susceptible to AM-induced toxicity, which may be an initiating event of an inflammatory response that precedes pulmonary fibrosis. (Supported by Medical Research Council of Canada Grant No. MT-13257).

378 METABOLIC FUNCTIONS OF ALVEOLAR TYPE II CELLS IN ACUTE SILICOSIS.

R D Levy, A F Hubbs, B S Ducatman, G Singh, V Vallyathan, L Bowman and P R Miles. *Health Effects Laboratory Division, National Institute for Occupational Safety and Health, Morgantown, WV and Department of Pathology and Laboratory Medicine, Veterans Administration Hospital, Pittsburgh, PA.* Sponsor: C Kommineni.

We have examined some metabolic functions of alveolar type II cells during experimental silicosis in rats. Consistent with previous studies, hypertrophied and hyperplastic alveolar type II cells and alveolar lipoproteinosis were observed at two and four weeks after intratracheal administration of 20 mg silica. Both hypertrophied and normal alveolar type II cells from all exposure groups contained immunohistochemically detectable lysozyme and surfactant apoprotein. Cytochrome P450 2B1 was immunohistochemically demonstrated in the Clara and normal type II cells of control and silica exposed rat lungs. However, the hypertrophied and hyperplastic alveolar type II cells contained no immunohistochemically detectable cytochrome P450 2B1. The concentration of P450 2B1 containing alveolar cells (positive cells/mm^2) was unaltered by silica. These findings support the hypothesis that during experimental silicosis, the hypertrophied type II cells are a newly-induced population of alveolar cells metabolically distinct from the pre-existing type II cells.

379 MUTATIONAL SPECTRA IN THE HPRT GENE OF RAT LUNG EPITHELIAL CELLS AFTER QUARTZ EXPOSURE.

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Previously we reported that exposure of rats to inflammatory doses of quartz and other particles results in an increased frequency of alveolar epithelial cells with mutation in the hprt gene. To better understand mechanisms of particle-induced mutation in the rat lung, the present study was undertaken to characterize the types of mutations occurring in the hprt gene of rat lung epithelial cells after *in vivo* quartz exposure. Briefly, rats were intratracheally instilled with saline or quartz (1-20 mg/kg body weight) and animals sacrificed 3-15 months after exposure. Alveolar epithelial cells were isolated and mutation in the hprt gene selected for by culture in 6 thioguanine (6TG) containing media. 6TG resistant colonies were expanded and RNA extracted. Mutations were characterized by direct cloning and sequencing of PCR amplified hprt cDNA. As reported previously the number of alveolar epithelial cells with hprt mutations was increased for cells from rats exposed to quartz. Comparison of the types of mutations generated revealed differences between saline and quartz exposed rats. Almost all hprt mutations in cells from saline exposed rats were point mutations, with only 1 frameshift and no deletions detected. In contrast, 47% of mutations found in rats after quartz exposure were point mutations with 40% frameshifts and 13% deletions and gene rearrangements. These data suggest that differences exist in the mechanisms underlying mutations occurring in the saline control and quartz exposed rats. Studies are continuing to examine mutational spectra associated with exposure to particles other than quartz.

380 *IN VITRO* TOXICITY IN RAT TYPE II PNEUMOCYTES AND ALVEOLAR MACROPHAGES OF TEXTILE PAINT COMPONENTS LINKED TO THE "ARDISTYL SYNDROME".

P H M Hoet, M Leyva, F L Clottens, M Demedts, B Nemery. *Laboratory of Pneumology, K.U. Leuven, Leuven, Belgium.* Sponsor: R Lauwerys.

In an attempt to elucidate the mechanisms for the severe pulmonary interstitial disease (Ardistyl syndrome) which affected textile printing sprayers in Spain (Moya, C. *et al.* Lancet 1994: 344: 498– 502) and in Algeria (Ould Kadi, F. *et al.* Lancet 1994: 344: 962– 963), the *in vitro* toxicity of components of the incriminated paint was tested in primary cultures of rat type II pneumocytes and alveolar macrophages. ®Acramin FWR (a polyurea), ®Acramin FWN (a polyamideamine), ®Acrafix FHN (a polyamine salt) or ®Acramoll W (a co-polymer of butylacrylate) were added, for 24 h, to the culture medium (Waymouth's medium with 10% FCS) in concentrations ranging from 0.000128 % to 2 % (v/v) of the commercial products. Acramoll W showed no toxicity. The viability of the type II pneumocytes, assessed as LDH release, diminished with increasing compound concentration, with TD_{50} values (95 % confidence intervals) of 18–52 ppm for Acramin FWR, 3–19 ppm for Acramin FWN and 16–65 ppm for Acrafix FHN. The toxicity to alveolar macrophages was in the same order of magnitude. Putrescine uptake, a specific function of type II pneumocytes, was significantly decreased during the first hour of exposure to 6.4 ppm of Acramin FWR, Acramin FWN or Acrafix FHN. The present study indicates that these polymers have a surprisingly high pulmonary toxicity *in vitro*, thus confirming previous *in vivo* observations.

