BREAKTHROUGH DISCOVERY
Cell that drives all allergies

Today when people have allergies and want to eliminate them, they must take allergy shots for a specific allergy such as pet dander or grass pollen. This treatment doesn’t always work, is limited to a few allergens at a time, can involve risk, and can take two to five years to build up immunity to the allergen.

What if, instead, there was one type of cell that could be targeted to affect all allergies and would be safer? Erik Wambre, PhD, at Benaroya Research Institute at Virginia Mason (BRI), has discovered a single type of cell that appears to drive all allergies that could change the trajectory of allergy research.

“This cell, which we named Th2A, could be a promising focal point for research to improve diagnosis, monitoring and treatment of allergies,” says Dr. Wambre. Additionally, these cells could be used as biomarkers, or indicators, that show whether a person has an allergy or is responding to allergy therapy. The research study was published in the latest issue of “Science Translational Medicine.”

“For the first time, BRI researchers have identified and are able to target a unique type of cell that causes allergies. Up until now, we couldn’t easily identify the ‘bad guy’ cells triggering allergies from the ‘good guy’ cells protecting the body,” says Steven Ziegler, PhD, who leads BRI’s Immunology Research Program. “This makes allergy research much more straightforward and opens the door to therapies that could target this common enemy and transform treatment.”

INCREASE IN ALLERGIES
Allergies affect 25 percent of the population or 50 million people in the U.S., and the incidence is increasing. It is estimated that by 2050 about one in two people will have allergies. Allergies occur when the body’s immune system makes a mistake and overreacts to a foreign substance (an allergen), such as pollen or animal dander, that in most people is generally harmless. Allergies can range from mild to severe. For some people, they can compromise quality of life and even be life-threatening.

BRI’s research, led by Dr. Wambre, began seven years ago, by examining a type of immune cell, called a Th2 cell, that helps orchestrate how the immune system responds to parasites, viruses and bacterial infections but also leads to allergies.

As Dr. Wambre and his colleagues analyzed human blood samples containing these cells, they

Continued on page 5
J ulie Poulsen learned she was allergic to peanuts at two years old. “I almost died in my mother’s arms after having a Snicker’s candy bar at a friend’s house,” says Julie. “I had over 20 reactions growing up in the early 90s.” Julie had to be cautious her whole life, reading labels, being aware of her surroundings, not accepting unfamiliar snacks and keeping her Benadryl and EpiPen close by.

She follows the latest research and discovered a peanut allergy oral immunotherapy clinical trial offered at Virginia Mason. Julie drives from Auburn, Wash., to participate in the study. She sees Virginia Mason allergists and BRI clinical researchers David Robinson, MD, and David Jeong, MD, who is also principal investigator for the study. “For the past year, I’ve taken a daily dose of the study medication,” she says. “After an initial food challenge to test my sensitivity, I started a dose and gradually increased it every two weeks for six months and then continued with a maintenance dose for another six months.”

The medication was either a peanut protein powder or a placebo powder. The research aimed to test if people could become desensitized to peanuts by taking small amounts of peanut powder each day and increase the dose until they no longer had a reaction to peanuts or had only a mild reaction.

BRI renown allergy researcher Erik Wambre, PhD, and his team are analyzing the blood samples from centers worldwide conducting the study. Dr. Wambre has discovered the allergen-specific T cells of the immune system that cause allergic disease. “Using our new tools and technology, it is now possible to look at blood samples of people with allergies and observe what these immune cells are doing,” says Dr. Wambre. “We can see how they respond to an allergen and to a vaccine like the peanut protein powder. If the vaccine is working, these cells decrease and then disappear.”

Though Julie didn’t know which medication she received at the time, she guessed after the first dose that it was the peanut protein because of mild reactions she experienced initially. Though the results of the clinical study have not been released, Julie personally had a good result.

TOLERATING PEANUT PROTEIN

“For me, it was a miracle! I can tolerate peanut protein now,” she says. “Trace amounts of peanut protein used to send me into anaphylactic shock. Swelling, vomiting, tightness in my throat, the use of Benadryl and an EpiPen used to be the drill. Now my body still recognizes when peanuts are introduced into my system, but instead of a full reaction, I just get a tingly tongue that subsides on its own, without medication, after 15 to 20 minutes.”

“The benefits of the result of my participation have been astounding,” she exclaims. “The peace of mind of not having to be on high alert has been totally worth the burden of a daily medication. I hope this research can help others with peanut allergies too. It was hard to grow up with a life-threatening allergy; I wanted the opportunity to improve or alleviate the burden for other families.”

Currently, she will have to take peanut protein on a daily basis to maintain her tolerance. “Based on my experience, I encourage anyone who can, to participate in clinical trials to help advance medicine.”

