Clinical Immunology Society
FOUNDATION

Support Research for Primary Immunodeficiences and Immune Dysregulatory Disorders

The Clinical Immunology Society is committed to…

- Research
- Education
- Novel approaches to therapy
- Excellence in patient care

$1M

Fundraising goal before money is dispersed

$100K

Pledge made by CIS

Jami Whaley's Story

The Whaley Family

My journey to a diagnosis of Common Variable Immunodeficiency (CVID) began with several life-threatening infections. An episode of meningitis 12 months prior to the birth of our daughter was terrifying, but we assumed it was related to my work in the Pediatric ICU. Three weeks after our first daughter was born, I had a sudden, unexplained fever. I spent four days in the hospital receiving antibiotics, but there was no explanation for this fever. It was assumed I had an infection related to my episiotomy. I returned to work when my daughter was three months old. Five days after returning to work, I had a diagnosis of sepsis and spent over a week in the hospital. After this, I did not return to work. At this point, the doctors were assuming the repeated infections were related to my splenectomy in 1994. When the sepsis returned nine weeks later, I was hospitalized, put on a 6-week course of oral antibiotics and instructed to visit an infectious disease physician. She ordered lab work that included immune studies, and referred me immediately to an immunologist. Finally, we had some answers but far more unanswered questions.

Now we had a diagnosis of sorts – an abnormal immune system with low levels of infection-fighting B cells and antibodies. This gave me an explanation for my recurrent infections, and a plan to manage them. But it did not tell me what this diagnosis meant for our daughter? Also, what about future children? We were told that CVID is not genetically inherited in many cases, but in some cases, it is, and thus there was a small but real chance that I could have passed it on to my daughter. Though she was young and asymptomatic, we requested that our daughter have immune studies when she was nine months old. Her B cells were normal and her immunoglobulin (IgG) level was slightly low. She had been a relatively heathy baby, with only two upper respiratory infections, but she was not responding to her immunizations. Therefore, she began receiving IgG replacement when she was 18 months old.

We want to support the Clinical Immunology Society Foundation as it promotes research in these rare diseases that affect the immune system.

We decided that we would like to have more than one child. Still not knowing if this was a genetic issue, we decided to proceed. Another daughter was added to our family in 2000, 23 months after our first-born. She had an upper respiratory infection at three weeks of age requiring hospitalization and continued to have respiratory and ear infections during her first year of life. Her immune studies were tested at 17 months of age at our request. Her immunoglobulin levels were also low. The hope was that both girls had transient hypogammaglobulinemia, and they would normalize their levels with age. We held off on starting her on replacement immunoglobulin until she was 4 years and 2 months. She still had a low immunoglobulin level, and was not responding to immunizations and boosters.

Our third daughter was born in 2002. We visited the National Institutes of Health (NIH) when she was just 7 weeks old. At the time, we presumably did not meet the criteria for any of the ongoing research studies. Our local immunologist

was phenomenal about trying to find a physician or scientist who would be interested in studying our family. She was in touch with the NIH and several other immunologists across the country. We were referred to the NIH for a second time in 2011 in the hopes of finding the underlying genetic defect in our family. Dr. Sergio Rosenzweig and his team began seeing us and checking lab work, x-rays, and other studies, including genetic sequencing. In June 2014, we were given a diagnosis with a specific genetic defect – Common Variable Immunodeficiency (CVID) caused by IKAROS haploinsufficiency. We now had an answer to our many questions, and we are so grateful to all the physicians and scientists who have advocated us, and solved our medical mystery.

Sergio Rosenzweig, MD, PhD, *Immunology and Laboratory Medicine, NIH Clinical Center*

