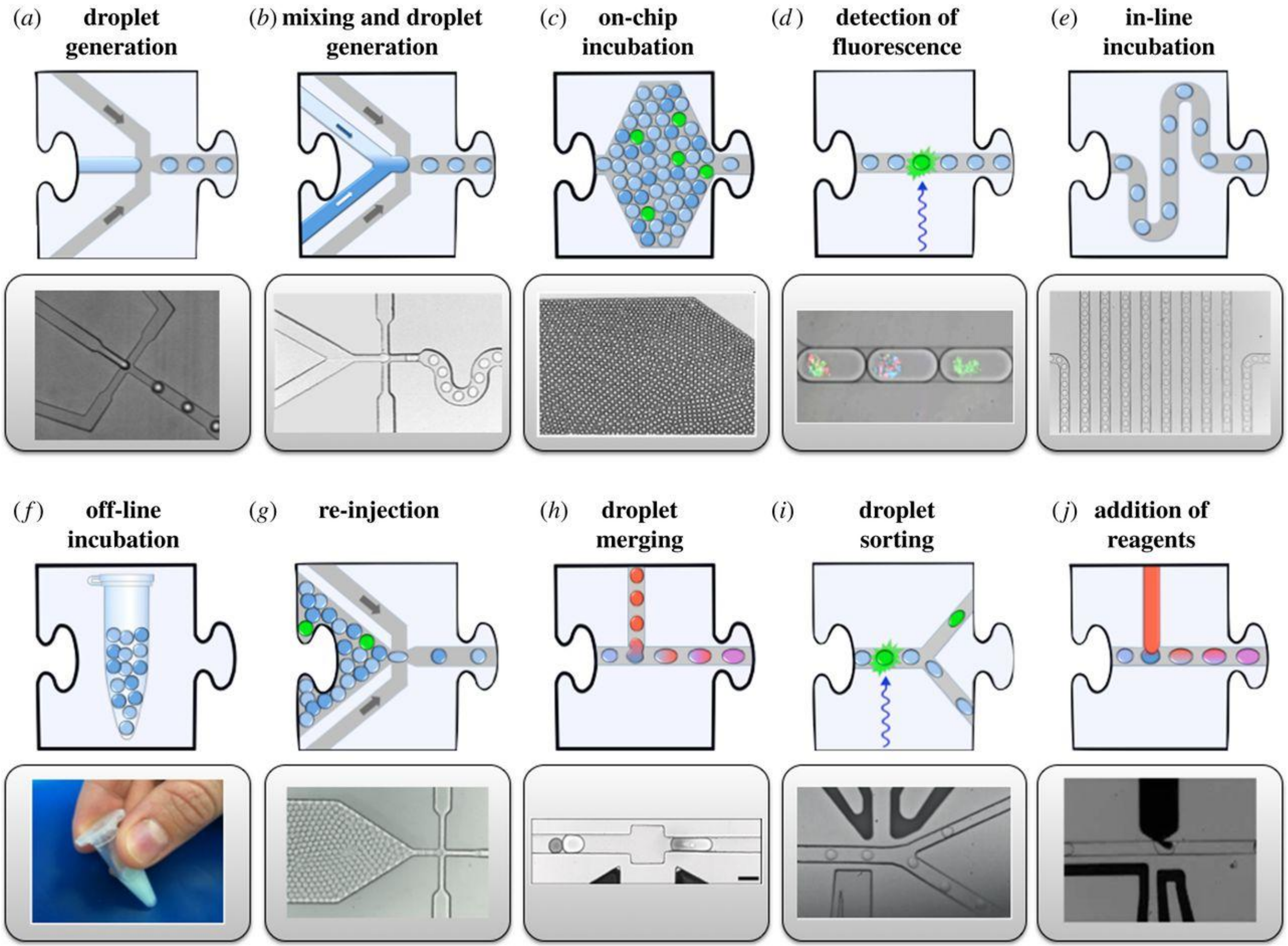
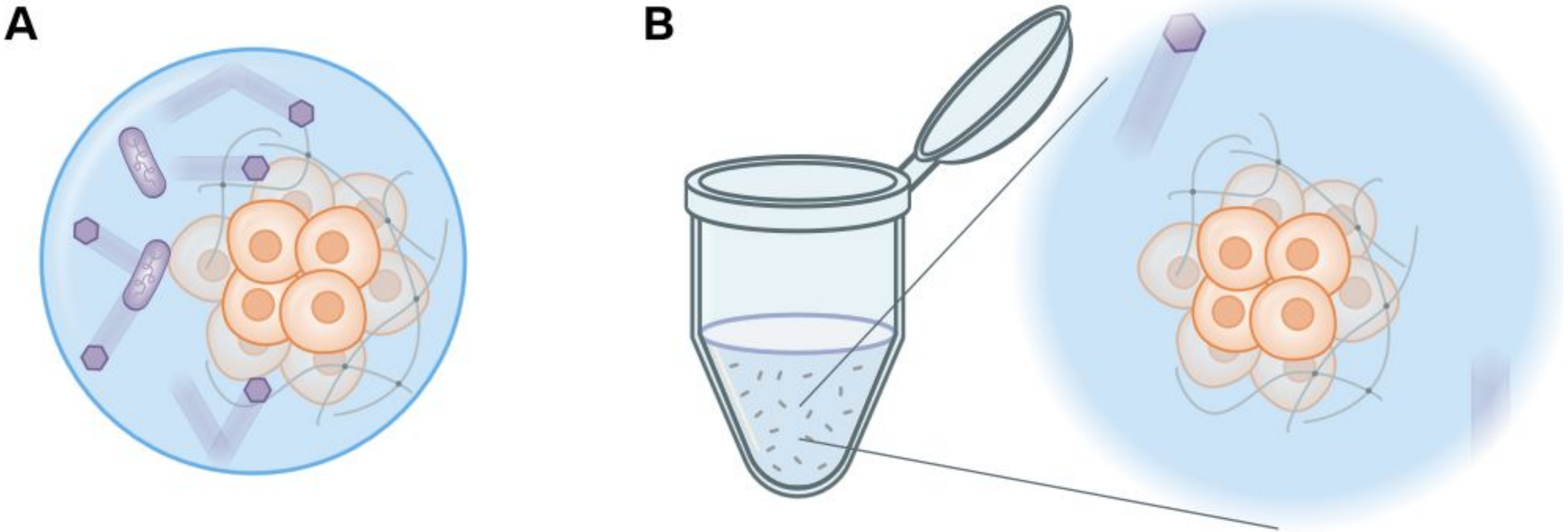


