

Spatial Biology as a Tool to to reveal Mechanisms of Immune Exclusion

SITC Immune Exclusion Virtual Summit
2023



Disclosures

Scientific Advisory Board & Stock Ownership: PrimeVax, BioAI

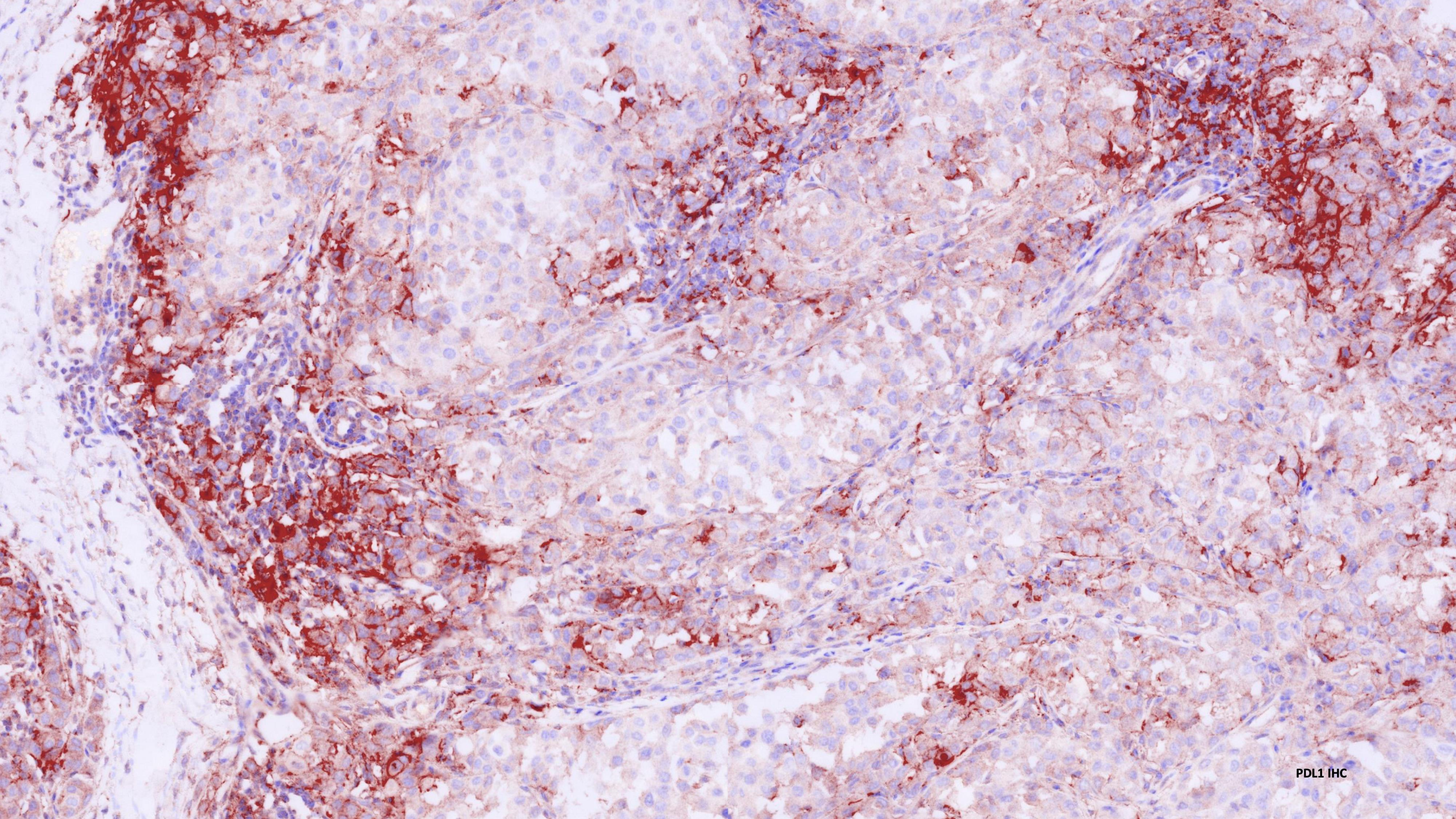
Scientific Advisory Board: Lunaphore

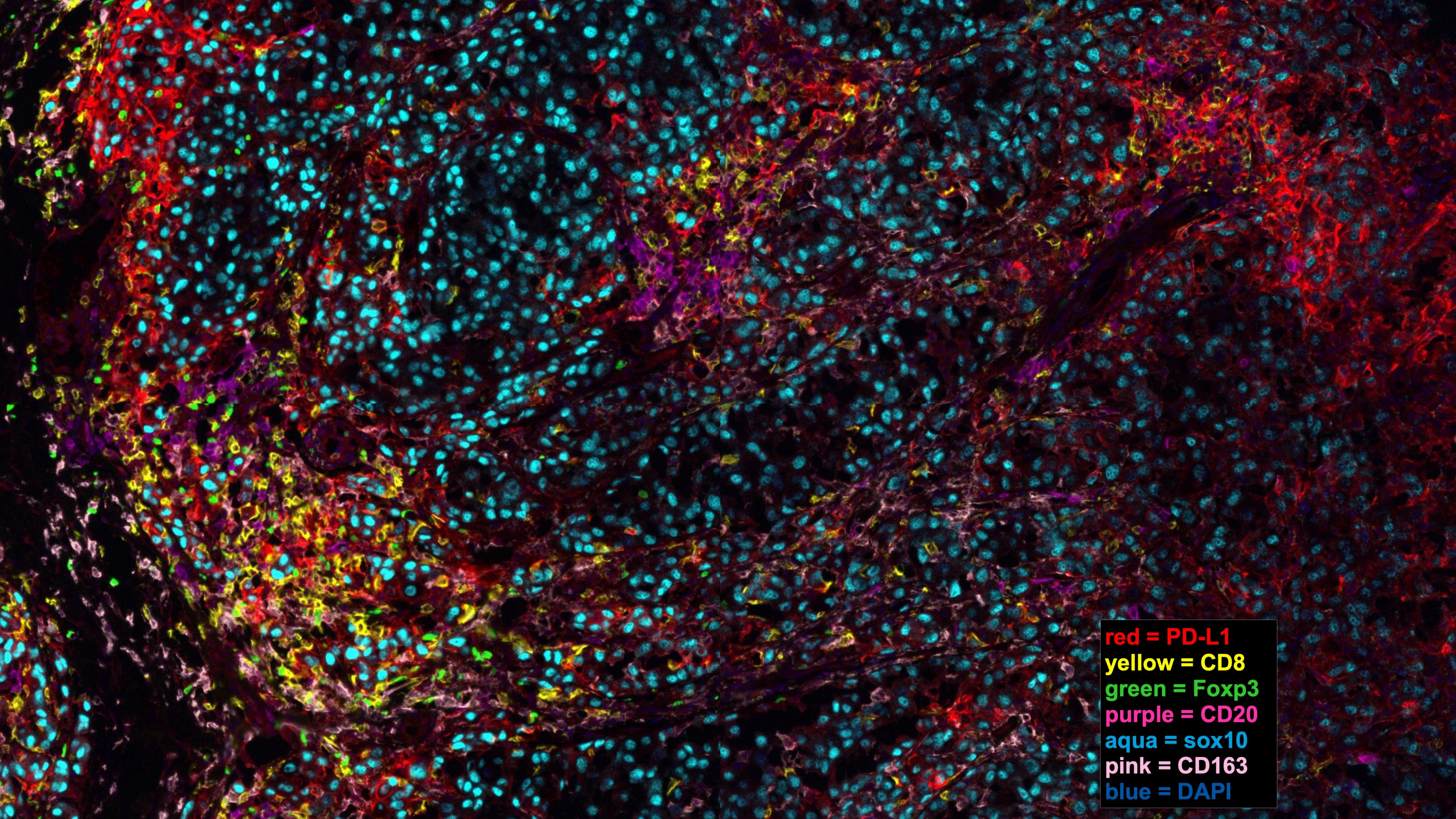
Patents: 10,275,880; 10,552,960; 11,164,316: Image processing systems and methods for displaying multiple images of a biological specimen & Image processing method and system for analyzing a multi-channel image obtained from a biological tissue sample being stained by multiple stains.

Patent pending: 20200388033: System and method for automatic labeling of pathology images.

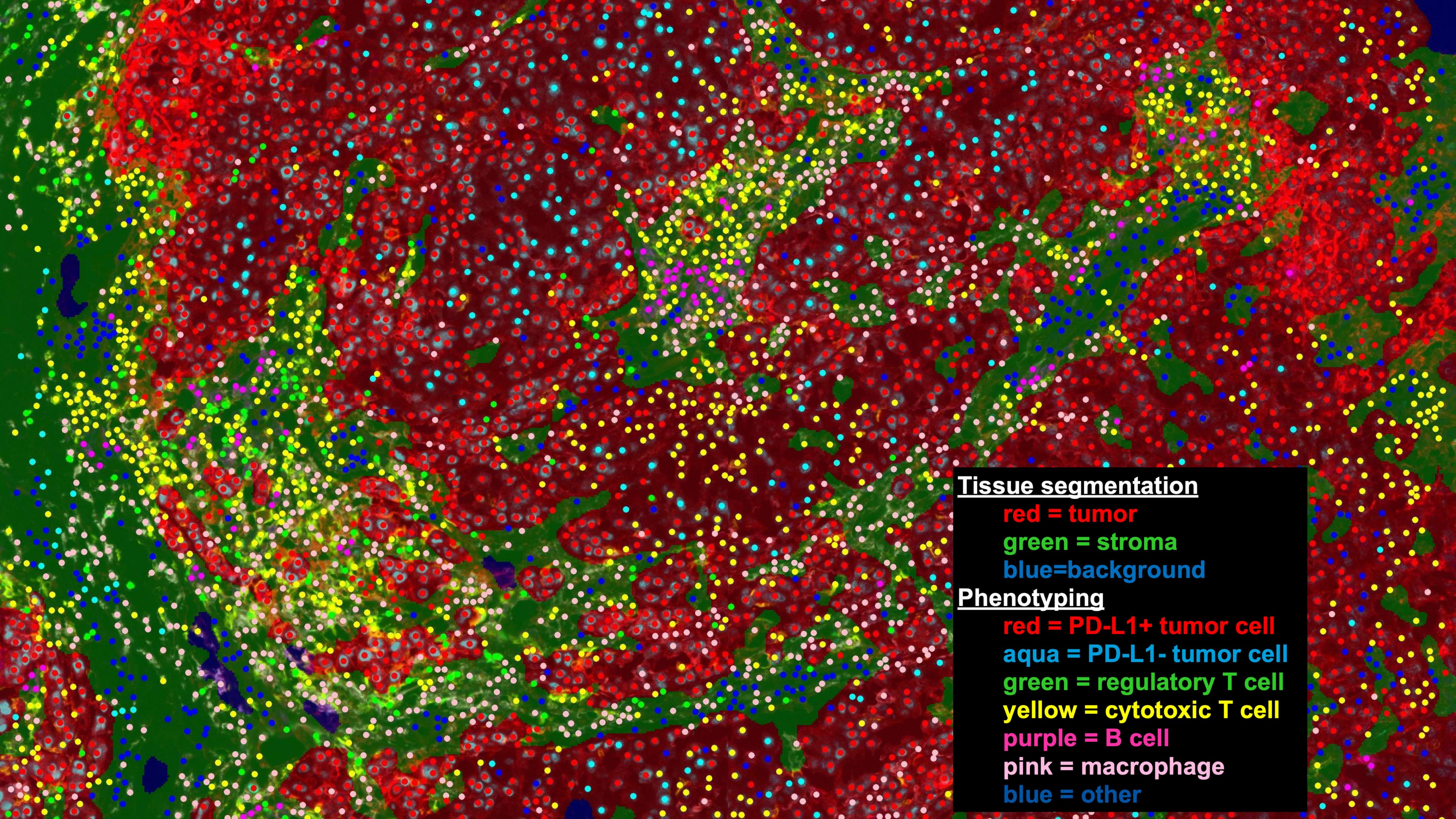
Research Support: MSFT End Customer Investment Funds (ECIF) program

Research Support: Illumina





red = PD-L1
yellow = CD8
green = Foxp3
purple = CD20
aqua = sox10
pink = CD163
blue = DAPI



Tissue segmentation

red = tumor

green = stroma

blue=background

Phenotyping

red = PD-L1+ tumor cell

aqua = PD-L1- tumor cell

green = regulatory T cell

yellow = cytotoxic T cell

purple = B cell

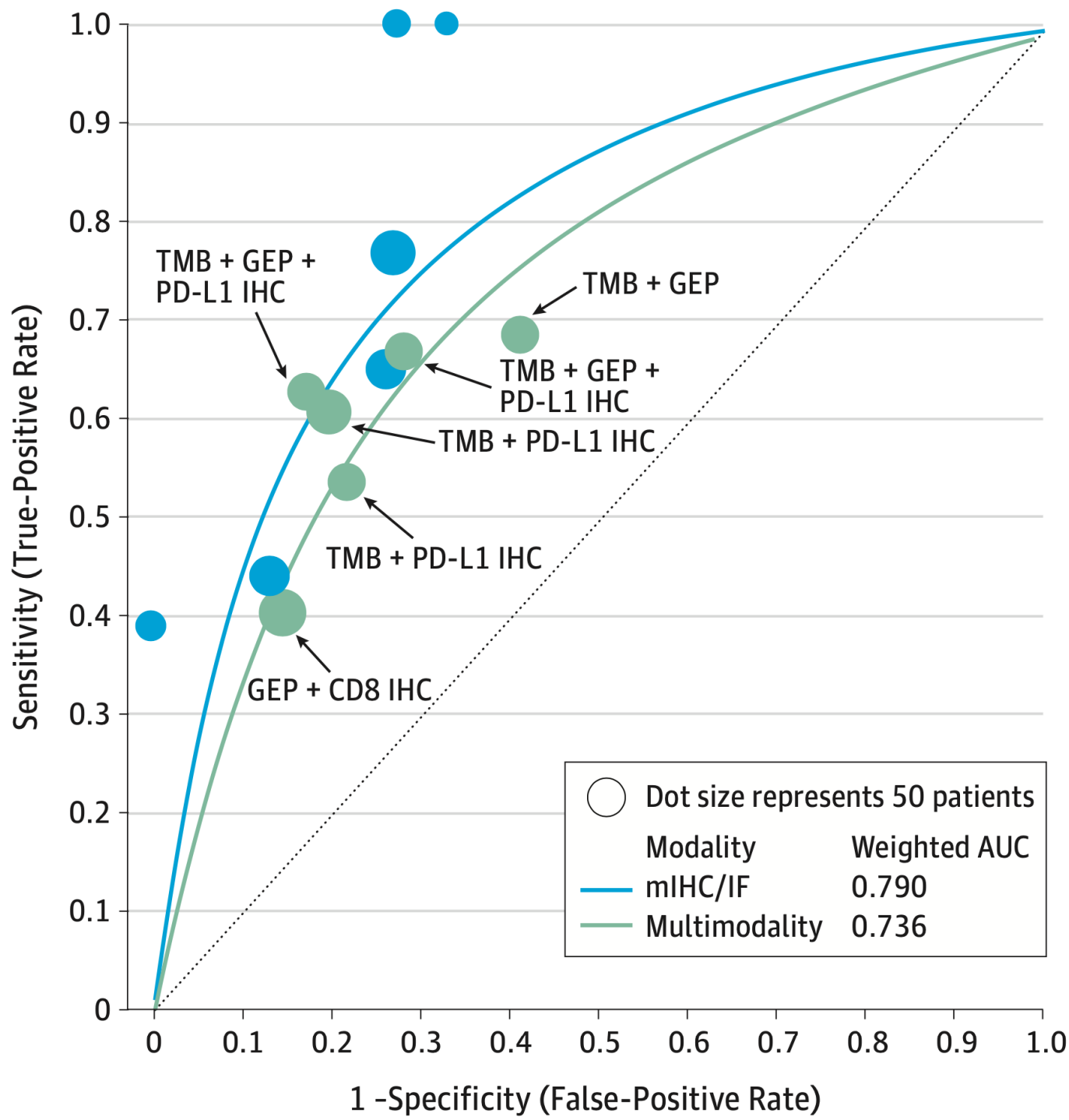
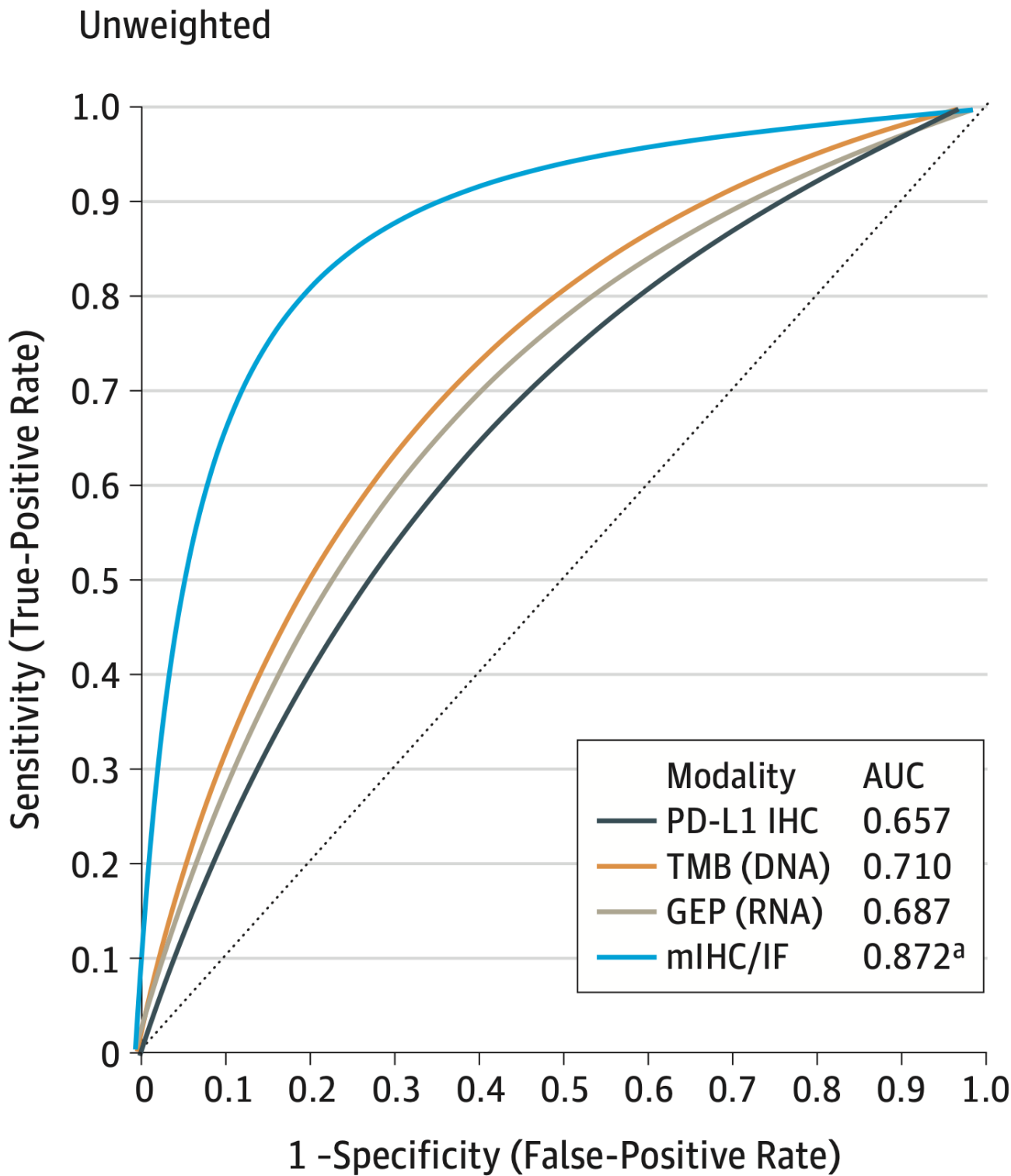
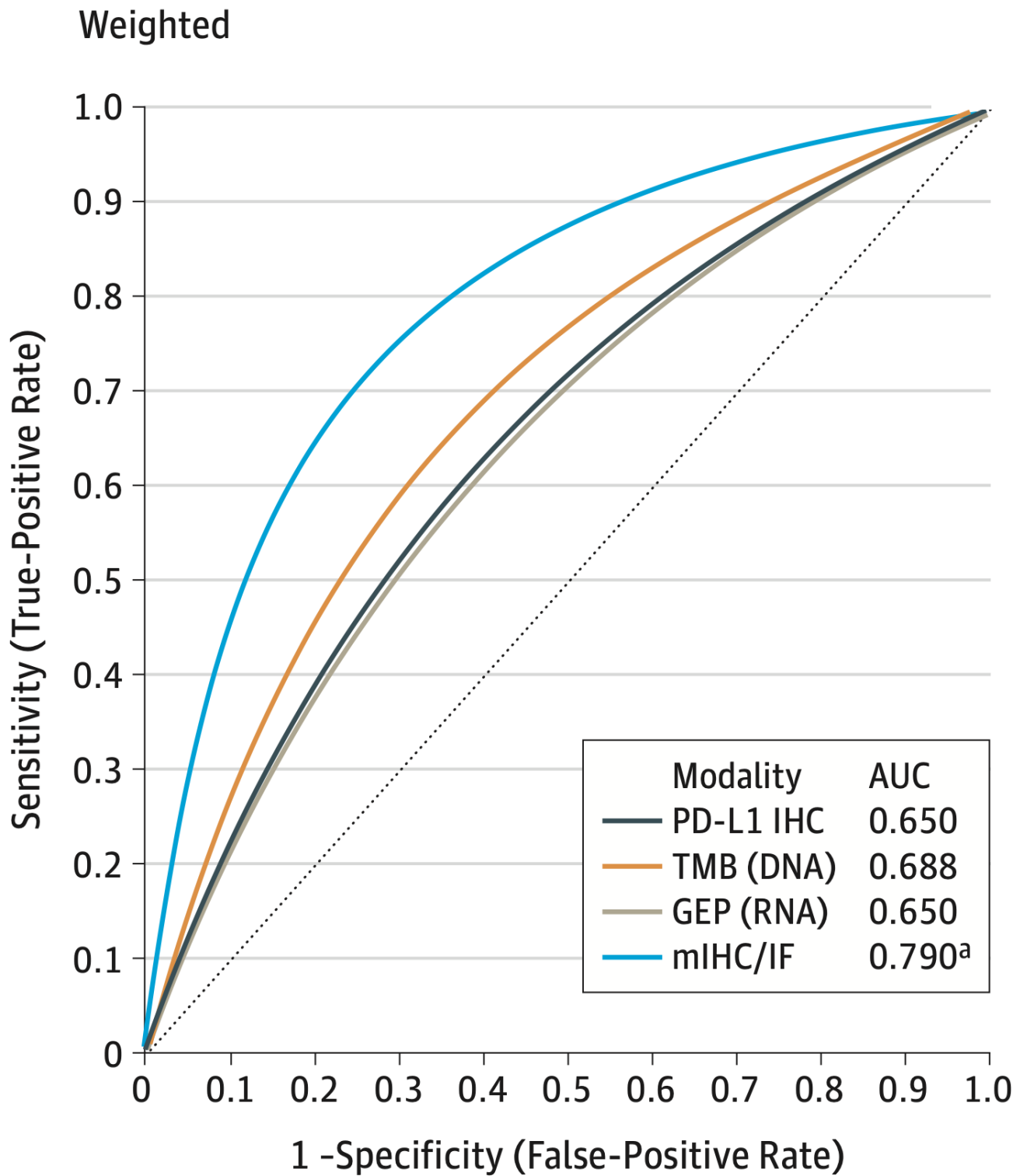
pink = macrophage

