News in Brief

American Academy of Allergy, Asthma & Immunology: Virtual annual meeting, February 26 to March 1, 2021

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After last year’s cancellation due to the pandemic, the annual meeting of the American Academy of Allergy, Asthma and Immunology was held at the end of February and provided an opportunity for clinicians and scientists to share the results of their research and learn about new and emerging therapies. In addition to the topics traditionally covered at the conference, e.g. therapies for allergic diseases, mechanisms of allergic inflammation, asthma or atopic dermatitis, research related to COVID-19 and COVID-19 vaccines (immunological profile, vaccine development, vaccine allergy etc.) were, unsurprisingly, extensively discussed. Below are a handful of studies presented during the scientific sessions and representative of the diversity of this conference.

Can the variable clinical phenotype of selective IgA deficiency be explained by gut microbiome/immune system interactions?

Peyton Conrey, along with co-first authors Lidija Denu and Kaitlin O’Boyle, as part of a collaboration between Dr. Sarah Henrickson and Dr. Michael Silverman’s labs at the Children’s Hospital of Philadelphia, Pennsylvania, USA, shared findings of a comparative study between patients with selective immunoglobulin A (IgA) deficiency and controls. While being the most common primary immune deficiency, only a third of affected patients are symptomatic and present with increased rates of allergy, infection and/or autoimmunity. In order to explain this variability in clinical phenotype, Ms. Conrey and her colleagues investigated the potential impact of IgA on the ability of gut microbes to access the systemic immune compartment.

To identify a potential link between the immune system and the gut, a cohort of 15 pediatric patients with selective IgA deficiency was recruited alongside a cohort of 17 controls composed of unaffected siblings of the patients living in the same household. Blood and stool samples were collected and used to perform high dimensional immune profiling, microbial flow cytometry and metagenomic sequencing. Specifically, patient’s or control’s serum was added to their stool microbes and antibody binding to these microbes was measured by microbial flow cytometry. Stool microbes were then sorted and sequenced. Significant alterations of the immune phenotype were observed with an increase in inflammatory cytokines, and a decrease in IgA+ and IgG+ B cells in patients. The access of commensal gut microbes to the systemic immune compartment was also affected with an absence of IgA-bound microbes but a higher proportion of IgG-bound microbes, confirming the initial hypothesis. The team is now conducting additional experiments in mice and humans to identify the mechanisms and to connect more precisely these alterations to the diverse phenotypes of IgA deficiency.

Androgen receptor signalling role in airway inflammation

Dawn Newcomb, from Vanderbilt University Medical center, USA reported the results of preclinical animal studies elucidating a mechanism behind the lower prevalence of asthma and type 2 airway inflammation in males compared to females. Previous studies evidenced that androgen signalling through the androgen receptor attenuates type 2 cytokine production, eosinophil infiltration into the airway, airway hyperreactivity and IgE production. In the present work, the team of Dr Newcomb hypothesized that androgen receptor signalling increases regulatory T cells (Tregs) suppressive function.

To test this hypothesis, Dr Newcomb and her colleagues developed a murine model by crossing Foxp3 fate mapping lineage mice with IL-13TdTTomato reporter mice, Foxp3 being the transcription factor for regulatory T cells. This model allows for the separate detection of current regulatory T cells, former regulatory T cells, Th2 cells and IL-13 former regulatory T cells. Male and female mice were submitted to a ten-day airway inflammatory protocol using a fungus (Alternaria) extract before harvesting their lungs and counting the different cell populations. No significant difference in the number of Tregs was observed between male and female mice after being challenged but the numbers of ex Treg, Th2 and IL-13 ex Treg cells were lower in male than in female mice. In a second series of experiments, three groups of male mice underwent the airway inflammatory protocol: a group with low concentrations of testosterone and androgens (due to gonadectomy), a group with restored levels after gonadectomy, and a group with endogenous levels of testosterone and androgens (who underwent a sham surgery). The two groups of mice with normal levels of androgens presented fewer number of ex Treg, Th2 and IL-13 ex Treg cells. These observations suggest that androgen receptor signalling is important for stabilizing regulatory T cell Foxp3 expression and provides a potential mechanism for decreased asthma prevalence in men compared to women.

