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An APC targeting therapeutic nanocarrier system that has intrinsic immunopotentiating effect

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Macrophage/ dendritic cells are major professional antigen presenting cells (APC) that are central in mounting protective immune responses against cancer and the many parasites, bacteria, and viruses. Thus, selective drug delivery to APCs has been the subject of much interest; in particular, when the pathogen can infect such cells and give rise to outbreak of so many deadly and hard to treat diseases in humans including tuberculosis, HIV, Rickettsial infections, and leishmaniasis. We describe the development of a nanocarrier that results in treatment shortening in *leishmaniasis* while enhances parasite specific immune responses in the infected host. Liposome entrapped amphotericin-B (AmB) is an effective antifungal and antiprotozoan agent that induces significant (nephro)toxicity at high doses and requires complicated dosing regimens to minimize its side effects. Since *Leishmania* species are obligate parasites in phagocytes, selectively delivering AmB to infected phagocytes improves efficacy, decreases toxicity, and simplifies dosing regimens. We developed a peptide-derivatized dendrimer (PDD) nanocarrier that complex with AmB and targets phagocytes via an MHC class II targeting peptide. In a murine model for *Leishmania* major infection, PDD-AmB efficiently targeted infected phagocytic cells reducing the AmB effective dose by 83% with improved pharmacokinetics. Moreover, since the MHC class II targeting peptide is a universal helper T-cell epitope, PDD-AmB complexes elicited parasite specific T-cell responses. Thus, by reducing and simplifying AmB dosing and consequent side effects, and stimulating T-cell responses, PDD-AmB complex is a potential candidate for further development and human clinical trials.

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