suggest that TRX possesses novel immunomodulatory properties as a result of its ability to modulate IL-1β production and/or signalling. In contrast, LF inhibits the activity of TNF-α. The bioactivity of these molecules following simple topical application demonstrates that these proteins can access the viable epidermis and may represent an opportunity for the development of novel anti-inflammatory reagents.

PS 96 PROTEIN ALLERGENICITY AND DIGESTIBILITY: COMPARISONS OF PEPSIN AND CATHEPSIN.

E. Foster, I. Kimber and R. J. Dearman. *University of Manchester, Manchester, United Kingdom.*

An association between protein allergenicity and resistance to pepsin digestion has been reported previously, however, such is not complete with examples of labile allergens and resistant non-allergens observed. Given the central role of antigen presenting cells, such as dendritic cells (DC), in the development of immune and allergic responses, the stability of allergens to intracellular processing may be more relevant than resistance to pepsin digestion. We have characterised the expression by DC of cathepsins (proteolytic enzymes), and compared the proteolytic activity of the most highly expressed cathepsin with pepsin. Cathepsin expression in bone marrow-derived DC (BMDC) and in mesenteric lymph node DC derived from BALB/c strain mice was characterised by flow cytometry. BMDC expressed detectable levels of cathepsin D, E and S, with cathepsin D being the most highly expressed, with a similar pattern observed in DC isolated from mesenteric lymph nodes. Digestion studies revealed that the allergens β-lactoglobulin (BLG), hen egg lysozme (HEL) and ovalbumin (OVA) were relatively resistant to pepsin, although bovine serum albumin (BSA) was labile, as were the non-allergens hemoglobin (HB) and horseradish peroxidise (HRP). In contrast, all 4 allergens were stable to overnight digestion with cathepsin D, although fragments were observed for BSA. HB was labile to cathepsin D whereas fragments were recorded for HRP. As intracellular digestion occurs under reducing conditions, the impact of prior chemical reduction was explored. Reduced BLG and OVA were labile to pepsin and fragments were observed following cathepsin D digestion. Generally, allergens were more stable than non-allergens to digestion by both enzymes and chemical reduction increased lability. Although a wider range of allergens and non-allergens needs to be examined, these data suggest that allergenicity correlates more strongly with resistance to digestion by cathepsin D than with pepsin.

PS 97 INHALATION OF *ORTHO-PHTHALALDEHYDE* VAPOR CAUSES SYSTEMIC SENSITIZATION AND ALLERGIC INFLAMMATION IN THE LYMPH NODES, NASAL MUCOSA, AND LUNG OF MICE.

V. J. Johnson, W. Wang, K. Fluharty, B. Yucesoy and J. S. Reynolds. *CDC/NIOSH, Morgantown, WV.*

Ortho-Phthalaldehyde(OPA) is increasingly being substituted for glutaraldehyde as a high-level disinfectant for sensitive medical devices. However, toxicological data on OPA safety is lacking. Safety concerns for glutaraldehyde include acute nasal toxicity and sensory irritation as well as sensitization leading to occupational rhinitis and asthma. Since OPA is a dialdehyde like glutaraldehyde and functions as a disinfectant due to its high reactivity for biological macromolecules, it is reasonable to expect similar respiratory hazards. Several case reports have been published supporting this hypothesis showing development of respiratory hypersensitivity reactions in healthcare workers and patients exposed to OPA. The purpose of this study was to determine if OPA is a respiratory sensitizer using a murine model. Mice were exposed via inhalation to OPA vapor 4 hrs/day for 3 days; rested for 11 days; challenged with OPA vapor 4 hrs/day for 3 days and then sacrificed 24 hrs after the final exposure. Lungs, nasal mucosa, head-draining lymph nodes (LN) and serum were collected and processed for cytokine gene expression and flow cytometry. OPA-specific antibodies were detected in the serum of exposed mice. OPA inhalation induced a dose dependent increase in LN IL-4 expression and B-cell proliferation. Importantly, there was a concomitant increase in IgE+ B-cells. Strong Th2 cytokine expression in the nasal mucosa increased with OPA dose whereas the inverse was observed for IFNγ expression, a cytokine expression pattern commonly observed in response to respiratory allergens. Th2 cytokine expression was also increased in the lung although to a lesser extent. These data demonstrate that OPA inhalation induces a predominant Th2 cytokine response in the respiratory tract and draining LN. Importantly, OPA inhalation induced isotype switching to IgE in the draining LN supporting the development of an allergic immune response. Overall, this study suggests that inhalation of OPA vapor in mice can induce respiratory allergy.

PS 98 CONTACT SENSITIZING POTENTIAL OF HEPTACHLOR IN FEMALE BALB/C MICE.