Image source: Liisa D. van Vliet et al. Interface Focus 2015

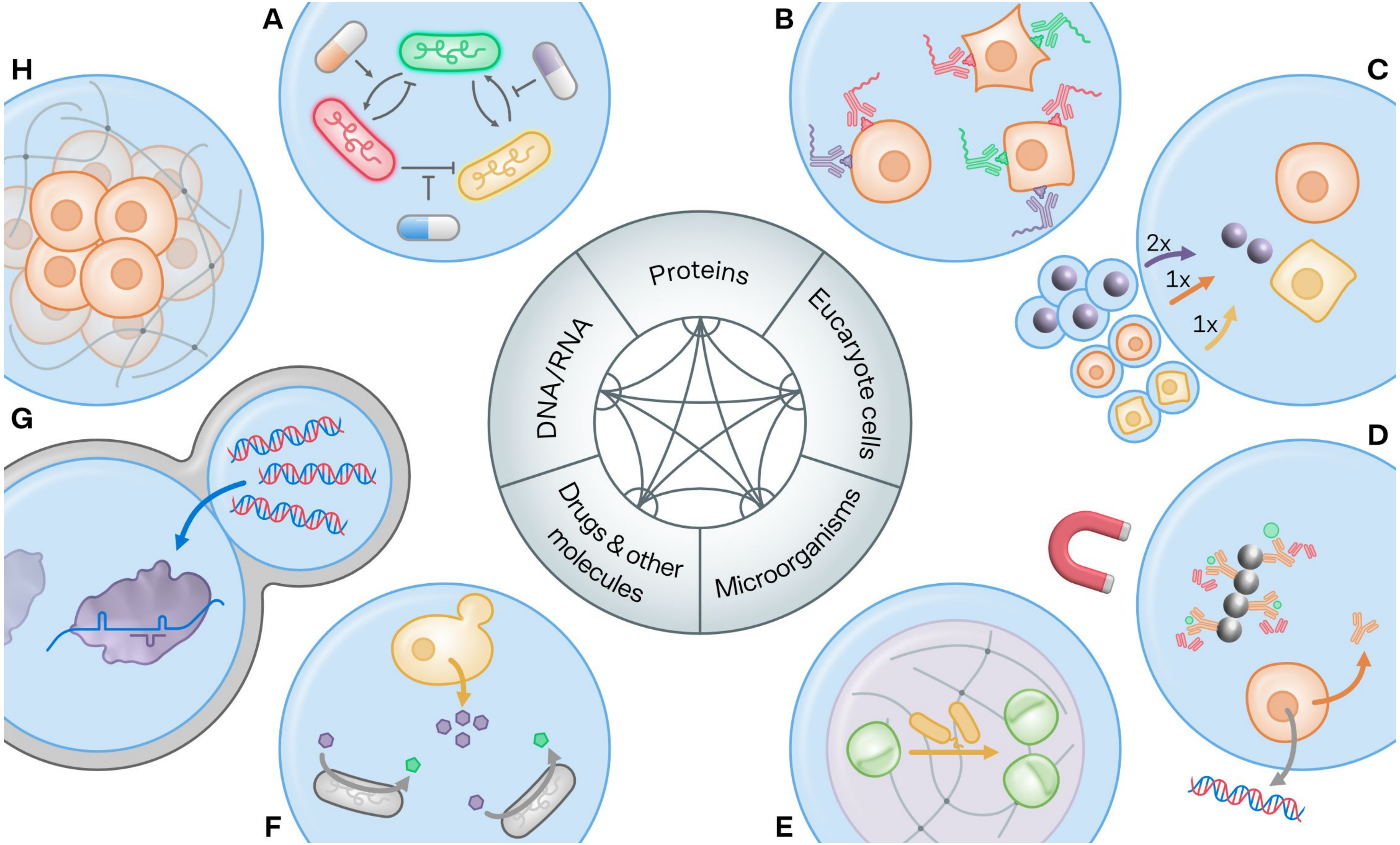
Interactions are best studied in droplets



