Further experiments are in progress to define the role of FOXO3a and FOXO1 in CSE-induced inflammation and autophagy. Overall, our results will provide important information about the therapeutic targets for the management of CS-induced inflammation/pathologies.

PS 3191 Cigarette Smoke Exposure Exacerbated Silica-Induced Pulmonary Toxicity

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Smoking, an avoidable life style factor, may modify the lung response to silica exposure including cancer and silicosis. Studies have shown that smoking induces oxidative stress and inflammation, etiological factors involved in the development and progression of cancer and silicosis. Nevertheless, the precise role of cigarette smoke (CS) exposure on the lung response to silica exposure and the underlying mechanisms are unclear. Therefore, the objectives of the present study were to determine the role of CS on lung response to silica exposure and the underlying mechanism. Male Fischer 344 rats were exposed by inhalation to air, crystalline silica (15 mg/m^3, 6 hrs/day, 5 days), CS (80 mg/m^3, 3 hrs/day, twice weekly, 6 months), or silica (15 mg/m^3, 6 hrs/day, 5 days) followed by CS (80 mg/m^3, 3 hrs/day, twice weekly, 6 months). The rats were euthanized 6 months following initiation of the exposures and lung response parameters including, lactate dehydrogenase (LDH) activity, oxidant production, cell counts, and cytokines in broncho-alveolar lavage (BAL) were assessed. Silica exposure resulted in significant lung toxicity as evidenced by lung histological changes, enhanced neutrophil infiltration, increased LDH levels, enhanced oxidant production, and increased cytokine levels. The CS exposure had only a minimal effect on the toxicity parameters. However, the combined exposure to silica and CS caused a significant increase in lung response, compared to silica or CS exposure alone. For example, CS or silica exposure alone resulted in neutrophil infiltration 5 and 150 times, respectively, compared to the air-exposed controls. The combined exposure to silica plus CS, on the other hand, caused a neutrophil infiltration that was 500 times higher compared to air controls suggesting a synergistic effect of silica and CS on lung toxicity. Global gene expression changes detected in the rat lungs correlated with the toxicity. Bioinformatic analysis of the gene expression data demonstrated significant enrichment in functions and pathways relevant to silica exposure which correlated with the lung toxicity. Unique pathways relevant to lung response to silica exposure, for example disruption of circadian rhythm signaling, were detected in the rat lungs exposed to silica and CS. Collectively our data demonstrated an exacerbation of silica-induced lung toxicity by CS exposure and the molecular mechanisms underlying the exacerbated toxicity.

PS 3192 Bioinformatics Approach Unravels Toxic Effects of Waterpipe Tobacco Smoking

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Waterpipe tobacco smoking (WTS), in Middle East known as shisha or narghile, is becoming more popular in Western societies, particularly among young people as an alternative form of tobacco use other than traditional cigarettes. The health risk associated with WTS is highly underestimated, despite the fact that waterpipe tobacco use is associated with greater carbon monoxide, similar nicotine, dramatically more smoke exposure and some of the same toxicants as cigarette smoking. The aim of this study was to investigate toxicities induced by light-use WTS. We analysed gene expression data (Walters MS *et al*, 2017) from small airway epithelium of waterpipe tobacco smokers and WTS impact on pathological changes and affected pathways. 282 signature genes (<.05, >.5) were detected from the whole genome analysis, as significantly dysregulated after exposure to WTS., By manually annotating and processing molecular information from the publicly available data (PubMed articles and FDA reports), we created a computational model of biological pathways describing cellular processes in human respiratory tissues and made the information computable. WTS exposure induced genes involved in immune responses, G-protein coupled receptor signalling, oxidative stress and mRNA regulation of translation. In addition, we annotated data about WTS toxic components (such as the ones from Hoffmann's list, Hoffmann D *et al,* 1998) and generated a comprehensive database of known side effects and protein targets of these toxicants. By applying bioinformatics analysis tools to gene expression data and combining with toxicants data, we have identified several pathologies that affect respiratory and circulatory system. We generated mechanistic hypothesis for each of these pathologies, supported by current knowledge. Together, these data indicate that even light-use waterpipe tobacco smoking is as much harmful as traditional cigarettes smoking, and may damage respiratory system.

