TOWARDS THE SEMI-SYNTHESIS OF PHOSPHORYLATED GLYCOSAMINOGLYCANS

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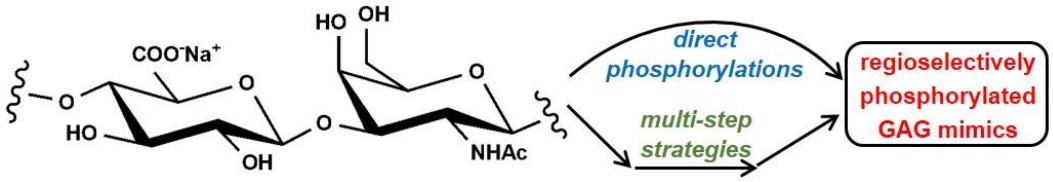
Glycosaminoglycans (GAGs) are highly negatively charged polysaccharides found in both vertebrates and invertebrates. They are typically composed of disaccharide repeating units, that are very often extensively decorated with sulfate groups. GAG sulfation is a dynamic, complex post-translational modification process that seems to be a result of evolution in order to let sulfated GAGs play key roles in many physiological and pathological processes in animals [1].
In the frame of developing artificial GAG mimics [2], an interesting topic concerns phosphorylated GAGs. Indeed, phosphate *vs.* sulfate differences in size, polarity, acid-base and chelation properties could lend unreported activities to phosphorylated GAGs, as indicated by an *in silico* study comparing the structural flexibility and intra- and intermolecular interaction patterns of native GAGs with their phosphorylated counterparts [3]. Actually, this theoretical investigation suggested that phosphorylated GAGs could bind proteins generally with a stronger affinity than their sulfated counterparts and the differences in the binding modes might be highly protein target-dependent. This would propose phosphorylated GAGs as promising, new species to specifically control biochemical processes where the mediating role of sulfated GAGs is crucial. Nonetheless, the preparation of phosphorylated GAGs is still rather underdeveloped [3-5]. In this communication we present the results of a screening of either multi-step strategies or direct phosphorylation methods – relying upon both standard and innovative phosphorylation reactions – applied on unsulfated GAG-like polysaccharides from microbial sources [6].



The final aim is to open a general, semi-synthetic access to phosphorylated GAG mimics, overcoming the several concerns regarding the phosphorylation of polysaccharides, *i.e.* harsh reaction conditions, poor yields and degree of phosphorylation, no regiochemistry control [7].

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