TumorMapr™: Unbiased Spatial Analytics And Explainable AI (xAI) Powers Precision Pathology

Poster #454

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Abstract

Background: It is now well understood that complex spatial relationships, the emergence of intermediate cell types and states, as well as communications between cells in tissues are critical components of disease progression and must be major drivers for solutions in precision pathology [1, 2, 3].

Problem: The current computational analyses of multi to hyperplexed fluorescence and/or mass spectrometry image datasets from patient pathology samples are not powerful enough to extract the maximum amount of information or to create the detailed knowledge that is required to advance precision pathology.

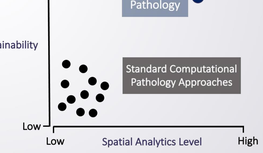
Solution: SpIntellx meets this challenge by harnessing the computational power of proprietary, unbiased spatial analytics and explainable artificial intelligence (xAI) to extract information and to create knowledge from patient primary disease pathology samples imaged on any of the existing fluorescence and/or mass spectrometry imaging platforms.

Results: In this work, we showcase results from applying TumorMapr on hyperplexed immunofluorescence dataset on colorectal cancer and hyperplexed imaging mass cytometry dataset on triple negative breast cancer discovering functional cell types (e.g., transitional cells) highly predictive of disease progression and response to therapy, and for identifying microdomain-specific network biology driving recurrence.

SpIntellx™

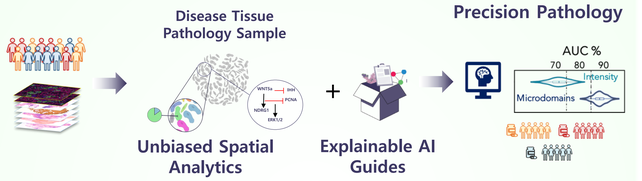
Power Precision Pathology: Going Beyond Computational Pathology by Leveraging Unbiased Spatial Analytics and Explainable AI

- **Next-generation spatial analytics** that harnesses parametric models to capture histological structures and statistical spatial relationships between all biomarkers to create unbiased analyses, not biased "spatial measurements" with deep learning
- **Truly explainable AI** that explains in pathologist's language the decisions made by algorithms, not black-box deep learning AI with biased heatmaps as explanations



TumorMapr™

An unbiased spatial analytics and explainable AI platform for creating knowledge from multi (<9 biomarkers) to hyperplexed (>9 biomarkers) fluorescence and/or mass spectrometry image datasets, from any platform.



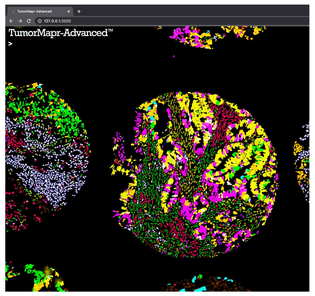
Revolutionizing Pre-Clinical and Clinical Workflows

Accelerated Drug Discovery | Optimized Clinical Trials | Advanced Companion Diagnostics | Personalized Therapeutic Options | Efficient and Accurate Clinical Workflows

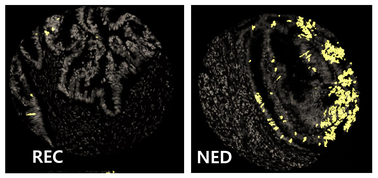
Results

Colorectal Carcinoma Study [4,5]: 213 patients, 51 Abs, immunofluorescence [6]

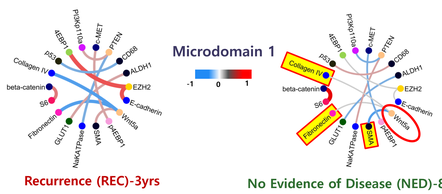
Unbiased Spatial Analytics and Automated Functional Cell Phenotyping



Transitional Cells Discovered Between FP2 & FP4

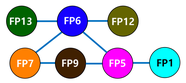


Spatial Systems Pathology Driving Recurrence



Regulatory switch driving the recurrence phenotype: sign changes in partial correlation plus co-occurrence of cell phenotypes

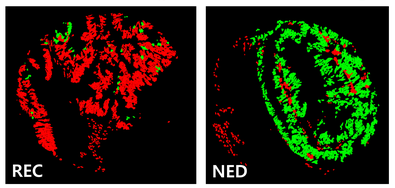
Unbiased and Automated Discovery of Microdomains Associated with CRC Recurrence



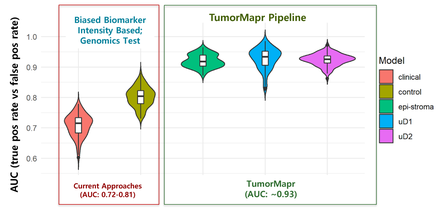
Functional Cell Phenotypes (FP)

Tumor Cell Types	FP1	FP2	FP7
Cancer Stem Cell Types	FP3	FP5	FP6
Fusion Cell Type	FP4		
Macrophage Cell Type	FP8		
Cancel Associated Fibroblast Cell Types	FP9	FP12	
Immune Cell Type	FP10	FP11	FP13

