cantly increased. In addition, 2-hydroxyiminostilbene, which is the metabolite of carbamazepine, activated inflammasomes of THP-1 cells. THP-1 cells whose inflammasome is activated increase high mobility group box 1 protein. These results support the hypothesis that the reactive iminoquinone metabolite can directly activate inflammasomes or it can cause the release of DAMPs from hepatocytes, which in turn, can activate inflammasomes. Inflammasome activation may be an important step in the activation of the immune system by carbamazepine, which in some patients can lead to hypersensitivity reactions.

1825 Potential Therapeutic Effects of Andrographolide in Attenuating Gut-Brain Inflammatory Surge in a Mouse Model of Gulf-War Illness

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Gulf war illness (GWI) is a chronic multisymptomatic disorder, which includes metabolic syndrome, gastrointestinal (GI) disturbances and neuroinflammation, that persists till date in affected veterans. Previously we reported that butyrate administration in mice with GWI decreased metabolic abnormalities and other GWI-associated symptoms. Most recently we found that a broad-spectrum antiviral drug has potent anti-inflammatory effects on GWI pathology. Andrographolide (AG), a labdane diterpenoid produced by the plant *Andrographis paniculata*, have a broad range of anti-inflammatory properties in various cell types. Currently, our lab studies the role of AG in combating gut and brain inflammation in GWI murine models. AG was selected based on its various beneficial effects which are crucial to overcome some of the toxicity associated with prolonged use of antiviral drugs. Adult C57BL/6J mice were exposed to GWI chemicals Pyridostigmine bromide and Permethrin for a week (GWT group) and treated with AG and Ribavirin (RB). Our results showed decreased expression of tight junction proteins Zona Occludin 1 (ZO1), Occludin, which significantly decreased in mice treated with AG alone or together with RB. Also, increased expression of Claudin-2 was observed, which is a signature of "leaky gut" in GWT models. Pro-inflammatory cytokine MCP1 expression was markedly decreased with RB, AG and combination of both in small intestine. These results indicate that AG alone or together with RB can provide increased protection from gut leaching in GWI mice model. Furthermore, our results showed that AG either individually or with RB significantly decreased the levels of CD11b, while increasing the levels of BDNF and blood brain barrier tight junction protein Claudin-5. This result clearly indicates that AG either singly or in combination had a significant impact in decreasing gut-associated inflammation and neurotoxicity and can be proposed as a potential therapeutic agent in GWI patients. *This study was supported by DoD Grant W81XWH1810374 and VA Merit Award I01CX001923-01 to S.C.*

1826 Single Cell Transcriptomics Reveals TCDD-Mediated Decrease in Gene Expression Associated with Erythropoiesis and Ribosomal Proteins in Early Phase of Human B Lymphopoiesis

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Persistent aryl hydrocarbon receptor (AHR) activation impairs B cell development by mechanisms not fully understood. Single cell RNA-Sequencing (scRNA-Seq) was employed to study the effect of AHR activation by 1 nM 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) on early stages (7 days of culture) of B lymphocyte development. An *in vitro* culture system supplemented with cytokines that drive B cell development from human cord blood derived $CD34^+$ hematopoietic stem and progenitor cells (HSPCs) was used. The objective was to determine how TCDD treatment modulates gene expression in differentiating HSPCs and to identify cellular transcriptomic heterogeneity. Using machine learning algorithms, we identified distinct cellular clusters in the scRNA-Seq dataset characterized by unique gene expression patterns, defined in part by expression of the AHR transcriptional target *CYP1B1*. *CYP1B1* induction was 2-fold higher in TCDD treated vs vehicle (VH; 0.02% DMSO) group, but not all TCDD treated cells expressed *CYP1B1*, indicating cellular transcriptional heterogeneity. Interestingly, *CYP1B1* expression was observed in 30% of the cells in VH group, suggesting endogenous AHR activation. Cells with higher *CYP1B1* expression in both treatment groups were associated with higher (>3.5 fold) expression of *CD14*, suggesting CD14 as a surface marker for high *CYP1B1* expression. In total, 90 genes were differentially regulated (log fold change difference > 0.25, p value < 0.01) by TCDD treatment. TCDD downregulated ribosomal protein encoding genes (11) and genes associated with erythropoiesis including drastic reductions in *HBD*, *HBB* and *HBG2*. Irrespective of treatment, most cells expressing genes associated with erythropoiesis and ribosomal proteins expressed 4-fold lower *CYP1B1* induction, suggesting that AHR activity is antagonistic to expression of these genes. This study demonstrates the presence of AHR activity in differentiating HSPCs, allows characterization of cells that are heterogeneous in AHR activity, and shows that genes associated with erythropoiesis and ribosome formation are suppressed by AHR activation early during B cell development. Further time course studies using scRNA-Seq will elucidate TCDD's effect on the cellular developmental trajectory from HSPCs to B cells.

