Biomedically Functional Sugars: Transforming Glycan-Based Drug Design Through Streamlined Methods and Novel Metabolic Glycan Tracking

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Complex sugars known as Glycosaminoglycans (GAGs) play a vital role in nearly all biological processes, from wound healing to the progression of diseases such as cancer and Alzheimer's. They are among the most complex, least understood, and most important biological macromolecules in all mammals. Despite the immense therapeutic potential of GAGs, their sheer complexity and related synthetic difficulties have greatly hindered their role in medicinal applications. Additionally, the absence of methods to study the spatial and temporal distribution of GAGs and recapturing their structures from in vivo significantly hampers our understanding of the mechanisms underlying glycan-based drug actions. I present my development of several new methodologies within synthetic glycan chemistry and glycomics that have addressed the previously mentioned limitations. Subsequently, a new set of synthetic glycan-based molecules that better mimic endogenous proteoglycans were developed and evaluated in vivo. Fibroblast growth factor(FGF) signaling drives cell proliferation, differentiation, angiogenesis, and development. The accumulation of this work led me to discover a new set of glycan-based molecules that modify FGF signaling, tested in vivo through Zebrafish embryonic development and ex vivo organ cultures. On top of this, the mechanisms of action of these new molecules are now able to be metabolically tracked. My work has addressed many of the shortcomings related to glycomics and glycan-based drug design. My innovations reshape glycomics, not only through synthetic glycan chemistry by proving new methods, notably one that accelerates glycosylation by over 1000x, but also glycan-based approaches for developing new, more effective disease treatments.

Awards Won: