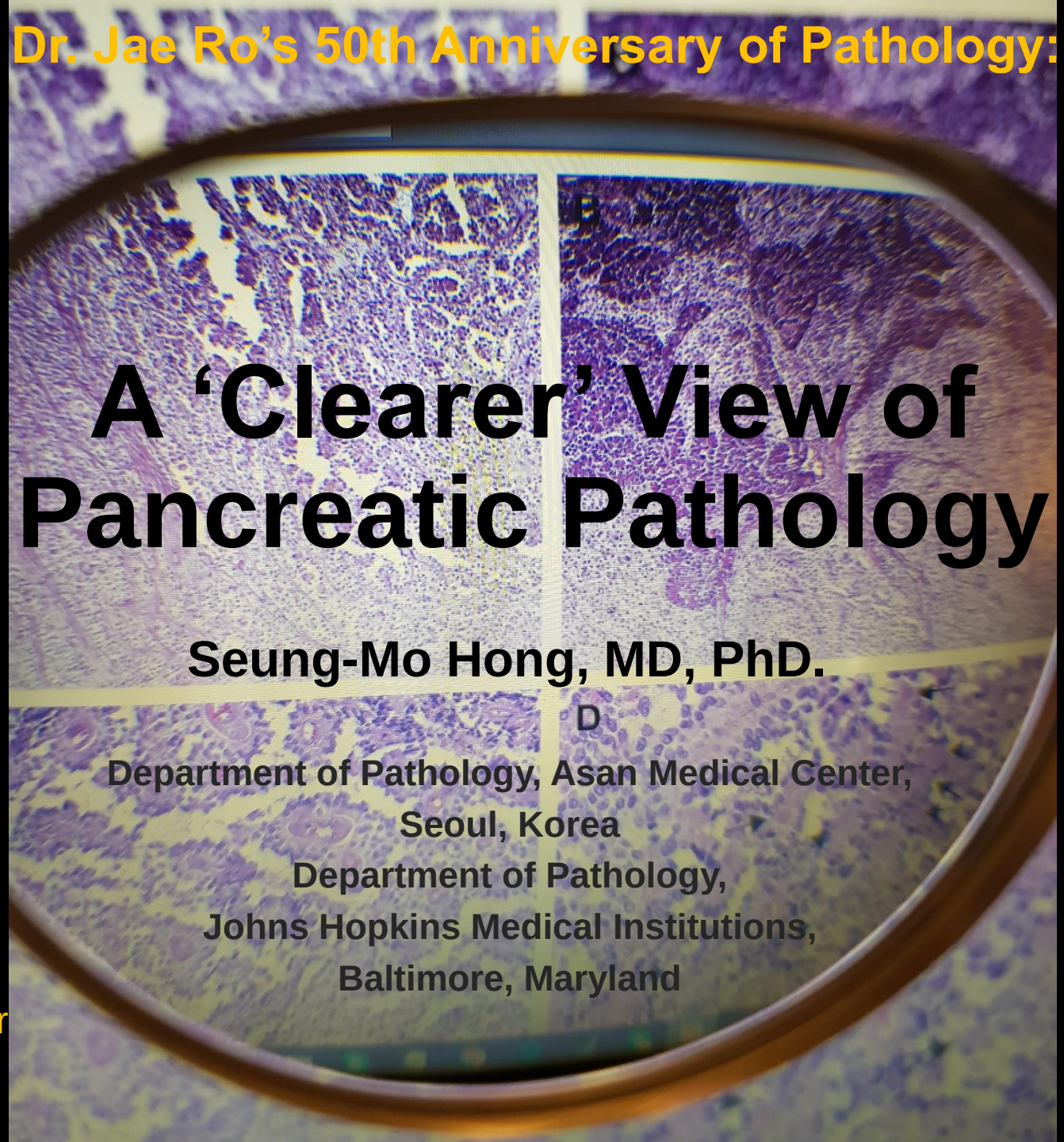
Celebrating Dr. Jae Ro's 50th Anniversary of Pathology: Do your BeST!



A 'Clearer' View of Pancreatic Pathology

Seung-Mo Hong, MD, PhD.

D

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Department of Pathology, Johns Hopkins Medical Institutions, Baltimore, Maryland

18th KOPANA Spring Seminar
National Harbor, MD
March 15, 2019

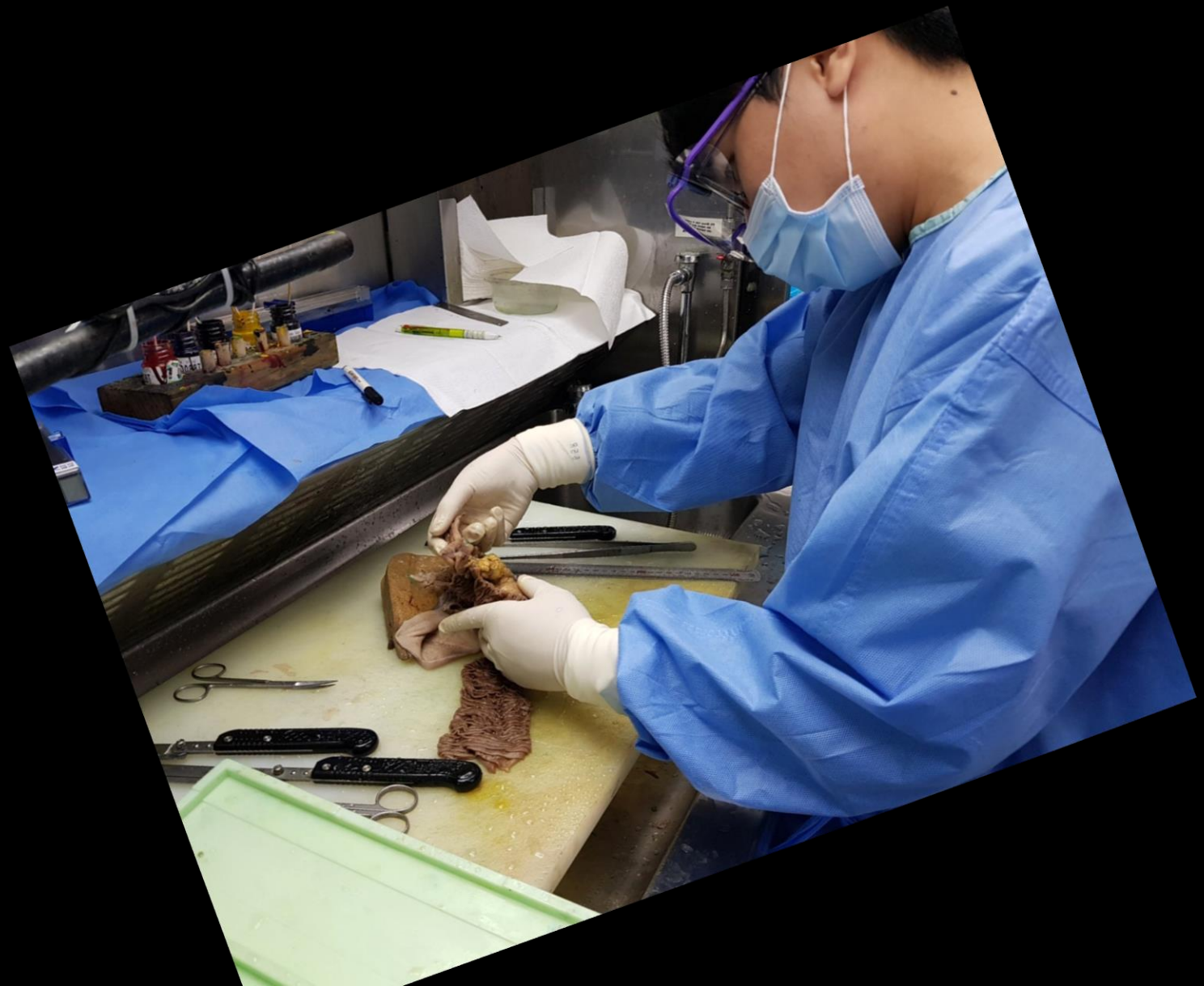
Dr. Ro's Do Your BeST!

- Basic
- Enjoy
- (effort) Study
- Think

Dr. Ro's Do Your BeST!

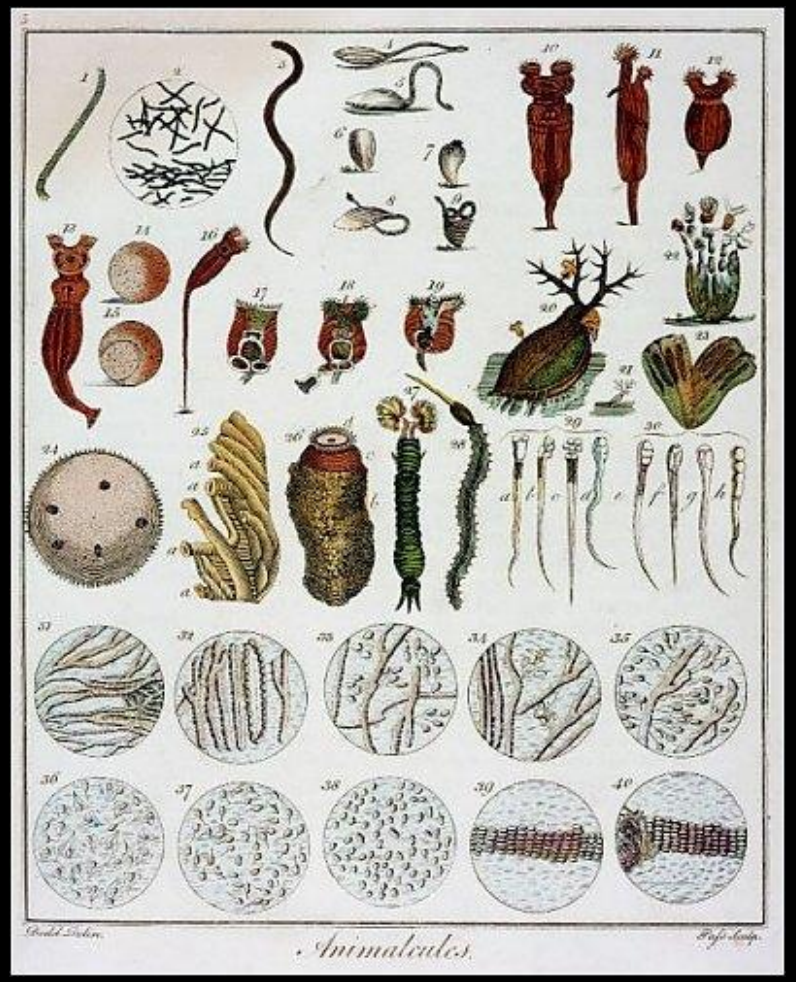
- **B**asic
- **E**njoying **S**tudy
- **T**hink

Gross examination



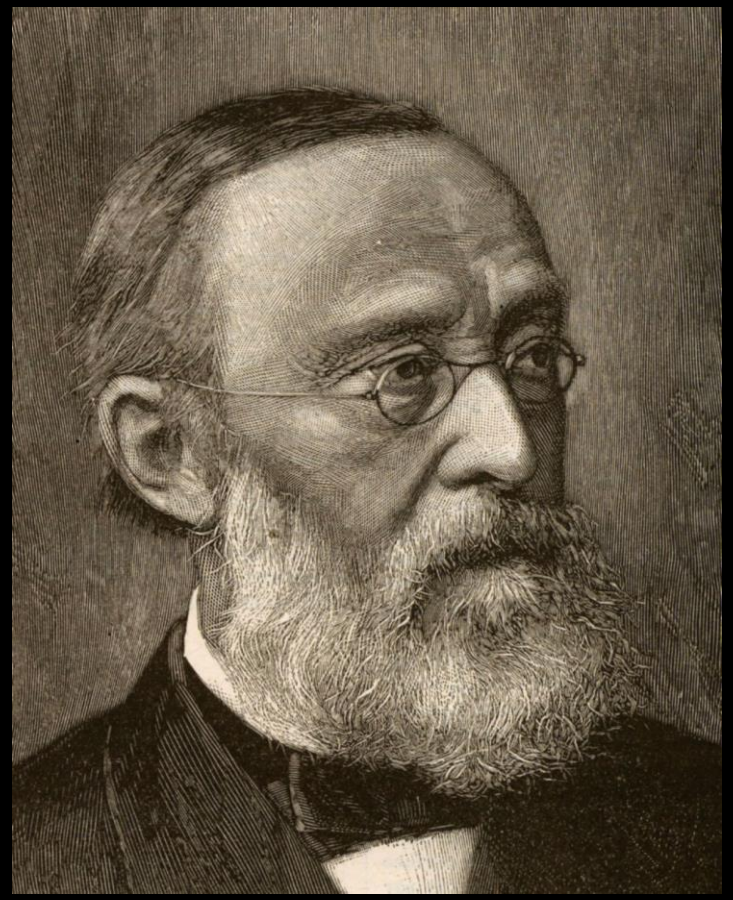
Antonie van Leeuwenhoek

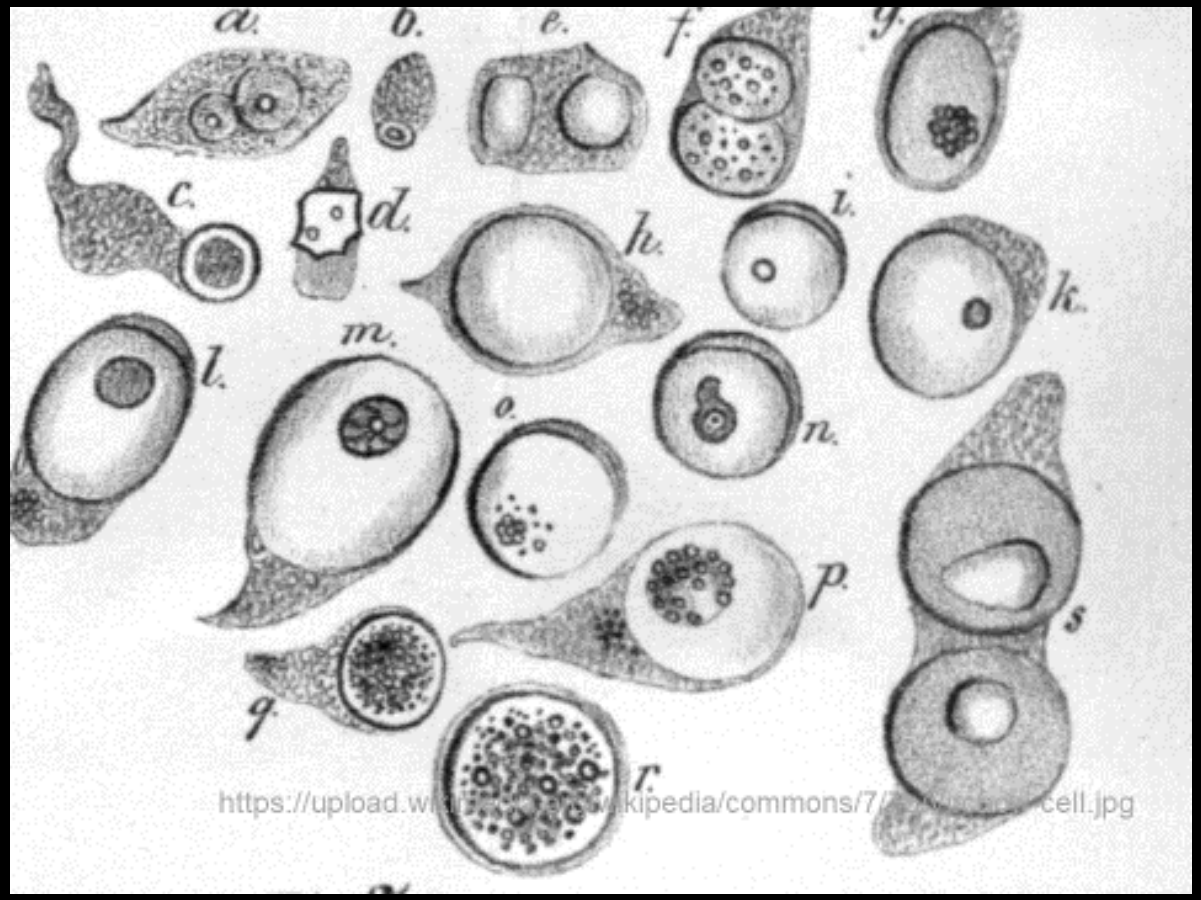
1795



https://commons.wikimedia.org/wiki/File:Animalcules_observed_by_anton_van_leeuwenhoek_c1795_1228575.jpg

