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Grant Title: Synthesis of heparan sulfate saccharides and their interaction with chemokines

Abstract

Heparan sulfate is an irregularly sulfonated polysaccharide that influences the activity of various proteins in the cell–extracellular interface. Acquiring well-defined compounds that reflects upon the complex structure of heparan sulfate is a huge challenge, but is a necessary requirement of structure–activity relationship studies. As a consequence, the optimal structures in heparan sulfate sought by numerous important proteins, such as cytokines, remain unknown. To improve our collective understanding about the role of heparan sulfate in chemokine function, we targeted the preparation of a heparan sulfate library and the evaluation of their interaction with a subset of chemokines. We achieved this by the modular assembly of linker-attached tetrasaccharide and hexasaccharides with only two orthogonally protected disaccharide building blocks. The desired diversity in the sugar was accomplished through divergent transformations. Thus, a reasonably sized heparan sulfate oligosaccharide library was assembled. Preliminary evaluations with chemokines by surface plasmon resonance assay showed length-dependence in affinity. The important fine details of the interaction are expected to be revealed in the near future.

