

Learning to Turn Off Lupus ... In the Brain

With infinite complexity, the human brain is an engineering marvel—yet for all its wonder, the brain cannot be shielded against lupus.

Understanding the causes of symptoms described by some patients as “fuzzy-headedness” ... “memory loss” ... and “trouble articulating thoughts and feelings”

is the focus of an intriguing investigation being conducted at Stony Brook University by **Lonnie Wollmuth, PhD**.



Dr. Lonnie Wollmuth

A recipient of the **Lupus Innovation Award (LIA)** from the **Lupus Research Alliance (LRA)**, Dr. Wollmuth is looking at neurobiological levels of brain function. He aims to obtain a greater understanding of the mechanisms of the “brain fog” reported by lupus patients and the means to treat it therapeutically. Dr. Wollmuth’s work is critical because the impact of lupus on the brain is not well understood—in part because common symptoms, like headaches, are not lupus specific.

By examining brain function—specifically the NMDA receptor—Dr. Wollmuth’s study will open avenues for new pharmacological interventions. These interventions will look to block the impact and repair the damage of lupus on this receptor molecule.

The NMDA receptor molecule is key to complex brain functions and is linked to cognitive abilities like learning, storing and retrieving information, and navigating our environment. In the brain, neurons interact at contact points called synapses. At a synapse, a chemical signal transmits electrical activity from an upstream cell to a downstream cell. In lupus, some antibodies disrupt the flow of electrical signals along these neural linkages.

“In some lupus patients, antibodies are produced to target the NMDA receptor, which alters the functioning of the receptor and may be linked to brain disorders,” explains Dr. Wollmuth. *“The NMDA receptor is central to brain function.”*

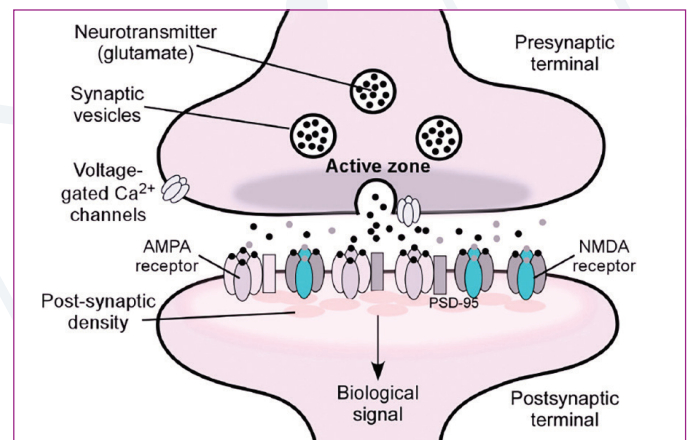
Dr. Wollmuth’s lab is looking at the interactions and effects of a subset of lupus autoantibodies called DNRABs. These experiments will yield vital information about patient-specific variations in the DNRAB/NMDA receptor interaction and, in turn, the altered NMDA receptor function.

An important element of the study is the analysis of DNRABs from diverse patients experiencing brain dysfunction to identify how variations in the DNRAB-NMDA receptor interaction contribute to clinical brain dysfunction and treatment potential.

Using murine models, Dr. Wollmuth’s team will assess the damage caused by specific antibodies and then look for ways to block the damage through various drugs and other neurological interventions. His work is laying the foundation for a new day of targeted personalized medical care for lupus patients with brain disorders.

Dr. Wollmuth will collaborate with **Betty Diamond, MD**—a prominent immunology researcher and LRA grantee—to examine polyclonal autoantibodies drawn from lupus patients, rigorously screened for neuropsychiatric disorders.

The LRA believes Dr. Wollmuth’s investigation has the potential to provide novel insights into the genesis and diversity of brain dysfunction in lupus and to lead the way to new treatments. His findings could also have ramifications for other autoimmune diseases that impact brain function.



NMDA receptors at synaptic terminal

IN THIS ISSUE

Learning to Turn Off Lupus ... In the Brain	1
Two Diversity Initiatives In Action	2
Achieving Diversity in Research	3
LRA in Action	4

BOLD NEW IDEAS

The LRA is delighted to announce the recipients of the **Lupus Innovation Award**. This funding mechanism provides early-stage support for highly innovative approaches to major challenges in lupus research.

