Construction of Various Multifunctional Envelope-type Nano Device (MEND) Based on Novel Assembly Technologies

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For efficient gene delivery to the nucleus, non-viral vectors need to overcome several barriers such as the plasma membrane, the endosomal membrane and the nuclear membrane. To overcome these obstacles, it is necessary to equip the delivery system with various functional devices. However, it is difficult to package all these functional devices into a single system to exert each of their functions at the appropriate time and at the correct location. Thus, we proposed a new packaging concept, which we call Programmed Packaging (Khalil, Kogure, Harashima et al., Gene Ther. in press). This concept consists of three components: 1) Programming: a program to overcome all barriers. 2) Design: the development of functional devices and their three dimensional assignment. 3) Assembly: the use of nano-technology to assemble all devices into a nano-size structure. Recently, we developed a novel non-viral gene delivery system "Multifunctional envelope-type nano device (MEND)" based on Programmed Packaging. MEND consists of a condensed nucleotides core and a lipid envelope, which can be equipped with various functional devices. Namely, various MENDs can be constructed in accordance with programs and designs for efficient gene delivery. Thus, innovative assembly technologies are required for construction of the various types of MENDs. In my presentation, I would like to talk about various type MENDs developed by novel assembly technologies, i.e., an octaarginine-modified MEND for efficient gene expression, a MEND equipped with ligand and pH-sensitive fusogenic peptide for receptor-mediated uptake and a nuclear localization signal-modified double membranous MEND for nuclear transfer.