UPPER RESPIRATORY TRACT
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W.69. IgA Levels in Nasal Washes from Immunodeficient Wistar Rats: Effects of Nasal Inoculation of Antigens

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Previous studies in our model of secondary immunodeficiency by immunohistochemistry on Nasopharynx-Associated Lymphoid Tissue and on isolated cells by cytometry have shown that CD5, CD4 and TCRαβ T cells were decreased but not IgA+ B cells. Rats protein deprived at weaning fed with 20% casein diet for 21 days (renourished group: R21) were compared simultaneously with well-nourished group (C60). The aim of the present study was to measure IgA levels in nasal washes from both groups, and from animals after intranasal instillation of OVA (C60-OVA and R21-OVA), and with IL-12 as adjuvant (C60-OVA-IL12 and R21-OVA-IL12). Antigen inoculation was performed directly on NALT at 0, 7, and 14 days, and nasal washes were obtained at day 21. IgA was measured with a commercial ELISA kit (Bethyl) and statistical analysis by ANOVA with Tukey-Kramer test. Results (ng/ml, X±SEM, C60: 9423±546; R21: 8915±979; C60-OVA: 6779±1733#; R21-OVA: 6821±994*; C60-OVA-IL12: 9769±988; R21-OVA-IL12: 12748±1161*# (*# $p<0.01$). Though significant differences were obtained between C60-OVA, R21-OVA and R21-OVA-IL12, only the difference between the last two groups is relevant. Therefore, IL-12 seems to act as adjuvant when co-administered with OVA in R21, probably due to permanent damage in the respiratory epithelium that allows IL-12 access to receptors on CD4+ T cells.

W.70. A Murine Model of Allergic Rhinitis with Sublingual Immunotherapy

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Sublingual immunotherapy (SLIT) has been considered to be a painless and efficacious therapeutic treatment for allergic rhinitis which is known as type-I allergy of nasal mucosa in a large number of clinical and basic trials. Putative immunological mechanisms of SLIT are induction of neutralizing antibodies with decrease in IgE/IgG4 ratio and/or induction of antigen-specific regulatory T cells (Tregs), however those remain controversial. Indeed, the amount of allergen needed in SLIT is 50 to 100 times more than that in subcutaneous desensitization. In this study, we constructed an efficient murine model of allergic rhinitis with sublingual immunotherapy, in which mice were sublingually administered with ovalbumin (OVA) followed by intraperitoneal sensitization and nasal challenge of OVA. Sublingually treated mice showed significantly decreased allergic responses as well as suppressed Th2 immune responses. Sublingual administration of OVA did not alter the population of $CD4^+CD25^+$ Tregs, but lead to up-regulation of Foxp3- and IL-10-specific mRNAs in lymphocytes of cervical lymph node (CLN). It was suggested that CLN cells were involved in the regulation of allergic responses possibly by the induction of Tregs and immunosuppressive cytokines in mice sublingually treated with antigen.

W.72. Murine Nasal Inductive and Effector Sites During Homeostasis and Group A Streptococcus Infection

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The nasal mucosa is the first site of contact for inhaled antigens and a critical site for host defense against pathogens. In rodents, the nasal-associated lymphoid tissue (NALT) is analogous to Waldeyer's ring in humans. The aim of this work was to further characterize the phenotypic and functional lymphocyte populations of NALT (inductive site) and nasal passages (NP, effector site) during homeostasis and infection with Group A streptococcus (GAS). BALB/c mice were given ~2 X 10^6 DO11.10 transgenic OVA-specific CD4 T cells via lateral tail vein. At various times post-transfer, NALT, NP, cervical lymph nodes (CLN) and spleen were harvested and analyzed by flow cytometry. In some experiments, animals were infected intranasally with PBS or 2.5 - 3 X 10^8 CFU Ova-expressing GAS. The low expression of CD62L in the NP is consistent with NP as an effector site. In naive mice, DO11.10 T cells were undetectable in the NP, but were seen in all 3 secondary lymphoid structures examined. Upon infection, only DO11.10 cells which had undergone a few rounds of division were detected in the nasal passage. Upon restimulation (*in vitro* and *in vivo*), DO11.10 T cells produced IL-2. Additionally, experiments supported a role for CD4 T cells in protective immunity to GAS.

W.73. The Unique Structure of the Palatine Tonsil of the Camel

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In the mouth and pharynx tonsils form a first line of defense against foreign antigens. The microanatomy of the palatine tonsils of the one humped camel is largely unknown. Palatine tonsils of 10 healthy adult male camels were obtained directly after slaughtering. The tonsils were examined macroscopically and by light, scanning and transmission electron microscopy. Palatine tonsils had the unique form of several spherical macroscopic nodules protruding into the pharyngeal lumen. These masses were numerous and close together in the lateral oropharyngeal wall, with a few solitary nodules in the dorsal wall. Each nodule had one or two apical openings to crypts, and was enclosed by an incomplete connective tissue capsule. The tonsillar crypt was lined with stratified squamous non keratinized epithelium. Several lymphocytes infiltrated the epithelial layer, forming patches of reticular epithelium. Lymphoid follicles with obvious germinal centers extended under the epithelial surface. Diffusely localized lymphocytes were seen in the interfollicular region. High endothelial venules, dendritic cells, macrophages and plasma cells

were observed among these lymphocytes. The unique arrangement of palatine tonsils in separate units with individual crypts results in a very large surface exposed to antigen and indicates a significant immunological role of palatine tonsils in the camel.

