Programmed Cell Death Ligand 1 Pathologist Training in the Time of COVID-19: Our Experience using Digital Solution

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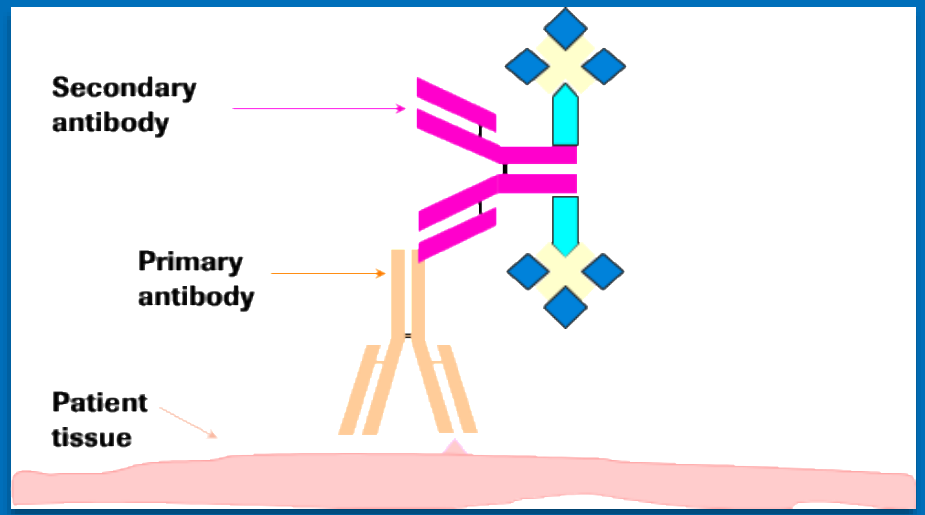
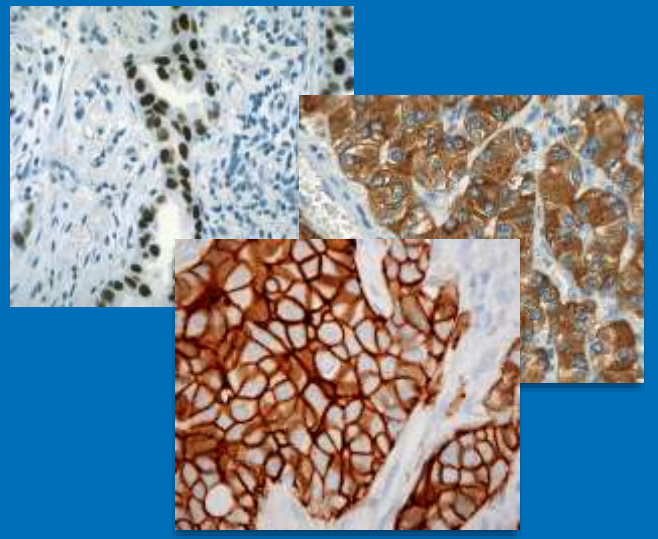
Digital Pathology Future Directions

- Multiplexing (MPX)
- AI and Image analysis
- Pathologist’s clinical decision support platforms
- Link to real time Big Data

What is multiplex IHC?

