

Molecular design of intracellular/intraparticle environment sensitive lipid-like materials and evaluation of physicochemical characteristics of nucleic acid carriers

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Gene therapy and nucleic acid therapeutics are expected to be a fundamental technology for realizing personalized medicine. Since the nucleic acids are membrane-impermeable anionic polymers, they can not reach to its site-of-action in cells by itself. For controlling an intracellular trafficking of the nucleic acids and maximizing its efficacy, nucleic acid carriers are being developed. One of the most studied nucleic acid carriers is a nanoparticle system which is referred as to lipid nanoparticles (LNPs). LNPs are generally composed of a series of multifunctional materials that are termed “Ionizable lipids”. Although they are termed as “lipids”, the structures of the materials are different from phospholipids. In this study, we applied conventional physicochemical evaluation methods that were used for liposomes to the LNPs which contained ssPalms, Ionizable lipids that we have developed. We will then discuss the environment sensitivity of the ssPalms from their physicochemical characteristics. Recently, we found that concentrated environment in the LNPs (O/W system) drive a characteristic organic reaction. We will report the development of a novel material that is based on the intraparticle reaction. Finally, we will briefly introduce our recent progress in a development of dried nucleic acid therapeutics.