

Taming complex protein glycoconjugate functions with chemical biology

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Abstract:

Protein glycoconjugates, protein products modified with glycan post-translational modifications, are often considered untamable biomolecules. A single protein glycoconjugate can exist as a mixture of heterogeneous unique protein glycoforms in living cells, resulting in innumerable possible interactions with glycan-binding proteins. These individual interactions can play diverse roles in orchestrating physiology and disease. However, current approaches to describe protein glycoconjugates and their interactions are limited, restraining our understanding of the consequent important and often critical functions they play. Using interdisciplinary approaches rooted in chemical biology and high-resolution mass spectrometry, I will outline our efforts to dismantle the complexity of protein glycoconjugates. These endeavors include the fabrication of defined proteoglycans to control cancer cell adhesion on matrices and the elucidation of the proteome-wide interactions of glycan-binding proteins and glycoproteins, as well as the development of synthetic small molecules that differentially engage various protein glycoforms.