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Abstract:

Our previous studies showed: (i) that growth arrested G0/G1 rat mesangial cells (RMCs) stimulated to divide in hyperglycemic medium initiate intracellular hyaluronan synthesis that induces autophagy and cyclin D3-induced formation of a monocyte-adhesive extracellular hyaluronan matrix after completing cell division; and (ii) that heparin inhibits the intracellular hyaluronan and autophagy responses, but after completing division, induces hyaluronan synthesis at the plasma membrane with formation of a larger monocyte-adhesive hyaluronan matrix. This study shows: (i) that the non-terminal trisaccharide of heparin is sufficient to initiate the same responses as intact heparin, (ii) that a fully sulfated tetrasaccharide isolated from bacterial heparin lyase 1 digests of heparin that contains a Δ-2S-iduronate on the non-reducing end does not, and (ii) that removal of the Δ-2S-iduronate to expose the fully sulfated trisaccharide (GlcNS(6S)-IdoUA(2S)-GlcNS(6S)) does. These results provide evidence that mammalian heparanase digestion of heparin and heparan sulfate exposes a cryptic motif on the non-reducing termini that is recognized by a receptor on dividing cells