

## **Preclinical Evaluation of a *Salmonella* Typhi Polysaccharide Vi-Diphtheria Toxoid (VI-DT) Conjugate Vaccine Candidate Against Typhoid Fever**

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**Background:** Typhoid fever continues to be a major public health problem according with estimates of World Health Organization. Conjugation of polysaccharides to an immunogenic protein revert the T-independent pattern of polysaccharides to a T-dependent pattern and induce immune response in infants. The aim of this work was to obtain and evaluate a conjugate candidate vaccine against this disease.

**Methods:** Vi polysaccharide of *Salmonella* Typhi was conjugated to diphtheria toxoid (Vi-DT) via a carbodiimide-mediated reaction. Analytic assays were done to formulations at 10µg/ml and 20µg/ml. Immunogenicity and protective capacity of conjugates were evaluated in BALB/c or C57BL/6 mice.

**Results:** All lots of conjugate formulations showed similar characteristics. Vi-DT conjugates were immunogenic in BALB/c mice and the immune response was dose dependent. The addition of at least a 50% of unconjugated Vi to Vi-DT, did not affect the conjugate's immunogenicity. Memory B cell and memory T cell responses after booster dose with a plain polysaccharide vaccine were induced. Conjugates were also protective after challenge with a *Salmonella* Typhi strain F9 and mucin as virulence inductor in C57BL/6 mice

**Conclusions:** These results demonstrated that Vi-DT conjugates are immunogenic and protective in animal models, encouraging us to continue the development of a conjugate vaccine against typhoid.