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Flagellin engineered Salmonella typhi Vi polysaccharide nanoparticulate vaccine: Class switching and memory antibody response

Jairam Meena, Robin Kumar and Amulya K Panda
National Institute of Immunology, India

Introduction: Salmonella typhi Vi capsular polysaccharide antigen (T cell independent antigen) is poorly immunogenic and antiphagocytic nature of Vi polysaccharide further limits its use as subunit vaccine. Like other non zwitterionic polysaccharides antigens Vi polysaccharide fails to generates antibody class switching, memory antibody responses and protection in children below 5 years of age. Non-zwitterionic polysaccharide antigens required conjugation with a carrier protein (T cell dependent antigen) for T cell presentation through MHC II pathway. Conjugation of polysaccharide antigen with T cell dependent antigen results in antibody class switching and memory antibody responses. Biodegradable polymer particles (PLA and PLGA) were extensively studied for drug delivery. In last decade, polymer particulate vaccines gained tremendous attention due to its depot effect and adjuvant activities. It has been reported that polymer particle entrapped antigens shows higher processing and presentation through MHC pathway as compare to the soluble antigens. In the current study, immunogenicity of PLA polymer particle (nano and micro) entrapped Salmonella typhi Vi polysaccharide antigen was evaluated. Further, flagellin (a TLR 5 agonist) is used as an adjuvant and ligand for targeted delivery of particles to the antigen presenting cells (APCs).

Results: Entrapment of Salmonella typhi Vi capsular polysaccharide antigen in to PLA polymer (45 KDa) particles (nano and microparticles) results in to higher antibody titer, antibody class switching and memory antibody response like glycoconjugate vaccines. Salmonella typhi Vi polysaccharide antigen is well known for its anti-phagocytic activity which limits antigen uptake into antigen presenting cell. Vi entrapped PLA polymer particles were flagellin (a TLR 5 agonist) tailored which enhanced the polymer particle uptake in antigen presenting cells and subsequently enhance the antigen payload in antigen presenting cells. Flagellin tailored PLA polymer particles significantly enhance the anti Vi IgM and IgG antibody responses. Furthermore polymer particle entrapped Vi antigen shows IgM to IgG antibody class switching and enhances the IgG2a, IgG2b, IgG3 subtypes as compared to the soluble Vi polysaccharide antigen.

Conclusions: Flagellin (a TLR 5 agonist) coating enhances the polymer particle uptake in antigen presenting cells. PLA polymer particle (nano and microparticle) entrapped Vi polysaccharide antigen results in higher anti Vi IgM and IgG antibody titer, antibody class switching and memory antibody response. PLA polymer particle entrapped Vi antigen results in higher IgG2a, IgG2b and IgG3 antibody subtypes.

jairam@nii.ac.in

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