Lauren Lippincott is not yet 35 years old, yet she lives with five autoimmune diseases. She’s not alone. About 25 percent of people with autoimmune diseases have a tendency to develop additional autoimmune diseases. For people who have more than one diagnosed autoimmune disease, it’s called polyautoimmunity. The combination of three or more diagnosed autoimmune disorders in one person is called Multiple Autoimmune Syndrome (MAS).

Scientists are investigating the exact reasons why people may get more than one autoimmune disease, but they agree that some of these diseases are linked through genetics and environmental causes, says Jane Buckner, MD, President of Benaroya Research Institute at Virginia Mason (BRI). “The gene defect that caused the immune system to attack the body and create an autoimmune disease could cause another autoimmune disease,” she explains.

BRI is a pioneer in understanding and discovering the commonalities between autoimmune diseases. “There’s a good reason that we say, ‘Progress against one autoimmune disease is progress against them all,’” emphasizes Dr. Buckner. “Underlying mechanisms in some of these diseases are similar, and as we figure out how one works, it gives us clues to how others work. As we more fully learn how the diseases operate, we can apply the right therapies to diagnose, treat, cure and ultimately prevent autoimmune diseases.”

Some diseases carry an increased likelihood of people having an additional autoimmune disease. These include rheumatoid arthritis, multiple sclerosis, autoimmune thyroiditis, Sjogren’s syndrome and others.

Living Well With Disease
At age 4, Lauren Lippincott learned she had type 1 diabetes. At age 12, after complaining about uncomfortably cold hands and feet, she was diagnosed with Raynaud’s disease. When Lauren was 16, her hair started falling out in patches — she had alopecia areata. At age 18, as a freshman in college, her joints suddenly locked up and she was in debilitating, chronic pain. She found out she had ankylosing spondylitis, a form of arthritis. At age 24, in an attempt to make her joints feel better, she tried different diets and was confirmed to have celiac disease and now must be gluten-free.

Lauren remembers clearly the day she learned that her diseases were all autoimmune diseases. “I was at a talk by the former head of BRI, Dr. Jerry Nepom, and he was describing the relationship between autoimmune diseases. Suddenly, I saw the names of my diseases show up on his PowerPoint slide,” she says. “It suddenly clicked that all of these seemingly random diseases were...”

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FROM ANGUISH TO ADVOCATE:
Helping People With Inflammatory Bowel Disease

Waiting a colonoscopy in a Tri-Cities, Wash., emergency room was the last place Angie Neal expected to find herself. The 33-year-old Olympia native was the epitome of health: She exercised regularly, ate healthy foods and had never been overweight. But when a concerned gastroenterologist ordered the additional exam, she knew it was serious.

“It was shocking,” Angie says of the test results. “I had never heard of inflammatory bowel disease [IBD] or, my official diagnosis, ulcerative colitis [UC].”

For nearly a year, Angie was symptom-free with a mesalamine treatment putting her condition into remission. Then, unexpectedly, she experienced a flare with new and much worse symptoms that didn’t respond to therapy.

Angie recalls, “I was severely dehydrated and stopped counting after 16 trips to the bathroom in one night. The night before I was finally admitted to the hospital, I was afraid to go to sleep for fear of dying.”

Over the next few months, Angie’s body was ravaged by her UC. On multiple occasions she was admitted to the hospital for weeks at a time. For much of the next year, with her symptoms back in remission, Angie worked to rebuild her body. But, as is the nature of this cyclical disease, she eventually experienced another severe flare.

DIFFICULT DECISIONS

Angie’s gastroenterologist consulted with Virginia Mason doctors about her condition and presented her with two options: She could take a monthly IV infusion of a drug called Remicade, or she could travel to Seattle to have her colon surgically removed. It was a difficult decision that, in the absence of a clinical trial, many UC patients must make.

“I had to think long and hard about it,” Angie says. “I felt I just couldn’t live through another flare like that again.” Ultimately, she chose the surgery, adding, “It was an undertaking.”