Variation of:

Leveraging interactions in microfluidic droplets for enhanced biotechnology screens
C. Vitalis & T. Wenzel
Current Opinion in Biotechnology, 2023/08

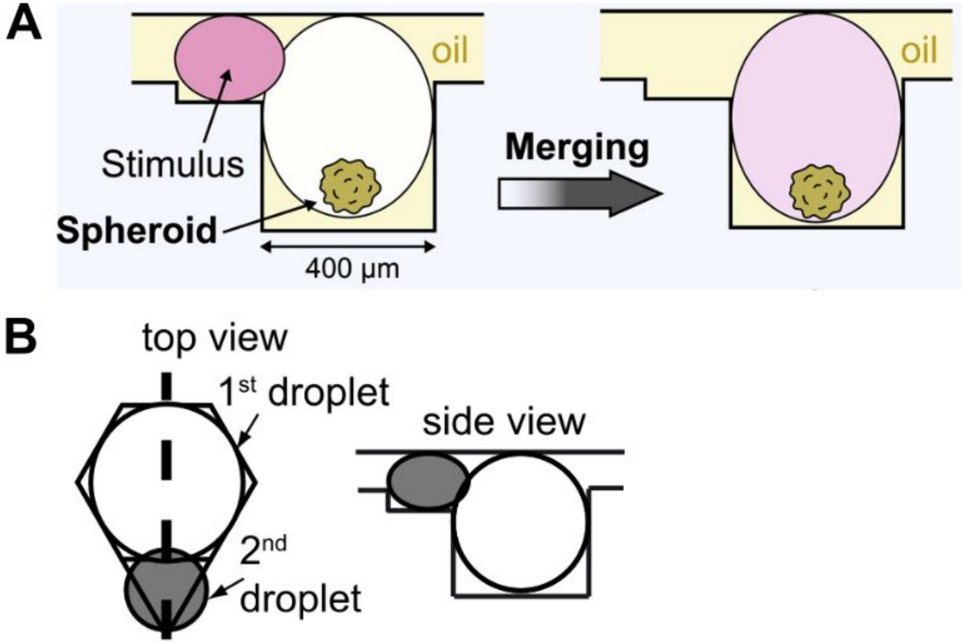
Many interactions can be studied in droplets

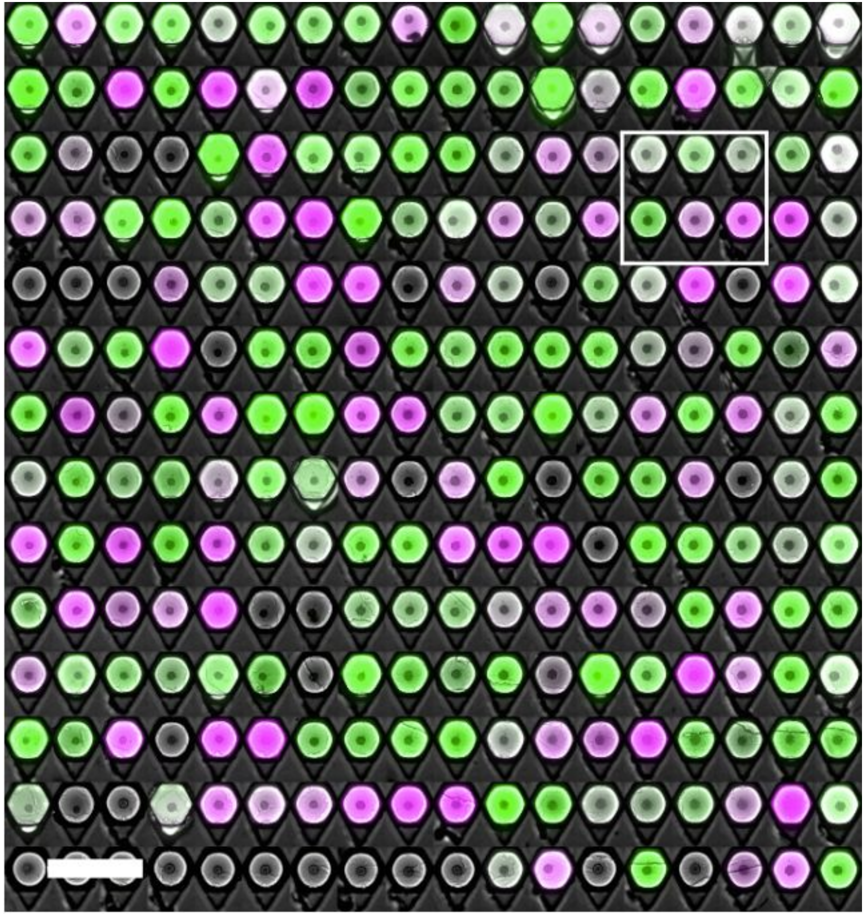


Leveraging interactions in microfluidic droplets for enhanced biotechnology screens
C. Vitalis & T. Wenzel
Current Opinion in Biotechnology, 2023/08

