LEADING A NEW CENTER FOR ASTHMA AND ALLERGY RESEARCH

Benaroya Research Institute at Virginia Mason (BRI) is now leading an Asthma and Allergic Diseases Cooperative Research Center in Seattle to study the immune system response to allergens in the lungs. One in four people in the United States struggles with allergies, asthma or both. BRI has made significant breakthroughs in understanding how these conditions occur.

The National Institutes of Health recently awarded BRI an $8 million grant to lead the center—a collaboration of researchers from BRI, UW Medicine and Seattle Children’s Research Institute. “Over the next five years, we will work together to gain insights into the lung epithelium—the interface between the inside of the lung and the outside environment—to inform the development of new treatments and therapies for allergies and asthma,” says Steven Ziegler, PhD, who will lead the center. He is the director of BRI’s Immunology Research Program and Academic Affairs.

IMPACTING LIVES
“Because we’re using cells from both children and adults, as well as a culture system that closely mimics the actual structure of the lung, our findings will positively impact the lives of people living with allergies and asthma,” says Dr. Ziegler. “This study wouldn’t be possible without collaboration; we’re grateful for the collegiality of the immunology community in Seattle, through which we’re able to fight immune system diseases together.”

The research will focus on testing whether the airway epithelial cells, the layer of cells forming the lung epithelium, is the major regulator of responses to outside attack from allergens and respiratory viruses. Based on previous studies, the scientists predict that airway epithelial cells from people with asthma will differ in how this regulation controls infections and allergic responses. Each project will test a different aspect of this response, with the epithelium providing the common link between them.

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I ndigo Philo was a freshman in college when she began to get painful stomach cramps and an overwhelming sense of urgency to go to the bathroom. She was diagnosed with ulcerative colitis, an autoimmune disease in which the body’s immune system attacks the intestines, resulting in intestinal inflammation, abdominal pain and bleeding. Ulcerative colitis is a chronic lifelong disease that has no cure.

Indigo’s diagnosis was 35 years ago when there weren’t a lot of treatment choices. She was allergic to sulfa drugs so she received steroids. “I was in and out of college and in and out of the hospital,” says Indigo. She met her husband while attending the University of Washington and then began to work.

“The world was a different place at that time. There were no accommodations,” she notes. “It was tough to talk about this debilitating disease to your boss and hard to manage. Pain and cramps might hit you anytime. Sometimes I’d feel overwhelming pain and cramps up to 20 times a day.”

NEW MEDICATIONS HELP
After about 25 difficult years, Indigo began taking new biologic medications. They work by suppressing or weakening the immune system. “When I had my first infusion, I felt better instantaneously,” exclaims Indigo. “I thought—this is what life is like for a normal person! I was able to travel to these beautiful caverns in Arizona called Kartchner Caverns that were an hour from the bathroom and not have anxiety.” While Indigo still has active periods of disease, her quality of life has improved greatly.

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Indigo learned about the BRI biorepository that supports scientists in finding ways to prevent, diagnose, treat and cure autoimmune and immune-mediated diseases. She joined and provided health information and a blood sample. Indigo also encourages her friends and family, many of whom have autoimmune diseases, to join.
Benaroya Research Institute is committed to fighting the more than 80 autoimmune diseases. Because autoimmune diseases all share a common cause—mistakes made by the body’s immune system—scientists can use breakthroughs made against one autoimmune disease to make progress against them all.

BRI scientists are now discovering a new, exciting commonality between autoimmune diseases. This research points to an early event that drives the development of autoimmunity and which could be targeted by new therapies. They are pioneering research into this critical driver of autoimmune diseases that is present in rheumatoid arthritis, type 1 diabetes, celiac disease and most likely multiple sclerosis. Their investigation focuses on proteins that are modified when the body experiences environmental stresses.

Generally, the immune system has a system of checks and balances so it can protect the body against infections without overacting, but certain stresses can disrupt that balance.

