UCSF Benioff Children's Hospitals

A NEWSLETTER FOR
FRIENDS AND SUPPORTERS

Connections

SUMMER 2023

Putting the Pieces Together:

Unpacking the Genetics of Autism

page 3

I am not a health professional

by training, but when UCSF Benioff Children's Hospitals approached me about becoming a board member, it felt right.

I have spent my career as a lawyer, community organizer, and public-policy advocate, and I've come back to health again and again. Working with low-income communities of color, I've seen firsthand how health, place, and race are connected.

Just consider the infant mortality gap. When I started the Urban Strategies Council, we found that the highest infant mortality rates were in poor, Black communities. With a diverse coalition of community leaders, we advocated for deliberate action to direct more resources to the communities that needed them most. That work led to the establishment of Alameda County's Healthy Start Program and a 50% reduction in infant mortality in targeted communities.

For people who live in historically neglected areas, good health depends on advancing racial equity by providing greater access to high quality health care and improved conditions in their communities. UCSF Benioff Children's Hospitals plays a crucial role in that work. We have an extraordinary opportunity to address some of the most urgent problems facing low-income communities of color across the Bay Area and beyond.

This year, we are undertaking an ambitious fundraising effort to transform our research campus in Oakland and create a new, state-of-the-art facility for pediatric blood disorders. This initiative will allow us to advance treatments and discovery for young patients suffering from debilitating blood conditions like sickle cell disease – patients who, historically, have been left behind by the health system.

I am so excited to be part of this work and everything that these hospitals stand for, and I look forward to partnering with the UCSF community to ensure that every child has an equitable health journey.

Sincerely,

Angela Glover Blackwell
Member, UCSF Benioff Children's Hospitals Board of Directors
Founder in Residence, PolicyLink

In Memory of Dr. Barbara Staggers

This past spring, we lost a legend: Barbara Staggers, MD, a trailblazing adolescent medicine physician who was beloved by her patients, their families, and her colleagues at our Oakland campus.

As the director of adolescent medicine at Children's Hospital and Research Center Oakland (now UCSF Benioff Children's Hospital Oakland), she launched school-based health clinics at Castlemont and McClymonds high schools and the Alameda County Juvenile Justice Center Medical Clinic. She was also a founding member of the Community Health and Adolescent Mentoring Program for Success (CHAMPS), which serves as a model enrichment program for youths interested in health care careers.

Dr. Staggers' dedication to health equity exemplified the values of UCSF Benioff Children's Hospitals. Her commitment to recognizing and addressing the social factors that influence teen health launched what is now known nationally as trauma-informed care, a framework for medical service that prioritizes knowledge and understanding of the patient's life experiences and trauma.

We are so grateful for Dr. Staggers' life, work, and legacy. Our entire community will miss her.

DISCOVERY

INVESTIGATING THE GENETICS OF AUTISM

AN INTERVIEW WITH ELLIOTT SHERR, MD

Curious about the genetics of autism? So is pediatric neurologist Dr. Elliott Sherr, who leads UCSF's effort to reveal the genes that give rise to autism spectrum disorder and develop treatments that will revolutionize how we care for children with developmental disabilities.

What is autism?

Autism is a relatively common genetic disorder. The US Centers for Disease Control and Prevention currently estimates that about one child in 40 has autism spectrum disorder, a broad range of conditions characterized by challenges with social skills, repetitive behaviors, speech, and nonverbal communication.

But those conditions are diverse. The brain is a complex place. More genes are expressed in the brain than anywhere else in the body, so interfering with how it functions can be varied and challenging.

Some kids will have autism and nothing else. But most of my patients have a constellation of neurodevelopmental challenges. They don't fit into a simple rubric. They might also have sensory disorders, like auditory or visual impairment.

Is autism always genetic?

It often is. There can be a family connection – one or more close relatives may have subtle features related to autism – which means there are many inherited genes working together to increase susceptibility. That probably makes up more than half of the cases that we have identified.

But it can also appear out of the blue, with no family connection. These cases are often caused by a new mutation in the DNA that isn't shared by other family members. I primarily work with these patients, where there's a unique change in the child's DNA that both causes and helps us understand the disorder.

How did you start thinking about the genetics of autism?

When I finished my training as a child neurology fellow, understanding the genetics of autism and intellectual disability was in its infancy. But UCSF had great expertise in brain imaging, which allowed us to connect the dots between cognitive-behavioral disorders and changes in brain structure.