Bioimaging in droplets for organoids and interactions

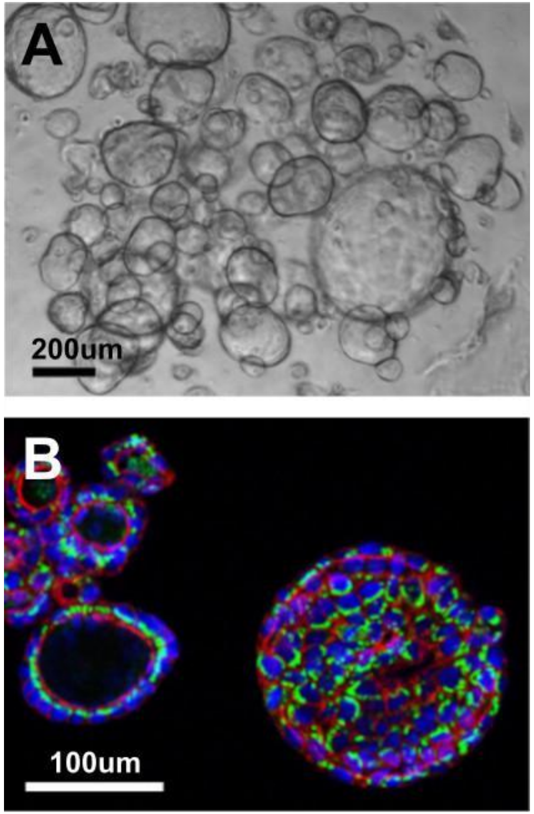
- **High throughput analysis of host-pathogen interactions in droplets**

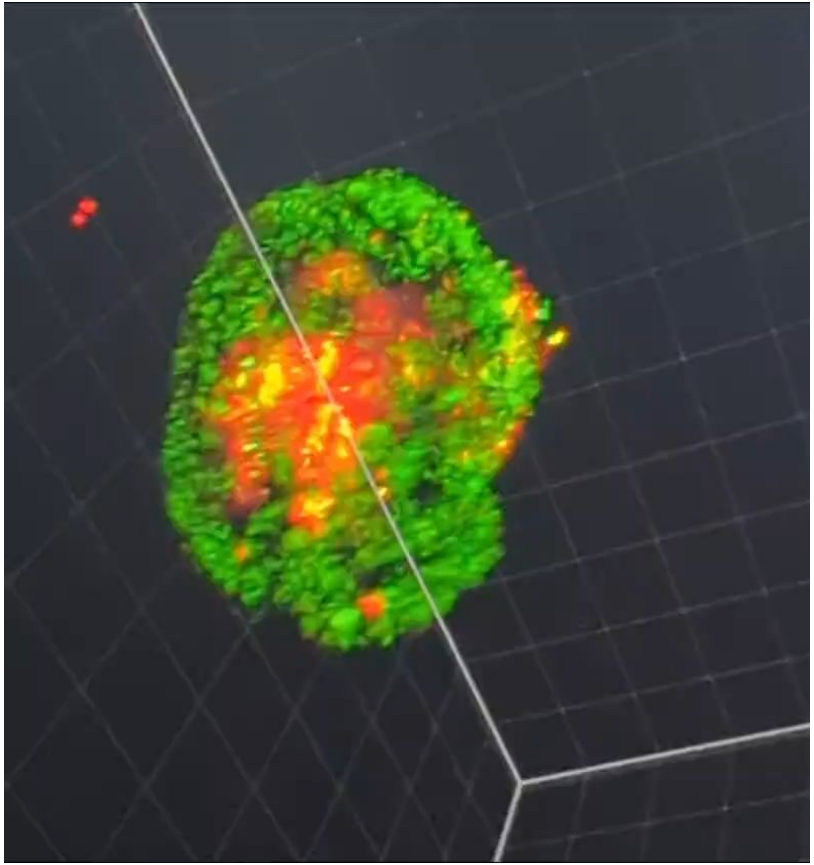




Tomasi et al. (Cell Reports. 2020)

