

and protein levels in the ear, but not in the lymph nodes or blood serum. *In vivo* administration of neutralizing anti-TSLP antibody impaired allergic responses augmented by dermal exposure to 3% triclosan during sensitization to ovalbumin. These effects include a significant decrease in skin pathology with a reduction in skin hyperplasia, redness and scabbing. There was also reduced cellularity of the skin draining lymph nodes, decreases in B cell frequencies, and reduced cytokine and GATA-3 transcription factor protein expression in Th2 CD4 T cells. These observations were further extended to human skin tissue cultures where we found that *in vitro* application of triclosan also induced TSLP expression. To our knowledge, this is the first report that triclosan can induce TSLP expression as a possible mechanism for augmenting allergic diseases.

**PS 672 Interrelationship of TDI- and HDI-Induced Respiratory Tract Irritation and Allergy in Rats**

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Brown Norway rats were skin-sensitized either with toluene diisocyanate (TDI) or 1,6-hexamethylene diisocyanate (HDI) by two topical administrations to pre-dispose them for respiratory allergy. This was followed by three subsequent inhalation priming exposures, each spaced by 2 weeks. Such protocol was shown to minimize any aggravation of irritation-related inflammation but to amplify the allergic inflammation. A dose-escalation bronchoprovocation challenge followed at either the first or fourth inhalation encounter with TDI or HDI. The escalation protocol utilized a constant concentration (Cconst) x variable bronchoprovocation time (tvar) protocol to quantify the elicitation-threshold Cxt in the absence and presence of prior inhalation priming exposures. The inhalation elicitation threshold dose on elicitation was determined based on measurements of neutrophilic granulocytes (PMN) in bronchoalveolar lavage fluid (BAL). The most appropriate Cconst was selected based on multiples ancillary pre-studies to achieve an 'optimal' penetration of the reactive and water soluble vapor into the bronchial airways at stable breathing conditions. PMNs in BAL of naïve and sensitized and inhalation primed rats were essentially identical at 900-1000 mg diisocyanate/m<sup>3</sup> x min. In summary, this study supports the conclusion that TDI- and HDI-induced respiratory allergy is likely to be caused by multiple, sequentially occurring mechanisms: first, dermal sensitizing encounters high enough to cause systemic sensitization (by circulating Th2-lymphocytes). Second, when followed by inhalation exposure(s) high enough to initiate and amplify an allergic airway inflammation (irritant threshold dose exceeded), then a progression into asthma may occur. The workplace human-equivalent threshold Cxt-product (dose), from 'asthmatic' rats, was estimated to be 0.003 ppmV when applying a time-dosimetry-susceptibility adjustment factor of 100. This threshold is in close agreement of the current ACGIH TLV® of TDI and HDI and published human evidence.

**PS 673 Differential Analysis of Protein Expression in RNA Binding Protein-Transgenic and Parental Rice Seeds Cultivated under Salt Stress and Allergenicity Test of the Rice Extracts**

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Transgenic plants tolerant to various environmental stresses are being developed to ensure a consistent food supply. We used a transgenic rice cultivar with high saline tolerance by introducing an RNA-binding protein (RBP) from the ice plant (*Mesembryanthemum crystallinum*); differences in salt-soluble protein expression between non-transgenic (NT) and RBP rice seeds were analyzed by two-dimensional difference gel electrophoresis (2D-DIGE), a gel-based proteomic method. To identify RBP-related changes in protein expression under salt stress, NT and RBP rice were cultured with or without 200 mM sodium chloride. Only 2 protein spots differed between NT and RBP rice seeds cultured under normal conditions, one of which was identified as a putative abscisic acid-induced protein. In NT rice seeds, 91 spots significantly differed between normal and salt-stress conditions. Two allergenic proteins of NT rice seeds, RAG1 and RAG2, were induced by high salt. In contrast, RBP rice seeds yielded 7 spots and no allergen spots with significant differences in protein expression between normal and salt-stress conditions. Therefore, expression of fewer proteins was altered in RBP rice seeds by high salt than those in NT rice seeds. We also assessed allergenicity of NT and RBP rice seeds cultured with or without 200 mM sodium chloride in mice. BALB/c mice were sensitized orally for three weeks with rice protein extracts in linoleic acid/lecithin emulsion, and after the sensitization, they were twice orally challenged with the protein extracts. Significant differences in systemic anaphylaxis score and antigen-specific IgG1 titer were not observed between NT and RBP rice fed mice groups.

