FUNDING PROGRAM FOR NEXT GENERATION WORLD-LEADING RESEARCHERS

Project Title: Development of a multi-coated nanoparticle for the control of intracellular trafficking and intra-nuclear disposition	
Name: Hidetaka AKITA	**Institution**: Hokkaido University

1. Background of research

"intracellular space" is full with various kinds of organelle (i.e. mitochondria, endosomes and Golgi apparatus), proteins and RNAs. As a next generation of Apollo Space Program, control of intracellular trafficking of nano-sized particle (nano; 10^{-9} m) in the invisible "intracellular space" for targeting a specific organelle will be one of the most innovated technology in the 21th century.

2. Research objectives

In this project, I'm planning the exogenous gene-encapsulating multi-layered nano-particles, to which various kinds of functional devices can be integrated. The nano-particles will be designed to overcome the cellular membrane barriers in stepwise manner, and to get to the nucleus. Also, we will identify the peptide sequence which can target the transcytosis-occurring cellular entry pathway, and apply it to the nano-particles for penetration of cell monolayers formed with endothelial cells. Finally, the disposition of intra-nuclear disposition of pDNA will be controlled for the efficient gene expression.

3. Research characteristics (incl. originality and creativity)

The multi-layered nano-particles can confer the temporal-spatial control of the functional exhibition of each modified devices, triggered by the step-wise decapsulation of the lipid envelopes. This concept can be realized only when pDNA was **encapsulated** by the lipid capsules, but not when pDNA forms electrostatic complex with a certain kinds of materials.

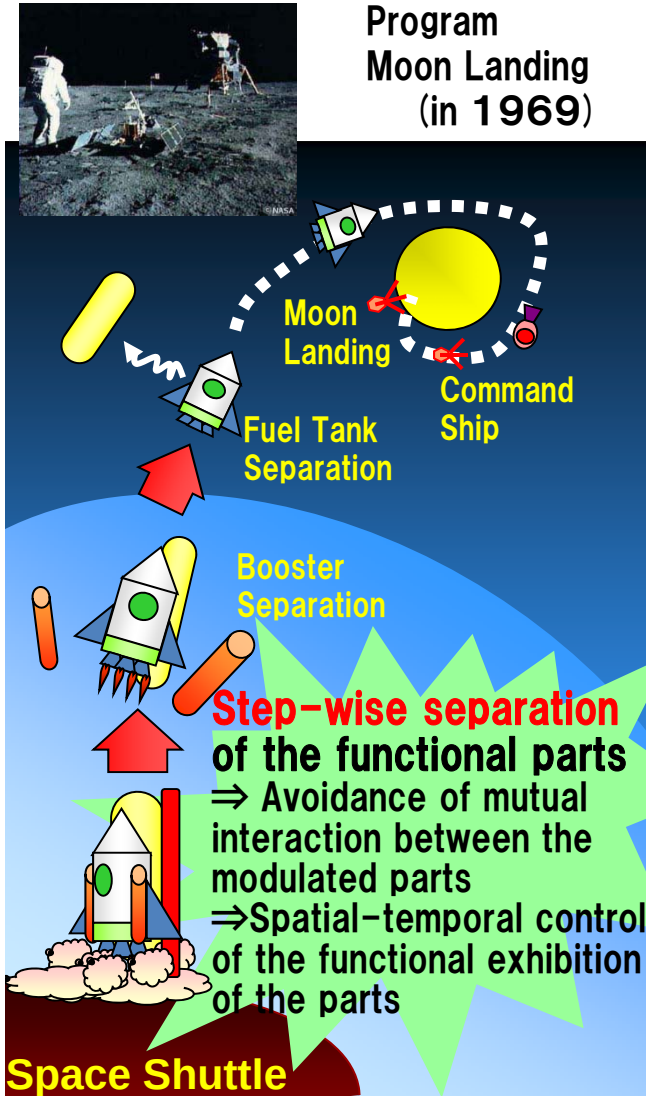
4. Anticipated effects and future applications of research

A definition of biotechnology-based drugs are now expanding from the low-molecular drugs to the macromolecules including proteins, antibody, DNA and nucleic acids (i.e. siRNA). For en effective function of these macromolecules, they must be delivered to the adequate tissue and furthermore proper organelle. The nano-particles which confer 1. the penetration of endothelial monolayer and 2. the intracellular trafficking of the targeting the organelle are a cutting-edge technology which can open a new-generation of biomedicine.

