treatments with welding fumes that are vastly different both chemically and physically. Welding fumes were collected from three different processes: gas metal arc-mild steel welding (GMA-MS); manual metal arc-hardsurfacing welding (MMA-HS); flux-cored arc-hardsurfacing welding (FCA-HS). Male Sprague-Dawley rats were treated by intratracheal instillation 1/wk x 7 wk with 0.5 mg/rat of the fume samples. Controls were treated with saline. Bronchoalveolar lavage was performed 4 days after the final treatment, and parameters of lung injury (lactate dehydrogenase and albumin) and inflammation (neutrophil influx) were assessed. Metal analysis indicated that the GMA-MS fume was primarily composed of Fe (1.08 μg Fe/gm total metal) and Mn (0.32 μg Mn/gm total metal), whereas the Mn content of the FCA-HS (2.0 μg Mn/gm total metal) and MMA-HS (1.8 μg Mn/gm total metal) fumes was ~6x higher than in the GMA-MS fume. The FCA-HS (0.07 μg Cr/gm total metal) and MMA-HS (0.304 μg Cr/gm total metal) fumes contained Cr which was present in only trace amounts in the GMA-MS fume. The FCA-HS and MMA-HS fumes were found to be more water-soluble than the GMA-MS fume. Significant elevations in lactate dehydrogenase, albumin, and the number of lung neutrophils were observed for the MMA-HS and FCA-HS groups compared to the GMA-MS and saline groups. No significant differences in lung injury and inflammation were observed between the GMA-MS and saline group. The greater lung response caused by the FCA-HS and MMA-HS fumes is likely due to the presence of Cr and higher levels of Mn. Results from this study indicate that welders who are exposed to fumes generated from specific processes may be at a greater risk for adverse pulmonary effects.

496 TOXICOKINETICS OF SURFACTANT PROTEIN AND INFLAMMATORY GENE EXPRESSION IN PRIMARY RAT LUNG ATII CELLS AND FIBROBLASTS EXPOSED TO PENICILLIUM CHRYSOGENUM AND STACHYBOTRYS CHARTARUM TOXINS.

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Not a great deal is known about the effects and modes of action of the spores and toxins of the majority of molds encountered in the indoor environment on lung biology. In vivo models of lung disease indicate that fungal spore and toxin exposures lead to a variety of species and toxin-specific inflammatory responses. However, it is unclear whether all the lung cells participate in these inflammatory changes. In this study we used gene expression profiling using custom made RT-PCR based microarrays to compare surfactant protein and inflammatory gene responses in primary fetal rat lung ATIIs and fibroblasts to atranones A&C from Stachybotrys chartarum (Sc) and melagrin and roquefortine C from Penicillium chrysogenum (Pc). In Pc-toxin exposed ATIIs, inflammatory genes were transiently up-regulated, generally in dose and time dependent ways, within 2 to 4 hr and de-expressed by 12 hr post exposure (PE), especially in meleagrin exposed cells. SP-A,-B &-C genes were down regulated at 4 hr PE. SP-D expression was unaffected by the Pc toxin exposures. Inflammatory genes were generally up-regulated in atranone A but down regulated in atranone C exposed ATIIs from 2 to 24 hr PE, and in a dose dependent fashion. SP-A & -C genes were down regulated in both atranone A & C exposed cells, while SP-B & -D expression was unaffected. In fibroblasts, gene expression was generally limited to SP-D up-regulation, while MIP-3α was down regulated, from 2 to 4 hr PE. The results indicate that toxins from two mold species common on damp materials in buildings provoke compound-specific toxic responses with different toxicokinetics. They also provide further insight into molecular mechanisms of spore and toxin induced lung disease onset and development, and may be useful in the identification of fungal specific molecular biomarkers of disease.

497 REPEATED EXPOSURE TO 1→3-β-GLUCAN SUPPRESSES LUNG DEFENSE RESPONSES AND SLOWS THE PULMONARY CLEARANCE OF LISTERIA MONOCYTOGENES IN RATS.