**PS 674 Lung Toxicity and Allergy Responses in Mice Exposed to Nanoparticle Silver**

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With expansive use of silver nanoparticles (AgNP) in medical applications and consumer products, potential for worker exposure during manufacturing has become a concern. The goal of the current study was to characterize the potential effects of AgNP in an ovalbumin (OVA)-induced allergy model in BALB/c mice. To characterize the effects of AgNP alone, mice were exposed via pharyngeal aspiration (PA) to physiological dispersion medium (DM), 6.1 µg, 18.2 µg, or 73 µg AgNP. Twenty nm diameter AgNP with 0.3% wt polyvinylpyrrolidone coating (NanoAmor, Inc.) were suspended in DM and sonicated before exposures. For all studies lung function was assessed using enhanced pause (Penh); bronchoalveolar lavage (BAL) was performed on the whole lung; BAL cells and fluid were retained for analysis of lung-associated injury, inflammation, phenotyping; and lymph nodes (LN) were harvested for enumeration and immune cell phenotyping. AgNP alone did not result in changes in Penh, while cellular responses in the lung indicated a dose-dependent injury and inflammation by post-exposure day 10, which began to resolve by day 29. Our previous studies have shown that exposure to AgNP prior to OVA-sensitization results in a trend for the development of airway reactivity. In this study, effects of AgNP on the elicitation phase were examined. Animals were sensitized with i.p. injections of OVA (dose) + aluminum hydroxide gel on days 1 and 10. To elicit an OVA-specific response, two PA challenges with OVA were given on days 19 and 28. AgNP were administered by PA on day 27. AgNP did not appear to significantly enhance Penh, and lung-associated LN total cell numbers, BAL cell numbers and IgE levels in serum were not increased above those of the allergy model control (OVA). The results indicate that although AgNP may have a moderate effect on airway resistance in the lung when administered before sensitization, they do not significantly alter the course of allergy development when given either prior to sensitization or during the elicitation phase.

**PS 675 Gene Expression Changes Induced by Skin Sensitizers in THP-1 Cells: Possible Relationship to Protein Binding Domains**

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The objective of our study is to generate a global view of transcriptional changes induced in target cells exposed to sensitizing chemicals with the goal of identifying common functional and regulatory pathways/molecules. Six replicate wells of THP-1 cells (human monocytic cell line) were exposed for 24h to single concentrations of 9 skin sensitizers (SS), 8 low molecular weight respiratory sensitizers (RS), and 9 non-sensitizers (NS) along with 11 vehicle control replicates. Cells were harvested for transcript profiling using the Affymetrix GeneTitan® U219 array plates. Statistical analyses at the individual gene level using cut-off values of a 1.5 fold-change with a false discovery rate <0.05 identified 181, 72, and 273 unique gene expression changes for the SS, RS and NS, respectively. The 181 unique genes for the SS were analyzed by hierarchical clustering. Examination of the SS heat map revealed possible clustering by protein reactivity domains. Enrichment analysis using MetaCore™ software (Thomson Reuters) was conducted on all of the SS and individual SS grouped by domain using genes common to all in the group. The most significant pathways for all SS grouped together and the SN2 electrophiles were similar and included cholesterol biosynthesis, TREM1 and GM-CSF signalling. The top pathways for the MA electrophiles were related to oxidative stress and the activation of antioxidant defense system. Pathways activated by the one SS classified as an acylating agent included immune response pathways associated with antigen presentation, complement, and histamine signalling. These results suggest that the nature of the hapten-protein binding chemistry may influence activation of specific cellular pathways in immune cells.

**PS 676 Increased Expression and Immunoregulatory Potential of microRNA 210 in a Murine Model of TDI Sensitization**

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MicroRNAs are single-stranded RNAs that exhibit functional significance through the regulation of gene expression; however, their roles in chemical sensitization have not been elucidated. Toluene 2,4-diisocyanate (TDI) is a low molecular weight chemical sensitizer that causes occupational asthma. In order to investigate



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