

- P016** The specificity of glycosaminoglycan interactions with hepatocyte growth factor / scatter factor (HGF/SF)
Krista R. Catlow¹, Jon A. Deakin¹, Mauro S. G. Pavão², Maryse Delehedde³, David G. Fernig³, Ermanno Gherardi⁴, John T. Gallagher¹ and Malcolm Lyon¹
¹*Cancer Research UK Department of Medical Oncology, University of Manchester, Christie Hospital, Manchester, UK.*
²*Universidade Federal do Rio de Janeiro, Rio de Janeiro, Brazil.*
³*School of Biological Sciences, University of Liverpool, Liverpool, UK.*
⁴*MRC Centre, Cambridge, UK*

We previously showed that HGF/SF binds with high affinity to both heparan sulphate (HS) and dermatan sulphate (DS). They are essential co-receptors for HGF/SF, probably through facilitating the formation of ternary signalling complexes with the Met receptor. The minimal effective oligosaccharide is a tetrasaccharide for HS/heparin, but a hexasaccharide for DS. The similar activities of HS and DS are surprising, considering their different positions and degrees of sulphation. We attempted to further elucidate the specificity of GAG recognition by investigating the binding and activation properties of (i) a range of HS/heparin species, both polymeric and minimal-size tetrasaccharides, which have been desulphated at specific positions, and (ii) some natural CS/DS structures possessing relatively unusual positions of sulphation. Our results confirm that HGF/SF demonstrates considerable flexibility in its GAG recognition, but that O-sulphation of hexosamine is the most critical sulphation required, and may be sufficient in the case of hexasaccharides, though additional sulphation is required for tetrasaccharides to bind.