Suppose a patient – let's call her Molly – comes in with severe autism. Molly has a set of clinical features, like autism, seizures, and visual impairment. Her brain imaging reveals another set of features, and she shares these exact features with a dozen other kids. These shared challenges tell us we're looking in the right direction and can figure out the cause of their condition. Knowing the cause becomes the springboard to a treatment plan.

Can you give an example?

One of the imaging features we look at is called agenesis of the corpus callosum, which is an anatomic structure that links the left and right sides of the brain. It's a big structure, like a superhighway – the 101, 280, 580, and 980 highways all put together. People with agenesis of the corpus callosum are born without that structure or with a smaller version.

Kids were coming into my clinic with autism and abnormalities of the corpus callosum, which prompted me to conduct a genetic analysis of this group. We found that a number of these patients also had mutations in a protein-coding gene called DDX3X, so we were able to identify DDX3X as a cause of autism.

What made this discovery unique?

Almost all the kids we identified early on with this mutation were female. And we were able to identify it as one of the four or five most common genetic causes of autism in girls. But it had been totally missed because so much of the autism research in the beginning focused on boys. Given this inadvertent scientific neglect of female patients, this was a good example of how important it is to pay closer attention to girls going forward.

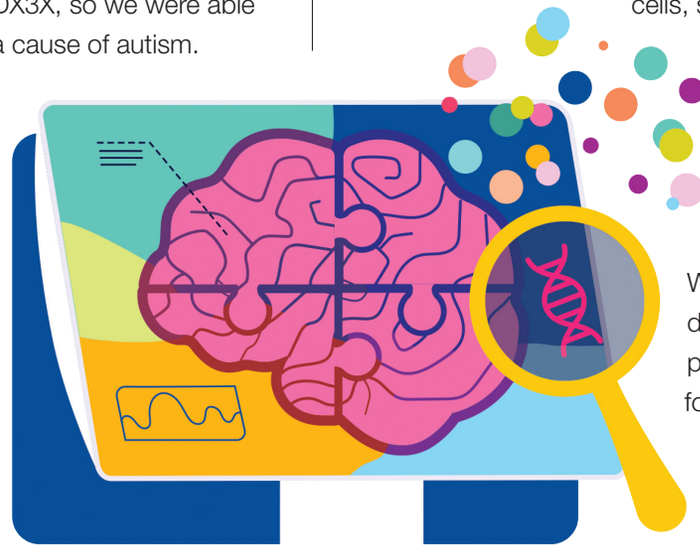
How can genetic insight impact treatment?

There's another gene called VAMP2. It produces a protein involved in neurotransmission, a crucial process that allows nerve cells in the brain to communicate.

We identified this mutation in several children with developmental delays, including a patient of mine. This patient was more than autistic. She was almost completely mute and didn't interact at all.

Knowing the cause becomes the springboard to a treatment plan.

We were aware of a multiple sclerosis (MS) drug called Ampyra that increases the stimulus from one nerve cell to another. MS is a disorder that can inhibit the interaction between nerve cells, so we reasoned that this drug might also help kids with mutations in this gene.



We gave this drug to my patient, and for her, it was profound, like an awakening. Within two weeks, she was speaking in full sentences. She started interacting deeply with family and friends. There were setbacks, but the turnaround was dramatic. A month after starting the medication, she attended her high school prom.

Should parents of children with autism pursue genetic testing?

If the child has autism and is dealing with more than one medical issue, the cause might be one of these mutations. In that situation, I would highly recommend genetic testing for the child. There won't always be a straight answer, but in some cases, there are remarkable opportunities to better understand the child's condition and push the treatment envelope.

TOPICS

Transforming the Asthma Landscape in the East Bay

A chronic challenge

Across the country, 9% of all school-age children suffer from asthma, making it the most common chronic childhood disease in the US. In Alameda County, that figure is 18% – double the national average.

The impact of air pollution

The highest rates of asthma are concentrated along the I-880 corridor, where traffic-related air pollution is most severe. In Oakland, San Leandro, Castro Valley, Hayward, and nearby communities, childhood asthma rates exceed the countywide average.

The role of race

Massive race-based disparities shape the incidence of asthma. In Oakland, Black children are five times more likely than non-Black children to die from asthma. In west and downtown Oakland, where people of color comprise 70% of the population, half of new childhood asthma cases are tied to traffic-related air pollution, compared with 1 in 5 cases in the Oakland Hills, where 70% of the population is white.

