POLYMERIC IgA ANTIBODY IN HUMANS AFTER VACCINATION AND IN DISEASE

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ABSTRACT

This thesis examines the relationship between antigen specific polymeric IgA (pIgA) antibody in serum and intestinal IgA antibody in humans.

The difficulties in assessing the human intestinal immune response, the requirement for a simpler method of indirectly assessing intestinal immunity and current knowledge regarding the origins of intestinal and serum IgA in humans are reviewed.

The development and validation of secretory component (SC) binding assays for antigen specific pIgA and total pIgA in human serum are described.

The relationship betwen pIgA antibody responses in serum and the IgA response in intestinal fluid was examined in normal subjects subject to oral vaccination with the live attenuated typhoid vaccine, Salmonella Ty21a and conventional parenteral typhoid vaccination. The serum pIgA response to oral typhoid vaccination and its relationship to the intestinal response was also examined in patients with alcoholic liver disease. In addition, antigen specific serum pIgA was examined in patients with a variety of disorders by looking for serum pIgA to gliadin in patients with Coeliac disease, to Escherichia coli lipopolysaccharide (E.coli LPS) in patients with alcoholic liver disease and Crohn's disease as well as to Campylobacter antigens in patients with Campylobacter enteritis. The immune response of a small sample of unselected patients with IgA nephropathy to oral typhoid vaccination was also investigated.

In normal subjects a short lived pIgA response to both oral and parenteral vaccination was detected whereas an intestinal immune response was only generated by delivery of an antigenic stimulus to the intestine. Levels of typhoid LPS-specific pIgA antibody related to total serum IgA antibody to typhoid LPS rather than intestinal anti-typhoid antibody.

Antigen specific serum pIgA was also detected in the patients with alcoholic liver disease but again there was no relationship to the levels of intestinal antibody. The SC binding assays were also successfully used to measure pIgA antibody in the other patient groups.

The main conclusion of the studies described in this thesis are that while a serum pIgA antibody response can be generated by delivery of an antigenic stimulus to the intestine there is no direct relationship between the level of the serum pIgA antibody and the antibody in the intestine. The regulation of serum pIgA and intestinal IgA appear to be independent.