Synthesis of the matriglycan, -3Xylα1-3GlcAβ1- oligomer and its interaction with laminin

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Matriglycan, a polysaccharide that is fundamental as a part of core M3 *O*-mannosyl glycan (OMG) composed of the repeating disaccharide -3Xylα1-3GlcAβ1-, interacts with laminin to stabilize muscle tissue (Fig. 1) [1]. Defects in the genes encoding processing enzymes associated with the formation of the core M3 OMG cause a form of muscular dystrophy. For example, FKTN, one of the processing enzymes to form OMG is inactive in patients of fukuyama congenital muscular dystrophy. Supply of the synthesized matriglycan from outside of the tissue may improve the conditions of muscular dystrophy. Recently, Boons and his co-workers reported the chemo-enzymatic synthesis of the matriglycan oligosaccharides [2]. We herein report the chemical synthesis of matriglycan-repeating oligosaccharides equipped with an alkyne linker to form glycoconjugates [3]. The key step in the formation of an α-linked xylosyl glycoside was resolved by solvent-specific separation from an anomeric mixture. Successful glycan elongation was regio- and stereoselectively executed to obtain $(\text{-3Xyl}\alpha\text{1-3GlcA}\beta\text{1})_n\text{-O}(C_2H_4O)_3CH_2C{\equiv}CH$ and the biotin conjugate. We investigated interactions between matriglycan oligosaccharides and laminin-G-like domains 4 and 5 of laminin-α2 using saturation transfer difference-NMR. The dissociation constant obtained from bio-layer interferometry was estimated to be 7.5×10^{-8} M in case of hexasaccharide. We also modified the matriglycan-conjugate to effectively interact with laminin. These results indicate that a chemical approach may be applied to the reconstruction of muscle tissue.

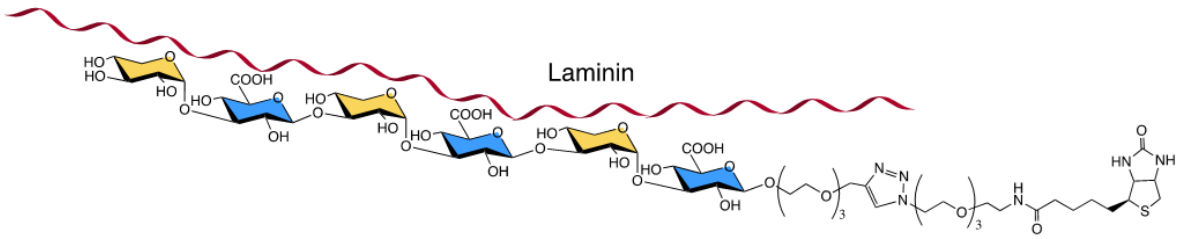

Fig. 1. Biotin-conjugated matriglycan hexasaccharide which interacts with laminin

Bibliographic references:

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