blue = other

Comparison of Biomarker Modalities for Predicting Response to PD-1/PD-L1 Checkpoint Blockade

A Systematic Review and Meta-analysis

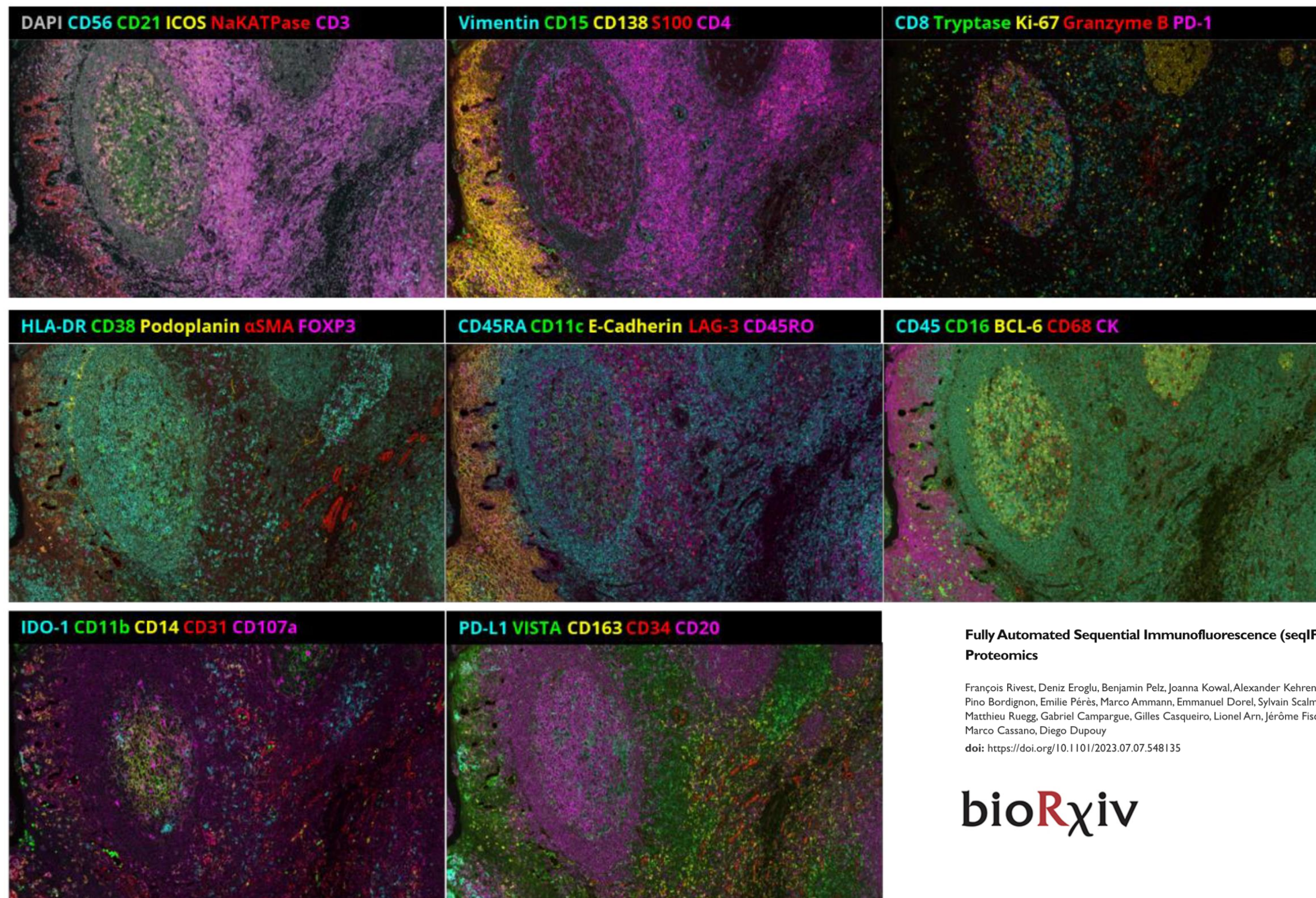
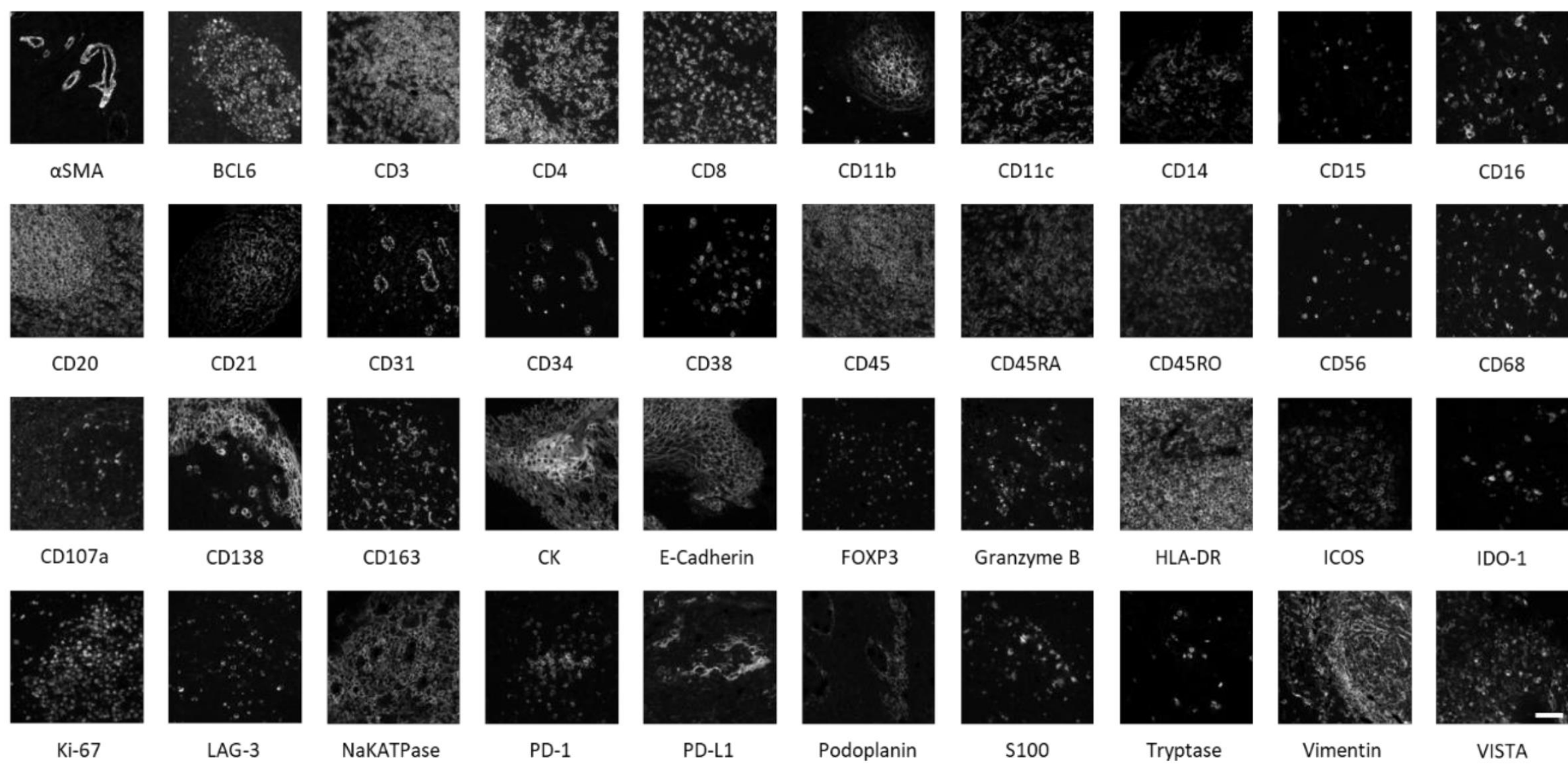
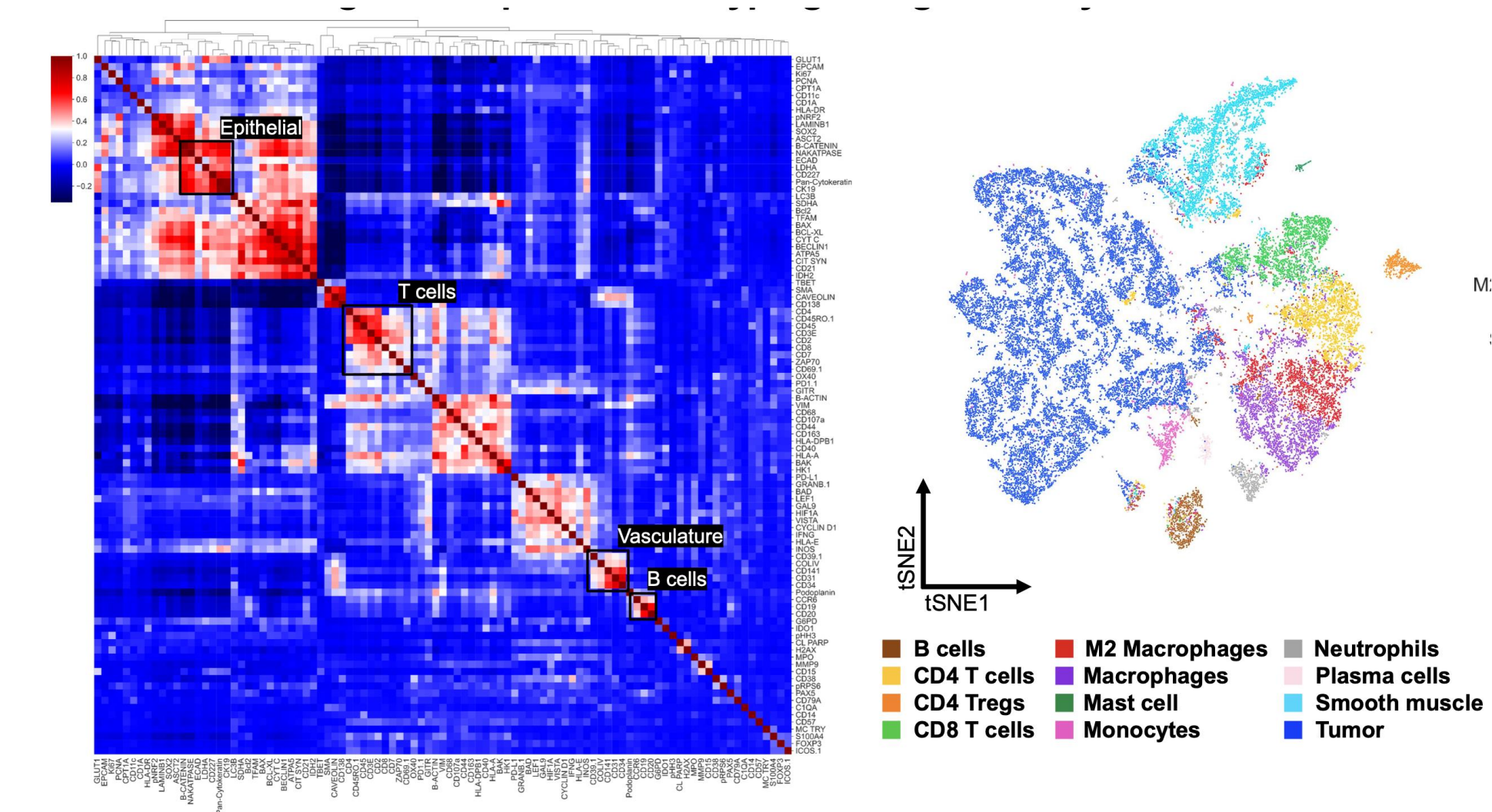
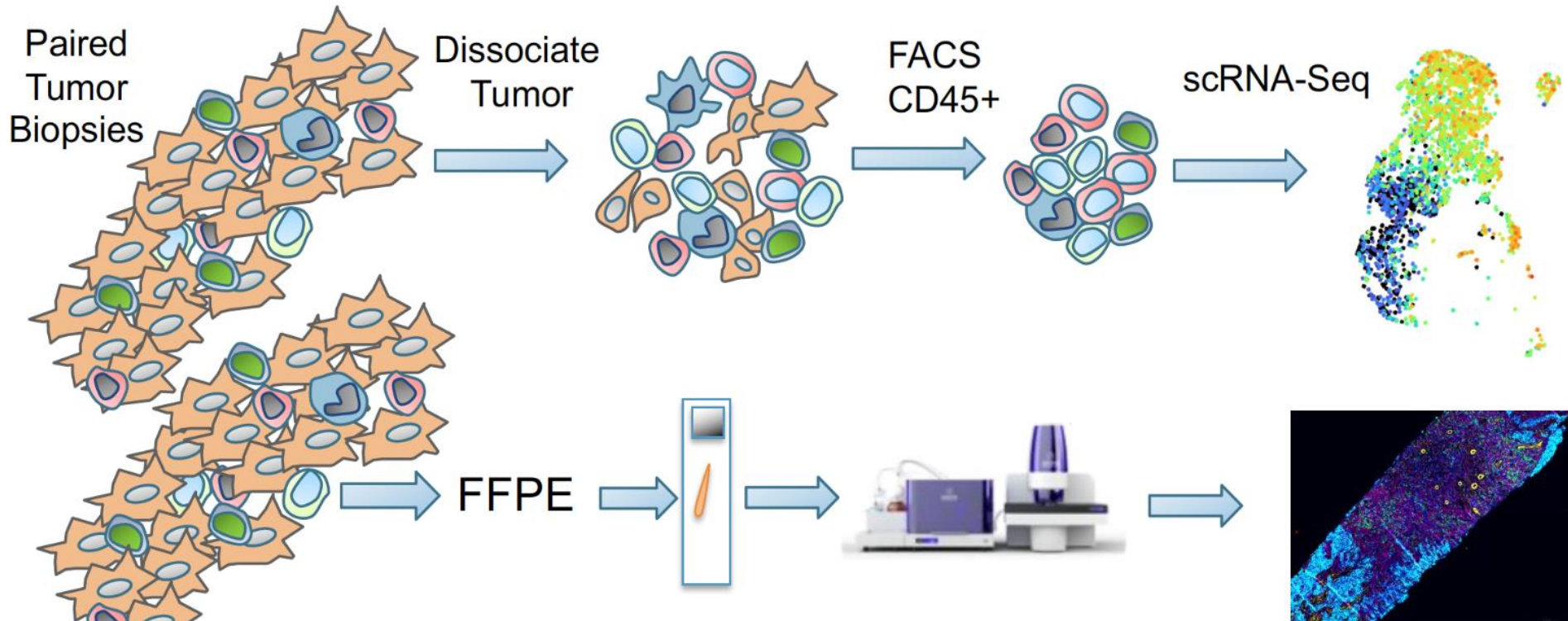
Steve Lu; Julie E. Stein, MD; David L. Rimm, MD, PhD; Daphne W. Wang, MS; J. Michael Bell; Douglas B. Johnson, MD; Jeffrey A. Sosman, MD; Kurt A. Schalper, MD, PhD; Robert A. Anders, MD, PhD; Hao Wang, PhD; Clifford Hoyt, MS; Drew M. Pardoll, MD, PhD; Ludmila Danilova, PhD; Janis M. Taube, MD



