Methods 27 healthy volunteers were randomly assigned to a vaccinated (n=14) or a control (n=13) group for Ty21a typhoid vaccine. Peripheral blood was collected from all volunteers prior to vaccination and 18 days following immunisation or recruitment. Mucosal samples (15 jumbo biopsies from duodenum (n=25) ± colon (n=18)) were collected from all volunteers at gastroscopy +/- sigmoidoscopy on day 18. Mononuclear cells were isolated from mucosal tissue by disruption and collagenase digestion, and from blood by centrifugation. Cells were stimulated with Ty21a or control antigens, and stained for surface phenotype and intracellular cytokine production. Antigen-specific IFN-γ, TNF-α, and IL-2 production was determined by flow cytometric analysis for CD8+/CD8+ and CD3+/CD8− (CD4+) lymphocytes. Humoural IgA, IgM and IgG responses in blood were examined in relation to mucosal and peripheral cellular responses.

Results Oral immunisation with Ty21a significantly increased the proportion of antigen-specific cytokine-producing CD8-positive (p<0.05) and CD8-negative (p<0.05) lymphocytes within the duodenal mucosa, but no specific response was seen in colon. CD8-negative lymphocytes within the duodenal mucosa adopted a significantly more poly-functional phenotype following vaccination, expressing 2 or 3 cytokines simultaneously, while in contrast antigen-specific cytokine-producing CD8-positive lymphocytes in the duodenal mucosa were mono-functional expressing a single cytokine. In blood, the proportion of antigen-specific cytokine-producing CD8-positive lymphocytes was increased (p<0.05) following oral vaccination, but there was no significant increase in cytokine-producing CD4-positive lymphocytes. Differences in functionality of antigen-specific cytokine responses were less marked in peripheral blood lymphocytes following vaccination.

Conclusion These data show an antigen-specific response in human gut mucosal lymphocytes following oral vaccination, and directly demonstrate different immune functionality of CD8-positive compared to CD8-negative mucosal lymphocytes. These responses were more informative than surrogate measurements in peripheral blood lymphocytes. The absence of a detectable cognate response from the colon may indicate compartmentalisation of the gut mucosal response to the embryological mid-gut, where typhoid antigen is likely presented at immune inductive sites.

Competing interests None declared.