PS 416 Exposure to Triclosan Augments the Allergic Response to Ovalbumin in a Mouse Model of Asthma.

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During the last decade there has been a remarkable and unexplained increase in the prevalence of asthma. These studies were conducted to investigate the role of dermal exposure to triclosan, an endocrine-disrupting compound, on the hypersensitivity response to ovalbumin (OVA) in a murine model of asthma. Triclosan has had widespread use in the general population as an antibacterial and antifungal agent and is commonly found in consumer products such as soaps, deodorants, toothpastes, shaving creams, mouth washes, and cleaning supplies. For these studies, BALB/c mice were exposed dermally to concentrations of triclosan ranging from 0.75-3% (0.375-1.5 mg/mouse/day) for 28 consecutive days. Concordantly, mice were intraperitoneally injected with OVA (0.9 ug) and aluminum hydroxide (0.5 mg) on days 1 and 10 and challenged with OVA (125 ug) by pharyngeal aspiration on days 19 and 27. Compared to the animals exposed to OVA alone, increased spleen weights, OVA-specific IgE, Interleukin (IL)-13 cytokine levels, and lung eosinophils were demonstrated when mice were co-exposed to OVA and triclosan. Statistically significant increases in OVA-specific and non-specific airway hyperreactivity (AHR) were observed for all triclosan co-exposed groups when compared to the vehicle and OVA controls. In these studies exposure to triclosan alone was not demonstrated to be allergenic, however co-exposure with a known allergen resulted in enhancement of the hypersensitivity response to that allergen, suggesting that triclosan exposure may augment the allergic responses to other environmental allergens.

PS 417 Oral Exposure to Genistin but Not Daidzein Increased Natutal Killer (NK) Cell Activity in Female B6C3F1 Mice.

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Genistin (GIN), the glycoside form of phytoestrogen genistein (GEN), is the predominant isoflavone found in soy products. The objective of this study was to determine if exposure to GIN (2, 6 or 20 mg/kg) by daily gavage for 28 days modulated immune responses in female B6C3F1 mice in comparison with daidzein (DAZ), another soy isoflavone. There were no significant changes in the body weight and absolute weights of thymus, spleen, lungs, kidneys, or liver in either GIN or DAZ-treated mice. However, exposure to GIN increased relative kidney weight (20 mg/kg: 11%). In contrast, exposure to DAZ decreased relative spleen weight (2 mg/kg: 21%; 6 mg/kg: 24%; 20 mg/kg: 24%), relative kidney weight (6 mg/kg: 15%), relative liver weight (6 mg/kg: 14%; 20 mg/kg: 14%;), and relative lung weight (20 mg/kg: 24%). In the thymus, GIN exposure increased the percentages of CD4+CD8+ cells (2 mg/kg: 22%; 20 mg/kg: 26%) and CD44-CD25- cells (20 mg/kg: 5%) but decreased the percentages of CD4+CD8- cells (20 mg/kg: 28%), CD4-CD8- cells (2 mg/kg: 41%; 20 mg/kg: 41%), and CD44-CD25+ cells (20 mg/kg: 53%). Exposure to DAZ increased the percentages of CD44-CD25- cells (2 mg/kg: 5%) while decreased that of CD4+CD8- cells (2 mg/kg: 30%), CD44+CD25+ cells (2 mg/kg: 51%), and CD44-CD25+ cells (2 mg/kg: 71%; 6 mg/kg: 45%; 20 mg/kg: 43%). In the spleen, GIN exposure increased the percentages of NK cells (20 mg/kg: 86%), T cells (20 mg/kg: 74%), and neutrophils (2 mg/kg: 148%) while DAZ exposure increased the percentages of T cells (20 mg/kg: 112%), CD4+ T cells (20 mg/kg: 58%), CD8+ T cells (6 mg/kg: 69%; 20 mg/kg: 133%) but decreased the percentage of neutrophils (20 mg/kg: 48%). In correlation with observed increased %NK cells, exposure to GIN but not DAZ increased NK cell activity. Taken together, the differential effects of GIN and DAZ suggest that both the estrogenic and non-estrogenic properties of these compounds contribute to their immunomodulatory roles (Supported in part by NIEHS contract NO1-ES05454).

PS 418 Neural Autoimmunity and Low-Level Mercury Exposure.