6764: Multi-Parametric Comparison of Ultra-high-Plex Spatial Phenotyping of Proteins in FFPE Head and Neck Tumor Biopsies

Aditya Pratapa¹, Shawn M. Jensen², Niyati Jhaveri¹, Christopher Paustian², Quyen C. Vu², Tarsem Moudgil², Yoshinobu Koguchi², Venkatesh Rajamanickam², Brady Bernard², Tanisha Christie², Brian Piening², Rom S. Leidner², Oliver Braubach¹, Bernard A. Fox²

¹Akoya Biosciences, Marlborough, MA; ²Providence Cancer Institute of Oregon, Earle A. Chiles Research Institute, Portland, OR



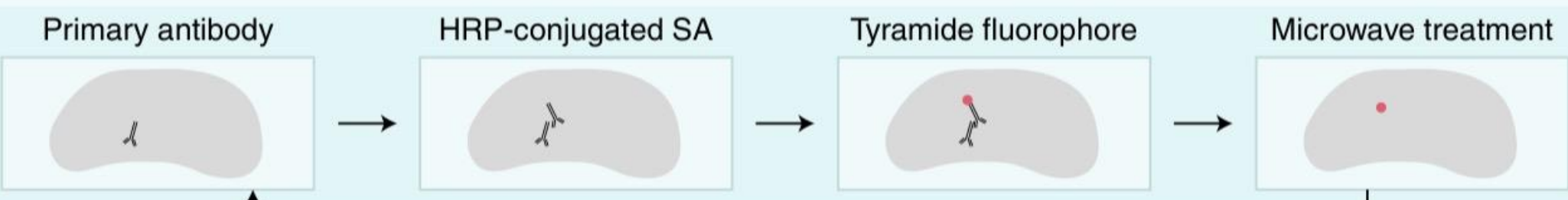
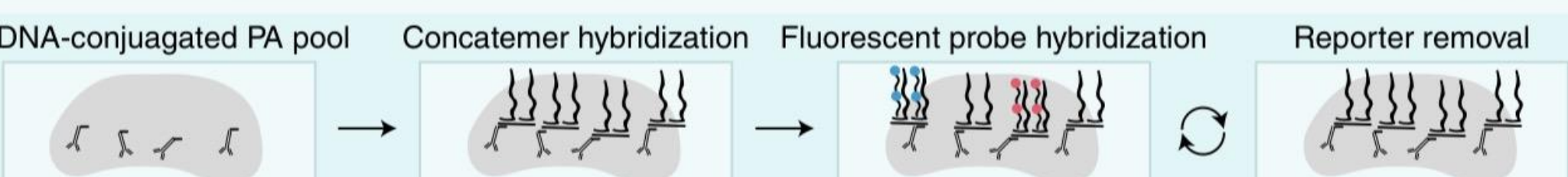
Fully Automated Sequential Immunofluorescence (seqIF) for Hyperplex Spatial Proteomics

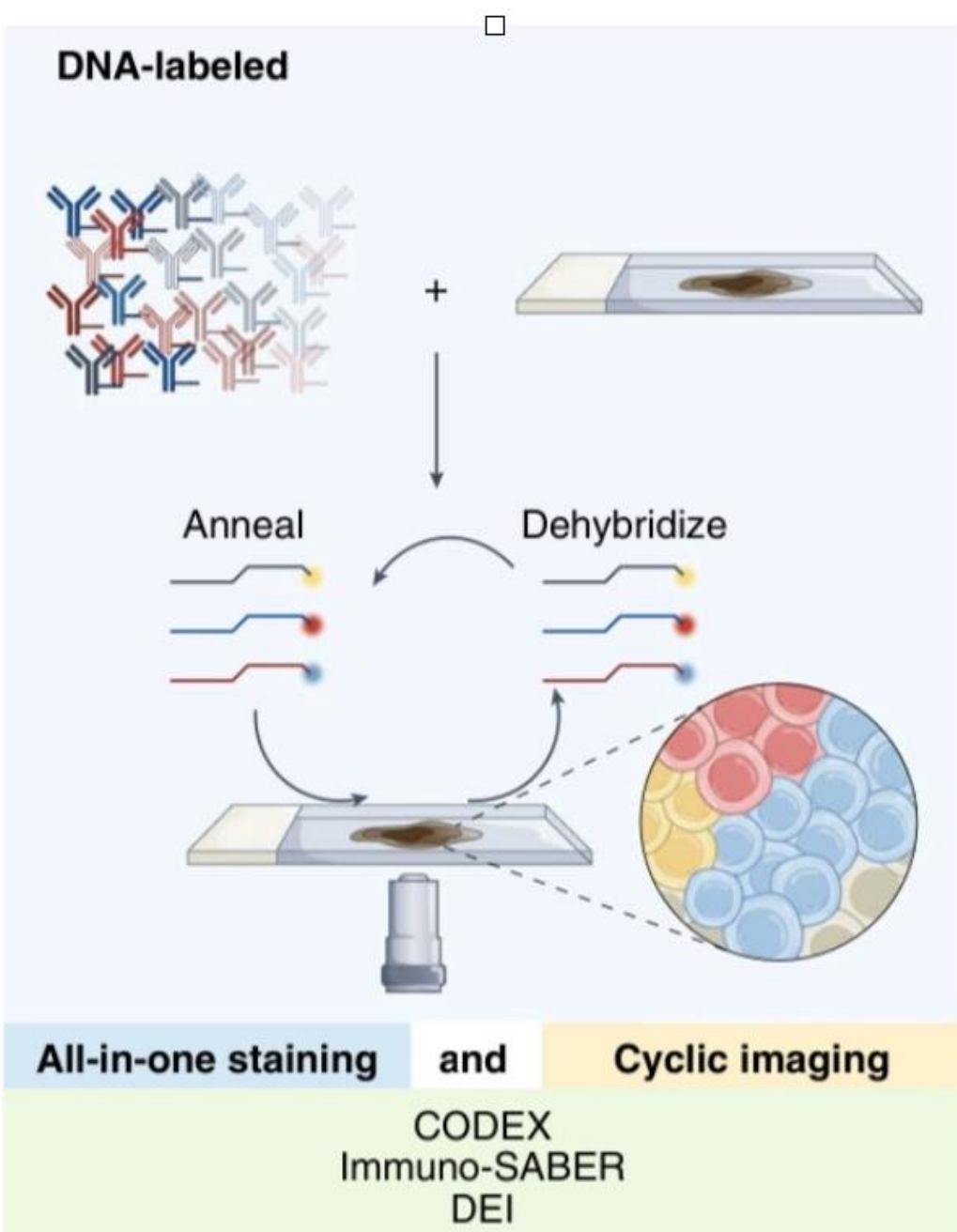
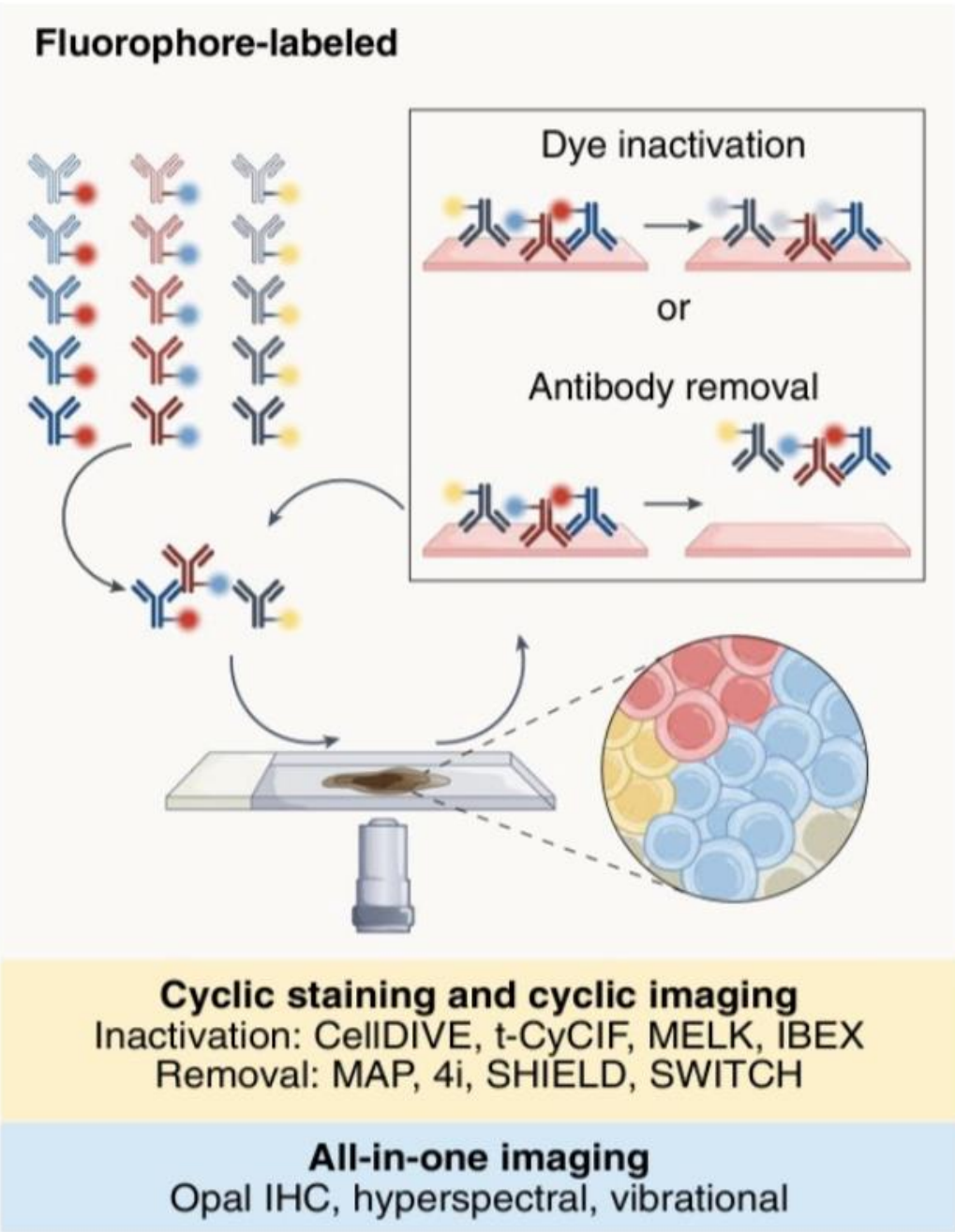
François Rivest, Deniz Eroglu, Benjamin Pelz, Joanna Kowal, Alexander Kehren, Maria Giuseppina Procopio, Pino Bordignon, Emilie Pères, Marco Ammann, Emmanuel Dorel, Sylvain Scalnazzi, Lorenzo Bruno, Matthieu Ruegg, Gabriel Campargue, Gilles Casqueiro, Lionel Arn, Jérôme Fischer, Saska Brajkovic, Pierre Joris, Marco Cassano, Diego Dupouy