Microneedle patch, a potential platform for peanut allergy immunotherapy

Michael Kulis, from the University of North Carolina at Chapel Hill, USA presented in the late-breaking session an evaluation of a new
immunotherapy platform that is being evaluated for patients with peanut allergy. Currently, only one immunotherapy treatment, an oral one called Palforzia®, has received FDA approval. In late stage development is an epicutaneous approach, called Viaskin®, that has shown promise in terms of safety but its efficacy response rate was limited to 35% of 4–11 year old, following 12 months of treatment in a clinical trial. Peanut antigens were applied on intact skin via a passive patch worn by the patient all day and replaced daily. In August 2020, the FDA did not approve this treatment due to several concerns including the patch not adhering to the skin for the required time. The team at UNC hypothesized that delivering antigens into the dermal layer of the skin, with a microneedle patch, might be a more efficient way to target the antigen presenting cells within the skin. This patch, developed by Moonlight Therapeutics, needs to be applied for only a few minutes and delivers the antigens within the skin as opposed to the surface.

In the presented study, Dr Kulis and his colleagues performed pre-clinical studies to evaluate the immunogenic and pharmacokinetic properties of peanut-protein loaded microneedle patches. First, the levels of peanut-specific immunoglobulins were quantified in three groups of naive mice administered different levels of peanut protein (placebo, 5 µg and 12.5 µg) via microneedle patches. The treatment was applied for 3 min, once a week for 3 weeks. Second, the safety of this approach was evaluated as the systemic absorption was compared between delivery via the microneedle patch and subcutaneous injections using measurement of Ara h 2, the most potent of the allergenic proteins identified in peanuts, in serum. The three weekly, 3-minute patch applications resulted in production of peanut-specific immunoglobulin, regardless of the applied dose. Ara h 2 was not detected in serum of the mice treated with the patch but was elevated in the mice after subcutaneous injections, indicating that the peanut protein administered via microneedles is not readily absorbed into circulation the way a subcutaneous injection of peanut protein is. If this type of profile holds in humans, it could mean that, despite administering the peanut proteins into the skin, the microneedle approach may be safe and not elicit systemic anaphylactic reaction. This pre-clinical data suggests that a microneedle patch could be a unique platform to administer peanut-specific immunotherapy using very low doses of peanut protein with a short application time. The team is now conducting additional studies to further understand the pharmacokinetics and investigate the desensitization mechanism of action.

House dust mite sublingual immunotherapy: an add-on treatment for atopic dermatitis?

Sarah Langer, MD, from Ribeirão Preto Medical School, University of Sao Paulo, Brazil, described a trial using house dust mite sublingual immunotherapy as an add-on treatment for patients with atopic dermatitis. Since 2007, a handful of studies have shown promising results following this approach in various populations (Asian and Caucasian, adult and children). However, none of these trials were both randomized and blinded. Additional well-designed trials are important to confirm these initial positive results, especially since sublingual immunotherapy products are already FDA-approved for other uses. Dr Langer and her colleagues conducted a randomized, double-blind, placebo-controlled trial evaluating the efficacy of dust mite sublingual immunotherapy drops.

In this registered trial (NCT03388866), 91 patients, all at least 3 years old, with atopic dermatitis (with a Severity Scoring of Atopic Dermatitis (SCORAD) score greater or equal to 15) and proven dust-mite allergy were enrolled. Patients were stratified by age (below vs above 12 years-old) to receive sublingual immunotherapy with extract from one of the most common dust mites Dermatophagoides pteronyssinus or placebo, 3 times a week, for 18 months. The primary outcome of the trial was a 15-point or greater decrease in SCORAD and the secondary outcomes were decreases in SCORAD, eczema area and severity index (EASI), visual analog scale of symptoms (VAS), pruritus score, investigator global assessment of 0 or 1 (IGA) and decrease higher than 3 points in dermatology life quality index (DLQI). 66 patients completed the study: 35 in the therapy group vs 31 in the placebo group. One severe allergic reaction was observed in the placebo group and caused cessation of treatment. The other reasons for discontinuation of treatment were pregnancy, withdrawal of consent, start of another treatment, loss to follow-up. At baseline, the average SCORAD score were respectively 48.1 and 45.7 in the treated and placebo groups. After 18 months, a higher proportion of patients under immunotherapy reached a 15-pt or greater decrease in SCORAD compared to the placebo group (74.2% vs 58%), although this difference was not significant. A higher number of patients with IGA 0 or 1 were found in the therapy group (40% vs 16%) and a larger significant decrease in SCORAD between baseline and end of treatment was observed (55.6% vs 34.5% decrease). The other indices did not significantly change. Further investigation of the efficacy of this therapy as an add-on treatment for atopic dermatitis is warranted. The team is currently assessing the immunologic responses to the treatment in laboratory experiments and conducting an open-label extension trial with a longer treatment period, to, hopefully, demonstrate a higher efficacy.

Declaration of Competing Interest

None.