

**48 House Dust Mite Group 2 Allergen Modulates LPS-Induced Responses in Airway Sensory Neurons**

Mayur Patil, MS<sup>1</sup>, Edward G. Brooks, MD<sup>2</sup>, Michael Henry, DDS, PhD<sup>1</sup>, Armen Akopian, PhD<sup>3</sup>; <sup>1</sup>UTHSCSA, San Antonio, TX, <sup>2</sup>Univ. Texas Health Science Center San Antonio, San Antonio, TX, <sup>3</sup>UTHSCSA, San Antonio, TX.

**RATIONALE:** Endotoxins like lipopolysaccharide (LPS) are effective sensitizers of the respiratory immune system. LPS-sensitized respiratory immune system undergoes maladaptive transformation after challenge with ovalbumin or *Der p 2* allergen. However, the types of cells and mechanisms which control this type of maladaptive transformation remain elusive. We hypothesize that airway sensory neurons could contribute to the respiratory immune system maladaptive transformation after sensitization by LPS and challenges by *Der p 2*. To address this hypothesis, we evaluated whether LPS and *Der p 2* could activate and modulate airway neurons.

**METHODS:** Activation and sensitization of neurons were examined using electrophysiology on rat airway jugular-nodose ganglia sensory neurons backtraced from bronchi. Neuropeptide release from airways was assessed using radio-immuno assay. Data were analyzed with ANOVA.

**RESULTS:** Our data indicates that LPS, but not *Der p 2* activates a subset of airway sensory neurons. Similarly, LPS but not *Der p 2* induced the release of CGRP from bronchi. Since *Der p 2* belongs to a family of proteins that can bind the LPS receptor - TLR4, LPS responses in the airway sensory neurons and bronchi preparations were modulated by *Der p 2*. In contrast, we did not detect modulation of *Der p 2* effects on airway neurons by LPS.

**CONCLUSIONS:** Activation of airway sensory neurons by LPS and modulation of these responses by *Der p 2* suggest a possibility that *Der p 2* can enhance LPS-induced release of factors from airway neurons and trigger airway inflammation and respiratory immune system maladaptive transformation.

**49 Effect of Recent Acetaminophen Usage in the Development of Asthma and Bronchial Hyperresponsiveness Is Modified by Toll Like receptor4 (rs1927911) Polymorphism**

Song I. Yang, MD<sup>1,2</sup>, Seung-Hwa Lee, BS<sup>3</sup>, Mi-Jin Kang, MS<sup>3</sup>, Ho-Sung Yu, BS<sup>3</sup>, Young Ho Jung, MD<sup>1,2</sup>, Ju-Hee Seo, MD<sup>4</sup>, Ji-Won Kwon, MD<sup>5</sup>, Byoung-Ju Kim, MD, PhD<sup>6</sup>, Ha-Jung Kim, PhD, DVM<sup>3</sup>, Young-Joon Kim, MS<sup>3</sup>, Hee-Suk Kim<sup>3</sup>, Kyungmo Hong<sup>7</sup>, So-Yeon Lee, MD<sup>8</sup>, Kang Seo Park, MD<sup>9</sup>, Jinho Yu, MD, PhD<sup>1,2</sup>, Soo-Jong Hong, MD, PhD<sup>1,2</sup>; <sup>1</sup>Childhood Asthma Atopy Center, Department of Pediatrics, Asan Medical Center, University of Ulsan College of Medicine, Seoul, South Korea, <sup>2</sup>Research Center for Standardization of Allergic Disease, Seoul, South Korea, <sup>3</sup>Asan Institute for Life Sciences, University of Ulsan College of Medicine, Seoul, South Korea, <sup>4</sup>Department of Pediatrics, Korea Cancer Center Hospital, Seoul, South Korea, <sup>5</sup>Department of Pediatrics, Seoul National University Bundang Hospital, Seoul National University College of Medicine, Seongnam, South Korea, <sup>6</sup>Department of Pediatrics, Haeundae Paik Hospital, Inje University College of Medicine, Busan, South Korea, <sup>7</sup>Goucher College, Baltimore, USA, <sup>8</sup>Department of Pediatrics, Hallym University Sacred Heart Hospital, Anyang, South Korea, <sup>9</sup>Department of Pediatrics, Presbyterian Medical Center, Jeonju, South Korea.