Rudolf Virchow



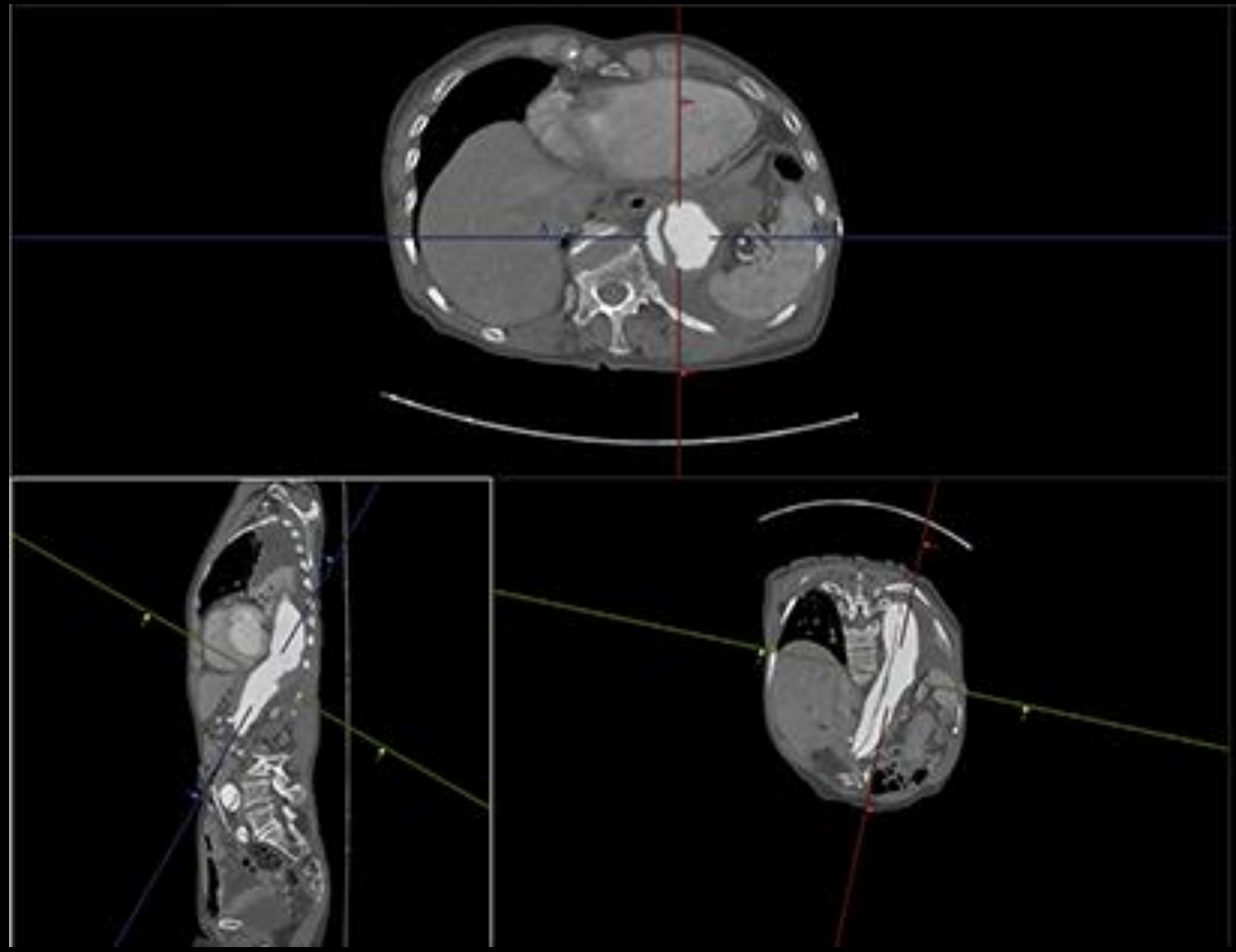


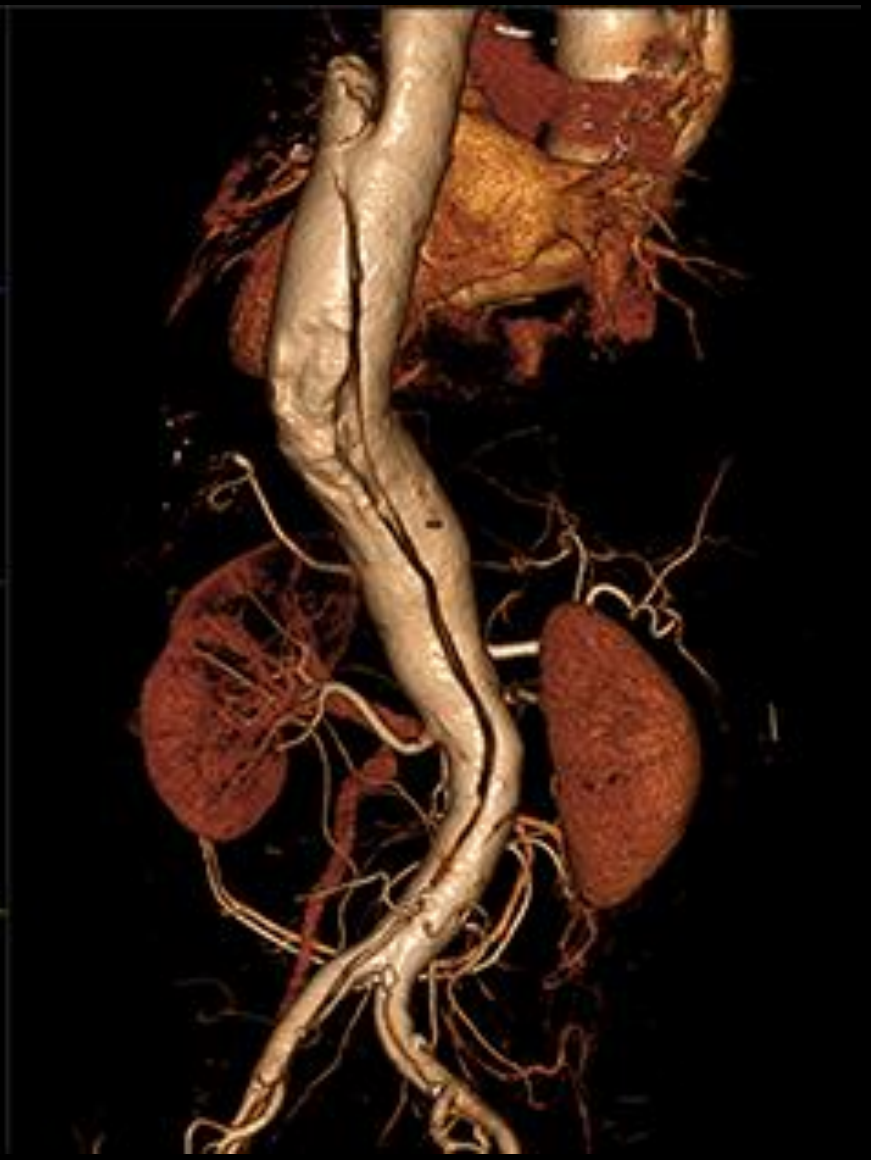
Father of pathology

https://www.britannica.com/biography/Rudolf-Virchow

Our view of disease is framed by 2D slide

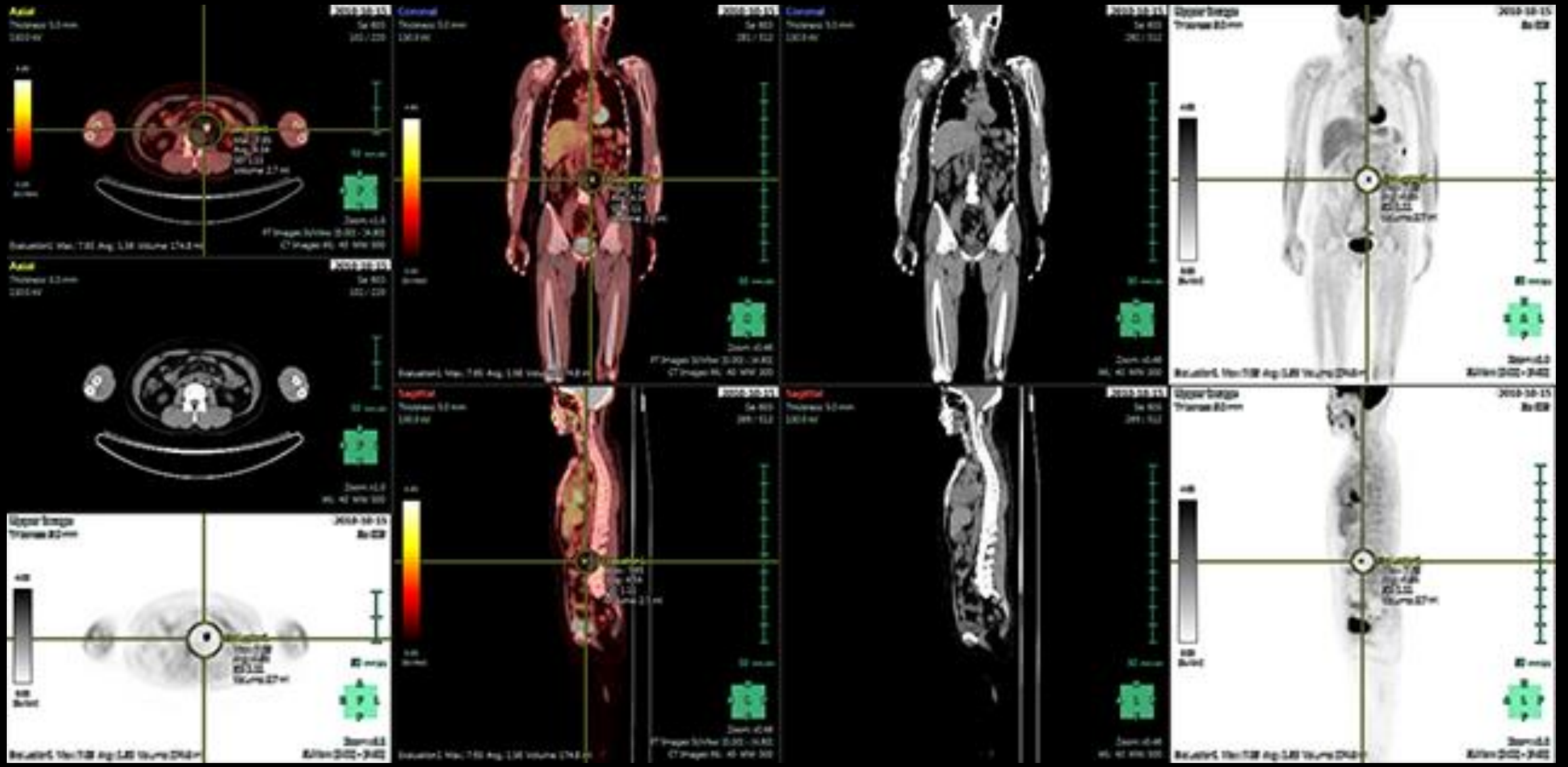
3D imaging in radiology





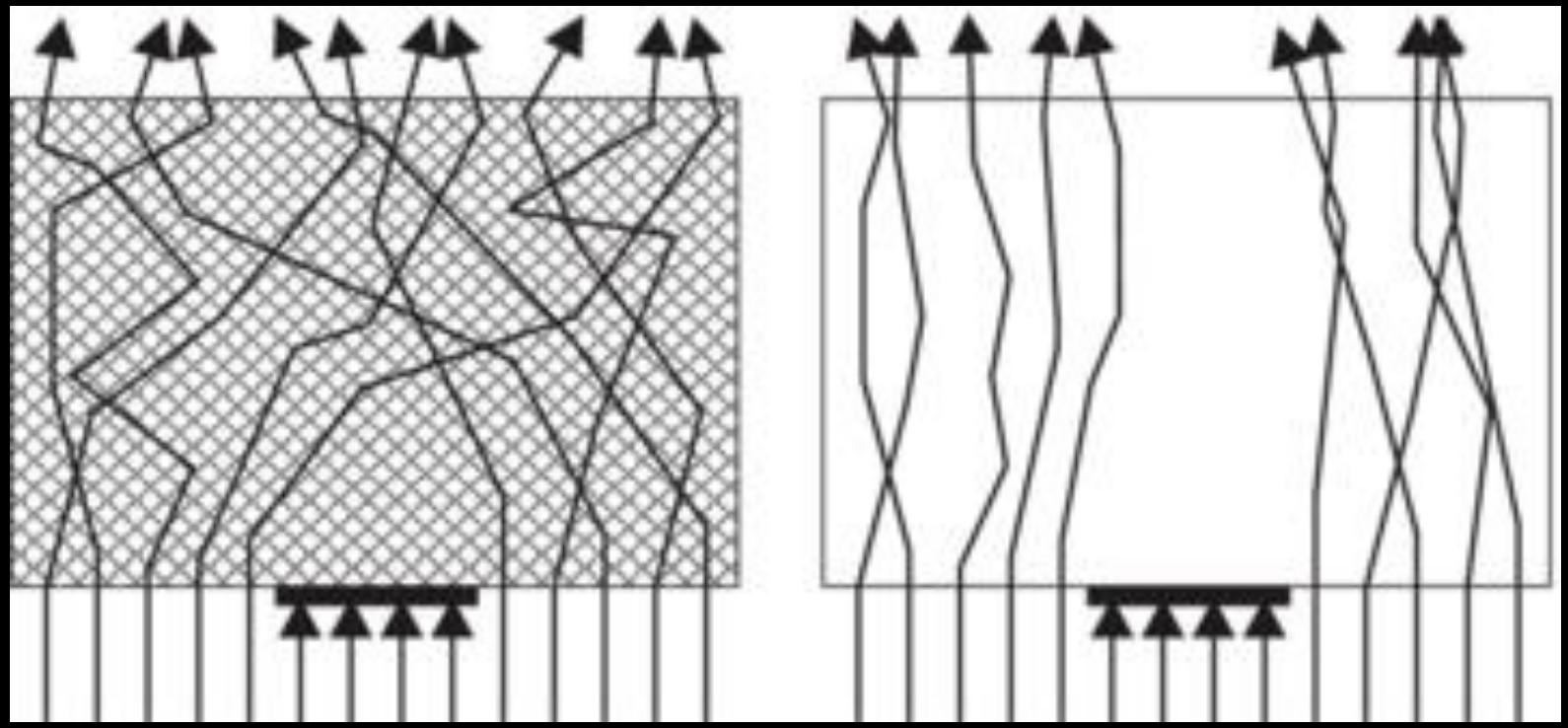
http://stage3dimaging.fujimed.com

3D imaging in nuclear medicine



http://stage3dimaging.fujimed.com

Clearing- 100 Year History

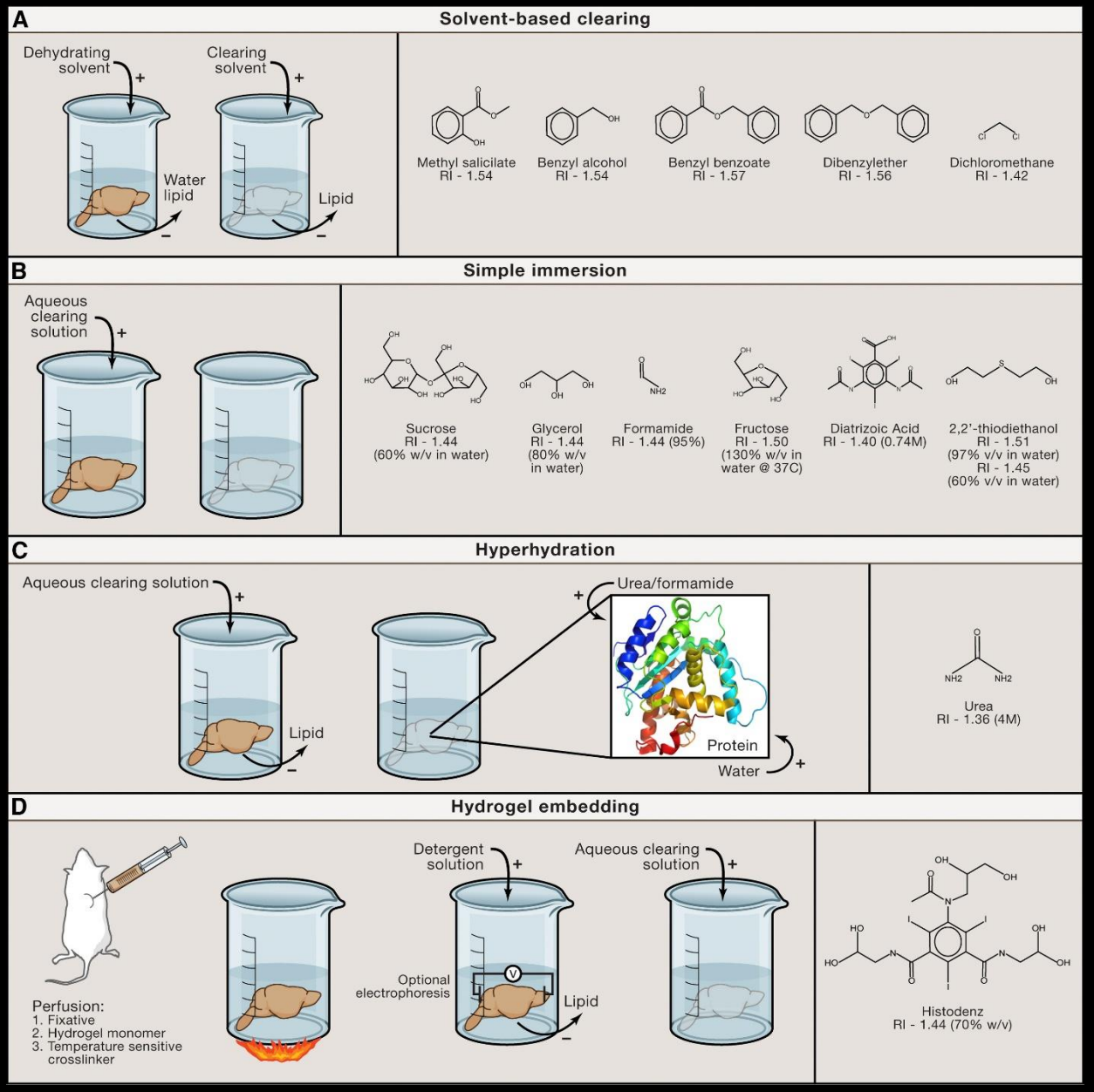


Werner Spalteholz 1914

Werner Spalteholz, Museum of Hygiene Dresden

http://iopscience.iop.org/article/10.1088/0957-0233/19/5/055710

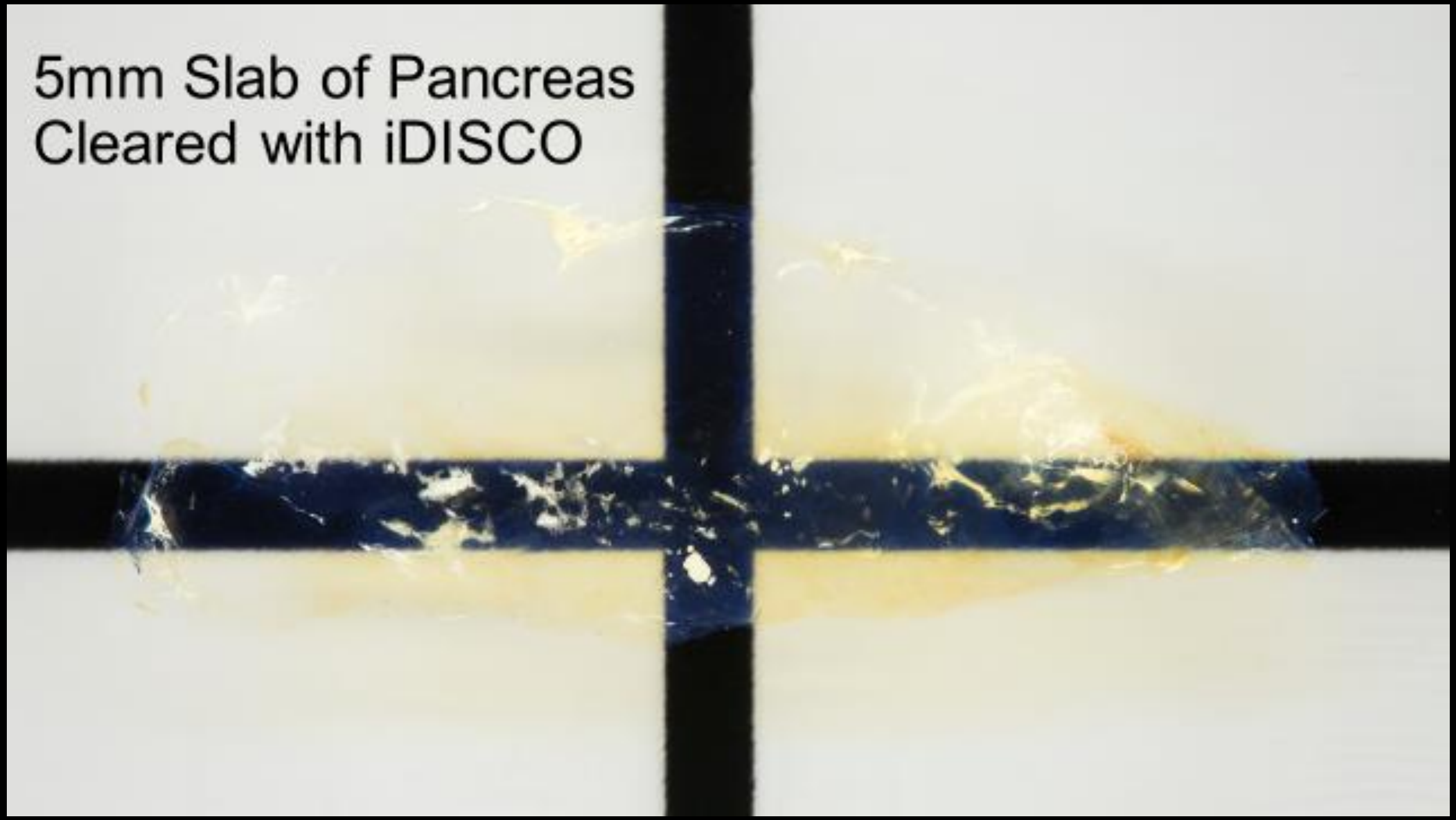
Tissue clearing techniques



Richardson DS et al. Cell 2015

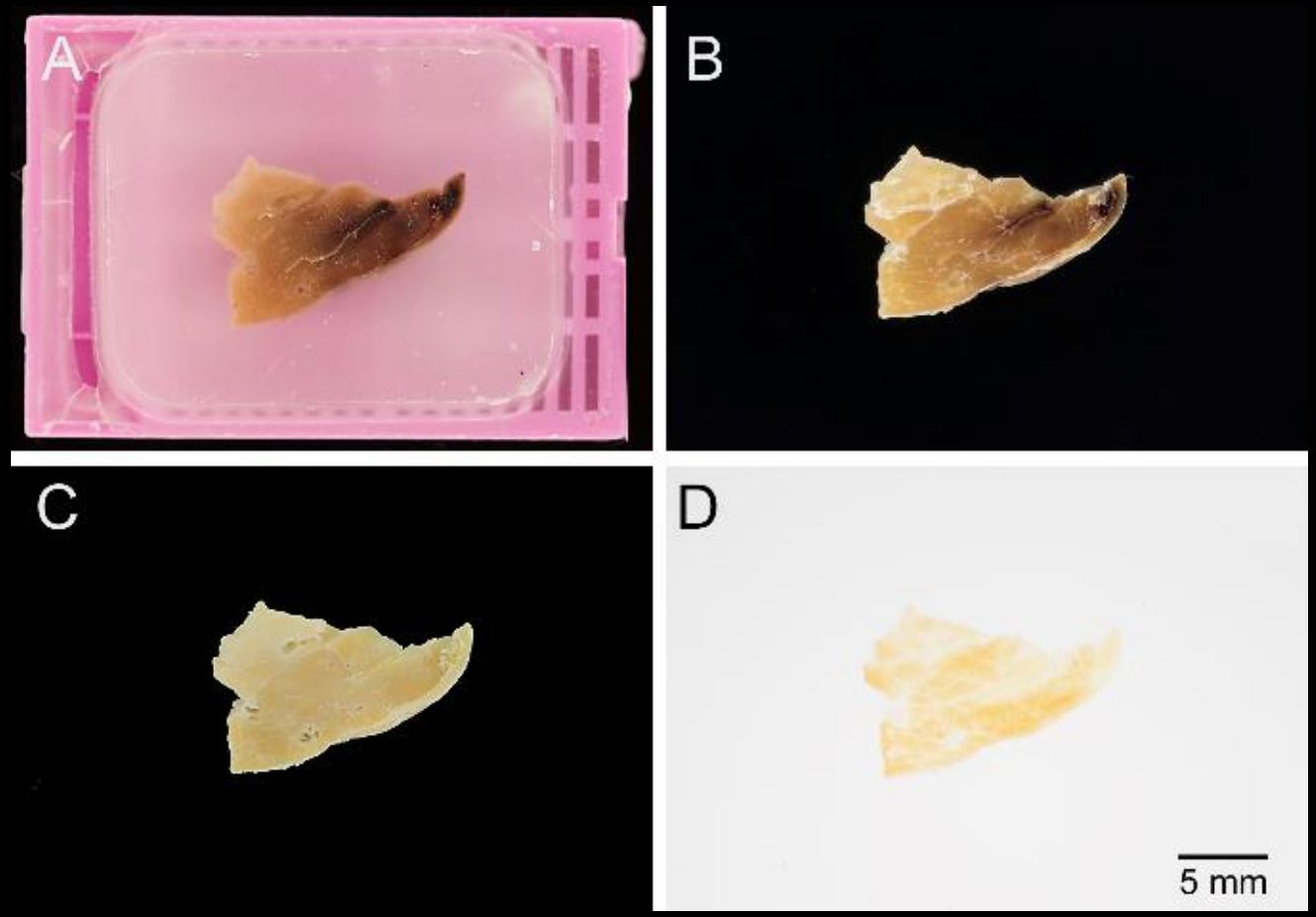
Human pancreas

- Modified iDISCO method [dibenzyl ether (DBE)] to clear the samples
- Dense fibrotic tissue
- Antibody penetration into dense tissues facilitated by gradually increasing antibody concentrations, centrifugal flow, and sonication

