What does it mean when scientists say they want to “prevent” a disease? “For the last 10 years or more, we’ve been making exciting discoveries that lead us to conclude that we can stop autoimmune diseases before they start in people who have a high risk of getting the disease,” says Jane Buckner, MD, President of Benaroya Research Institute at Virginia Mason (BRI).

While the Institute continues to look for the best therapies to treat autoimmune and allergic diseases, BRI researchers agree that the best way to cure diseases will be to prevent them from taking hold in the first place. Preventing type 1 diabetes is fully underway and rapidly making progress.

Now prevention work is quickly advancing in rheumatoid arthritis (RA). How do scientists plan to prevent RA? “We can now identify people at high risk of getting RA, and we are studying them to learn what occurs to trigger the disease,” says Dr. Buckner, leader of this work at BRI. “Then we will find ways to intervene, so they don’t get it.”

The ultimate goal, she explains, would be to develop a simple blood test that could be used routinely in the doctor’s office to determine a patient’s risk for the disease. For those at high risk, an individualized therapy would be provided to prevent RA from developing before symptoms occur.

Two studies are critical in making progress to identify individuals at risk of developing RA. The first, now completed, is SERA (Studies of the Etiology of Rheumatoid Arthritis) and the second, recently launched, is TIP-RA (Targeting Immune Responses for the Prevention of Rheumatoid Arthritis).

RISK FACTORS

People considered at high risk for RA are those who have a parent, sibling or child with the disease, as there is a genetic connection. In the general population, one in 100 people have rheumatoid arthritis, but for people with a close relative with arthritis, as many as one in 20 have the disease.

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RA is an autoimmune disease in which the body’s immune system mistakenly begins to attack its own tissues, primarily the synovium, the membrane that lines the joints. Because of this autoimmune response, fluid builds up in the joints, causing joint pain and systemic inflammation. This can lead to deformity of the joints and injury in other organs in the body.
During SERA, a study led by the University of Colorado which BRI participated in, Dr. Buckner and others followed volunteers who gave their medical histories and donated blood over time. They analyzed people before and after they developed RA. They also studied people who were at high risk but didn’t develop the disease.

Scientists learned that people develop autoantibodies called anti-cyclic citrullinated peptide (CCP) and rheumatoid factor (RF) up to 10 years before symptoms of the disease begin. Researchers also discovered that more of these autoantibodies are produced six months to a year before the disease occurs and that the immune system becomes more active.

“Our findings show there is an opportunity to intervene in this disease before it develops,” says Dr. Buckner. “Now we’ve started a new study, TIP-RA, to increase the number of people observed and to use new tools we’ve developed to understand disease. We’re also looking in-depth at people’s lifestyle and environment.” Besides the University of Colorado, Denver, TIP-RA also includes two new collaborators, bringing many perspectives to the work. They are the University of California, San Diego and Stanford University.

Benaroya Research Institute brings its expertise at how T cells contribute to RA. T cells are important in the immune system response because they tell the other immune system cells what to do in response to a virus or bacteria. They are key when the immune system makes a mistake and causes an autoimmune disease.

“We now have the capacity to take a small amount of human blood and look in-depth at specific T cells targeting the joints in RA, so we can understand what makes them become harmful and attack the body,” says Dr. Buckner. “We think these are the cells that cause RA. Now we can make incredibly rapid progress with our samples from our generous volunteers. Once we understand what starts RA, then we can develop approaches to stop it before it takes hold.”

Find resources and the full article on the Autoimmune Life blog: BenaroyaResearch.org/blog

THREE SISTERS HONOR THEIR MOTHER

Three sisters, Jeanne, Marilyn and Carol Kleyn, all joined the early research project SERA and the follow-up TIP-RA study. Their mother, Peggy Kleyn, was diagnosed with RA around 76 years of age.

“As a physical therapist, I have seen patients severely impacted by RA,” says Marilyn. “I helped my mother get the correct treatment early on. RA is a devastating disease and if there’s anything we can do to be proactive I’m all in.”