Improving IHC to provide more information



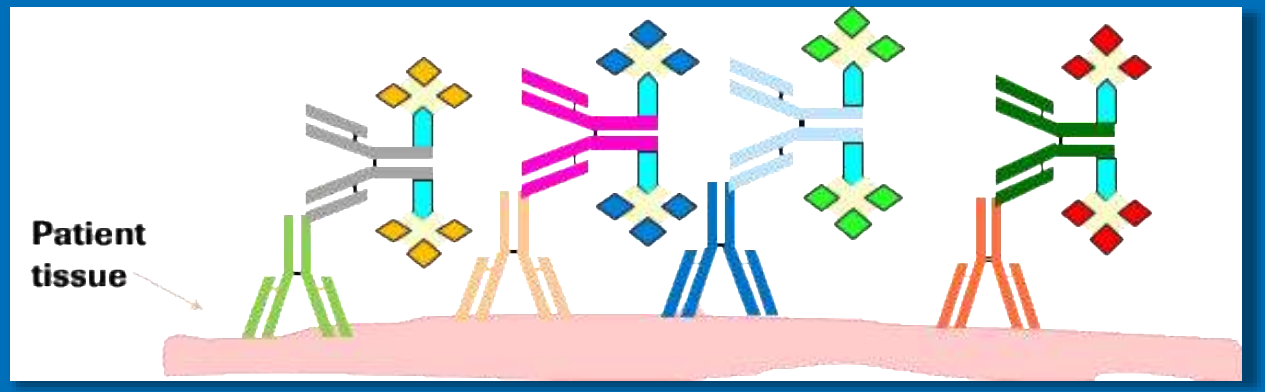


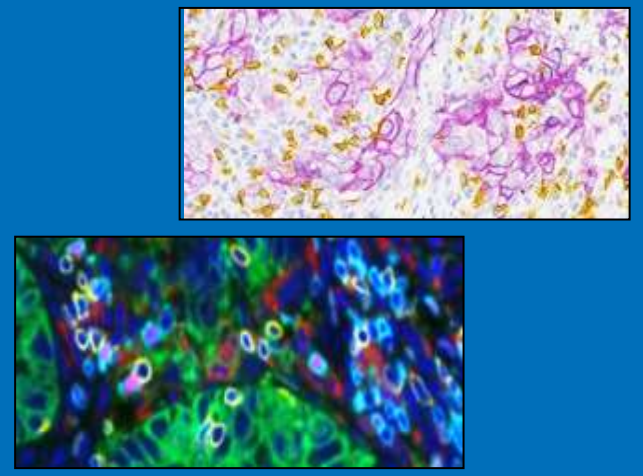
- *Conventional IHC utilizes a single antibody that recognizes a specific protein in a single sample of patient tissue*

- *For the pathologist, this allows for identification of a single biomarker within the sample.*
- *Providing information on the cellular and spatial location of the biomarker and protein expression of the biomarker*

What is multiplex IHC?

Improving IHC to provide more information





- *Multiplex IHC utilizes multiple antibodies (2 or more) each recognizing a different protein in a single sample of patient tissue*

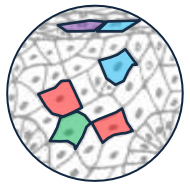
- *Visualization of the multiple biomarkers can be performed using chromogenic or immunofluorescent tags*
- *Evaluation of multiplex IHC can be performed using standard manual interpretation or digital image analysis*

Why multiplex IHC?

Key drivers behind multiplexing as the future of IHC

Increasing Complexity

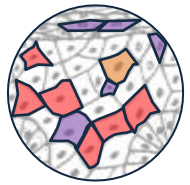
Tissue Conservation



PD-L1 + / - or
NTRK + / - or
MLH1 + / - or
CD8 + / -

Markers that would otherwise be stained on separate slides are combined to conserve tissue

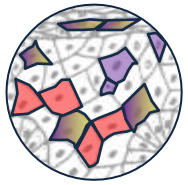
Relative Expression



PD-L1 high +
FoxP3 low +
CD8 high

Comparison of the % of cells expressing one marker versus another marker(s), taken as a signature

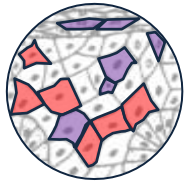
Co-Expression



PD-L1+ +
CD8/IFN+ : CD8/IFN-

Multiple markers expressed on the same cell (used to characterize cells at a granular level)

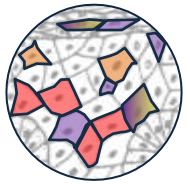
Intercellular Context



PD-L1, CD8 densities in tumor +
PD-L1, CD8 densities in tumor margin;

Location of multiple markers in the context of the cell or tumor microenvironment (e.g., proximity to tumor)

