mask and whether the NHP model was nasal or mouth breathing was performed to determine the concentration of CO_2 within 3 different mask designs. Providing 6 L/minute to the mask using the CFD model with a TV of 30 mL, RR of 30 breaths per minute, 100% mouth breathing and 0% nasal breathing produced 2.5% CO_2 within a Philips Respironics® ProfileLite single port mask. The CO_2 decreased to 0.7% using dual ported masks (designated as 15-22 Mk1 and IPM). A similar CO_2 concentration of 2.7% was produced with the Philips Respironics® ProfileLite mask with 100% nasal breathing at the same TV and RR. Hyper-ventilating conditions (TV=15mL TV, RR=70 breaths per minute) and 100% mouth breathing, produced a CO_2 concentration of 2.4%. The results using the 15-22 Mk1 and IPM masks under these conditions gave CO_2 concentrations of 0.5% to 0.7%. Decreasing the airflow to 3 L/min from 6 L/min increased CO_2 in the Philips Respironics® ProfileLite mask to 2.8%,=; however, there was a marked increase with both dual ported 15-22 Mk1 and IPM masks to 1.4%. Increasing the airflow to 9 L/minute from 6 L/minute decreased CO_2 in the Philips Respironics® ProfileLite mask to 2.5%, however, there was a marked decrease with both dual ported 15-22 Mk1 and IPM masks to 0.4%. Intentionally raising or lowering the angle of the mask on the 3D printed NHP model by 7.5° did not result in a significant change in CO_2 concentration (<0.1% from baseline in terms of ventilated CO_2) for the IPM mask. In conclusion, using a dual ported mask significantly reduces CO_2 concentration in the mask. Reduced CO_2 improves safety and the animal experience allowing for improved welfare and study integrity. However, decreasing mask airflow reduces the clearance in the mask and increases the CO_2 concentration, especially in the dual port designs.

PS 4585 Myeloid Heterogeneity Mediates Air Pollution–Induced Acute Exacerbations of Pulmonary Fibrosis

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Epidemiological evidence indicates that exposure to particulate matter is linked to the development of idiopathic pulmonary fibrosis (IPF) and increases the incidence of acute exacerbations of IPF (AE-IPF). In addition to accelerating the rate of lung function decline, exposure to fine particulate matter ($PM_{2.5}$) is a risk factor for increased mortality in IPF subjects. Mice were intratracheally administered bleomycin and exposed to $PM_{2.5}$ daily for 7 days after fibrosis was early (day 14) or extensively established (day 21). Monocyte/macrophage subsets were determined by FACS analysis in BAL cells from mice exposed to bleomycin and $PM_{2.5}$. Fibrotic progression was analyzed by micro-CT imaging. Exposure to $PM_{2.5}$ in mice with established pulmonary fibrosis led to monocyte recruitment. Although monocyte-derived macrophages were recruited to the lung in bleomycin-injured mice treated with $PM_{2.5}$, there was no difference in the number compared to bleomycin-injured mice receiving vehicle. $PM_{2.5}$ exposure promoted the recruitment of monocytes expressing $Ly6C^{hi}$ to the lung. This resulted in progression of fibrosis and reduced lung aeration. $Ly6C^{hi}$ monocytes isolated from fibrotic mice exposed to $PM_{2.5}$ showed enhanced expression of proinflammatory markers compared to fibrotic mice exposed to vehicle. Moreover, IPF BAL cells treated *ex vivo* with $PM_{2.5}$ showed an exaggerated inflammatory response. Therapeutically targeting $Ly6C^{hi}$ monocytes inhibited fibrotic progression in mice after $PM_{2.5}$ exposure. These observations suggest that enhanced recruitment of $Ly6C^{hi}$ monocytes with a proinflammatory phenotype drives AE-IPF fibrosis after exposure to $PM_{2.5}$ and targeting these cells may provide a novel therapeutic target to protect against AE-IPF.

PS 4586 Effect of Crystalline Silica and Welding Fume on Lung-Associated Gene Changes in the Rat