The sisters had many reasons to join the studies besides honoring their mother. “We all joined to find out if we had any biomarkers of the disease and, of course, to help the research, especially since there were three of us participating,” says Carol. “I’m sure it also made Mom feel good to know we were having early checks.”

Like many families with one autoimmune disease, a different autoimmune disease is often found within the family because of genes shared between autoimmune diseases. Marilyn was diagnosed with idiopathic thrombocytopenic purpura (ITP) in her 30s. BRI scientists work to apply what they learn from one disease to other diseases.

Carol and Marilyn do not have the autoantibodies that put them at high risk for RA, but Jeanne does. Because their mother did very well on a new biologic drug for RA for a number of years, Jeanne wasn’t too concerned about an initial reporting about her autoantibodies for RA. But as her mother’s health deteriorated, until her recent death at age 91, Jeanne became concerned.

“My mother was mentally bright and active, and then the RA caused her to have interstitial lung disease and she slowly deteriorated,” says Jeanne. “So now I’m very glad to know I’m at high risk.” In consultation with her doctors, Jeanne has decided to go on a medication that may aid in preventing the disease. Though this will change her status within the research study, researchers will continue to follow her progress. The next step for RA prevention research studies will be to test medications to slow or stop the disease.

Find resources and the full article on the Autoimmune Life blog: BenaroyaResearch.org/blog
The Morris family was celebrating Christmas when they realized their nine-year-old son, Jordan, needed to go to the doctor. Recently he had been losing weight, urinating often, extremely thirsty and exhausted. His mother, Leslie Morris, a nurse, suspected type 1 diabetes (T1D). Jordan loved sports and the day after Christmas he was dressed in his soccer uniform, ready to go to a tournament, when they broke the news that he had to go to the doctor instead.

“Jordan was also very responsible and learned quickly that the more he took care of himself, the better he felt.”

When they learned about diabetes research, Jordan's siblings rolled up their sleeves to be tested for the disease through Type 1 Diabetes TrialNet. TrialNet, led by BRI, is an international network of researchers who are exploring ways to prevent, delay and provide early treatment for T1D.

By giving less than a teaspoon of blood and health histories, family members can help find the answers for causes and cures for type 1 diabetes. Relatives of people with the disease are selected to participate because they are 15 times more likely to develop the disease than the regular population.

LEARNING IF YOU'RE AT RISK

The simple blood test can also tell families whether a member is at risk of developing T1D years before symptoms appear. “Detecting the disease at its earliest stage is very important,” says Carla Greenbaum, MD, chair of TrialNet and director of BRI’s Diabetes Research Program. “You may be able to join a research study looking for ways to slow down or stop the disease. You can start treatment early and aggressively if needed. Also, participating in risk screening helps kids avoid serious complications before diagnosis.”

“We felt it was important for the kids to be tested and know if they had two or more autoantibodies

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Most parents would expect their six-year-old twin boys to have safe, carefree and somewhat similar childhood experiences. Imagine their surprise when Rachael Crickman and Stephanie Cooper learned their son Zephyr had a severe food allergy, while his twin brother, Zachary, did not.

When Zephyr was nine months old, he was diagnosed with food allergies after a life-threatening reaction to eggs. Since it is common for children to be allergic to both eggs and peanuts, Zephyr was tested and found to be allergic to peanuts, too. While he no longer has a serious reaction to eggs, Zephyr deals daily with a life-threatening peanut allergy. Consequently, Zephyr’s life is very different from that of his twin brother. Zephyr must be constantly vigilant about food, while his twin brother can be much more carefree.

DAILY VIGILANCE

Food allergies can have a tremendous impact on daily life. Most people with food allergies practice avoidance. However, as Rachael and Stephanie know, accidental exposure to peanuts can happen if they are not vigilant and would be life-threatening for their son.

“It can be very isolating to be a child living with a peanut allergy,” says Rachael. “There is a lot of fear regarding mundane things like someone else’s lunch. Zephyr understands he could die if he ate peanuts.”

It’s not easy on the parents either. Rachael explains that it’s difficult and scary to send your child “to camp, school, temple, and the world, not knowing how vigilant others will be checking for food allergens. Peanut is found everywhere because of peanut flour, peanut oil and other peanut products.”

