Weill Cornell Medicine

MAP-IT: Spatial Protein Interactome Mapping in Human Tissue Sections Using Photocatalytic Labeling

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Background & Unmet Need

- Protein-protein interactions (PPIs) represent a promising class of potential drug targets
- However, PPIs are typically identified in settings (e.g., cells, lysate, or model organisms) which lack crucial features of human physiology, limiting biological and clinical relevance
- Identifying PPIs directly in patient tissue may uncover physiologically-relevant interactions, but developing such methods remains challenging
- Proximity labeling, in which a photocatalyst or enzyme at a protein of interest (POI) generates reactive intermediates which flag nearby protein interactors, is a potentially attractive strategy
- However, current applications of tissue-based proximity labeling, such as µMap-FFPE, are limited by large labeling radii and high false positive rates
- **Unmet Need:** Improved methods for PPI discovery in human tissue samples

Technology Overview

- **The Technology:** MAP-IT, an optimized photocatalytic proximity labeling method for direct PPI mapping in primary human tissue sections
- Photocatalyst-decorated secondary antibodies are paired with primary antibodies to target labeling of endogenous POIs in intact tissue samples
- Selective blue-light irradiation of subcellular locations or specific cell types can be used to facilitate spatial interrogation of protein interactions
- The inventors have further developed a customized microscope setup and neural network-powered spatial segmentation to automatically identify and irradiate regions of interest
- **PoC Data:** MAP-IT successfully profiled and spatially deconvoluted the interactome of CD45 for interactions in B vs. T cells in human tonsils
- Global tissue irradiation with MAP-IT was used to identify interactors of EGFR which are exclusive to colon cancer tissue but absent in healthy tissues

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Jacob Geri
Sarah Faulkner
Charles Warren
Noah Yardeny
Jih Kai Yeh

Publications:
Burdette et al. ChemRxiv. 2026. (pre-print)

Patents:
PCT Application Filed

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Technology Applications

- Identification of PPIs unique to certain tissue types, subcellular structures, mesoscale structures, or disease states for research use or target identification for novel therapeutics
- Identification of protein interaction pairs for development of bispecific antibodies and next-generation AND-gated biologics

Technology Advantages

- Enables direct target discovery in human samples with a disease state of interest
- Tight labeling radius enables identification of PPIs with low false positive and false negative rates
- Spatially-specific activation enables the identification of location or cell-type specific interactions
- Integration of neural networks for image-guided irradiation provides a high flexibility and scalability

Supporting Data / Figures

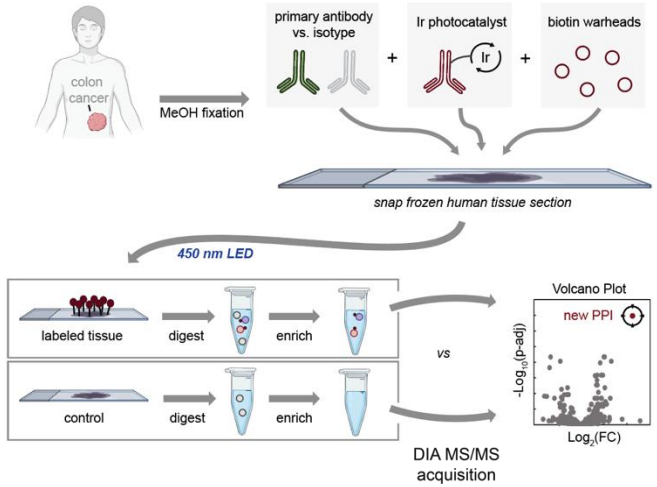

Figure 1: MAP-IT workflow for protein interaction discovery in human tissue sections.

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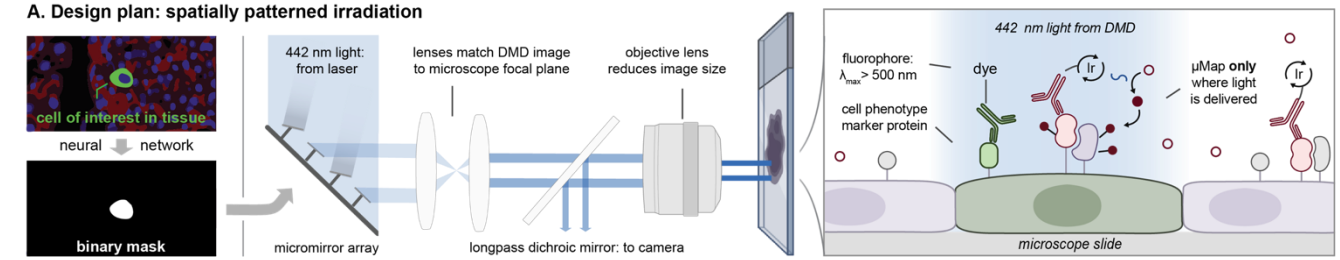