**MODIFIED PROTEINS**

“We have found that when the body undergoes stresses such as a viral infection, it increases enzymes in the body that modify or alter its own proteins. These modified proteins can activate T cells to mistakenly attack and destroy healthy cells in the body, causing autoimmune disease,” says Eddie James, PhD, who is conducting a number of studies regarding T cell responses toward these proteins.

In 2014, BRI President Jane Buckner, MD, and Dr. James identified T cells that react to such modified proteins in the joints of people with rheumatoid arthritis (RA). They were able to demonstrate that the number of these T cells was increased in the blood of people with RA but that they were reduced with immune modulating treatments. Dr. James later demonstrated that similar T cells are present in people with type 1 diabetes and hopes to extend this research into other autoimmune diseases such as multiple sclerosis.

**DISCOVERY OF A COMMON DRIVER**

Dr. James is seated with laboratory members standing from left to right: research technicians Gabriele Blahnik-Fagan and David Arribas-Layton with Hai Nguyen, PhD, postdoctoral research associate.

These discoveries open up a whole new area of research, and Dr. James is now collaborating with many other groups to study the recognition of modified proteins. These include:

**University of Colorado and Karolinska Institutet, Sweden**—Drs. Buckner and James are collaborating with these institutions to see how the altered proteins affect people with RA. For instance, they plan to look at family members who are at high risk for developing RA and to perform studies to determine whether effective therapies eliminate these T cells. This collaborative work will also include structural studies to investigate why modified proteins are so effective at activating T cells.

**University of Pittsburgh**—Dr. James is working with Jon Piganelli, PhD, to see how the altered proteins affect type 1 diabetes (T1D). In T1D, the immune system mistakenly attacks beta cells in the pancreas. Beta cells create insulin that the body needs to live. “Beta cells may be the most stressed cells in the immune system,” says Dr. James. “Every time you eat, the beta cells have to release insulin and then restock. The stress can alter proteins in a way that causes T1D. Our collaborators have developed some anti-stress molecules. We want to see whether treating beta cells to block these stress pathways has the potential to slow down the disease process.”

**Yale University**—Dr. James is collaborating with Mark Mamula, PhD, to see if there are new biomarkers that can measure responses to modified proteins in type 1 diabetes. These studies would help further define at-risk family members who should be considered for prevention studies.

For more information, visit BenaroyaResearch.org/EddieJames.
**WIMPRESS FAMILY BATTLES DIABETES, SUPPORTS RESEARCH**

In the 1950s, when Jack Wimpress, a talented Boeing aerodynamics engineer, and his late wife, Doris, a dedicated nurse, began their family, they were a statistical anomaly. “Three out of four of our children developed type 1 diabetes,” says Jack. “Everyone told us that this wasn’t possible.”

Luckily, between a nurse and an engineer, they could plan and manage the rigid treatment their children’s disease required. “We had the whole family on a diabetic diet with carbohydrates, protein and starches measured separately for each child,” says Jack. “We had to measure blood sugar levels through the urine instead of the blood. We never had a day off; their care was 24/7. It was hard when the children had high or low blood sugars resulting in insulin reactions.”

Disease research. Jack has given every year since 1979 with several major gifts along the way. He has also attended programs at BRI to keep updated on progress. In August, Jack spoke at the Grapes on the Green fundraising event for BRI about his experience raising his family and the importance of supporting research.

**DEVASTATING COMPLICATIONS**

“Some people think living with type 1 diabetes is not a big deal, but the complications associated with it can be devastating,” says Jack. His children encountered major complications, including blindness, kidney failure, heart disease and poor blood flow to the feet. Two underwent pancreas transplants. While today there are nine grandchildren and 14 great grandchildren and lots of love, those with diabetes have suffered greatly. Jack hopes research can change this for other families.

“Type 1 diabetes has proven to be a very complicated disease and the solutions are very difficult,” says Jack. “It requires a broad-based research team with much expertise. Benaroya Research Institute has those qualities. That’s why I give and I hope others will give BRI the support it deserves.”