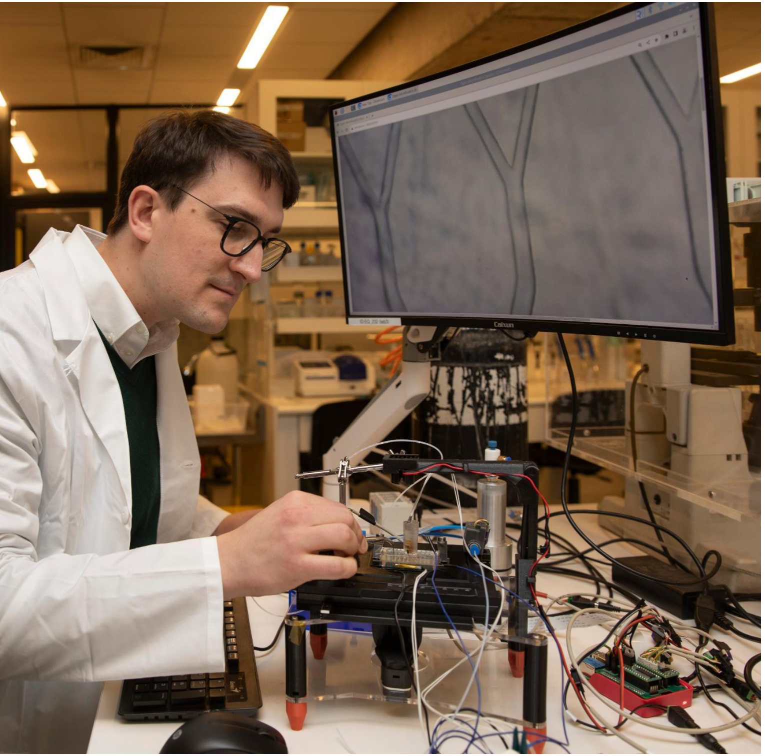
Organoid cultivation under controlled conditions on chip

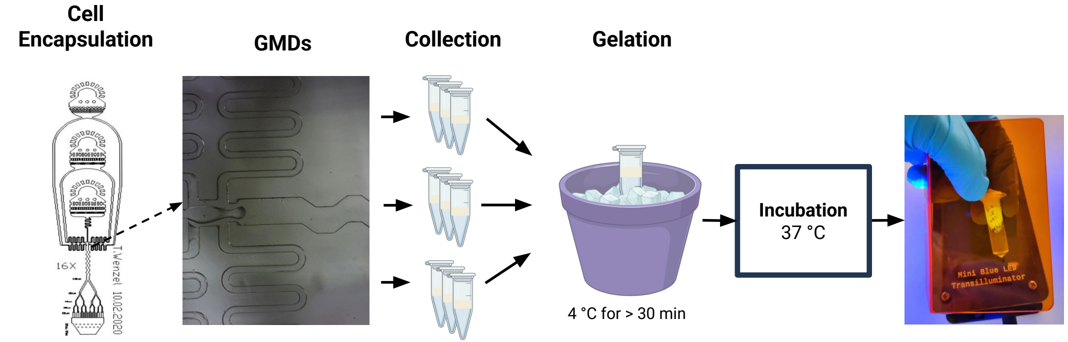




Droplet Microfluidic Workstation for Microgels

Instituto de Ingeniería Biológica y Médica

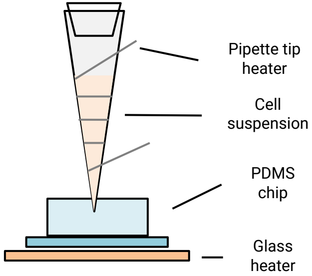




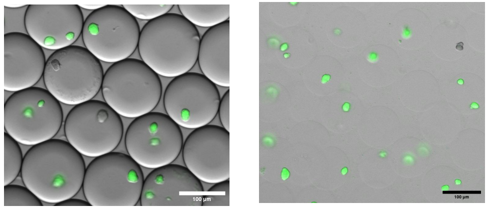
Cell Encapsulation **GMDs** **Collection** **Gelation**

4 °C for > 30 min

Incubation
37 °C



sfGFP expressing *E. coli* colonies inside of gel microdroplets (Scaler bar: 100 µm)



in oil

in buffer

Manuscript in revision

Detailed documentation
and open license

Strobe-enhanced microscopy stage

by Pierre Padilla-Huamantinco, Matías Hurtado-Labarca, and Tobias Wenzel
Latin American Hub for Bioimaging Through Open Hardware (LIBRE hub)

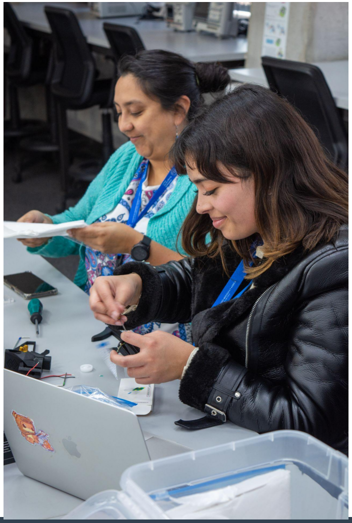
- **Strobe-enhanced microscopy stage**
- **Build the 3-level microscopy stage**
  - Print the plastic parts
  - Laser cut the acrylic parts
  - Assemble the focus mechanism
  - Assemble the basics optics module
  - Attach parts to the top plate
  - Attach parts to the

3-level microscopy stage

Before you start building the station, you will need to source all the components listed in our bill of materials (HTML, CSV), which is given on the next page.

