Cells were collected on Day 25 of ALI culture following 5 days of woodfire smoke (WFS) exposure for downstream experiments. Results from three distinct burns on the SMPS and APS demonstrate a pine bark combustion profile with most particle diameters between 100-1000nm. Mass of particulate matter distribution across transwells and experiments were confirmed consistent at 189 ± 13.82 ug. Fluorescence fingerprinting using excitation emission matrix (EEM) revealed two distinct and similar peaks to that published of EEM from woodsmoke derived humic-like substances, demonstrating the relevance of our exposure system to biomass burning in ambient wood and wildfire situations. To interrogate changes to the mucociliary epithelium after WFS exposure, we performed global RNA sequencing on ALI cultures to identify broad gene expression changes following WFS exposure. We identified global downregulation of transcription of cilia related pathways and an upregulation of stress related pathways; such as MAPK and Reactive Oxygen Species. Proteomic abundance and phosphorylation were performed using mass spectrometry, which revealed a downregulation of cilia related protein abundance (RSPH4A/IFT88/DNAL1), coupled with a global downregulation of phosphorylation of those proteins. Functional analysis of beating cilia in these cultures revealed a dose dependent decrease in ciliary movement for each day of WFS exposure, resulting in complete abolition of ciliary movement following 5 days of WFS exposure (15 minutes total). Interestingly, this ciliary injury was prevented by the addition of a 100uM dose of Pimasertib added to the top and bottom of the transwells 30 minutes prior to WFS exposure each day. Treatment with Pimasertib demonstrated a dose dependent response with a 58.4% protection of ciliary movement when WFS was combined with 100nM Pimasertib and an 82.1% protection of ciliary movement when treated with 1uM Pimasertib. To confirm the role of ERK signaling in reducing ciliary movement, we performed the same ciliary movement tests with the addition of an ERK activator, BCI. Following addition of BCI to ALI cell cultures, ciliary movement decreased by 20.33% as compared to room air controls. Finally, we investigated the ultrastructure of ciliated cells following WFS exposures and MEK inhibitors. The ciliary axoneme consists of nine outer doublet microtubules surrounding two central singlet microtubules (9+2), known as the central pair. The central pair plays a key role in ciliary motility. Transmission Electron Microscopy (TEM) analysis revealed normal 9+2 ciliary axonemes across the control samples, and 100% loss of the central pair following WFS. The central pair loss was prevented by the addition of Pimasertib treatment during exposure. **Conclusions:** We have created a novel exposure chamber to mimic acute environmental exposures of the human proximal airway to wildfire smoke, woodfire smoke, and biomass burning in a uniform and highly reproducible manner. Here we show that WFS is responsible for reducing MCC in the airway by damaging the central pair of proteins in ciliary axonemes in a dose dependent manner. We also show that MAPK signaling regulates these ciliary proteins and inhibition of MEK with Pimasertib preserves ciliary ultrastructure and therefore ciliary movement. Pimasertib therefore has potential to be used as a mitigator of airway disease in WFS exposed individuals, especially in those with underlying lung disease.

3477 Whole body inhalation of polycarbonate emissions generated during 3D-printing process alters metabolism and redox status in rat liver

M. Bodas, S. Guppi, *K. Mandler*, W. McKinney, A. K. Knepp, S. Keeley, L. Battelli, *Y. Qian*, and *T. A. Stueckle*. National Institute for Occupational Safety and Health, Morgantown, WV.