doi: <https://doi.org/10.1101/2023.07.07.548135>

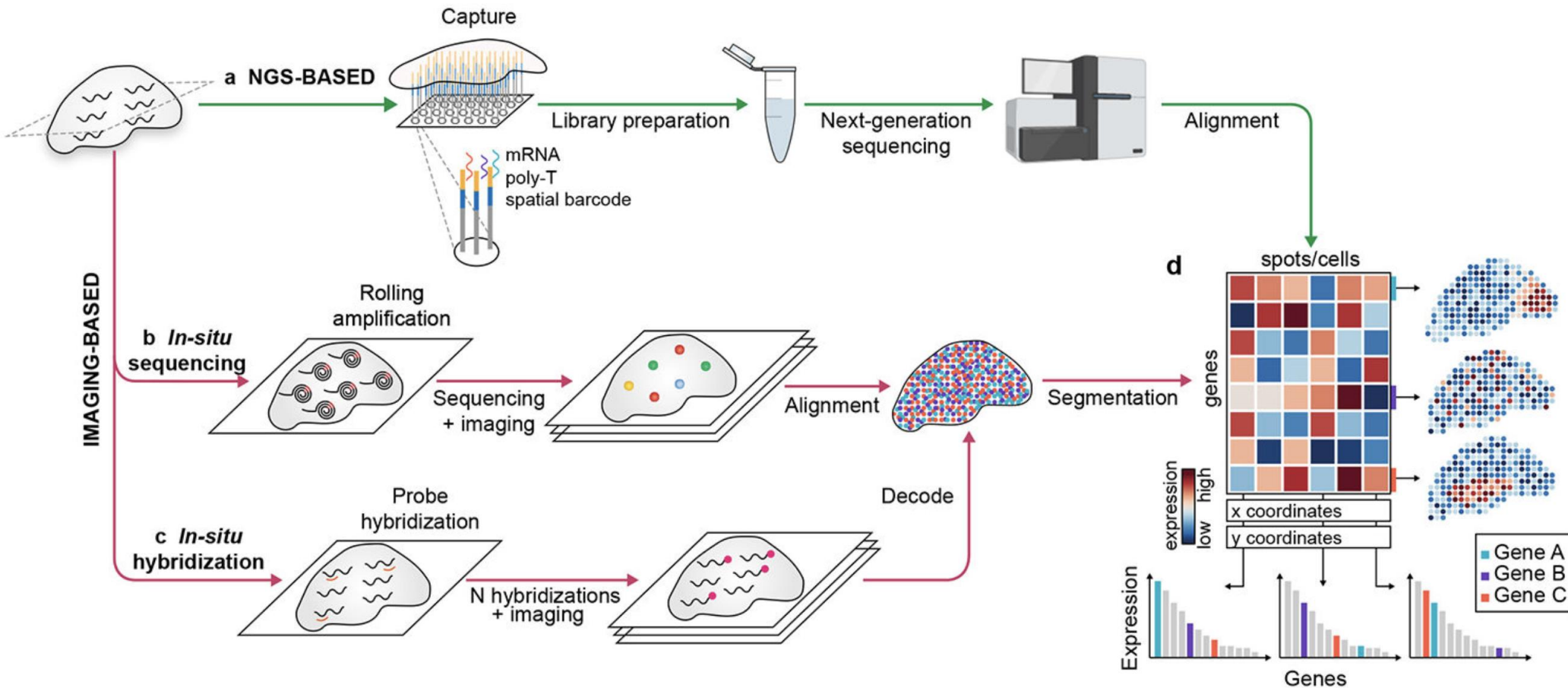
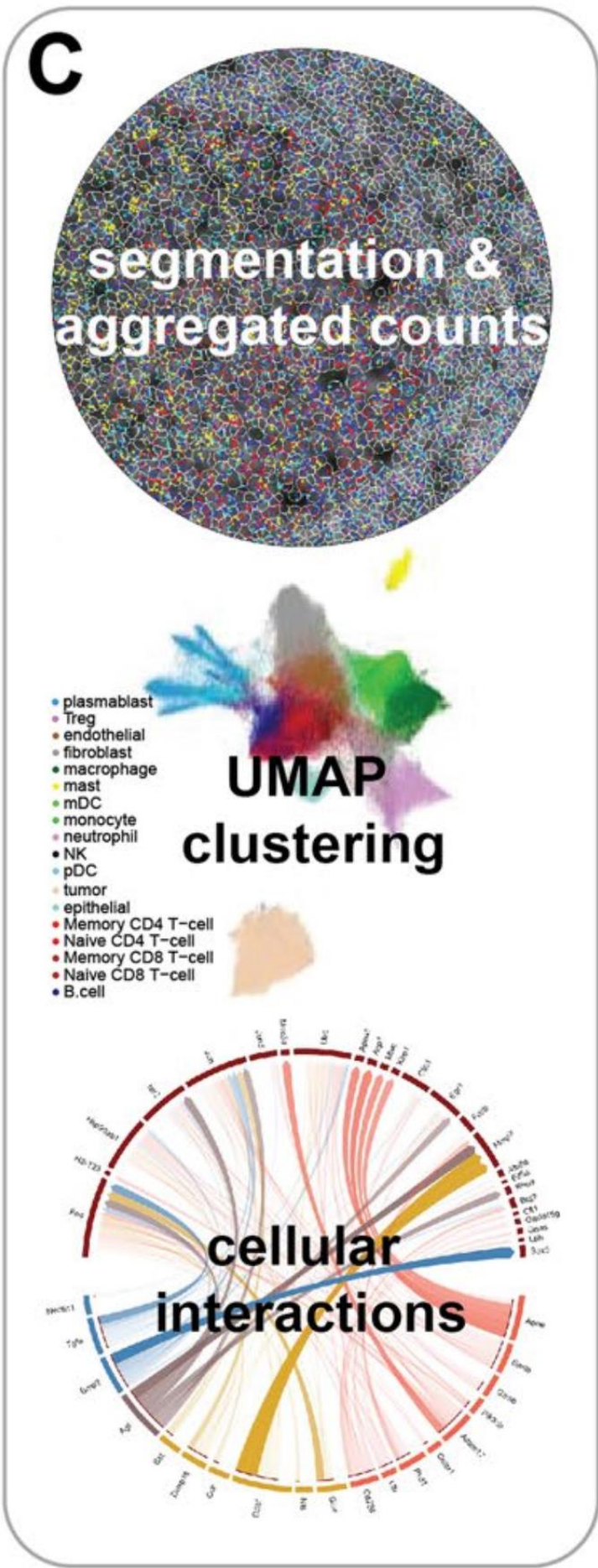
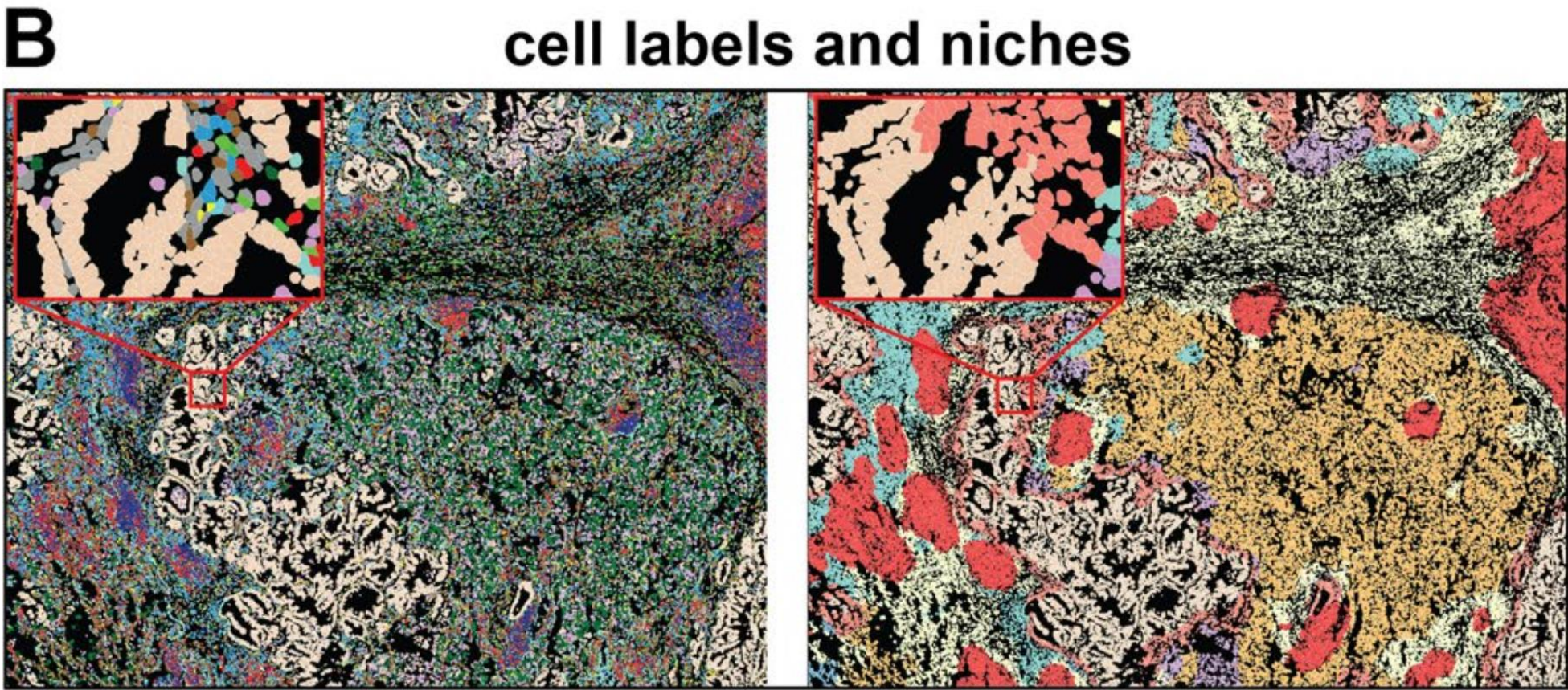
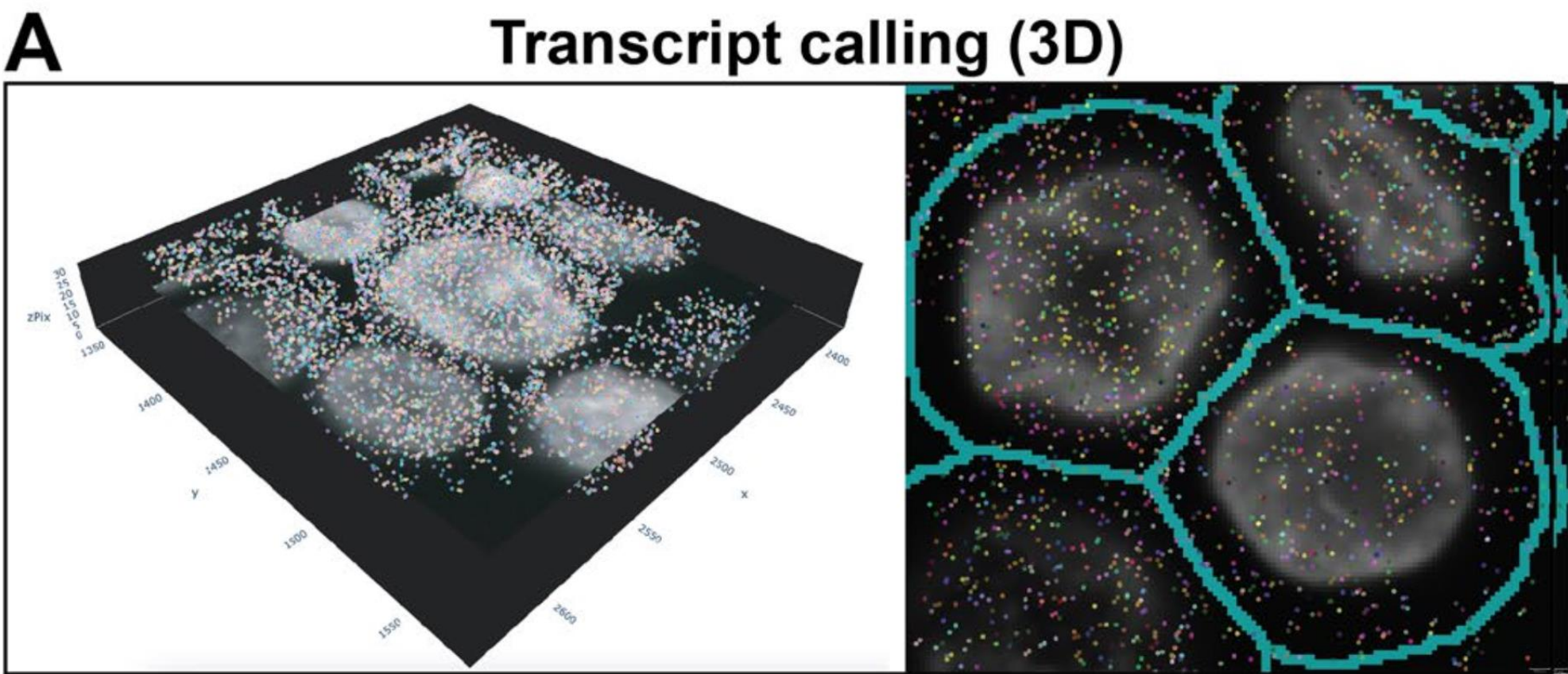
bioRxiv

Spatial Proteomics

				No. of targets	Tissue prep.
Iterative	miHC			30	FFPE
	OPAL			10	FFPE
	CyclIF			60	FFPE
Iterative (fluorescence)	REAdye_lease and REAfinity			100 (400)	FFPE
	CODEX			60	FF* FFPE
	Immuno-SABER			10 (50)	Whole-mount FF* FFPE