Inter-marker spatial context

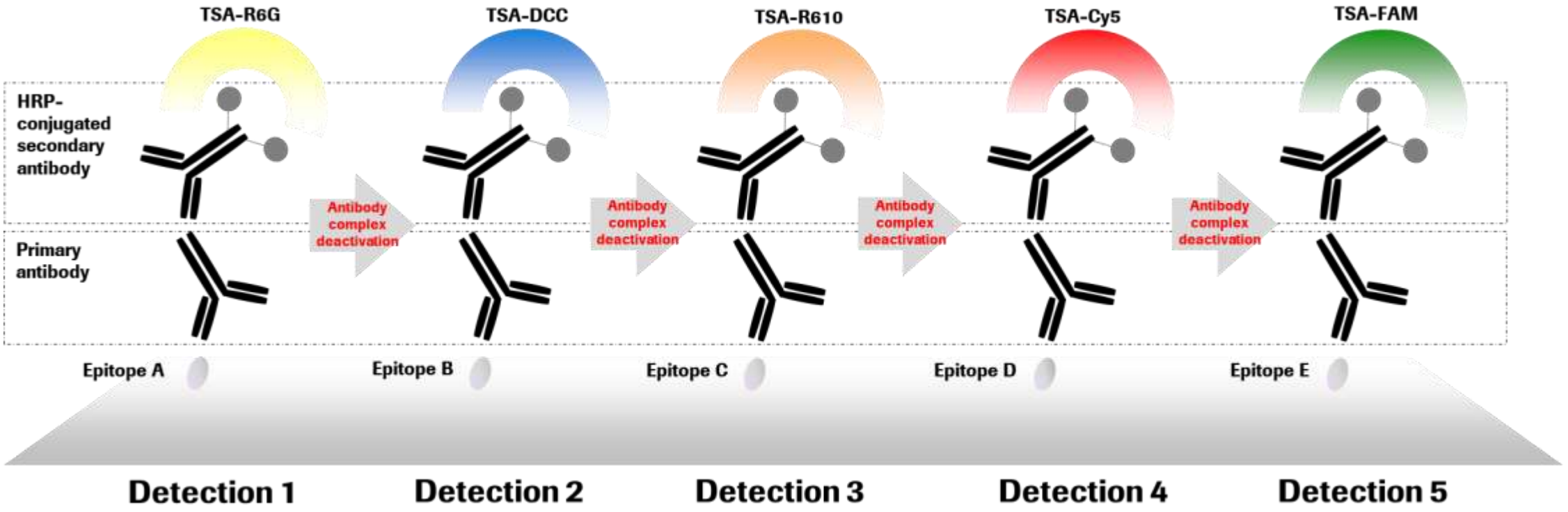


PD-L1, CD8/IFN+, FoxP3 proximity index in tumor
PD-L1, CD8/IFN+, FoxP3 proximity index in tumor margin

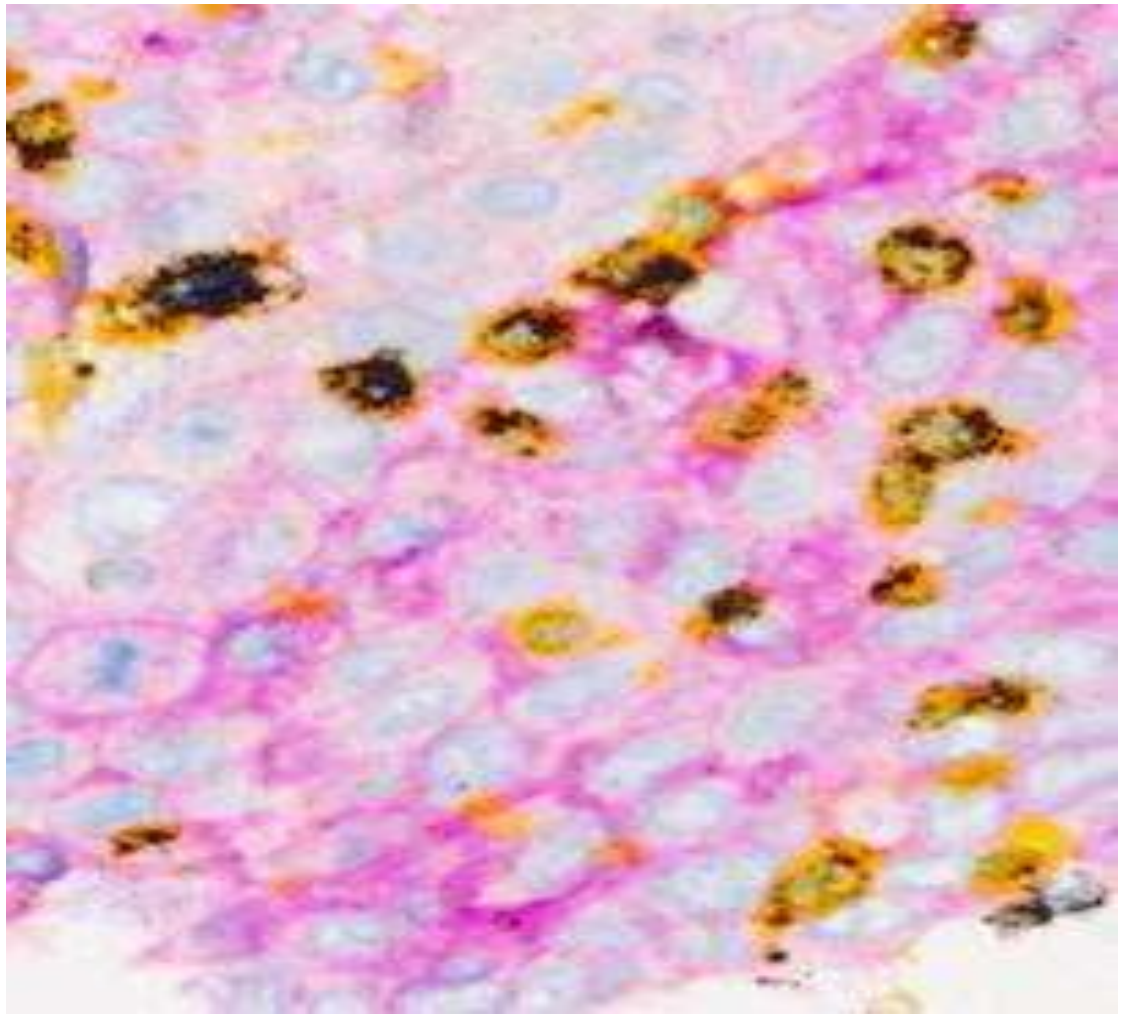
Spatial orientation of markers in respect to one another (e.g., PD-L1/PD-1 interaction score)

