Fluorogenic capture of glycan-lectin interactions

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Abstract
Glycosciences are transforming our understanding of living organisms, and technological innovation in chemical glycobiology is often a stepping stone toward novel therapeutic interventions. Within glycosciences, shortcomings of traditional biochemical techniques have driven the development of sophisticated chemical strategies to quantify glycan-processing enzymes or to decipher sugar recognition in increasingly complex environments. Non-covalent glycan recognition by glycan-binding proteins (lectins) is ubiquitous across all kingdoms of life, but capturing and studying these interactions is notoriously challenging due to low intrinsic affinities and multivalency effects. Photo-crosslinking strategies are often implemented in chemical probes, metabolic reporters or exo-enzymatic labeling, yet the direct visualization of cross-linked species remains problematic. Our group designed photoactive dyes based on aryl azides with extended conjugation and aromatic fluorination that remain nonfluorescent until reactive nitrene intermediates covalently trap glycan-binding proteins, thereby appending a permanent fluorescent tag to the lectin target. This strategy works in complex environments and can be applied to lectins of various specificities.

In this talk, I will introduce strategies developed in our lab toward fluorogenic capture of sugar-protein interactions and the further development of trifunctional scaffolds that present any glycan (mono- to oligosaccharides), include our fluorogenic photocrosslinker, and can be conjugated to biotin tags or multivalent carriers. Because these approaches unlock new ways to map glycan–protein recognition events, I will also present our efforts toward expanding the color palette of fluorogenic photocrosslinking for capturing sugar-protein binding events at the cell surface. Looking ahead, this approach could be integrated with metabolic reporting and exo-enzymatic labeling while also offering unique features that could enable spatiotemporal mapping of glycan-protein interactions on live membranes. This capability could help illuminate the dynamics of recognition at the cell surface.