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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

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**Tissue Conservation**

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

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

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**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

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**Co-Expression**

- PD-L1+ + CD8/IFN+ vs CD8/IFN-

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

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**Interacellular 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)

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**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-L1 interaction score)
What multiplex technology do we have at RTD?

Fluorescent and chromogenic
IF MPx_TSA-Fluorophores Greatly Enhance Detection Sensitivity

Detecting 5 biomarkers on a single slide

DAPI CD31 FAP MHCI CD8 panCK in Gastric carcinoma
DiagRelatlimab (REL) plus nivolumab (NIVO) versus NIVO in first-line advanced melanoma: Primary phase III results from RELATIVITY-047 (CA224-047). Lipson et al. ASCO 2020

- 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.