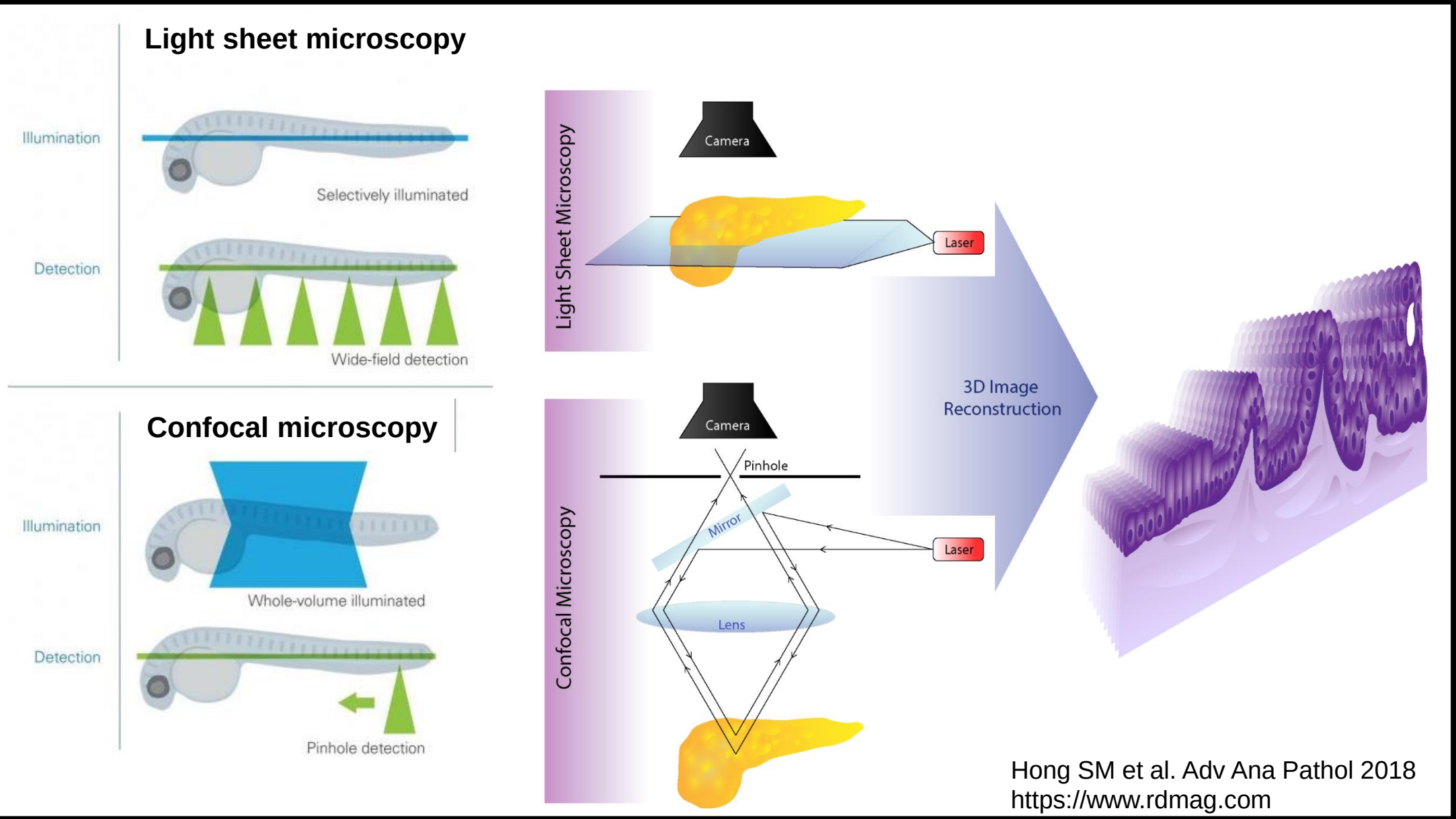


Noe M et al. Am J Pathol 2018

Formalin-fixed paraffin-embedded tissues also can be cleared



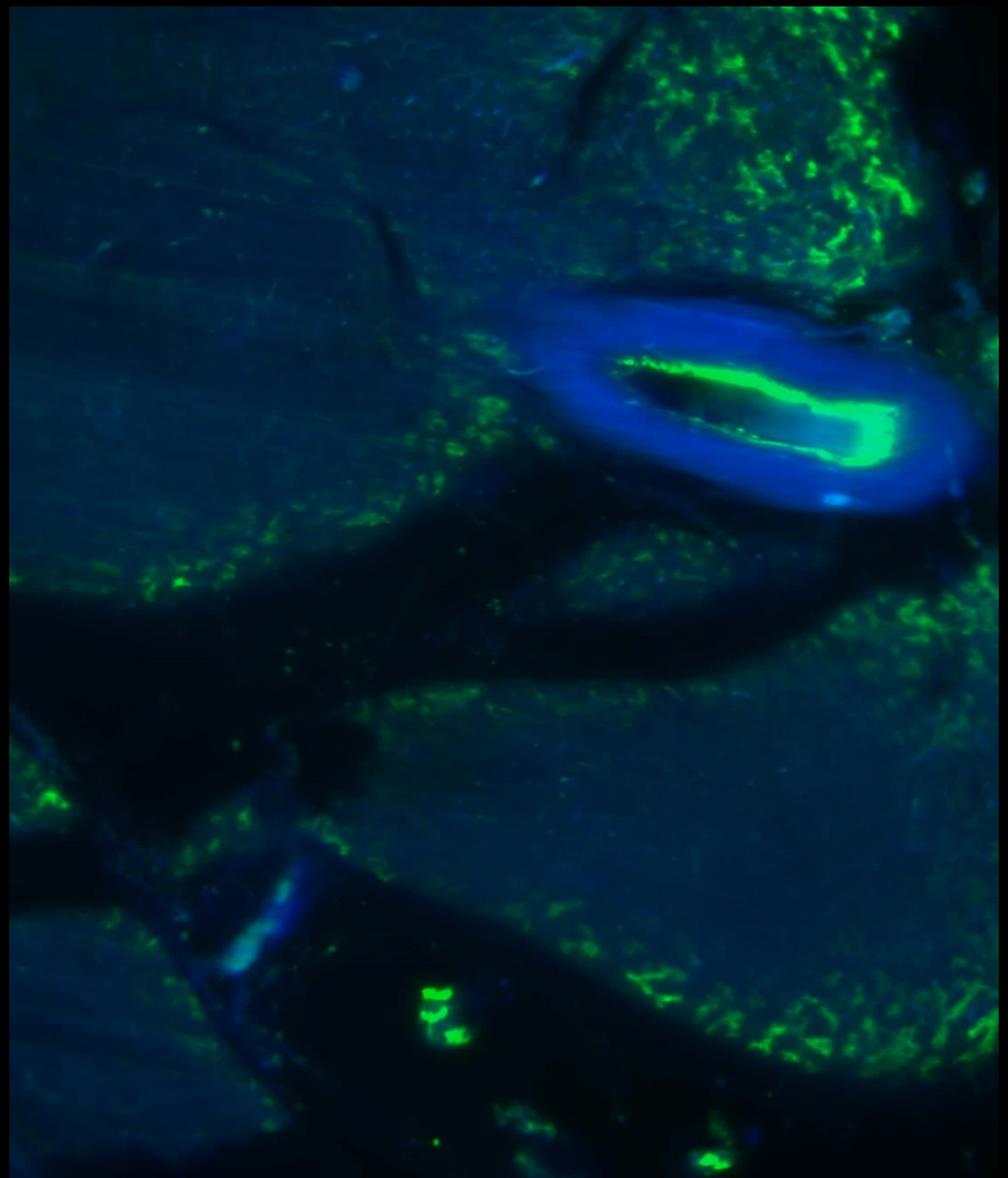
Imaging of cleared tissue

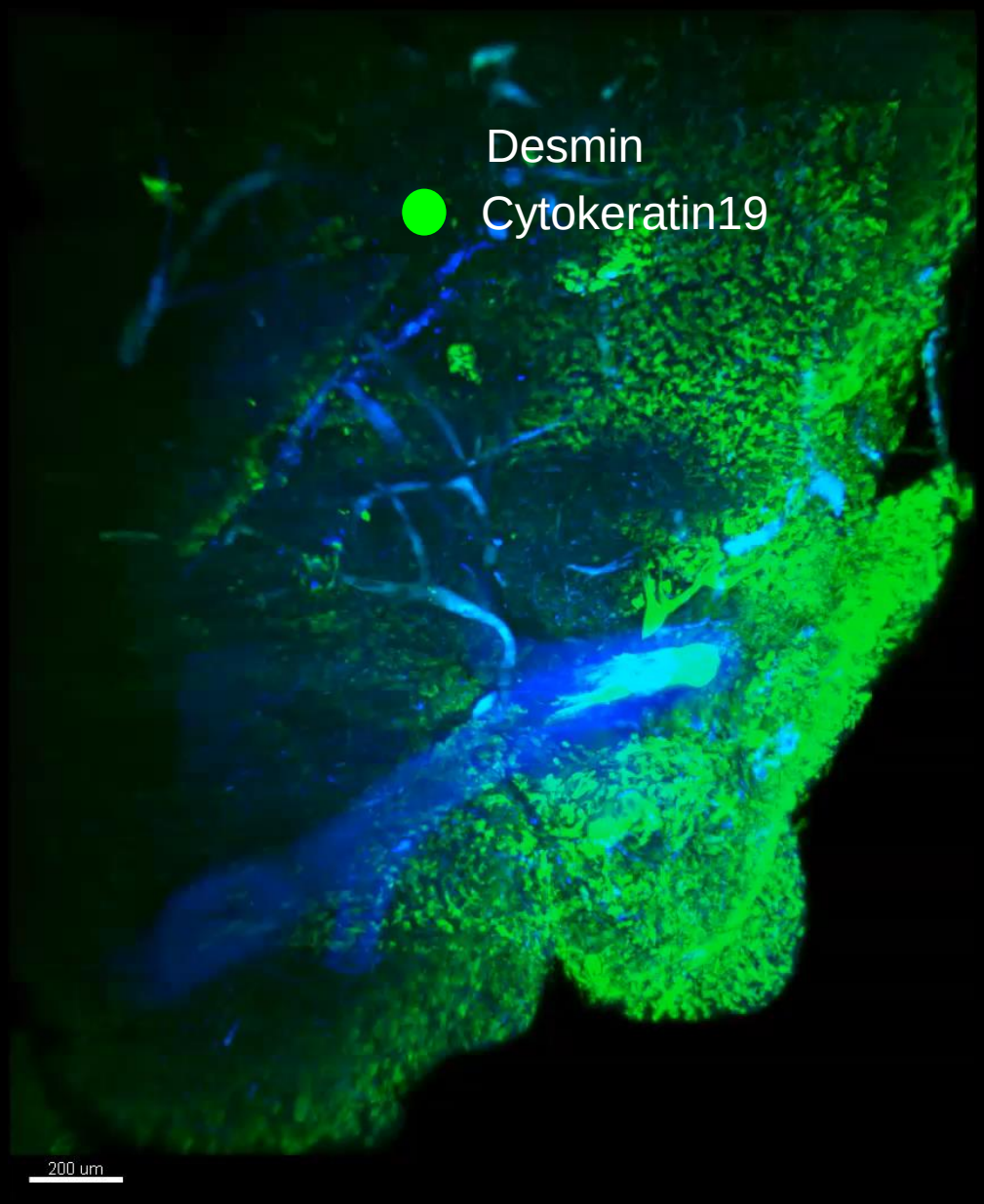


Hong SM et al. Adv Ana Pathol 2018
https://www.rdmag.com

Normal pancreas

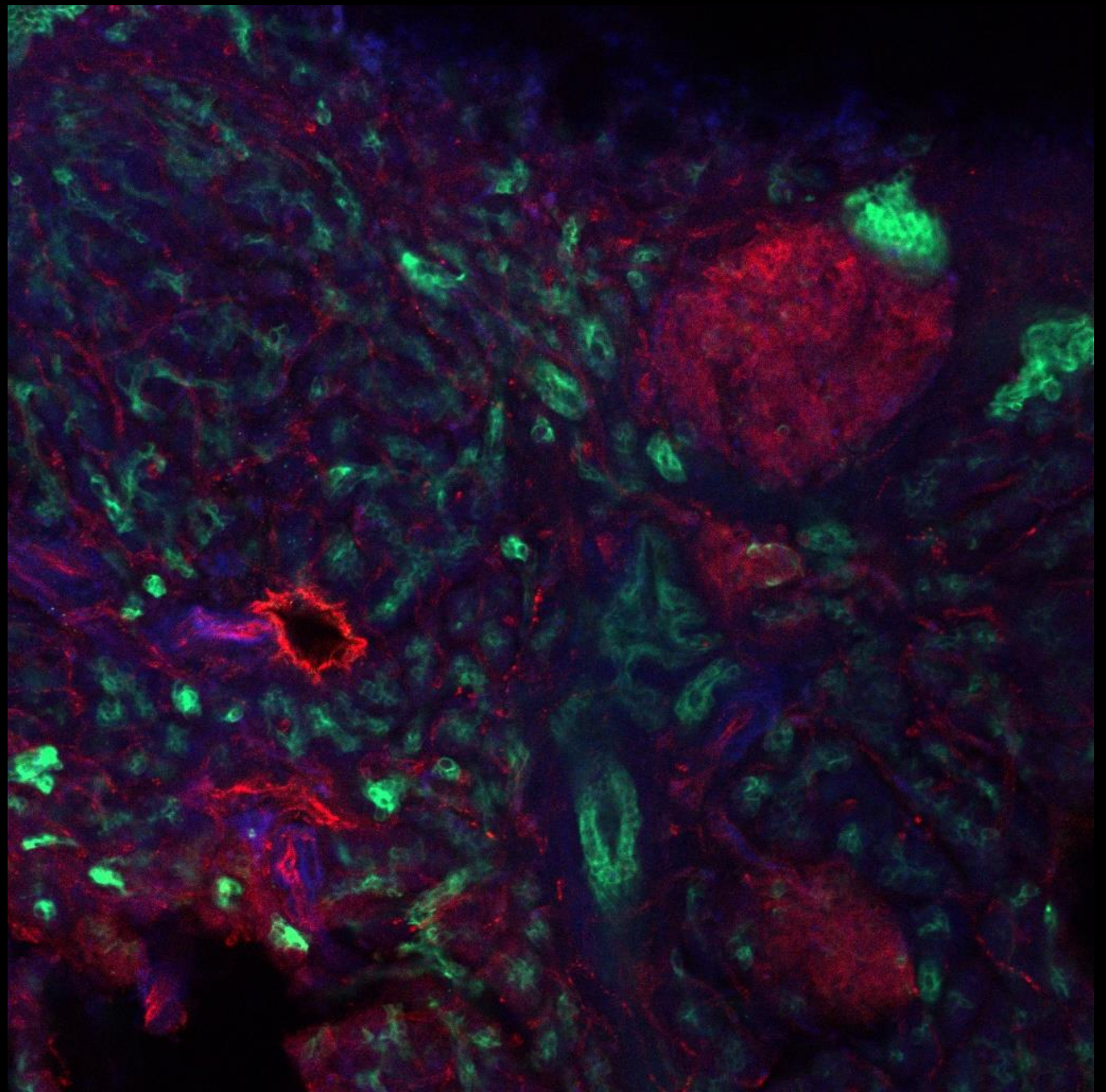
Cytokeratin 19 Desmin Auto-fluorescence





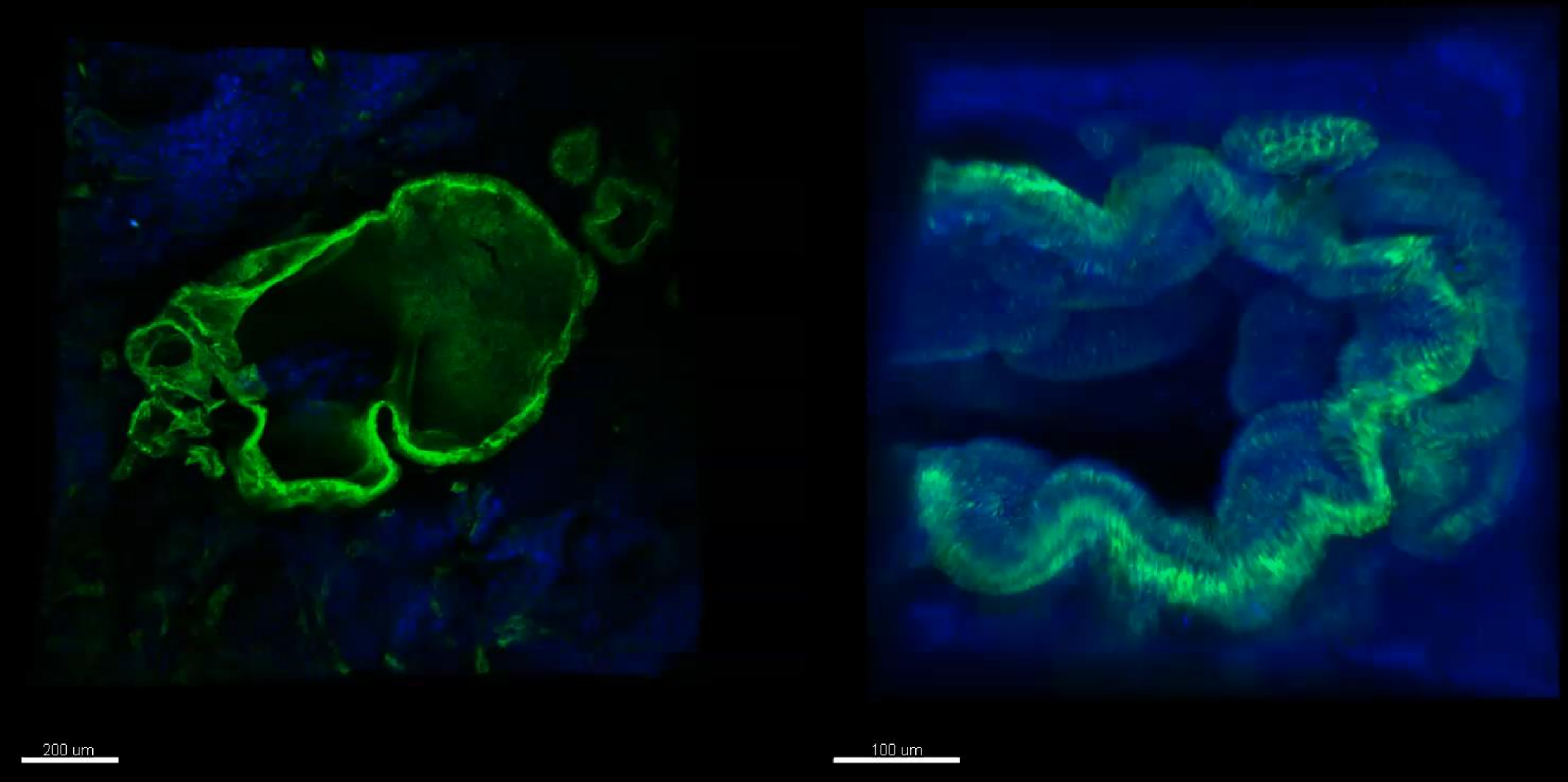
Normal pancreas

Cytokeratin 19 Desmin CD31



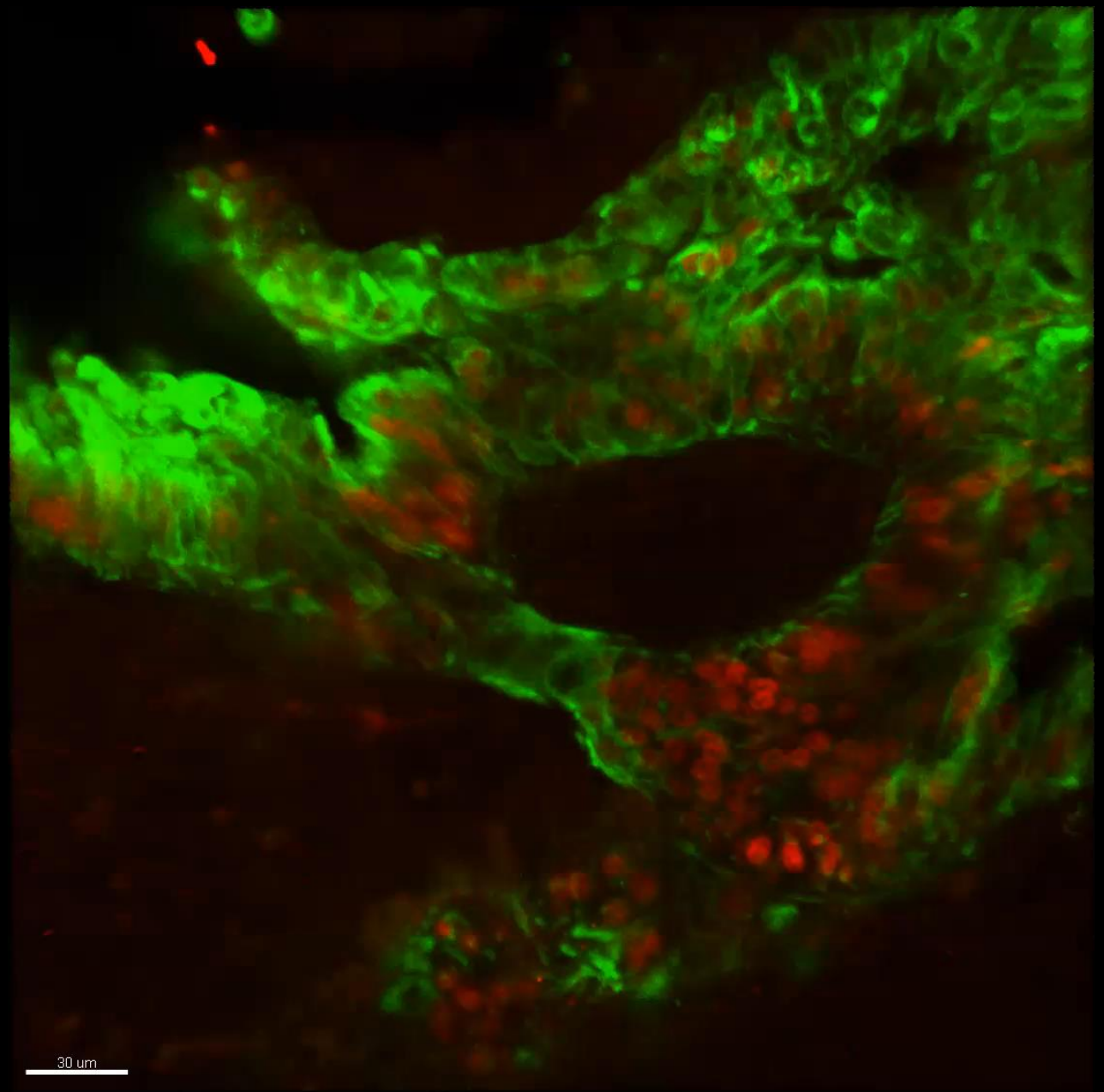
Still Image

All PanINs are not created equal

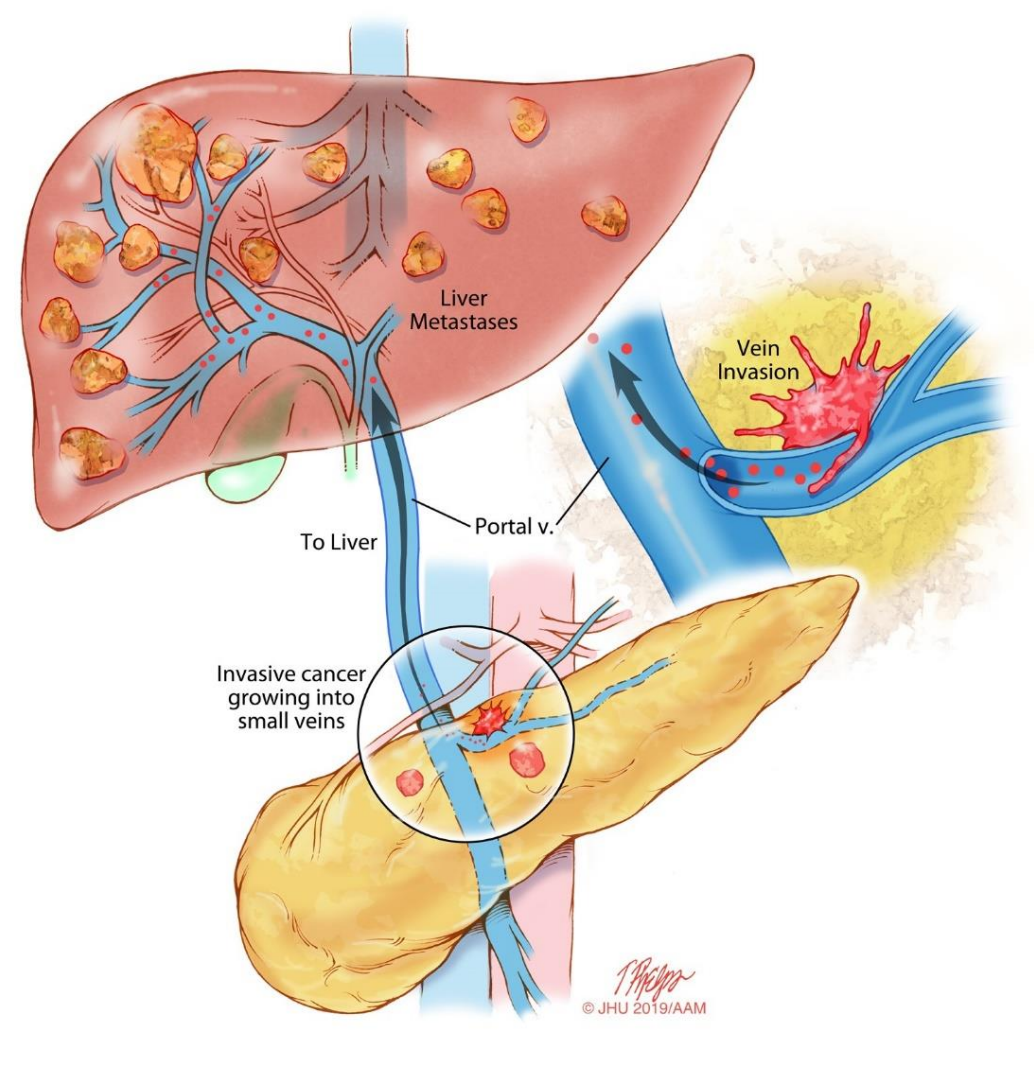


Ductal adenocarcinoma

Cytokeratin 19 p53



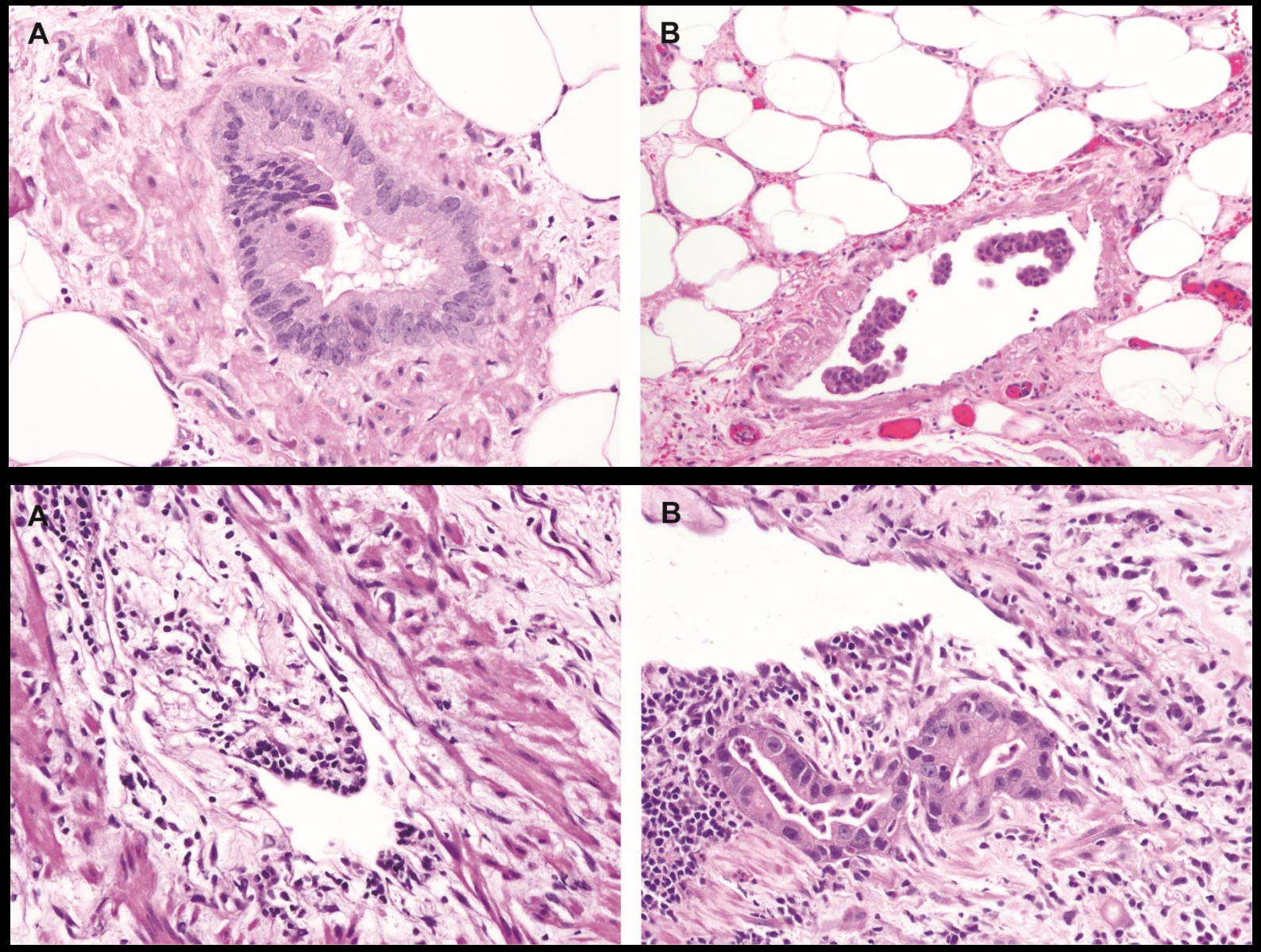
Vascular invasion



- Observed in 70% of surgically resected pancreatic cancer
- Much higher prevalence than cancers from other organs
- Associated with metastases and a poor prognosis
- Neoplastic cells replace endothelial cells and grow along inner wall of the vessels
- Unique histologic features: PanIN-like histologic feature