For more information on giving to BRI, visit BenaroyaResearch.org/support-us.

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**END-OF-YEAR GIVING**

Contributing to BRI provides vital funds to continue innovative research, invest in new ideas and new investigators, and purchase cutting-edge equipment. Every gift, large or small, makes a difference. You can give online at BenaroyaResearch.org/support-us or by returning the enclosed donor envelope.
**LEADING A NEW CENTER**  
Continued from front page

**OTHER AWARDS**

This latest grant follows a $2.9 million grant recently awarded to BRI to expand studies of interleukin-33, a protein that helps drive the immune response to allergic reactions. BRI researchers discovered this critical pathway in peanut allergy may also extend to other food allergies.

Culture of airway epithelial cells, with cilia on upper surface, similar to what is seen in the human lung.

BRI and Virginia Mason Medical Center were also recently selected to join the Food Allergy Research & Education Clinical Network, an initiative that aims to accelerate the development of drugs as well as improve the quality of care for patients with food allergies. BRI and Virginia Mason are one of 28 leading research and care sites nationwide that provide high-quality clinical and subspecialty food allergy expertise and services, and that are focused on applying new evidence-based knowledge to this important field. These centers also meet high standards for clinical care, teaching and clinical research.

Also, BRI Assistant Member Erik Wambre, PhD, was recognized last year with a Food Allergy Research & Education investigator award to support research in food allergy, specifically peanut allergy.

**LEADING INNOVATION**

"These grant awards speak to the tremendous work taking place at BRI and other research institutions in the region. Together, we are a leading source of innovation and progress in the fight for human health," said BRI President Jane Buckner, MD. "Only through these collaborations among investigators will we be able to turn the tide against these lifelong diseases so that we can move beyond treating and containing them, and instead focus on preventing them from ever taking hold."

For more information visit BenaroyaResearch.org/news and also do a web search for “Lung in a Dish.”

**ALL IN FOR RESEARCH**  
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When her physician retired, Indigo began to look for a new partner in her health care and she interviewed several doctors. “I met Dr. James Lord and he was calm, thoughtful, intelligent and compassionate. I thought this is the doctor for me.”

**BIOREPOSITORY SUPPORTS RESEARCH**

James Lord, MD, PhD, practices gastroenterology at Virginia Mason Seattle Medical Center and is a researcher at Benaroya Research Institute. He informed Indigo about the BRI biorepository, which collects, processes, stores and distributes biospecimens to support scientific research. BRI scientists use the donated biologic samples and medical histories to study ways to prevent, diagnose, treat and cure autoimmune and immune-mediated diseases.

Indigo has joined the biorepository and has recruited five family members to join—people with and without immune system diseases. A number of autoimmune diseases are present in Indigo’s family, including multiple sclerosis, rheumatoid arthritis and type 1 diabetes. Joining the fight against one autoimmune disease can lead to progress against them all.

“I’m excited about the research and of course I’d love a cure,” says Indigo. “But short of a cure, I’m really happy that BRI and Virginia Mason are truly committed to helping people with autoimmune diseases. They give me great hope that really smart people are working to make a difference.”

For more information visit BenaroyaResearch.org/biorepositories.
You’re invited to join us for a unique opportunity to learn about medical research at Benaroya Research Institute at Virginia Mason.

- Overview of BRI with a lead researcher
- Laboratory tour of BRI led by scientists
- Discussion with board members and other guests

**UPCOMING 2017 DATES**

Join us for lunch from noon to 1:30 p.m. on the following dates:
- January 27
- March 31
- May 12
- July 21
- September 22
- December 8

Register at BenaroyaResearch.org/ScienceFriday.

For more information, contact Rachel Martin at 206-342-6519 or RMartin@BenaroyaResearch.org.

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**THANK YOU!**

We are grateful for the support of the **2016 Illuminations Luncheon Sponsors.** The October 28 program showcased BRI breakthrough science to fight autoimmune diseases and raised a record $153,000. Thank you to all our sponsors, donors and attendees.

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