Phylogenetic Approach to Mine Novel β-1,4-Galactosyltransferases for Glycoengineering

Seonghun Kim, Jae Kap Jeong, Doo-Byoung Oh, Ohsuk Kwon, Hyun-Ah Kang

Protein Therapeutics Research Center, Korea Research Institute of Bioscience & Biotechnology, 52 Eoeun-dong, Yuseong-gu, Daejeon, 305-333, KOREA
E-mail: seonghun@kribb.re.kr, Tel: 82-42-860-4393, Fax: 82-42-860-4594

β-1,4-Galctosyltransferase (β4-GalT) is a key enzyme involved in the biosynthesis of glycoproteins found mainly in mammalian species (1). From a systematic search of databank, using human β4-GalT as a query sequence, we have identified 114 putative β 4-GalT sequences in 34 organisms belong to four kingdoms except plant. Phylogenetic tree analysis indicated that β4-GalTs would be split into two distinct groups; Eukaryotic β4-GalT and Bacterial β4-GalT. Multiple amino acid sequence alignments of eukryotic β4-GalTs showed these transferases have a typical Golgi type II transmembrane domain at their N-terminal region and share four conserved motifs involved in transferring galactose from UDP-galactose to *N*-acetylglucosamine (2). Eukaryotic β4-GalTs were further divided into 8 subfamilies, including β4-GalT I, II, III, IV, V, VI, VII, and *Strongylocentrotus* group; An ortholog to the ancestor present before the split of β 4-GalT I, II, III, and IV was detected in arthropods. An ortholog to the ancestor before the split of β4-GalT V and VII was found in sea urchin. All bacterial β4-GalTs, however, were grouped into a single family. Interestingly, most bacterial enzymes were detected from parasitic microorganisms in the human body, reinforming the notion that bacterial β4-GalTs could plays an important role in establishing the host-parasite relationship. Database mining and subsequent phylogenetic analysis of enzymes involved in the *N*-glycan synthesis allows us to identify novel bacterial enzyme useful to engineer glycosylation pathways for the production of humanized glycoproteins.

Recent Publication

1. Meynial-Salles, I and Combes, D. *J. Biotechnol.* 46, 1-14 (1996)
2. Qasba, P.K., Ramakrishan, B. and Boeggeman, E. *Trends Biochem. Sci.* 30, 53-62 (2005)