Function and Fate of Cellular Carbohydrates

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Carbohydrates are involved in a myriad of cellular functions. In the form of glycoconjugates they modulate activity and physicochemical properties of proteins and lipids, and they are themselves involved in molecular recognitions processes. However, our understanding of the underlying mechanisms is just at the beginning and methods for their elucidation need further development. Challenges in current glycobiology include the elucidation of the mechanisms of multivalent carbohydrate-protein interactions and the development of tools to monitor glycan structures in cells and organisms. This lecture gives an overview of our group's activities in these fields. To unravel the molecular details of carbohydrate-protein interactions we employed X-ray crystallography and, more recently, distance measurements in the nanometer range by EPR spectroscopy using spin-labeled carbohydrates. In contrast to proteins, that are routinely labeled by genetic methods, such as expression as GFP fusion proteins, comparable methods are not available for glycans. We employed metabolic oligosaccharide engineering for monitoring glycans in different cell lines as well as in zebrafish. To increase the repertoire of existing bioorthogonal ligation reaction, we developed a new ligation method based on a Diels-Alder reaction with inverse-electron-demand of electron deficient 1,2,4,5-tetrazines and terminal alkenes. Since this reaction is orthogonal to the azide-alkyne cycloaddition (click reaction), detection of two different sugars (one alkene-labeled the other azide-labeled) is possible within one experiment.