What sets us apart

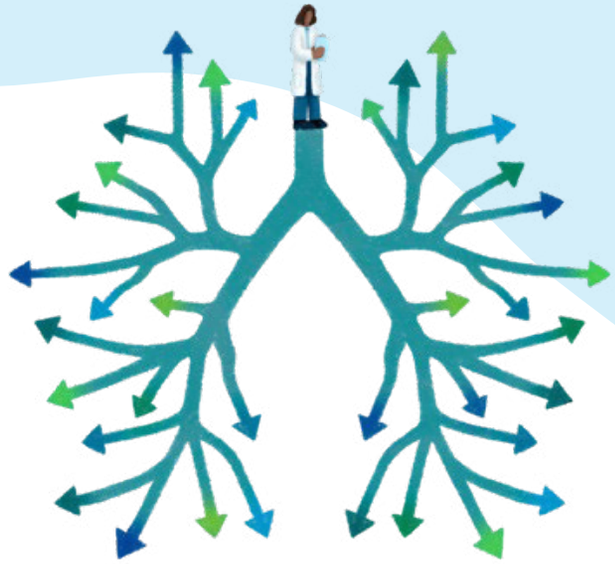
UCSF Benioff Children's Hospital Oakland plays a crucial role in preventing and treating asthma exacerbations in the East Bay. We provide asthma care at our main hospital, emergency department, and Pulmonology Clinic, as well as through our satellite clinics, Federally Qualified Health Center, school-based health clinics, and other locations.

Growing needs

But demand is on the rise. Since 2019, our Pulmonology Clinic caseload has risen by 4% each year. More children than ever are suffering the ill effects of traffic-related air pollution, and our care delivery channels struggle to keep up.

Our vision

We believe that children in Alameda County deserve better. With additional investment, we can move the dial on asthma prevention and care for underserved children across the region by creating a comprehensive, evidence-based system that reaches deeper into communities and addresses the social determinants of health.



The impact

With our partners' support, we can transform asthma prevention and care in the East Bay – for every child, of every background.

PHILANTHROPY

Nothing Short of a Miracle

The Parkers from left: Cat, Vic, Lew, Jen, Gus, and Anna.

Every hour. That's how often Lew Parker had seizures on the worst days.

Lew's parents, Jen and Vic, walked through life in fear. They spent their days in a constant state of vigilance; the specter of a medical emergency lurked around every corner. They stopped traveling and going out for dinner. They were afraid to drive with Lew in the car. His three older siblings came to see the world – and their lives – through the lens of their little brother's condition.

"It flattened us," Jen says. "It was always a little scary at our house. We knew something devastating could happen at any moment."

But the Parkers also knew they were lucky. They could afford to pay out of pocket for medicine, special education, family therapists, and around-the-clock care. A night nurse stayed at Lew's bedside in case a seizure struck while he was asleep.

"And even so, we barely slept," Jen recalls. "Even with all that scaffolding, we barely held it together."

Coping with Epilepsy

At birth, Lew seemed healthy. Over the next three years, he developed normally and hit every milestone: He talked and walked and dribbled a soccer ball on time. He just had the occasional seizure when he got sick.

On their own, brief febrile seizures – convulsions in children often caused by a spike in body temperature – are common and without long-term consequences. But the pattern concerned Lew's neurologist, UCSF's Joe Sullivan, MD, who recommended genetic testing. Lew's test results revealed that he suffered from a severe form of epilepsy.

Over the next seven years, the seizures increased in intensity and frequency. Available medications didn't work, and the side effects were physically and cognitively debilitating. Lew's development became delayed. He spoke less and less.

But Dr. Sullivan was determined. He experimented with new drug combinations in a complex and delicate process of trial and error. He enrolled Lew in a clinical trial testing a novel therapy. And he showed up for the Parkers in ways that went far beyond medicine. He was the family's rock.

"Dr. Sullivan is unique," Jen says. "He is clinically excellent *and* he's an empath. He cares so much. He became one of the most important people in our lives."

Finding Meaning

The Parkers weren't alone. Dr. Sullivan helped many of his families navigate the daily challenges of caring for a child with epilepsy – everything from arranging extended childcare and transportation to the hospital to accessing experimental drugs, psychological care, and special education.

Over the years, Jen and Vic learned how essential this was for struggling families. At an epilepsy support group, Jen met parents who had traveled to UCSF from the Central Valley with five children in tow because they didn't have childcare at home. Other parents spoke about watching their children 24 hours a day, seven days a week, without any outside help. They missed work and lost income. The school system was impossible to navigate. Their mental health deteriorated.