R. P. Frawley[1], W. Auttachoat[2], M. J. Smith[2], R. D. Brown[2], T. L. Guo[2], K. L. White Jr[2] and D. R. Germolec[1]. *[1]National Toxicology Program, National Institute of Environmental Health Sciences, Research Triangle Park, NC and [2]Department of Pharmacology and Toxicology, Virginia Commonwealth University, Richmond, VA.*

Heptachlor (HPT) is a chlorinated cyclodiene insecticide that was used extensively in the 1950's through 1980's in agriculture, and in commercial and domestic buildings. Banned by the Environmental Protection Agency (EPA) for most uses (except for fire ant control in underground power cable boxes) since 1988, low levels of HPT residues persist in the environment. Human exposure can occur through contact with contaminated soil or building materials; consumption of contaminated meat, fish or dairy products; or production and application of HPT insecticides. The objective of this study was to evaluate the sensitization potential of HPT in female BALB/c mice following dermal exposure using the ICCVAM-validated local lymph node assay (LLNA) in combination with a measurement of irritancy, and the mouse ear swelling test (MEST). Sensitization was evaluated at concentrations that did not induce overt toxicity. HPT was applied to the dorsa of both ears daily for three days. There was no increase in ear swelling 24 hr following the third application at 0.2%-5.0%, indicating that HPT is not an irritant. Cervical (auricular) lymph node cell proliferation was statistically increased (72 hr post-application) at 2% HPT relative to the vehicle control, however, the increase did not reach a sensitization index (SI) of 3. In the MEST, mice sensitized with 1% and 2% HPT and challenged with 2% HPT exhibited significant increases in percent ear swelling, compared to the vehicle irritancy control, at 24 hr, but not at 48 hr, post-challenge. In summary, based on lack of irritancy and on statistical significance in the LLNA and MEST, HPT can be characterized as a sensitizer, but not an irritant.

PS 99 HUMAN LINE1 PROMOTER ACTIVITY IS ENHANCED BY CHEMICAL AND DRUG-INDUCED STRESS IN HEPG2 CELLS.

N. Terasaki, M. Kajikawa and N. Okada. *Department of Biological Science, Graduate School of Bioscience and Biotechnology, Tokyo Institute of Technology, Yokohama, Japan.* Sponsor: J. Sugimoto.

Long interspersed element 1 (LINE1), which is one of retrotransposons, constitutes 17 % of the human genome. 80-100 human LINE1 elements are currently active and can mobilize into a new location of the genome, resulting in alteration of the genomic information. Therefore, active LINE1 elements are considered as a sort of endogenous mutagens. In previous studies, some stresses, for example, heat shock, gamma radiation, UV irradiation and some agents are reported to induce mobilization of retroposons. In this study, to investigate widely what chemicals and drugs have the potential to enhance the LINE1 promoter activity, we established a reporter gene assay system in HepG2 cells using human LINE1. We cloned the 5'-UTR of L1.3, which is one of the most active human LINE1s, in the upstream of a luciferase gene and used it in the assay. The LINE1 promoter activity was measured at 6 and 24 hours after exposure to compounds. We assessed 106 compounds which include anticarcinogenic agents, nonsteroidal antiinflammatory drugs (NSAIDs), hypolipidemic agents, statins and some compounds that induce ER stress, oxidative stress, mitochondrial dysfunction etc. More than 1.5-fold increase of the LINE1 promoter activity was observed by the treatment of 9 compounds (merbarone, benzo(a)pyrene, exo1, iodoacetamide, citrinin, cyclosporine A, fenofibrate, bezafibrate, diflunisal and salicylamide) at both 6- and 24-hour points. Other 12 compounds also elevated the LINE1 promoter activity by 1.2- to 1.5-fold. These results suggest that various toxicants and drug stresses might have the potential to cause genomic mutations in a human body by inducing LINE1 mobilization. Therefore, we should keep in mind the possibility of activation of retrotransposons during drug discovery processes.

PS 100 *IN UTERO* BISPHENOL A EXPOSURE ALTERS METASTABLE EPIALLELE AND GLOBAL DNA METHYLATION PATTERNS IN MOUSE OFFSPRING.

M. S. Nahar, C. Weinhouse, O. S. Anderson, T. R. Jones, S. A. Liberman, L. S. Rozek and D. C. Dolinoy. *Environmental Health Science, University of Michigan, Ann Arbor, MI.*

Genetically identical individuals such as monozygotic twins and inbred mice often display phenotypic discordance, even after controlling for environment. Therefore, epigenetic plasticity has been proposed to play a role in the diverse phenotypes of individuals. Metastable epialleles variably express loci in genetically identical individuals due to epigenetic marks established early in development. Strikingly, these

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Deadline for Proposals for SOT 2012 Annual Meeting Sessions: April 30, 2011

WHY SUBMIT A PROPOSAL?

