

## NEXT-GENERATION CHEMICAL TOOLS FOR IMPROVED GLYCOPROTEIN ANALYSIS

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Glycoproteins are involved in all essential cellular processes ranging from intercellular communication to pathogen recognition and immune modulation. Aberrant glycosylation has been recognized as a hallmark of many diseases including cancer, neurodegenerative, or metabolic diseases. However, the glycobiology underlying the pathology in these diseases is fragmented at best. In particular, a correlation between altered glycan structures and resulting consequences for protein function are mostly missing. The structural complexity and heterogeneity of glycans complicates a detailed analysis with currently available methods.

Our research applies chemical biology to elucidate how aberrant glycosylation can modulate the structure and function of proteins and thereby contribute to the pathogenesis of certain diseases. To this end, we develop new chemical tools and apply novel concepts for improved glycoprotein analysis. This includes the synthesis of various next-generation chemical probes. Using established concepts of solid phase synthesis, we customize complex multi-functional probes that carry bioorthogonal handles, such as azides, alkynes or tetrazines for covalent attachment to chemically engineered glycoproteins. These probes allow efficient enrichment, isolation and multi-modal analysis of glycoproteins in multiple coordinated experiments. We apply these tools in state-of-the-art technologies, such as live cell imaging and intact chemical glycoproteomics to decipher aberrant protein glycosylation in a class of rare genetic glycosylation defects; so-called Congenital Disorders of Glycosylation as well as in some types of malignant cancers.

Other probes are equipped with diazo groups or sulfated and phosphorylated glyco-oligomers and can be used to study glycan-mediated pathogen infections. Our main focus is to contribute to a better understanding of the role that glycans play in disease development as a basis for designing suitable diagnostic and therapeutic concepts.