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Co-Delivery of Albendazole and OTS964 by Lipid-Coated Calcium Phosphate (LCP) Nanoparticles to Treat Metastatic Cancers

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The leading reason of death for the majority of patients with cancer is metastasis. Currently, 90% of chemotherapeutic treatments fail during the metastasis stage of cancer due to drug resistance. A promising approach to combat the drug resistance is combination therapy by at least two therapeutic agents. OTS 964 is a novel anti-cancer drug targeting TOPK pathway which is highly expressed in the circulating tumour cells. On the other hand, albendazole is recently recognized as an anti-cancer drug inhibiting tubulin polymerization. The combination of OTS 964 and albendazole not only can be employed as an effective tool against drug resistance but also can act against metastasis by targeting the marker of metastatic cells.

In this work, we employed pH-responsive lipid-coated calcium phosphate (LCP) nanoparticles for co-delivery of albendazole and OTS 964 (OTS-ABZ-LCP). OTS-ABZ-LCPs were tested against B16F0 melanoma cells, B16F10 metastatic melanoma cells and HUVEC cells. Cell toxicity, apoptosis induction, ROS and VEGF level and cell migration ability were measured to investigate the mechanism of action.

OTS-ABZ-LCPs were highly effective against B16F0 and B16F10 melanoma cells while showing no significant toxicity against healthy cell line, HUVEC. The results revealed that albendazole and OTS kill cancer cells in a synergistic fashion through inducing synergistic apoptosis induction. The treatment not only reduced VEGF expression in cancer cells but also decreased their migration ability and metastatic properties.

Co-delivery of albendazole and OTS 964 in LCP form can be a promising tool to overcome drug resistance in cancer cells as well as targeting metastasis with minimum toxicity to healthy organs. Further *in vivo* studies are required to confirm the results and move toward clinical trials.

Biography:

Dr. Fatemeh Movahedi did her bachelor in Sharif University of Technology (2007) the leading university in Iran. She did her master in IUST (2012). Later, she pursued her research in drug delivery in Nanyang Technological University (NTU) in Singapore and then moved to Australia and started her PhD in Australian Institute for Bioengineering and Nanotechnology, The University of Queensland under supervision of Professor Zhiping (Gordon) Xu. Fatemeh Movahedi's research is to develop a new nanoplatform to efficiently deliver albendazole for cancer therapy. Her research is focused on optimizing LCP nanoparticles to carry albendazole and enhancing the delivery efficacy *in vitro* and *in vivo* for cancer therapy.