Spatial Transcriptomics



Science

Current Issue

HOME > SCIENCE > VOL. 381, NO. 6657 > THE DAWN OF SPATIAL OMICS

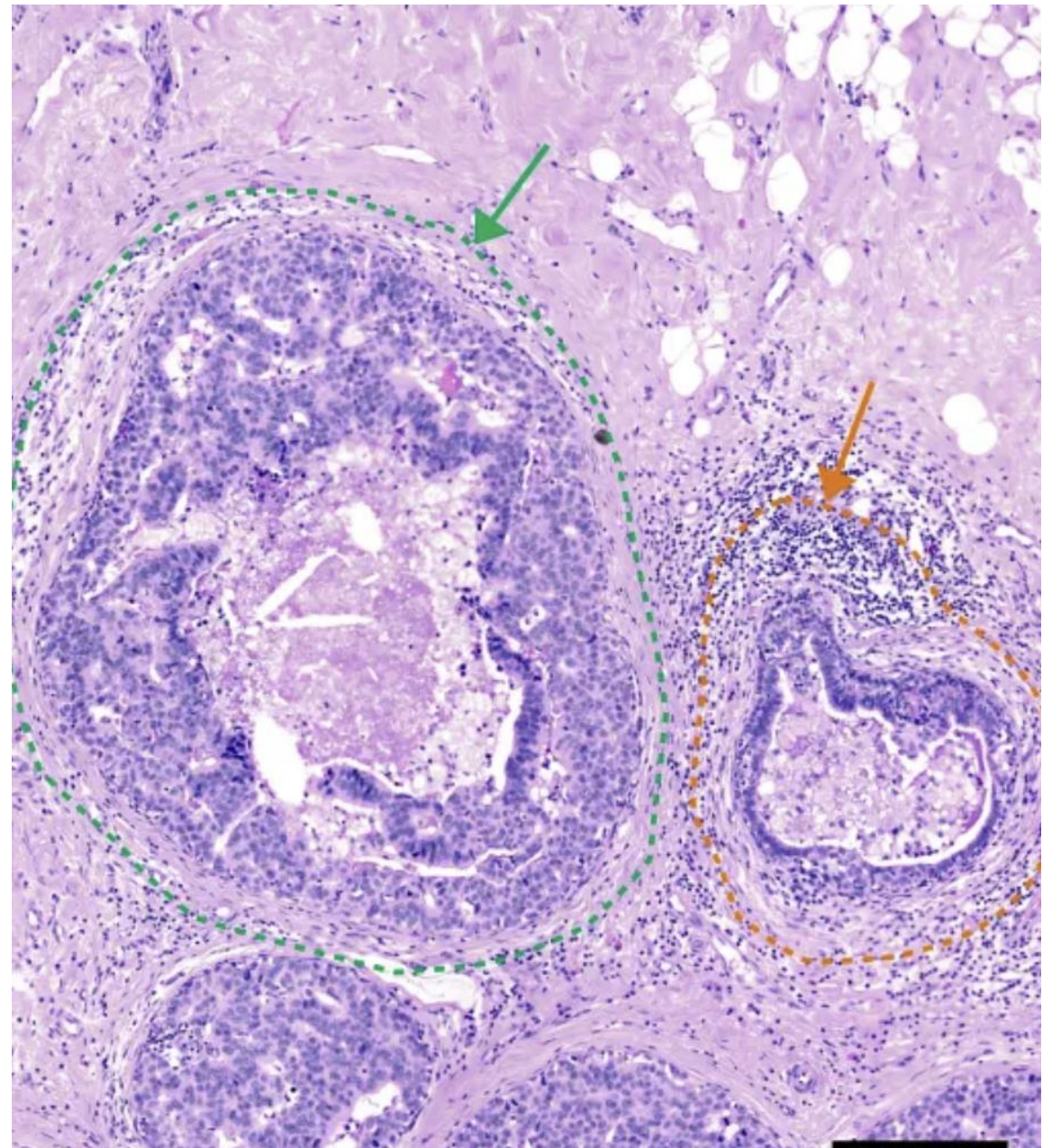
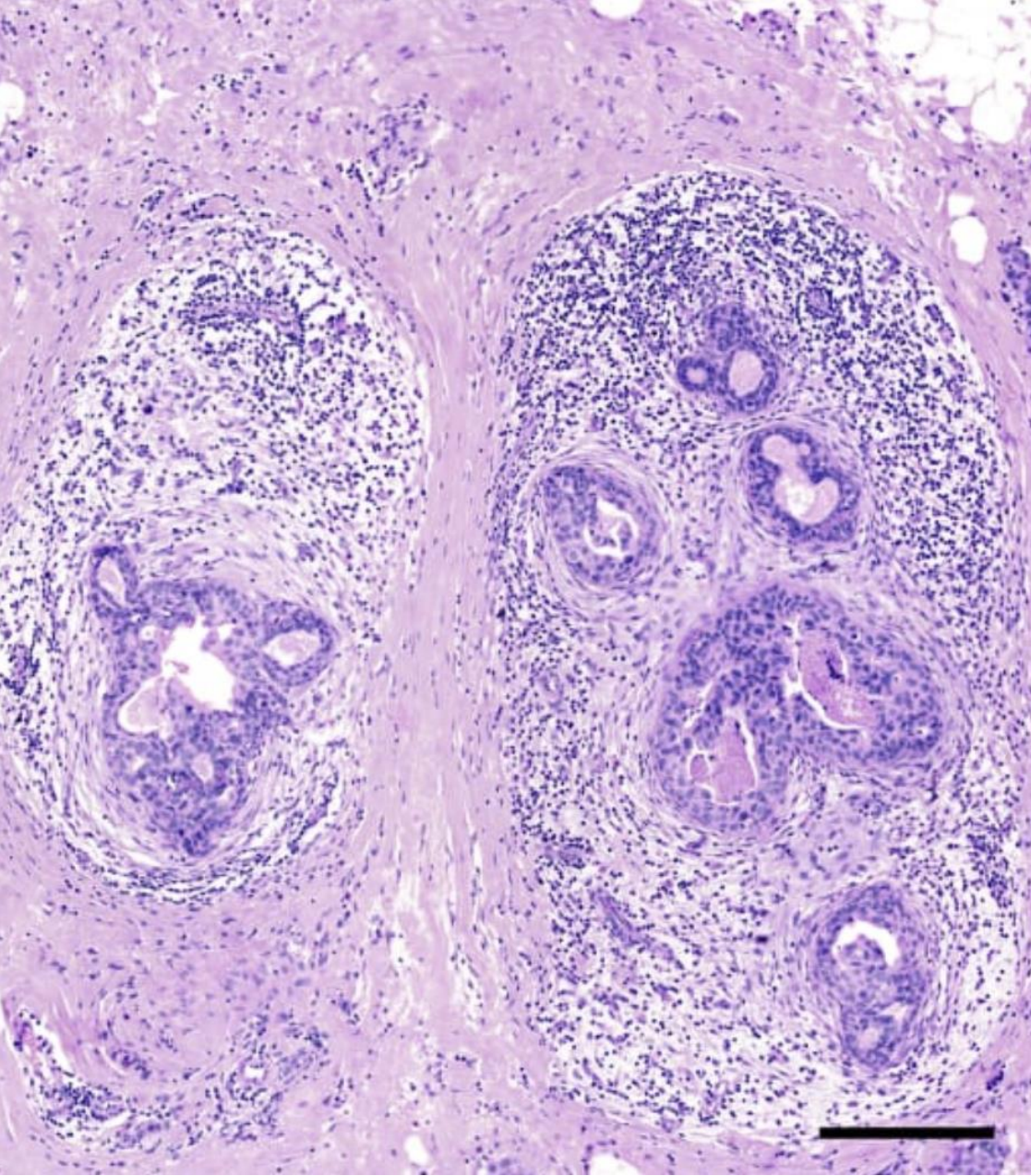
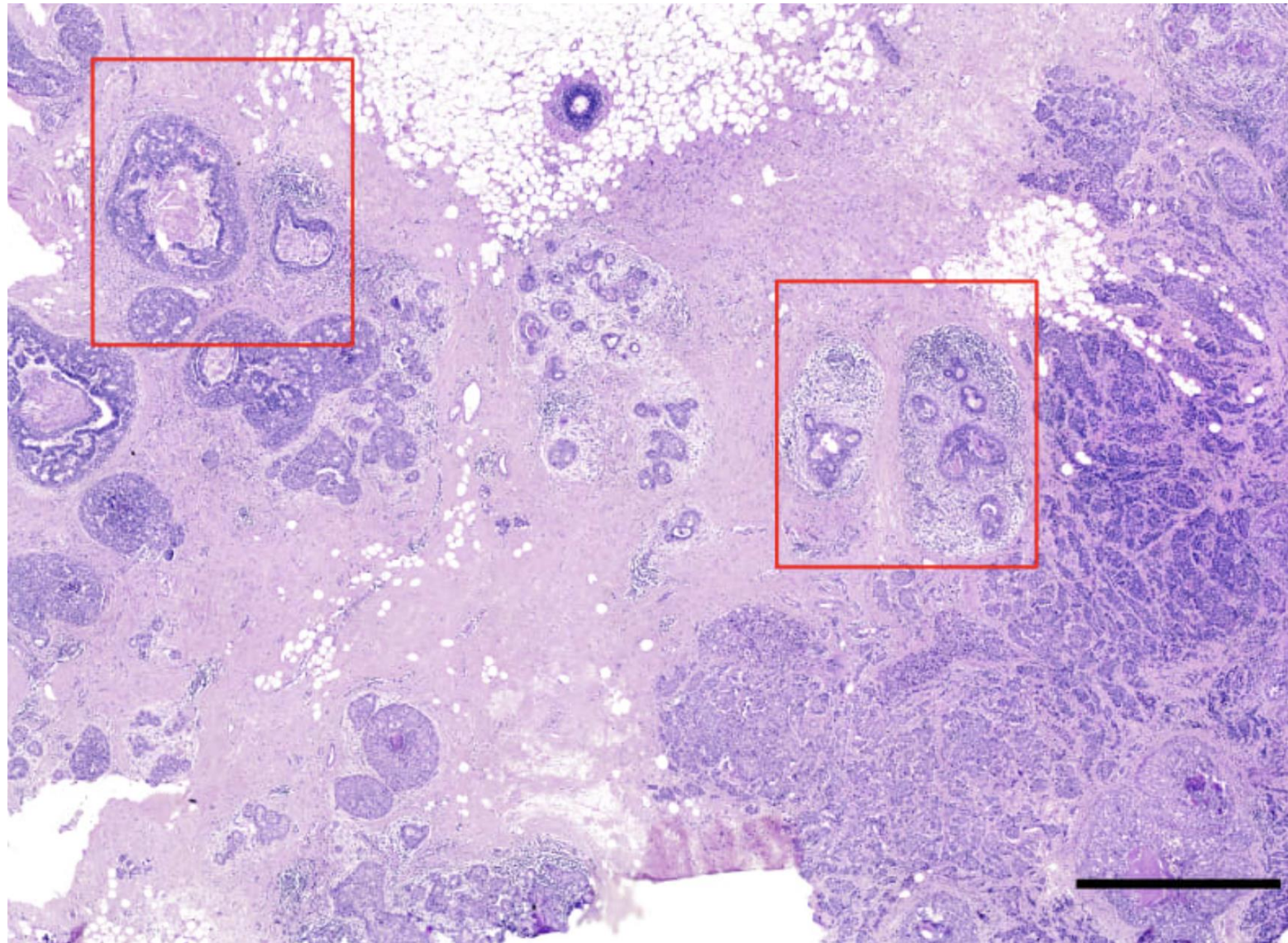
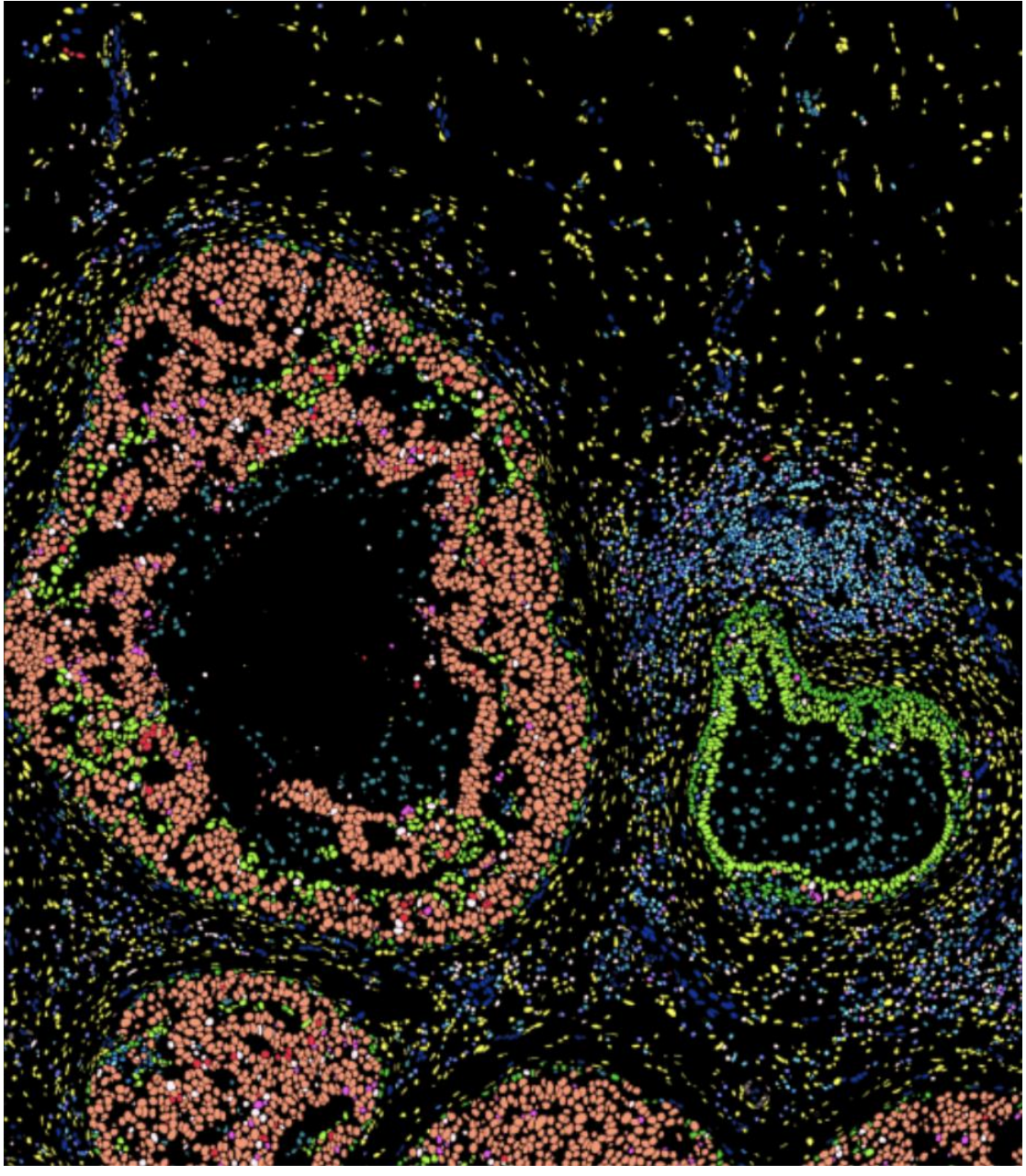
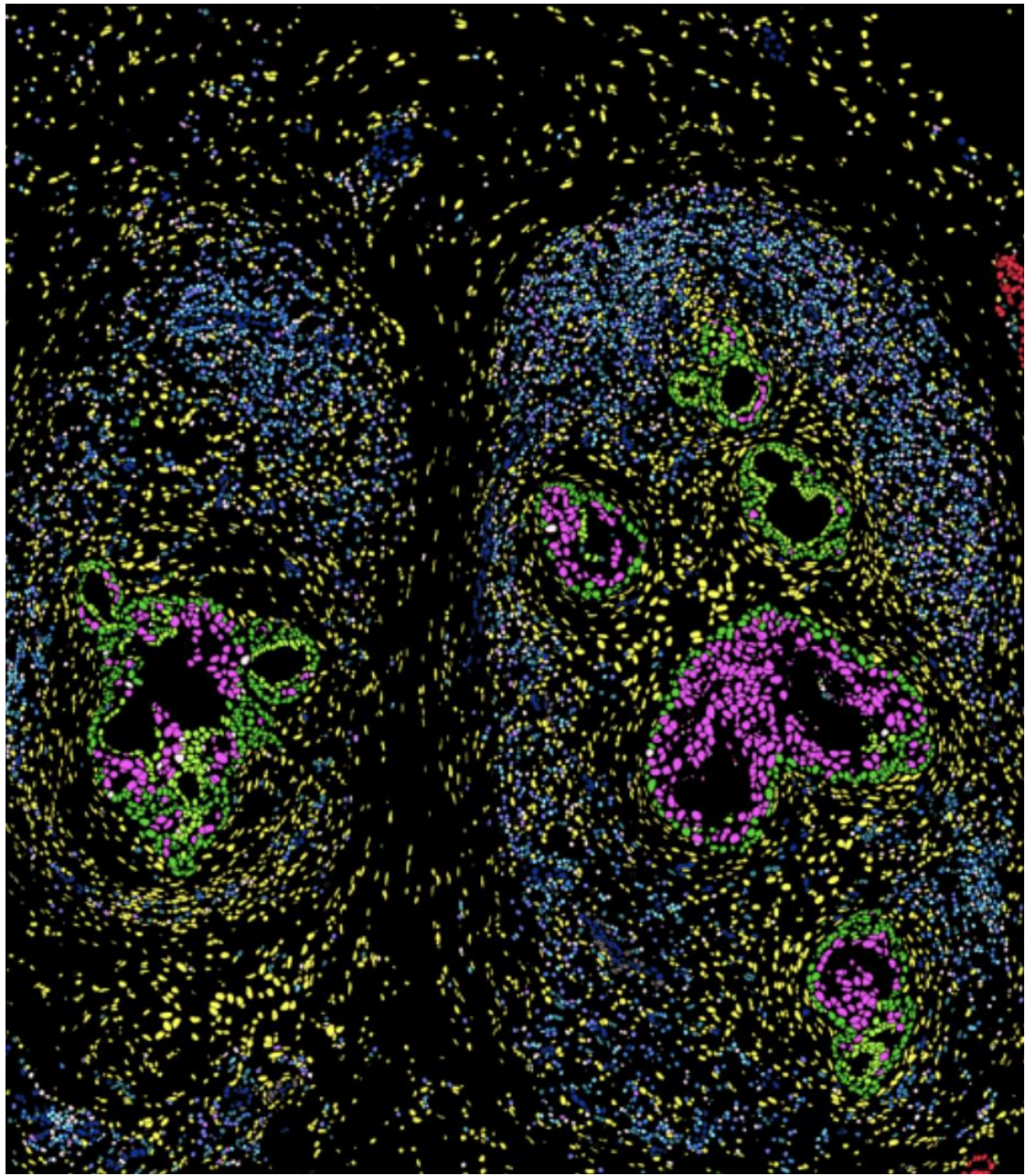
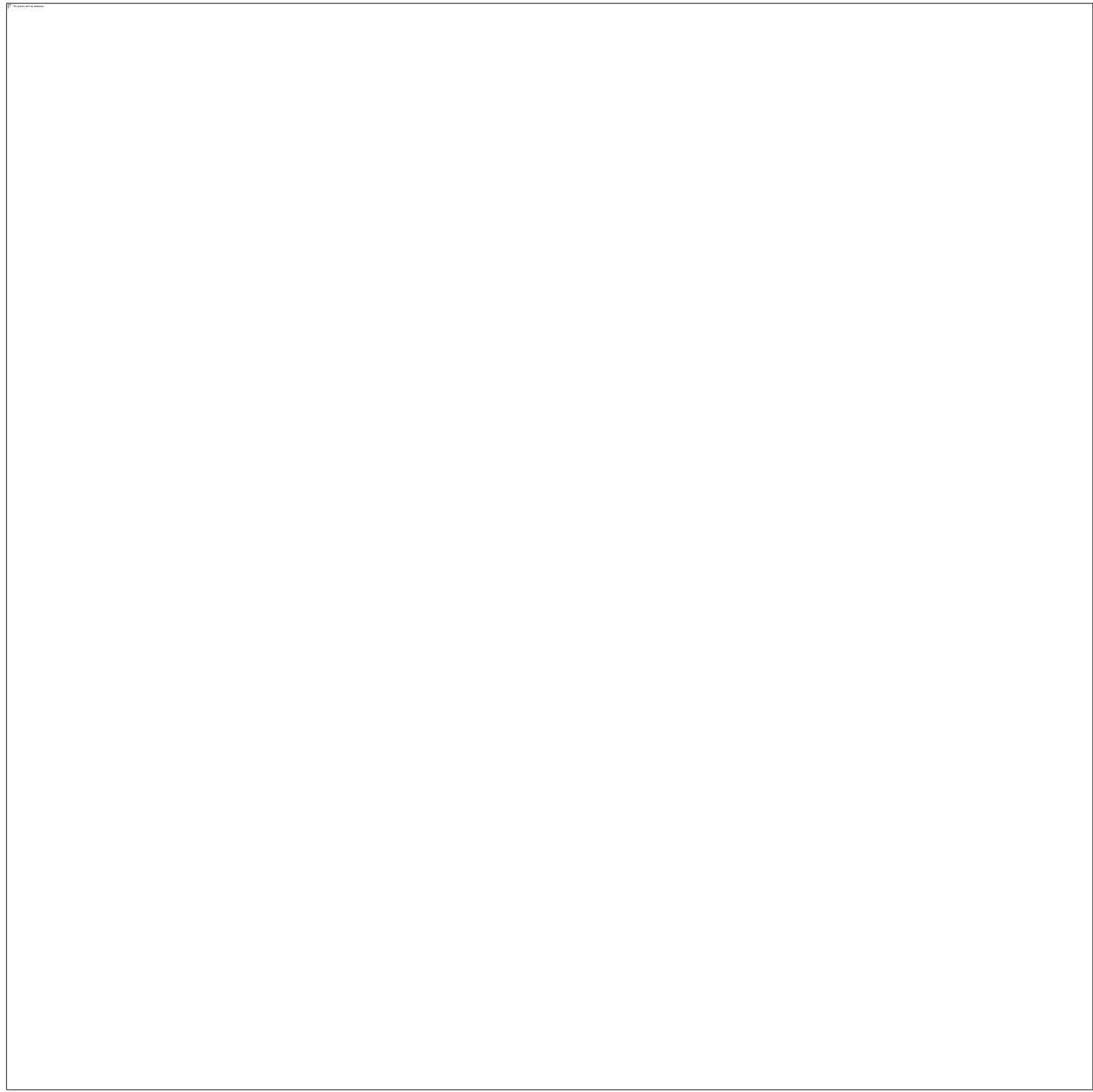
REVIEW | SPATIAL OMICS

The dawn of spatial omics

DARIO BRESSAN , GIORGIA BATTISTONI , AND GREGORY J. HANNON  [Authors Info & Affiliations](#)

SCIENCE • 4 Aug 2023 • Vol 381, Issue 6657 • DOI: 10.1126/science.abq4964

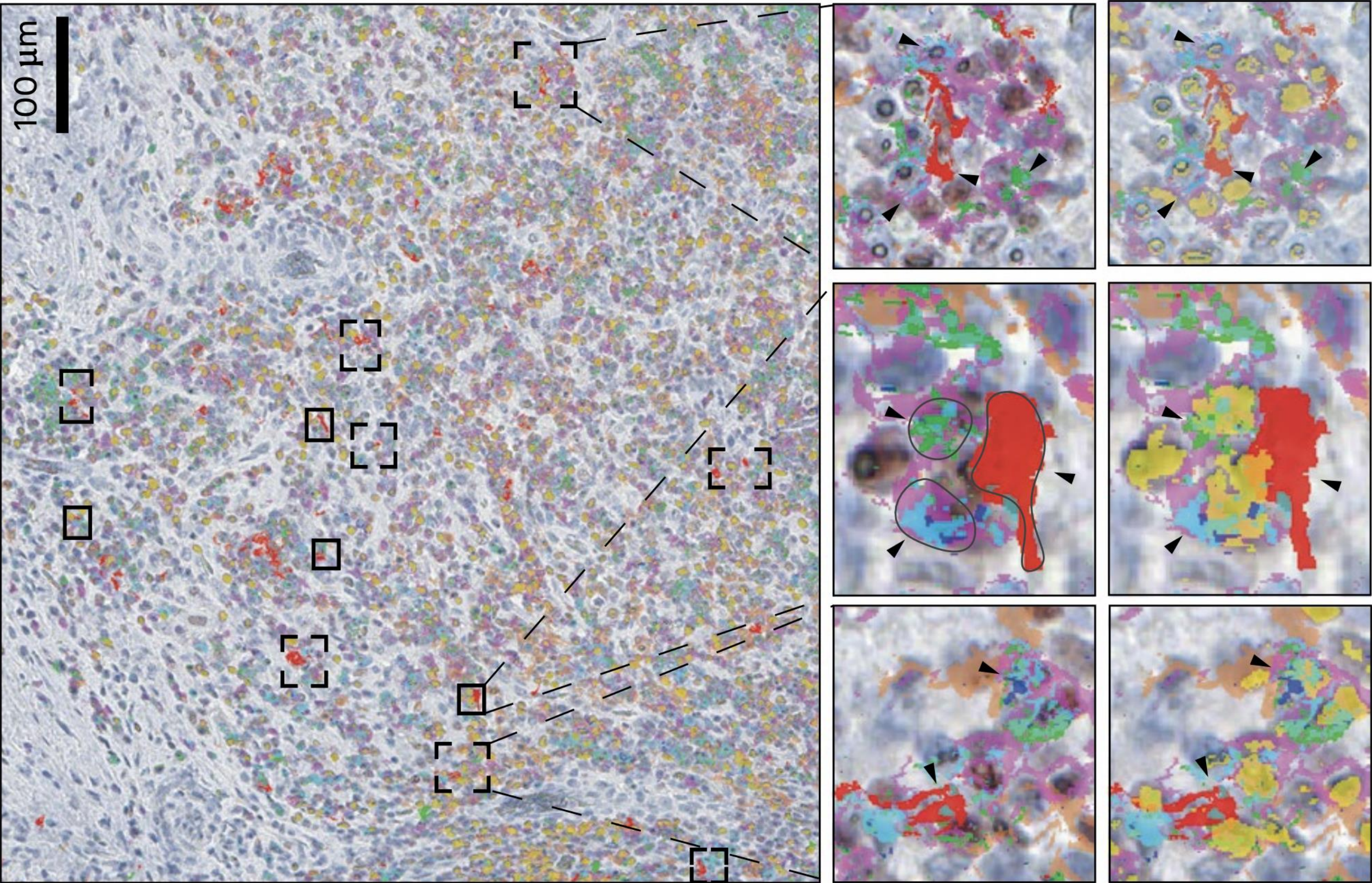
14,089



Intratumoral dendritic cell–CD4⁺ T helper cell niches enable CD8⁺ T cell differentiation following PD-1 blockade in hepatocellular carcinoma