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Multiple Sclerosis (MS) is an autoimmune disease of the central nervous system (CNS) involving demyelination; the mechanism of disease pathology involves stimulated auto-reactive T cells that are elicited against myelin proteins and primarily strikes more women than men. Mercury (Hg), a heavy metal found in many consumer products and as an environmental contaminant, affects the immune system, although there is little data linking low-level Hg exposure to the development of autoimmunity. Contrarily, high-level Hg exposure has proven to be toxic to the human CNS, specifically on neurons and glial cells. Since glial cells are CNS-resident immune lineage cells, we hypothesized that low-level Hg pre-exposure will increase neural autoimmunity in the animal model of MS, experimental autoimmune encephalomyelitis (EAE), induced with myelin oligodendrocyte glycoprotein (MOG). Adult C57BL/6 male mice were first pre-treated with $HgCl_2$ or PBS every other day by subcutaneous injection for 2 weeks pre-disease induction, then divided into 3 groups: (1) Hg only, (2) disease (MOG_{35-55} peptide) only, and (3) Hg+ disease. Clinical scores were recorded daily until day 25 when mice were euthanized. Brain, spinal cord, and spleen tissues were collected and analyzed for 9 cytokines (pro- & anti-inflammatory) using a multiplex assay. Hg alone raised levels of both pro-inflammatory and anti-inflammatory cytokines in the spinal cord; however, in diseased animals, Hg did not have the same effects and only increased IFN-γ in the brain. Low-level Hg alone is insufficient to prompt disease in males but exposure does upregulate cytokine levels in the CNS (IFN-γ) when disease is present. These data indicate that low-dose Hg interacts with components of the CNS milieu, specifically cytokine-producing cells of the immune system. Future studies will focus on exploring sex-specific effects of disease severity with Hg pretreatment in female mice of the same animal model.

PS 419 Modulation of HIV_{GP120}-Specific T Cell Responses by Δ^9-Tetrahydrocannabinol *In Vitro* and *In Vivo*.

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Approximately 25% of HIV patients use marijuana for its putative therapeutic benefit; however, it is unknown how cannabinoids affect the immune status of immunocompromised HIV patients. A surrogate *in vitro* mouse model was established to investigate the effects of cannabinoids on the early stages of the anti-HIV response. Specifically, T cell responses to HIV_{gp120} were induced using gp120-expressing antigen presenting cells and target cells. $CD8^+$ T cell proliferation and gp120-specific IFNγ production were observed, which was suppressed or enhanced by Δ^9-tetrahydrocannabinol (THC), the predominant psychoactive compound in marijuana, depending on the magnitude of cellular activation. To further determine the molecular mechanisms by which THC differentially modulates T cell responses, PMA/ionomycin (Io) or anti-CD3/CD28 were used as stimuli. THC suppressed or enhanced IFNγ or IL-2 production under optimal or suboptimal activation, respectively, but increased intracellular Ca^{2+}, regardless of the activation levels, suggesting that appropriate or excessive Ca^{2+} affected T cell activation differentially. To determine whether THC has similar effects *in vivo*, a mouse model to stimulate HIV_{gp120}-specific response has also been established. Vector plasmid VRC2000 or gp120-expressing plasmid VRC_{gp120} was injected intramuscularly into mice. The gp120-specific IFNγ response was detected by ELISPOT, when splenocytes were restimulated with the pool of gp120-derived peptides 81-84, which were identified as the putative immunodominant ones among 211 tested peptides. The THC effect on the gp120-specific response *in vivo* will be characterized. Overall, our data will provide in-depth understanding of cannabinoid effects on HIV antigen-specific T cell responses *in vitro* and *in vivo*. (Supported by NIH DA07908)

PS 420 Cannabinoid Enhancement of Humoral Immunity in CB_1/CB_2 Null Mice Is Correlated with Enhanced Splenic Norepinephrine (NE) Concentration.

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Cannabinoid compounds, such as Δ^9-tetrahydrocannabinol (THC), are immune suppressive as evidenced, in part, by their ability to inhibit T cell-dependent B cell responses. In response to sheep erythrocytes, THC suppresses immunoglobulin M (IgM) antibody production in a cannabinoid receptor (CB) 1 and/or CB2-dependent manner. Moreover, previous studies demonstrated that the magnitude of IgM production in response to sheep erythrocytes was higher in CB1/CB2 null mice as compared to wild type mice, suggesting endogenous cannabinoid control of humoral immunity. Thus, the focus of the present studies was to determine the mechanisms by which cannabinoids regulate humoral immunity. A direct comparison of female and male wild type and CB1/CB2 null mice demonstrated that CB1/CB2 null mice produce more circulating IgM and IgG, even in the absence of immune

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