Angie’s procedure, called a colectomy, involved two major surgeries spread out over two months. The first operation removed her entire large intestine, connected her small intestine to her rectum and created a temporary ostomy to divert waste until everything healed. Two months later, in the second operation, her ostomy was removed.

LEARNING ABOUT RESEARCH

During this time, Angie learned about the research being conducted at Virginia Mason and Benaroya Research Institute and joined the BRI Biorepository. The Inflammatory Bowel Disease Biorepository is a confidential list of people with inflammatory bowel diseases (IBD), such as Crohn’s disease and ulcerative colitis, who are willing to donate a blood sample and provide health information to support scientific research. Researchers use the biorepository to better understand the causes and long-term health effects of gastrointestinal and immune-mediated diseases, as well as to explore better treatment options.

ANGIE’S ADVICE FOR A NEW PATIENT

“Stay positive and don’t harbor resentment. Take comfort in knowing you can do the things you want, but they may have to be modified now. You can maintain control of your life. And, yes, you can do this.”

Angie’s recovery was long and challenging. With the support of her Virginia Mason team, she successfully modified her hydration, diet and exercise routine. In fact, Angie was so impressed by her experience, she moved to Seattle with the hope of working at Virginia Mason. And in 2016, she joined the Digestive Disease Institute at Virginia Mason as a clinical research coordinator.

“Having lived the experience, my work is both interesting and personally meaningful,” Angie says. “I know exactly what my patients are going through and they truly appreciate that I’ve been there.” She adds, “And while it was the right choice for me, I understand most of my patients are trying to avoid colectomy. That’s why it is a privilege to be part of research I’m passionate about at an institute that is so highly regarded.”

Find the full article on the Autoimmune Life blog: BenaroyaResearch.org/blog.
Some diseases occur together more frequently, such as type 1 diabetes and celiac, because of a shared gene that predisposes for these diseases. In people who have three autoimmune diseases or more (MAS), researchers and physicians have identified groups of diseases that cluster together. This may be a helpful tool for doctors diagnosing additional autoimmune diseases in one person since there are more than 80 different disorders.

BE ALERT FOR SYMPTOMS

“While we don’t want people to worry about getting more than one autoimmune disease, we do want them to be alert for another one if symptoms do occur,” says Dr. Buckner. “Then they can be diagnosed and treated early on. Also, in some cases, the combination of diseases may require a change in medication.”

Some people may not realize that they have two or more autoimmune diseases because they are treated by different doctors for different things. For instance, a patient may have ulcerative colitis, which affects the gut, and see a gastroenterologist for care. Meanwhile she may also develop vitiligo, which affects the skin, and see a dermatologist for care. The patient might not be aware they are both autoimmune diseases. “It would be helpful for her to know that they are both autoimmune diseases and inform both of her doctors, so they can coordinate her care,” notes Dr. Buckner.

Multiple Autoimmune Diseases in Down Syndrome

BRI scientists are studying multiple autoimmune diseases in people with Down syndrome. “Patients with Down syndrome have a 15- to 100-fold greater chance of getting autoimmune diseases such as type 1 diabetes and celiac disease, and we want to understand why,” says BRI Principal Investigator Bernard Khor, MD, PhD. “We think it’s related to excessive DYRK1A, a protein that can prevent the body from shutting down unnecessary inflammatory responses. It is also a main gene in Down syndrome.

If we’re correct, we might stop autoimmune diseases in these patients using DYRK1A inhibitors that are in development. Then we can go back to the broader patient populations with type 1 diabetes and other autoimmune diseases to understand who else might benefit from DYRK1A inhibition.”

To study this, BRI recently established the first Down syndrome biorepository in the Pacific Northwest, led by Dr. Khor and Rebecca Partridge, MD, head of the Virginia Mason Down Syndrome Program. Blood samples donated by participants with Down syndrome, including those with and without autoimmune diseases, will be used to move research forward.

