Development of Liposome-Based Nasal Drug Delivery Systems to Enhance Mucosal Defense for Radical Allergy Treatment

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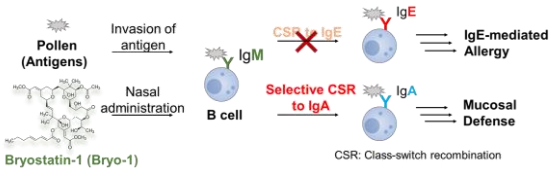
Allergic symptoms occur by the overproduction of IgE antibodies, and symptomatic treatments with antihistamines are provided.[1] For radical treatments, development of medicines with enhancement of IgA antibody production on nasal mucosa as well as deliver them to antigen-presenting cells (APCs) in the nasal mucosa are essential. Bryostatin-1 (Bryo-1) is expected to be an ideal drug for the radical treatment of allergies. Bryo-1 showed high activity for inhibition of IgE-related allergic reactions with enhancing the defense of nasal mucosa against antigens through the selective production of IgA antibody by nasal administration (Scheme 1).[2]



Scheme 1. Strategy to enhance the mucosal defense though selective class-switching to IgA.

In this study, we have developed basic liposome carriers (LNPs) for the APCs-targeting nasal DDS. The IgA class-switching drugs, Bryo-1, was incorporated into LNPs with different surface charges, neutral LNPs (DOPC), cationic LNPs (DOTAP/DOPC) and anionic LNPs (DOPS/DOPC), to enhance interaction with both the nasal mucosa and APCs through electrostatic and receptor-mediated interactions, as well as resist mucociliary clearance.

Bryo-1@LNPs were prepared using the thin-film method, with surface charges varied depending on the ionic lipids and an incorporation ratio of about 85%. The interaction between LNPs and RAW264.7 cells were determined by FACS analysis *in vitro*. The result showed that charged LNPs increased uptake efficiency, demonstrating the stronger interaction between cells and charged LNPs. Additionally, the class-switch recombination (CSR) activity of Bryo-1@LNPs was evaluated according to the germline transcript (GLT) levels of IgA and IgE using real-time PCR. As the result, all Bryo-1@LNPs exhibited CSR activity towards B cells by increasing GLTα expression and reducing GLTε expression. Finally, the effect of Bryo-1@LNPs on OVA-allergy model mice was investigated. The OVA-specific IgA and IgE level in mouse saliva and serum were determined using ELISA. As a result, the efficiency of intranasal administration of Bryo-1 in promoting IgA production and reducing IgE level can be enhanced by incorporating it with cationic and anionic LNPs. The increased IgA production indicates a strengthening of mucosal defense.

Consequently, the present study highlighted that charged LNPs are highly efficient DDS carriers of Bryo-1 for the radical treatment of allergies.

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