significantly decreased (78% of control). Pyridostigmine depleted cardiac GSH and GSSG concentrations (40% and 45% of control), respectively while lipid peroxidation was increased (116% of control). Exercise significantly decreased cardiac GSH-Px activity (78% of control) and depleted GSH concentration (75% of control). The combination of pyridostigmine and exercise decreased cardiac CAT and GSH-Px activities (56% and 72% of control), GSH concentration and GSH/GSSG ratio (73% and 47% of control), respectively and increased GSSG concentration (133% of control). The data suggest that pyridostigmine and exercise interaction perturb the cardiac antioxidant defense system leading to oxidative stress in mice (Supported by US Army contract # DAMD17-97-C-7066.)

961 COMBINATION OF PHENOLIC COMPOUNDS WITH ARACHIDONIC ACID INDUCES "FUTILE THIOL PUMPING" AND OXIDATIVE STRESS IN EPIDERMAL HUMAN KERATINOCYTES.

A A Shvedova[1], Y Y Tyurina[2], V A Tyurin[2], B Jeffries[1], C Kommineni[1], V Castranova[1], and V E Kagan[2,3]. [1]*Health Effects Laboratory Division, National Institute for Occupational Safety and Health, Morgantown, WV;* [2]*Departments of Environmental and Occupational Health, and* [3]*Pharmacology, University of Pittsburgh, Pittsburgh, PA.*

In human epidermis, active metabolism of arachidonic acid to prostaglandins is regulated by prostaglandin H synthase (PHS) which is also known to catalyze xenobiotic biotransformation. In particular, peroxidase activity of PHS may catalyze one-electron oxidation of phenolic compounds to their phenoxyl radicals. The phenoxyl radical may attack intracellular thiols to regenerate the phenolic compound that may repeatedly undergo peroxidase-catalyzed oxidation. This thiol-supported redox-cycling of phenolic compounds (i.e,. "futile thiol pumping") has been demonstrated in keratinocytes exposed to acetaminophen (Mason et al., 1989). n the present work, we tested whether redox-cycling of phenolic compounds can induce peroxidation of membrane phospbolipids and deplete antioxidants in keratinocytes. We used a fluorescence-HPLC assay for quantitation of membrane phospholipids metabolically prelabelled with oxidation-sensitive natural fluorescent fatty acid, cis-parinaric acid (PnA). We found that a combination of phenol/arachidonic acid or cresol/arachidonic acid caused a pronounced oxidation of major phospholipids: phosphatidylcboline, phosphatidylethanolamine, and phosphatidylserine in keratinocytes. Exposure to phenol (cresol) + arachidonic acid decreased total antioxidant reserves in keratinocytes as measured by luminol-enhanced chemiluminescence in the presence of a water-soluble azo-initiator, AAPH. Measurements with a thiol-reagent, ThioGlo-1™ showed that phenol (cresol) + arachidonic acid depleted GSH and oxidized protein sulfhydryls in keratinocytes. Electron microscopy revealed characteristic apoptotic nuclear fragmentation in keratinocytes exposed to a combination of phenolic compounds with arachidonic acid. These results suggest that peroxidase activity of PHS may he involved in phenol (cresol)-induced "futile thiol pumping" in human epidermal keratinocytes.

962 ROLE OF p53 TUMOR SUPPRESSOR GENE IN THE TOXICITY OF TCDD, ENDRIN, NAPHTHALENE AND CHROMIUM (VI) IN THE LIVER AND BRAIN TISSUES OF MICE.