The Parkers saw how deeply Dr. Sullivan cared for these families – how he simultaneously provided world-class clinical care, led potentially lifesaving research studies, and offered emotional and logistical support to parents with far fewer resources than their own.

Jen and Vic had reached a low point with Lew's condition. "The wheels were coming off," Jen says. "But we had to find something positive to do amid all the stress."

As a first step, they funded a research coordinator to help Dr. Sullivan advance promising clinical trials and bring new therapies to patients. Then they helped launch the Pediatric Epilepsy Center of Excellence (PECE), a groundbreaking model of wraparound care for families affected by epilepsy.

Lew and Dr. Sullivan in clinic.

PECE provides access to innovative treatments, as well as psychological care, educational support, and a patient concierge who ties it all together.

Dr. Sullivan says PECE is a crucial part of his work. "Now we can address the whole patient, the whole family, the whole day, the whole week, better than our group of physicians and nurses could ever do alone." PECE has become a model of care that UCSF Benioff Children's Hospitals hope to replicate across its programs.

Lew's Transformation

After years in distress, Lew finally experienced a turning point at age 7, in 2017: Thanks to a groundbreaking clinical trial, Dr. Sullivan identified a new drug that worked. After Lew received it, a few days passed without a seizure, then a week. A month. A year. In the past five years, he has had only one seizure.

Lew is now 13. "His transformation has been profound," Jen says, "like someone plugged him in." After years of barely speaking, he's talking nonstop. Last year, he started reading. He makes up stories and articulates ideas that astound his family. He lives in the moment. He's funny. He's happy.

Through it all, PECE has been a lifeline. Working with Dr. Sullivan, listening to families, and hosting fundraising events have given the Parkers another purpose. In 2022, they took this work a step further by establishing the Murphy Parker Endowed Professorship in Pediatric Epilepsy, which will secure PECE's leadership, research, and service for years to come.

"I look back and think, I don't know how we got here," Jen says. "There are no guarantees, but it feels like nothing short of a miracle. That's all thanks to Dr. Sullivan."

ONCOLOGY

Siya's Cure

Siya Gupta says the fifth day after her 10th birthday was the scariest day of her life. That's when she was diagnosed with acute lymphoblastic leukemia (ALL), the most common childhood cancer.

As with every ALL patient, nearly all of the cells in Siya's bone marrow were cancerous when she was diagnosed. But unlike with most ALL patients, 80% of Siya's bone marrow cells were still cancerous after treatment. Chemotherapy usually reduces the share of cancer cells in the bone marrow of ALL patients to under 1%.

"I've been doing this job for 12 years, and that was the smallest reduction in leukemia cells I have ever seen after a month of chemotherapy," says Elliot Stieglitz, MD, a pediatric hematologist and oncologist at UCSF Benioff Children's Hospitals. "Historically, less than 10% of patients like Siya who don't respond to conventional treatments survive."

Dr. Stieglitz knew he needed to shift gears. He told the family about another option: chimeric antigen receptor (CAR) T-cell therapy, a revolutionary form of cellular immunotherapy. Unlike chemotherapy, which attacks tissue throughout the body,

I hope my story inspires people.

– Siya Gupta

CAR T-cell therapy genetically alters a patient's own cells to recognize, target, and destroy *only* the cancerous cells.

Early evidence indicates that this approach not only minimizes the debilitating side effects that often come with chemotherapy but also has the potential to keep more patients in remission for longer.

Siya remembers the anticipation leading up to the day of the procedure. She was scared. She knew that CAR T-cell therapy could put her in remission but that a new therapy carried the risk of the unknown. But she trusted Dr. Stieglitz. He had always encouraged her to ask questions and express her concerns. She knew he believed that the potential benefits outweighed the risks.

Infusion day came. Doctors talked the family through the procedure one last time. When the infusion began, the room fell silent. Siya recalls, "I remember thinking, 'It'll be fine. You're going to be OK.' But even though I was assuring myself, I was secretly praying. And I knew everyone else in the room was praying for me too."

Siya experienced minimal side effects – just a low-grade fever, which meant that her immune system was responding to the treatment. One month later, Dr. Stieglitz and his team repeated the bone marrow analysis. Siya was leukemia-free. She was in remission.

With Siya in remission, Dr. Stieglitz and his team were able to perform a successful bone marrow transplant. Three years later, she is still leukemia free.

