

Less Risk and Greater Efficacy In Pediatric Lupus Nephritis Treatment

There is no doubt about it. The research into the mechanisms of pediatric lupus nephritis conducted by **Elena Hsieh, MD**, at the University of Colorado, Anschutz Medical Campus, is driven by her genuine concern for the wellbeing of children—and a lifelong passion for science.

With her new grant from the **Lupus Research Alliance (LRA)**, Dr. Hsieh—who is a *researcher, clinician, and mother*—is working on a multi-dimensional investigation that has the potential of lessening risks and greatly improving outcomes for children with this disease.

Underscoring the importance of pursuing this critical line of inquiry is the fact that children with lupus commonly develop kidney disease—known as lupus nephritis. Worse still, lupus nephritis is often more severe in pediatric patients than in adults. Sadly, the disease will progress in many of these children, resulting in end-stage renal disease or kidney failure.

“In addressing the needs of children with lupus, we need to better understand the underlying immunological abnormalities in lupus in order to design and use treatments with less toxicity and greater efficacy,” explained Dr. Hsieh.

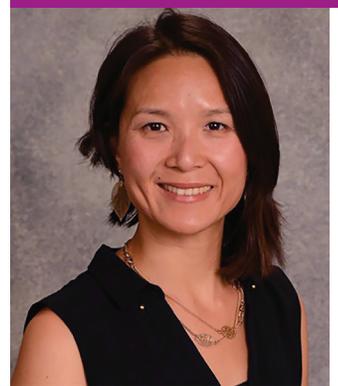
In pediatric populations, physicians try to minimize procedures and rely on peripheral blood and urine studies. But this approach has its limitations. *“We don’t always know what is happening at the level of the organ that is affected. That’s why it’s important to go back to the idea that any autoimmune or immunodeficiency disorder is really a dysregulation of the immune system. If we can identify which part of the immune system is not working properly, then we can target therapy,”* explained Dr. Hsieh.

Working toward this aim, Dr. Hsieh and her team will use innovative technologies that allow for the precise characterization of individual cells in tissues (called MIBI) and in peripheral blood (called CyTOF) and comparisons with samples from patients with other autoimmune or non-autoimmune kidney diseases.

Dr. Hsieh envisions the creation of a “map” of the immune-specific cells that are involved in causing kidney disease. Comparing the “kidney immune maps” may provide invaluable information for the entire lupus scientific community. Dr. Hsieh hopes to illuminate a pathway

to understanding the mechanisms that drive kidney disease specifically in lupus.

Another goal of this investigation is to compare lupus patients’ kidney biopsies with a similar precise map of the immunological features identified in their own peripheral blood cells using CyTOF. *“The identification of relationships between what is happening in the kidney and what is seen in the blood will help doctors make critical decisions about what medicines to use without having to do a kidney biopsy,”* said Dr. Hsieh.



Dr. Elena Hsieh

As a researcher, Dr. Hsieh is grateful to the LRA for enabling her to develop a novel approach that has the potential to significantly improve outcomes for children with the disease, offering new hope to their families.

And as a physician and a mother, she is thankful on a more individual level: *“Patient care is up-close and personal, and I see how severe flares can devastate the lives of children and their parents. This is why I am sincerely thankful to the LRA for the means to identify immunologic pathways that could have a dramatic impact on children with this disease.”*

“Pediatric diseases—like lupus nephritis—are, in general, terribly underfunded and understudied. That’s why funding structures like those of the LRA are so vital. The LRA strongly supports areas that are traditionally less well funded and makes a big impact on the progress of care from diagnosis to treatment.”

—Dr. Hsieh

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NEW GRANTEES = NEW IDEAS AND APPROACHES

The LRA is proud to announce that the following seven scientific investigators were selected grantees for our **2020 Lupus Innovation Award** to help propel their ideas.

This grant mechanism—funded through donor gifts—provides support for pioneering, high-risk, high-reward approaches to major challenges in lupus research.

