PIgR / IgA
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W.49. Neonatal Fc Receptor Dependent Acquisition of Allergic Protection

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The mechanism(s) responsible for the reduced risk of allergic disease in breastfed infants are not fully understood. Using a murine model of allergic airway disease (AAD) we demonstrated the ability of breast milk from allergic mothers to protect offspring from AAD is dependent on intact maternal B cell immunity (Breastfeeding Medicine; in press). Offspring nursed by wildtype ovalbumin (OVA)-immune foster mothers are protected from OVA-induced AAD; whereas, offspring nursed by B cell deficient OVA-immune foster mothers, are not. The aim of this study was to investigate the role of offspring FcRn in this maternally transferred protection. Naïve C57BL/6J-FcRn+/- or -FcRn-/- offspring were nursed by wildtype foster mothers with a history of Th2-type immunity to OVA. Levels of maternal OVA-specific antibodies absorbed from breast milk were determined in weanling FcRn+/+, FcRn+/-, or FcRn-/- mice. Interestingly, transfer of OVA-specific antibodies from mothers to breastfed offspring (irrespective of Ig isotype [IgG1, IgA, or IgE]) was dependent on offspring FcRn expression. Furthermore, when offspring were challenged, protection from OVA-induced AAD was dependent on offspring FcRn. Although maternal transfer of IgG is known to occur via FcRn, these data suggest FcRn expression promotes acquisition of other Ig isotypes and associated protective factors from breast milk.

W.50. Differential Distribution of PIgR in Mouse Organs

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Background and Aim: In spite of the relevance of the mouse as an experimental animal for immunological research, there is no specific monoclonal antibody (moAb) against mouse polymeric immunoglobulin receptor (mpIgR) molecule. Recently, we generated specific moAbs against mpIgR and the specificities and reactivities of them has been reported (Scand. J. Immunol., 2008, 68, 543–551). With these moAbs, we succesfully established ELISA system allowing the estimation of mpIgR and free secretory component (fSC), which is the extracellular part of the pIgR, in the biological samples. In the present study, we attempted to estimate the concentrations of mpIgR in the lysates of several mouse organs. Methods and Results: Eight-weeks old C57BL/6 mice and Sprague-Dawley rats were obtained from Clea Japan (Tokyo, Japan). The mice organs (small and large intestine, brain, kidney and liver) were obtained and lysates were prepared by Dounce's homogenizer. Total protein concentrations were estimated and 100 μg of total protein was applied to ELISA. The highest concentration of pIgR was detected in the lysate of the small intestine. Conclusions: These results indicated that pIgR molecule is differentially distributed along the intestinal tract and may suggest the regional differences of pIgR functions.

W.53. Induction of the Polymeric Immunoglobulin Receptor by Colonic Bacteria through TLR-dependent Activation of NF-kB

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Commensal bacteria signal through Toll-like receptors (TLRs) to enhance innate immune functions of intestinal epithelial cells (IECs). We found that stimulation of the HT-29 human IEC line with the commensal bacterium *E. coli* Nissle (EcN) induced expression of the polymeric immunoglobulin receptor (pIgR), the epithelial IgA transporter. However, induction of pro-inflammatory genes by EcN was significantly lower in HT-29 cells than in the THP-1 human monocyte cell-line. Whereas expression of TLR4 and MyD88 were similar in THP-1 and HT-29 cells, expression of TLR2 was 2000-fold higher in THP-1 cells. Importantly, expression of the TLR decoy receptor SIGIRR was higher in HT-29 cells. Induction of pro-inflammatory genes in HT-29 cells by EcN was transient, and was blocked by either NF-kB or MAPK inhibitors. By contrast, the slow and sustained induction of pIgR was blocked by NF-kB inhibitors but enhanced by MAPK inhibitors. We found that expression of pIgR was significantly reduced in the colons of MyD88-deficient mice, consistent with its regulation by TLR-mediated responses to commensal bacteria. We conclude that unique pathways of MyD88-dependent TLR signaling in IEC may promote intestinal homeostasis by inducing expression of protective molecules like pIgR while limiting expression of pro-inflammatory genes. Supported by NIH and CCFA.

W.54. Reactivity of Human Milk and Myeloma IgA to Various Bacteria

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Human milk IgA plays a crucial role in the defense of suckling newborns against environmental antigens (e.g. pathogens)

during the early postnatal immune system adjustment. Apart from the specific IgA - pathogen interactions, the antibody-independent pathway through the abundant glycan side-chains linked to the IgA molecules was described. Our aim was to determine which form of IgA is the most efficient in reacting with various commensal and pathogenic bacteria (e.g., *E. coli*, *B. distasonis*, *S. typhimurium*). Samples of whole colostrum (1–4 days postpatrum), of purified colostral IgA and of different myeloma IgA1 or IgA2 were evaluated by ELISA and FACS analysis for their capacity to bind various bacteria. Our results indicate that purified colostral IgA has the highest reactivity with most of bacteria tested when compared to the other IgA preparations. Interestingly, one myeloma IgA1 sample consisting of a mixture of polymeric and dimeric molecular forms exhibited a relatively high reactivity to bacteria. These results contribute to the understanding of the mechanisms by which human milk IgA exercises its antibacterial activity and protects infants against enteric infections.