# Rational design of protamine nanocapsules as antigen delivery carriers

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**Abstract**

Current challenges in global immunization indicate the demand for new delivery strategies, which could be applied to the development of new vaccines against emerging diseases, as well as to improve safety and efficacy of currently existing vaccine formulations. Here, we report a novel antigen nanocarrier consisting of an oily core and a protamine shell, further stabilized with pegylated surfactants. These nanocarriers, named protamine nanocapsules, were rationally designed to promote the intracellular delivery of antigens to immunocompetent cells and to trigger an efficient and long-lasting immune response. Protamine nanocapsules have nanometric size, positive zeta potential and high association capacity for H1N1 influenza hemagglutinin, a protein that was used here as a model antigen. The new formulation shows an attractive stability profile both, as an aqueous suspension or a freeze-dried powder formulation. In vitro studies showed that protamine nanocapsules were efficiently internalized by macrophages without eliciting significant toxicity. In vivo studies indicate that antigen-loaded nanocapsules trigger immune responses comparable to those achieved with alum, even when using significantly lower antigen doses, thus indicating their adjuvant properties. These promising in vivo data, alongside with their versatility for the loading of different antigens and oily immunomodulators and their excellent stability profile, make these nanocapsules a promising platform for the delivery of antigens..

**Keywords**

Protamine, Nanocapsules, Antigen delivery, Vaccine, Influenza vaccine, Adjuvant.