(e.g. macrophages) that recruit neutrophils to the lung. Furthermore, the attachment of HA to neutrophils migrating to the lung may reduce their adhesion to the extracellular matrix and facilitate their influx into alveolar spaces.

1039 MOUSE STRAIN DIFFERENCES IN BERYLLIUM HYPERSENSITIVITY

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Due to its unique physico-chemical properties, beryllium (Be) is an indispensable metal for many national defense programs in aerospace, electronics, and weaponry. Exposure to beryllium is an occupational hazard that can cause chronic beryllium disease (CBD), an irreversible, debilitating granulomatous lung disease, in as many as 3-5% of exposed workers. CBD begins as an MHC Class II-restricted, Th1 hypersensitivity, and the Human Leukocyte Antigen, *HLA-DPB1 E*^{69}, is associated with risk of developing CBD. Previously, we found that mice with the human *HLA-DPB1*1701* transgene, which in humans is correlated with increased risk of development of CBD, had an increased hypersensitivity response over their control counterparts. We employed the mouse ear swelling test to determine if different inbred mouse strains (AKR, Balb/c, C3H/HeJ, C57/BL6, DBA/2, FVB/N and SJL/J) would display varying hypersensitivity responses to beryllium. In two separate experiments, mice were placed into either group: control/control (skin sensitized with vehicle and challenged with vehicle) or Be/Be (skin sensitized with beryllium sulfate and challenged with beryllium sulfate). Beryllium sensitized and challenged Balb/c, C57/BL6, DBA/2, and SJL/J strains had significant ($p<0.001$) ear swelling over their control counterparts. The FVB/N and C3H/HeJ strains, however, had small but not statistically significant increases in ear thickness. This indicates that there may be genes that modulate the augmentation of the beryllium hypersensitivity response by the *HLA-DPB1 E*^{69} genotype. Uncovering the genes responsible for the hypersensitive phenotype in mice may prove useful in learning more about the mechanisms involved in chronic beryllium disease.

1040 MATERNAL ALLERGIC PHENOTYPE IMPACTS ALLERGIC RESPONSES OF OFFSPRING

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Epidemiological evidence supports non-genetic maternal influence on allergy development in offspring. Using established mouse allergy/asthma models, we tested the hypothesis that maternal allergic phenotype impacts the development of allergic responses in offspring. Four maternal cohorts were established. 1) Allergic-Ovalbumin (OVA) in alum injected intraperitoneally (IP); 2) Tolerant- OVA aerosol exposure; 3) Procedural controls-IP/aerosol saline treatments 4) Naïve controls no treatments. Subsequently, allergic, tolerant and procedural control phenotype dams received 10-day OVA or saline aerosol during gestation (naïve controls were not treated). Dams and litters of all groups were sampled at term (19-21 days of gestation) and at weaning. One half of the remaining offspring from all groups received 10 days of OVA aerosol at 4-5 weeks of age. Half of these animals were sampled at 6 weeks of age. Previously unexposed offspring and the remaining exposed offspring received OVA aerosol at 10-11 weeks of age. Offspring were sampled at 12 weeks of age. Three maternal phenotypes were identified (no significant differences between control and naïve dams). Immune and inflammatory characteristics of the established maternal phenotypes persisted unchanged through time, repetitive challenges, and multiple pregnancies. Offspring demonstrated no differences related to gender or number of exposures. Offspring from allergic dams produced significantly higher levels of OVA-specific IgG1 and IgG2a isotypes compared to offspring of tolerant, control, and naïve dams. IgE levels and inflammatory histopathology tended to be more pronounced in offspring of tolerant, control, or naïve dams than in the offspring of allergic dams. Thus, maternal allergic phenotype influences development of allergic responses in offspring.

1041 MORPHOMETRIC CHARACTERIZATION OF INFLUENZA-INDUCED EPITHELIAL INJURY, REGENERATION, AND MUCOUS CELL METAPLASIA WITH CORRELATION TO INFLAMMATORY CELL INFILTRATE IN THE PULMONARY AIRWAYS OF C57BL/6J MICE