W.74. Expression of Toll-like Receptors in Human Nasal Polyps

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Nasal polyps (NP) represent a chronic and recurrent inflammatory affection of nasal mucosa (NM) but little is known about their etiopathogenesis. Our hypothesis is that chronic stimulation of innate immune mechanisms at the level of nasal mucosa may contribute to the development of NP in predisposed individuals. Toll-like receptors (TLR) represent key innate immune receptors that recognize various non-self as well as self "danger signaling" antigens. In this study we investigated expression of TLR1-10 in human NP and non-affected human NM in both intraepithelial and lamina propria compartments. Biopsies of NP were obtained from 17 patients with NP and 3 patients with NP and aspirin intolerance, whereas mucosal biopsy specimens of the inferior turbinate were obtained from the same NP patients (n=11) as well as from 3 healthy controls. Using indirect immunohistochemistry, frozen tissue sections were stained for TLR1-10. Number of infiltrating cells expressing TLR3, TLR4, and TLR5 were significantly higher in biopsies of NP compared to NM. Similarly, quantitative evaluation detected substantial differences in numbers of TLR7, TLR8, TLR9, and TLR10 positive cells in NP. Interestingly, TLR4 showed abundant expression in epithelium of NP, while we did not detect any positivity of TLR4 in epithelium of NM. Remarkable number of TLR3 expressing cells in epithelium was also found in NP and not in NM biopsies. No difference in expression of TLR1, TLR2, and TLR6 were found in NP compared to NM specimens and no significant differences were found between NP patients with and without aspirin intolerance. Increased expression of selected TLRs maybe relevant not only to inflammatory pathogenesis of nasal polyps but also to possible environmental agents involved in the etiology of the disease.

W.75. Analysis of NKp46+ Cells in Nasopharynx-associated Lymphoid Tissue (NALT) and Nasal Cavity

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NKp46 (CD335) is a newly identified surface marker expressed on Natural Killer (NK) cells. Expression of NKp46 is uniquely found on NK cells from immature to mature stage, and not found on Natural Killer T (NKT) cells. Recently some groups reported about gut NKp46+CD3- cells. Unlike other regions, mucosal NKp46+CD3- cells do not possess characteristics of NK cells, such as cytotoxicity nor interferon production. Instead they control gut mucosal immunity through production of IL-22. Here we would like to report about NKp46+ cells in Nasopharynx-Associated Lymphoid Tissue(NALT) and nasal cavity, we have recently identified. This is a quite unique population for its surface marker expression and cellular functions.

W.76. Immunoglobulin D Enhances Immune Surveillance by Activating Antimicrobial and Immunostimulating Programs in Basophils

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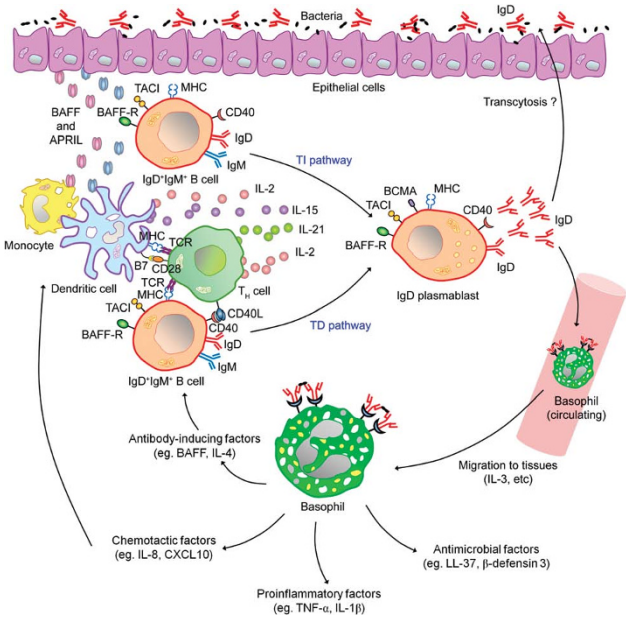

Immunoglobulin D (IgD) is an enigmatic antibody isotype that B cells co-express with IgM through alternative RNA splicing. We found active IgM-to-IgD class switch DNA recombination in B cells from the upper respiratory tract. This process required activation-induced cytidine deaminase, occurred through T cell-dependent and T cell-independent pathways, and generated IgD-secreting plasmablasts reactive to respiratory bacteria. Secreted IgD bound to circulating basophils through a calcium-mobilizing receptor that induced antimicrobial and immunostimulating factors including cathelicidin, interleukin-1 and interleukin-4 upon IgD cross-linking. By showing dysregulation of IgD-armed basophils in autoinflammatory syndromes, our data indicate that IgD orchestrates an ancestral surveillance system at the interface between immunity and inflammation.