Now 13, Siya has spoken widely about her experience with CAR T-cell therapy, including encouraging donors to partner with UCSF to fund research on treatments like the one that saved her life. "I hope my story inspires people," she says. "I am very, very proud to call myself a cancer survivor."

ORTHOPAEDICS

XAVIER: A SECOND OPINION

Xavier Gatlin is a competitor.

He started playing basketball at age 3. By second grade, he was playing competitively, and a year later, he was traveling up and down the West Coast with an elite club team. At the end of that season, his team was ranked number-one in the West.

Then, in 2017 when he was 8, Xavier fell during a game, and another player landed on his knee. He came out of the game, went back in, then came out again, limping and in pain.

"It seemed a bit unusual because Xavier tends to have a pretty high pain threshold," says Johanna, Xavier's mom. "So the fact that he didn't want to keep playing was alarming to us."

Over the next few days, Xavier's knee continued to hurt. At school, he didn't want to play during recess. The family pediatrician recommended rest, ice, and ibuprofen, and the pain subsided. But every time Xavier got back on the basketball court, the pain came back.

Johanna and Kang Su, Xavier's dad, took their son for an MRI, which revealed a small cyst in the knee area attached to the anterior cruciate ligament (ACL). Xavier was referred for physical therapy and diligently followed his treatment plan. But six weeks later, doctors found that the physical therapy actually had aggravated the injury.

Xavier was frustrated. He wanted to tough it out. He did everything doctors recommended, rested the knee, felt better, and got back on the court, only for the pain to return. "It finally got to the point where he just couldn't play," says Johanna. "He would come out wincing in pain. We were following the doctors' advice, but we just couldn't bear to see him like that anymore."

Xavier's mobility began to decline. The pain grew from intermittent to constant. The family decided to travel from Seattle to San Francisco to get a second opinion at UCSF. Xavier was scheduled for surgery with Nirav Pandya, MD, a world-renowned pediatric orthopaedic surgeon who specializes in sports medicine for young athletes.

Dr. Pandya and Xavier following knee surgery.

The surgery wasn't straightforward. Dr. Pandya would only know what procedure to perform after he saw the inside of Xavier's knee. "It could be a simple cyst removal, it could be a partial or full ACL reconstruction, it could be a meniscus repair," says Johanna. "But he prepared us for each scenario. We knew exactly what to expect with each possibility."

Dr. Pandya removed the cyst. During the operation, he found that the meniscus was torn, so he repaired it. The procedure was a success.

Johanna says that with Dr. Pandya's support and detailed guidance, Xavier was able to take control of his recovery and focus his energy on healing, despite the pressures to get back on the court. And even after a long hiatus, he hasn't missed a step: Now in the seventh grade, Xavier's game is better than ever. He can touch the rim and has his sights set on dunking by the eighth grade.

Johanna and Kang Su say it's great to see their son doing what he loves again. But they're even more grateful that they got a second opinion from UCSF and a recovery plan that gave their son the time he needed to heal – both physically and emotionally.

"Xavier is doing great," says Kang Su. "He beats me consistently at one-on-one now."

UCSF Benioff Children's Hospitals

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Meet our Patient Ambassadors

Elena Sweet
Age: 11
Diagnosis: Ewing sarcoma
Loves: Theater and acting

Krystie Gomes
Age: 14
Diagnosis: Osteosarcoma
Loves: Volleyball and soccer

Manvir Guleria
Age: 10
Diagnosis: Stomach cancer
Loves: Traveling and music

Oli Roth
Age: 17
Diagnosis: Ulcerative colitis
Loves: Art, music, poetry, and cats

Oliviya Viertel
Age: 6
Diagnosis: Acute lymphoblastic leukemia
Loves: Princesses, coloring, and dress up

Riley Falkoff
Age: 19
Diagnosis: Arrhythmia
Loves: Singing and dancing

Ripley Shair
Age: 6
Diagnosis: Congenital heart defect
Loves: Art, swimming, and bike riding

Skylar Bailey
Age: 17
Diagnosis: Regional pain syndrome
Loves: Music, dirt bikes, and nature

Their stories could fill volumes: The little boy who had open heart surgery when he was just a month old. The teen grappling with ulcers in her digestive tract. The fourth grader who worries about cancer when he should be learning karate. Despite all they've been through, these young people are determined to give back to others through our Patient Ambassador Program. Each year, these remarkable kids share their stories in a variety of ways, including community events, media interviews, videos, and more. To read more about them and learn how you can nominate a patient, visit http://tiny.ucsf.edu/ambassadors.