SELECTED TALK:

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Precision labeling and photo-crosslinking of glycoconjugates through cell-surface glyco-engineering

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Glycans and glycoconjugates mediate vital biological processes such as cell growth, differentiation, and immune recognition through selective interaction with glycan-binding proteins. Dysregulation of glycan-mediated signaling is implicated in disease states including cancer, inflammation, and pathogen infection. However, detecting these native interactions is very challenging with current methods. The biosynthesis of glycans is not template driven, meaning that their structures are not specifically encoded in the genome. As a result, traditional gene knockout or overexpression approaches are not ideal for studying specific glycan structures and their interactions. Moreover, monovalent glycan-protein interactions are typically short-lived and have low affinities, making it difficult to capture and isolate interacting partners. A multivalent display ideally within the context of cell surfaces is thus necessary to study relevant glycan/protein binding. Recognition of glycan ligands can also be dependent on interactions with terminal sugar epitopes, glycan subclass-specific presentation, and conjugation to specific protein or lipid anchors. Thus, despite their importance, the specific glycoconjugates involved in these critical biological processes are largely unknown and consequently there is a need for novel tools to discover and probe these interactions.

Introduction of photo-crosslinking groups into cellular glycans provides an attractive strategy to capture, isolate and analyze native binding partners involved in glycan-protein interaction complexes. Herein, we present a precision labeling and photo-crosslinking approach through cell-surface glyco-engineering using a photo-crosslinking CMP-Neu5Ac (CMP-sialic acid) derivative by exogenous enzymatic transfer. Our toolset harnesses the inherent specificity of various sialyltransferases to install sugar probes with high linkage and class specificity on to native glycans on live cells. These crosslinking probes are then used to interrogate sialic acid-based interactions between glycoconjugates and important receptors such as Siglecs, which are involved in modulation of the immune system and are heavily implicated in cancer, infectious disease, and neurobiology. This presentation will discuss the utility of this strategy for the discovery and analysis of glycan-protein interactions and as an exciting tool to improve our fundamental understanding how these interactions play a role in human health and disease.