high amount of hemoglobin, cytosolic samples had to be sub-fractionated into three different fractions (I, II, and III) by size exclusion chromatography. While the protein profiling in P-RBCs cytosolic fraction III is underway, separation and quantitation of other fractions revealed 11 membrane proteins, 9 (fraction I) and 25 (fraction II) cytosolic proteins increased significantly (≥ 2.5 fold) in P-RBCs as compared to V-RBCs. Our preliminary studies with membrane proteins suggest that the increased protein spots might be identified as ankyrin, adducin, anion exchange, 4.1 or 4.2 proteins. Identification of the increased proteins by LC-MS/MS and their functional categorization is in progress.

325 LUNG INFLAMMATION AND CARDIOVASCULAR OUTCOMES - WHOLE BLOOD GENE EXPRESSION STUDIES IN A LIPOPOLYSACCHARIDE (LPS) PHARYNGEAL ASPIRATION MOUSE MODEL.

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Recent animal and epidemiological studies suggest that pulmonary inflammation (e.g. ultrafine particulates) can trigger negative cardiovascular outcomes although the mechanism(s) resulting in systemic effects are not well established. Expression profiling of blood samples is becoming a useful tool for disease screening and identification of new biomarkers. In this study, it was hypothesized that lung inflammation results in activation of systemic gene expression related to cardiovascular disease. Prior to analyzing models of occupational exposure, pharyngeal aspiration of LPS was characterized with intraperitoneal (IP) injection as a positive control. C57BL/6 mice were treated with LPS (0.1mg/kg) and sacrificed 2hr post exposure. Whole blood and tissues were harvested for analysis of mRNA transcripts related to inflammation and coagulation. Expectedly, IP LPS resulted in a marked inflammatory response in the blood, heart and lung and pharyngeal aspiration of LPS resulted in a significant lung inflammation. Interestingly, whole blood showed similar gene expression induction of macrophage-inflammatory protein-2 (MIP-2) and tumor necrosis factor alpha (TNFα) following LPS by pharyngeal aspiration or IP injection. Extrapulmonary tissues were mostly unaffected by instillation of LPS into the lung. In conjunction with inflammation, changes in tissue factor (TF) and plasminogen activator inhibitor-1 (PAI-1) have been associated with increased risk of cardiovascular disease. Neither TF nor PAI-1 gene expression was elevated in blood following IP LPS although PAI-1 was strongly induced in the heart and lung. Following pharyngeal aspiration of LPS, both TF and PAI-1 were significantly increased in the lung and whole blood but not in the heart. In conclusion, lung inflammation results in activation of inflammatory and coagulation biomarkers associated with cardiovascular diseases and blood gene expression studies can identify biomarkers which predict cardiovascular outcomes in occupational-related respiratory exposures.

326 OVINE MATERNAL STRESS DURING LATE PREGNANCY ALTERS OFFSPRING FEBRILE RESPONSIVENESS TO SYSTEMIC ENDOTOXIN CHALLENGE LATER IN LIFE.

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Epigenetic programming of the neuroendocrine-immune axis during fetal development may contribute to variation in the febrile response and subsequently influence an individual's resistance to pathogenic infection later in life. In this study gender-specific changes in the ovine febrile response to systemic Escherichia coli lipopolysaccharide (LPS) were examined over time using infrared imaging, and an assessment was carried out to determine if maternal inflammatory stress experienced during late pregnancy influences febrile responsiveness of the offspring later in life. Pregnant sheep were allocated to 3 treatment groups and challenged with saline, or E. coli LPS (400 ng/kg x 3 consecutive days, 1.2 μg/kg) commencing on gestation day 135. Offspring of these stressed sheep were challenged with 400 ng/kg of LPS at six months of age and infrared energy emitted from the ear and eye was measured hourly for 6 hours post challenge to determine tissue temperatures; these measurements were compared with rectal temperatures. As expected, eye and rectal temperatures increased and then returned to basal levels within 6 hours of the LPS challenge. Ear temperature measurements on the other hand, decreased rapidly and then increased such that basal measurements were exceeded. This response was more pronounced in the females and is likely attributed to peripheral vasoconstriction. Female eye and rectal temperature was also higher than male offspring during LPS challenge, and the change in eye temperature was significantly different between the two different female LPS treatment groups. Overall, these results demonstrate that prenatal stress alters the ovine febrile response to LPS later in life, females have higher body temperatures than males, and infrared imaging is sufficiently sensitive to detect these subtle changes in body temperature.

