the mother to the fetus and plays a critical role in fetal development. Changes in placental FA homeostasis may result in abnormal fetal development. This study demonstrates the effects of DEHP, MEHP and EHA on the mRNA and protein expression of PPARα, β, and γ, and fatty acid transfer conferring proteins in a rat placental cell model (HRP-1). HRP-1 cells were grown as monolayers and treated with DEHP, MEHP and EHA in a dose and time dependent manner for RNA and protein isolation. RT-PCR were performed under optimized conditions and normalized to β-actin expression using gene specific primers for PPAR isoforms and fatty acid transporters including fatty acid transport protein 1 (FATP1), plasma membrane fatty acid binding protein (FABPpm) and heart cytoplasmic fatty acid binding protein (hFABP). Western and slot blotting was utilized to support the RT-PCR results. All mRNA and protein expressions of each target of interest were observed in the HRP-1 cell at baseline. In the DEHP, MEHP and EHA treated cells, the expression of PPARα and γ, FATP1, and hFABP were up regulated in a dose and time dependent manner. PPAR β, FABPpm demonstrated variable expression in these samples, consistent with literature reports. These results demonstrate that DEHP, MEHP and EHA can influence the expression of proteins involved in FA homeostasis in a rat placental cell line. This implies that these compounds may contribute to aberrant placental FA homeostasis through peroxisome proliferation and potentially result in abnormal fetal development. Financial support from NAAR.

1480 6-HYDROXYDOPAMINE-INDUCES OXIDATIVE STRESS AND TOXICITY IN HUMAN NEUROBLASTOMA CELLS.

C. hu, M. A. Tirmenstein, P. K. Narayanan, H. C. Thomas and L. W. Schwartz. *GlaxoSmithKline, King of Prussia, PA.*

6-Hydroxydopamine (6OHDA) has been implicated in the pathogenesis of Parkinson's disease (PD) and is frequently used in animal models of PD. Previous studies have demonstrated that 6OHDA is selectively toxic to catecholaminergic cells and is toxic to the human dopaminergic neuroblastoma cell line, SH-SY5Y, *in vitro*. Studies suggest that formation of free radicals by 6OHDA is an important causative factor in cellular toxicity in SH-SY5Y, but there is no direct evidence for 6OHDA-induced oxidative stress in SH-SY5Y cells. In our study, we examined cellular *via*bility, reduced to oxidized glutathione ratios, ATP levels, and mitochondrial membrane potential ($\Delta\Psi m$) in SH-SY5Y cells treated with 6OHDA at concentrations of 50 – 500 μM and 5 – 50 μM for 4 and 24 h, respectively. 6OHDA produced slight but significant increases in cell death after 4 h. After 24 h, a concentration-dependent increase in cell death was observed, but only the highest dose (50 μM) induced significant increases. After a 4 h incubation, 6OHDA decreased reduced glutathione (GSH) and increased oxidized glutathione (GSSG) levels in a concentration dependent manner resulting in substantial reductions of GSH/GSSG ratios. 6OHDA induced a dramatic (12-fold) concentration-dependent elevation of GSH at 24 h . Significant ATP depletion occurred in cells treated with 6OHDA at ≥ 100 μM for 4 h and at ≥ 25 μM for 24 h. The $\Delta\Psi m$ of SH-SY5Y cells was also decreased by 6OHDA (≥ 50 μM) at 4 h. These findings demonstrate that 6OHDA induces mitochondrial dysfunction, oxidative stress and toxicity, in SH-SY5Y cells.

1481 A MODEL OF TOXICANT-INDUCED OXYGEN FREE RADICAL PRODUCTION FROM ISOLATED BOVINE RESPIRATORY CHAIN COMPLEX I.

J. E. Johnson[1, 2], K. Choksi[2] and W. R. Widger[2]. *[1]Optometry, University of Houston, Houston, TX and [2]Department Biology and Biochemistry, University of Houston, Houston, TX.* Sponsor: D. Fox.

The free radical theory of toxicant-induced injury and aging states that cell metabolism and function progressively decline in response to oxidative stress produced by reactive oxygen species (ROS). ROS production also is implicated in neurodegenerative disorders such as Parkinson's, Alzheimer's, and mitochondrial diseases. Multiple sites within the mitochondrial respiratory chain are hypothesized to produce ROS. The extent to which respiratory chain complex I contributes to ROS production is a topic of debate and clinical importance. Our aim was to determine whether ROS production co-isolated with respiratory complex I. Piericidin A, a potent inhibitor of complex I, and ubiquinone-1 (Q1) were used to stimulate ROS production from complex I. The ROS production was measured by two independent techniques: superoxide dismutase- (SOD) and catalase-sensitive oxygen consumption and SOD-sensitive cytochrome c reduction. Oxygen turnover and SOD-sensitive cytochrome c turnover were 150 - 550 per min. and 0 - 1000 per min., respectively. Q1-dependent ROS production was linear and non-saturating with increasing Q1 concentrations, suggesting that thie ROS production was largely nonspecific. Diphenyleneiodonium inhibited complex I ROS production, indicating that the site of ROS production was prior to the piericidin A block, possibly at one or more iron-sulfur centers and/or the flavin mononucleotide (FMN). Most importantly, the ROS production co-isolated with complex I FMN indicating that complex I is a potential site of mitochondrial ROS production. These results have mechanistic and therapeutic relevance for the diagnosis and treatment of free radical-induced injury in many tissues, especially those with high aerobic demand such as heart, kidney, and brain. Supported by the Welch Foundation Grant E-1381.

