

P002 Design, synthesis and biological evaluation of small molecule heparin / heparan sulphate (H/HS) analogues as GAG-protein interactions inhibitors

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Cancer growth involves the proliferation and invasion of cancer cells, the stimulation of tumour angiogenesis, and the metastasis of tumour cells through the vasculature. Key factors in these cellular activities are growth factors such as HGF/SF (hepatocyte growth factor / scatter factor) and FGFs (fibroblast growth factors). These signalling events involve the binding of the growth factor to their receptor, a transmembrane tyrosine kinase. This binding can only take place in the presence of heparin/ heparan sulphate (H/HS). Given the potential significance of therapies based on control of glycosaminoglycane (GAG)-protein interactions, the development of structurally simpler mimics is an attractive area for investigation. Based on previous studies of bioactive heparin fragments, we designed and synthesized a series of small, non-sugar, aromatic molecules as possible mimics of H/ HS, but intended to bind to the growth factor without promoting receptor activation and downstream signalling. Here we present the design and synthesis of these compounds and the interesting discoveries we have made by evaluating their biological properties against HGF/SF and FGF-2.