1827 Alterations in the Mouse Skin and Gut Microbiome and Skin Integrity following Dermal Exposure to the Antimicrobial Chemical Triclosan

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It is increasingly being recognized that the microbiome plays an important role in human health. Dysbiosis of the microbiome has been shown to alter immune responses and has been associated with increased risk of allergic disease. Triclosan is an antimicrobial chemical used in the healthcare field as a high level disinfectant. In humans, triclosan exposure has been associated with an increase in food and aeroallergy and asthma exacerbation. Although not directly sensitizing, dermal exposure to triclosan has been shown to augment allergic responses to experimental allergens in mouse models. However, the impact of dermal exposure to antimicrobials, such as triclosan, on the microbiome and skin integrity is unknown. This study investigated the impact of dermal exposure to triclosan on the skin and gut microbiome and on the skin integrity in mice. Mice were dermally exposed to 2% or 3% triclosan or acetone vehicle control once daily for either 7 or 28 consecutive days. Swabs were used to collect skin commensal bacteria prior to exposure and over the course of the exposure period. Following the final triclosan exposure, skin was collected to assess expression of skin integrity genes and fecal pellets were collected to assess gut commensal bacteria. Following bacterial DNA extraction from skin swabs and fecal pellets, composition of the skin and gut microbiota was determined by 16S rRNA gene sequencing. Triclosan exposure decreased the relative abundance of Proteobacteria and increased the abundance of Firmicutes, specifically the families Lachnospiraceae and Ruminococcaceae, on the skin. Triclosan exposure also led to increased abundance of Lactobacillaceae in the gut. Seven days of triclosan exposure altered the expression of two skin integrity genes, filaggrin 2 and keratin 14, in the skin. Taken together, dermal exposure to triclosan altered the composition of commensal bacteria in both the skin and gut of mice and altered the expression of skin integrity genes, suggesting that triclosan can both induce dysbiosis of the microbiome and alter skin integrity and that this may contribute to the observed alternations in immune function.

1828 Effects of THC and CBD Treatment on IL-1β Secretion in TLR7- and TLR8-Stimulated Monocytes from HIV-Negative and HIV-Positive Subjects

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Δ^9-tetrahydrocannabinol (THC) and cannabidiol (CBD) are two immune modulating cannabinoids present in *Cannabis sativa*. THC is the primary psychotropic constituent, acting on CB1 receptors in the central nervous system and CB1 and CB2 receptors on immune cells. CBD, is non-psychotropic and possesses low affinity for both CB1 and CB2 receptors. The primary molecular target by which CBD mediates biological activity has yet to be identified. Cannabis is commonly used by human immunodeficiency virus (HIV)-infected individuals, with a prevalence of about half of those afflicted. Previous research has shown that THC and CBD can have immunosuppressive and anti-inflammatory properties. Here we report on the immune modulating activity of THC and CBD in activated monocytes, when stimulated through various toll-like receptor (TLR) pathways. The objective of this study was to determine the effects of THC and CBD on monocyte IL-1β secretion in HIV- and HIV+ individuals when activated through TLR7 and TLR8 pathways. When activated through TLR7 by R837, monocytes isolated from HIV- and HIV+ donors showed similar IL-1β secretion profiles. THC treatment in combination with R837 resulted in a concentration-dependent decrease in monocyte IL-1β secretion, while CBD augmented secretion. Stimulation through TLR8 by ssRNA40, also showed a concentration-dependent decrease in IL-1β secretion from monocytes isolated from both HIV- and HIV+ donors. Interestingly, CBD

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Preface

This issue is devoted to the abstracts of the presentations for the Continuing Education courses and Scientific Sessions of the 59th Annual Meeting of the Society of Toxicology, held at the Anaheim Convention Center, Anaheim, California, March 15–19, 2020.

An alphabetical Author Index, cross-referencing the corresponding abstract number(s), begins on page 542.

The issue also contains a Keyword Index (by subject or chemical) of all the presentations, beginning on page 580.

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