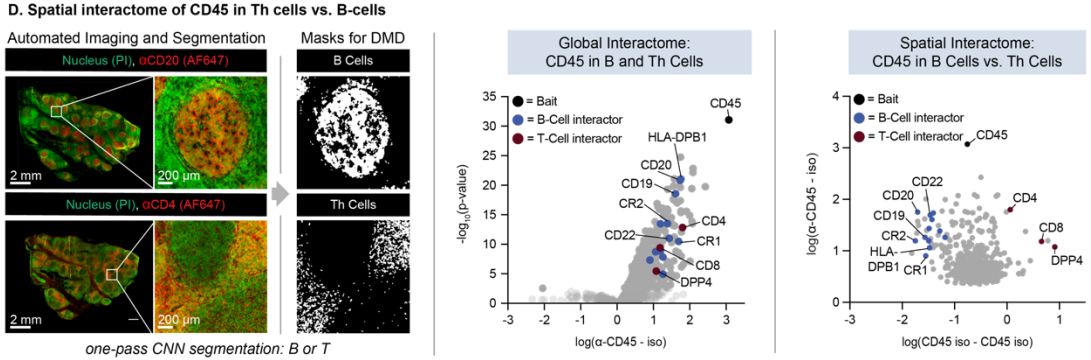

Figure 2: Top: Workflow for spatially resolved interaction discovery using neural network-guided irradiation **Bottom:** Global vs. spatial interactome for CD45 in B versus Th cells.

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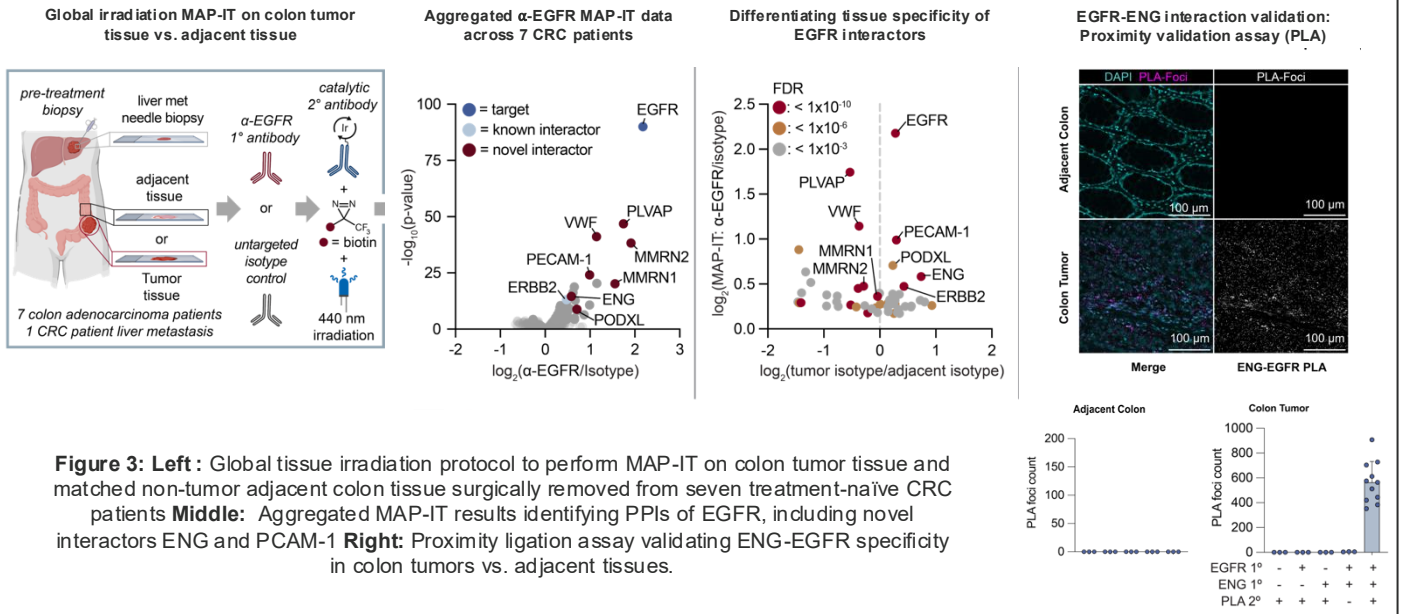

Figure 3: Left : Global tissue irradiation protocol to perform MAP-IT on colon tumor tissue and matched non-tumor adjacent colon tissue surgically removed from seven treatment-naïve CRC patients **Middle:** Aggregated MAP-IT results identifying PPIs of EGFR, including novel interactors ENG and PCAM-1 **Right:** Proximity ligation assay validating ENG-EGFR specificity in colon tumors vs. adjacent tissues.

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