Multi-layer engineered nanoliposomes as a novel tool for oral delivery of lipid core peptide-based vaccines against group A streptococcus (GAS)

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The aim of our project is to develop a novel oral nano-vaccine delivery system against group A streptococcus (GAS) by encapsulating lipid core peptide (LCP) antigens into the liposomes. We synthesized the LCP construct by attaching lipoamino acids (Toll-like receptor-2 agonist) with J-14 (B-cell epitope derived from GAS M-protein) and P25 (universal CD4+ T-helper epitope) using microwave assisted solid-phase peptide synthesis. The optimized LCP-loaded liposome formulations were prepared and their surface were coated with oppositely charged polyelectrolytes [negatively charged sodium alginate and positively charged trimethyl chitosan (TMC)] and characterized by dynamic light scattering (DLS) and transmission electron microscopy (TEM). Loading efficiency of the LCP-loaded formulations was ~80%. DLS and TEM measurements showed spherical monodisperse particles before and after three layers coating with alginate-chitosan-alginate with final size of ~165 nm and ~195 nm, respectively. Positively-charged formulations (LCP-loaded liposomes and double-layered TMC-coated liposomes) had a significant uptake by dendritic cells and macrophages compared to single and triple-layered liposomes. Developed formulations showed an enhanced colloidal stability of liposomes in simulated gastric and intestinal fluid. In vivo oral immunization studies were conducted in Swiss outbred mice and double-layered TMC-alginate-coated liposomes showed higher J-14 specific mucosal IgA and systemic IgG production in the mucosal fluids and serum as compared to vaccine formulated with a standard mucosal adjuvant. Taken together, our results suggest that layer-by-layer engineered nano-architecture formulations as a promising novel strategy for oral delivery of lipopeptide-based vaccines.

Figures: Polyelectrolyte coated nano-liposomes for oral vaccine delivery. Schematic representation of multi-layered nano-liposomes and TEM images of (A) LCP-loaded uncoated liposomes, (B) Alg-coated liposomes, (C) TMC-Alg-coated liposomes, (D) Alg-TMC-Alg-Coated liposomes (bar; 500 nm).