

#501 A complete pipeline for high-plex spatial proteomic profiling and analysis of neural cell phenotypes on a Spatial Molecular Imager and a Spatial Informatics Platform.

Michael Rhodes^{*1}, Shiloh A Bonnett¹, Alyssa Rosenbloom¹, Mark Conner¹, Tiên Phan-Everson¹, Zachary Lewis¹, Giang Ong¹, Yan Liang¹, Emily Brown¹, Liuliu Pan¹, Aster Wardhani¹, Mithra Korukonda¹, Carl Brown¹, Dwayne Dunaway¹, Edward Zhao¹, Dan McGuire¹, Sangsoo Woo¹, Brian Filanoski¹, Rhonda Meredith¹, Kan Chantranuvatana¹, Brian Birditt¹, Hye Son Yi¹, Erin Piazza¹, Jason Reeves¹, John Lyssand¹, Vikram Devgan¹, Gary Geiss¹, Joseph M Beechem¹

¹NanoString® Technologies, Seattle, Washington, USA

Abstract

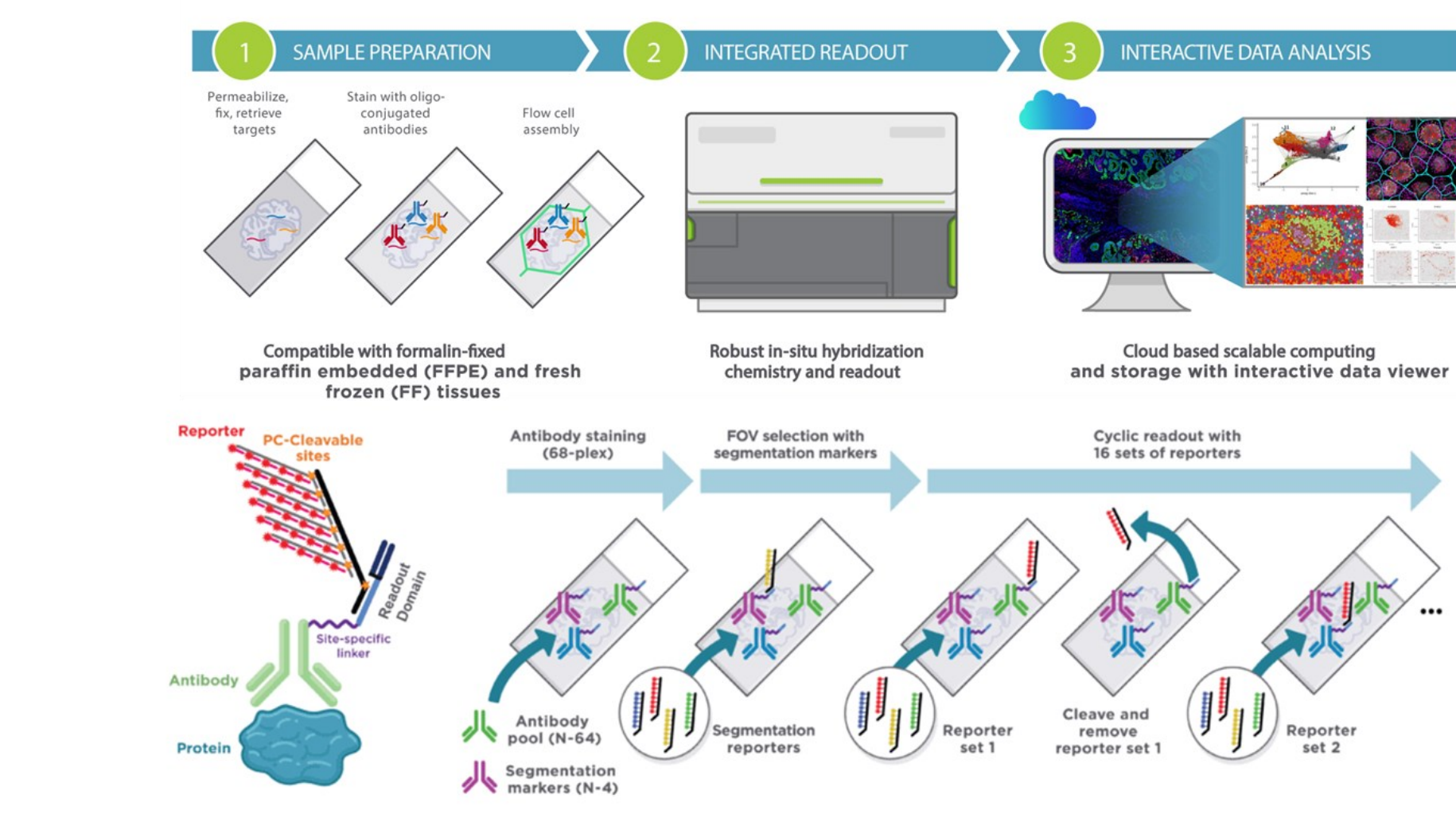
The brain is complex and heterogeneous where cell function and cell-to-cell communication are critical for rapid and accurate performance. The ability to explore protein-driven activities at high resolution within the spatial context of their immediate environment is critical to gain comprehensive pictures of brain development, activity, aging, disease or dysfunction, and inflammatory responses. Many existing approaches for high-plex single-cell spatial proteomics face issues around simplicity, speed, scalability, and big data analysis.

Here, we present an integrated workflow that addresses key concerns around high-plex proteomics. The CosMx™ Spatial Molecular Imager (SMI) and AtoMx™ Spatial Informatics Platform comprise an end-to-end workflow that efficiently handles highly multiplex protein analysis at plex sizes exceeding 68 targets. The CosMx protein assays use oligonucleotide-conjugated antibodies, that are detected using universal, multi-analyte CosMx readout reagents. The CosMx Mouse Neural Cell Typing and Alzheimer's Pathology panel is optimized to comprehensively profile neural cell lineages across the brain as well as the progression of Alzheimer's disease (AD). Furthermore, 80% of the antibodies making up both panels are cross-reactive with human tissue antigens. The AtoMx spatial informatics platform provides full analysis support, including whole-slide image viewer, and methods for performing built-in or fully customizable analyses for cell typing, ligand-receptor analysis, neighborhood analysis and spatial differential expression.

The CosMx protein assay reagents were validated on the FFPE adult mouse brain, mouse embryo, and Alzheimer's positive human brain. We used the CosMx Mouse Neural Cell Typing and Alzheimer's Pathology panel with the CosMx SMI to identify multiple neuronal subtypes, different reactive states of astrocytes and microglia, cell degeneration and proliferation. In a single-cell exploration of mitochondria, we noted distinct patterning of key immune targets based on their immediate microenvironment. Additionally, evaluated the co-expression patterns and activation states of microglia within 200 μm from the amyloid plaque and tau tangles.

The CosMx SMI is a high-plex spatial multi-omics platform that enables the detection of > 68 proteins at subcellular resolution. In combination with the high-plex CosMx Mouse Neural Cell Typing and Alzheimer's Pathology panel, we present a flexible and scalable informatics platform, a robust solution for comprehensive neural and disease phenotyping that captures the complexity of neuronal and glial cellular activity with full spatial context.

CosMx Spatial Molecular Imager (SMI) and AtoMx Spatial Informatics Platform



CosMx Mouse Neuroscience Protein Panel (64-Plex) Content