1482 LACK OF INHIBITION BY MELATONIN OF THE TOXIC AND PROLIFERATIVE EFFECTS OF DIETARY DIMETHYLARSINIC ACID ON RAT UROTHELIUM.

M. Wei, S. M. Cohen, M. Cano and L. L. Arnold. *Path/Micro, University of Nebraska Med. Ctr, Omaha, NE.*

Arsenic is a known human carcinogen of the skin, lung, bladder, and possibly other internal organs. Dimethylarsinic acid (DMA), a major organic metabolite of arsenic in most mammals including humans, has been shown to be a bladder carcinogen in rats when administered in the diet or in the drinking water. Oxidative stress has been suggested as a mechanism for DMA-induced carcinogenesis. Our recent results suggest that the induction of cytotoxicity with necrosis and consequent regenerative proliferation of the urothelium may be involved in the process of DMA-induced urinary bladder carcinogenesis. Dimethylarsinous acid (DMA^{III}) generated from reduction of DMA, probably contributes to the process. To determine whether an antioxidant, melatonin, could inhibit the cytotoxic and proliferative effects of DMA, female F344 rats were concurrently treated with 1000 ppm melatonin and 100 ppm DMA in the diet. Histopathology, bromodeoxyuridine (BrdU) immunohistochemistry and scanning electron microscopy (SEM) were used to evaluate proliferative and cytotoxic changes in the urothelium. Melatonin did not show significant inhibitory effects on urothelial proliferation when compared with DMA alone. The BrdU labeling index was significantly increased in the DMA-treated rats with or without melatonin and by light microscopy there was no difference between the DMA and the DMA plus melatonin groups. However, there was the suggestion of a slight protective effect against DMA-induced cytotoxicity based on SEM observations. These results show that melatonin had little inhibitory effect on DMA-induced urinary bladder toxicity or proliferation in the rat. In addition, melatonin (0.2 mM) did not inhibit DMA (0.6 mM) or DMA^{III} (0.4 μM)-induced cytotoxicity *in vitro*

1483 CARBON NANOTUBE EXPOSURE CAUSED FORMATION OF FREE RADICALS, INDUCTION OF OXIDATIVE STRESS AND CYTOTOXICITY IN HUMAN KERATINOCYTES AND BRONCHIAL EPITHELIAL CELLS.

E. Kisin[1], A. R. Murray[2], D. Schwegler-Berry[1], V. Z. Gandelsman[3], M. R. Ganther[2], V. Castranova[1, 2, 4] and A. A. Shvedova[1, 2]. *[1]PPRB, NIOSH, CDC, Morgantown, WV, [2]Physiology and Pharmacology, WVU, Morgantown, WV, [3]Advanced Technology Group, NASA-JSC/SAIC, Houston, TX and [4]GSPH, University of Pittsburgh, Pittsburgh, PA.*

Carbon nanotubes are new members of carbon allotropes similar to fullerenes and graphite. Because of their unique electrical, mechanical and thermal properties, carbon nanotubes are being evaluated for novel applications in the electronics, aerospace and computer industries. Exposure to graphite and carbon materials has been associated with increased incidence of skin and lung diseases, e.g., carbon fiber dermatitis, hyperkeratosis, naevi, asthma, COPD, pneumoconiosis and cancer. However, the potential toxicity of single wall carbon nanotubes (SWCNT) has yet to be completely evaluated. The present study investigated adverse effects of SWCNT using a cell culture of immortalized human epidermal keratinocytes (HaCaT) or bronchial epithelial cells (BEAS-2B). Exposure to SWCNT resulted in ultra-structural and morphological changes in cultured human cells. Treatment of keratinocytes and bronchial epithelial cells with SWCNT for 18 hr caused oxidative stress and cellular toxicity indicated by the formation of hydroxyl radicals, accumulation of peroxidative products, antioxidant depletion, loss of cell *via*bility and apoptosis. These data suggest that dermal and respiratory exposure to unrefined SWCNT may lead to dermal and pulmonary toxicity due to accelerated oxidative stress.

1484 GREEN CHEMISTRY CATALYST CAUSES DEPLETION OF GSH, OXIDATIVE STRESS AND CYTOTOXICITY IN KERATINOCYTES IN THE PRESENCE OF H_2O_2.

J. Kisin[1], Y. Y. Tyurina[2], E. Kisin[3], C. P. Horwitz[1], T. J. Collins[1], V. E. Kagan[2], V. Castranova[3, 4] and A. A. Shvedova[3, 4]. *[1]Carnegie Melon University, Pittsburgh, PA, [2]GSPH, University of Pittsburgh, Pittsburgh, PA, [3]PPRB, NIOSH, Morgantown, WV and [4]WVU, Morgantown, WV.*

The Pollution Prevention Act of 1990 (US CODE, 42) is a national policy to prevent or reduce pollution to protect human health and the environment. A practical, inexpensive, green chemical process for degrading environmental pollutants is

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Preface

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An alphabetical Author Index, cross referencing the corresponding abstract number(s), begins on page 443.

The document also contains a Keyword Index (by subject or chemical) of all the presentations, beginning on page 473.

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