Their parents and siblings can advance science by joining the Healthy Control Biorepository.

Genetic Links in Diseases

“Some genes contribute to multiple diseases, showing us that there are common causes, and helping explain why different autoimmune diseases can occur in a single family or even in a single individual,” says Karen Cerosaletti, PhD, a BRI Principal Investigator who studies genetics in lupus, type 1 diabetes and other autoimmune diseases.

Key genes that appear in multiple autoimmune diseases.

“Our research can point to specific defects that can be targeted therapeutically and may allow us to group patients so that we can direct therapies to the groups who are most likely to benefit from them,” explains Dr. Cerosaletti. Some of these genetic connections, many of which are studied at BRI, are illustrated above. This is the
type of analysis that is helping move treatments away from emphasis on the tissue that is being attacked toward a focus on the pathway (type of cell) that needs to be fixed — pathways that are sometimes shared by patients with different diagnoses.

Dr. Buckner’s laboratory has discovered why a group of genes linked to autoimmunity promote diseases including type 1 diabetes, multiple sclerosis and lupus. The genes include PTPN22, IL2RA, PTPN2, BANK1, IFIH1 and TYK2.

“Once we learn about the genes that are critical in an autoimmune disease, we go back to our research participants who have autoimmune diseases that are in our biorepositories,” says Dr. Buckner. “They have donated blood and provided their medical histories. We can see if they have that gene and whether that gene has created a defect in the cells or that pathway that’s causing an autoimmune disease. They teach us about the disease and which therapeutics will work, and then we can apply it to the general population in clinical studies.”

Understanding Type 1 Diabetes

Dr. Buckner and Carla Greenbaum, MD, Director of BRI’s Diabetes Research Program, recently wrote a scientific paper emphasizing how past scientists, studying patients with multiple autoimmune diseases, discovered that type 1 diabetes was an autoimmune disease. This opened the door for treatments of the disease and led the way so that today, there are clinical trials for the prevention of type 1 diabetes.

“This discovery was also important in showing that autoimmune diseases had common mechanisms,” says Dr. Buckner. “This is why it’s vital that we don’t study just one disease but look broadly across diseases. We learn from one disease and see how we can apply that information to another. That is how we can accelerate research and optimize our abilities to help people with autoimmune diseases as quickly as possible.”

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

Dr. Buckner and Carla Greenbaum, MD, research autoimmune diseases.

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not random at all; it was a moment of crystallization, of connecting HUGE dots. It felt empowering to learn more about my body and what I had been living with.”

Lauren takes a positive approach to dealing with her diseases. “I try very hard not to view myself as a sick person. I focus hard on what my body can do and has done for me, and I’m still able to feel deep gratitude for my life. My body helped me come back from a stroke (unrelated to autoimmune issues), and it gave me the gift of my young son. My experiences with my health also pushed me to pursue a career as a therapist who counsels others navigating a chronic illness, and working with my people — resilient, strong, tired, beautiful fighters trying to love the bodies that have often betrayed us — gives me so much courage and offers me so much grace in the face of disease.”

Lauren advises others not to worry about having more than one autoimmune disease. “Please do not allow fear to rule your life. Having a rich, full life is possible with one or five autoimmune diseases! Lean on your family and friends, focus on your strengths and shore up where you need support.”

Lauren also gets strength from BRI’s commitment to find the causes and cures for autoimmune diseases. “I take comfort in BRI’s no-nonsense approach in searching for the root cause of autoimmune disease and not just because I have so many that need solving! Every time I see their tagline, ‘progress against one is progress against them all,’ I’m reminded that BRI’s combined effort to tackle the enormous beast that is autoimmune disease is the best strategy for beating them.”

