Characterization of Specific Cell-Surface Heparan Sulfate-Protein Interactions

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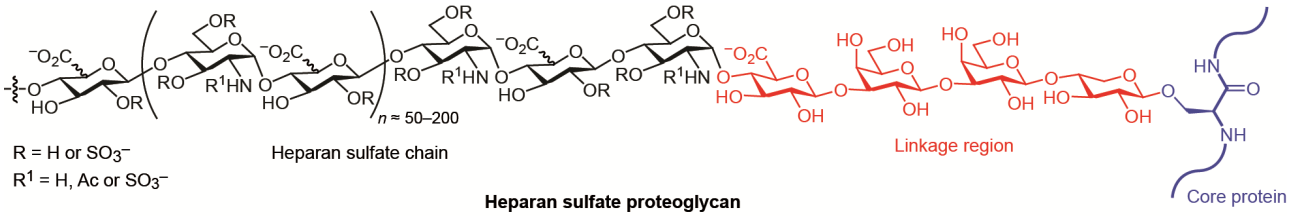
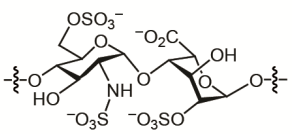
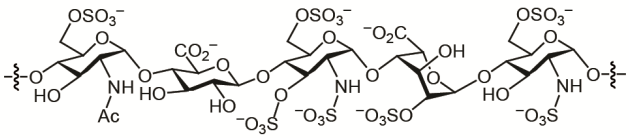
Heparan sulfate (HS) is a linear polysaccharide that is widely distributed on the cell surface, where it exists as proteoglycan component. The HS chain is initially assembled as a simple 1→4-linked copolymer of *N*-acetyl-α-D-glucosamine and β-D-glucuronic acid (GlcA), but the seemingly regulated but non-template driven modifications cause extensive microheterogeneity along the sugar backbone comprised of around 50 to 200 disaccharide units. These modifications, which include *N*-deacetylation, *N*-sulfonation, GlcA 5-C epimerization forming α-L-iduronic acid, and multiple *O*-sulfonations, are implemented by several enzyme isoforms of varying specificities and are always incomplete, accounting to theoretically 48 disaccharide variations. The myriad of functional group patterns decorating the sugar backbone allowed HS to encode a high density of structural information. Such array of modifications is responsible for mediating or modulating protein activity. Keen interests are focused in deciphering the molecular level details of the HS–protein interactions because they may present therapeutic opportunities. Here, chemical synthesis of HS oligosaccharides in conducting structure–activity relationship studies will be presented.



Heparan sulfate proteoglycan



Major repeating unit of heparin



Antithrombin-binding sequence