Hidetoshi Arima et al., J Pharm Drug Deliv Res 2016, 5:3(Suppl)
http://dx.doi.org/10.4172/2325-9604.C1.008

Potential therapeutic application of dendrimer/cyclodextrin conjugates with targeting ligands as advanced carriers for gene and oligonucleotides drugs

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So far, we have reported that gene, shRNA and siRNA transfer activity of PAMAM dendrimers (G2-G4) was strikingly increased by conjugation with α-cyclodextrin (α-CyD) through both an increase in the endosomal escaping effect and a decreasing in cytotoxicity of the dendrimers. However, the PAMAM dendrimer conjugates with α-CyD (α-CDEs) have no cell-selective gene and oligonucleotides transfer activity. Therefore, we have recently prepared various α-CDEs having targeting ligands such as folate, lactose and mannose/fucose as non-viral vectors to deliver DNA, shRNA, siRNA, miRNA and decoy DNA to tumor cells, hepatocytes and Kupffer cells, respectively, since they possess cell-selective entry, endosomal escaping ability, serum resistance and high safe profile. Most recently, we demonstrated that 2PAMAM dendrimer (G3) conjugates with glucuronylglucosyl-β-cyclodextrin (GUG-β-CDE (G3)) provided superior properties to α-CDE (G3). Also, we fairly recently found that sacran, a megamolecular polysaccharide derived from *Aphanothece* sacrum, enhanced cellular uptake and the RNAi effect of siRNA complexes with α-CDEs via a formation of ternary complexes. I will introduce the recent progress of α-CDEs and GUG-β-CDEs as cell-selective non-viral vectors.

Biography

Hidetoshi Arima has completed his PhD from Kumamoto University and worked in Eisai Co., Ltd. in Japan. He has then moved to Tokyo University of Pharmacy and Life Sciences, and came back to Kumamoto University, Japan, 1998. He was a Visiting Researcher in 2001 in University of Southern California, CA, USA. He is a Professor in Graduate School of Pharmaceutical Sciences, Kumamoto University, Japan. He has published more than 190 papers in reputed journals and has been serving as an Editorial Board Member of *Scientific Reports* and so on.

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