Hyper-plexed biomarker imaging using the MultiOmyx™ platform enables novel systems biology insights for the diagnosis and treatment of disease

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Targeted fluorescent imaging of tissue specimens provides insight into the presence, relative abundance, and location of biomarkers significant for the diagnosis and treatment of diseases. Existing methods are spectrally limited in the number of biomarkers that can be imaged on the same tissue section. Serial sections are routinely used to mitigate this limitation but that approach does not allow comprehensive profiling of individual cells, and equivalency is compromised by tissue heterogeneity. We describe a novel multi-omic, hyper-plexed tissue analysis platform, MultiOmyx, which enables the simultaneous analysis of ~60 protein and nucleic acid biomarkers at the subcellular level in intact tissue sections.

The information produced by MultiOmyx, combined with sophisticated analytics algorithms, enables new systems biology analyses and insights. Proprietary algorithms have been developed to segment the images hierarchically at the level of tissue regions, individual cells, and sub-cellular organelles, and to register expression profiles. Relative biomarker abundance is quantified within each of these levels to provide a comprehensive dataset of biomarker profiles in a hierarchical spatial context within intact tissues. Comprehensive biomolecular expression and spatial features profiled across subjects, tissues, histological regions, cells, and sub-cellular compartments open up new opportunities in big-data systems biology research.

Novel image and data visualization tools enable interpretation of hierarchical spatial profile information that may not be apparent from numerical datasets. We have developed a visual analysis software tool called Layers™ that enables images to be queried and viewed with annotations based on biomarkers, tissue regions, or cells fitting combinatorial criteria. As a relatively simple example, immune cell infiltration into a tumor can easily be viewed by color coding the biomarkers that correspond to immune cell phenotypes. (Fig. 1.) For analyses where more general combinations of biomarkers must be considered, cells having a specified biomarker profile can be identified using software tools that resemble those used in flow cytometry but can be viewed and analyzed in the intact tissue context. Additionally, cells can be clustered using multiple included clustering techniques and visualized in “cell families” having similar molecular and morphological phenotypes to aid profile interpretation and hypothesis generation.

Combining pathway information with the spatial analysis of protein and nucleic acid biomarker profiles further enables deep pathway-oriented insights. We have prototyped a Cytoscape plugin which integrates protein and nucleic acid data pertaining to the different –omic technologies, including NGS and MultiOmyx, with specific cancer pathway information. (Fig. 2) Integrating measurements from MultiOmyx and other -omic techniques can bridge the shortcomings of uni-modal data, generating integrative, novel systems biology insights.

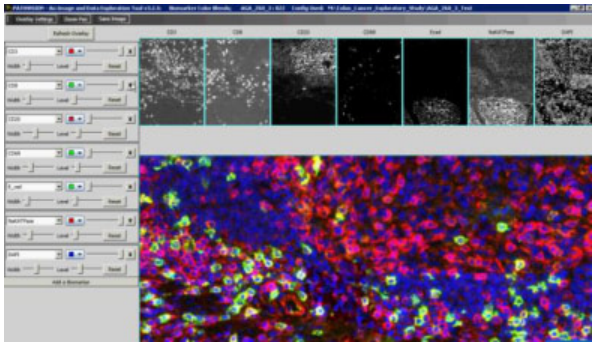

Fig. 1. Tumor infiltration visualized with T cells in red, B cells in yellow.

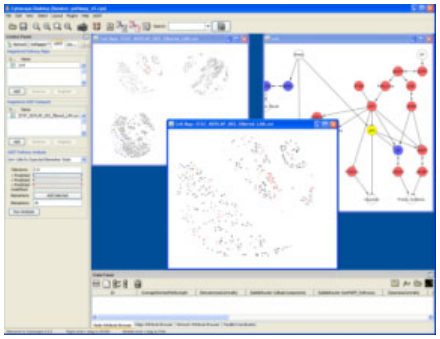

Fig. 2. Plug-in to Cytoscape to visualize MultiOmyx data in a pathway context.