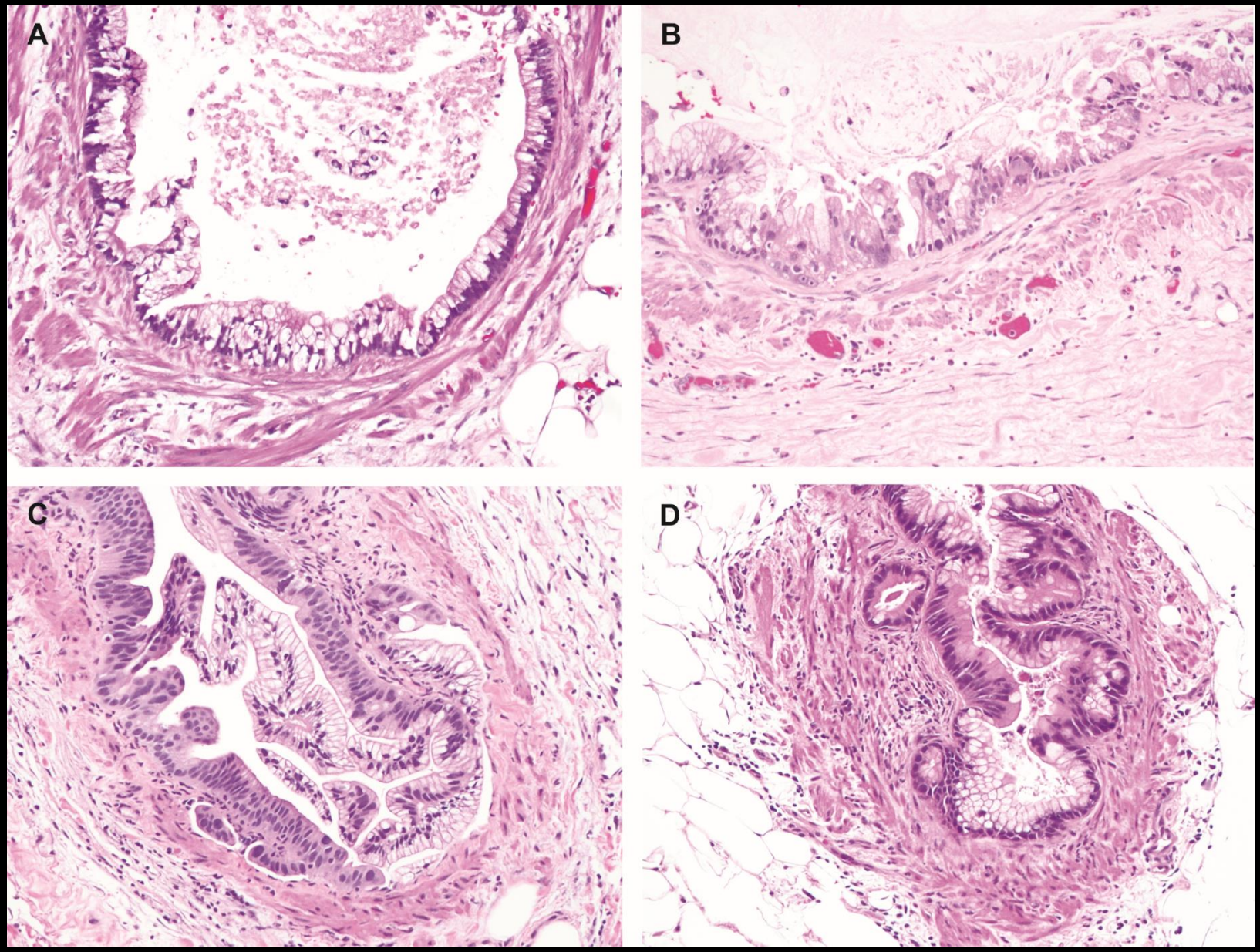
Hong SM et al. Am J Surg Pathol 2012
Hruban RH et al. J Pathol 2019

