REGIO- AND STEREOSELECTIVE SYNTHESIS OF THE BIOTIN-CONJUGATED KERATAN SULFATE OLIGOSACCHARIDE

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Keratan sulfate (KS), an acidic linear polysaccharide, is one of the members of glycosaminoglycan (GAG). KS is composed of repeating disaccharide, -4)βGlcNAc(1-3)βGal(1- having different sulfation patterns at the primary hydroxyl groups. L4 is one of the subclasses of KS, sulfated at all primary hydroxyl groups. Together with other GAG members, KS also acts as hydrating role in cornea and cartilage tissues, and exhibits various bioactivities. Imagama et al. demonstrated the inhibitory effect of KS towards axonal growth. Although the sulfation patterns were unclear, they suggested the glycan length might be 6-8 saccharide stretch [1]. KS oligosaccharides with defined structure including sulfated positions can be a powerful tool to investigate the role of KS at a molecular level. We herein report the effective synthesis of KS L4 oligosaccharide as biotin-conjugate. The target oligosaccharide was attributed to form the glycan-backbone without protection at some hydroxyl groups during the 2+2n glycosylation procedures. We employed the unprotected glycosyl acceptors at 2,3,4- and 2,4-positions of galactose (Gal) residues at the non-reducing terminal and the inside residues, respectively, for the coupling reaction. *O*-3 of the non-reducing terminal predominantly reacted to give the desired 1-3-linkage. The primary hydroxyl groups of Gal and *N*-acetylglucosamine (GlcNAc) moieties were regiospecifically protected with orthogonally removable NAP (2-naphthylmethyl) and TBDPS (*tert*-butyldiphenylsilyl) groups, respectively. Formation of all type of sulfation patterns may be available with the versatile protection. In addition, our oligosaccharide was formed as 2-aminoethyl glycoside. The short linker made it possible to connect the appropriate functional group. Complete sulfation and the subsequent deprotection were performed for the oligosaccharide substrates to form the biotinylated KS-L4 oligosaccharide (Fig. 1).

Figure 1.

Reference:

1. S. Imanaga *et al*, *J. Neurosci.*, **2011**, *31, 17091*-17102.