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Development of non-viral nanoDDS for DNA: Analysis, control of the intracellular trafficking and beyond

A category of biomedicine is now expanding from low-molecular drugs to the recombinant protein, antibody, and nucleic acids (i.e. siRNA, mRNA and plasmid DNA). While the gene therapy approach has faced technical and/or regulatory impediments, a large number of clinical trials are still ongoing worldwide. One crucial success is the first approval of the Glybera® (UniQure) by the European Medicinal Agency (EMA) as a first gene-based medication

Gene expression efficacy is rate-limited by the multiple processes (i.e. cellular uptake, endosomal escape, cytoplasmic transport and nuclear delivery). Adequate design to overcome these barriers is a minimum requirement. Our quantitative and mechanism-based information on differences in transfection efficiency between viral and artificial cationic vectors revealed that post-nuclear delivery processes (i.e. transcription and translation) predominantly contributed to the poor transfection efficacy in artificial ones in dividing cells. In other words, the process of the post-organelle delivery process (intra-organelle disposition) should be taken into the consideration.

In this presentation, I'll propose two strategies to enhance/maximize these processes. First strategy is to develop a neutral nanoparticle in those the use of the cationic material is minimized. As an example, I'll focus on the concept of SS-cleavable and pH-activated lipid-like materials (ssPalm), that are designed to collapse in response to the intracellular environment to accelerate the "decapsulation/release" of nucleic acids (DNA and siRNA).

As another strategy, I'll propose a particle that mounts a "Switch-on" function as a trigger of signal transduction, and stimulation of transcription. As an example, I'll summarize the dendritic cell-targeted gene delivery for the DNA vaccine.

Biography

Hidetaka Akita received Ph.D. degrees (Pharmaceutical Sciences) from The University of Tokyo in 2002. After a Research Fellowship for young scientists from the Japan Society for the Promotion of Sciences (JSPS), he was appointed to the Faculty of Pharmaceutical Sciences, Hokkaido University. He was promoted to the rank of an associate professor in 2010.

In 2010, he received the Incentive Award from The Academy of Pharmaceutical Science and Technology, Japan (APSTJ). In 2011, he won The Pharmaceutical Society of Japan Award for Young Scientists. In 2013, he won The encouragement award from The Japan Society of Drug Delivery System.

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