showed similar levels of apoptosis as wild-type (WT) B cells. Furthermore, addition of CB2 select antagonist (SR144528) caused significant inhibition in apoptosis. Similarly, B cells from CB2 KO mice showed similar levels of sensitivity to CBD; However, addition of CB1 antagonist (SR141716) failed to inhibit the response because CB1 agonist appeared to act as a reverse agonist. We also investigated the role of transient receptor potential Vanilloid type 1 (TRPV1) which is known to be a ligand for CBD. Upon blocking the TRPV1 receptor, with Capsazepine (CPZ), a selective TRPV1 antagonist, CBD-induced apoptosis was not altereed. Pre-treatment of B lymphocytes in vitro with Caspase 3, 8 and 9 suggested a potential cross talk between the extrinsic and intrinsic pathways of apoptosis. Together, our data suggested that the anti-inflammatory properties of CBD can be attributed, at least in part, to apoptosis in activated B cells (Supported in part by NIH grants R01ES09098, P01AT003961, R01ES019313).

PS 1667 EFFECTS OF PBDES CONGENERS (BDE-209 AND BDE-47) ON HUMAN HEPATOMA CELLS (HEPG2) PROLIFERATION AND VIABILITY.

D. J. Dorta and A. O. de Souza. *Quimica, Faculdade de Filosofia, Ciências e Letras de Ribeirão Preto - Universidade de Sao Paulo, Ribeirão Preto, SP, Brazil.*

INTRODUCTION: Polybrominated diphenyl ethers (PBDEs) are an important class of flame retardants used, nowadays, in a variety of electronic equipment. Factors such as their high lipophilicity and bioaccumulation have raised concerns about their toxic potential. In fact, recent studies reported that PBDEs have been shown toxic effects and they may vary depending on the studied specie. OBJETIVE: This work investigated the effects of the PBDE congeners -209 and -47 on the proliferation and viability of HepG2 cells. METHODOLOGY: Firstly, cell proliferation test was performed using the sulforhodamine B (SRB) colorimetric assay to evaluate the inhibitory potential of these congeners and then the cell viability test (MTT assay) was performed. In both tests, cells were incubated at 37°C, in an atmosphere containing 5% CO2 and 96% relative humidity for 24 hours before starting the treatment. Then, cells were treated with PBDEs (0.1μM, 0.5μM, 1μM, 5μM, 10μM and 25μM) for 24 and 48 hours. For the SRB assay, the dye was added and left at room temperature for 1h. Subsequently, the cells were washed twice and SRB attached to the cells membrane was extracted using Tris buffer, pH 8.0. The absorbance of the dye was then measured in a spectrophotometer at 540 nm wavelength. For the MTT assay, after the exposure time to the PBDEs, the cells were reincubated with MTT 0.5% solution for 3 hours for the formation of formazan crystals, which were solubilized with dimethyl sulfoxide and glycine buffer solution. The absorbance was analyzed at 570 nm wavelength. RESULTS: Both congeners evaluated are capable of inhibiting cell proliferation and significantly decrease cell viability at doses starting at 5μM, however in a bigger extension for BDE -47 CONCLUSIONS: According to these results, the PBDEs congeners -209 and -47 showed a significant potential for inhibit cell proliferation in HepG2 cells and induce cell death. Financial support: FAPESP, CAPES

PS 1668 HYDROXYL RADICALS MEDIATES CISPLATIN-INDUCED APOPTOSIS IN HUMAN HAIR FOLLICLES DERMAL PAPILLA CELLS AND KERATINOCYTES THROUGH BCL-2-DEPENDENT MECHANISM.

S. Luanpitpong[1, 3], P. Chanvorachote[3], V. Pongrakhananon[1, 3], L. Wang[2], U. Nimmannit[4] and Y. Rojanasakul[1]. *[1]West Virginia University, Morgantown, WV, [2]National Institute for Occupational Safety and Health, Morgantown, WV, [3]Chulalongkorn University, Bangkok, Thailand and [4]National Nanotechnology Center, Pathumthani, Thailand.*

Induction of massive apoptosis of hair follicle cells by chemotherapy has been implicated in the pathogenesis of chemotherapy-induced alopecia (CIA), but the underlying mechanisms of regulation are not well understood. The present study investigated the apoptotic effect of cisplatin in human hair follicle dermal papilla cells (HFDPC) and HaCaT keratinocytes, and determined the role of reactive oxygen species (ROS) in the process. Treatment of the cells with cisplatin induced ROS generation and a parallel increase in caspase activation and apoptotic cell death in HFDPC and HaCaT cells. Inhibition of ROS generation by antioxidants, N-acetyl cysteine and reduced glutathione, inhibited the apoptotic effect of cisplatin, indicating the role of ROS in the process. Studies using specific ROS scavengers further showed that hydroxyl radical, but not hydrogen peroxide or superoxide anion, is the primary oxidative species responsible for the apoptotic effect of cisplatin. The mechanism by which hydroxyl radical mediates the effect of cisplatin was shown to involve down-regulation of anti-apoptotic protein Bcl-2 through ubiquitin-proteasomal degradation. Bcl-2 was also shown to have a negative regulatory role on hydroxyl radical. Together, our results indicate an essential role of hydroxyl radical in cisplatin-induced cell death of hair follicle cells through Bcl-2 regulation. Since CIA is a major side effect of cisplatin and many other chemotherapeutic agents with no known effective treatments, the knowledge gained from this study could be useful in the design of preventive treatment strategies for CIA through localized therapy without negatively affecting the chemotherapy efficacy.