Instructions

Open Hardware Droplet Workstation



PLOS BIOLOGY

OPEN ACCESS

ESSAY

Open hardware: From DIY trend to global transformation in access to laboratory equipment

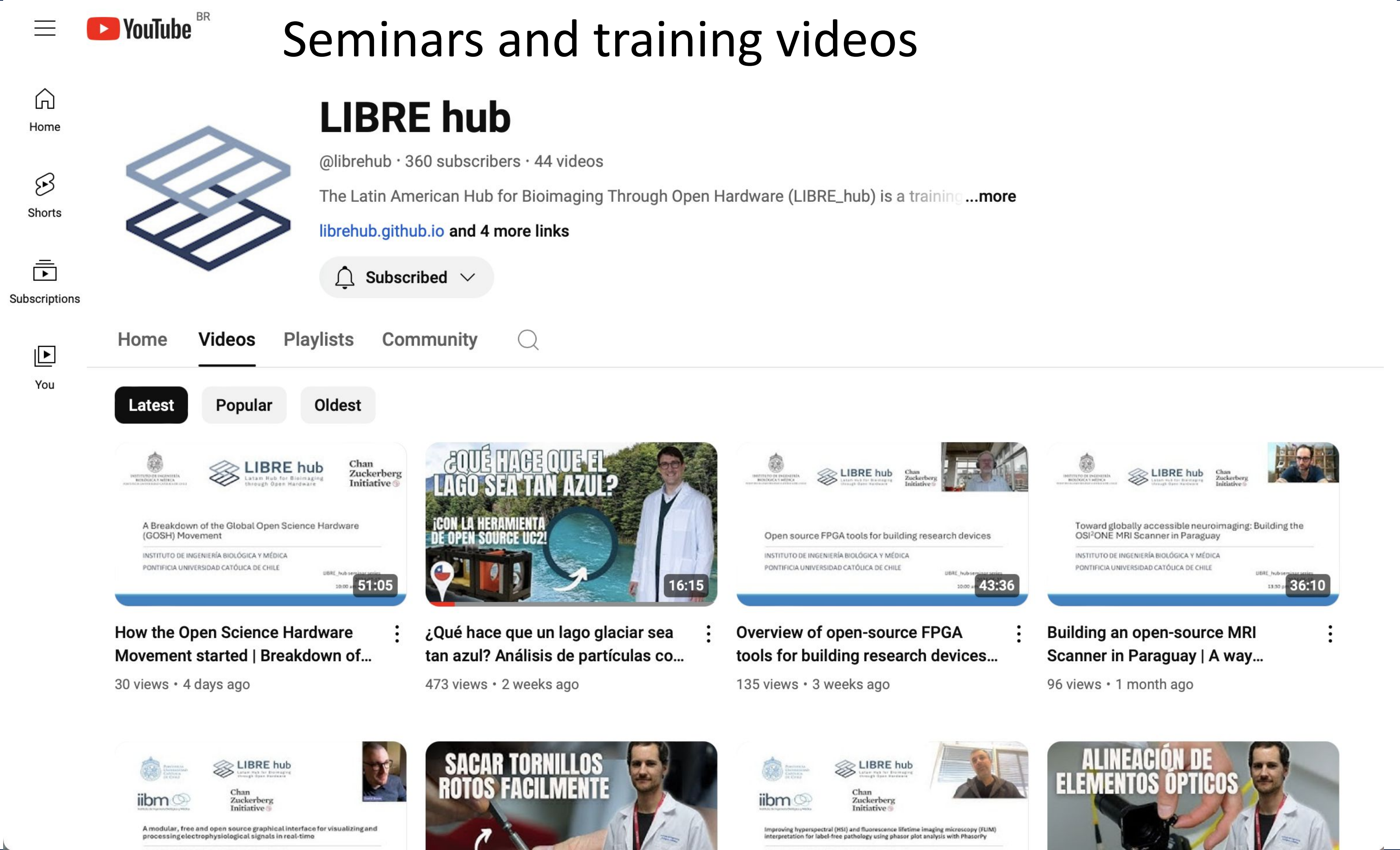
Tobias Wenzel

Published: January 17, 2023 • https://doi.org/10.1371/journal.pbio.3001931

Abstract

Open hardware solutions are increasingly being chosen by researchers as a strategy to improve access to technology for cutting-edge biology research. The use of DIY technology is already widespread, particularly in countries with limited access to science funding, and is catalyzing the development of open-source technologies. Beyond financial accessibility, open hardware can be transformational for the access of laboratories to equipment by reducing dependence on import logistics and enabling direct knowledge transfer. Central drivers to the adoption of appropriate open-source technologies in biology laboratories around the world are

Seminars and training videos



LIBRE hub

@librehub · 360 subscribers · 44 videos

The Latin American Hub for Bioimaging Through Open Hardware (LIBRE_hub) is a training ...more

