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Synthetic and application studies of carbohydrate-based molecular transporters as a drug delivery vector

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The Blood Brain Barrier (BBB) is composed of densely packed endothelial cells which surrounds the vessels of the brain. Endothelial cells of brain capillaries are tightly joined through tight junctions. Thus most molecules in blood plasma such as chemicals as well as pathogens are excluded from the brain. Due to this unique barrier property, brain can be effectively protected from common infectious and inflammatory processes. On the other hand, when the brain is in trouble by a certain disease, the BBB becomes the major hurdle for drug delivery to the brain. In addition, many kinds of efflux pumps are present in the endothelial cells in the brain. For these reasons, the development of CNS (central nervous drug) drugs with the BBB permeability is the major issue in pharmaceutical research. Employing the G8 sorbitol-based molecular transporter, we have prepared AZT and 5-FU conjugates to examine their delivery to the mouse brain. The transporter has two selectively protected-primary hydroxyl groups. One hydroxyl group was conjugated to the drug of interest, while the other was used to attach a fluorophore via suitable linkers. For AZT and 5-FU conjugation, we utilized the succinate ester linker, which can be enzymatically cleaved to release the drug after successful delivery to tissues.

Biography

Jungkyun Im has obtained his PhD degree in 2010 from Pohang University of Science and Technology in the field of Bioorganic Medicinal Chemistry. During the PhD course, he has synthesized glycodendrimer, molecular transporter, stereoisomers of kinase inhibitor etc. In particular, to overcome the problems in the drug delivery across biological barriers, he prepared a series of novel molecular transporters based on carbohydrate as a scaffold. The G8 (containing eight guanidine units) sorbitol-based molecular transporter was found to be highly effective in cellular uptake as well as crossing the BBB. Employing the G8 sorbitol-based molecular transporter, he has prepared AZT (the first drug approved by FDA for the treatment of AIDS), and 5-Fu (the drug approved for the treatment of solid tumors) conjugates to examine their delivery to the mouse brain.

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