Luckily, Zephyr has the full love and support of his family as he deals with his allergy. Rachael and Stephanie practice with the boys how to administer epinephrine injections in case Zephyr has a serious allergic reaction. “Zachary is kind and very protective of Zephyr, which helps us in our vigilance,” says Stephanie. “The boys are best friends and competitors—they delight in each other and crack each other up.”

LOOKING TO RESEARCH FOR HOPE

While managing their daily challenges, the entire family looks to research for hope. Rachael and Stephanie learned about the cutting-edge research being conducted at Benaroya Research Institute from Zephyr’s Virginia Mason allergist, Mary Farrington, MD. Virginia Mason physicians and BRI scientists work closely together on many aspects of allergy research.

“We ultimately wanted to contribute to science and help make the world safer for people with severe food allergies,” say Stephanie and Rachael. That led to Zephyr and Zachary joining the BRI biorepository.

At BRI, a crucial tool for advancing medical research is the collection of biological samples called a biorepository. These samples are mostly blood donations from volunteers, like Zephyr and Zachary, which are analyzed by scientists and used in research to identify ways to prevent, diagnose, and treat a variety of conditions.
that would show that they would get diabetes,” says Leslie. “Then we could follow them as it developed and get them the right care.” None of the siblings have the markers.

“To all those considering contributing to research, I want to thank you,” says Jordan. “This is going to be a group effort to find a cure. And I want to thank my family. I wouldn’t be where I am in sports or life without my family. To hear they’re helping with research and supporting me means everything to me.”

**JORDAN MORRIS FOUNDATION**

“I’d like to give back to the diabetes community and help young people with the disease,” says Jordan about launching the Jordan Morris Foundation. “I want to be available to talk to kids, inspire them to accomplish their goals and help them with some tips or advice.” Jordan’s community outreach includes a website, visits to hospitals and schools and other opportunities. Learn more at JordanMorrisFoundation.com.

*Find resources and the full article on the Autoimmune Life blog: BenaroyaResearch.org/blog*

**TWINS Continued from page 4**

treat and, hopefully, cure many types of autoimmune and allergic diseases.

While Zephyr donated a sample to the Allergy and Asthma Biorepository, Zachary donated blood to the Healthy Control Biorepository. By bravely donating their blood samples, Zephyr and Zachary became superheroes and partners with BRI scientists in the fight against autoimmune and allergic diseases. Though Zachary does not have an autoimmune disease or allergies, his contribution is invaluable for scientists who look for differences between the immune systems of those with and without disease.

**BREAKTHROUGH SCIENCE**

Samples donated to the BRI biorepositories by participants were crucial in a recent breakthrough in allergy research. Scientists at BRI, led by Erik Wambre, PhD, made the discovery that could change allergy research worldwide. They identified a single type of cell called TH2A that appears to drive all allergies. This is a promising discovery because the cell can be targeted for new treatments and possible cures for all allergies, not just one.

As part of his allergy research, Dr. Wambre is also working to better understand the mechanisms behind innovative oral immunotherapies, which are currently in trials at Virginia Mason. The research is testing if people can become desensitized to peanuts by taking small amounts of peanut powder each day, increasing the dose until they no longer have a reaction to peanuts or have only a mild reaction. Rachael and Stephanie became aware of the clinical trials and are interested in allowing Zephyr to participate in them.

*Find resources and the full article on the Autoimmune Life blog: BenaroyaResearch.org/blog*
JOIN OUR CHAMPIONS

Generous donors who give $1,000 or more annually in support of Benaroya Research Institute at Virginia Mason (BRI) are members of our BRI Champions Giving Circle. Champion gifts provide a reliable stream of funding, enabling our scientists to make great strides in their research. Our Champions support also brings hope and relief to the more than 20 million people living with autoimmune diseases. We are grateful and appreciative of our BRI Champions. Without their support, our discoveries and advancements would not be possible.

Please consider joining our efforts to fight autoimmune and immune system diseases at the Champion level. As a member, you will receive an insider’s look into the research occurring because of your support, as well as special invitations to learn more about science.

To join, visit BenaroyaResearch.org and click on Support Us.

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