Find the full article on the Autoimmune Life blog: BenaroyaResearch.org/blog.
IMMUNE SYSTEM DISCOVERY: New Strategy May Stop Breast Cancer

The study of a protein, critical in causing asthma, allergies and other diseases, has led scientists at Benaroya Research Institute at Virginia Mason (BRI) to discover a new strategy for stopping breast cancer.

BRI researchers Emma Kuan, PhD, and Steven Ziegler, PhD, have pinpointed how the protein, called thymic stromal lymphopoietin (TSLP), causes breast cancer tumors to survive and grow. Even more significant, the researchers showed that blocking TSLP can significantly inhibit the growth of breast tumors and halt metastasis to the lungs. This discovery opens the door to new strategies that could stop breast cancer tumors from growing and spreading. It may also be applied to other tumors that involve TSLP.

“Breast cancer becomes especially dangerous once it spreads to other parts of the body,” Dr. Kuan says. “Our work suggests that blocking TSLP could prevent this from happening and potentially save the lives of women worldwide.”

The research was published recently in *Nature Immunology*. TSLP was discovered 15 years ago by the Ziegler Laboratory, as well as other labs, to initiate the inflammatory cascade that leads to the development of asthma, allergies and other diseases.

Researchers had previously found elevated TSLP levels in several different tumor types, but its role in tumor biology was unclear. Drs. Kuan and Ziegler solved this mystery by using preclinical models to investigate what happens to breast cancer tumors when TSLP is taken away.

“The tumors can get started without TSLP, but they need it in order to stay alive and metastasize through the body,” Dr. Ziegler says.

Once the researchers determined that TSLP was critical, they set out to uncover how it worked — and became the first to discover that tumors turn immune cells into accomplices that express TSLP. Importantly, the researchers found that the same cells that make TSLP in the models also make TSLP in human breast cancer patients, and human breast tumor cells respond to TSLP in the same way.

When Drs. Kuan and Ziegler used an antibody to block TSLP, it stopped tumors in their tracks — even when they had already started growing. Within six weeks, the tumors had shrunk significantly, more of their cells were dying and they had stopped spreading to the lungs. This suggests that anti-TSLP therapy could work in human patients with existing tumors.

“Blocking TSLP could potentially contain not just breast cancer, but many other tumors that have elevated TSLP — including pancreatic cancer, cervical cancer and multiple myeloma,” says Dr. Kuan.

HOPE FOR CLINICAL TRIALS

A drug that blocks TSLP has already been developed, and initial trials have shown that it’s safe in patients with asthma, so scientists are hopeful clinical trials could be launched for cancer patients in the relatively near future.

For their research, Drs. Ziegler and Kuan used samples from BRI’s new biorepository, the Virginia Mason and Benaroya Research Institute Tumor Repository (VM BRITE). The biorepository houses the medical history and blood and tumor samples of research participants with a variety of cancers.

“As BRI studies the immune system and tries to understand why it veers off course, we learn how it relates to other diseases such as cancer,” says BRI President Jane Buckner, MD. “We want to pursue these discoveries to improve the lives of people with autoimmune diseases, cancer and hopefully many other diseases.”

*Find the full article on the Autoimmune Life blog: BenaroyaResearch.org/blog.*
BRI SEAFAIR TRIATHLON
What: Swim, bike, run at the Benaroya Research Institute Seafair Triathlon. This is a unique opportunity to participate in one of two endurance-testing races: an Olympic distance triathlon (1-mile swim, 20-mile bike ride, 10K run) or a sprint distance triathlon (half-mile swim, 12-mile bike ride, 5K run). There will be opportunities to fundraise for BRI.
When: July 22, Seward Park
Contact: Visit sea-tri.com.

BOEING CLASSIC GOLF TOURNAMENT
What: The Boeing Classic is 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: Aug. 24–26 at The Club at Snoqualmie Ridge
Contact: 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: Aug. 24, 6 p.m., at The Golf Club at Newcastle
Contact: Visit VirginiaMasonFoundation.org/events, or call 206-223-7521.