The LRA congratulates each of these brilliant researchers as they bring new insights to lupus research:

Simone Caielli, PhD

Erythroid Mitochondrial Dysfunction in Lupus Pathogenesis
Joan & Sanford I. Weill Medical College of Cornell University

Joyce Chang, MD, MSCE

Mechanisms of Vascular Injury and Dysfunction in Pediatric Lupus
The Children's Hospital of Philadelphia

Keith Elkon, MD

cGAMP as an Immune Transmitter of the Interferon Response
University of Washington

Elena Wen-Yuan Hsieh, MD

Multiplexed Single-cell Imaging in Pediatric Lupus Nephritis
University of Colorado Denver, AMC and DC

Vipin Kumar, PhD

Targeting a Novel Population of Innate-like CD8+ Treg in Lupus
The Regents of University of California, San Diego

Zahi Touma, MD, PhD

Modeling Cognitive Impairment in Patients with Systemic Lupus Erythematosus
University Health Network

Hu Zeng, PhD

Targeting mTORC2 for Lupus Treatment
Mayo Clinic

Vascular Injury and Dysfunction In Pediatric Lupus

While children with lupus can experience manifestations similar to adults with the disease, children present with more acute illness, more frequent flares, and increased risk of major organ involvement—including those of the heart.

With her LRA grant, **Joyce Chang, MD, MSCE** from Children's Hospital of Philadelphia, aims to understand why children with lupus are more prone to heart attacks and strokes—and how to prevent these conditions from happening in the first place.

"We currently do not know how to monitor or prevent early blood vessel injury in child-onset lupus," said Dr. Chang. *"My investigation will examine whether a specific pathway is involved in the initial injury that causes vascular dysfunction and premature plaque formation."*

Specifically, Dr. Chang is looking at the role of neutrophils—the most abundant immune cell type—and their role in the initiation and perpetuation of tissue damage to the heart. *"So, it's possible that there's a sort of mechanistic link between neutrophil-induced inflammation in lupus and some of the accelerated plaque formation that we see,"* explained Dr. Chang.

Understanding that mechanism and how lupus can cause injury to blood vessels—specific to children and adolescents—will allow Dr. Chang and her team to make two important advances. They will be able to quantify factors to determine a patient's lupus-related risk of having a heart attack or stroke. And they aim to determine potential ways to intervene and inhibit neutrophil activation or some form of its downstream effects.

"Because neutrophils play a major role in fighting infection, we need to find their specific attribute that causes blood vessel injury," added Dr. Chang. *"Then we can target that attribute rather than trying to wipe them out completely."*

The LRA recognizes the importance of Dr. Chang's work because there are health care disparities with lupus—and especially pediatric lupus. Likewise, Dr. Chang acknowledges the role the LRA plays: *"The LRA really drives scientific lupus research—and without that support, many of the studies of early investigations, like mine, might never get off the ground. I'm deeply grateful for this opportunity."*

Dr. Chang's investigation has the potential to support future studies that could lead the way to therapies that are beneficial in supporting cardiovascular health in adolescents and young adults with lupus.

"As a researcher and a clinician, I enjoy taking care of my pediatric lupus patients, most of who are teenagers. Adolescence can be a time of great personal growth—so to take care of them is especially rewarding."

—Dr. Joyce Chang



Dr. Joyce Chang

FACES OF LUPUS

Lupus Advocate. Human Rights Defender. Teenager. Aaliya Wears All These Hats ... and More

It takes a brave, compassionate person to look beyond the personal pain of lupus and look for ways to create greater good. And it is even more remarkable when that person is a teen—like **Aaliya Qassim**.

She has been coping with lupus for much of her young life—but her spirit remains unbroken. Aaliya, now 17, is grounded by an inner strength, a comprehensive world view, and a passion to advocate for those in need—especially others with lupus.

As a child, Aaliya was a curious, eager learner who devoured books. So, it was shocking when she suddenly couldn't make sense of the printed words. That was the first sign. By April of 4th grade, Aaliya was in and out of the emergency room more times than she can remember.

That same year, Aaliya and her parents were completely taken off guard when she was unable to stand. For the next several months, this brave young girl mastered the physical art of getting around in a wheelchair—while developing the mental fortitude to forge ahead at school.

"Doctors didn't know what was going on with me—even though my father has lupus. But they did shock my parents—telling them the situation was so critical I had a 50-50 chance of survival," Aaliya said remembering that scary time.

By age 11, doctors began to connect the dots and Aaliya finally received a formal diagnosis of lupus. *"I was shocked, confused and lupus was a word I definitely did not want to hear,"* Aaliya shared.

But she had to face it—her lupus involvement was that severe. The disease attacked her internal organs and joints, even though Aaliya looked healthy to the outside world. That irony about lupus greatly shaped her outlook. *"That's the frustrating thing about lupus ... because I am struggling. I may not have a broken arm or wear a cast, but I'm struggling in my own way—even if people can't see it,"* Aaliya shared.