Research characteristics— Design philosophy of gene-carrier development

Engineering innovation in 20th century

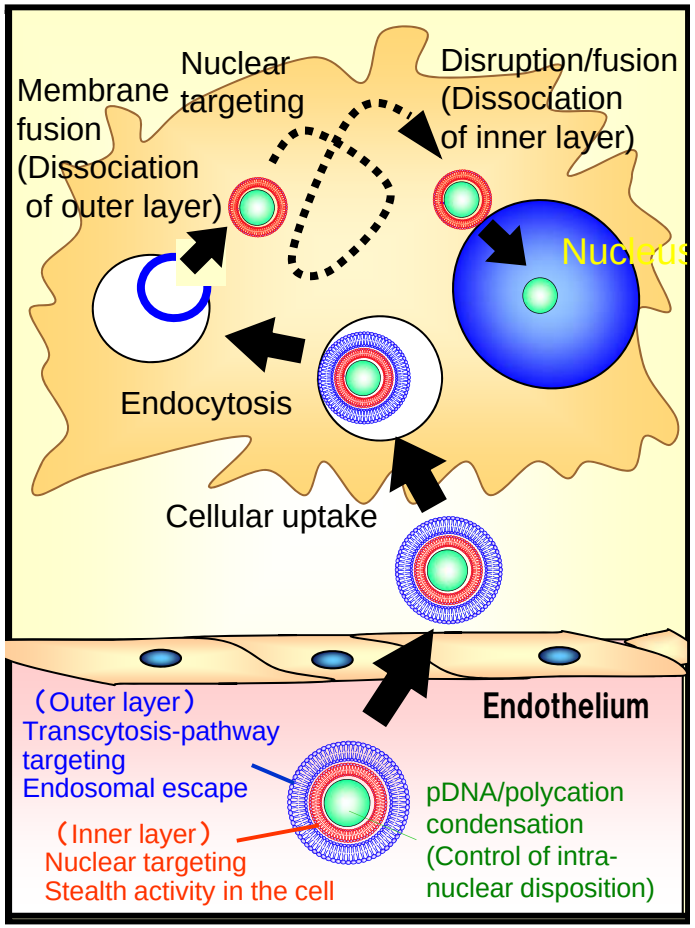
Apollo Space Program Moon Landing (in 1969)



Step-wise separation of the functional parts
⇒ Avoidance of mutual interaction between the modulated parts
⇒Spatial-temporal control of the functional exhibition of the parts

Engineering innovation in 21th century

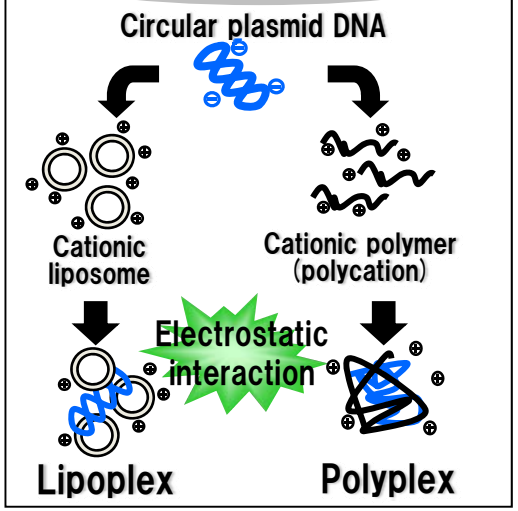
Control of a trafficking of nano-particles in the 'intracellular space'



Design concept:
Step-wise functional exhibition of the modified devices, triggered by the dissociation of the part of the nano-particle

pDNA-encapsulation is a minimum requirement to realize this concept

Conventional Gene vector



Fundamental technology