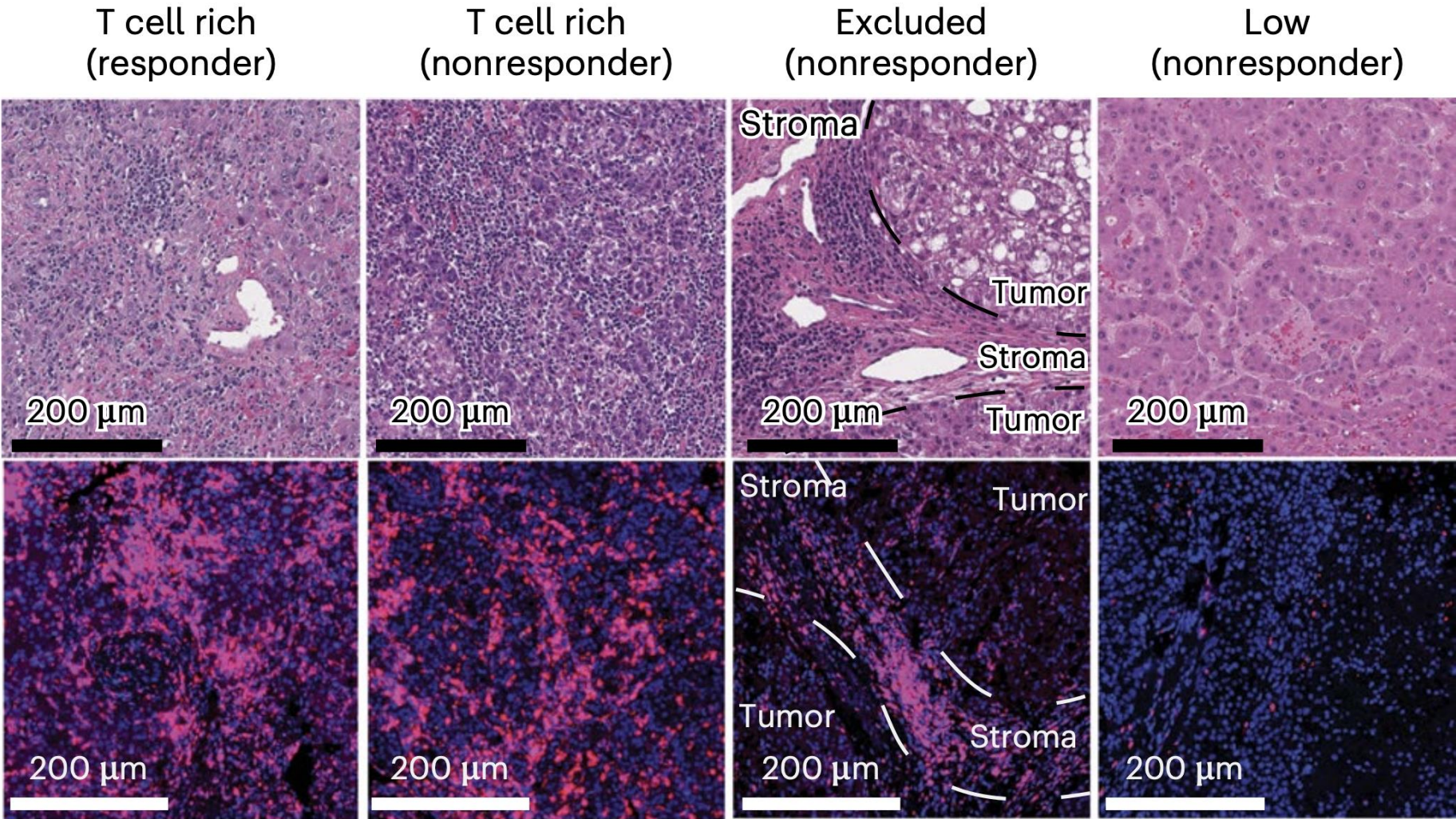
Received: 9 June 2022
Accepted: 10 April 2023
Published online: 15 June 2023
Check for updates

Assaf Magen^{1,2,3,13}, Pauline Hamon^{1,2,3,13}, Nathalie Fiaschi⁴, Brian Y. Soong^{1,2,3}, Matthew D. Park^{1,2,3}, Raphaël Mattiuz^{1,2,3}, Etienne Humblin^{1,2,3}, Leanna Troncoso^{1,2,3}, Darwin D'souza⁵, Travis Dawson⁵, Joel Kim^{1,2,3}, Steven Hamel^{1,2,3}, Mark Buckup^{1,2,3}, Christie Chang^{1,2,3}, Alexandra Tabachnikova^{1,2,3}, Hara Schwartz^{1,2,3}, Nausicaa Malissen^{1,2,3}, Yonit Lavin^{1,2,3}, Alessandra Soares-Schanoski^{1,2,3}, Bruno Giotti⁶, Samarth Hegde^{1,2,3}, Giorgio Ioannou^{1,2,3}, Edgar Gonzalez-Kozlova^{1,2,3}, Clotilde Hennequin^{1,2,3}, Jessica Le Berichel^{1,2,3}, Zhen Zhao⁷, Stephen C. Ward⁸, Isabel Fiel⁷, Baijun Kou⁴, Michael Dobosz⁹, Lianjie Li⁴, Christina Adler⁸, Min Ni⁸, Yi Wei⁸, Wei Wang⁹, Gurinder S. Atwal⁴, Kunal Kundu⁹, Kamil J. Cygan¹⁰, Alexander M. Tsankov⁶, Adeeb Rahman⁴, Colles Price¹⁰, Nicolas Fernandez¹⁰, Jiang He¹⁰, Namita T. Gupta¹⁰, Seunghee Kim-Schulze^{1,2,3}, Sacha Gnjatic^{1,2,3}, Ephraim Kenigsberg¹⁰, Raquel P. Deering⁴, Myron Schwartz^{1,2,3,14}, Thomas U. Marron^{1,2,3,15}, Gavin Thurston^{1,2,3}, Alice O. Kamphorst^{1,2,3,13} & Miriam Merad^{1,2,3,6,12,13,14}



Without TCF1

With TCF1



CD3

CD8

CD20

DCLAMP

PD-1

CXCL13

TCF1

500 μm

mregDC
Progenitor CD8
CXCL13⁺ T_H

CD3⁺IL21⁺CH25H⁺
CD3⁺IL21⁺CH25H⁻

- Akoya
 - PhenoCycler/Imager
- Vizgen
 - Merscope
- IonPath
 - MIBIscope
- Lunaphore
 - Comet, Labsat
- Nanostring
 - GeoMx, CosMx..
- 10xGenomics
 - Xenium, Visium...
- ...



Advances and prospects for the Human BioMolecular Atlas Program (HuBMAP)

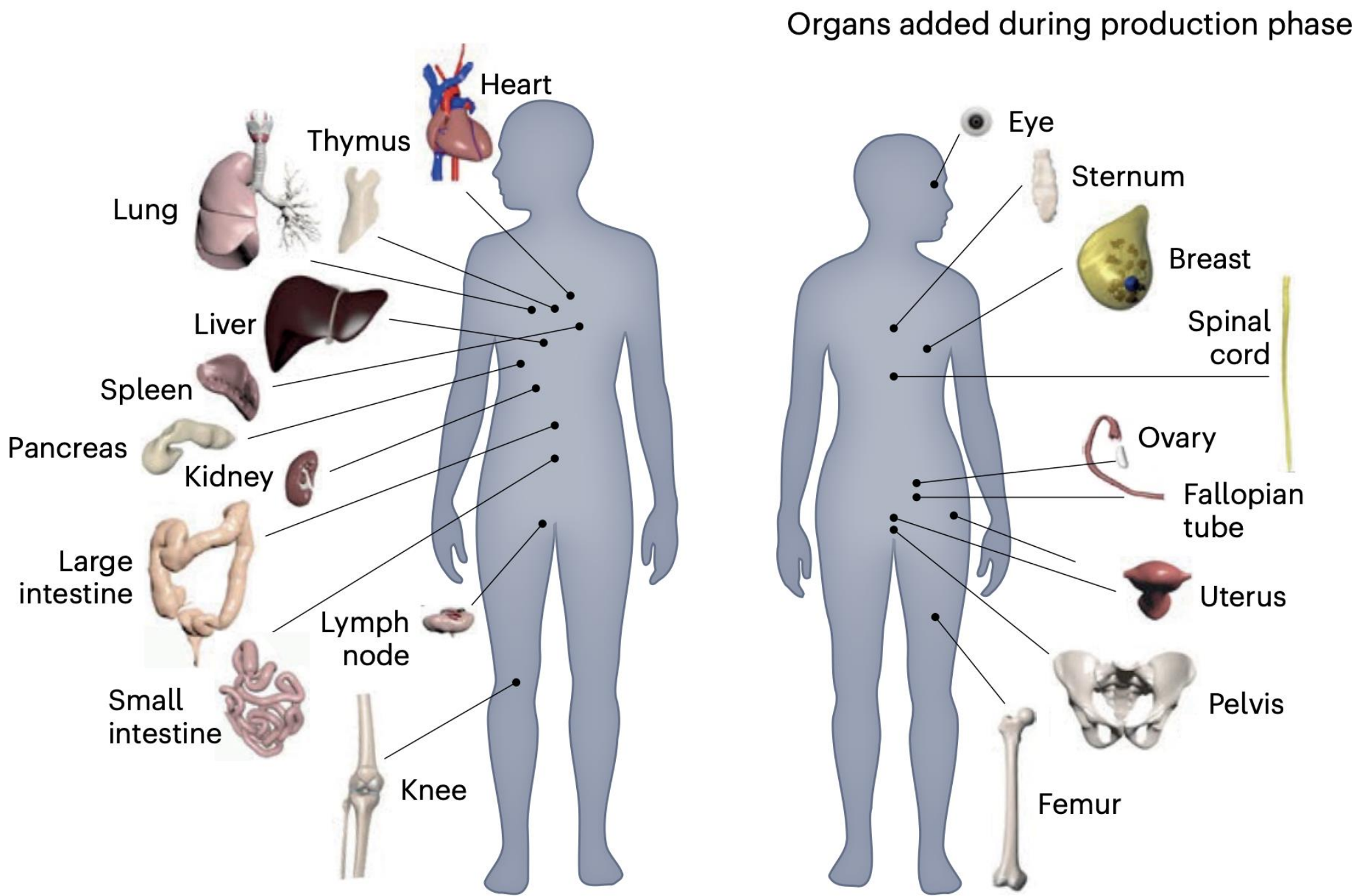
Received: 6 March 2023

Accepted: 22 June 2023

Published online: 19 July 2023

 Check for updates

Sanjay Jain ^{1,2,3,79}✉, Liming Pei ^{4,79}✉, Jeffrey M. Spraggins ^{5,79}✉, Michael Angelo⁶, James P. Carson⁷, Nils Gehlenborg⁸, Fiona Ginty⁹, Joana P. Gonçalves ¹⁰, James S. Hagood ¹¹, John W. Hickey ¹², Neil L. Kelleher ¹³, Louise C. Laurent¹⁴, Shin Lin¹⁵, Yiing Lin ¹⁶, Huiping Liu ¹⁷, Alexandra Naba ¹⁸, Ernesto S. Nakayasu ¹⁹, Wei-Jun Qian ¹⁹, Andrea Radtke ²⁰, Paul Robson ²¹, Brent R. Stockwell²², Raf Van de Plas²³, Ioannis S. Vlachos^{24,25}, Mowei Zhou²⁶, HuBMAP Consortium*, Katy Börner ^{27,79}✉ & Michael P. Snyder ^{28,79}✉



Core technologies
Single cell + spatial omics

New technologies
Demonstration projects

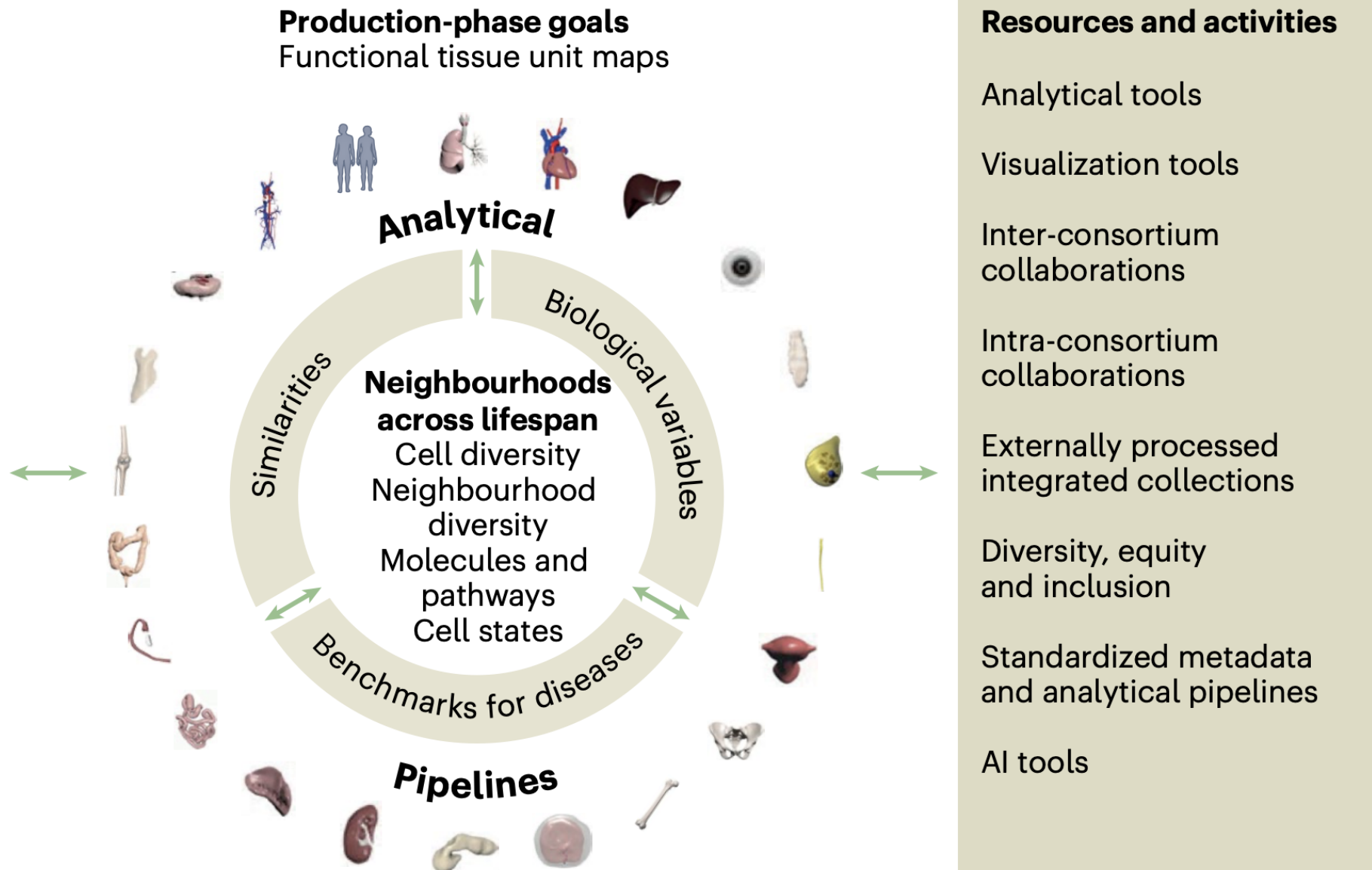
Spatially resolved transcriptomics
•CosMX •10x Xenium
•MERFISH

