Anti-Vi Isotype and Subclass-Specific Assays for Serum and Plasma Antibody Quantification

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Background: Typhoid Vi-vaccine trials incorporating measures of vaccine immunogenicity typically assess serum anti-Vi antibody titres. The aim of this study was to repurpose commercial Vi antibody immunoassay kit components to develop and optimise serum IgA, IgM, and IgG_{1-3}-specific anti-Vi antibody assays. A secondary aim was to validate the use of plasma samples (rather than serum) for anti-Vi antibody quantification with the unmodified commercial kit.

Methods: One hundred and eleven participants enrolled in a typhoid vaccine trial were randomised to receive an active typhoid vaccine (Vi-polysaccharide/Vi-tetanus toxoid) or control, prior to oral *Salmonella* Typhi challenge one month later. Participants were actively observed for clinical or bacteriological confirmation of typhoid diagnosis. Anti-Vi IgG titre was quantified in all participants, and IgA, IgM, and IgG_{1-3} in 36 participants before vaccination, one month after vaccination, and one month after infection. Matched post-vaccination plasma and serum samples from 39 participants were also assayed using an unmodified commercial immunoassay kit (VaccZyme™ Human Anti-*Salmonella* Typhi Vi IgG Enzyme Immunoassay Kit, The Binding Site).

Results: Preliminary results indicate that post-vaccination anti-Vi pan-IgG, IgA, IgM, and IgG_{1-3} titres significantly correlated with protection from *S*. Typhi infection. Vaccine-specific levels of protection will be calculated upon completion of the vaccine trial in December 2016. Post-vaccination plasma and serum anti-Vi IgG titres were significantly correlated, with corresponding mean plasma titres 12% lower than in serum.

Conclusion: This project successfully optimised the VaccZyme™ Kit for anti-Vi IgA, IgM, and IgG_{1-3} quantification within a clinical trial context, for use as a possible correlate of protection. Furthermore, a correlation between serum and plasma anti-Vi IgG titres was demonstrated, suggesting that the kit may be suitable for use with plasma samples. Our findings bear relevance for teams seeking to investigate the humoral immune response to typhoid vaccination and challenge, with further potential applications in serosurveillance.