OS02-5 Dynamic analysis and control of intracellular trafficking of gene-encapsulating nano-carrier based on a real-time imaging

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Gene therapy is promising cures for intractable diseases. However, low delivery efficiency of the therapeutic nucleic acid is a significant obstacle in the clinical application of non-viral gene therapy. An ultimate goal of drug delivery system research is the ability to target delivery of the therapeutic gene to specific organs and organelle (i.e. nucleus). Especially, cytoplasmic transport is also a crucial barrier for macromolecules. The diffusion of large-sized DNA (>250bp) is greatly impeded and is dependent on the size of the molecule, most likely due to restriction by actin cytoskeletal filaments. Viruses develop sophisticated machinery for overcoming these biological barriers and are able to successfully deliver their genomes to the nucleus. We recently developed a multi-functional envelope-type nano-device (MEND), in which complex and/or condensed particles formed with pDNA and polycations were encapsulated in the lipid envelope. This structure confers a surface modification of various types of functional devices to overcome the biomembrane barriers (i.e. endosomal membrane and nuclear membrane). One of the unique examples is octaarginine (R8)-modified MEND, which is taken up via macropinocytosis pathway, and circumvent from lysosomal degradation. It somehow reached the nuclear periphery, achieving a transfection activity as high as that for adenovirus in dividing cells. However, the issue of specifically how the R8-modified liposome (R8-Lip) travels through the cytoplasm remains largely unknown.

In this presentation, the mechanism for the nuclear accumulation of R8-MEND will be focused by single particle tracking studies. In addition, I'll show our recent approached to improve a function of R8-MEND from the point of view of control of the intracellular trafficking.