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The present study was designed to determine the kinetics of airway epithelial injury and remodeling in the pulmonary airways of C57BL/6J mice after infection with influenza virus A/PR/8/34 (PR8). Mice were intranasally instilled with 50 plaque forming units (pfu) of virus or its respective vehicle, saline. Animals were sacrificed at 3, 7, 10, 15, or 21 days post-infection (DPI). Lungs were lavaged with saline to collect bronchoalveolar lavage fluid (BALF), then formalin fixed for immunohistochemical analysis. Total and differential cell counts were performed on the BALF. Peak inflammatory cell infiltrates occurred at 10 DPI. The early inflammatory response was marked by the presence of neutrophils at 3 and 7 DPI with an adaptive immune response consisting of lymphocytes at 7,10, and 15 DPI. Using image analysis and standard morphometric techniques, airway epithelial cell densities and volume densities of intraepithelial mucosubstances (Vs) were determined at generation 5 of the left lung lobe. Influenza treatment resulted in significant airway epithelial cell apoptosis (Caspase-3 + staining) at 7 DPI, with regeneration (PCNA + staining) at 10 DPI. Viral-induced mucous cell metaplasia (MCM) was evident at 10, 15, and 21 DPI. The results of this study indicate that the onset of MCM immediately follows viral-induced apoptosis and occurs during and after regeneration of airway epithelium. The role of neutrophil and lymphocyte-derived inflammatory mediators in the development of viral-induced MCM is yet to be determined. In addition, these studies serve as a starting point from which to ascertain the role of immune suppressive compounds such as delta9-tetrahydrocannbinol in mediating the clearance of PR8 and modulating epithelial changes. (Supported by The MSU Foundation NIH grant DA07908).

1042 PRE-EXPOSURE TO ZYMOSAN ENHANCES LUNG DEFENSE MECHANISMS AND ACCELERATES THE PULMONARY CLEARANCE OF A BACTERIAL PATHOGEN IN RATS

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Although bacteria and fungi are common etiological agents which are known to induce pulmonary inflammation, complicated interactions may exist when the lungs are exposed to both concurrently. The objective of the present investigation was to determine the effects of pre-exposure to zymosan (a 1->3-β-glucan from baker yeast) on bacterial (Listeria monocytogenes) infection in male Sprague-Dawley rats. On day 0, rats received a single dose of zymosan A (2.5 mg/kg body weight) via intratracheal instillation or vehicle control (saline). On day 3, rats were intratracheally inoculated with 5x105 bacteria, and bacterial clearance was determined by measuring colony-forming units cultured from the left lungs. Rats were euthanized on days 6, 8, and 10, and bronchoalveolar lavage (BAL) was performed on the right lungs. Inflammation and lung injury were assessed by measuring (1) neutrophil (PMN) infiltration and (2) albumin, total protein and lactate dehydrogenase levels in BAL fluid. Alveolar macrophage activation was determined by chemiluminescence. Immune response was assessed by immunophenotyping of lymphocytes and lymphokine production. Immunophenotyping was performed on BAL cells and lung-associated lymph node cells. Lymphokine production was measured using lymph node cells treated with or without concanavalin A stimulation. Zymosan pre-exposure accelerated the clearance of the bacteria from the lungs compared to the control group. Zymosan-treated rats also had a smaller PMN infiltration in the lung compared to control, however, a greater number of lymphocytes was present in lymph nodes of the rats. Lung injury parameters were lower in zymosan-treated rats at days 6 and 8. Activation of macrophages recovered from zymosan-treated rats was elevated at day 6 compared to control. These results strongly suggest that pre-exposure to zymosan enhances the lung immune response and attenuates pulmonary infection in rats.

1043 RADIATION-INDUCED PULMONARY FIBROSIS: EFFECT OF THE COMBINED ACTION OF EXTERNAL RADIATION AND CERIUM-144 ON THE DEVELOPMENT OF FIBROUS PROCESS IN THE RATS LUNG

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The biological effects of combined action of inhaled beta-particle-emitting radionuclides and external radiation are not well known. The nonneoplastic diseases induced by an inhaled, relatively insoluble form of cerium-144, are related with the development of fibrous process. Fibrosis is the formation or development of excess fibrous connective tissue in an organ or tissue as a reparative or reactive process, as opposed to formation of fibrous tissue as a normal constituent of an organ or tissue. Pulmonary fibrosis has unusual amino acid composition. It contents large amounts of proline, as well as two amino acids hydroxyproline and hydroxylisine. An investigation was carried out on the effect of the combined action with gamma-rays and incorporation of cerium-144 on the development of fibrous process in the lungs of rats. One dose external radiation and 3 different activities Ce-144 were applied. In the first step of the present experiment adult male Wistar rats (30/group) were

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Preface

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An alphabetical Author Index, cross referencing the corresponding abstract number(s), begins on page 500.

The issue also contains a Keyword Index (by subject or chemical) of all the presentations, beginning on page 534.

The abstracts are reproduced as accepted by the Program Committee of the Society of Toxicology and appear in numerical sequence.

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