Jami's story is one of resilience, perseverance and collaboration. Jami was healthy as a child but started having repetitive, invasive, life-threatening infections as an adult. At the time, she was diagnosed with CVID, and placed on immunoglobulin replacement therapy, and did very well thereafter. As a health care provider herself and also as an astute patient, she knew CVID could run in families so she requested her newborn daughters to be tested for immunodeficiency. And her doctors listened to her. Although the first results were essentially normal, they insisted on follow-up testing. Their reasoning was that Jami was healthy as a child too, and thus her daughters may also be asymptomatic during childhood but would develop symptoms later in life. Jami's intuition was remarkable because over time, her two older daughters started showing signs of progressive attrition of their humoral immune system with low B cells, immunoglobulins and declining specific antibody responses. They also started to show an increased incidence of infections, which in the context of their antibody deficiency, prompted initiation of immunoglobulin replacement. Her daughters, like her, did well with treatment; however, there were still several questions that were unanswered. Why was this happening? What was the genetic defect causing this familial form of CVID? Jami was fortunate to have a very committed team of pediatricians and immunologists, who facilitated her visit to the National Institutes of Health (NIH). We along with several other immunology colleagues from around the US and the world are studying patients with primary immunodeficiencies precisely to answer these sorts of questions so we can diagnose them early and provide a timely and appropriate treatment. We commenced our studies on Jami's family and soon realized they shared common features with other patients seen by colleagues from around the country and the globe. We found out that Jami and her family were part of a larger cohort of individuals (a total of 29 from 6 families) followed in New York, Utah, Georgia, Colorado, Texas, Norway and Switzerland who had a genetic defect in a gene called IKAROS, an important molecule for the development of B cells and other cells in the immune system. We are continuing to learn from IKAROS, Jami, her daughters, and other patients with IKAROS deficiency, so that we can apply this knowledge to new patients, and understand these immunodeficiency diseases better.

This is precisely the mission of the CIS Foundation, which seeks to foster intellectual curiosity and collaborative research within our physician and scientist community, so we can help our resilient and perservering patients with immunodeficiencies to lead better and more wholesome lives.

Elias Argirokastritis' Story

Evelyn Argirokastritis, *Elias' Mother*

I was very worried something was wrong with my son within five hours of his birth. I called the pediatrician but was assured it was some form of allergy or sensitivity. This was the beginning of our journey going from specialist to specialist, week after week, culminating in an emergency room admission when he was two months old. I was overwhelmed trying to advocate for my son and feeling like I was not being heard.

After a two week stay in the hospital with Elias' case being tossed between various specialties - oncology, infectious disease, and allergy there was still no answers. I asked for Elias to be transferred to the C.S. Mott Children's Hospital based on a gut feeling that someone there would know how to help. Elias was very frail upon transfer but he was fighting hard to stay strong to allow the doctors to continue unraveling the diagnostic dilemma. We met Dr. Walkovich, and she had a good sense from the very beginning that he had a rare primary immunodeficiency, and my mind was set at ease knowing that she knew how to help him.

We are committed to supporting the Clinical Immunology Society, whose mission it is to support, educate and train physicians in immunology, so that patients like my son may have a chance at a normal life.

Dr. Walkovich diagnosed Elias with a rare X-linked immunodeficiency called NEMO (NF kappa B essential modulator) syndrome, and she organized a medical team to address his pressing clinical issues. We are so grateful we eventually found a competent team of physicians who could

Date of Transplant: October 3, 2018

help my son. We are fortunate that Elias is doing very well considering the trials he has had to endure from birth. We have found a cord blood donor and he was transplanted on October 3, 2018. For us, especially Elias, the key element was that we found a doctor who had training in immunology and could immediately recognize he had a severe immunodeficiency, and who worked relentlessly to get him an accurate diagnosis. She has worked relentlessly to manage him and select appropriate therapy for him.

Kelly Walkovich, MD, *Pediatric Hematology-Oncology, and Immunology, University of Michigan, Ann Arbor*

When I first met Elias, I noted he was a beautiful baby, but he was burdened by a diagnostic conundrum, and I was very drawn to help him in every way I could. Similar to many other patients with rare primary immunodeficiency disorders, Elias' symptoms of rashes, oral ulcers, elevated white blood cell count and difficulty gaining weight appeared seemingly disconnected, akin to scraps of fabrics waiting to be sewn together to complete a quilt with a specific pattern. There was no apparent sense of which diagnostic direction to pursue in the early stages of his evaluation. However, Elias was blessed with a highly motivated family whose dedicated sleuthing uncovered generations of crucial family history, which suggested an X-linked genetic inheritance. To complete solving the diagnostic puzzle for Elias many medical disciplines pitched in and completed various pieces with additional laboratory data, which ultimately resulted in a diagnosis. Immunology is embedded in nearly every field of medicine, and as a pediatric hematologist/oncologist, I am grateful for the training I received through CIS from the PID Summer School and the ongoing mentorship within CIS, both of which allowed me to contribute to "stitching" together Elias' story and positively intervening with a diagnosis and therapy plan.

Please consider contributing to the CIS Foundation Fund to support the care of patients like Elias by educating the next generation of clinical immunologists.