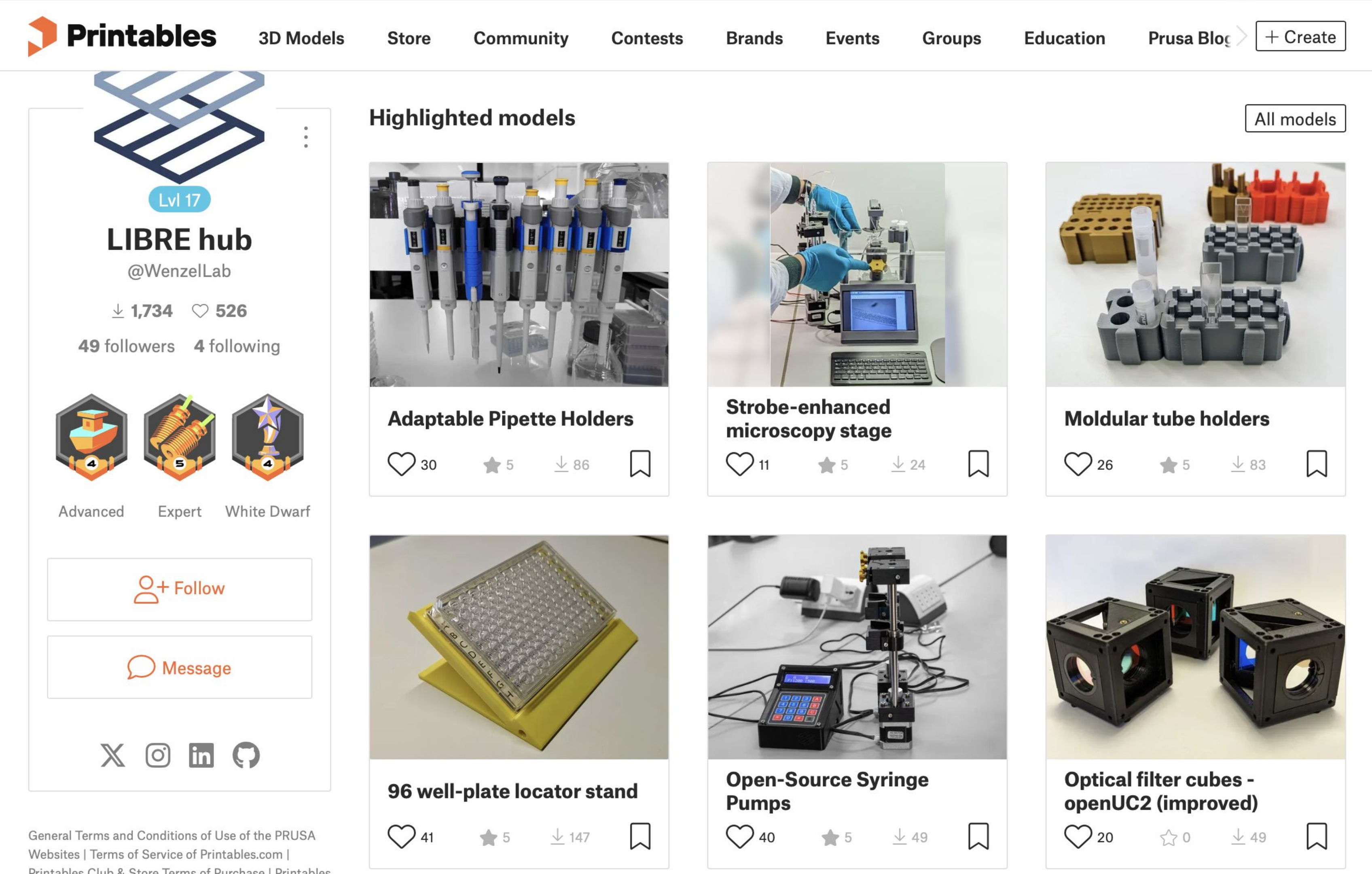
librehub.github.io and 4 more links

How the Open Science Hardware Movement started | Breakdown of...
51:05 · 30 views • 4 days ago

¿Qué hace que un lago glaciar sea tan azul? Análisis de partículas co...
16:15 · 473 views • 2 weeks ago

Overview of open-source FPGA tools for building research devices...
43:36 · 135 views • 3 weeks ago

Building an open-source MRI Scanner in Paraguay | A way...
36:10 · 96 views • 1 month ago



LIBRE hub

@WenzelLab

1,734 ♡ 526

49 followers 4 following

Highlighted models

Model	♡	★	Downloads
Adaptable Pipette Holders	30	5	86
Strobe-enhanced microscopy stage	11	5	24
Moldular tube holders	26	5	83
96 well-plate locator stand	41	5	147
Open-Source Syringe Pumps	40	5	49
Optical filter cubes - openUC2 (improved)	20	0	49

