

ALLERGIES & ASTHMA RESEARCH FACT SHEET

More than 25 percent of Americans, or 70-75 million people, suffer from allergies and asthma and these numbers are increasing. Symptoms range from coughing, sneezing and a runny nose to rashes, hives, lower blood pressure, difficulty breathing, asthma attacks and even death.

Allergies and asthma occur when the body's immune system reacts to a foreign substance (allergen) that usually is considered harmless to the body. The allergen is eaten, breathed into the lungs, injected or touched. People can have an allergic reaction to a wide variety of substances including tree, grass and weed pollen, mold and dust mites, cat, dog and rodent dander, food such as milk, eggs, soy, peanuts, tree nuts, fish and shellfish, drugs such as penicillin and insects such as bee stings.

Allergies can range from mild to severe. For some people they can compromise quality of life and even be life-threatening. This research is aimed at finding better ways to help these patients with less side-effects and risks.

Better Vaccines for Allergies

Benaroya Research Institute is a worldwide leader in investigating better ways to diagnose, treat and cure allergies and asthma. One century after its first introduction, allergen-specific immunotherapy (also called allergy vaccine therapy) remains the primary treatment for certain types of allergies. In this therapy, patients are vaccinated with increasing larger doses of the substances to which they are allergic with the goal of improving the body's immune tolerance to the allergen. A major drawback to current therapies is that they require months to years of treatment. In some cases, the allergy shots may also cause life-threatening symptoms such as low blood pressure and anaphylactic shock that can lead to death.

Scientists at BRI, led by William Kwok, PhD, with David Robinson, MD, Virginia Mason Allergy and Asthma Clinic, and Erik Wambre, PhD, and others are taking a new approach to improve allergy vaccine therapy. Our researchers are using tetramers — biomarkers discovered at BRI — to identify the piece of the allergen molecule (peptide) that causes a person to react. Using this small part of the allergen avoids the adverse reactions that can occur when the whole allergen is utilized. Tetramers are also employed to monitor patients and understand the immune responses that lead to allergic reactions.

BRI scientists have learned that over the duration of the allergy vaccine therapy, the pathogenic cells that react to the allergens eventually are depleted. This helps BRI to propose a new paradigm for understanding why duration and allergy dose are key factors for successful allergen-specific immunotherapy. This work is funded by a \$5.3 million grant from the National Institutes of Allergy and Infectious Diseases.

Critical Factor in Asthma & Allergies

In a significant discovery, Steven Ziegler, PhD, Director of the BRI Immunology Program, and his team identified a key factor that helps initiate the inflammatory cascade that leads to the onset and progression of asthma and allergies. In the last several years, Dr. Ziegler and colleagues have studied this factor called Thymic Stromal Lymphopoietin (TSLP) and found it is a critical component

of the underlying mechanism of allergic disease. This has led to studies of food allergies, lung infections, asthma, eczema, and even bronchitis in pediatric patients.

BRI's studies have shown an elevated level of TSLP in people with all of these diseases, suggesting that it may be the underlying cause. BRI scientists find that allergens turn on too much TSLP in some people, leading to an inappropriate response that can lead to diseases such as asthma as well as other allergies. The goal is to find a way to modify TSLP in these people so the immune system doesn't overact.

Lung Infection Research

Additional research is being conducted on lung infections through an \$11.7 million National Institutes of Health (NIH) research grant recently awarded to BRI. Dr. Ziegler will lead the researchers from BRI and the University of Washington, including Thomas Wight, PhD, and Daniel Campbell, PhD, from BRI. The goal is to understand what drives the inflammatory response to lung infections, and then learn how best to control that response to eliminate the associated disease progression. These diseases include influenza, pneumonia, chronic bronchitis, tuberculosis, HIV/AIDS-related respiratory illness, SARS and asthma.

Biomarkers for Asthma

Dr. Wambre is leading a team to find a unique biomarker that initiates and drives allergies. The hope is to identify a biomarker at the top of the allergic chain reaction that will predict the onset of allergy before the first symptoms are experienced and will lead to novel vaccine approaches as well as to develop a simple blood test to predict the likelihood of resolution of an allergy during therapy. BRI received a \$2.2 million grant from the National Institutes of Health to fund this project.

In another area, Dr. Wight has partnered with Drew Ayars, MD and Susan Potter-Perigo, PhD, from the University of Washington to understand whether tissue matrix components can be used as clinical markers of asthma severity. The tissue matrix consists of materials produced by cells in the lung in response to inflammation, contributing to progression of the disease. These biomarkers may be used to manage therapy for patients' asthma control and airway damage.

Community Support

BRI needs community support to continue its crucial work of unlocking the immune system and eliminating autoimmune and immune-mediated diseases. For more information about supporting BRI please call (206) 583-6083 or visit BenaroyaResearch.org/donate-now.