Quantification of antibody secreting cell responses in a human challenge model of Salmonella Typhi infection

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**Background:** Forty adult volunteers were recruited to a study of Salmonella Typhi (S. Typhi) infection in human volunteers. To determine the host response to infection, participants received a S.Typhi challenge dose of 1-5 x 103 or 1-5 x 104 colony forming units (CFU). The antibody secreting cell (ASC) response in infected individuals was studied to characterise the development of immunity following infection.

**Methods:** An enzyme-linked immunospot (ELISpot) assay was developed as a quantitative method to characterise the IgG, IgM and IgA response to S. Typhi O (LPS), capsular (Vi) and flagellar (H) antigens. Quantification was performed at baseline (day 0), day 7 and day 10 post challenge, and 48 hours following typhoid diagnosis (defined by bacteraemia or a persistent raised temperature). Spot forming cells were quantified and are presented as the number of antibody secreting cells per 106 PBMCs.

**Results:** Secretion of typhoid antigen-specific IgG, IgM and IgA from PBMCs was detected by ELISpot on day 7 and day 10 following challenge with S. Typhi. The results demonstrate a 6, 8 and 18-fold increase in specific ASC responses to O, Vi and H antigen respectively at the point of diagnosis of typhoid in individuals who met the case definition.

**Conclusion:** We describe a rapid ELISpot method for detecting typhoid antigen-specific B cell responses. The data acquired from study of these volunteers indicates the development of strong immune responses to important surface antigens of S. Typhi, in those who develop enteric fever.

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