Integrated omics of the cancer microenvironment

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Abstract
Proteomics technologies and bioinformatics have matured to the point that quantification of proteins from cancer biospecimens is routine. The resulting ability to correlate protein expression patterns with genomics information forms the basis of the proteogenomics initiative. However, proteomics workflows apply only to unmodified peptides and those with phosphorylation or other small, predictable post-translational modifications. The availability of signaling molecules to cancer cell surfaces depends on the glycosylation structure of the surrounding extracellular matrix (ECM). The molecular structures of molecules in the ECM also control mechanical stimulus of cancer cells. Glycosylation of ECM molecules is heterogeneous and escapes characterizing using standard proteomics bioinformatics workflows. To characterize site specific glycosylation requires customized analytical and bioinformatics workflows.

We analyzed expression of glycosaminoglycans (heparan sulfate and chondroitin sulfate), proteins and glycoproteins from two human glioblastoma biospecimen cohorts. These results demonstrate that site specific glycosylation distinguishes glioblastoma (GBM) subtypes and reflect underlying disease mechanisms. This demonstrates feasibility of using site specific glycosylation to understand cancer mechanisms and tumor heterogeneity.

Biography

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Dr. Joseph Zaia, Ph. D. is a Professor in the Dept. of Biochemistry, Cell Biology and Genomics and Associate Director of the Center for Biomedical Mass Spectrometry (CBMS) on the Boston University Medical Campus (www.bumc.bu.edu/BUCBM). His primary research interest concerns structural biochemistry of proteoglycans and glycoproteins. He has extensive experience with methods for compositional analysis of glycosaminoglycan (GAG) oligosaccharides using liquid chromatography-mass spectrometry and sequencing using tandem mass spectrometry. His group has pioneered methods for analysis of GAGs from
cultured cells, wet tissue, and histological slides from vertebrate and invertebrate sources. He has used these methods to study tissue-specific patterns of expression of heparan sulfate, activity of extracellular Sulf enzymes and mammalian heparanase. He has also developed bioinformatics software for interpretation glycan and glycopeptide liquid chromatography-mass spectrometry data.

Dr. Zaia collaborates widely with investigators regarding roles of proteoglycan and glycoprotein expression in human diseases. He organized an American Society for Mass Spectrometry tutorial on glycomics and glycoproteomics and participates regularly in short courses on these topics at international conferences. He organized an Association of Biomolecular Resource Facilities interlaboratory study on protein glycosylation and is a member of the Minimum Information Required for a Glycomics Experiment working group.

Selected publications: