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Abstract

Treating "Liquid Tumors" with Nanomedicines: Liposomal Drug Delivery in Cancer-Hematological Malignancies and Beyond

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Abstract:

Background: Hematological malignancies (HM) are a collection of malignant transformations originating from cells in the primary or secondary lymphoid organs. Although, many chemotherapeutic drugs are clinically available for the treatment of HM, the use of these agents is limited due to dose-related toxicity and lack of specificity to tumor tissue. Moreover, the poor pharmacokinetic profile of most of the chemotherapeutics requires high dosage and frequent administration to maintain therapeutic levels at the target site. Liposome encapsulation has been proven to improve therapeutic window of anticancer drugs. Small size of liposomes allows them to extravasate and accumulate at malignant sites passively by means of the EPR effect.

Aims: We developed and studied liposomal formulations of glucocorticoids and proteasome inhibitors in two clinically more relevant mouse tumor models: a spontaneous MMTV/neu mouse model of breast cancer. In this model, the transgenic mice develop mammary tumors after several months, showing slower and clinically more relevant tumor growth kinetics compared to many subcutaneous xenograft models; and a humanized mouse model of multiple myeloma with a reconstituted human hematopoietic niche. The human bone environment is mimicked by interaction of myeloma cells to bone marrow stromal cells. Moreover, angiogenesis is developed within and around the tumor bearing scaffolds.

Results: Liposomal formulations of prednisolone and dexamethasone substantially improved their pharmacokinetic profile and therapeutic efficacy in advanced mouse models of breast cancer and multiple myeloma respectively. Liposomal bortezomib resulted in complete tumor regression in a humanized mouse model of multiple myeloma with cell-derived and patient-derived xenografts.

Conclusion: Liposomal encapsulation of glucocorticoids prednisolone and dexamethasone, and proteasome inhibitor bortezomib improved anti-tumor efficacy in advanced mouse models of solid tumor and multiple myeloma.

Biography:

Dr Anil Kumar Deshanri has completed his PhD in 2018 from University Medical Center Utrecht, The Netherlands. He is working as a Scientis Pre-Clinical Pharmacology at Sun Pharma Advanced Research Company Limited, a leading pharmaceutical company in India. He has published 8 papers in reputed journals and has more than 12 years of research experience in industry and academia. His research interest is to establish advanced animal models for cancer research and to develop nanomedicine drug delivery systems for cancer and inflammatory disorders.

Publication of speakers:

1. Anil Kumar Deshantri; Nanomedicines for the treatment of hematological malignancies
2. Anil Kumar Deshantri; Liposomal prednisolone inhibits tumor growth in a spontaneous mouse mammary carcinoma model
3. Anil Kumar Deshantri; Liposomal dexamethasone inhibits tumor growth in an advanced human-mouse hybrid model of multiple myeloma
4. Anil Kumar Deshantri; Liposomal drug delivery in an in vitro 3D bone marrow model for multiple myeloma
5. Anil Kumar Deshantri; Biofabrication of cell-derived nanovesicles: a potential alternative to extracellular vesicles for regenerative medicine.

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