**RATIONALE:** The risk of asthma has been increasing with usage of acetaminophen which is a potential source of oxidative stress. Toll like receptor 4 (TLR4) plays not only a critical role in innate immunity but also recognizes the low molecular weight (LMW) forms by oxidative stress. The LMW is critical in initiating inflammatory responses.

**METHODS:** We undertook a population-based cross-sectional survey by using ISAAC questionnaire with 2,428 elementary school children in Korea. Current asthma was defined as diagnosis ever and symptom during the past 12 months. Bronchial hyperresponsiveness (BHR) in asthma was represented as PC<sub>20</sub>≤16. TLR4 (rs1927911) was genotyped using TaqMan assay.

**RESULTS:** Family history of asthma was a risk factor in asthma diagnosis ever and current asthma (aOR 1.974, p=0.047; aOR 2.867, p=0.030, respectively), but acetaminophen usage or TLR4 polymorphism was not. However, subjects who acetaminophen usage with family history of

asthma were increased the risk of asthma diagnosis ever and current asthma (aOR 2.552, p=0.032; aOR 4.635, p=0.009, respectively). CT+TT genotype of TLR4 polymorphism with acetaminophen usage had increased risk of asthma diagnosis ever (aOR 2.079, p=0.024), but not current asthma. Family history of asthma (aOR 1.987, p=0.036) and acetaminophen usage (aOR 1.469, p=0.014) were the risk factors for BHR. Although TLR4 was not the risk factor for BHR, CT+TT genotype of TLR4 polymorphism with acetaminophen usage had increased risk of BHR (aOR 1.741, p=0.038).

**CONCLUSIONS:** Acetaminophen usage to genetically susceptible subjects may affect the susceptibility of asthma and BHR. This effect may be modified by TLR4 polymorphism.

**50 Disposition of Toluene Diisocyanate (TDI) Following Dermal Exposure**

Donald H. Beezhold, PhD, FAAAAI, Ajay Nayak, PhD, Stacey Anderson, PhD, Brett Green, PhD, Paul Siegel, PhD; CDC/NIOSH, Morgantown, WV.

**RATIONALE:** Diisocyanates are highly potent allergens that cause work-related asthma and allergic disease. We describe a model for dermal exposure to diisocyanates using toluene diisocyanate (TDI) as a prototypic hapten that covalently modifies proteins to characterize the dermal exposure route.

**METHODS:** Ears of BALB/c mice were dosed a single time with TDI (0.1%, 4% and 15%) in acetone. Vehicle exposed mice served as controls. Ears and draining lymph nodes were collected at various time points between 1 hour and 15 days post-exposure and were processed for histology and immunochemical assessment. Monoclonal anti-TDI-haptenated protein (TDI-hp, mAb) and anti-langerin (CD207<sup>+</sup>) were used to examine antigen localization and processing using immunohistochemical confocal microscopy.

**RESULTS:** Hematoxylin and eosin stained sections of mouse ears exhibited edema, followed by infiltration of immune cells, epidermal sheathing, hyperplasia, and remodeling. At early time points staining for TDI-hp was found localized to the stratum corneum and in hair follicles and sebaceous glands. Immunostaining for TDI-hp was observed between 1 hour to 4 days post exposure, but could no longer be detected at later time points. Immunohistochemistry showed co-localization of CD207<sup>+</sup> positive Langerhans cells and TDI-hp in the hair follicles. Co-localization of antigen and dendritic cells was observed in the lymph nodes by 48 hrs.

**CONCLUSIONS:** TDI-hp were located mainly in the stratum corneum but the hair follicles and associated sebaceous glands appeared to be the hapten route of entry with subsequent migration of TDI-hp to the lymph nodes. These studies show the utility of TDI mAb for characterizing dermal and systemic exposures.