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Towards the development of self-adjuvanting vaccine against group A streptococcus

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Peptides are of great interest to be used as vaccine antigens due to their safety, ease of manufacturing and specificity in generating immune response. There have been massive discoveries of peptide antigens over the past decade. However, peptides alone are poorly immunogenic, which demand co-administration with strong adjuvant to enhance their immunogenicity. Recently, fibril-forming peptides such as Q11 and lipoamino acid-based carrier have been identified to induce substantial immune responses when covalently linked to peptide epitope. In this study, we have incorporated either Q11 or lipoamino acids to a peptide epitope (J14) derived from M protein of Group A Streptococcus to develop self-adjuvanting vaccines. J14, Q11 and lipoamino acids were also conjugated together in a single vaccine construct in an attempt to evaluate the synergy effect of combining multiple adjuvants. Physicochemical characterization demonstrated that the vaccine constructs folded differently and self-assembled into nanoparticles. Significantly, only vaccine constructs containing double copies of lipoamino acids (regardless in conjugation with Q11 or not) were capable to induce significant dendritic cells uptake and subsequent J14-specific antibody responses in non-sizes dependent manners. Q11 had minimal impact in enhancing the immunogenicity of J14 even when it was used in combination with lipoamino acids. These findings highlight the impact of lipoamino acids moiety as a promising immunostimulant carrier and its number of attachment to peptide epitope was found to have a profound effect on the vaccine immunogenicity.

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Optimization of nuclear-localization in a Multicomponent Non-viral Gene Delivery System

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Gene Therapy is a technique utilized to treat diseases caused by missing, defective or overexpressing genes. Although viral vectors transfect cells efficiently, risks associated with their use limit their clinical applications1,2. Nonviral delivery systems are safer, easier to manufacture, more versatile and cost effective3. Previously studied gene delivery systems can successfully get through the cell membrane and release into cytoplasm4. However, the translocation onto the nuclear membrane and enter into the nucleus become a major challenge for gene delivery. In the current research, a library of multicomponent gnonviral gene delivery system incorporating a cationic Dendron (DEN), a cell penetrating peptide (TAT), an endosomal-disrupting peptide (GALA) and nuclear localization species (NLS) were produced (Figure 1). Four NLSs (SV40 T-antigen, nucleoplasmin, Dexamethasone and Retinoic acid) were selected to identify which one has the most efficient nuclear localization activity, and therefore is the best optimize gene delivery system.

Peptide based components were synthesized by standard solid phase peptide synthesis, and GALA was conjugated to the system by 'click chemistry'. After finishing synthesis, these four different delivery systems will be tested and compared for DNA condensation ability, cellular uptake, and transfection efficiency. Delivery system without NLSs will be used as a negative control in the biological experiments

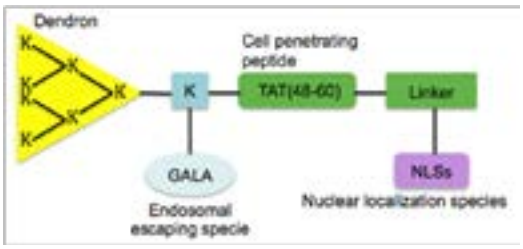

Figure 1: Schematic presentation of multicomponent non-viral gene delivery system construct

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