For more information on peanut and food allergy studies, visit BenaroyaResearch.org/clinical-allergies.
Exciting and innovative new treatments for inflammatory bowel diseases (IBD), which includes Crohn’s disease and ulcerative colitis, are now being offered in clinical research trials at Virginia Mason supported by BRI. “There is a rich pipeline of exciting new drugs and approaches that is bringing us steady progress in finding better solutions to fit individuals and their diseases,” says Michael Chiorean, MD, director of the IBD Center of Excellence and Digestive Disease Institute research at Virginia Mason. “Scientists and immunologists are discovering new molecules and pathways to target in IBD. This results in more options for people who can’t find a drug that works for them, become immune to the drugs that used to work for them or experience difficult side effects from their current drug. The new medications are more targeted, which may work better and may have fewer side effects.”

In some cases, the latest drugs can be life changing. “One of our research participants who hasn’t responded to any previous therapy went on a clinical trial, responded to the drug and is off steroids for the first time in years,” says Dr. Chiorean. “Another participant could only work the graveyard shift because he had to go to the bathroom every 20 minutes. With the clinical research drug, he went into remission, received a daytime job with a promotion and moved out of state. Now he chooses to fly back to Seattle for his follow-ups.”

Crohn’s disease and ulcerative colitis are autoimmune diseases in which the body’s overactive immune system attacks the intestines, resulting in intestinal inflammation, abdominal pain, diarrhea and bleeding.

Clinical research in IBD with Drs. Chiorean, Lord and Boden is working to make advancements in three areas:

1. BETTER DRUGS
“The efficacy of current drugs for inflammatory bowel disease is about 30 to 35 percent, so we are looking for more and better drugs to help patients,” says Dr. Chiorean. “Crohn’s disease and, to some extent, ulcerative colitis are probably many different diseases that we tend to lump together, so there are not just one or two drugs that will solve the problem for everyone. Since these are individualized diseases, we need individualized approaches including diverse classes of drugs and probably combinations of drugs. Among many interesting therapeutics in clinical trials, we have a new drug called mongersen. In the last 30 years, all efforts in IBD were aimed at turning off the overactive immune system to stop it from damaging the intestines. Mongersen is the first drug that turns on the regulatory part of the immune system to boost certain cells that deactivate the attacking immune cells.” Dr. Chiorean and his team select clinical research trials based on their patient population. They conduct regular reviews of their practice to evaluate the type of patients, disease type and severity they encounter to identify the most critical needs that are not satisfied by currently approved therapies and may be offered through a clinical trial.

2. IMPROVED DRUG DELIVERY
Some clinical studies test the ways drugs are delivered to see if they can be more convenient for patients while still being as effective. For instance, if a drug is given as an infusion, requiring a person to come to the clinic once a month for several hours, it is tested as an injection taken daily. A drug given as a weekly or monthly injection may be tested as an oral pill. If the drug is more convenient, it will be easier for patients to take it regularly as prescribed, thereby increasing compliance, improving their quality of life and their symptoms.

3. PERSONALIZED MEDICINE
At BRI, Dr. Lord leads research to find ways to best match an individual with the best medicine right away without trial and error. This research is being conducted by using the Inflammatory Bowel Disease Biorepository, a large, confidential sample repository containing tissue and blood specimens from people with IBD who are willing to provide health information to support scientific research. Scientists use these samples and data in laboratory analysis to better understand the causes and long-term health effects of IBD. They can also explore better treatment options for patient care and identify targets for novel therapies.

JOINING CLINICAL STUDIES
Dr. Chiorean encourages people who have not found a good medication for their IBD to consider joining a clinical trial. “People are sometimes hesitant about...
A t Benaroya Research Institute, we are delighted to receive and learn about how new donations come to the Institute. Many come regularly from ongoing supporters. And some are unexpected and may even be anonymous. Some are designated for a specific scientist or program or to help fight a specific disease or to honor a family member or friend. However they come, all donations are special to us because with every dollar, people are showing hope and trust in our work and dedication to conquer diseases and improve people’s lives.

Recently, we received one of our surprise donations. It came from Penn Mason McClatchey Sr., the grandson of one of the founders of Virginia Mason, John Blackford, MD. In 1920, Dr. Blackford and a group of physicians pioneered an innovative approach to healthcare—multispecialty medicine—and opened a hospital and a clinic that grew to include a research center, all in one place to provide the finest patient care possible.

**GIVING TO DIABETES RESEARCH**

When Penn received part of an annuity from his mother’s estate that was originally owned by Dr. Blackford, his first thought was to donate the proceeds to BRI. “Not only was my grandfather a founder, but while my mother was a chemistry student at University of Washington in 1941, she held a summer job at Virginia Mason titrating blood sugars for the kids with diabetes,” says Penn.

Penn and his wife, Ann, also happen to have three sons with type 1 diabetes, Mason, William and Forester, though no one in the larger family group has the disease. “We all live in the Southeast, or they would probably be patients of Virginia Mason and participate in BRI research,” he notes. “Please designate this money for type 1 diabetes research towards BRI’s efforts to cure this disease. I’m sure my grandfather would be pleased.”