Poised and articulate, Aaliya was the inspiration for the annual Rally Against Lupus event, which she co-founded with her uncle Nadeem Meghji, a member of the LRA Board of Directors. She is also an incredible lupus awareness advocate—and welcome addition to the LRA's Young Leaders Board. It's a perfect match—as this group of young people is devoted to helping others cope with lupus. *"Letting people know that they are not alone is one of the powerful ways I can contribute to lupus awareness and social justice."* Aaliya concluded.

The LRA is grateful to Aaliya for sharing her story and for already leaving her mark on the world.



Keynote speaker Aaliya Qassim at the 2019 Rally Against Lupus



LRA GALA GOES ONLINE

For the first time in our history, the LRA **Breaking Through Gala** will become an online celebration: the *Lupus Research 2020 Virtual Fundraising Event*. Using the latest technology, we will be hosting an exciting virtual **FUNdraiser** on November 23 at 7:00 PM EST.

Boasting star-studded performances and surprise celebrity guests, the Lupus Research Alliance will lead the charge to unite the global lupus community through the power of science. This unparalleled virtual experience hosted by **Willie Geist** of *Sunday TODAY*, and Co-Host of *Morning Joe*.

The event will also give the LRA the opportunity to publicly acknowledge and celebrate the extraordinary contributions of champions of the lupus community, **Jenny and Spencer Zwick** of Solamere Capital and the **LRA Board of Directors**.

With a national viewership, the global lupus community—researchers, physicians, and supporters—will join up with us on one night, behind one goal - to help fund the research urgently needed to discover new treatments and a cure.

Donate at <https://give.lupusresearch.org/virtualgala> to be added to the list for access to our broadcast and stay tuned for future announcements.

Lupus News Corner

COVID-19 Won't Stop the Jets' Support

In getting ready for another season of football, the NY Jets welcomed fans and friends to this year's kickoff ... virtually on September 10, 2020.

In a video presentation, Bob Wischusen—radio voice for the NY Jets—exuded excitement about the upcoming season in spite of COVID-19.

"For 20 years we've done a Kickoff Luncheon and, of course, this is the first year we're doing it virtually, but we still thought it was important to acknowledge the commencement of the Jets' season and to raise money for the NY Jets Foundation and the LRA," said Bob.

The LRA is extremely grateful for the continued support of the NY Jets. "This incredible enterprise has been an avid supporter of lupus research and we are tremendously grateful for the Jets' commitment, especially during this difficult year," said Kenneth M. Farber, President and CEO of the LRA.



Redefining Lupus Trials Amid COVID-19 and Beyond



Lupus Therapeutics, the clinical trial innovation division of the LRA, orchestrated a webcast on August 24, 2020 to discuss important considerations regarding clinical trial participation during COVID-19.

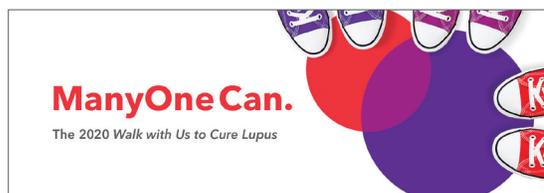
The program featured a diverse, expert panel about clinical trial innovation and why COVID-19 may be the spark needed to empower patients and drive clinical trial innovation. To read a more detailed article, go to www.lupusresearch.org

ManyOne Can!

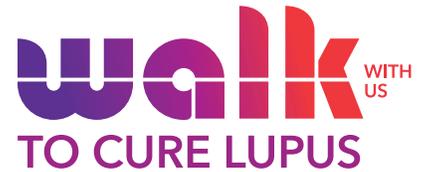
Using the latest technology, we created the world's largest lupus Walk event on September 12, 2020.

The event featured inspirational speakers, lupus research updates, and interactive activities to celebrate as one community. By walking with us virtually, participants propelled lupus research for millions worldwide.

No one individual can do it alone—but **ManyOne Can!**



Visit lupusresearch.org to make a donation, learn more about lupus and our funded lupus research, or find out about our *Walk with Us to Cure Lupus* program.



100% of all donations goes to support lupus research programs because the Lupus Research Alliance Board of Directors funds all administrative and fundraising costs.

For the latest, up-to-date information about lupus you can join our online community on:



facebook.com/lupusresearchalliance



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youtube.com/lupusresearchorg



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