Charlie Luckesen's Story

Katie Luckensen, *Charlie's Mother*

For the first year of my baby's life, our family lived in unremitting dread of every cough, every sneeze, and every cry. We agonize over every person who comes into contact with Charlie because there is the incessant apprehension that this will be the time he gets sick, and he will not recover from it.

When Charlie was one week old our family's world completely changed when the newborn screening came back, which showed that Charlie had an abnormal newborn screen for Severe Combined Immunodeficiency (SCID). After discussing our options with Charlie's immunologist, Dr. Cathy Collins, we decided to admit him into the hospital so he could be placed in reverse isolation in an effort to keep him healthy. After several additional diagnostic tests, we were told that Charlie did not have SCID but a partial deletion of one of his chromosomes, number 22, resulting in a condition called 22q11 deletion syndrome. We subsequently learned that Charlie was even more unusual because he was one of a small subset of patients who have Complete DiGeorge Syndrome, which meant that he had no functional thymus, which was essential for normal development of his immune system. Many of Charlie's doctors had never treated a patient with complete DiGeorge Syndrome. They had never seen this condition before and had only read about it in medical journals. We were told the only treatment option for him was a thymus transplant, which could only be performed at Duke University, on a research basis. We were given no definitive answer on when he would be able to get a thymus transplant.

We support the efforts of the Clinical Immunology Society, which is educating physicians in this complex specialty, and recently developed the Thymic Defects Taskforce, to address the critical need to expand thymus transplantation and treatment for this particular subgroup of patients.

We kept Charlie in isolation in the hospital for eight long months. After a great deal of prayer and consultation with doctors, we decided to take the risk and bring Charlie home to help with his social and behavioral development, which was beginning to lag behind other children his age. During this past year, for the most part, we have kept him healthy. There have been setbacks and various problems but Charlie's doctors have been diligent in working with us to treat each issue as quickly and accurately as they could. Through Facebook we have been able to connect with families all over the world who have children living with Complete DiGeorge Syndrome, both pre- and post-transplant.

Our other three young children are now homeschooled and live in isolation so as to not endanger Charlie's life. We know every mark on his skin and his latest laboratory test results. We constantly disinfect anything and everything that might come near Charlie. We are always watching for some sign that things are going wrong and that he has some bacteria, virus or fungus.

If we had been told in the beginning what we was in store for us we would have completely crumbled under the reality of it all. My six-year-old frequently asks, "What will happen if Charlie dies?" This is heartbreaking because we can't even tell him that won't happen because without functional T cells this possibility is all too real. My son has a fatal genetic condition that will kill him unless he gets a new thymus.

Cathy Collins, MD, PhD, *Pediatric Immunology, Rady Children's Hospital/UCSD*

We are so fortunate in the United States to have access to the newborn screening program, which can identify babies at risk for immunodeficiencies like Severe Combined Immunodeficiency (SCID) and complete DiGeorge Syndrome (DGS).

My patient, Charlie, was diagnosed with severe T cell lymphopenia (very low T cell counts) when he was less than 10 days old, and shortly thereafter we found the cause was an absence of the thymus, an organ where the T cells (a key cell of the immune system) undergoes development resulting in complete DGS. T cells are absolutely critical to normal functioning of the immune system, and their lack results in serious complications and premature death.

The Clinical Immunology Society has been committed to educating physicians but also facilitating dialogue and discussion, and supporting research to identify and develop new treatments for various immune system disorders.

Another key point in Charlie's case was that the early diagnosis by newborn screening identified cardiac problems that are part of the DGS diagnosis. Had we not known this diagnosis, he might have remained undiagnosed and developed serious heart issues. Even though Charlie received an early diagnosis, he has not been able to receive specific treatment for his condition.

This is because patients with complete DGS need a thymus transplant, but there is only one center in the US that can provide this treatment, and it is challenging to ensure that every patient who needs this type of treatment can receive it in a timely manner. We have been able to keep Charlie well thus far through the tireless efforts of his family, and prophylaxis with antibiotics and immunoglobulin replacement. He spent 8 months in the hospital avoiding exposure to infections, and his parents made the tough choice to home school their other children in order to make his home environment as safe as possible. We urgently need greater accessibility to the life-saving treatment that children like Charlie need, which is thymus transplantation or some other way to restore a normal thymus to allow his immune system to develop normally.

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HELP US REACH OUR GOAL

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