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Improvement of anti-tumor responses by DC-Sign mediated antigen-targeting using glycan modified liposomes: A potential anticancer vaccine

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Abstract

Dendritic cells (DC) are key antigen presenting cells that have the unique ability to cross present tumor-derived antigens on MHC class I, resulting in effective priming of cytotoxic T lymphocytes (CTL). DC express C-type lectin receptors that bind and subsequently mediate the uptake of carbohydrate structures appended to glycoproteins. Here we have explored the specific expression of the C-type lectin receptor, DC-SIGN to specifically target antigens to DC, to improve anti-tumor responses.

Glycan-modified stealth and non stealth liposomes containing ovalbumin (OVA) as the model antigen were prepared from a mixture phospholipids and utilizing the thin film hydration method. The linkage of the glycans to the liposomes was confirmed in an ELISA. Specific binding and uptake of glycan-modified liposomes to DC-SIGN was assessed by measuring the mean fluorescence upon incubation of bone marrow derived dendritic cells (BMDCs) of hSIGN Tg mice with graded numbers of liposomes at 4 and 37^0C. Both the stealth and non stealth liposomes showed conjugation of ligand on the liposome surface in ELISA when stained with anti-Lewis^B antibodies. However the stealth liposomes failed to show any signal in the ELISA after staining with DC-SIGN-Fc suggesting improper conjugation or unavailability of the ligands for binding to DC-SIGN. In the binding studies the non stealth liposomes showed 8 fold higher binding to BMDCs compared to the stealth liposomes. Our results demonstrate that DC-SIGN targeted glycan modified liposomes could be used for the efficient induction of anti-cancer immune responses and serve a potential anticancer vaccine.

Biography

Medha Joshi is Ph.D in pharmaceutics form Institute of chemical Technology, Mumbai, India. She has post doctoral experience for more than four years from Free University of Berlin, Germany and Utrecht University, The Netherlands. She has worked for Ocean Nanotech, AR for production and development of lipid based nanoparticle systems for diagnostics purpose. Currently she is Assistant Professor in the Pharmaceutical Sciences department at Midwestern University's Chicago College of Pharmacy, IL. She has expertise in lipid based drug delivery systems including micro emulsions, liposome technology and targeted drug delivery. She holds intramural grants and a grant from Alzheimer's disease foundation to support her research. Apart from research, she is the course director and instructor for Pharmaceutical calculations course in pharmaceutics sequence of the Doctor of Pharmacy curriculum at Chicago College of Pharmacy. She has been the awarded for the best poster presentation couple of times at drug delivery symposiums and conferences. She is the reviewer of many international drug delivery journals. She holds more than 13 publications in top drug delivery international journals. She is the member of various drug delivery and pharmaceutical organizations and associations.