Scientists are discovering that the immune system is much more complex than previously thought.

A critical factor in whether people develop an autoimmune disease is “cell communication.” BRI principal investigator Adam Lacy-Hulbert, PhD, is studying cell communication in the gut.

Two autoimmune diseases, Crohn’s disease and ulcerative colitis (UC), also known as inflammatory bowel disease (IBD), occur in the gut. The body’s immune system mistakenly attacks the intestines, resulting in intestinal inflammation, abdominal pain and bleeding.

“The gut is fascinating because it is filled with bacteria and food that is technically foreign to the body, but they are an integral part of the body,” he says. “Usually the immune system would fight against foreign material, but within the gut it needs to sort out how to respond to a variety of things both good and bad for the body. These include infections, viruses, bacteria, food and medications.”

Dr. Lacy-Hulbert is studying special rare cells, called dendritic cells, which organize communications. They are the “teachers” that tell the “student” immune cells or T cells what to do. “Dendritic cells bring in the T cells and teach them what to respond to and how to respond to it. We research how dendritic cells make the decision to react to foreign materials and how they communicate it to the immune cells. This communication is vital because if the dendritic cells get it wrong and if they tell T cells to attack something that is part of the body, it can cause autoimmune disease.”

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We all know you can give blood to help ill or injured people who need it, but did you know you can also donate blood for research? Benaroya Research Institute collects blood samples and medical histories for researchers to use in their quest to prevent, treat and eliminate autoimmune and immune diseases.

The samples and information are stored in the BRI Immune Mediated Diseases Biorepository. It’s one of BRI’s most important assets, with more than 9,000 participants donating over 250,000 samples of blood and tissue, as well as medical histories collected since 2000 to support BRI scientists in their fight against diseases.

WHY GIVE?
Researchers use the samples to compare similarities and differences at the cellular and genetic level and identify biomarkers with distinct cell characteristics that are associated with the progression of disease. Using these biomarkers, BRI scientists are able to advance their understanding of how and why autoimmune and immune-mediated diseases develop, identify how genetic risk factors influence the immune system to cause disease and develop targets for new therapies. Scientists use samples from people with diseases and without diseases (Healthy Control Biorepository) for comparison.

HONORING A GRANDMOTHER
Meeko Garcia joined the biorepository in honor of his grandmother. “Joining the Healthy Control Biorepository carries a greater meaning beyond giving blood,” he explains. “This was an important and sentimental step that I took in honor of my grandmother who had diabetes. Every single donation provided to BRI benefits the overall mission in finding cures for autoimmune diseases.”

He found it easy to give. “Participation was easy and convenient,” he notes. “I contacted BRI and expressed interest in donating,” he adds. “The staff was accommodating with my schedule and expertly guided me through the whole process. My appointment took about 45 minutes.” All of the information gathered is kept confidential.

COMPANY SUPPORT
Meeko is strategic account manager for National Purchasing Partners (NPP), a group purchasing organization owned by Virginia Mason Health System. The company leverages the combined purchasing power of its membership to provide discounted products to its members including government, construction, hospitality and others.

“Because of our relationship with Virginia Mason, revenues from NPP actually end up supporting crucial research at BRI,” Meeko says. “Many of my co-workers have taken part in the donation process and are also excited to be part of the great cause. Autoimmune diseases touch many lives, and every supporter puts us that much closer to finding a cure.”

BRI BIOREPOSITORIES
A collection of blood samples and health information researchers use to help treat, prevent and eliminate diseases.

- Allergy and Asthma
  - Peanut
  - Tree-nut
  - Shrimp
  - Grass
  - Tree
  - Others

- Diabetes
  - Type 1 (T1D)
  - Family members of individuals with T1D

- Infectious Diseases
  - Japanese encephalitis virus
  - Yellow fever
  - Flu
  - Others

- Inflammatory Bowel Diseases
  - Crohn’s disease
  - Ulcerative colitis
  - Celiac
  - Others

- Neurologic Diseases
  - Multiple sclerosis
  - Amyotrophic lateral sclerosis (ALS)
  - Others

- Rheumatic Diseases
  - Rheumatoid arthritis
  - Lupus
  - Relapsing polychondritis
  - Others

- Healthy Controls
  - People without autoimmune disease

- Juvenile Arthritis
- Idiopathic Thrombocytopenic Purpura
- Lambert-Eaton Syndrome
- Vasculitis
- Autoimmune Polyglandular Syndrome
- Inflammatory Bowel Disease
- Lupus
- Scleroderma
- Systemic Lupus Erythematosus
- Thyroiditis
- Type 1 Diabetes
- Type 2 Diabetes
- Ulcerative Colitis
- Uveitis
- Vasculitis
- Vasovagal Syncope
- Wegener’s Granulomatosis
- Wilson’s Disease
How do you study children and adults who suffer from asthma, allergies or respiratory diseases? Without direct access to the lung for experiments, researchers find it challenging to study the molecules and cells that cause these conditions.

