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Vaccine nanocarriers: Coupling intracellular pathways and cellular biodistribution to control CD4 vs CD8 T cell responses

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Abstract

Nanoparticle delivery systems are known to enhance the immune response to soluble antigens (Ags) and are thus a promising tool for the development of new vaccines. Our laboratory has engineered two different nanoparticulate systems in which Ag is either encapsulated within the core of polymersomes (PSs) or decorated onto the surface of nanoparticles (NPs). Previous studies showed that PSs are better at enhancing CD4 T cells and antibody titers, while NPs preferentially augment cytotoxic CD8 T cells. Herein, we demonstrate that the differential activation of T cell immunity reflects differences in the modes of intracellular trafficking and distinct biodistribution of the Ag in lymphoid organs, which are both driven by the properties of each nanocarrier. Furthermore, we found that Ags within PSs promoted better CD4 T cell activation and induced a higher frequency of CD4 T follicular helper (Tfh) cells. These differences correlated with changes in the frequency of germinal center B cells and plasma cell formation, which reflects the previously observed antibody titers. Our results show that PSs are a promising vector for the delivery of Ags for B cell vaccine development. This study demonstrates that nanocarrier design has a large impact on the quality of the induced adaptive immune response.

Keywords

Vaccine design, antigen presentation, T follicular helper cells, germinal center, dendritic cells

Abbreviated title

Intracellular pathways and cellular biodistribution of vaccine nanocarriers