Using synthetic oligosaccharides to accelerate the investigation of heparan sulfate biology

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Heparan sulfate is a sulfated polysaccharide that participates in a wide range of physiological and pathophysiological functions. A central issue in the investigation of the biology of heparan sulfate is to determine the contribution of specific sulfate saccharide sequences to the functions. Our laboratory has developed a chemoenzymatic method to synthesize homogeneous oligosaccharides.

The method has been shown for its ability of preparing structurally complex oligosaccharides in gram quantities, providing a new technology for the development of heparan sulfate-based therapeutics. In addition, we use this synthetic approach to prepare ^{13}C-labeled disaccharide and oligosaccharide calibrants to improve the LC-MS/MS-based analysis of heparan sulfate isolated from biological sources. The inclusion of ^{13}C-labeled calibrants permits the quantitation of heparan sulfate. In the presentation, I will discuss how to exploit the anti-inflammatory activity of a synthetic 18-mer (octadeca-saccharide) in mouse models:

1) protecting against acute liver injury caused by drug overdose;

2) preventing organ damage from sepsis.

I will also show an example to connect 3-O-sulfated heparan sulfate, and Alzheimer's disease. The findings offer new lines of evidence for justifying the efforts for developing heparan sulfate-based therapeutics.