Label-free technologies
•Stimulated Raman spectroscopy

HiFi sequencing

Optical coherence tomography

Proteomics
•Single-cell proteome
•Phosphoproteome



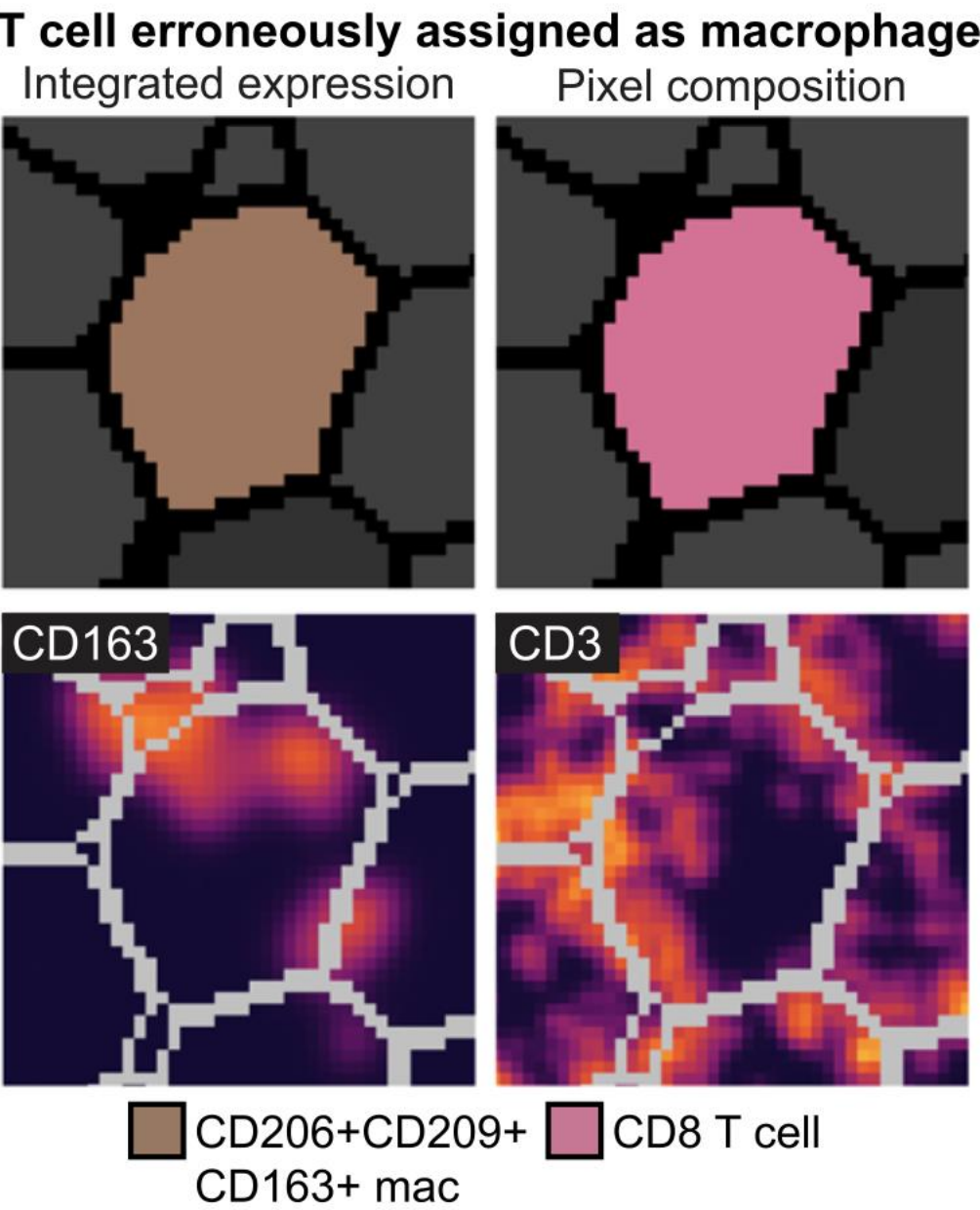
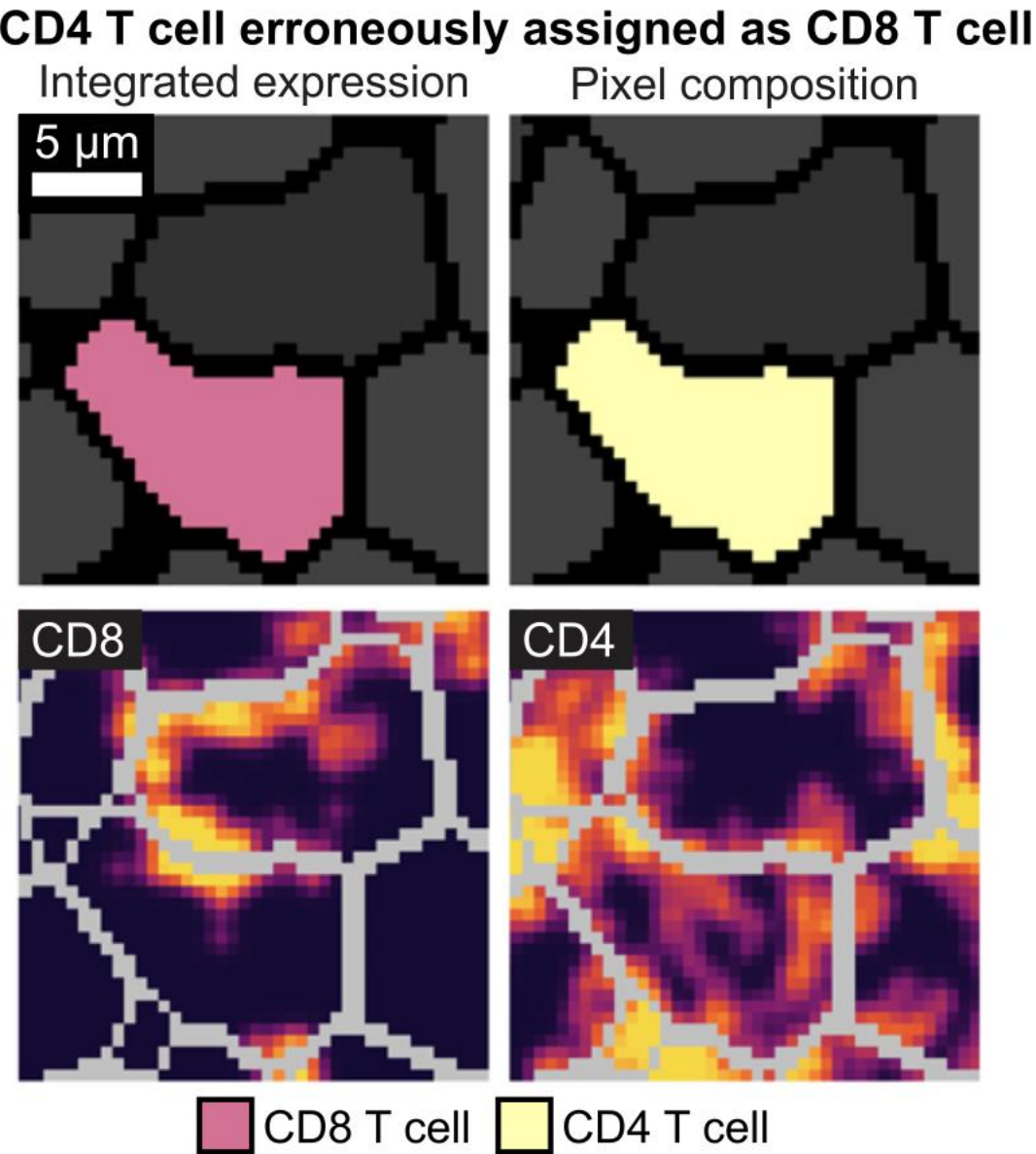
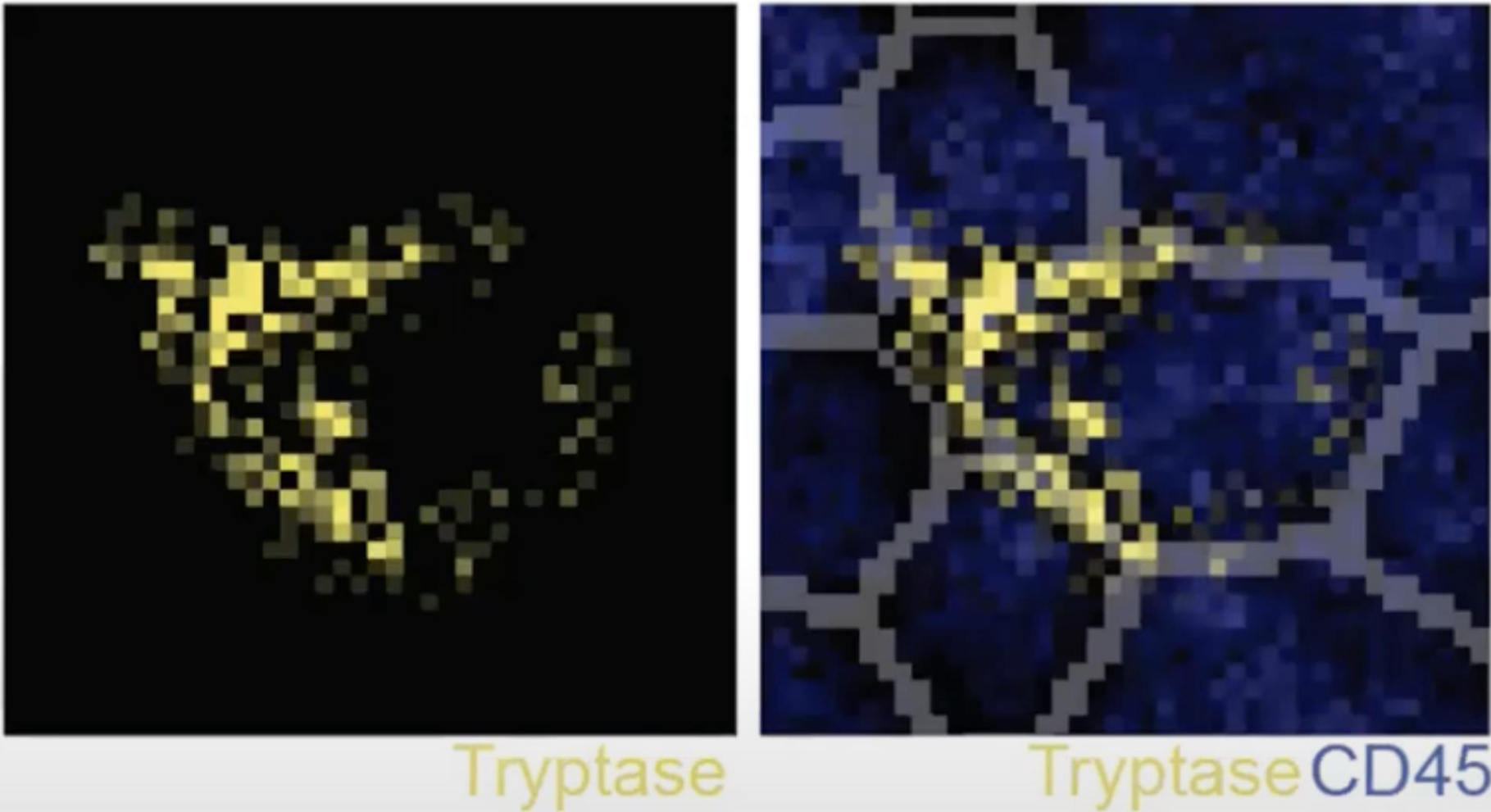
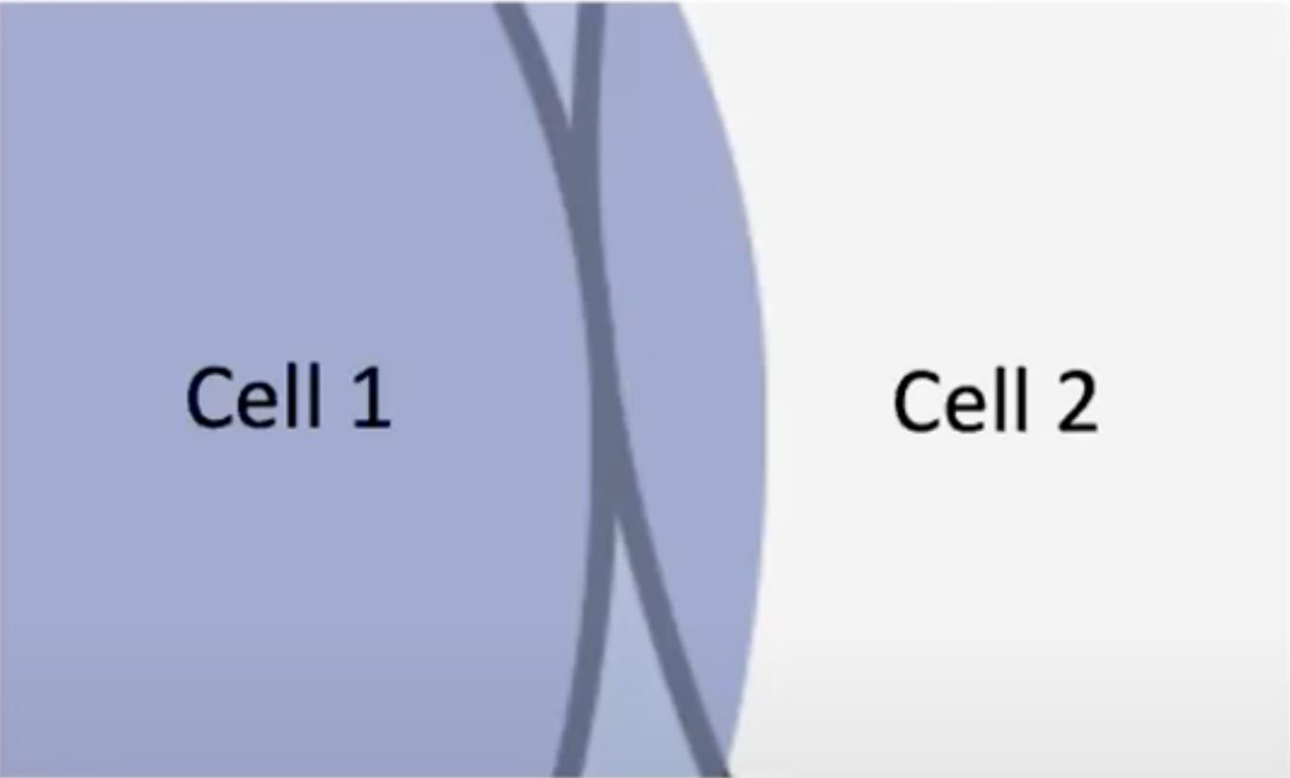
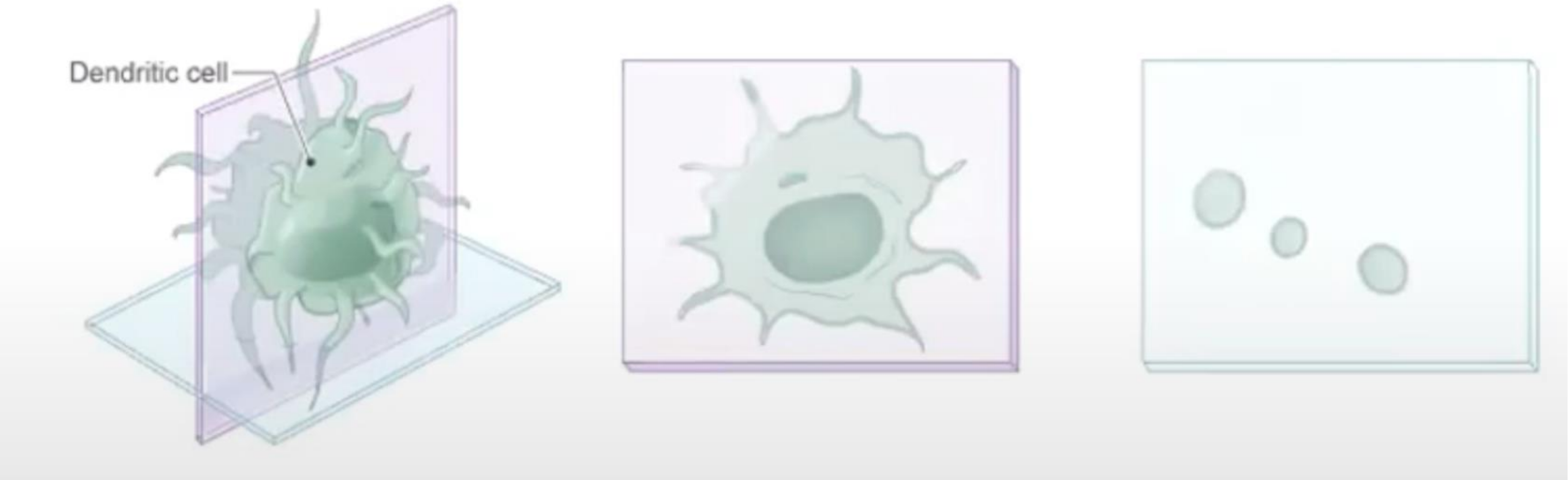
Robust phenotyping of highly multiplexed tissue imaging data using pixel-level clustering

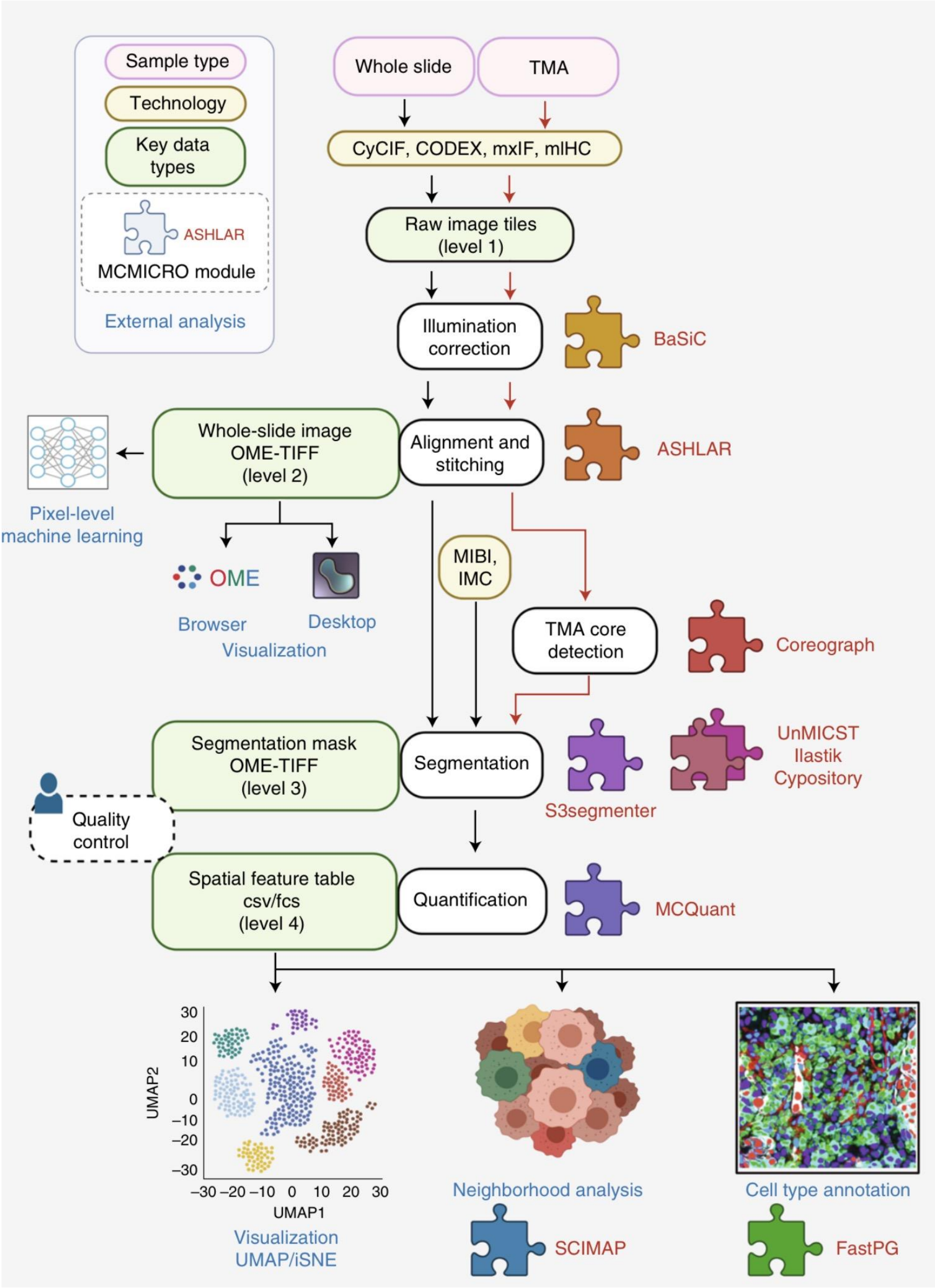
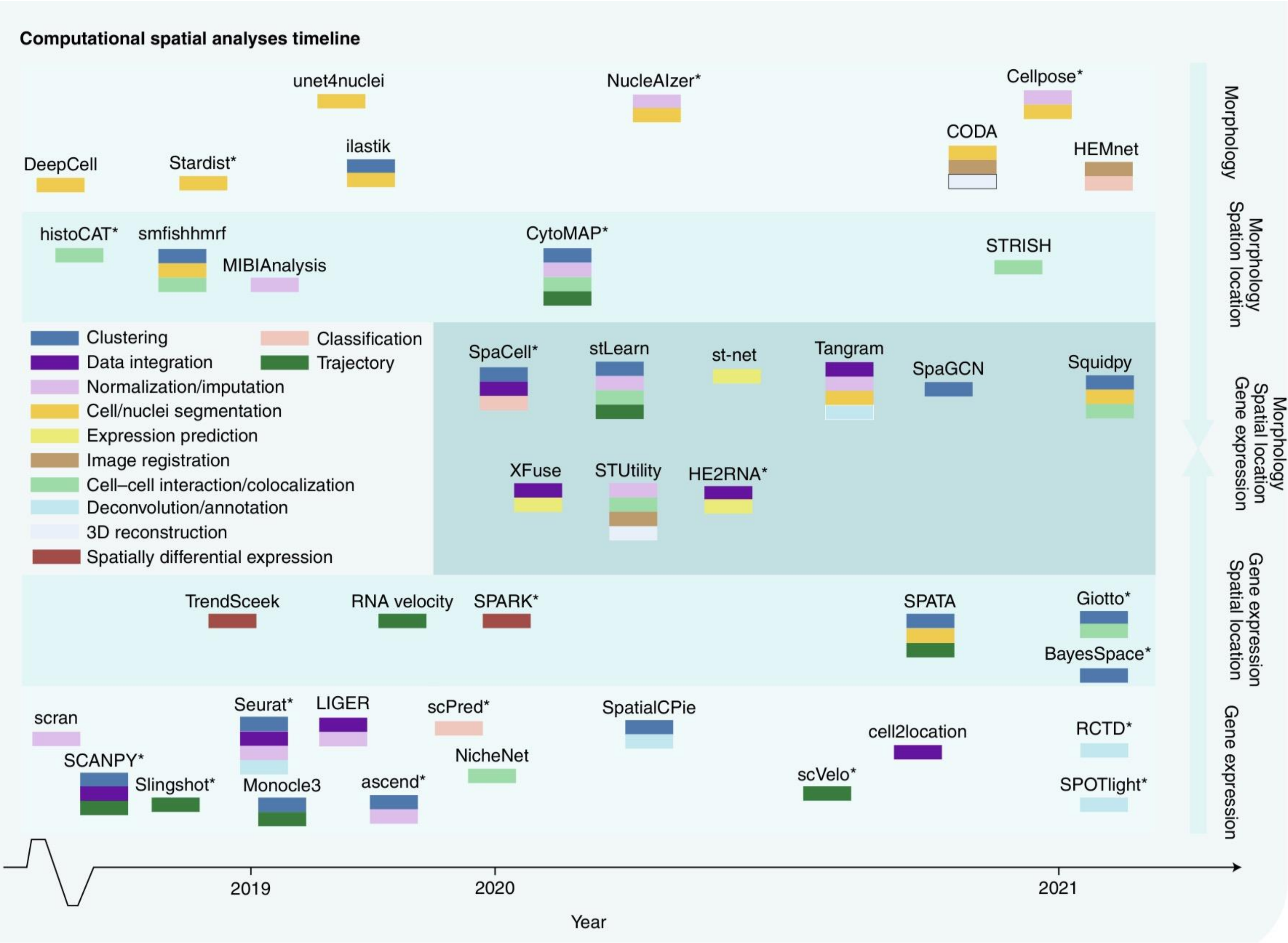
Received: 28 March 2023

Accepted: 11 July 2023

Published online: 01 August 2023

Candace C. Liu¹, Noah F. Greenwald ¹, Alex Kong¹, Erin F. McCaffrey¹,
Ke Xuan Leow¹, Dunja Mrdjen¹, Bryan J. Cannon ¹, Josef Lorenz Rumberger^{2,3},
Sricharan Reddy Varra ¹ & Michael Angelo ¹✉







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Unstructured Data

Example clinical trial with eligibility criteria highlighted

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ClinicalTrials.gov

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Save this study

Cabozantinib in High Grade Neuroendocrine Neoplasms

The safety and scientific validity of this study is the responsibility of the study sponsor and investigators. Listing a study does not mean it has been evaluated by the U.S. Federal Government. Know the risks and potential benefits of clinical studies and talk to your health care provider before participating. Read our disclaimer for details.

