Evaluation of Coated α-galactosylceramide Liposomes as Delivery Vehicles for Oral Vaccines for Atopic Conditions
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Purpose
The main limitations for oral delivery of liposomal vaccines are their inherent instability under the conditions found in the gastrointestinal (GI) tract and induction of an insufficient immune response. The aim of this study was to characterise α-galactosylceramide (α-galcer) liposomes designed to have improved stability in the GI tract through coating with either silica nanoparticles (SNP), chitosan or PEG and to then evaluate their effectiveness in suppressing antigen specific IgE induction in an allergic mouse model.

Methods
Liposomes made from dipalmitoylphosphatidylcholine, cholesterol and α-galcer and loaded with ovalbumin (OVA), were coated with SNP, low molecular weight chitosan or PEG and characterised for size, size distribution, Zeta potential and surface morphology. Stability tests were conducted by incubating the formulations in simulated gastric fluid at 37°C for 2 hours and assessing antigen retention, particle size and polydispersity. Storage stability was assessed at 4°C for 28 days. The optimised formulations were administered to OVA sensitised mice and assessed for serum OVA specific IgE response and cytokine release from restimulated splenocytes.

Results
Particle size increased upon coating with SNP and chitosan and the surface charge matched the respective negative and positive charges of the coating components. The stability results showed coated particles had improved retention of the model antigen during incubation in the simulated gastric condition but appeared to flocculate into large agglomerates. Antigen retention under 4°C storage conditions was similar between formulations, with the majority of the antigen being retained over the 28 day period, although coated particles exhibited an increase in particle size. Administration of formulations to OVA sensitised mice in a pilot study showed a partial suppression of the induction of OVA specific IgE by the SNP coated liposomes and a slight decrease in the production of IFN-γ by OVA-restimulated splenocytes.

Conclusion
The in vitro findings suggest that the electrostatically coated formulations may have greater antigen retention but the gastric simulated conditions caused the coated particles to aggregate. Preliminary in vivo data suggests that oral administration of the SNP coated liposomes could possibly suppress the antigen specific IgE induction in the mouse allergy model.