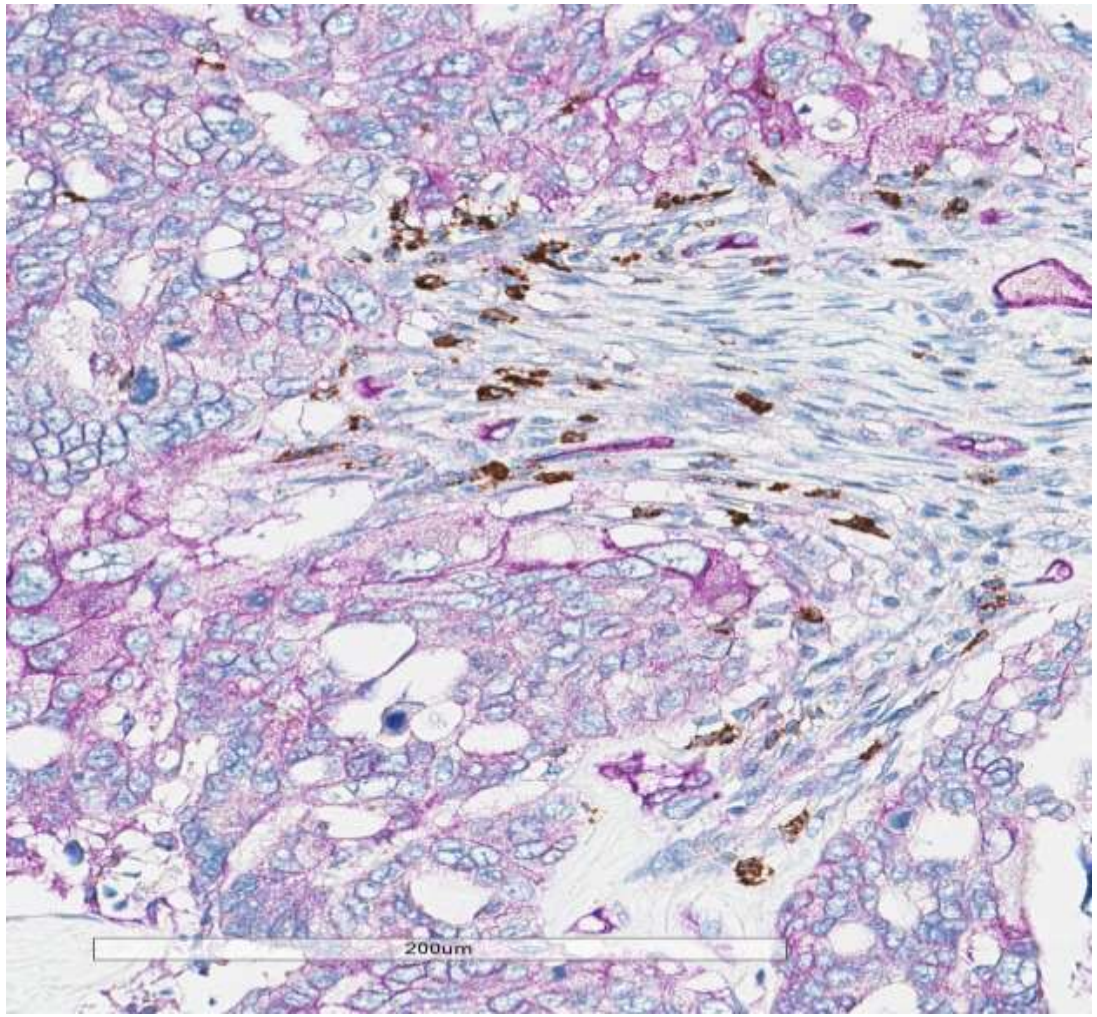
What multiplex technology do we have at RTD?