Vascular invasion

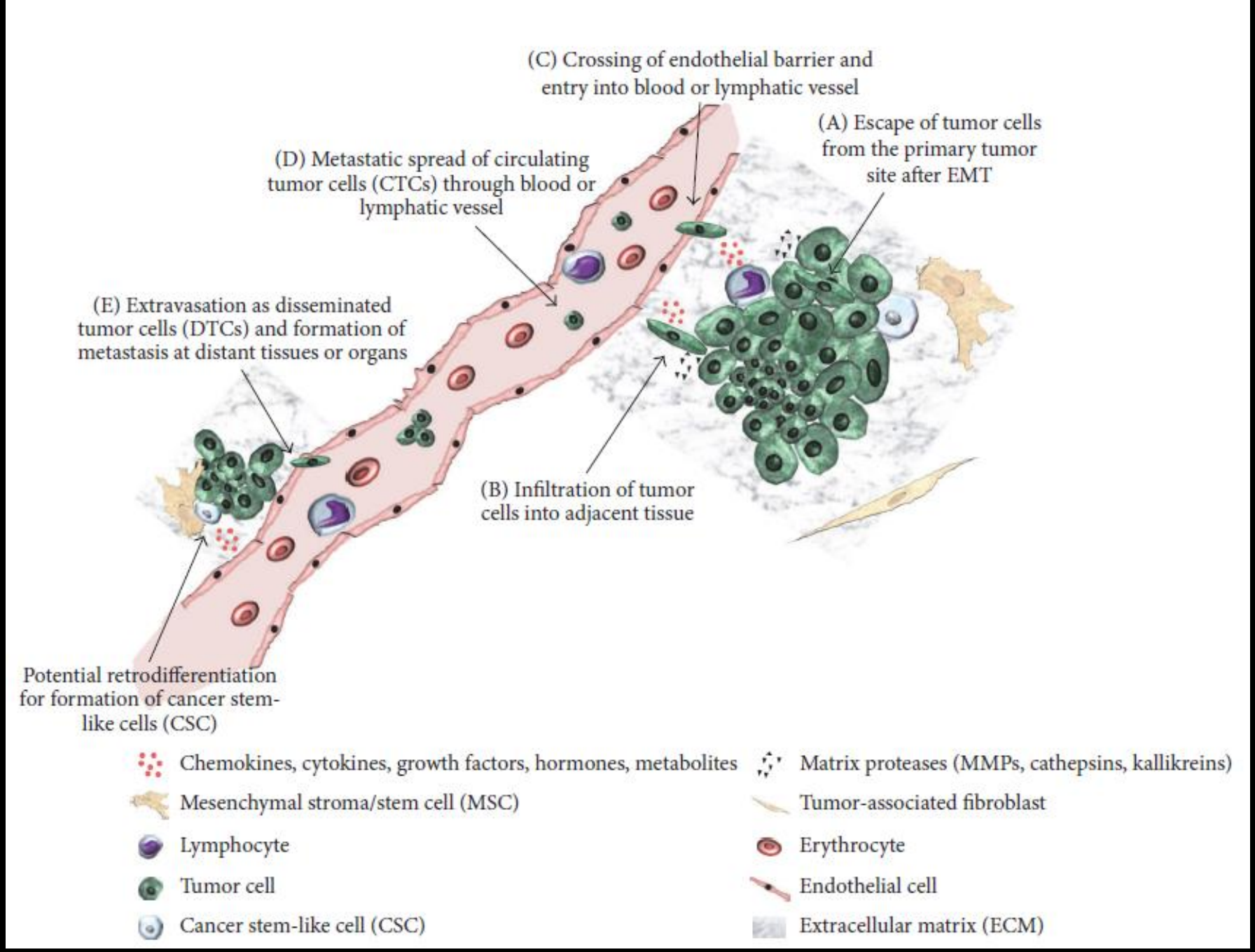


Hong SM et al. Am J Surg Pathol 2012

Vascular invasion

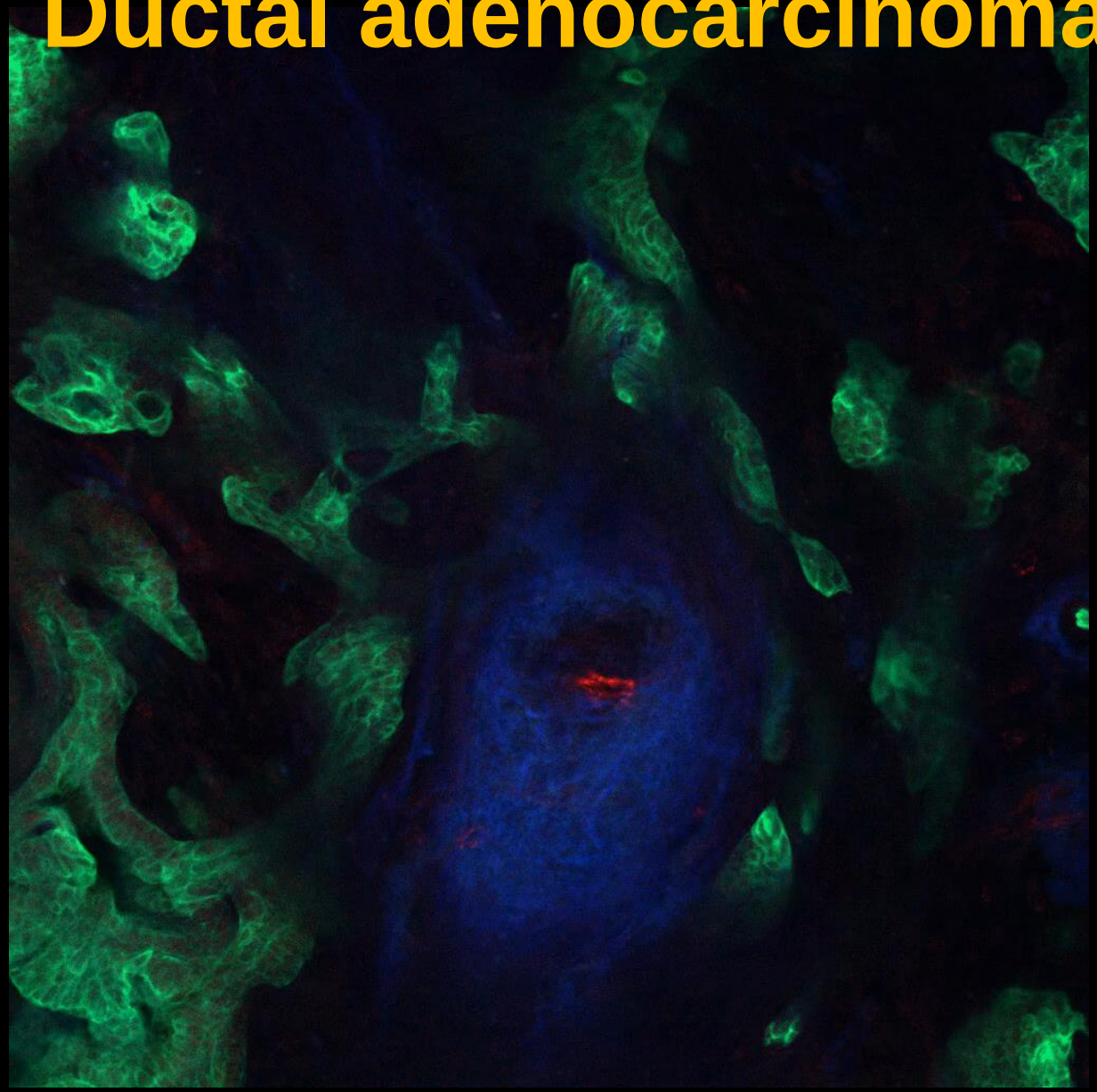


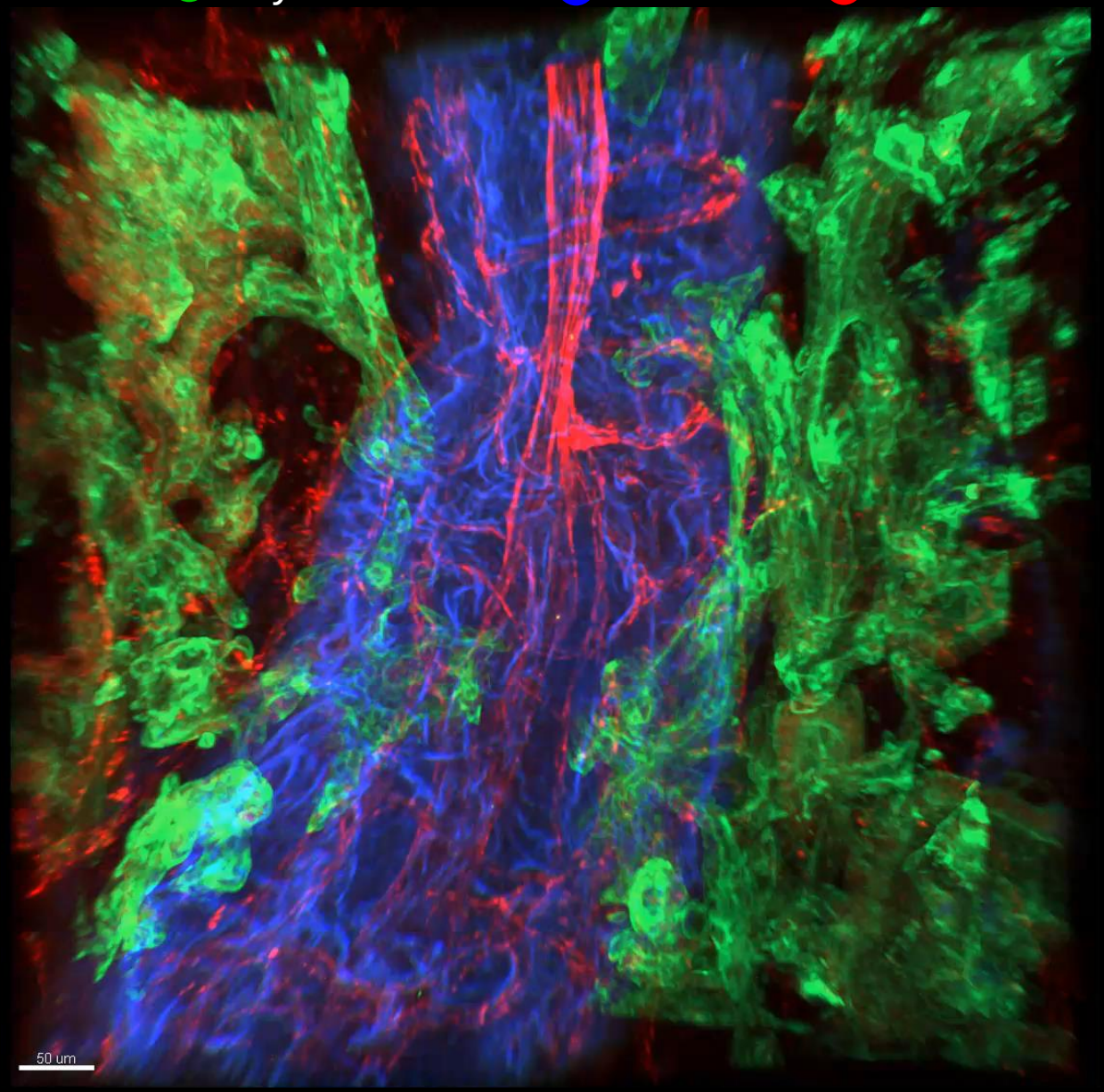
Hong SM et al. Am J Surg Pathol 2012



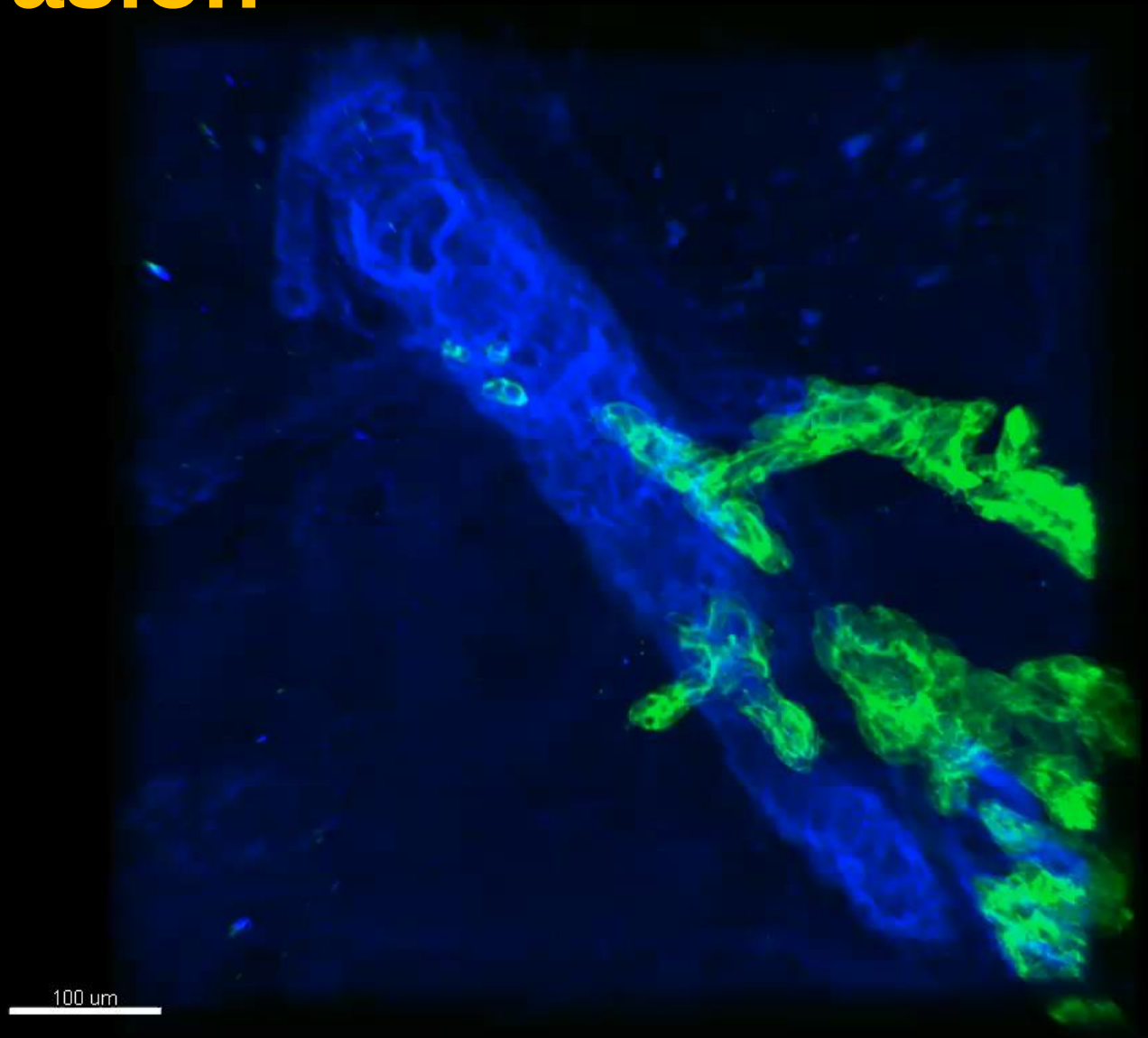
Melzer C et al. Biomed Res Int 2017

Ductal adenocarcinoma





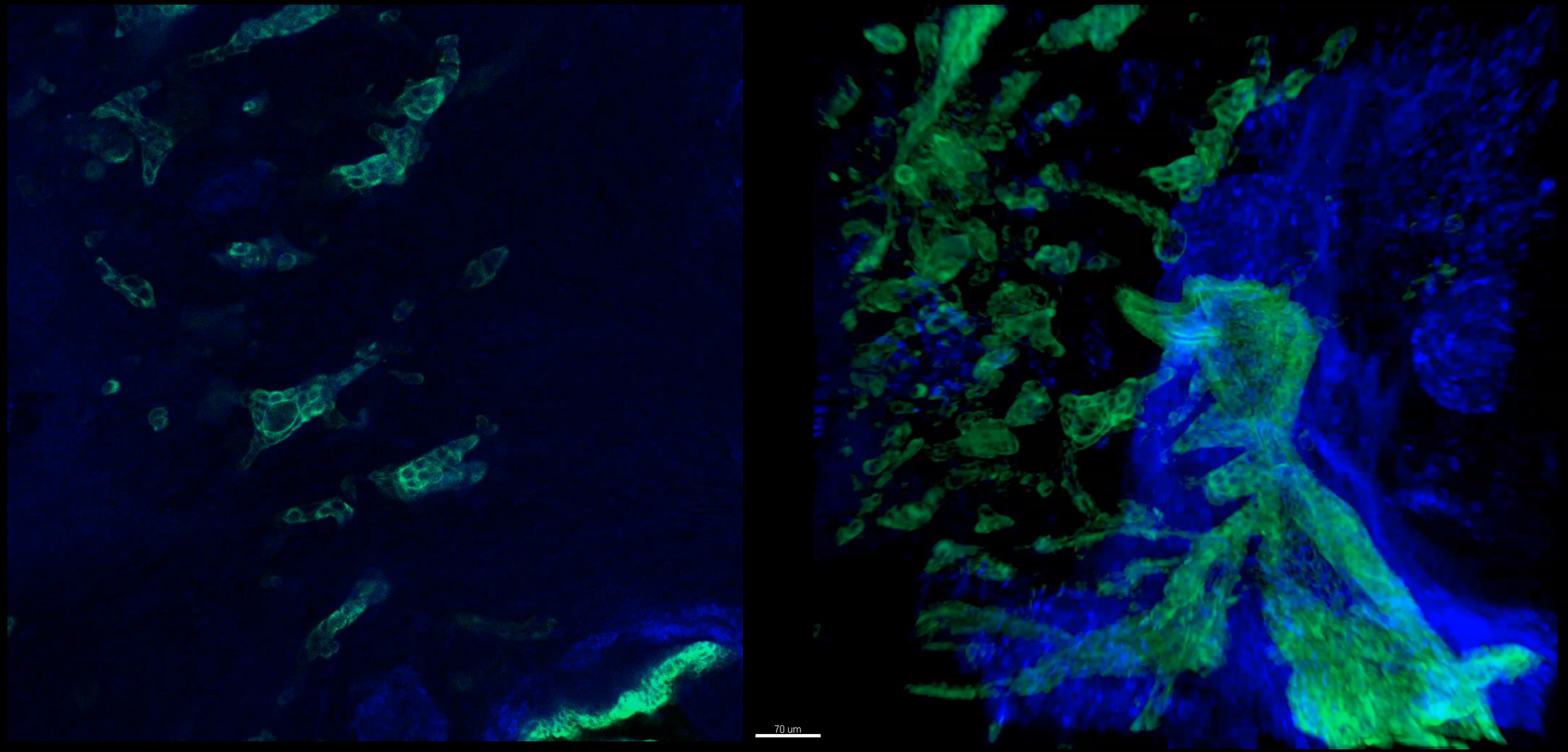
Vascular invasion



Long tubes of neoplastic cells approaching and then paralleling muscular veins

Vascular invasion

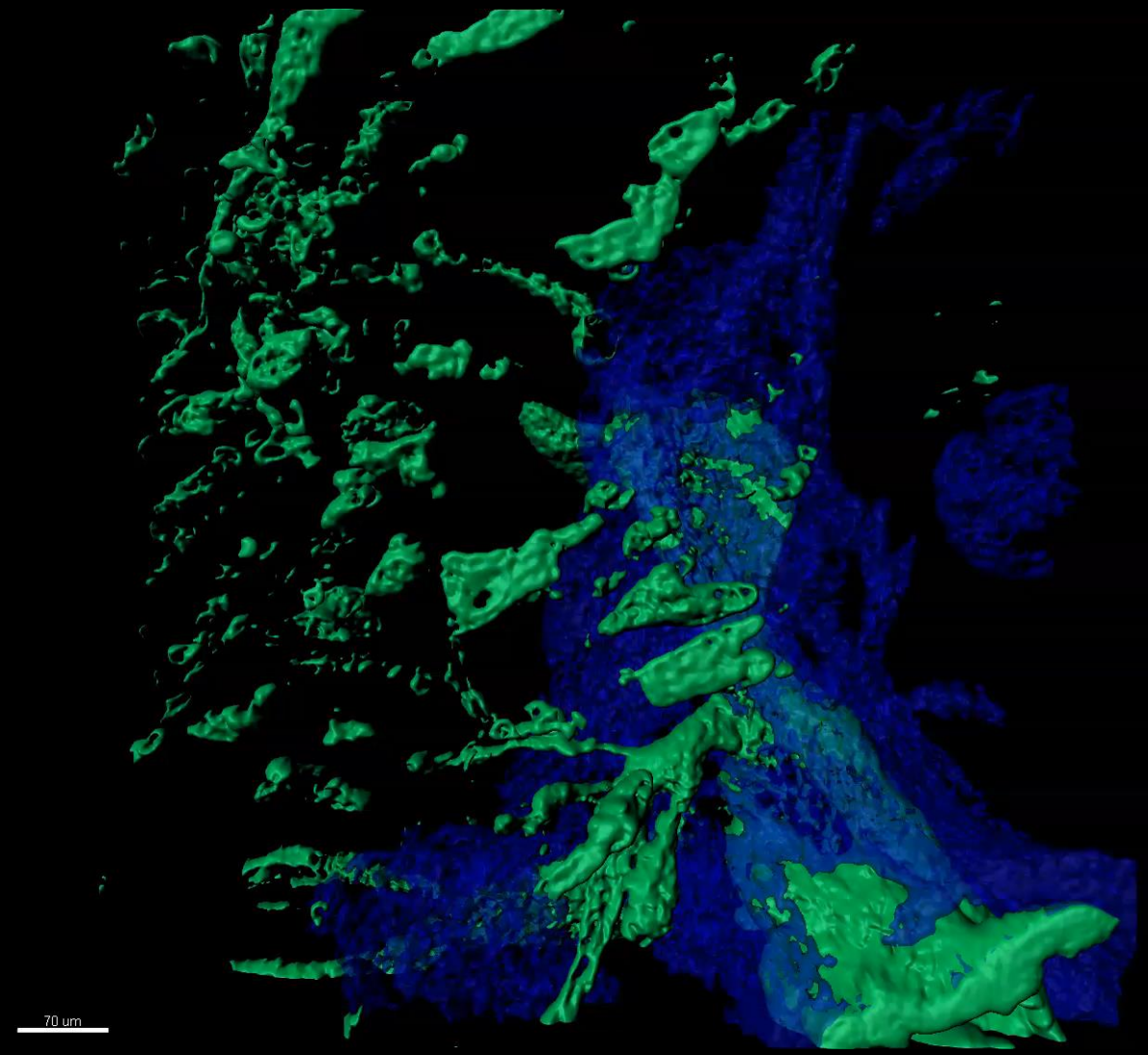
Cytokeratin 19 Desmin

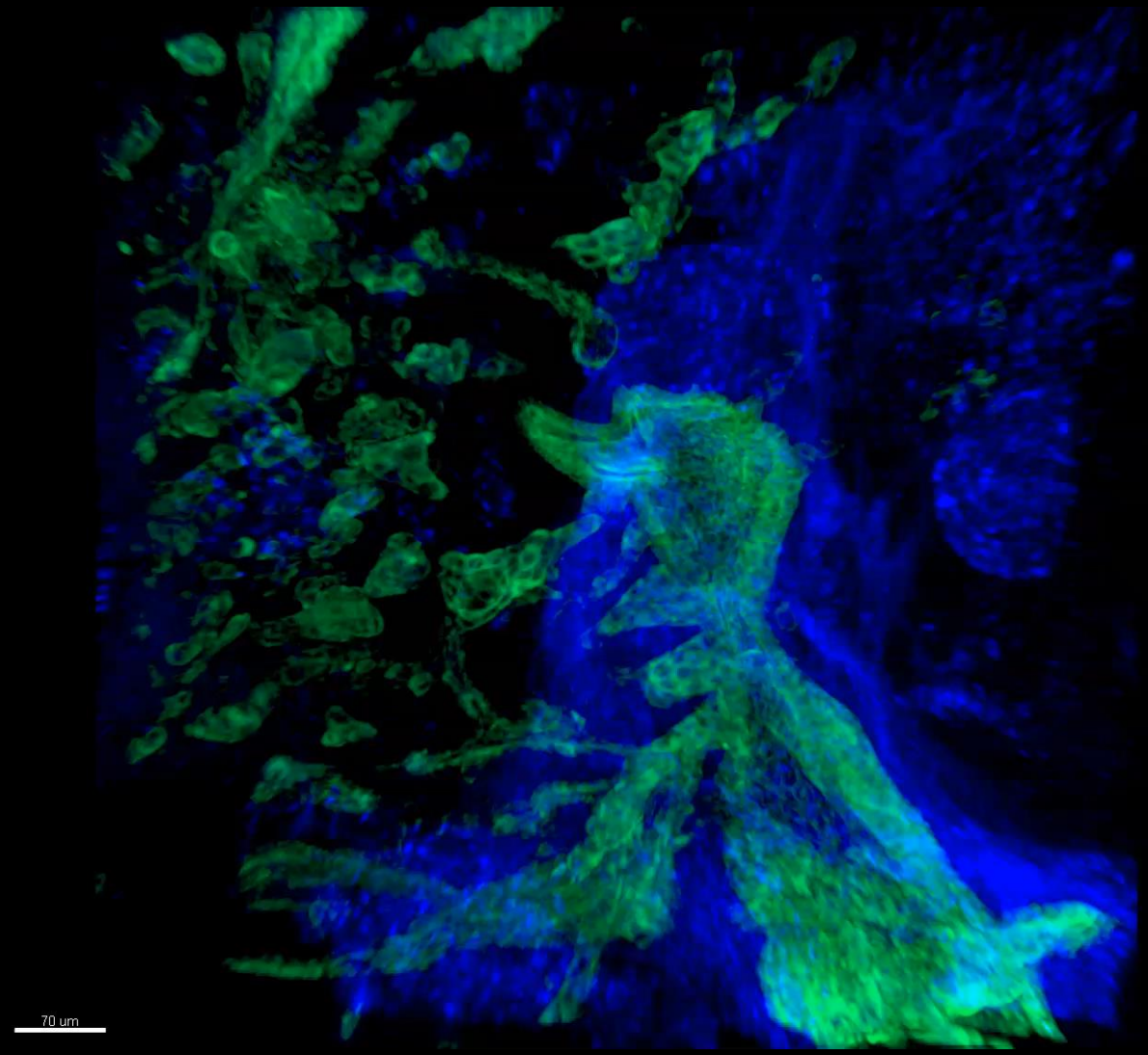


Multiple points along individual vessels at which the neoplastic cells traverse into/out of the vessels