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Thank you! Let’s discuss…

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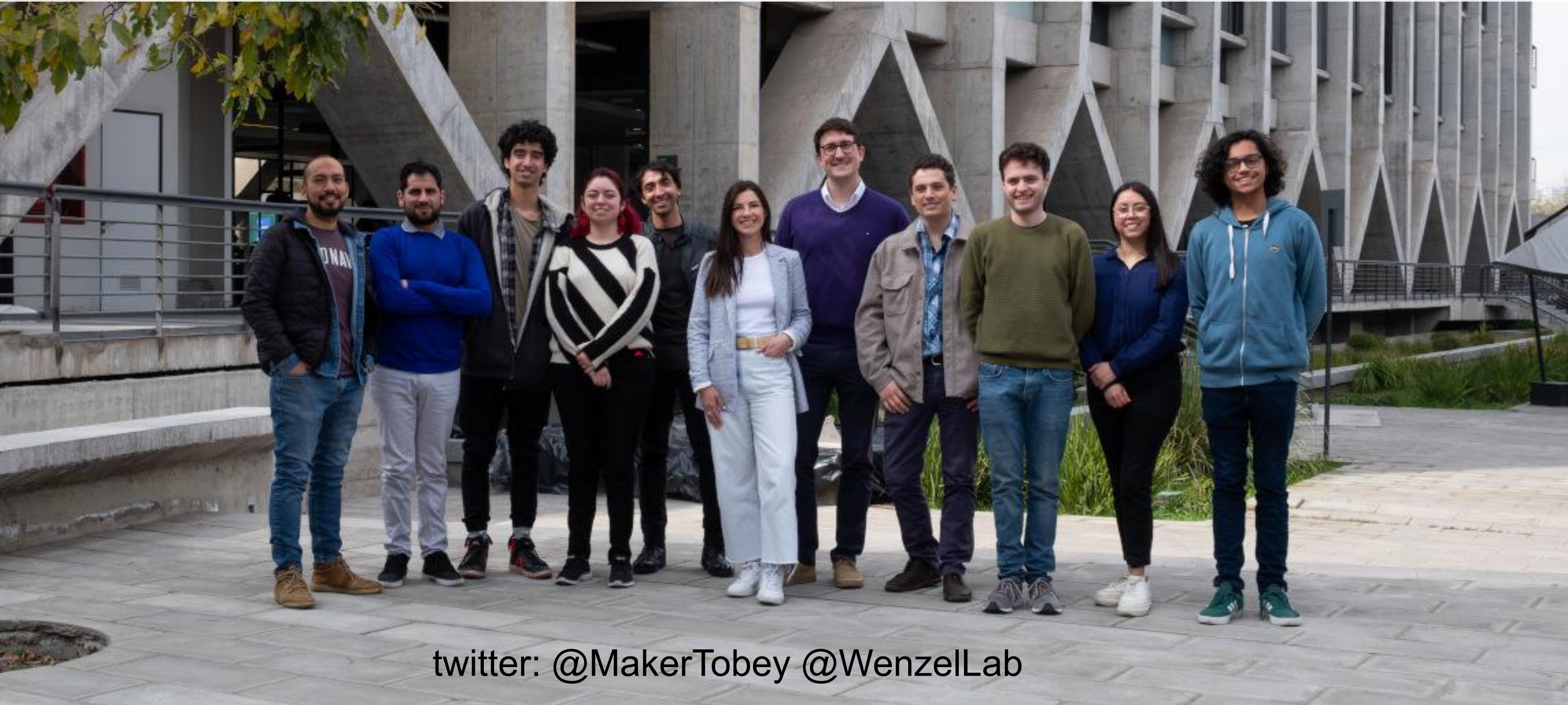
Ministerio de Educación
Gobierno de Chile

FONDECYT
Fondo Nacional de Desarrollo Científico y Tecnológico

Chan
Zuckerberg
Initiative

CIFAR



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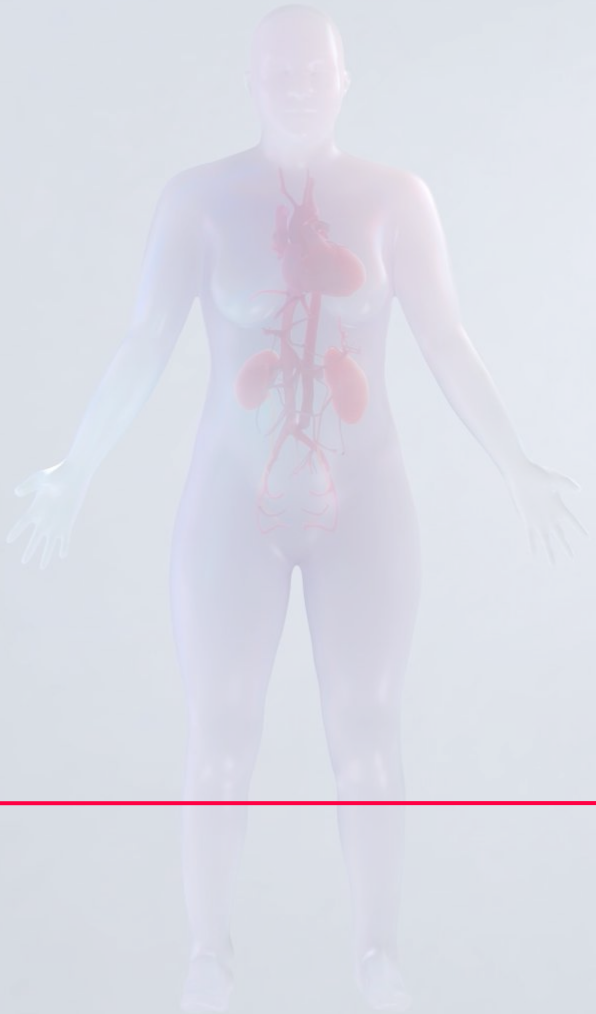

Q&A

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

Thank you