Microdomain 1: Tumor Promoting | **Microdomain 2: Tumor Restraining**



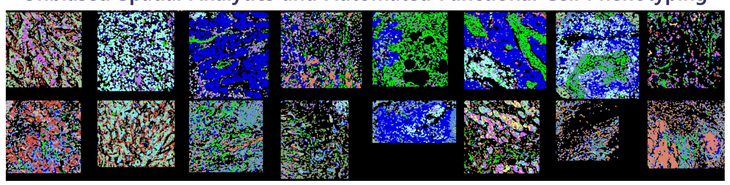
Prediction Model



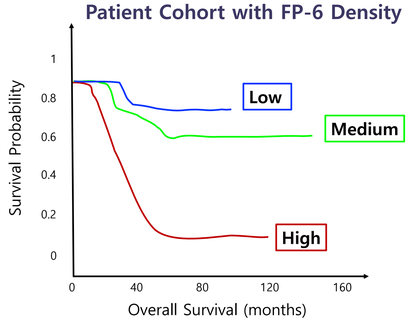
Colon Cancer Study: Prognostic Test Vastly Superior to Current Approaches in Predicting the 5-Year Risk of Recurrence in Colorectal Cancer Patients

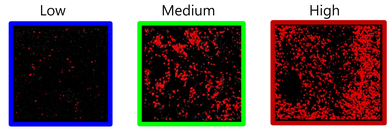
Triple Negative Breast Cancer Study: 49 patients, 34 Abs, imaging mass cytometry (IMC) [7]

Unbiased Spatial Analytics and Automated Functional Cell Phenotyping



Stratifying Triple Negative Breast Cancer Patient Cohort with FP-6 Density

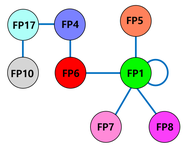




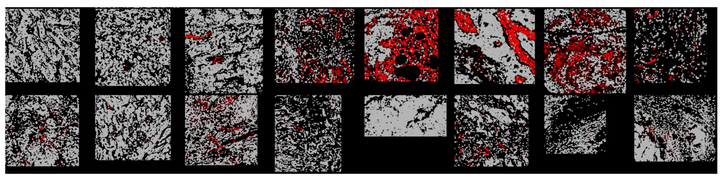
Functional Cell Phenotypes (FP)

Tumor Cell Types	FP11	FP16	FP17
	FP18	FP26	
Epithelial Cell Types	FP5	FP6	FP7
	FP8	FP9	FP10
	FP12	FP13	
Immune Cells with Tumor Characteristics	FP14	FP15	FP19
	FP2	FP3	FP4
Immune Cells Type	FP1		
Fibroblast	FP20		
Macrophages	FP21	FP24	
T-cells	FP22		
Leukocytes	FP23		
B-cells	FP25		

Unbiased and Automated Discovery of Microdomains Associated w/ Recurrence in Triple Negative Patient Cohort

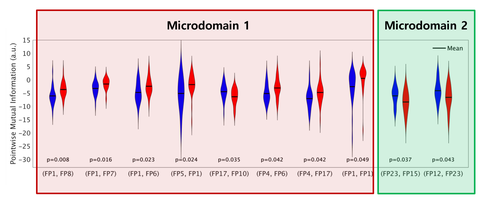


Microdomain 1: Tumor Promoting | **Microdomain 2: Tumor Restraining**



Microdomain 1: Tumor Promoting (red)

REC (top row, recurrence within 2 years); NED (bottom row, no evidence of disease in 8 years)



Discovery of ten statistically significant FP-pairs using pointwise mutual information [8] analysis

Discussion

TumorMapr Software-as-a-Service (SaaS)

- **Why Unbiased Spatial Analytics? [4,5]**
  - **Identify** functionally relevant transition cell states and fusion cell types
  - **Discover** heterogeneous microdomains associated with disease progression and outcomes
  - **Reveal** pathway interactions, signaling networks, potential molecular targets and drugs with microdomain-specific spatial systems pathology
- **Why Explainable AI? [9]**
  - **Explain** why a particular recommendation is made in a clinician understandable language
  - **Build** trust and confidence in decisions recommended by the algorithms
  - **Deliver** information and actionable knowledge with xAI guides to pathologists and disease specific clinicians who remain in full control to make the final decisions

Colorectal Carcinoma Study

- TumorMapr applied to CRC primary tumor tissue samples automatically identified 13 unbiased FP's and two corresponding recurrence-associated microdomains [4,5].
- Microdomain-specific partial correlation analysis of biomarker pairs shows a strikingly significant difference between the two patient cohorts. We find that within the evolving tumor microenvironment, the molecular signaling networks within each microdomain undergo a regulatory switch to confer a recurrence phenotype supported by cancer stem cell maintenance and immunosuppression.
- Any level of the FP hierarchy can be used for the spatial analysis of a tumor sample. We previously reported the use of the first level of this hierarchy (epithelial and stromal domains) to successfully predict the risk of 5-year recurrence in CRC with AUC 0.89 [4]. With further spatial dissection of the recurrence-associated microdomains, we improved the prognostic accuracy to an AUC 0.93 [5].

Triple Negative Breast Cancer Study

- TumorMapr applied to triple negative breast cancer tissue samples generated by IMC [7] automatically identified 26 unbiased FP's and two corresponding recurrence-associated microdomains [4,5].
- The 26 unbiased FP's have heterogenous properties, with the density of FP-6 being a prognostic indicator for stratifying triple negative patients.
- Spatial analysis of the triple negative patient cohort results in two recurrence-associated microdomains containing tumor promoting and suppressing properties.

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Acknowledgements

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- The computational and systems pathology intellectual property (US patent application 62/847,622) from this work is owned by the University of Pittsburgh and is exclusively licensed to SpIntellx Inc., Pittsburgh, PA (http://www.spintellx.com).