Vascular invasion

Cytokeratin 19 Desmin

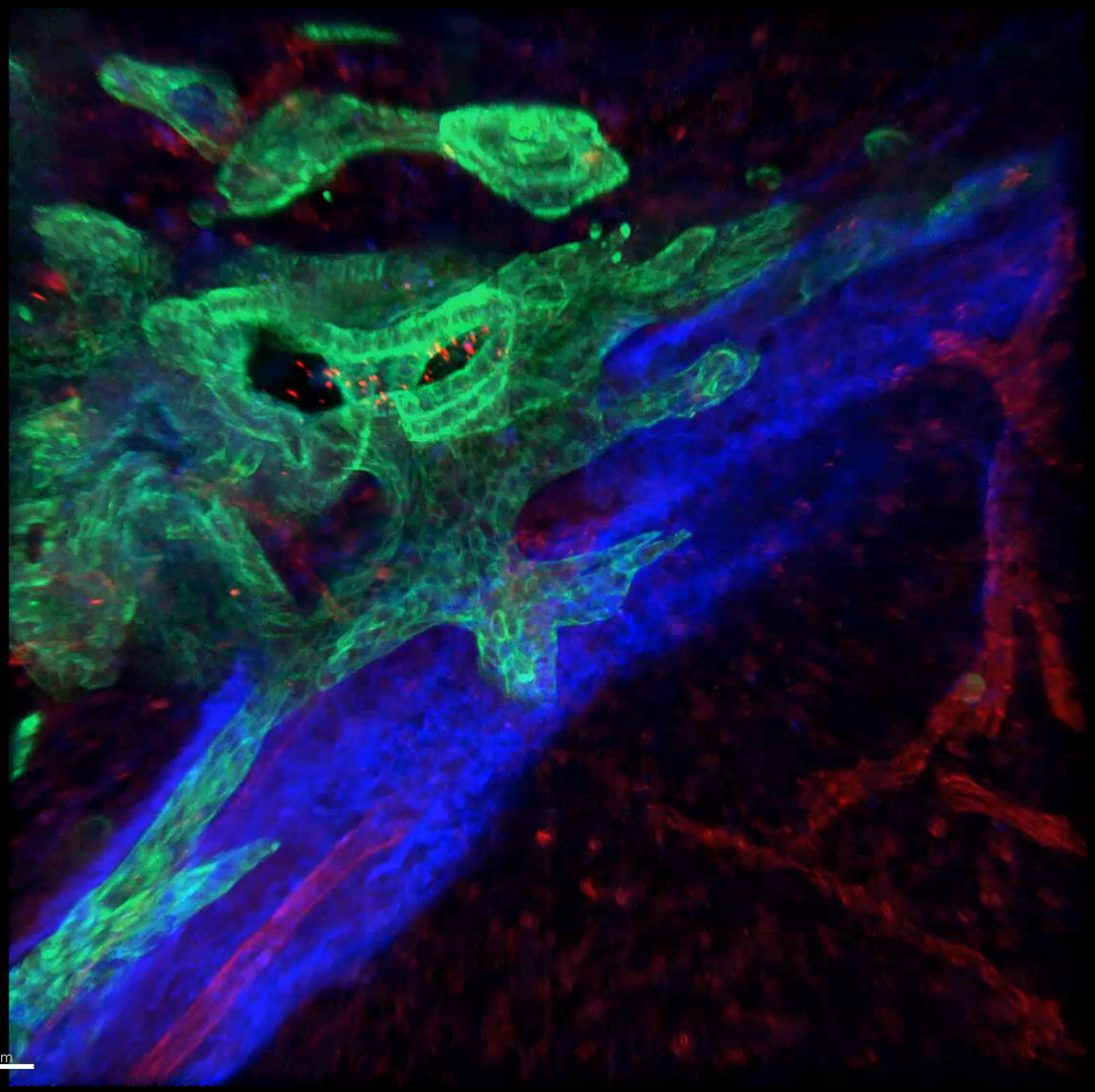




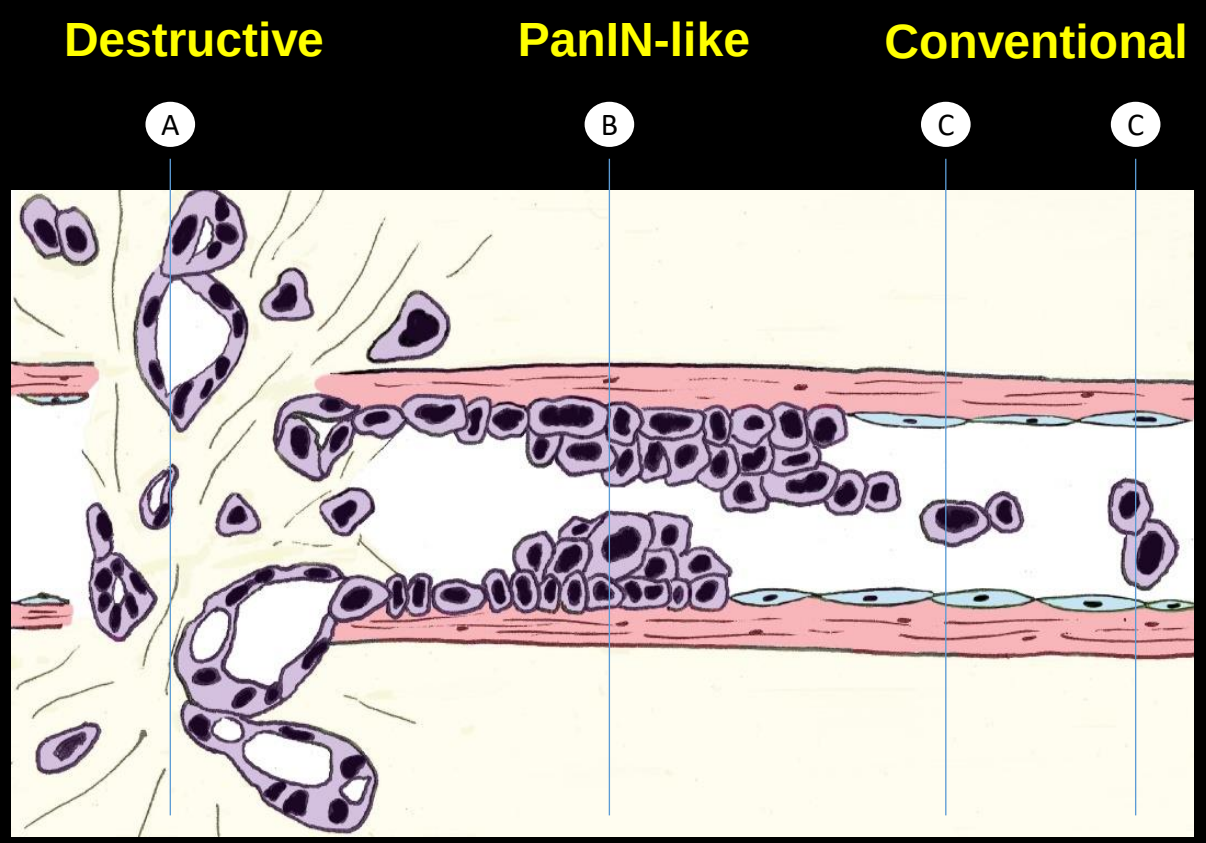
Multiple points along individual vessels at which the neoplastic cells traverse into/out of the vessels

