Highly multiplexed, multiomic and multimodal tissue imaging using novel photocleavable mass-tags

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While the advent of mass spectrometric imaging (MSI) has extended the metabolomic/proteomic capabilities of mass spectrometry to the spatial dimension, it is generally limited to untargeted analysis of small molecules and proteolytic protein fragments. We have developed a novel spatialomic approach based on photocleavable mass-tags (PC-MTs) for facile labeling of probes including antibodies, lectins and nucleic acids which enables highly multiplexed MSI of targeted macromolecules in tissues. This approach, termed MSI-IHC, significantly exceeds the multiplexity of both fluorescence and previous cleavable mass-tag based methods. In addition, when combined with direct label-free MSI of small biomolecules, it provides an integrated workflow to study the spatial distribution and interaction of small molecules and larger macromolecules in a single tissue specimen. High-plex MSI-IHC has been achieved on brain, tonsil and cancer tissues using a variety of probe classes, reflecting the known molecular composition, anatomy and pathology of the targeted biomarkers. Novel dual-labeled fluorescent-PC-MT-probes extend the utility of this new approach to multimodal imaging. Overall, MSI-IHC holds significant promise for use in the fields of tissue pathology, tissue diagnostics, therapeutics and precision medicine as well as in R&D aimed at understanding the mechanisms of human disease.

Biography:

Dr. Mark Lim (Ph.D.) is the Executive Vice President and Chief Scientific Officer at AmberGen Inc. He has over 20 years' experience in the biotechnology industry and has been awarded over 15 patents which underlie key technologies in the biotechnology industry, including in the fields of proteomics, genomics/transcriptomics and diagnostics. His early work on photocleavable linkers and protein engineering contributed to the commercialization of a variety of novel reagents including PC-Biotin, PC-Phosphoramidites and fluorescent suppressor tRNAs. These reagents currently underlie several novel commercial techniques widely used in the proteomics/transcriptomics fields. Dr. Lim now leads AmberGen's mass spectrometric-based tissue imaging and blood-based biomarker detection and diagnostics projects. He is co-inventor of AmberGen's PC-PURE technology for photo-affinity biomarker

enrichment which facilitates enhanced diagnostics as well as AmberGen's photocleavable bead mass spectrometry technology for multiplex biomarker detection. Dr. Lim has successfully developed novel blood-based immunodiagnostics for cancer and allergy. He also spearheaded an R&D effort which led to the discovery of two novel autoantigen biomarkers for the autoimmune liver disease primary biliary cirrhosis, with the diagnostic assays currently undergoing FDA-clearance and CE Mark. Most recently, he led the development of a novel method for tissue diagnostics and spatialomics which is based on mass spectrometry imaging of whole proteins using photocleavable mass-tags [Yagnik, Liu et al. (2021) J Am Soc Mass Spectrom 32(4): 977-988, https://pubs.acs.org/doi/10.1021/jasms.0c00473].