381 OZONE-INDUCED SIGNAL TRANSDUCTION IN RESPIRATORY EPITHELIAL CELLS: ROLE OF PROTEIN KINASE C.

I Jaspers, E Flescher, L C Chen. *Nelson Institute of Environmental Medicine, New York University Medical Center, Tuxedo, NY.*

We have previously shown that ozone-exposure induces the DNA-binding activity of the transcription factors NF-kB and NF-IL6 as well as the expression of IL-8 in respiratory epithelial cells. Phosphorylation of NF-kB and NF-IL6 allows their translocation into the nucleus and binding to the IL-8 promoter region. We, therefore, investigated whether protein kinase C (PKC) may be an essential step in the signal transduction leading to IL-8 production in ozone-exposed respiratory epithelial cells. In this study, we examined whether PKC is activated in ozone-exposed epithelial cells and whether the PKC inhibitors Calphostin C and Chelerythrine inhibit the ozone-induced expression of IL-8. Activity of PKC was measured in A549 cells, a human alveolar type-II-like cell line, exposed to 0.1 ppm ozone or air. Both air- and ozone-exposed cells displayed increased PKC activity. The effects of Calphostin C and Chelerythrine on the expression of IL-8 were measured at the transcriptional and translational levels. A549 cells exposed to 0.1 ppm ozone for 5 hours showed significantly increased expression of IL-8 as compared to air-exposed cells, which was not inhibited by Calphostin C or Chelerythrine. From these results we conclude that the ozone-induced signaling cascade leading to expression of IL-8 in respiratory epithelial cells is PKC-independent. (Sponsored by EPA R819342 and DAMD17-95-1-5058).

382 ALPHA PARTICLES LIKE THOSE EMITTED BY RADON INCREASE INTRACELLULAR SUPEROXIDE AND HYDROGEN PEROXIDE PRODUCTION IN HUMAN LUNG FIBROBLASTS.

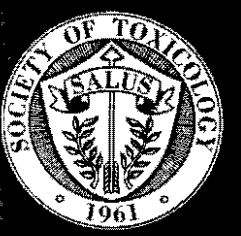
P K Narayanan, E H Goodwin, and B E Lehnert. *Life Sciences Division, Los Alamos National Laboratory, Los Alamos, NM.*

The mechanism(s) by which high-LET alpha(α)-particles like those emitted by inhaled radon and radon progeny cause lung cancer has not been elucidated. Conceivable, DNA damage induced by α-particles may be mediated by the generation of reactive oxygen species in addition to direct α-particle-DNA interactions. In this study, we set out to examine this possibility by assessing the intracellular generation of superoxide (O_2^-) and hydrogen peroxide (H_2O_2) in normal human lung fibroblasts following exposure to α-particles. Ethidium bromide (EB) and 2',7'-dichlorofluorescein (DCF), fluorescent products of the membrane-permeable dyes hydroethidine (HE) and 2',7'-dichlorofluorescin diacetate (DCFH-DA), were used to flow cytometrically monitor the intracellular production of O_2^- and H_2O_2, respectively. Irradiation of fibroblasts with α-particles (0.04 – 0.19 Gy) caused significant increases in intracellular O_2^- and H_2O_2 production when compared to sham irradiated fibroblasts. Our results to date are consistent with the possibility that α-particles may mediate their DNA-damaging effects at least in part *via* an ROS-related mechanism. [Supported by and conducted under the auspices of the U.S. Department of Energy].

383 THE CHANGE OF SURFACTANT-ASSOCIATE PROTEIN SP-B, C RNA EXPRESSION AND K-RAS MUTATION IN RAT TYPE II PNEUMOCYTE TREATED WITH EXTRACT OF AIRBORNE PARTICLES.

Z Xian-si. *Dept. Preventive Medicine, School of Basic Medicine, Shanghai Tiedao University, Shanghai, P.R.China.* Sponsor: J R Landolph.

In this study, type II pneumocytes isolated from rat lung incubated in DMEM medium containing some doses of organic extract of urban airborne particles for certain time, and then refresh the medium with that containing TPA every three days. The cells were collected to extract DNA for detecting DNA adducts and K-ras mutation. The DNA adducts was detected with 32P-postlabeling assay, and K-ras gene was detected with Southern hybridization after the DNA was amplified with PCR. Meanwhile, some of the cells used



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Preface

This issue of *The Toxicologist* is devoted to the abstracts of the presentations for the symposium, platform, poster / discussion, workshops, roundtables, and poster sessions of the 36th Annual Meeting of the Society of Toxicology, held at the Cincinnati Convention Center, Cincinnati, Ohio, March 9-13, 1997.

An alphabetical Author Index, cross referencing the corresponding abstract number(s), begins on page 371.

The issue also contains a Keyword Index (by subject or chemical) of all the presentations, beginning on page 395.

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