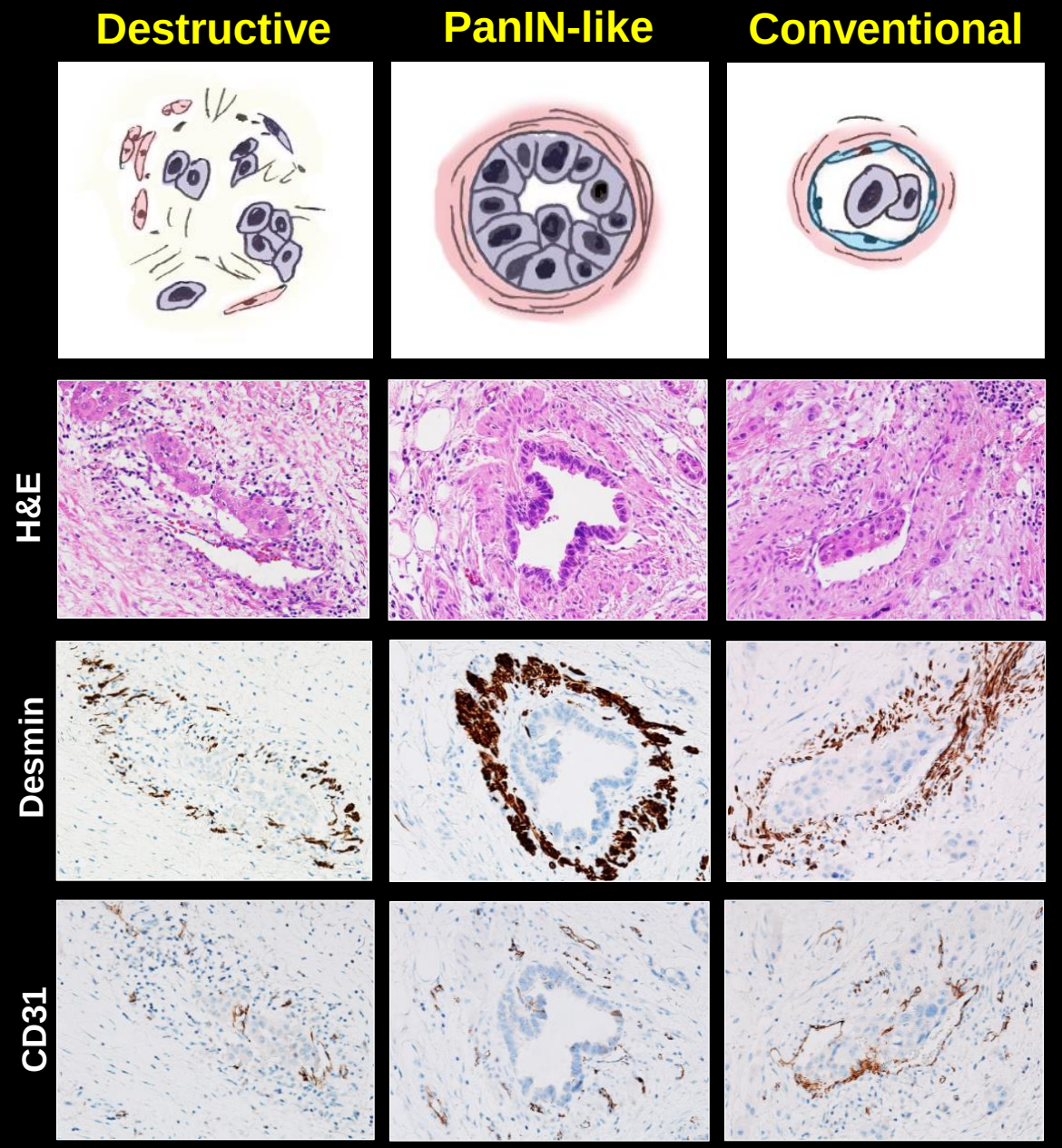
Vascular invasion

Cytokeratin 19 Desmin CD31



Vascular invasion

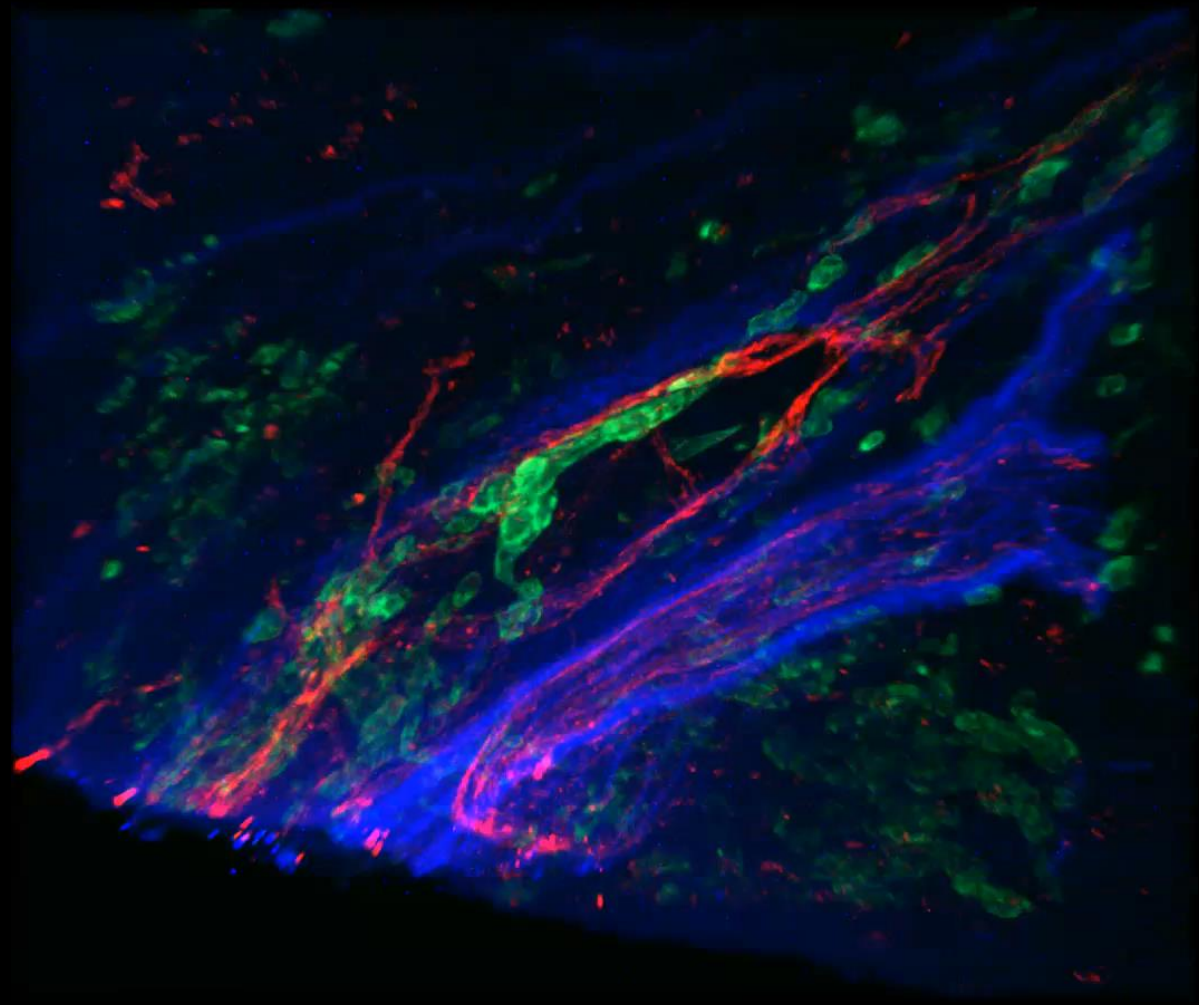




Shin J & Hong SM Unpublished data

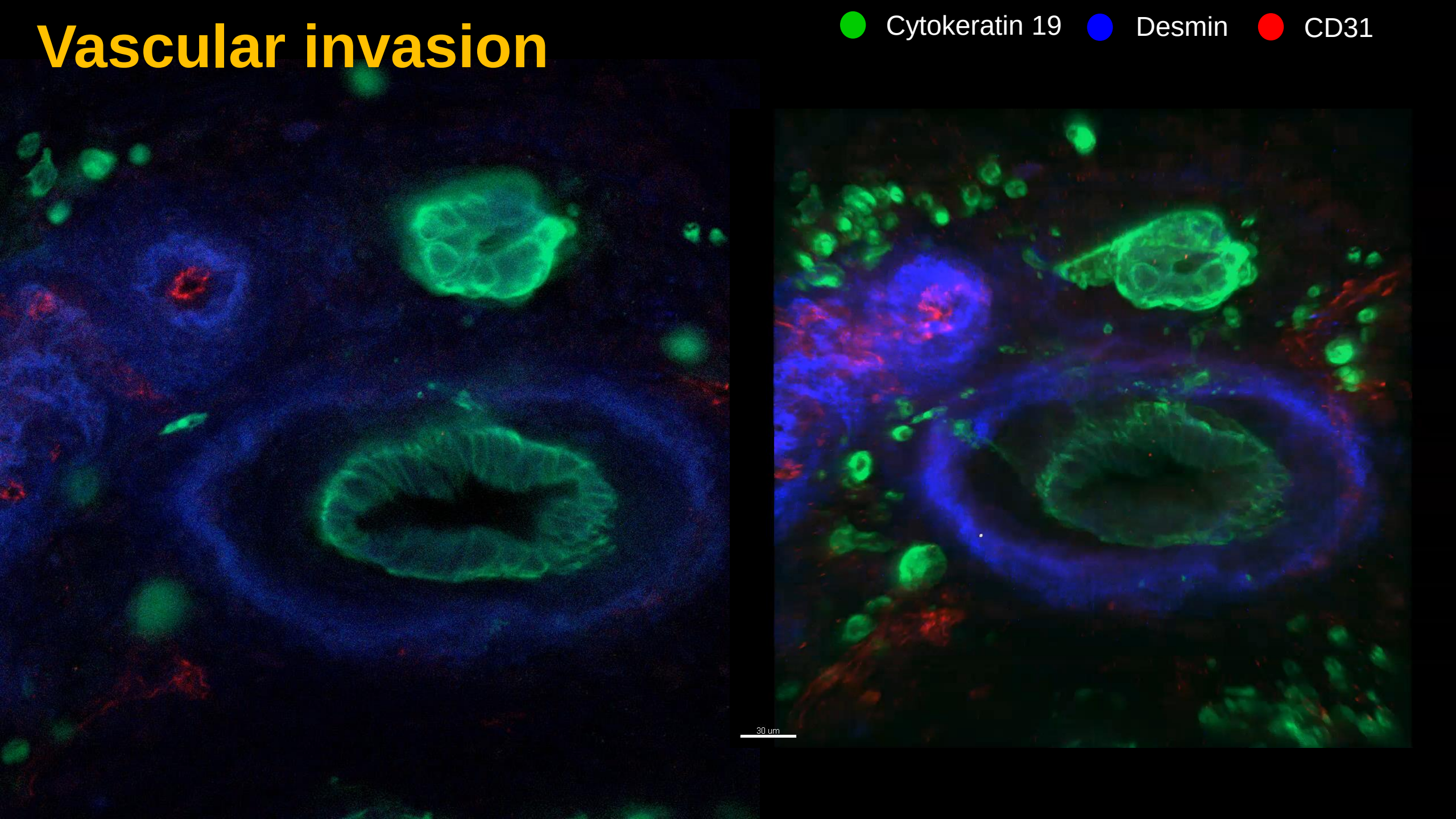
Vascular invasion

Cytokeratin 19 Desmin CD31



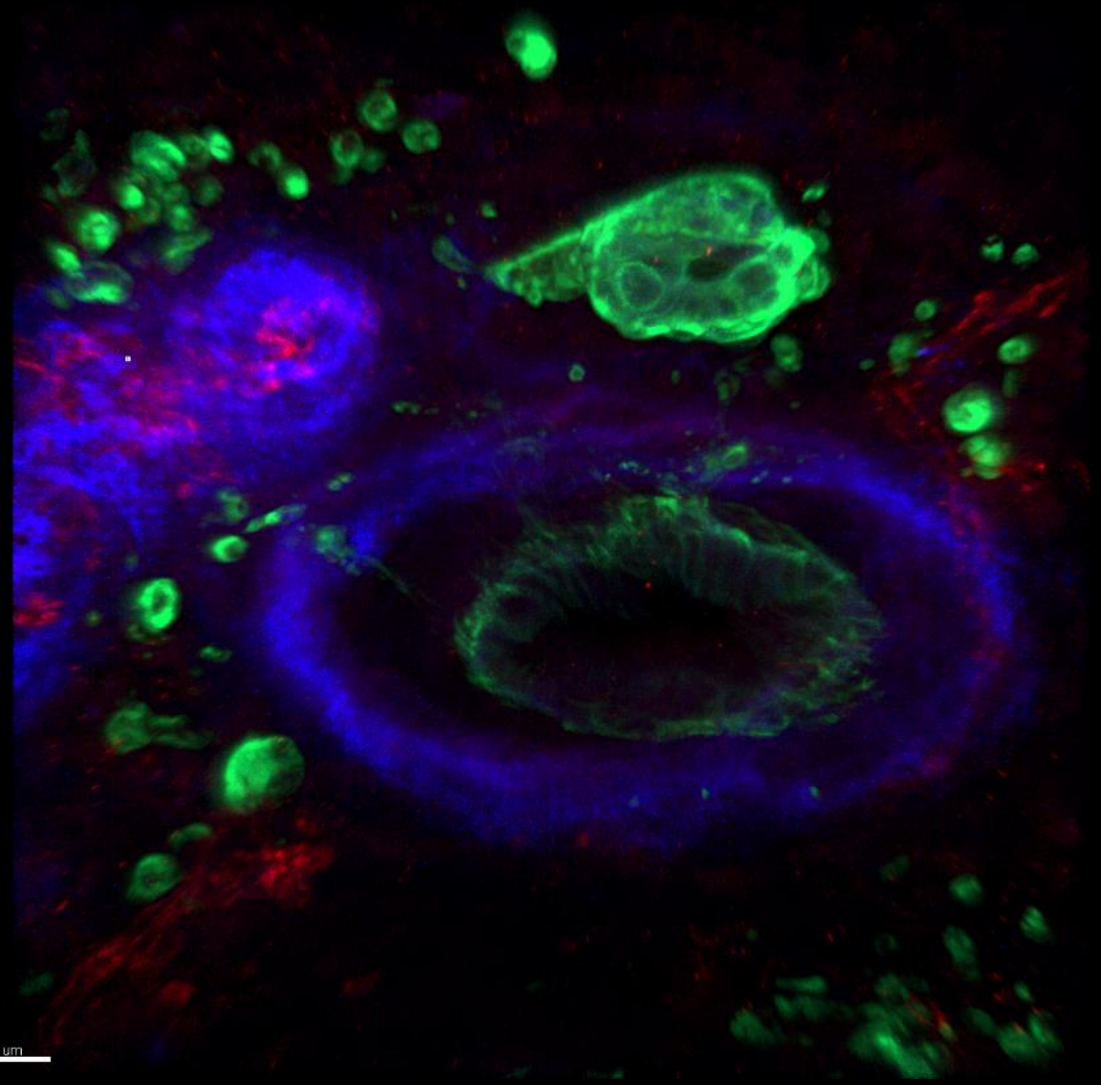
Vascular invasion

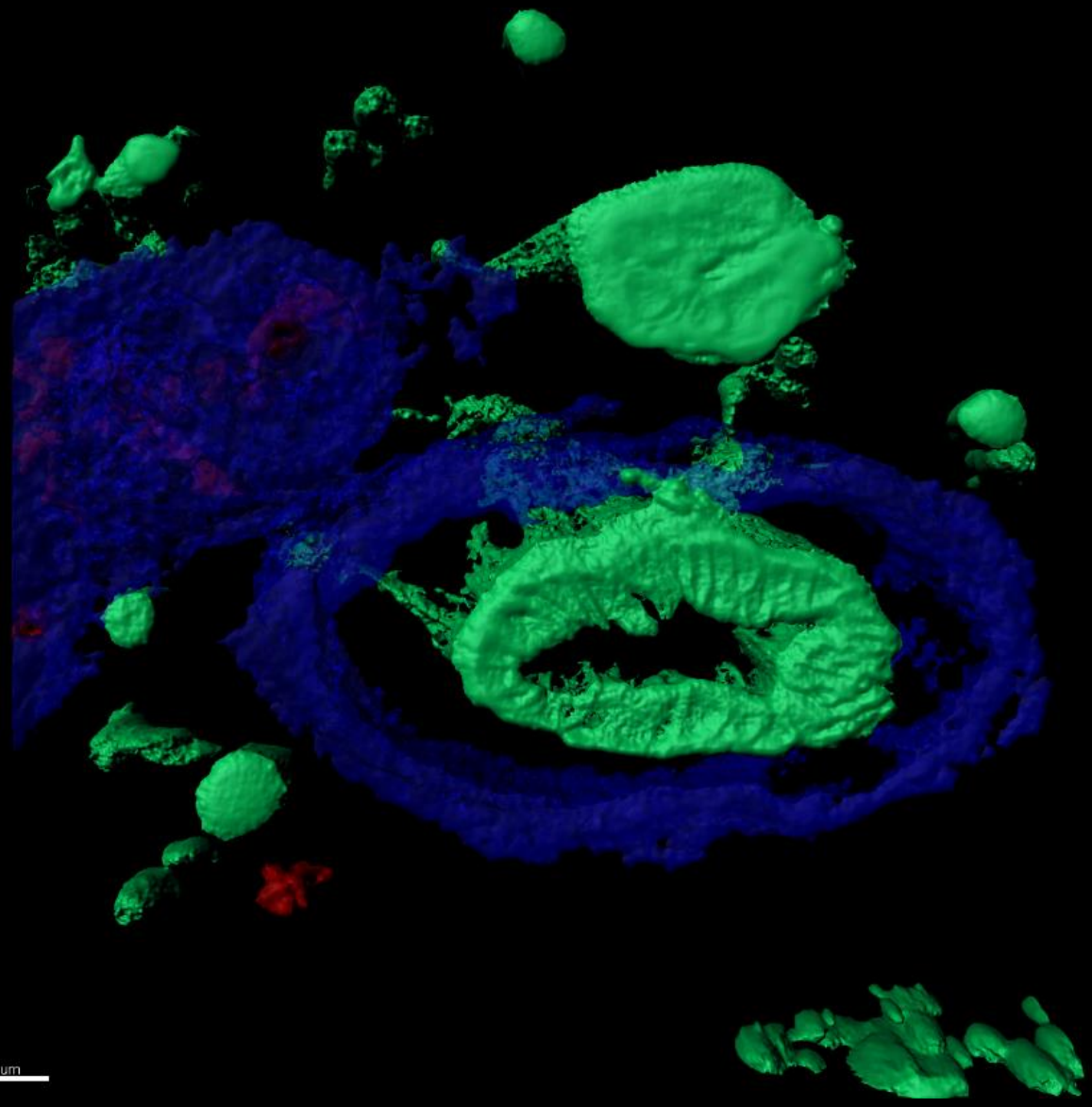
Cytokeratin 19 Desmin CD31



Vascular invasion

Cytokeratin 19 Desmin CD31

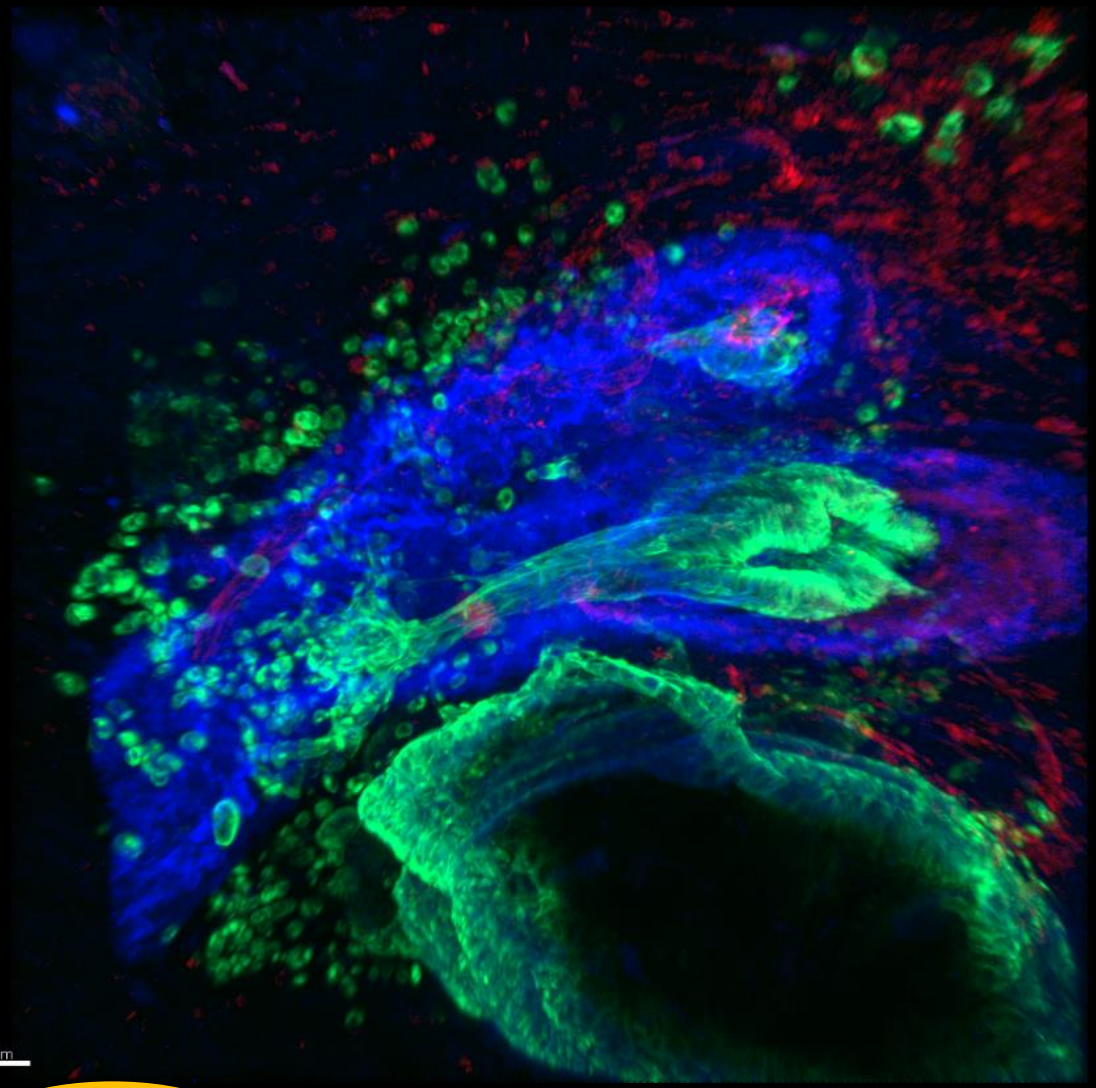


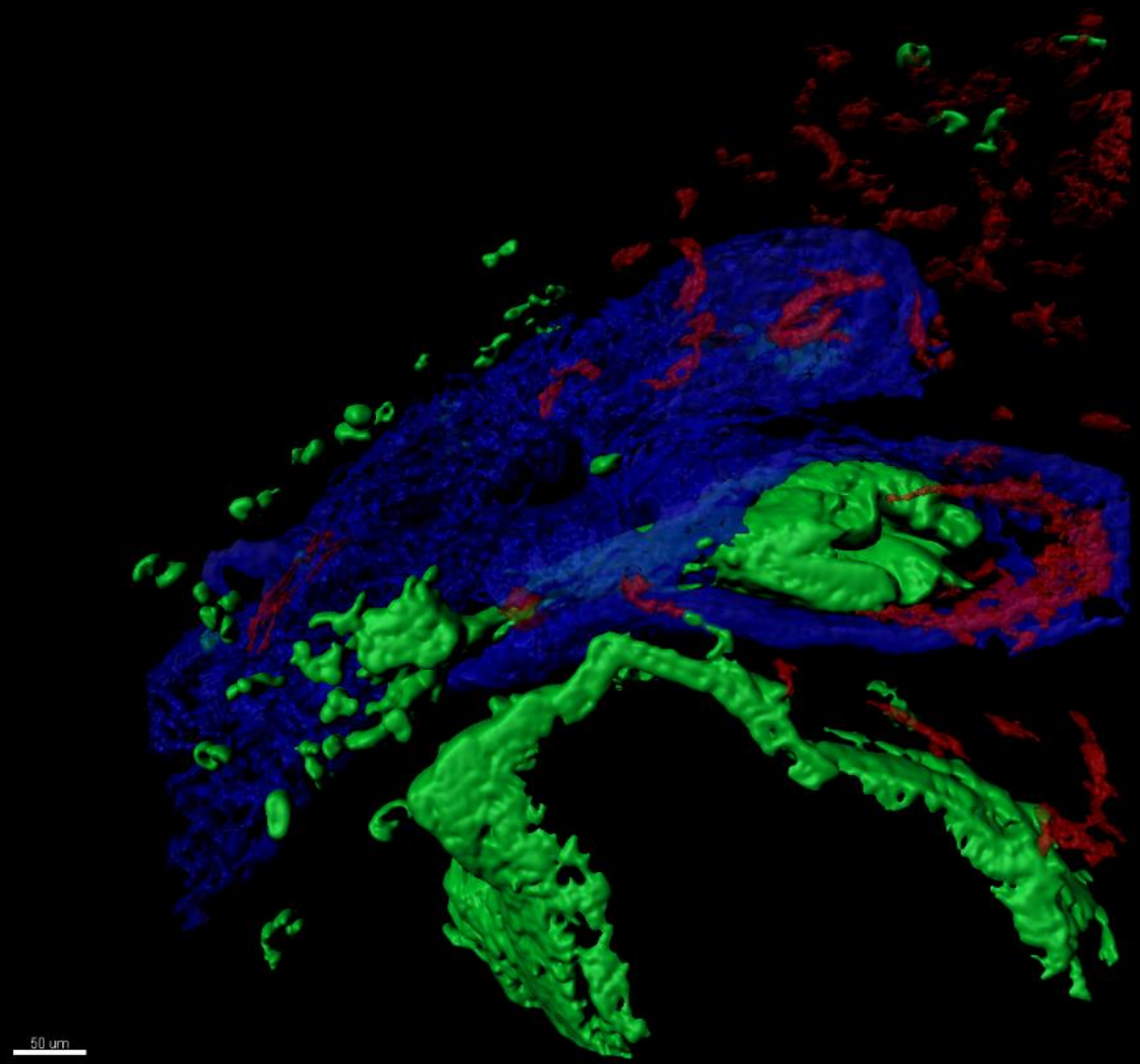


Still Image

Vascular invasion

Cytokeratin 19 Desmin CD31





Still Image

Summary of vascular invasion

- Long tubes of neoplastic cells approaching and then paralleling muscular veins
- Multiple points along individual vessels at which the neoplastic cells traverse into/out of the vessels
- Formation of loose cancer cell cords or networks inside of venous walls
- Replacement of the endothelial cells by neoplastic cells
- Intraluminal growth and extension of the cords of neoplastic cells
- Detachment of single cells at the leading edge of the intraluminal growth
