SATURDAY

208 A Single Dose Of Fel d 1 Monoclonal Antibodies Regulates Molecular Signatures of Asthma In Nasal Mucosa Upon Cat Allergen Challenge In A Phase 2 Study

Meagan OBrien, MD[1], Kaitlyn Gayvert[2], Matthew Wipperman[2], Fredreic de Blay, PhD[3], Alina GHERASIM, MD[4], Nathalie Domis[5], Pretty Meier[2], Michelle DeVeaux[2], Lorah Perlee, PhD[6], Gary Herman[2], Wei Keat Lim[2], Jennifer Hamilton[7], Sara Hamon[2]; [1]Regeneron Pharmaceuticals, [2]Regeneron Pharmaceuticals, Inc, [3]Nouvel Hopital Civil, [4]Alyatec, [5]ALYATEC® Environmental Exposure Chamber, [6]Regeneron Pharmaceuticals Inc, [7]Regeneron Pharmaceuticals, Inc.

RATIONALE: Allergies to cats are a major risk factor in the development of asthma. We aimed to investigate the effect of a single dose of Felis domesticus allergen 1 (Fel d 1) monoclonal antibodies (REGN1908/1909) on asthma signatures in a clinical trial assessing efficacy of the antibodies for prevention of early asthma responses (EAR) by cat allergen in cat-allergic mild asthmatic subjects (NCT03838731).

METHODS: Subjects were randomized to receive single-dose REGN1908/1909 600 mg (n=29) or placebo (n=27) prior to cat-allergen exposure in a controlled environmental exposure unit. Cat exposure occurred at baseline and day 29 to assess prevention of EAR, defined as a decrease of ≥20% from baseline FEV1. Nasal brushings were done post-cat allergen exposure at baseline and day 29 to assess nasal mucosal changes in gene expression with RNA sequencing. Differential fold change analysis, a novel placebo-controlled method of analyzing gene expression changes, was used to assess how previously published type 2 (GSE152004) and epithelial (GSE85567) asthma signatures were impacted by treatment within clinical subpopulations based on EAR.

RESULTS: REGN1908/1909 significantly suppressed EAR occurrence versus placebo on day 29 (44.8% vs 88.0%). When controlling for exposure time, subjects receiving REGN1908/1909 demonstrated improvement in asthma signatures compared to placebo both in the patient subpopulation that experienced an EAR (normalized enrichment score [NES] = -1.72, p<0.001) or those that did not (NES = –2.07, p<0.001).

CONCLUSIONS: Suppression of asthma signatures by Fel d 1 monoclonal antibodies was a sensitive molecular assessment as it occurred in REGN1908/1909-treated subjects regardless of whether they experienced an EAR.

209 Investigation of Specific IgG4 and IgE Antibodies to Cat Allergen Among 296 Subjects in the Project Viva Birth Cohort: Evidence that a Low Ratio of sIgG4:sIgE is a Significant Risk Factor for Asthma and Asthma Severity

Behnam Keshavarz, PhD[1], Lisa Workman, BA[1], Samuel Ailsworth[1], Diane Gold, MD[2], Emily Oken, MD, MPH[2], Sheryl Rifas-Shiman, MPH[3], Jeffrey Wilson, MD, PhD[1], Thomas Platts-Mills, MD PhD FAAAAI[1]; [1]University of Virginia, [2]Harvard T.H. Chan School of Public Health, [3]Harvard Medical School Department of Population Medicine.

RATIONALE: We investigated IgE and IgG4 antibodies to cat allergen and asthma in the Viva Cohort at age 13 years to better understand the tolerance induced by living with a cat.

METHODS: ImmunoCAP assays for sIgE and sIgG4 used cut-offs of 0.84 and 70 ng/ml respectively. Values for sIgG4 to sIgE ratios were calculated for cases with positive results to both isotypes. Cat ownership in the last year was taken as high exposure. Moderate severe asthma (MSA) was defined as current asthma cases who reported two or more acute episodes in the last year.

RESULTS: Full data was available for current asthma, MSA and cat exposure as well as specific sIgG4 and sIgE antibodies to cat extract for 296 subjects including 82 with current asthma. Among the 47 subjects with IgE to cat and a cat at home, the geometric mean ratio of sIgG4:sIgE among the 32 children without current asthma was 69.8 while the ratio for the 15 children with current asthma was 12.8 (p<0.01). Moreover, 10 of 13 subjects with asthma, who lived with a cat and had a sIgG4:sIgE ratio of less than 50, had MSA.

CONCLUSIONS: In keeping with previous results, exposure to cat did not cause an increased prevalence of sIgE to cat. However, among subjects with exposure to cat a ratio of sIgG4: sIgE lower than 50:1 was a significant predictor of current asthma and asthma severity. Our results suggest that children with a ratio of sIgG4: sIgE less than 50:1 might benefit from cat specific intervention.

210 Chemerin Deficiency Exacerbates Ozone-Induced Increases in Airway Responsiveness

Albert Pilkington, PhD[1], Michiko Takahashi[2], Yutaka Takahashi[3], Theresa Boots[1], Richard Johnston, PhD[1]; [1]National Institute for Occupational Safety and Health, [2]Kobe University Hospital, [3]Nara Medical University, Kashihara, Japan.

RATIONALE: Intranasal insufflation of chemerin, a non-chemokine chemoattractant, decreases the severity of airway hyperresponsiveness (AHR) following antigen sensitization and challenge, an atopic asthma stimulus, *via* suppression of CCL2 secretion. However, the effect of chemerin on AHR induced by ozone (O_3), a non-atopic asthma stimulus, is unknown. Furthermore, chemerin reduces alignment of collagen, and when collagen is present in excess in the lung interstitium, this decreases quasi-static respiratory system compliance (C_{stat}). Therefore, based on these observations, we hypothesized that C_{stat} is decreased and the severity of O_3-induced AHR increased in mice genetically deficient in chemerin (chemerin-deficient mice).

METHODS: Wild-type (C57BL/6J) and chemerin-deficient mice were exposed to filtered room air (air) or O_3 (2 parts/million) for three hours. Twenty-four hours following cessation of exposure, C_{stat} was calculated from the deflationary limb of pressure-volume curves obtained from air-exposed mice while responses to methacholine for respiratory system resistance (R_{RS}) and compliance (C_{RS}) were determined in air- or O_3-exposed mice using the forced oscillation technique.

RESULTS: C_{stat} was reduced in chemerin-deficient as compared to wild-type mice following air exposure. Compared to genotype-matched, air-exposed controls, responses to methacholine for R_{RS} and C_{RS} were significantly increased and decreased, respectively, following O_3 exposure. However, increases in R_{RS} and decreases in C_{RS} following O_3 exposure were exacerbated in chemerin-deficient as compared to wild-type mice.

CONCLUSIONS: In chemerin-deficient mice, decreases in C_{stat} may result from genotype-related differences in lung collagen alignment while increases in the severity of O_3-induced AHR may be a consequence of the inability to suppress CCL2 secretion in the lung.