327 EXPOSURE OF MICE TO CIGARETTE SMOKE *IN UTERO* INDUCES AIRWAY HYPER-RESPONSIVENESS (AHR) IN EXPOSED OFFSPRING LATER IN LIFE.

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More than a million infants are born each year in the U.S. after *in utero* exposure to maternal cigarette smoke (CS). Accumulating epidemiologic data suggest that exposure to CS *in utero* poses a substantial risk for respiratory disease/atopy/asthma in the next generation. While these findings carry extensive clinical consequences, few studies are available to provide insight into the possible mechanisms by which these effects might occur. Thus, a toxicologic study was performed to test the hypothesis that prenatal exposure to CS from maternal smoking persistently enhances airway reactivity (a defining feature of asthma) and related biologic parameters in the exposed offspring, and that these effects were sex-dependent. Pregnant CD1 mice were exposed daily (by inhalation) for 4 hr/d (5 d/wk) from gestational day 4 to parturition to mainstream CS at a concentration equivalent to smoking <1 pack of cigarettes per day (PM = 16 mg/m^3; CO = ≤25 ppm). In the absence of effects on maternal weight gain, litter size or offspring sex ratio, prenatal exposure to mainstream CS significantly enhanced airway reactivity (compared to the sex/age-matched, air exposed controls) in 5-wk-old female (but, not male) offspring in response to bronchoprovocation challenge with acetylcholine (ACH); AHR was observed in the absence of any pulmonary inflammation, lung cell damage, overt pulmonary pathology, or elevated serum IgE levels. In contrast, airways of prenatally exposed older female offspring (4-mo-old) were significantly less responsive to ACH challenge (compared to controls). These studies suggest that: prenatal exposure to CS has long-term effects on offspring respiratory health; effects of prenatal CS exposure on offspring airway function are gender-dependent; mechanisms other than airway inflammation may underlie changes in offspring bronchial reactivity in response to *in utero* CS exposure; and, even modest smoking during pregnancy may increase the offspring's risk of respiratory dysfunction later in life. Funded by IFSH.

328 AGE-RELATED CHANGES IN ADRENAL RESPONSIVENESS, GRANULOCYTE TRAFFICKING, AND SERUM IL-6 CONCENTRATIONS IN FEMALE SHEEP SYSTEMICALLY CHALLENGED WITH ESCHERICHIA COLI LIPOPOLYSACCHARIDE.

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The production of inflammatory mediators has been associated with senescence of both the neuroendocrine and immune systems and may contribute to a number of age-related diseases. In this study, this process of "inflamm-ageing" was investigated using an ovine model of acute systemic inflammation. Seven mature ewes (4-5 years old) and 7 ewe lambs (6 months old) were challenged intravenously with 400 ng/kg Escherichia coli lipopolysaccharide (LPS). Temperature measurements and venous blood samples were obtained at baseline, and 2, 4, 6, and 24 hours post-LPS administration to assess changes in serum interleukin-6 (IL-6), cortisol, and haptoglobin concentrations, the percentage of blood granulocytes, and biochemical markers of hepatotoxicity and liver function. Basal IL-6 concentrations in the adult sheep were dramatically higher than those of the younger animals, and the response to LPS challenge was significantly different over time between age groups. Serum cortisol concentrations increased in both age groups in response to LPS challenge however, the response was significantly greater in the adult versus the young animals. In both age groups the percentage of blood granulocytes decreased 2 hours, and increased 6 hours post LPS challenge. The 2-hour decrease however, was significantly more pronounced in the young versus adult sheep. Significant differences between the age groups were not observed for either haptoglobin, or temperature, and there was no evidence of hepatotoxicity in either group of animals. Overall, these results indicate that inflamm-ageing also occurs in ruminants, and that the sheep may be useful large animal model for studying the ageing neuroendocrine and immune systems.