- In many cases, the neoplastic cells retained a ductal morphology (cohesive cells forming tubes) throughout the process

2D versus 3D

Summary of my talk

- Incorporation of the new techniques (tissue clearing, advanced microscopies, and multiple antibody labeling), will provide new insights into pancreas pathology and will be widely applicable to other diseases.
- Dual or triple 3D visualization with cytokeratin 19 and desmin with/without CD31 immunofluorescence labeling demonstrates that sustained epithelial-mesenchymal transition is not required for venous invasion in pancreatic cancer.

Acknowledgements

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DongJun Jung

Asan Medical Center, Seoul, Korea

Junyoung Shin

University Hospital Heidelberg, Germany

Matthias M. Gaida

Wednesday, March 20, 2019
Poster Board #: 145

Immunolabeling of Cleared Human Pancreata for Multiple Markers Provides Insights into Pancreatic Anatomy and Pathology

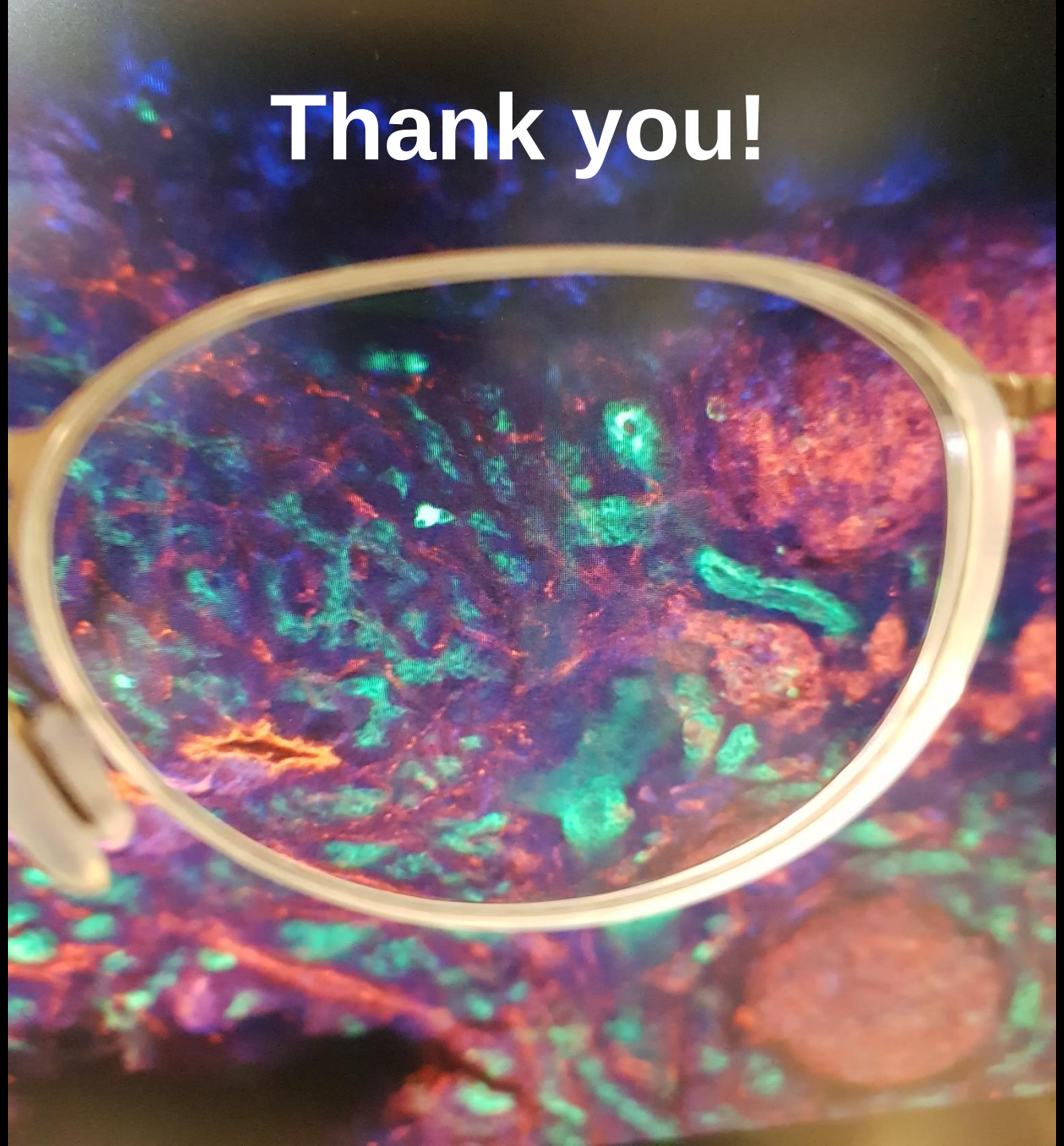
Celebrating Dr. Jae Ro's 50th Anniversary of Pathology: Do your BeST!

TO SIR, WITH LOVE

Do Your BeST!

- **B**asic
- (effort) **S**tudy
- **T**hink
- **E**njoy

2009 Boston, MA at USCAP annual meeting


Thank you!