D Bagchi, J Balmoori, M Bagchi, X Ye, C B Williams, and S J Stohs. *Creighton University Health Sciences Center, Omaha, NE, USA.*

It has been postulated that tumor suppressor genes are involved in the cascade of events leading to the toxicity of diverse xenobiotics. Therefore, we have assessed the comparative effects of 0.01 LD_{50}, 0.10 LD_{50} and 0.50 LD_{50} doses of TCDD, endrin (EN), naphthalene (NAP) and chromium (VI) (CrVI) on lipid peroxidation (LP), DNA fragmentation and enhanced production of superoxide anion (cytochrome c reduction) in the liver and brain tissues of TSG-P53 deficient mice in order to determine the role of p53 in the toxic manifestations produced by these diverse xenobiotics and compare these data with C57BL/6J mice. In general, p53 deficient mice are more susceptible to all four xenobiotics. Dose-dependent effects were produced by the four xenobiotics which were studied in both the p53 deficient mice and the C57BL/6J mice. At a 0.50 LD_{50} dose, TCDD, EN, NAP and CrVI induced 2.5-, 2.3-, 3.7- and 3.3-fold greater increases in hepatic LP in p53 deficient mice as compared to the C57BL/6J mice. At this dose in brain tissues 1.8-, 2.4-, 3.0- and 2.1-fold greater increases in LP occurred in p53 deficient mice as compared to the C57BL/6J mice. Similar results were observed with respect to DNA fragmentation and production of superoxide anion. The results support the hypothesis that p53 tumor suppressor gene plays a role in the toxicity of structurally diverse xenobiotics.

963 AUTOFLUORESCENCE IN PRIMARY RAINBOW TROUT HEPATOCYTES INTERFERES WITH MEASUREMENT OF OXIDATIVE ACTIVITY VIA THE EXOGENOUS PROBE, DCF, BUT PROVIDES INTRINSIC MEASURE OF CELLULAR OXIDATIVE STATE.

T R Henry, R D Johnson, D B Lothenbach and P K Schmieder. *USEPA, NHEERL, Mid-Continent Ecology Division, Duluth, MN, USA.*

The compound 2',7'-dichlorodihydrofluoroscein diacetate (DCF-DA; Molecular Probes) is a probe commonly used to detect oxidative activity in live cells. Studies were undertaken to measure reactive oxygen species generated in freshly isolated rainbow trout hepatocytes exposed to a variety of redox cycling compounds, including 1,4-napthoquinone (NQ) and diquat (DQ). During our studies we found unusually high background levels of fluorescence (Ex: 490nm; Em: 520nm) in control, NQ- and DQ-treated cells loaded with DCF-DA. Similar levels of fluorescence were observed in freshly isolated cells which were not loaded with DCF-DA, indicating that the fluorescence in not due to the oxidized metabolite, DCF. It was determined that the background fluorescence apparent immediately upon isolation correlates with cell density, indicating that it is endogenous autofluorescence. The fluorescence was observed to increase with time in culture up to 24 hours post-isolation, reaching a maximum fluorescence up to an equivalent of 50 pmol DCF. This temporal change in autofluorescence confounds interpretation of measurements of DCF fluorescence as an indicator of oxidative activity. However, the autofluorescence itself may be a useful endogenous indicator of the oxidative state of the cells. Examination of the rainbow trout hepatocyte autofluorescence using multi-photon excitation microscopy indicates that it is consistent with previous reports of autofluorescence of flavoproteins and pyridine nucleotides in mammalian cells. Exploitation of these intrinsic fluorescent molecules will provide a means of monitoring cellular oxidative activity in future mechanistic studies of cellular responses to oxidants in rainbow trout heptocytes.

964 MAITOTOXIN-1 INDUCES LIVER AND PLASMA LIPID PEROXIDATION IN CF-1 MICE TREATED WITH SUBLETHAL ORAL DOSES.

J Matta and M Milad. *Dept. of Pharmacology & Toxicology, Ponce School of Medicine, Ponce, PR.*