PS 1669 LC-ESI/MS REVEALS UNUSUAL OXYGENATED LYSO-PHOSPHATIDYLSERINES PRODUCED AFTER OXIDATION AND HYDROLYSIS BY PLASMA LIPOPROTEIN-ASSOCIATED PHOSPHOLIPASE A2 OF SN-1, SN-2-DILINOLEOYL-PS.

V. A. Tyurin[1, 2], Y. Y. Tyurina[1, 2], C. H. Macphee[3] and V. E. Kagan[1, 2]. *[1]Center for Free Radical and Antioxidant Health, University of Pittsburgh, Pittsburgh, PA, [2]Environmental and Occupational Health, University of Pittsburgh, Pittsburgh, PA and [3]GlaxoSmithKline, King of Prussia, PA.*

Oxidation and hydrolisis of phospholipids (PL), containing oxidizable residues in sn-2 position, play an essential role in the production of signaling molecules - oxygenated fatty acids (FA) and lyso-PL. The presence of oxidizable FA - in both sn-1 and sn-2 positions - may yield - upon oxidation and hydrolysis by phospholipases A2 (PLA2) - a large variety of oxidized species and non-oxidized species with potentially effective regulatory propensities. In particular, oxidative/hydrolytic metabolism of doubly polyunsaturated phosphatitdylserines (PS) may play a central role in the molecular mechanisms of apoptosis and clearance of apoptotic cells. We present the results on structural characterization of oxygenated molecular species of PS containing linoleic acid in sn-2 position (C18:0/C18:2) and in both sn-1 and sn-2 position (C18:2/C18:2) formed in cytochrome c/H2O2 driven reaction. Oxidation of PS(C18:2/C18:2) resulted in formation of products at m/z 798, 814, 830 and 846, which included OH, OOH, OH/OOH and 2OOH groups, respectively. We characterized PS hydrolysis products (lyso-PS and free FA, FFA) formed by lipoprotein-associated PLA2 - secreted type VIIA PLA2 and cytosolic type VIIB PLA2. PS was preferable substrate for VIIA PLA2. Accumulation of hydrolysis products was markedly greater after hydrolysis of oxidized PS than non-oxidized PS. The products were mainly oxygenated FFA and non-oxidized lyso-PS. Hydrolysis of oxidized PS (C18:2/C18:2), led to generation of a great variety of both oxygenated and non-oxygenated lyso-PS and FFA. We suggest that both oxidatively modified FFA and lyso-PS may represent important signals facilitating and regulating execution of apoptotic and phagocytotic programs essential for control of inflammation. Supported by OH008282, U19AI068021, HL70755, HL094488, GlaxoSmithKline.

