BIOMEDICAL NANOTECHNOLOGY : THE DEVELOPMENT OF ACTIVE TARGETING DRUG DELIVERY SYSTEM NANOPARTICLES BASED ON MOLECULAR ASSEMBLY OF LIPIDS, PROTEINS, AND SUGAR CHAINS

Noboru Yamazaki
Nanotechnology Research Institute, AIST, Tsukuba, Ibaraki 305-8565, Japan
E-mail: n.yamazaki@aist.go.jp
http://www.aist.go.jp/RIODB/db072/

Active targeting drug delivery system (DDS) is attracting increasing interest in the biomedical nanotechnology. Ligand/receptor-mediated targeting has emerged as a novel paradigm in the active targeting DDS, and sugar chain/lectin-based targeted system is expected to be a promising research field. A large number of biological events such as cell-cell recognition, adhesion, growth regulation, and inter- and intracellular routing have been shown to involve sugar chains of glycoproteins and glycolipids for correct and efficient molecular interplay. Today, various families of proteins, i.e., animal lectins, which participate as receptors in such interactions and specifically recognize the structural features of sugar chain ligands, are increasingly being discovered to play salient roles in biological carbohydrate-protein recognition systems. By studying cellular functions of animal lectins, we have been developing a novel type of glycoprotein(or glycolipid)-liposome conjugates for active targeting DDS. We here present the current state of our research in this area, including establishment of a method to prepare an innovative type of sugar chain-conjugated liposomal nanoparticles and their applications for analyzing carbohydrate-protein recognition functions in a model system *in vitro* and *in vivo*. This approach is aimed at the design of a novel type of active targeting DDS which is based on the molecular assembly of lipids, proteins, and sugar chains.

We have established a method to prepare a series of glycoprotein (or glycolipid)-liposome conjugates [1-5]. Analyses of these preparations proved homogeneity and stability (Fig. 1). The *in vivo* stability was also satisfactory, which fulfilled a prerequisite for considering applications in biological systems. A model and *in vitro* assays demonstrate that this type of sugar chain-bearing liposomes has carbohydrate-specific activities and is useful as a biosensing probe. A biodistribution assay indicates the potential usefulness of these sugar chain-liposome conjugates as efficient drug-targeting devices which exploit cellular functions of carbohydrate-binding proteins, i.e., animal lectins (Fig. 2). Whereas some level of expertise and experience in developing carbohydrate-mediated drug delivery systems based on glycolipid-bearing liposomes has been attained, the tailor-made design and applications of glycoprotein-bearing liposomes are less explored. As a step to address this issue, efforts are directed to design and construct high-functional glycoprotein(or glycolipid)-liposome conjugates which display various sugar chains on the liposomal surface, and an example is illustrated in Fig. 1. By applying this kind of approach or by developing further techniques, we expect to provide new insights into the underlying mechanisms of carbohydrate-protein interactions on membrane surface, and to define applications in biomedical nanotechnology such as biosensing and drug delivery systems.

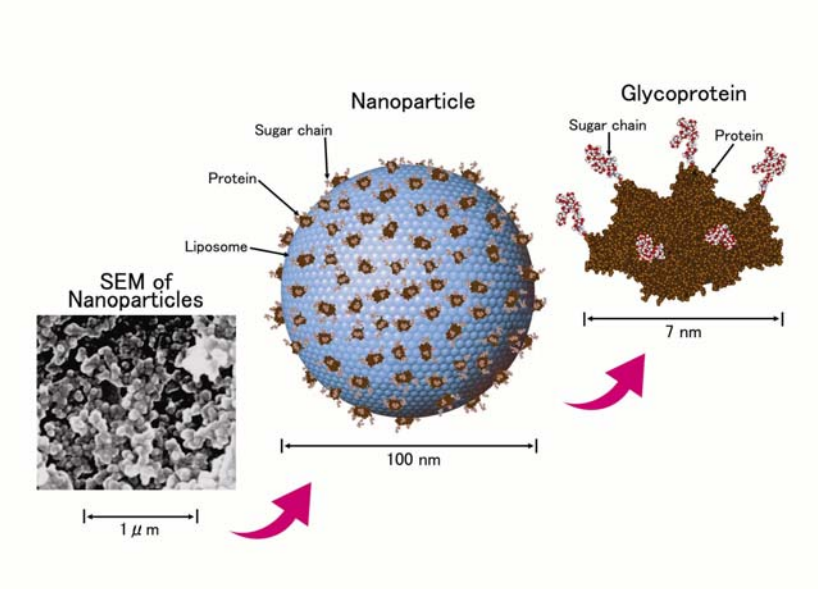

Fig. 1 Molecular Assembly of Our DDS Nanoparticles

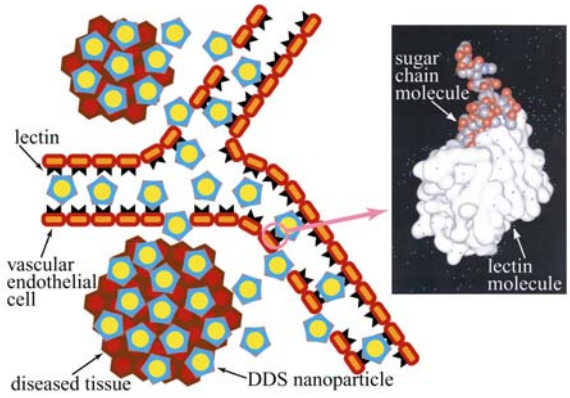

Fig. 2 Diagram of the Active Targeting

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This work is supported by the Dynamic Nanotech Research Promotion Program Grant DNR002.