hepatic fire-fly luciferase activity was observed in siblings from two of the breedings. Treatment of *CYP1A1*-luciferase transgenic mice with differing doses of TCDD ranging from 8 to 32 μg/kg demonstrated a concordance of liver induced luciferase activity with the accumulation of microsomal cyp1a proteins. Thus, these studies demonstrate the potential usefulness of a transgenic mouse model for examining the regulatory properties of the human *CYP1A1* gene. (Supported by Superfund Grant ES10337)

533 SMOKING INCREASES HUMAN NASAL EPITHELIAL CYTOCHROME P450 1A1 GENE TRANSCRIPTION.

R. Brundage[1], T. Rossignol[2], R. Hanshaw[1], M. Lucas[2], D. Fekedulegn[1], G. Opheim[2], M. Kashon[1], V. Castranova[1] and D. Weissman[1]. *[1]ASB/HELD, NIOSH, Morgantown, WV and [2]Madigan Army Medical Center, Ft. Lewis, WA.*

Respiratory tract carcinogenesis, mediated by polycyclic aromatic hydrocarbons (PAH) such as those associated with cigarette smoke, is in part due to induction of cytochrome P450 1A1 (CYP1A1) mRNA and protein expression with subsequent carcinogenic activation of PAH by CYP1A1. Respiratory epithelium is a key target tissue for these events. We therefore hypothesized that CYP1A1 mRNA expression level could be noninvasively monitored in human nasal epithelium, the most easily sampled respiratory epithelium, as a potentially pre-carcinogenic health effect of exposures to inhalants such as cigarette smoke. Subjects were healthy office and garage workers. Demographic, smoking, and occupational histories were obtained by questionnaire. Nasal epithelium was collected using Rhinoprobes(Tm) to obtain scrapings from subjects inferior turbinates. Tissue samples were stabilized using RNLater(Tm) to inhibit RNAses. RNA was extracted using Trizol(Tm). Isolated RNA was reverse transcribed, and abundance of mRNA encoding CYP1A1, IL-8, and G3PDH was evaluated by real time TaqMan(Tm)PCR. Cycle threshold (CT) was used as a measure of the mRNA level in each sample, standardized between samples by using the CT for G3PDH, and the following equation used to calculate a delta CT: CT (CYP1A1 or IL-8) minus CT (G3PDH) = delta CT. Data demonstrated a significant increase ($p < 0.001$) of CYP1A1 expression in current smokers (n=16) as compared to non-smokers (n=17) or former smokers (n=23) in our study group. No significant differences were seen in IL-8 expression levels between these groups nor were any associations apparent between occupational exposures and expression levels of CYP1A1 or IL-8. We conclude that CYP1A1 gene expression can be monitored noninvasively in human nasal epithelium, and that expression level can be modulated by exposures to agents such as cigarette smoke.

534 ROLES OF THE AH RECEPTOR IN OXYGEN-MEDIATED INDUCTION OF PULMONARY AND HEPATIC CYTOCHROME P4501A ENZYMES AND IN THE ATTENUATION OF HYPEROXIC LUNG INJURY.

B. Moorthy[1], S. E. Welty[2], X. I. Couroucli[1], R. Barios[3], S. R. Kondraganti[1] and W. Jiang[1]. *[1]Pediatrics, Baylor College of Medicine, Houston, TX, [2]Pediatrics, The Ohio State University, Columbus, OH and [3]Pathology, Baylor College of Medicine, Houston, TX.*

Administration of supplemental oxygen is frequently encountered in infants suffering from pulmonary insufficiency. However, hyperoxia causes lung damage in experimental animals, and may do so in humans. The mechanisms of oxygen-mediated lung injury are not completely understood. In the present investigation, we tested the hypotheses that: (i) hyperoxia would modulate pulmonary and hepatic cytochrome P450 (CYP)1A1/1A2 expression by Ah receptor (AHR)-dependent mechanisms; and (ii) AHR (-/-) mice would be more susceptible to hyperoxic lung injury than wild type (C57BL/6J) [(AHR (+/+)] mice. Two month-old adult male AHR (+/+) and AHR (-/-) mice were maintained in room air or exposed to hyperoxia (greater than 95% oxygen) for 24-72 h, and pulmonary and hepatic CYP1A1/1A2 expression was studied. Extent of lung injury was determined by measuring lung weight/body weight ratios and by histology. Hyperoxia caused significant increases in pulmonary and hepatic ethoxyresorufin O-deethylase (EROD) (CYP1A1) activities and pulmonary CYP1A1 mRNA levels in AHR (+/+), but not AHR (-/-) mice, suggesting that AHR-dependent mechanisms contributed to CYP1A1 induction. On the other hand, hyperoxia augmented hepatic CYP1A2 expression in AHR (+/+) as well as AHR (-/-) animals, suggesting that AHR-independent mechanisms contributed to this phenomenon. AHR (-/-) mice exposed to hyperoxia were more susceptible to hyperoxic lung injury, as indicated by significantly higher lung weight/body ratios, increased pulmonary edema, and enhanced neutrophil recruitment into the lungs than similarly exposed wild type animals. Taken together, our results support the hypothesis that there is a mechanistic link between the AHR, induction of CYP1A enzymes, and development of hyperoxic lung injury. (Supported in part by NIH grant ES09132 and by the American Lung Association.)

