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Particle formed by ssPalm as a nanoDDS platform for the genes and nucleic acids

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Recently, we design a nanoparticle which is neutral at physiological (cytoplasmic) pH to avoid mRNA interactions, and is degradable for the effective release of DNA or nucleic acids in response to the cytoplasmic environment. The key molecule to realize this concept is an ionizable lipid-like material; we refer to as SS-cleavable Proton-Activated Lipid-like Material (ssPalm). This molecule mounts dual sensing motifs that can respond to the intracellular environment; positively charged tertiary amines responsible for an acidic compartment (endosome/lysosome) for membrane destabilization, and disulfide bonding that can be cleaved in reducing environment (cytosol). The liposomal nanoparticle formed with ssPalm (LNPssPalm) was stable for at least 24 h in serum. The dynamic flow of LNPssPalm, with evidence for no aggregate formation and rapid liver accumulation was verified after the intravenous administration by *in vivo* intravital real-time confocal laser scanning microscopy. Moreover, the long-lasting gene expression (>2 weeks) in the liver without no production of the inflammatory cytokines were conferred. Furthermore, the surface modification of the LNPssPalm with PEG prolonged the blood circulation, and resulted in the successful gene expression in tumor tissue. As a 2nd generation of ssPalms were developed, in those fat-soluble vitamins such as vitamin A or vitamin E was used as a hydrophobic scaffold. Selection of the adequate hydrophobic scaffold and further molecular tuning in tertiary amines resulted in the development of the hepatic siRNA delivery system. Collectively, ssPalm is one of the promising platforms as a carrier for genes and siRNA.

Biography

Hidetaka Akita received PhD 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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