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A major source for the occupational diseases that result in significant morbidity and mortality is exposure to dust often containing toxic agents, such as silica and/or welding fumes. More than 424,000 workers in the U.S. and close to one million workers worldwide perform welding as part of their work duties. Because there is little information regarding the number or the health effects of workers who are exposed to both crystalline silica and welding fumes while carrying out work duties, this study was designed to assess the possible health effects on this unique population of workers. Male Fischer 344 rats weighing approximately 200 g were exposed to air or silica (15 mg/m^3, 6 hours/day, 5 days). At 5- and 11-months post-silica exposure, rats received gas metal arc stainless steel welding fumes (20 mg/m^3, 4 hours/day, 4 days/week for 4 weeks) by whole-body inhalation. At 1-day post welding fume exposure bronchoalveolar lavage was conducted to assess pulmonary toxicity. Lung expression gene changes were also assessed. The BAL results showed that both silica and welding fume exposures resulted in lung toxicity, at both post-exposure time points. The silica alone, welding fume alone, and the silica + welding fume exposure all resulted in a significant increase in neutrophil and macrophage infiltration at both 6-and 12-months post welding fume-exposure. For example, at 12-months post-exposure silica or welding fume exposure, alone, resulted in neutrophil infiltration of 250 and 625 times, respectively, compared to air controls. The exposure to silica + welding fume, however, caused neutrophil infiltration that was 1392 times higher compared to air controls. The induction of pulmonary inflammation in the exposed rats also caused a significant elevation in the measured cytokine levels, at both post-exposure timepoints. Although silica alone, welding fume alone, and the silica + welding fume exposures all caused this elevation, the elevation was most significant in the silica + welding fume exposure group at both 6- and 12-months post-exposure. Global gene expression changes in the lungs were also detected in all exposure groups, at both 6- and 12-months post-exposure. For example, silica exposure alone resulted in 750 significantly differentially expressed genes (SDEGs), while the welding fume alone group had 2255 SDEGs, and the silica + welding fume exposure had 1910 SDEGs, at 12-month post-exposure. The bioinformatic analysis at 12 months post-exposure showed the top 3 disease and function pathways in the welding fume and welding fume + silica exposure groups are respiratory system tumor, lung tumor, and lung cancer. Additionally, gene transcripts associated with lung cancer development were significantly expressed. Specifically, MMP7, MMP12, and FOLR4 (all genes associated with lung cancer development) have more than 3-fold higher expression rates in the welding fume + silica exposed lungs compare to the silica alone exposed lungs. Past studies have demonstrated that stainless steel welding fumes, which contain significant levels of nickel (Ni) and chromium (Cr), induce more lung injury and inflammation, and are retained in the lungs longer than mild steel welding fumes, which contains mostly iron. Previous studies have shown that Ni and Cr are key contributors to the development of lung cancer in stainless steel welders. Our study, assessing the pulmonary toxicity outcome to a mixed exposure of welding fume and crystalline silica concluded that the combined exposure caused a greater expression of disease/injury markers and functional pathways associated with lung cancer. Taken together, these results suggest a potentially enhanced effect of the silica + welding fume exposure on genes associated with lung tumor and lung cancer development.

PS 4587 Lung Toxicity in Rats after Inhalation of Aerosols Generated during Thermal Spray Coating Using Different Consumable Materials

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Thermal spray coating (TSC) is an emerging industrial process in which molten metal is sprayed at a high velocity onto a surface as a protective coating. Little is known about the physical and chemical properties of the particles generated and the potential health effects associated with exposure to TSC aerosols. A computer controlled TSC generator and inhalation exposure system has been developed to perform animal studies to mimic workplace exposures. Male Sprague-Dawley rats were exposed by whole-body inhalation to aerosols (25 mg/m^3 x 4 hours/day x 4 days) generated from electric arc wire TSC using different consumable wires including a Fe-Cr stainless-steel wire (PMET731), a Ni-based wire (PMET885), and a Zn-based wire (PMET540). Control animals were exposed to filtered air. Bronchoalveolar lavage (BAL) was performed at 4 and 30 days after the last of the 4 day exposures to assess lung toxicity. BAL fluid lactate dehydrogenase (LDH) was measured as a marker of lung cell toxicity, and total recovered BAL cells were counted as an index of lung inflammation. Animal body weights were measured throughout the post-exposure period to assess general health. The TSC aerosols were generated in a closed spray booth and piped into an animal exposure chamber where they were collected and characterized. The metal composition of each was determined by ICP-AES, including the stainless-steel wire [PMET731 (66% Fe, 26% Cr)], the Ni-based wire [PMET885 (97% Ni)], and the Zn-based wire [PMET540 (99% Zn)]. The particles generated regardless of composition were poorly soluble, complex metal oxides that were arranged as chain-like agglomerates and were similar in size distribution with mass median aerodynamic diameters (MMAD) that ranged from 310 - 378 nm as determined by MOUDI. Inhalation of the Ni-based (PMET885) aerosol caused a significant decrease in body weight compared to the air control at all time points assessed post-exposure for 30 days, whereas the Zn-based (PMET540) and Fe-Cr stainless-steel (PMET731) aerosols had no effect on body weight post-exposure. Exposure to the Ni-based (PMET885) aerosol caused a significant increase in lung injury (BAL fluid LDH activity) and inflammation (total BAL cells recovered) at both 4 and 30 days after exposure. Inhalation of the Zn-based (PMET540) aerosol caused a slight but significant increase in BALF LDH and total BAL cells recovered at 4 but not at 30 days compared to air control. Exposure to the Fe-Cr stainless-steel TSC aerosol had no significant effect on lung toxicity post-exposure. Results of this pilot comparison study of different TSC aerosols indicate that varied lung responses (e.g., Ni >> Zn $\geq$ Fe-Cr) are likely dependent on the type of consumables used.

PS 4588 Differential Mucus Secretion in Several Mouse Strains in Response to Cigarette Smoke Exposure

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Mucus hypersecretion from airway goblet cells induced by cigarette smoke (CS) or other particulate matter exposure is a major feature of chronic bronchitis. Several CS exposure studies with mice have been reported to date. The effects of CS exposure on the respiratory system are not necessarily consistent. Thus,

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