535 ALLEVIATION OF HYPEROXIC LUNG INJURY IN THE NEWBORN RAT BY RETINOIC ACID.

X. I. Couroucli[1], W. Jiang[1], H. W. Strobel[2] and B. Moorthy[1]. *[1]Pediatrics, Baylor College of Medicine, Houston, TX and [2]Biochemistry, The University of Texas-Houston Medical School, Houston, TX.*

Supplemental oxygen is frequently used in infants having pulmonary insufficiency, but prolonged hyperoxia contributes to the development of chronic lung disease in these infants. Hyperoxic exposure during the newborn period leads to acute lung injury and abnormal lung maturation in rats. Cytochrome P450 (CYP) enzymes have been implicated in lung injury induced by hyperoxia. In this investigation, we tested the hypothesis that neonatal exposure of rats to a combination of retinoic acid (RA) and hyperoxia would lead to decreased susceptibility of these animals to lung injury and improved lung maturation in adulthood, compared to those exposed to hyperoxia only, and that modulation of cytochrome P450 (CYP)1A and/or CYP4F4 expression contributes to the beneficial effects of RA. Newborn Fisher rats were maintained in room air or exposed to hyperoxia (≥95% O_2) for 7 days. Some animals were treated i.p. with RA (0.5 mg/kg) or vehicle (saline), once daily for 5 days. Animals were sacrificed 1 or 30 days after termination of hyperoxia, and lung injury was assessed by measuring lung weight/body weight (LW/BW) ratios and by histology. Pulmonary CYP1A1 and CYP4F4 expression was studied by RT-PCR. Exposure of animals to hyperoxia alone for 7 days showed higher LW/BW ratios at 1 day compared to those exposed to RA + hyperoxia. Hyperoxia significantly suppressed CYP1A1 mRNA expression at 1 day, and this effect was potentiated by RA treatment. On the other hand, while hyperoxia dramatically attenuated CYP4F4 expression, this effect was counteracted by pretreatment with RA. At the 30 day time point, the oxygen-exposed animals showed retarded alveolarization. In contrast, RA + hyperoxia-exposed animals showed improved alveolarization. The differential regulation of CYP1A and CYP4F4 expression by hyperoxia and hyperoxia + RA suggests that these enzymes may contribute to the beneficial effects of RA in alleviating lung damage induced by hyperoxia. (Supported in part by NIH grant KO8 HL04333 to XC)

536 EFFECTS OF LIGHT AND DARK BEERS ON HEPATIC CYTOCHROME P450 EXPRESSION IN MALE RATS RECEIVING ALCOHOLIC BEVERAGES AS PART OF TOTAL ENTERAL NUTRITION.

J. Badeaux[3], H. Hardy[3], N. Floyd[3], T. Fletcher[3], M. Ferguson[3], K. Hale[3], T. Dallari[3], M. J. Ronis[1,3] and T. M. Badger[2,3]. *[1]Pediatrics, University of Arkansas for Medical Sciences, Little Rock, AR, [2]Physiology, University of Arkansas for Medical Sciences, Little Rock, AR and [3]Arkansas Children's Nutrition Center, Little Rock, AR.*

Alcoholic beverages contain many congeners in addition to ethanol. Therefore, consumption of alcoholic beverages may have considerably different effects on expression of hepatic microsomal monooxygenases than the relatively selective induction of CYP2E1 observed following ethanol consumption. In the current study we compared the effects of two beers: larger (a light roasted beer) and stout (a dark roasted beer) infused intragastrically into groups of N = 10-13, 300 g male Sprague-Dawley rats for 21 d using a system of total enteral nutrition (TEN) with a group of rats infused an equivalent amount of ethanol isocalorically. At the end of the infusion period, rats were sacrificed and liver microsomes prepared. Cytochrome P450s CYP1A1/2, CYP2B1, CYP2E1, CYP3A and CYP4A expression was assessed by Western immunoblot analysis. In addition monooxygenase activities were assayed for the following substrates: ethoxy-, methoxy-, pentoxy- and benzyloxyresorufin, tesosterone, midazolam, erythromycin and p-nitrophenol. No effects of larger or stout were observed on relative expression of CYP2E1or CYP2B1 or activity towards p-nitrophenol or pentoxyresorufin. However, higher expression of CYP1A2, CYP3A and CYP4A were observed in stout-infused relative to larger and ethanol-infused rats ($p \leq 0.05$). In addition, although no differences were observed in alkoxyresorufin, midazolam or testosterone metabolism between groups, stout-infused rat had greater erythromycin N-demethylase activity (a CYP3A substrate) and higher lauric acid 12-hydroxylase activity (a CYP4A substrate) than other groups ($p \leq 0.05$). Therefore stout contains congeners which are inducers of cytochrome P450s other than CYP2E1. Supported in part by R01 AA08645 (TMB).

537 EFFECTS OF CHRONIC ETHANOL ON HEPATIC CYP2C11 IN MALE RATS: INTERACTIONS WITH THE JAK2-STAT5B PATHWAY.

T. M. Badger[2,3], M. J. Ronis[1,3], Y. Chen[3] and L. He[3]. *[1]Pediatrics, University of Arkansas for Medical Sciences, Little Rock, AR, [2]Physiology, University of Arkansas for Medical Sciences, Little Rock, AR and [3]Arkansas Children's Nutrition Center, Little Rock, AR.*

Chronic alcohol consumption results in altered expression of many genes. These effects are often secondary to alterations in hormonal actions. GH is secreted from the pituitary gland in a sexually dimorphic pulsatile pattern and this secretory pat-