The following 11 grantees bring bold and innovative ideas to the LRA's scientific portfolio:

Gregory Barton, PhD

University of California, Berkeley
Identification of new genes that restrict TLR7 responses to self-nucleic acids

Nunzio Bottini, MD, PhD

University of California, San Diego
Targeting the proteoglycan switch for lupus therapy

Jason Cyster, PhD

University of California, San Francisco
Role of metabolite-receptor pathway in protection from lupus

Maria Gutierrez-Arcelus, PhD

Boston Children's Hospital
Insights into lupus heterogeneity by single-cell profiling of B cell activation

Bart Lambrecht, MD, PhD

VIB-UGent Center for Inflammation Research
Linking the microbiome and B cell repertoire to lupus nephritis

James Oates, MD

Medical University of South Carolina
Targeting pathogenic endothelial dysfunction in lupus nephritis

Joshua Ooi, PhD

Monash University of South Carolina
Targeted regulatory T cells (Tregs) to treat lupus nephritis

Zaida Ramirez-Ortiz, PhD

University of Massachusetts Medical School
Mechanisms of SCARF1 in regulating SLE

Joanne Reed, PhD

Westmead Institute
Beyond serology: Improving the prediction and treatment of lupus with single cell Omics

Betty Tsao, PhD

Medical University of South Carolina
The role of polyamine catabolism in the development of lupus

Lonnie Wollmuth, PhD

Stony Brook University
Diversity of anti-NMDA receptor autoantibodies in lupus patients

Two Diversity Initiatives In Action

The LRA is leading the way on two fronts to remove barriers that inhibit people of color from participating in lupus clinical trials and seeking careers in lupus scientific research.

Clinical Trials: Partnering with Those at Greatest Risk

With its clinical affiliate **Lupus Therapeutics (LT)**, the LRA has officially launched **Project CHANGE** to increase meaningful, equitable, and supported clinical trial awareness, participation, and engagement among African Americans/Black people living with lupus.

A collaborative team in three pilot locations will partner with this population and their communities to tailor a specific action plan that addresses their unique needs. *For an insider's point of view from Director of Health Equity, Ebony Scott, see highlighted story below.*

Supporting Research Pathways for Minorities

The LRA's **Diversity in Lupus Research Program** is working to alleviate the lagging representation of minorities in scientific research through three important mechanisms:

The **Career Development Award to Promote Diversity in Lupus Research** provides up to \$600,000 over four years to outstanding early-career underrepresented minority scientists.

The **Postdoctoral Award to Promote Diversity in Lupus Research** provides qualifying postdoctoral research fellows with \$170,000 over two years.

The **Administrative Supplement to Promote Diversity in Lupus Research** supports promising underrepresented minority trainees working with LRA-funded researchers or investigators supported by the NIH or DOD who have reviewed LRA grant applications within the past three years.

*"Advancing racial equity in scientific research has been important to the LRA since our inception," says **Kenneth M. Farber, LRA President and CEO**. "Today, our work continues with renewed focus to achieve even greater diversity among professionals on the front lines of lupus research."*

AN ENLIGHTENED PERSPECTIVE

"I have family members who cope with lupus. I have family members who have died from lupus. So, I understand the reluctance that many feel—including those most vulnerable—about participation in lupus clinical trials. That's why Project CHANGE is so important.

We are looking to increase participation and retention in lupus clinical trials among the very people most touched by the disease—people of color.

Greater participation means that these groups can begin to understand more about symptoms ... more about side effects—and to become more empowered in knowledge.

As with all health disparities, those most affected are those most vulnerable. I feel a duty to provide these communities with the tools and resources that can start to diminish health inequities—because I look like people from these communities. That's my goal with Project CHANGE."



Ebony Scott

—Ebony Scott, Director of Health Equity

Achieving Diversity in Research

Janet Lubov, Research Fellow at UMass Chan Medical School and **Juan Rivera-Correa, PhD**, at the Hospital for Special Surgery attest to the fact that a brilliant mind capable of making substantial contributions to lupus research is not limited by ethnicity or the color of one's skin.

These two researchers have been selected to be part of the LRA's Diversity in Lupus Research Program—and each is already making invaluable contributions to LRA-funded studies being led by Principal Investigators **Jillian Richmond, PhD** and **Alessandra Pernis, MD**, respectfully.

Ms. Lubov, a medical student who is also pursuing a master's degree, works remotely as a dermatology research fellow in Dr. Richmond's lab. There, she is part of a team that is using gene expression profiling to better understand the genetics and epigenetics of lupus and other dermatologic conditions.

"Dr. Richmond's style of mentoring, her network of colleagues and access to advanced biotechnology, encourages growth and autonomy in a rigorous but nurturing environment," Ms. Lubov said about her experience.

In praising Ms. Lubov's attention to detail and eagerness to be a contributing team player, Dr. Richmond said that she will *"make a superb physician-scientist."*

In his postdoctoral fellowship, Dr. Rivera-Correa has the good fortune of working with lupus research expert Dr. Pernis on an exciting investigation that is looking at Autoimmune/Age-associated B cells (ABC).