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Chronic exposure to low levels of mold has been reported to increase susceptibility to respiratory infections. Currently, the mechanism is not well understood. This study investigated lung defense effects after repeated low-dose zymosan (a 1→3-β-glucan from yeast cell wall) exposure on bacterial infection (Listeria monocytogenes) in male Sprague-Dawley rats. On days 0, 3, 7 and 10, rats received one dose of zymosan A (0.6 mg/kg body weight each dose) via intratracheal instillation or vehicle control (saline). On day 17 (one week later), rats were intratracheally inoculated with $5x10^5$ bacteria. Rats were euthanized on days 20, 22, and 24. Bacterial clearance was determined by measuring colony-forming units cultured from the left lungs. Bronchoalveolar lavage (BAL) was performed on the right lungs. Inflammation and lung injury were assessed by measuring (1) neutrophil (PMN) infiltration and (2) albumin and lactate dehydrogenase levels in BAL fluid. Multiple zymosan treatments induced greater lung injury and inflammation as indicated by elevations in PMN, LDH, and albumin at days 22 and 24 compared to control. In addition, repeated low-dose exposure to zymosan slowed the clearance of the bacteria at day 20 and 22 compared to controls, suggesting a possible suppression in lung immune responses. In contrast, previous results have shown that a single acute dose of zymosan at a concentration (2.5 mg/kg body-weight) equivalent to the total of the four repeated concentrations used in the current study enhanced lung immune responses and increased the rate of bacterial clearance from the lung. This study demonstrated the importance of treatment concentration and dosing regimen in understanding lung immune effects associated with 1→3-β-glucan exposure.

498 90 DAY INHALATION TOXICITY STUDY WITH DISK-SHAPED POTASSIUM OCTATITANATE PARTICLES (POT; TERRACESS TF) IN RATS.

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Fibrous particles such as asbestos and some man-made fibers have been known to produce carcinogenic or fibrogenic effects upon inhalation. Non-fibrous, disk-shaped potassium octatitanate particles (POT; Terracess TF) have been manufactured to avoid potential fiber toxicity. Four groups of 20 male and 15 female rats each were exposed to POT aerosol at concentrations of 0, 2, 10, or 50 mg/m3 for a 90 day period followed by a 15 week recovery period. The mass median aerodynamic equivalent diameter of the aerosols ranged from 2.5 to 2.9 μm. Lung burdens of POT were determined in 5 males/group at the end of the exposure period and after 3 and 15 weeks recovery. The clearance ½ times for POT were estimated to be in the order of 2 to 3 months for the 2 and 10 mg/m3 groups and 6 to 9 months for the 50 mg/m3 group. There were no POT related adverse effects in clinical observations, body weights, clinical pathology, or neurobehavioral measurements. At the end of the 90 day exposure, a slight increase in lung-to-body weight ratios was observed at 50 mg/m3 in males; this effect was not seen during the recovery periods. Female lung weights were normal. Microscopically, inhaled POT particles were mostly phagocytized by alveolar macrophages (AMs) in the alveoli and alveolar walls maintained their normal structure at 2 and 10 mg/m3. At 50 mg/m3, some alveoli were distended and filled with aggregates of particle laden AMs. The alveolar walls showed slight Type II pneumocyte hyperplasia but neither active inflammation nor alveolar fibrosis was present. The lung responses and lung clearance rates of POT were comparable to those of "nuisance" type dusts at these concentrations. The slower clearance rates at 50 mg/m3 and the presence of aggregated particle-laden AMs in alveoli at this level were considered signs of alveolar "overloading" and 50 mg/m3 was considered an effect level; the NOAEL was 10 mg/m3.

499 ESTABLISHMENT OF A BIOASSAY FOR DETECTION OF LUNG TOXICITY DUE TO FINE PARTICLE FROM BASED ON RESULTS OF DOSE RESPONSE STUDY.

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In order to establish an appropriate bioassay for detection of lung damage after fine particle expose, sequential histopathological changes were examined after intratracheal instillation to quartz, as a typical lung toxic agent, into F344 male rats.
Experiment 1: A total of 60, 10-week-old male F344 rats, were randomely separated into 6 groups and each group was consisted 10 rats. Groups 1-4 were exposed to 4mg, 2mg, 1mg and 0mg (control) quartz (DQ-12) suspended in saline (0.2ml) using an aerolizer and subgroups were sacrificed 5 rats on Days 1 and 28 thereafter. Groups 5 and 6 were exposed to 4mg and 0mg (air only) quartz powder without suspension using special aerolizer and sacrificed on the same days. All groups underwent assessment of lung histopathology.
Experiment 2: A total of 72, 10-week-old male F344 rats, were randomly separated into 6 groups. 60 rats (5 groups) were exposed by intratracheal instillation to quartz, titanium dioxide, hydrotalcite and β-cyclodextrin, 2mg/rat, suspended in 0.2ml saline (established by Experiment 1) and subgroups of 6 rats were sacrificed on Days 1 and 28. 12 rats were exposed by intratracheal instillation to 0.2ml saline as control groups, remaining 12 rats were not exposed as untreated group and subgroups of 6 rats were similarly sacrificed on the same days. All groups underwent assessment of lung histopathology and immunohistochemical demonstration of BrdU and iNOS as end-point markers.
From Experiment 1, 2mg quartz suspended in 0.2ml saline were suggested to be most appropriate for sensitive detection of inflammatory changes. By histopathology and immunohistochemical assessment, the level of toxicity were considered

