Biosynthetic Mechanism and Functions of Glycosaminoglycans in *Caenorhabditis elegans*

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Glycosaminoglycans (GAGs) such as heparan sulfate (HS) and chondroitin sulfate (CS) have been implicated in numerous pathophysiological phenomena of vertebrates and invertebrates. The biosynthesis of GAGs is initiated by the addition of Xyl to specific serine residues in the core protein, followed by the sequential addition of two Gal residues and a GlcA residue, forming the tetrasaccharide linkage structure. Then, HS polymerization with alternating GlcNAc and GlcA is achieved by an enzyme complex composed of EXT1 and EXT2 in the *EXT* gene family, which were first identified as causative genes of a genetic bone disorder, hereditary multiple exostoses. Alternatively, chondroitin polymerization with alternating GalNAc and GlcA takes place on the linkage tetrasaccharide by the action of a complex consisting of chondroitin synthase (ChSy) and chondroitin polymerizing factor (ChPF), a unique protein factor required for the polymerization. So far, the functionally redundant, multiple glycosyltransferases involved in GAG biosynthesis have been cloned. This redundancy makes it difficult to investigate the biosynthetic mechanism and functions of GAGs by gene knockout or characterization of individual glycosyltransferases. To investigate the biosynthetic mechanism and functions of GAGs *in vivo*, we have been using lower organisms such as *Caenorhabditis elegans*, because they are predicted to have few glycosyltransferases and a simple mechanism for GAG production. In fact, only two homologous genes, *rib-1* and *rib-2*, of the mammalian *EXT* genes and a *ChSy* ortholog (*sqv-5*) and a *ChPF* ortholog (*pfc-1*) were identified in the *C. elegans* genome. In this lecture, recent advances in the study of the biosyntheis and functions of GAGs in *C. elegans* will be presented.