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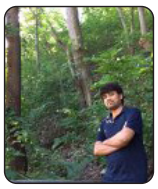
Abstract



In vivo Targeting of Liposomally complexed DNA Vaccines to Dendritic Cells induce Long Lasting Protection against Melanoma Tumor

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Abstract:

Background: Since Dendritic cells (DCs) are responsible for both in the instigation of adaptive immune response and the tolerance initiation, manipulation of DCs with DNA vaccines in vivo encoding tumor-associated antigens is considered as an efficient approach to combat cancer [1].

Objective: Developing a simple & economical in vivo DCs targeting delivery system as well as achieving long-lasting immunity which is a substantial scientific task in DNA vaccination [2].

Methods: In the present study, we developed an efficient mannose receptor (MR)-selective in vivo DC-targeting liposomal formulation of a novel cationic amphiphile-consisting mannose-mimicking di-shikimoyl- and guanidine head-group and two n-hexadecyl hydrophobic tails (DSG in short form).

Results: Genetic immunization with the liposomes of DSG/p-CMV-GFP complex showed a significant expression of green fluorescence protein in the CD11c+ DCs of the neighboring lymph nodes compared to the control liposomes of BBG/p-CMV-GFP complex. MR-facilitated in vivo DC-targeted genetic immunization (s.c.) with the electrostatic complex of liposomes DSG/pCMV-MART1 induced long-lasting (270 days post tumor challenge) melanoma immune response under prophylactic conditions. Remarkably, under therapeutic settings in vivo genetic immunization (s.c.) with the liposomes of DSG/pCMV-MART1 complex significantly inhibited the melanoma growth and improved the overall survivability (OS) of tumor melanoma bearing mice.

Conclusion: Our studies show that this efficient non-viral delivery system can deliver DNA vaccines to DCs in vivo and can thus be used to developing potential vaccines for various infectious diseases and cancers.

Biography:

Gopi Krishna Moku did his M.Sc from Osmania University, Hyderabad, India in 2009. Later he worked as Associate Research Scientist at Advinus Therapeutics Pvt Ltd, Pune. In 2010 he joined CSIR-Indian Institute of Chemical Technology, Hyderabad, India and received his PhD in 2016 under the supervision of Dr. Arabinda Chaudhuri. During his Ph.D he worked on the development of cationic amphiles for use in targeted chemotherapy and DNA vaccination. Later, in May 2016 he joined as a postdoctoral research associate at Department of Pharmaceutics, University of Minnesota, Twin Cities, Minnesota, USA, where he worked on development of mesenchymal stem cell based drug delivery systems. In July 2019, he joined Kakatiya Institute of Technology and Science, Warangal, India and he is currently working as an assistant professor. His research interests include cancer immunotherapy, cancer biology and targeted chemotherapy. He has 10 publications in reputed Journals and 2 US granted patents.

Publication of speakers:

1. J. Banchereau, R. M. Steinman, Nature 1998, 392, 245–252.
2. Z. Hu, P. Ott, C. Wu, Nat. Rev. Immunol. 2018, 18, 168–182.

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