Fluorescent and chromogenic



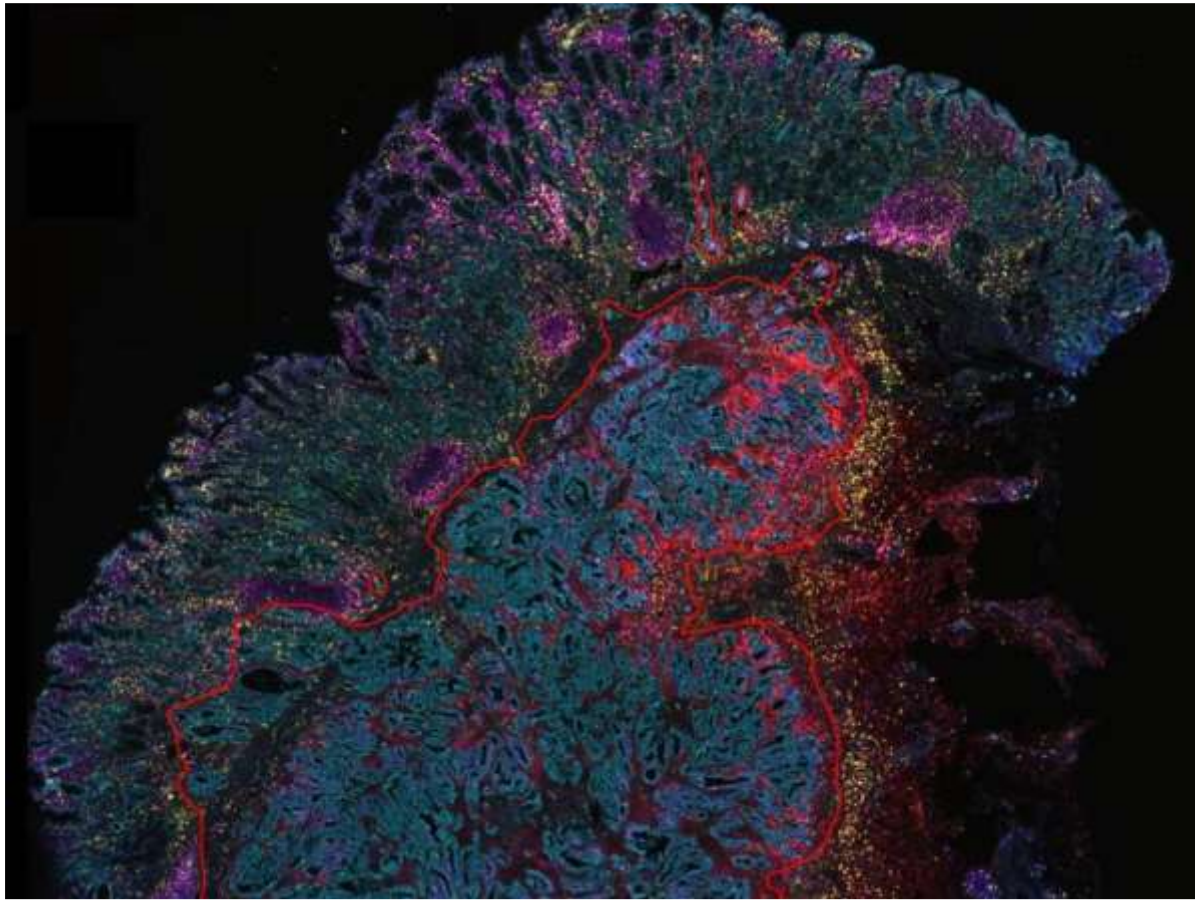
Multiplexing Panels

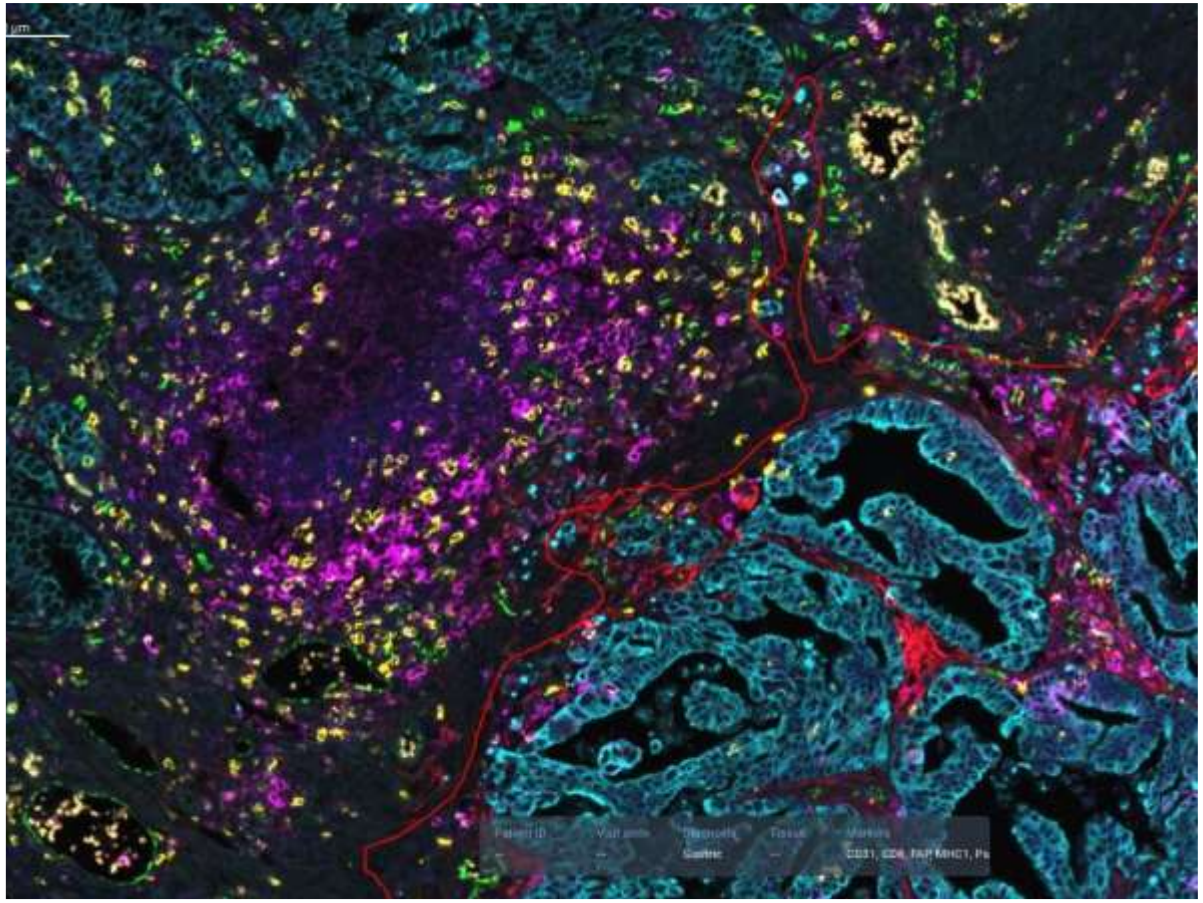




IF MPx_TSA-Fluorophores Greatly Enhance Detection Sensitivity

Detecting 5 biomarkers on a single slide





DAPI CD31 FAP MHCI CD8 panCK in Gastric carcinoma

Courtesy of GNE team

DiagRelatlimab (RELA) plus nivolumab (NIVO) versus NIVO in first-line advanced melanoma: Primary phase III results from RELATIVITY-047 (CA224-047). Lipson et al ASCO 20201

- Phase III study demonstrated a clinically meaningful benefit by dual inhibition of the LAG-3 and PD-1 pathways.
- RELA+NIVO FDC showed statistically significant PFS benefit when compared to NIVO monotherapy in patients with advanced melanoma.