ClinicalTrials.gov Identifier: NCT04412629

Recruitment Status : Recruiting

First Posted : June 2, 2020

Last Update Posted : December 20, 2022

See Contacts and Locations

View this study on Beta.ClinicalTrials.gov

Study Details

Tabular View

No Results Posted

Disclaimer

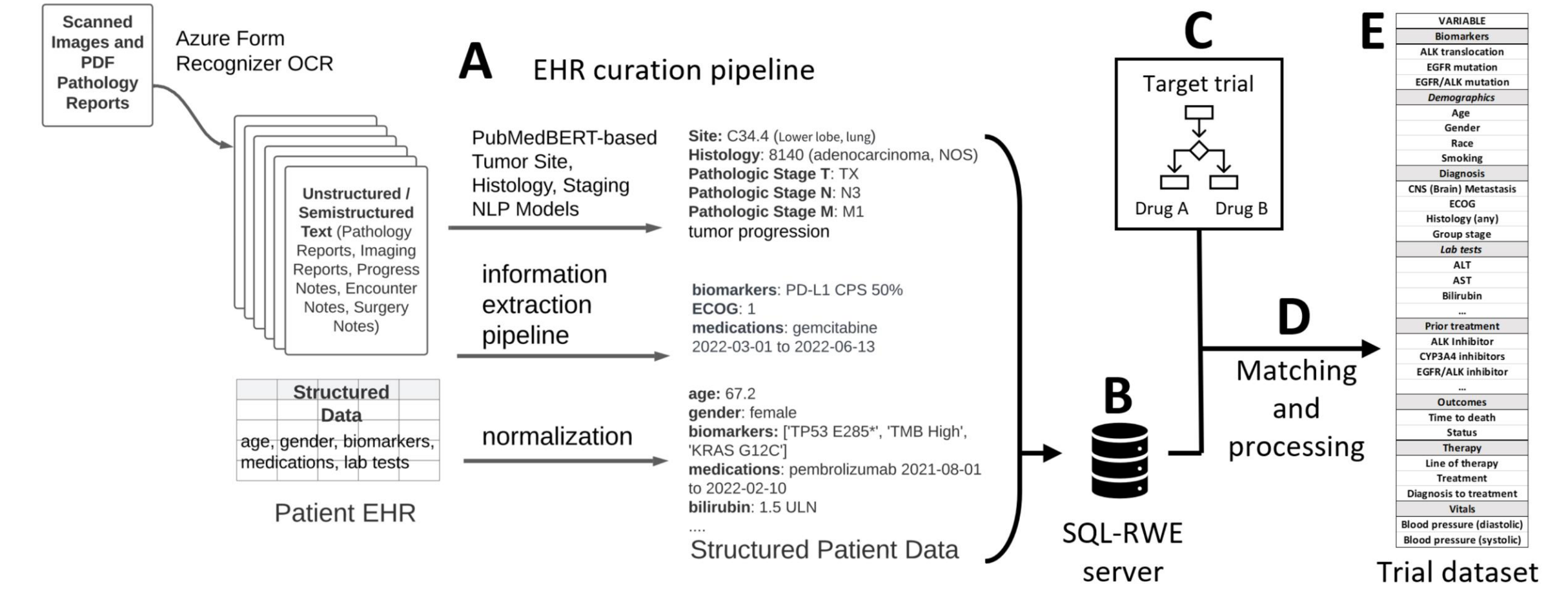
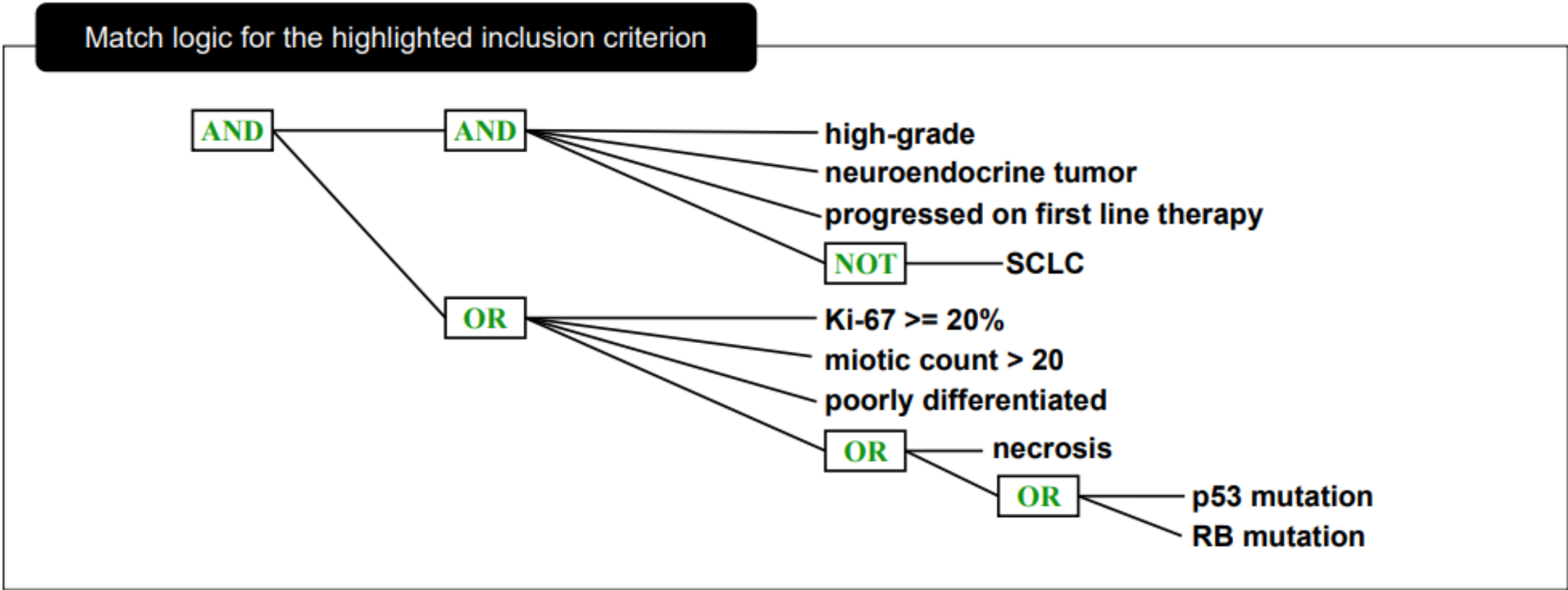
How to Read a Study Record

Eligibility Criteria

Go to

Inclusion Criteria:

-Histologically or cytologically confirmed high-grade neuroendocrine tumor that has progressed on first line therapy, excluding small cell lung cancer (SCLC). High grade includes any neuroendocrine neoplasm with a Ki-67 of >=20% or with mitotic count of more than 20 mitoses per high power field or any poorly differentiated neoplasm or any neoplasm lacking these that is deemed high grade by pathology consensus, based on other markers (necrosis or IHC demonstrating p53 or RB mutation).



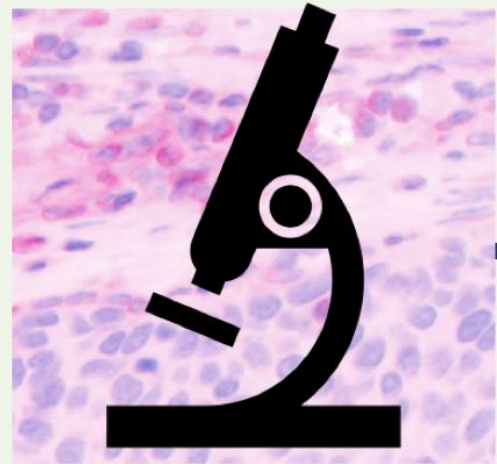
	Histology			Biomarker			Histology+Biomarker		
	Precision	Recall	F1	Precision	Recall	F1	Precision	Recall	F1
SciSpaCy	9.2	16.8	11.8	36.4	5.3	9.3	7.4	10.8	8.8
Criteria2Query	23.2	34.8	27.8	22.0	12.0	15.5	9.6	17.4	12.4
GPT-3.5 (zero-shot)	36.0	20.6	26.2	48.3	18.7	26.9	30.7	14.6	19.7
GPT-4 (zero-shot)	43.0	41.3	42.1	31.0	17.3	22.2	27.8	21.1	24.0
GPT-4 (3-shot)	42.7	54.8	48.0	39.4	37.3	38.4	27.3	32.4	29.6

Structuring of oncology trial eligibility criteria, evaluated on complete match logic in DNF form (a specific representation of Boolean logic)

- Structuring trial eligibility criteria: $T_{\text{spec}} \rightarrow T_{\text{structured}}$;
- Structuring patient records: $P_{\text{EMR}} \rightarrow P_{\text{structured}}$;
- Matching: $\text{Match}(T_{\text{structured}}, P_{\text{structured}}) \rightarrow \{\text{yes}, \text{no}\}$;

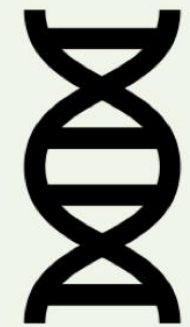
Data Mining

Tumor imaging



CNN layer

Tumor genomics



Real-world data



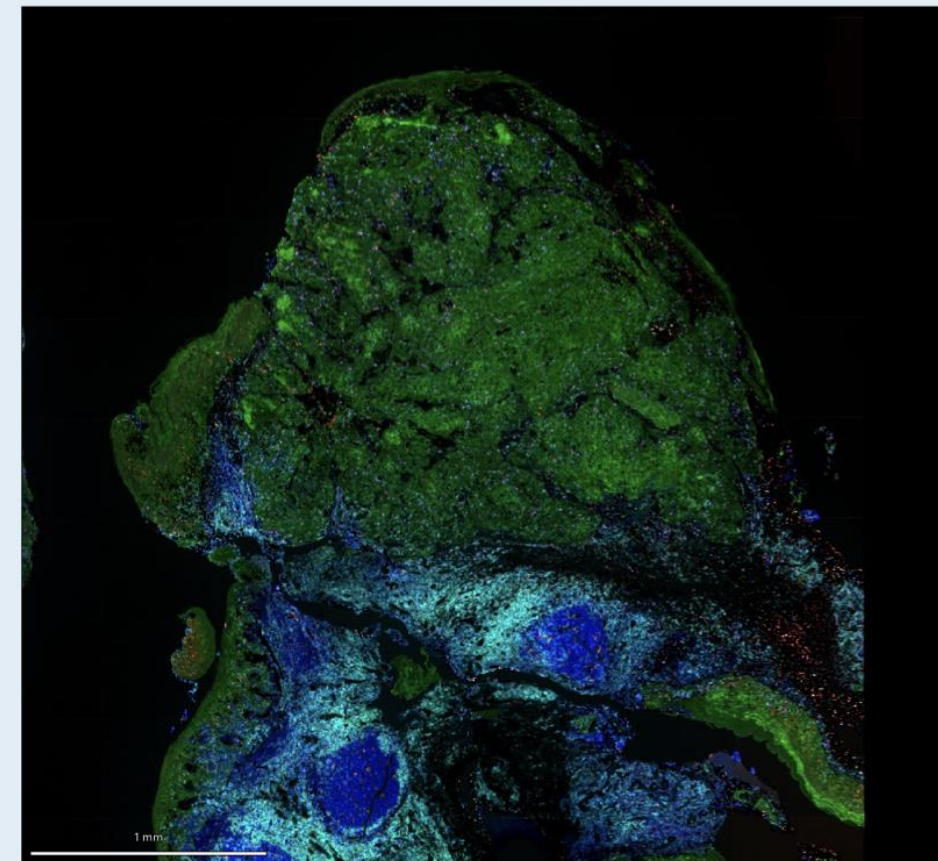
LLM/NLP layer

Scale: 1,000,000s

Discovery

Lunaphore
COMET

Hyperplex
immunofluorescence



XENIUM

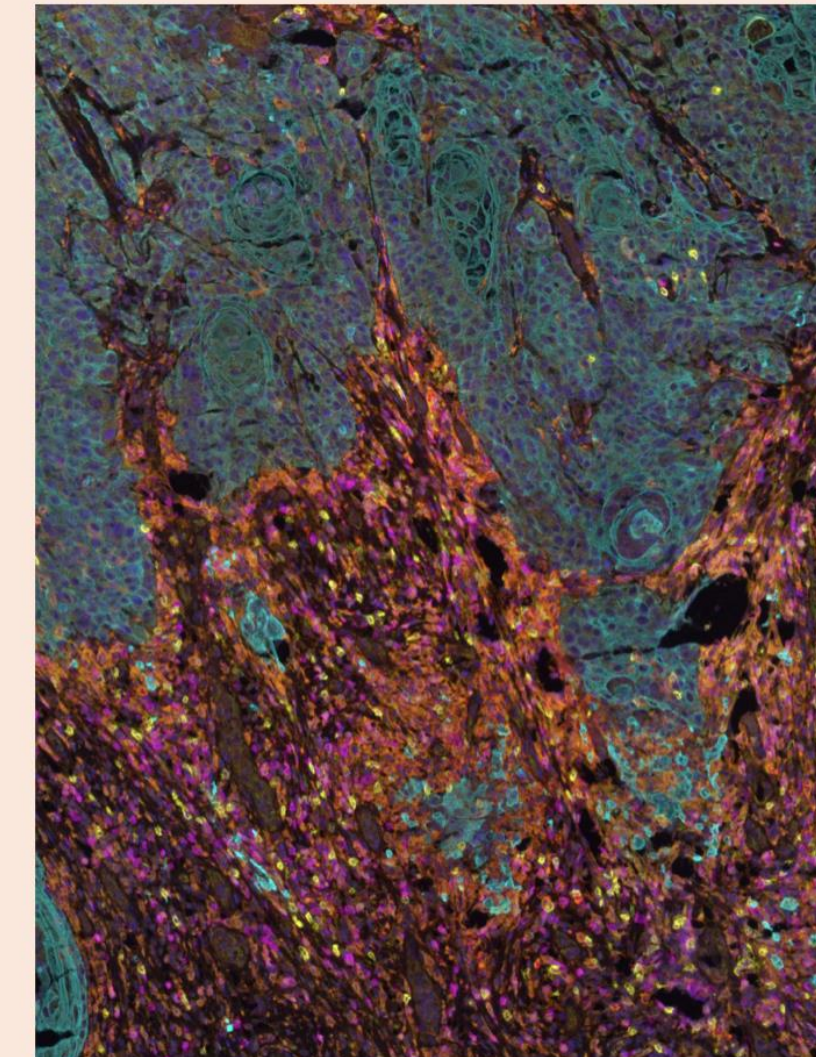
GeoMx

100s-1,000s

Routine/Clinical Phenotyping

Akoya Phenoimager
HT

Validated panels



1,000s-10,000s

Panel
development

Acknowledgements:

Piening Lab:

Alexa Dowdell
Fred Robinson
Racheli Ben Shimol
Angela Crabtree

Prov Genomics:

Brian Piening
Tucker C. Bower
Benjamin Cosgrove
Eric Shull
Christine MOUNG-WEN
Jacob Abel

Prov HI Team:

Soohee Lee
Roshanthi Weerasinghe

Fox Lab:

Bernie Fox
Shawn Jensen

MSFT Research:

Hoifung Poon
Rajesh Rao
Naoto Usuyama
Cliff Wong

...

EACRI:

Walter Urba
Bryan Bell
Eric Tran
Rom Leidner

Support:

Providence Foundations of
Oregon
Elsie Franz-Finley

Funding:

Nightingale Open Science
MSFT ECIF

Acknowledgements:

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Providence Foundations of
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MSFT Research:

Hoifung Poon
Rajesh Rao
Naoto Usuyama
Cliff Wong

...

EACRI:

Walter Urba
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Rom Leidner

THANK YOU!

Funding:

Nightingale Open Science
MSFT ECIF