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Cheorl-Ho Kim

Sungkyunkwan University, Korea

Carbohydrate xenoantigens in pig to human xenotransplantation

NeuGc is acted as an immune rejection antigen in pig to human xenotransplantation, as it is called as a non-Gal xenoantigen, a next xenoantigen to overcome after elimination of major Gal xenoantigen by knocking out the α-1,3-galactosyltransferase in the pig to human xenotransplantation. In the previous study, we isolated two promoter regions of P1 and P2, which are responsible for transcriptional regulation and located on upstream regions of the two alternative transcripts of 5'pcmah-1 and pcmah-2, respectively. Among them, promoter P2 was demonstrated to be responsible for basal house-keeping expression of the gene (BBRC). However, since the intestine tissues is important for the selective expression of the gene in responses to the pathogenic infection in pigs, the intestine specific regulatory mechanism of the gene promoter is the best interest of the pig NeuGc biosynthesis. Then, it is in this study reported that the 5'pcmah-1 promoter containing exon 1a and common ORF region (exon 2 to exon 14) is intestine specific in the pig. From the luciferase reporter assays using serial construction of each deleted promoter, it was demonstrated that promoter P1-1600 region relative to upstream region of 5'pcmah-1 is preferentially active in IPI-2I cells than in PK15 cells, corresponding with both mRNA expression patterns. Both promoters lack TATA box, but contain two Sp1 binding sites overlapped in the P1-260. Each mutation of Sp1 binding sites resulted in the reduction of luciferase activities in P1-542, indicating that in the proximal promoter region, Sp1 binding sites are crucial to regulate the intestine specific level of pcmah expression in the IPI-2I cells. In addition, the treatment with mithramycin A (25 nM to 100 nM) decreased the luciferase activity of P1 promoter in a dose-dependent manner. EMSA analysis revealed that the probes containing each Sp1 binding site bind to Sp1 and Sp3. Taken together, the results indicate that Sp1/3, or Sp1 bind to their putative binding sites on the P1 promoter regions of pcmah gene and positively regulate the promoter activity in pig cells

Biography

Cheorl-Ho Kim has completed his PhD from The University of Tokyo and was positioned as a senior scientist from Korea Research Institute of Bioscience and Biotechnology. He is a Professor of Molecular Glycobiology, SungKyunKwan University, Korea, leading organization of Korea, which is cooperated with the SamSung Group. He has published more than 341 papers in reputed journals and serving as an Editorial Board Member, Executive Editor and Editor-in Chief of the international journals. His work was contributed to the mechanisms of glycan-mediated Hepatis B viral oncogenesis and invasion, sialoglycan-mediated leukemic differentiation and vascular biology. He is being serves as an Editor-in-Chief of *Journal of Glycobiology*, Editor-in-Chief of *Journal of Microbial and Biochemical Technology*, Executive Editor of *Journal of Glycomics and Lipidomics*, Editor of *eCAM*, Editor of *The Peer Journal* and Editor of *Current Pharmaceutical* Biotechnology.

chkimbio@skku.edu

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