



NSI Meeting Announcement

Date: Wednesday, November 8, 15:00 – 16:00

Venue: Rikshospitalet, Auditorium 1 (Green)

Guest lecture

by

Professor Per Brandtzæg

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“Secretary Immunity: Past, Present and Future”

Abstract

In 1961 Lars Å. Hanson (Göteborg) showed that breast milk IgA contains an antigenic epitope not present on serum IgA. Thomas B. Tomasi's (1965) work in Henry G. Kunkel's laboratory at the Rockefeller Institute (New York), resulted in the first physicochemical characterization of secretory IgA (SIgA). Its additional antigenic portion was identified as an epithelial ~80-kDa glycoprotein called 'secretory piece', now designated secretory component (SC).

In the late 1960s and early 1970s at least six models were suggested to explain how IgA could be selectively exported to external secretions as SIgA, but they all turned out to be wrong. Our laboratory published in 1973-74 that mucosal plasma cells produce dimeric IgA with a small associated peptide called joining (J) chain. In 1968 we had provided the first evidence that the large pentameric IgM molecule, like dimeric IgA, is also translocated to secretions by an active process. We then proposed that there must be a common epithelial transport mechanism for these two polymeric immunoglobulins, with SC acting as a transmembrane receptor. This was a unique biological concept based on collaboration between two different cell types to produce the hybrid SIgA and SIgM molecules. An important basis for this novel concept was the 'key-and-lock' function of membrane SC and J chain. Membrane SC (~100-kDa) is now usually referred to as the polymeric Ig receptor (pIgR).

The SIg system represents the most important antibody-dependent defence of the body. We have calculated that at least 80% of the body's antibody production takes place in the gut. In 1999 we generated a knockout mouse with deficient pIgR/SC. This strain has been exploited in many collaborative studies to learn how SIgA antibodies protect the mucosae and how homeostatic backup mechanisms develop to compensate for a defect barrier function when SIgA is lacking. SIgA antibodies function both by performing antigen exclusion and by virus and endotoxin neutralization within epithelial cells. SIgA is thus persistently containing commensal bacteria outside the epithelial barrier but can also target invasion of pathogens and penetration of harmful antigens.

The clinical importance of SIgA is highlighted by the fact that pathogens generally enter the host via the mucosae. Most of the about 40 000 children under 5 years of age dying every day, succumb from mucosal infections. In the developing world, the risk of dying from diarrhoea in infancy is 20 times higher without breast-feeding than with exclusive breast-feeding. Nevertheless, it has been difficult to exploit the SIg system for active immunization, although some effective mucosal vaccines have been approved for human use. Particularly the successful oral administration of attenuated live vaccines against poliovirus and rotavirus stimulates optimism for the future. Nasal vaccine administration may be advantageous for certain infections, and it also elicits systemic immunity. WHO and GAVI therefore show a keen interest in developing needle-free mass vaccination.

Refreshments will be served

Welcome all!



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