It turns out that the McClatcheys support diabetes research in many ways and connect with BRI even though they live in the Southeast. All three sons participate in Type 1 Diabetes TrialNet, which is led by BRI with Carla Greenbaum, MD, Diabetes Research Program director, as chair. TrialNet is an international network that conducts clinical studies to evaluate new approaches to predict, prevent, delay and reverse the progression of type 1 diabetes.

**FAMILY FIGHTS THE FIGHT**

Mason, the oldest son, is a diabetes researcher starting his postdoctoral work at Vanderbilt University School of Medicine and Forester is a contributing writer to the Beyond Type 1 blog. William is studying film and worked as an intern on a type 1 diabetes documentary called the “Human Trial.” The family also supports JDRF, which in turn supports research projects at BRI.

The McClatcheys are especially intrigued by BRI’s approach to applying the breakthroughs we make against individual autoimmune diseases to make progress against them all. One son has four autoimmune diseases and another has two. They were diagnosed at young ages—5, 9 and 16. They also have a daughter who doesn’t have any autoimmune diseases.

“One technology is getting better all the time and we’re grateful for that, but diabetes is such a difficult disease,” says Penn. “It’s hard to always be thinking about what you eat and if you need more insulin. It’s 24/7.”

We’re hopeful a trip can be planned to introduce the McClatchey family to breakthrough diabetes research at BRI and to the legacy of a grandfather that has grown into a large, innovative medical system of 6,000 team members and nine locations. “My grandfather would be humbled and amazed,” says Penn.
discovered a specialized subtype of cell, which they called Th2A, that is present in people with allergies but almost entirely absent from people who don’t have allergies. They performed tests to confirm that Th2A cells play a pivotal role in at least six common allergies—including peanut, grass pollen, mold, cat dander, dust mite and tree pollen.

The research team also analyzed Th2A cells in blood samples from participants in a clinical trial of a new therapy for peanut allergies. Dr. Wambre and his colleagues found that the Th2A cells were activated when participants were exposed to the peanut allergen or an environmental pollen. Also the number of Th2A cells decreased as participants became desensitized to the peanut allergen during the study.

“This is the first time we’ve had a way to accurately measure the allergy process and assess whether therapies are working,” says Dr. Wambre. Even more important, researchers can now pursue therapies that potentially disarm Th2A cells and stop allergies.

The study’s results have already caught the attention of leading allergy research and advocacy organizations including Food Allergy Research & Education (FARE), which awarded Dr. Wambre a five-year Mid-Career Investigator Award in 2015.

“This could make allergy research much more directed, since scientists can now focus on the specific cells involved in generating allergies,” says James R. Baker Jr., CEO and chief medical officer of FARE, which funds research on new allergy therapies. “We’re hopeful that studying Th2A cells will quickly improve our understanding of how allergies develop and lead to therapeutic approaches to block allergies. This would improve the lives of allergy sufferers tremendously.” BRI and Virginia Mason are members of the FARE Clinical Network Centers of Excellence.

A strong collaboration between Wambre’s laboratory, BRI’s Translational Research Program including the biorepository team, allergy research participants and Virginia Mason’s Drs. Jeong, Robinson and Farrington helped to make this discovery possible.

BRI studies diseases caused by imbalances of the immune system, including autoimmune diseases, allergies and asthma, among others. Autoimmune diseases occur when the immune system mistakenly attacks its own healthy tissues. Allergies and asthma occur when the body’s immune system overreacts to substances that are generally considered harmless. When BRI scientists were studying the immune system in autoimmune diseases, they discovered significant cells and mechanisms that pertained to allergies and asthma. They continue to pursue these areas in efforts to rebalance the immune system and improve human health.

For more information and to see a video, visit BenaroyaResearch.org/wambre-PR-2017.
BRING IT ON.

Benaroya Research Institute at Virginia Mason
1201 Ninth Avenue
Seattle, WA 98101-2795

ANNOUNCEMENTS

ILLUMINATIONS LUNCHEON AND RESEARCH SHOWCASE
What: Join the fight against autoimmune diseases by attending the Illuminations Luncheon. Hear BRI researchers discuss their latest discoveries in diagnosing, treating and even preventing autoimmune diseases.
When: Friday, Oct. 27. New location: Sheraton Hotel, Seattle
10:30-11:30 a.m. Check-in and Research Showcase
11:30 a.m.-1:00 p.m. Lunch and Program
Contact: BenaroyaResearch.org/bri-events or Illuminations Luncheon event manager at 206-583-6514 or Events@VirginiaMason.org.

AUTOIMMUNE LIFE BLOG
Our website has an exciting new tool: a comprehensive blog where anyone can find out about everything autoimmune. Accessible to all, Autoimmune Life exists to build community, share breakthroughs and provide resources about autoimmune diseases and allergies. And the best part is, you don’t need to be a scientist to join the conversation. BenaroyaResearch.org/Blog.

Copyright © 2017 Benaroya Research Institute at Virginia Mason (BRI). All rights reserved. BRI is a world-renowned nonprofit medical research institute focused on diseases of the immune system. For more information, visit BenaroyaResearch.org or call 206-342-6500.