PS 3193 Toxicological Evaluation of E-vapor Aerosols Using *In Vitro* Regulatory Cytotoxicity and Genotoxicity Assays under Air-Liquid and Air-Agar Interface Conditions

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Users of electronic nicotine delivery systems (ENDS) inhale generated aerosols; therefore, it would be ideal to conduct *in vitro* toxicity testing using systems that mimic direct aerosol exposures to the apical surface of cells or bacteria, i.e., air-liquid interface (ALI) or air-agar interface (AAI). Here we evaluated a cig-a-like device with base formulation (containing humectants and 4% nicotine) and three commercially available cig-a-like ENDS (containing humectants, varying flavors and a range of nicotine concentrations (2.4%-4.8%)) using the Vitrocell®- 24/48 [ALI] and Ames 48 [AAI] exposure modules and regulatory cytotoxicity (neutral red uptake (NRU)) and genotoxicity (Ames) assays. The lung adenocarcinoma cell line, A549 was used for the cytotoxicity assay and was exposed to either air or to e-vapor aerosols at varying puff numbers (50-400 puffs). For the Ames assay, 5 *Salmonella* strains (TA98, TA100, TA102, TA1535 and TA1537) were used and exposed to either humidified air or to 400 puffs of aerosol from each test article. Aerosols were generated using a modified CORESTA CRM 81 puffing regimen (55ml puff volume, 5 sec puff with 30 sec interval). Concentration of the deposited nicotine in the insert was measured as marker of exposure. In the NRU assay, the base formulation was cytotoxic only at 400 puffs (39.1±30.1 % viability), while all three tested e-vapor products showed a concentration dependent cytotoxicity with the estimated IC50 ranging from 72-146 puffs. In the Ames assay, the base formulation and two of tested e-vapor products were found to be negative, however, one e-vapor product was positive in strain TA1535 (>18-fold increase above air control) following exposure to 400 puffs of e-vapor aerosol. The study was repeated with varying puff numbers (50-400) using strain TA1535, wherein a concentration dependent increase in response was observed in comparison to air treated group. In summary, the employed ALI and AAI *in vitro* testing conditions were able to detect varying degrees of cytotoxic and genotoxic hazard in e-vapor aerosols, demonstrating the potential use of direct aerosol testing as part of the toxicological evaluation of e-vapor products.

PS 3194 Thirdhand Smoke Adhesion to and Removal from Indoor Fabrics: Factors Affecting Human Exposure and Remediation

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Thirdhand smoke (THS) consists of residual tobacco smoke that settles and remains on indoor surfaces after smoking has ceased. Remediation of these chemicals is important in reducing exposure to THS. In this study, we investigated the affinity of THS chemicals to common household fabrics that are not washed frequently (e.g. draperies and upholstery) and could act as chemical reservoirs. Cotton, terry cloth, polyester, and wool carpet fabrics were washed four times before being placed in a chamber designed for THS exposure smoke exposure. They were then exposed for 1, 6, 12 or 18 months to 696, 1569, 1795, 3617mg of smoke, respectively. THS was extracted from each fabric at a concentration of 0.1g of fabric/mL of PBS, DMSO, or cell culture medium. Extraction media were examined using fluorescence spectroscopy at various wave lengths. Nicotine, nicotine alkaloid and tobacco specific nitrosamine (TSNA) concentrations in extracts were quantified using liquid chromatography-tandem mass spectrometry (LC-MS/MS). Affinity of nicotine to terry cloth and polyester was compared by exposing each fabric to 10 mg/ml of nicotine, and quantifying the amount of nicotine recovered after extraction using high performance liquid chromatography (HPLC). Our results showed that THS chemicals in fabric extracts autofluorescence, and fluorescence was proportional to the time and amount of THS exposure received by the fabrics. THS autofluorescence was not detected in extracts from polyester and wool carpet at any of the excitations tested. Nicotine, nicotine alkaloid, and TSNA concentrations were higher in THS extracts from cotton and terry cloth than in polyester and wool carpet. Using fabrics spiked with 10 mg of nicotine, we showed that extraction efficiency was much higher from terry cloth (7mg) than from to polyester (0.11mg). The absorption into and release of THS from fabrics varied with the type of fabric. Human exposure to THS could be influenced by fabric type, and remediation techniques may need to vary depending on the fabrics reservoirs being treated.

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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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