Human consumption of tropical fish containing polyether marine toxins (e.g. maitotoxins) can cause acute and chronic ciguatera fish poisoning. We tested the hypothesis that oral ingestion of maitotoxin-1 (MTX-1) causes significant increases in liver and plasma lipid peroxidation. Mice (CF-1 strain, n=5/dose/time interval) were gavaged with 0% (control), 0.1%, 1%, 10%, 25%, 50%, 75% of the MTX-1 LD_{50} (130 ng/kg, Calbiochem) and groups were sacrificed after either 3, 6, 24 or 72 h. Analysis was done of liver and plasma lipid peroxidation (HPLC), plasma protein, ALT and AST activities. MTX-1 caused a significant increase ($p<0.01$, 2-way ANOVA) in liver and plasma lipid peroxidation in many animals. This effect was more pronounced in liver than in plasma and varied substantially depending on dose utilized and time interval sampled. In the 3 h group a maximum effect was found; liver lipid peroxidation increased nearly 1800% relative to controls in animals treated with 75% of the LD_{50}. MTX-1 caused an increase of at least 300% in plasma lipid peroxidation in the 3 h group treated with 50% of the LD_{50}. These effects were abolished in animals treated with alpha tocopherol (100 μ M) after MTX-1 exposure. Collectively, these studies suggest that lipid peroxidation is a mechanistic component of acute ciguatera fish poisoning.

964A SHIFT IN FTIR (FOURIER TRANSFORM INFRARED) ABSORPTION SPECTRA OF AMIDE BOND-VIBRATION IN METHYL-CARBAMATE (METHOMYL) EXPOSED RAT SPLEEN CELLS IS RELATED TO DISRUPTION OF CYTOSKELETON.

T Suramana[1], R Sindhupak[2], N Dusitsin[2], T Posayanonda[3], and P Sinhaseni[3]. [1]*Department of Forensic Medicine, Faculty of Medicine;* [2]*Institute of Health Research;* [3]*Pesticide Safe Use Unit and Department of Pharmacology, Faculty of Pharmaceutical Sciences, Chulalongkorn University, Bangkok, Thailand.*

Oxidative stress caused by many toxicants to red blood cells can lead to apoptosis and release of lactate delydrogenase enzymes in plasma of exposed rats. We earlier reported that rats exposed to 8 mg/kg methomyl (s-methyl N -[(methylcarbarnoyl) oxy] thioacetimidate) showed transient increase of lactate dehydrogerase isozyne (type 4) in plasma and the elevated level which suhsided on day 2 after exposure. N-acetyl-cysteine, a free

An Official Journal of the
Society of Toxicology
Supplement

38th ANNUAL MEETING

TOXICOLOGICAL SCIENCES

Formerly Fundamental and Applied Toxicology

The Toxicologist

Oxford University Press

Volume 48, Number 1-S, March 1999

The Toxicologist

An Official Publication of the Society of Toxicology

and

Abstract Issues of

TOXICOLOGICAL SCIENCES

An Official Journal of the Society of Toxicology

Published by Oxford University Press, Inc.

Abstracts of the 38th Annual Meeting

Volume 48, Number 1-S

March 1999

Preface

This issue of *The Toxicologist* is devoted to the abstracts of the presentations for the symposium, platform, poster / discussion, workshop, roundtable, and poster sessions of the 38th Annual Meeting of the Society of Toxicology, held at the Ernest N. Morial Convention Center, New Orleans, Louisiana, March 14-18, 1999.

An alphabetical Author Index, cross referencing the corresponding abstract number(s), begins on page 419.

The issue also contains a Keyword Index (by subject or chemical) of all the presentations, beginning on page 444.

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

Copies of *The Toxicologist* are available at $45 each plus $5 postage and handling (U.S. funds) from:

Society of Toxicology
1767 Business Center Drive, Suite 302
Reston, VA 20190-5332
http://www.toxicology.org

© 1999 SOCIETY OF TOXICOLOGY

This abstract book has been produced electronically by Coe-Truman Technologies, Inc. Every effort has been made to faithfully reproduce the abstracts as submitted. However, no responsibility is assumed by the organizers for any injury and/or damage to persons or property as a matter of products, instructions or ideas contained in the material herein. Because of the rapid advances in the medical sciences, we recommend that independent verification of diagnoses and drug dosage be made.