1. To present new developments in toxicology.
2. To provide attendees an opportunity to learn about state-of-the-art technology and how it applies to toxicological research.
3. To provide attendees an opportunity to learn about the emerging fields and how they apply to toxicology.

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The Scientific Program Committee will continue the thematic approach for the 2012 Annual Meeting. Additional details regarding the themes will be available on the SOT Web site.

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Continuing Education—Emphasis on quality presentations of generally accepted, established knowledge in toxicology
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Symposia—Cutting-edge science; new areas, concepts, or data

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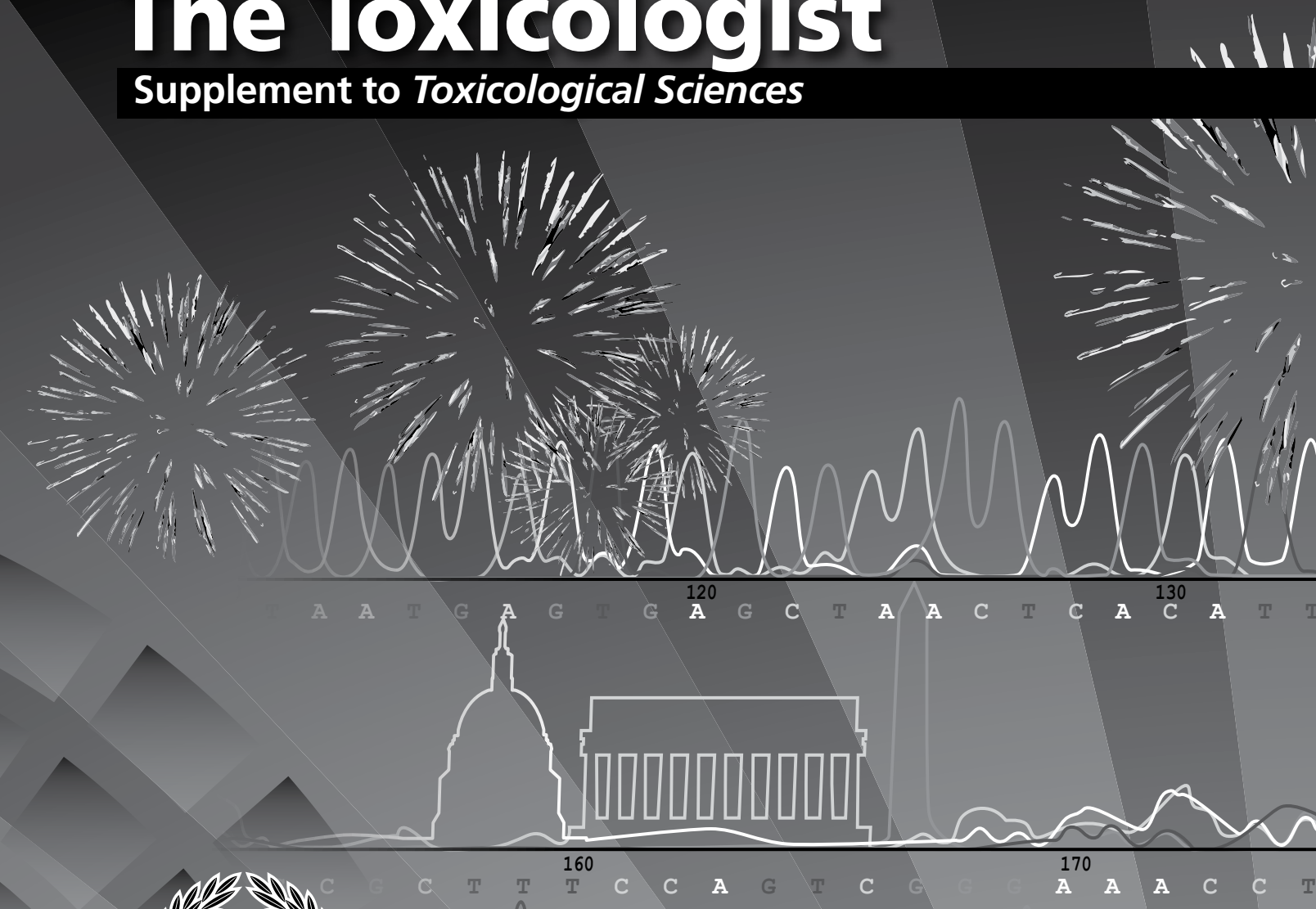

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Preface

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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