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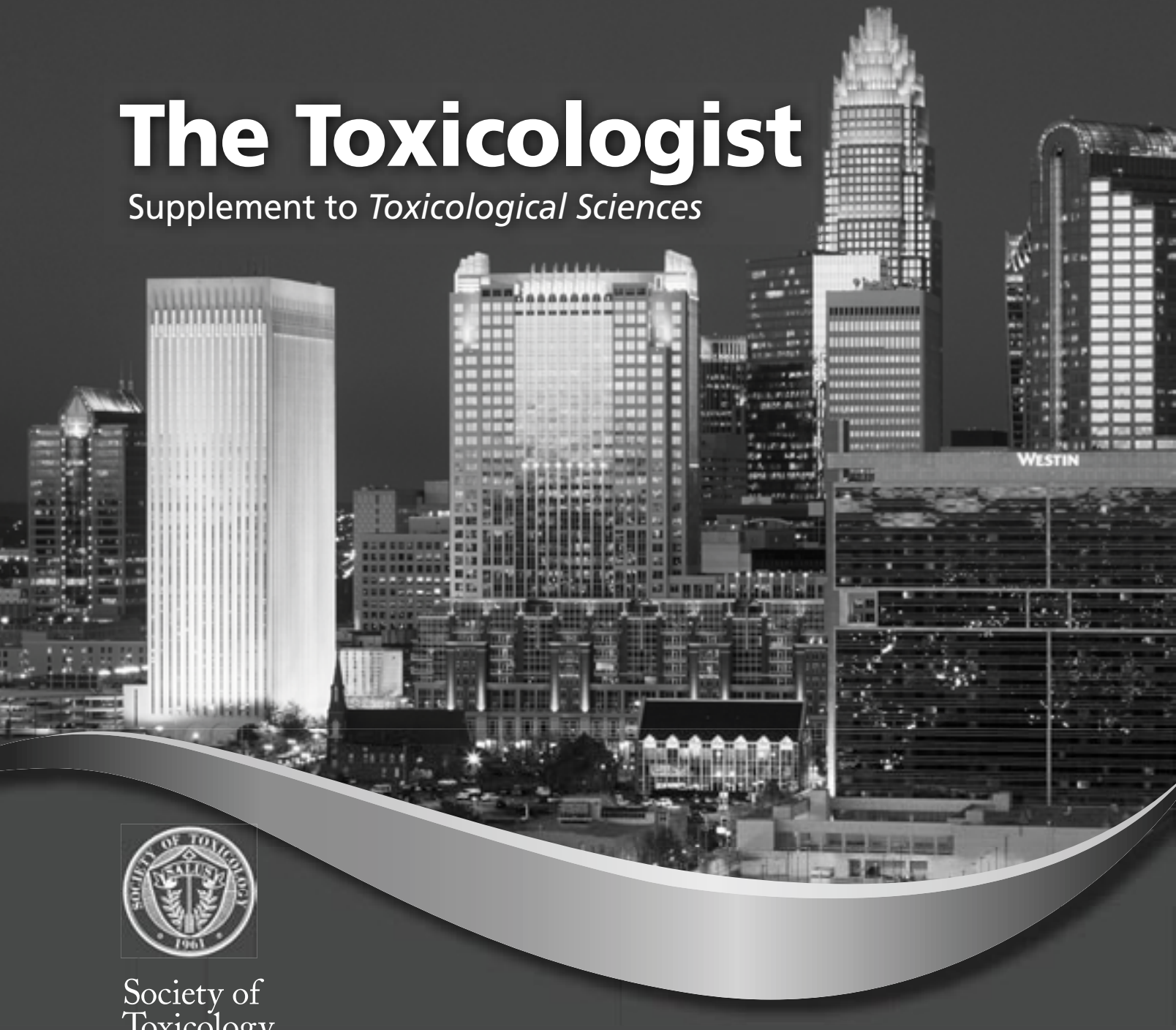

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Preface

This issue of *The Toxicologist* is devoted to the abstracts of the presentations for the symposium, platform, poster discussion, workshop, and poster sessions of the 46th Annual Meeting of the Society of Toxicology, held at the Charlotte Convention Center, Charlotte, March 25–29, 2007.

An alphabetical Author Index, cross referencing the corresponding abstract number(s), begins on page 449.

The issue also contains a Keyword Index (by subject or chemical) of all the presentations, beginning on page 480.

The abstracts are reproduced as accepted by the Program Committee of the Society of Toxicology and appear in numerical sequence.

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