329 EFFECTS OF LATENT *IN UTERO* AND PERINATAL TCDD EXPOSURE IN POST-NATAL C57BL/6 AND SNF1 MURINE OFFSPRING.

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TCDD [2,3,7,8-tetrachlorodibenzo-p-dioxin] and its congeners have a long and well-documented history of causing damage from both acute and chronic exposure. However, the potential risks associated with latent in utero and perinatal exposure

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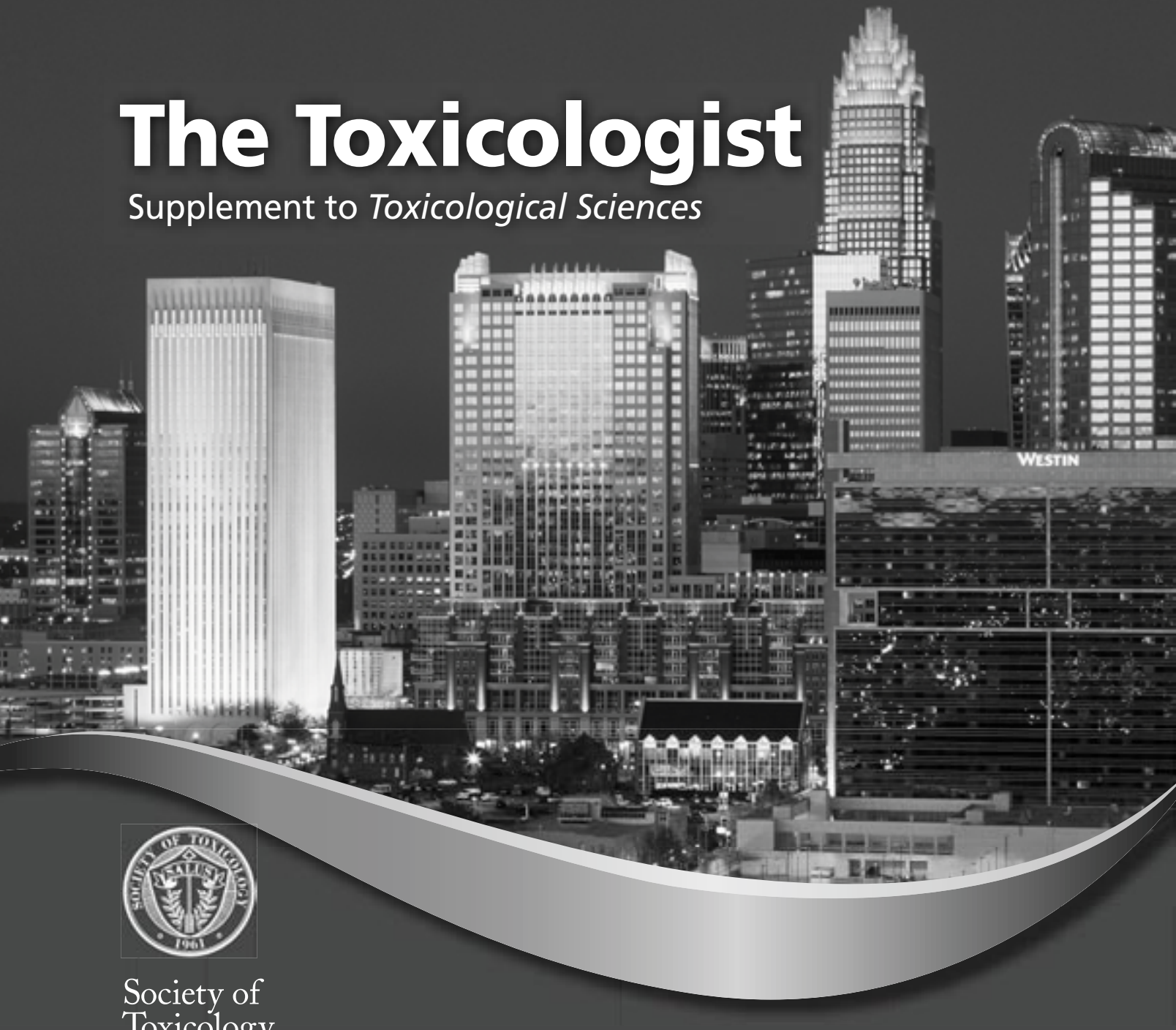

Society of Toxicology

46th Annual Meeting and ToxExpo™

Charlotte, North Carolina

An Official Journal of the Society of Toxicology

www.toxsci.oxfordjournals.org

OXFORD UNIVERSITY PRESS

ISSN 1096-6080
Volume 96, Number 1, March 2007

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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