But Benaroya Research Institute (BRI) and Seattle Children's Research Institute (SCRI) scientists have tackled this problem by creating a “lung in a dish” and conducting exciting new experiments. Lead investigators are Steven Ziegler, PhD, BRI director of the Immunology Research Program and Academic Affairs, and Jason Debley, MD, of SCRI. They have also collaborated with BRI’s Erik Wambre, PhD, on allergies and Tom Wight, PhD, on the connecting tissue of the lung.

MODEL SYSTEM

“We've created a model system of the human lung in a laboratory dish,” says Dr. Ziegler. “We can replicate the environment of what you'd find in a lung by taking bronchial brushings from children and growing the cells in a special tissue culture system called air-liquid interface culture, which mimics what is seen in the airways.” Through SCRI, scientists have samples of cells from 200 children, 75 children with asthma, 50 who are at risk of developing asthma and 75 who are healthy.

An important part of the experiments is studying the lung epithelium. It is the cell layer in the lungs that serves as the interface between the inside of the lung and the outside environment. “It’s a barrier for bacteria and viruses in the lung, but it’s also a sensor. It’s a smart barrier,” explains Dr. Ziegler. “We've learned that it senses potential threats and determines whether or not to mount a response. For individuals prone to allergy and asthma, the epithelium incorrectly initiates immune responses to pollen or other innocuous environmental allergens.” The immune cells will then release chemicals which cause sneezing, itching in the nose and other reactions.

In addition, Dr. Debley says, “The epithelial response to infection and injury in asthma seems to be dysfunctional, sending signals to other cells in the lung that lead to airway scarring and narrowing, and ultimately a decline in lung function. Our model system using human cells from carefully characterized children with and without asthma is greatly expanding our understanding of mechanisms that drive childhood asthma, which we are optimistic...
Cece credits her Virginia Mason care team for getting answers and helping her find the best treatments so she can continue with her active life of traveling, spending time with friends and supporting important causes.

“I give to Virginia Mason because of the wonderful, lifesaving care I receive from all of my doctors there,” Cece explains. “How could I not donate? And I give to BRI because of all the inspiring work the Institute does to find causes and solutions for so many diseases. The hospital, doctors, nurses, BRI, board members, staff and those who generously donate all exemplify transforming healthcare. I am proud to play a small part in Virginia Mason’s and BRI’s journey and call VM my healthcare provider.”

For more information on giving to BRI, visit BenaroyaResearch.org/support-us.
Dr. Lacy-Hulbert and his team discovered that a certain gene is essential for dendritic cells to generate a population of T cells and to tell them to become regulatory cells that can control the immune response and avoid autoimmune diseases. Their research has described the complicated way that the dendritic cells instruct the T cells to activate and become T regulatory cells. They also discovered that if they block this process in a model system of the gut, ulcerative colitis develops.

“Our next step would be to test this in human samples,” says Dr. Lacy-Hulbert. “Then we can see if the dendritic cells make the wrong decision, can we reverse it? We are also studying the bigger picture of communications by studying the messages that are sent from the epithelial cells that form the barrier between the gut and the body. They are constantly sending messages that interact with other cells in the gut. We need to understand them better as well.”

For more information, visit BenaroyaResearch.org.
BOEING CLASSIC GOLF TOURNAMENT
What: The Boeing Classic, an official PGA Champions Tour event featuring the legends of golf 50 years of age or older. The event will benefit Benaroya Research Institute.
When: Monday - Sunday, Aug. 22-28 at TPC Snoqualmie Ridge
Contact: For more information and ticket options, please visit BoeingClassic.com.

EXECUTIVE WOMEN’S DAY
What: Executive Women’s Day at the Boeing Classic is an opportunity for women business leaders to learn from each other and network in an engaging forum.
When: Tuesday, Aug. 23 at TPC Snoqualmie Ridge
Contact: For more information and ticket options, please visit BoeingClassic.com.

GRAPES ON THE GREEN
What: Join us for this lively wine tasting, multicourse dinner and auction that kicks off the Boeing Classic Tournament weekend. This event benefits Benaroya Research Institute.
When: Friday, Aug. 26 at The Golf Club at Newcastle.
Contact: For more information and tickets, visit VirginiaMasonFoundation.org.

ILLUMINATIONS LUNCHEON
What: Become a BRI insider by attending this luncheon to learn about the latest breakthrough research at BRI. Attend as a guest, table host, or table sponsor, or become an event sponsor.
When: Friday, Oct. 28
Contact: For more information and ticket options, please visit VirginiaMasonFoundation.org.