Background and Purpose: Three-dimensional printing (3D Printing), i.e. additive manufacturing, is a burgeoning technology which has applications in various industries, such as healthcare, education, consumer goods, and personal care products. It has also found great utility in industrial manufacturing applications in the automobile, aerospace, and construction sectors. Fused filament fabrication (FFF) is a widely used 3D printing method that works by melting and extruding plastic filament layer by layer. Polycarbonate (PC) filament-based FFF process is known to release ultrafine particles (UFPs) and volatile organic compounds (VOCs), which might pose an inhalation hazard. Recent studies from our group have found that rats exposed to inhaled 3D printer emissions at a concentration of 2.5 mg/m^3 using PC filament demonstrated systemic adverse effects on various components of the neuroendocrine system, but no significant pulmonary toxicity. The present study was designed to examine whether whole body inhalation of emissions generated during the PC FFF printing process leads to metabolic and redox changes in the liver. **Methods:** Six to seven weeks old male Sprague-Dawley rats, each weighing about 200-225 grams, were purchased from Hilltop Lab Animals and housed in ventilated polycarbonate cages. The rats were housed in a facility that provided a controlled environment with HEPA-filtered air and acclimated for at least seven days before study initiation. Rats were fed a standard irradiated diet and filtered tap water *ad libitum*. The study protocol was reviewed and approved by the CDC-Morgantown Institutional Animal Care and Use Committee, which is accredited by AAALAC International. Whole body inhalation exposure of rats was performed using an in-house 3D-printer emissions inhalation exposure system. Briefly, rats were exposed to either filtered air (*air control group*) or 3D printer-PC filament emissions (2.5 mg/m^3, 63 nm mean particle electric mobility diameter; *3D-PC group*), for a time course of 1, 4, 8, 15 and 30 days (4 hours per day; 4 days per week). Twenty-four hours after the last exposure, rats were euthanized by intraperitoneal injection of pentobarbital. Liver tissue was harvested and stored in RNAlater for quantitative real-time PCR (qPCR) or immediately frozen at -80°C for biochemical analyses. Total RNA was used to perform qPCR to quantify the changes in expression of genes related to inflammation, oxidative stress, and metabolism. Homogenized liver tissue lysates were prepared and used to evaluate changes in markers of redox status including reduced and oxidized glutathione, glutathione S-transferase (GST), and lipid peroxidation. Differences between treatments were assessed using 2-way analysis of variance followed by post-hoc student t-tests. Non-parametric data were compared using Wilcoxon multi-comparison tests. **Results:** The genes selected for qPCR were grouped into five categories, namely (1) inflammation, (2) oxidative stress, (3) glucose/glycogen metabolism, (4) fatty acid metabolism, and (5) sterol metabolism. The data suggests that Day 1 exposed rats had elevated expression of genes related to inflammation (e.g. *TNFα*), glucose (e.g. *Slc2a3*), fatty acid (e.g. PPAR*α/γ, Thrsp*), and sterol metabolism compared to air controls. The rats exposed for 8 days showed comparable levels of gene expression (or suppression in some genes, e.g. *Scd1*) in fatty acid and sterol metabolism-related genes as compared to air controls, while genes related to inflammation remained elevated. In rats exposed for 30 days, the expression of *IL-1β* remained elevated while other inflammation-related genes were similar to air controls. Moreover, *Thrsp*, *Hmgcs1*, and *Hmgcr* still retained elevated levels while all other genes showed no difference from air controls. GST activity significantly increased 5-fold for all Day 4 animals compared to Day 1 animals. At Day 8 PC-exposed animals had significantly lower GST activity as compared to air controls. All animals in remaining exposure days showed similar GST activity compared to Day 1 animals. Total glutathione levels in all animals at Day 4 were significantly lower than Day 1 animals, while PC-exposed animals at Day 8 had significantly lower total glutathione than time-matched air controls. All remaining time points and treatments possessed comparable total glutathione as Day 4 animals. Reduced glutathione showed an exposure time-dependent decrease starting at Day 4. By Day 8 reduced glutathione had decreased by 10-fold in both PC and air control animals and remained low in all later time points. Lipid peroxidation did not change in all animals with increasing exposure time until a significant increase in all Day 15 and 30 animals. **Conclusions:** Collectively, whole body PC FFF exposure at 2.5 mg/m^3 induced rat liver biomarkers associated with inflammation, oxidative stress, glucose, fatty acid, and sterol metabolism, which partially resolved with repeated exposure over time. PC exposure depleted total glutathione stores and subsequent GST activity faster than air control animals over 8 days of repeated exposure, potentially subjecting long term exposed animals to xenobiotic-induced metabolic changes, damage, and redox stress.

3478 Lung toxicity profile of inhaled copper-nickel welding fumes in rats

P. C. Zeidler-Erdely, *J. R. Roberts*, *V. Kodali*, T. Meighan, L. Grose, T. Eye, W. McKinney, S. Stone, J. L. Cumpston, H. D. Leonard, *A. Erdely*, and *J. M. Antonini*. CDC-NIOSH, Morgantown, WV.

Background and Purpose: Welding processes create inhalable fumes rich in iron (Fe) that may also contain known toxic metals such as chromium (Cr) and nickel (Ni). Welding aerosols derived from copper-nickel (CuNi) consumables have not been investigated as thoroughly as those from mild (Fe-rich) and stainless-steel (Fe-rich + Cr + Ni) welding consumables. The study objective was to determine the pulmonary toxicity in rats exposed by inhalation to CuNi welding fumes generated using gas metal arc welding. **Methods:** Male Sprague-Dawley rats (n=6/group/timepoint) were exposed to CuNi welding aerosols by whole-body inhalation for 3 hours/day for 3 days at 40 mg/m^3 or filtered air. Rats were sacrificed and bronchoalveolar lavage (BAL) was done at 1, 4, 6, and 8 days post-exposure. BAL fluid lactate dehydrogenase (LDH) activity was measured as a marker of general lung cytotoxicity and recovered BAL cells were counted and differentiated under light microscopy to assess lung inflammation and cell influx. Animal body weights were assessed throughout the exposure and post-exposure periods. **Results:** Characterization of the fume indicated that >95% of the particles were between 0.1 and 1 µm in diameter, with a mass median aerodynamic diameter of 0.43 µm. Metal content of the fume was Cu (~76%) and Ni (~12%). All animals gained weight throughout the exposure period. Body weight (% increase) was significantly different between air- and CuNi fume-exposed at the 1-day post-exposure timepoint only. CuNi welding fume significantly increased LDH levels and polymorphonuclear leukocytes in the BAL fluid at all timepoints post-exposure. Lung cytotoxicity was increased in the CuNi fume-exposed group by 10-fold on 1- and 4-days post-exposure, and 8- and 4-fold at 6 and 8 days. Total cell BAL cells were also increased at all timepoints and were 4- and 5-fold at 1 and 4 days, respectively, and remained elevated at 8 days post-exposure (~3.5-fold). **Conclusions:** The results suggest that short-term exposure to inhaled CuNi welding fume causes significant acute lung toxicity in rats with no resolution of the inflammatory lung response by 8 days.

3479 Cadmium exposure modulates fibroblast-to-myofibroblast transition signaling

I. Sundar, C. Prasad, S. Duraisamy, K. Madduru, K. Cushing, and J. Hagen. University of Kansas Medical Center, Kansas City, KS.

Background and Purpose: Cadmium (Cd) is a toxic heavy metal linked to adverse health effects and is widely present in the environment due to sources such as volcanic emissions, forest fires, coal-fired plants, smelting industries, soldering, and

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