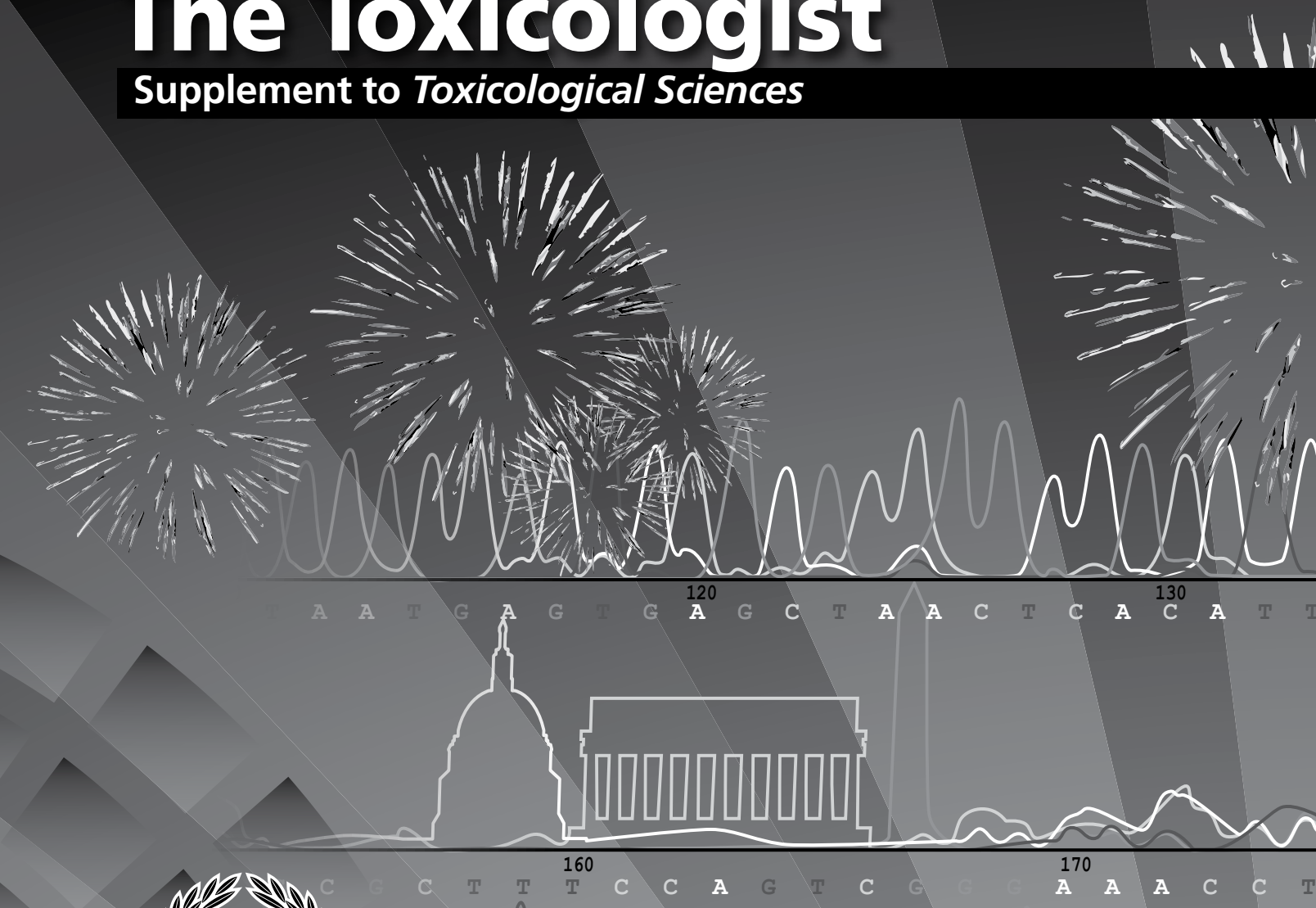
PS 1670 GROWTH INHIBITION OF BENZO(A)PYRENE (BAP)-EXPOSED HT29 HUMAN COLON CANCER CELLS BY RESVERATROL.

A. C. Huderson, J. N. Myers and A. Ramesh. *Biochemistry & Cancer Biology, Meharry Medical College, Nashville, TN.*

The magnitude of human exposure to BaP through diet has generated a great deal of interest with regard to the association of ingested BaP with gastrointestinal carcinogenesis. Studies conducted in our laboratory have already shown that oral administration of BaP causes tumors in the colon of APC^{Min} mice. Given the fact that colon cancer ranks 3rd among cancer-related mortalities, and in the United States alone around 60,000 lives are lost every year to colon cancer, it is necessary to evaluate the effect of anti-carcinogenic compounds on colon cancer initiation and progression. In this study we investigated the anti-carcinogenic effects of resveratrol (RVT) on BaP-induced apoptosis in the human colon cancer cell line HT29. HT-29 cells were cultured in Dulbecco's Modified Eagle Medium: Nutrient Mixture F-12 (DMEM/F12) supplemented with 10% FBS and antibiotics (Penicillin/Streptomycin). Initially cells were revived by the addition of 1mL of HT-29 cell frozen stocks to 20mL of media. Every 2 -3 days the media was changed until the cell grew to be 80% confluent. After cells were observed to be healthy, DMSO stocks were made of the cells using 90% FBS and 10%DMSO. Cells were seeded onto a 6 well plate or a T75 flask at a density of 20,000cells/well or 500,000 cells respectively. The cells were then synchronized overnight by serum starvation (DMEM/F12 media, 1% FBS) method. Cells were treated with 5μM of BaP simultaneously with 40μM of RVT. After a 24, 48, 72, and 96 hour exposure period, cells were counted using Beckman coulter counter. Resveratrol alone or simultaneously with BaP caused growth inhibition of the HT29 cells when compared to the no treatment and DMSO treatment groups. A progressive decrease in growth inhibition of cells was noticed with an increase in duration of exposure to BaP and RVT. Studies are in progress to see if this preventive effect is concentration-dependent both for the anti-carcinogenic agent and the carcinogen. This study was funded by the NIH grants 5T32HL007735-12, 1RO1CA142845-01A1, 1RO3CA130112-01, and 1S11ES014156-01A1.

The Toxicologist

Supplement to *Toxicological Sciences*



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An Official Journal of the Society of Toxicology

OXFORD UNIVERSITY PRESS

ISSN 1096-6080
Volume 120, Supplement 2
March 2011

www.toxsci.oxfordjournals.org

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Preface

This issue of *The Toxicologist* is devoted to the abstracts of the presentations for the Continuing Education courses and scientific sessions of the 50th Annual Meeting of the Society of Toxicology, held at the Walter E. Washington Convention Center, March 6–10, 2011.

An alphabetical Author Index, cross referencing the corresponding abstract number(s), begins on page 578.

The issue also contains a Key Word Index (by subject or chemical) of all the presentations, beginning on page 606.

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

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