In murine models, ABCs can produce pathogenic autoantibodies—and inappropriate expansion of ABCs

have also been observed in people with lupus.

In her lab, Dr. Pernis is mentoring Dr. Rivera-Correa as they examine the mechanisms that control the growth and function of these cells. Dr. Pernis and her team are also looking to identify new targets for drugs that could help prevent tissue damage and disease progression.

"Dr. Rivera-Correa has been of invaluable assistance in my lab—translating the information obtained from our murine studies to lupus patients," said Dr. Pernis.

It's a win-win situation for them both. *"This investigation is allowing me to gain a broad background in cellular immunology, in signaling pathways, and in mouse models with autoimmunity,"* said Dr. Rivera-Correa. *"I am especially grateful to the LRA and Dr. Pernis for this opportunity."*



Janet Lubov



Dr. Juan Rivera-Correa

HARNESSING THE POWER OF ALL MINDS

Through its **Diversity in Lupus Research Program**, the LRA is fostering the development of talented and promising young scientists from underrepresented backgrounds by giving them the opportunity to work alongside LRA Principal Investigators. Meet the teams!

Marta Alarcon-Riquelme, MD, PhD

is mentoring
Olivia Castellini Perez, BS

Elena Hsieh, MD

is mentoring
Olivia Anne Bailey, PhD

Alessandra Pernis, MD

is mentoring
Juan Rivera-Correa, PhD

Jillian Richmond, PhD

is mentoring
Janet Lubov, BSN

Roger Sutton, PhD

is mentoring
Johanna Villarreal, BS

Zahi Touma, MD, PhD

is mentoring
Carolina Muñoz-Grajales, MD, PhD

Victoria Werth, MD

is mentoring
Thomas Vazquez, BS

LRA in Action

Not Just 31 Days!

May is **Lupus Awareness Month** and the LRA aims to accomplish two goals during the 31 days of May and every day throughout the year.

First, we recognize the awesome strength, passion, and optimism characteristic of people with lupus and those who love them. And secondly, we aim to educate the general public on: life with lupus, how the body's immune system goes haywire and starts attacking itself, and how to recognize the symptoms ... because knowledge is power.

Join us every month of the year—in celebrating the lives of people with lupus, their support networks, and the LRA-funded scientists who are leading the way to improved diagnosis and therapies on a number of fronts by taking part in the ManyOne Can movement—and learn how each person can make a difference in advancing new lupus treatments and a cure.

Visit us at LupusResearch.org, and on **Facebook**, **Twitter** and **Instagram** for accounts of trials and triumphs, scientific exploration and promising discoveries, disease awareness and advocacy successes.

Celebrating Every Walker—Over 20 Years!

Great things have come from 20 years of the LRA's Walk with Us to Cure Lupus signature fundraising walkathon—including \$42 million in funding for the world's most pioneering lupus research!

Every step that walkers took brought us closer to finding more effective treatment options. In addition to raising funds, participants shared their stories and spirit—effectively raising awareness of the disease and camaraderie among the lupus community.

Each and every participant in the newly rebranded **ManyOne Can Walk with Us to Cure Lupus** events drives lupus research forward. Join us in 2022! Northern Michigan—June 11, Mid-Atlantic—October 1, NYC—October 22, Dallas—October 22, and San Diego—November 5.



The graphic features the Lupus Research Alliance logo and the 'ManyOne Can Walk with Us to Cure Lupus' logo. It lists the dates for the 2022 walks in various locations. A 'JOIN US' button is prominently displayed. At the bottom, it marks the 20th anniversary of the walk program.

LRA's 2022 Walks

- South Florida - **Saturday, April 9**
- Virtual Walk - **Saturday, May 7**
- New Jersey - **Saturday, May 14**
- Northern Michigan - **Saturday, June 11**
- Mid-Atlantic - **Saturday, October 1**
- New York City - **Saturday, October 22**
- Dallas - **Saturday, October 22**
- San Diego - **Saturday, November 5**

20TH Anniversary of our Walk Program!

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

 twitter.com/lupusresearch

 youtube.com/lupusresearchorg

 pinterest.com/lupusresearch

 instagram.com/lupusresearchalliance

 lupusresearch.org/community



©2022 Lupus Research Alliance. All Rights Reserved. Lupus Research Update is published by the Lupus Research Alliance. Contents herein may not be reproduced, republished, or distributed without the prior written permission of the Lupus Research Alliance. To request permission to reproduce, republish, or distribute any part of this newsletter, contact us at **212-218-2840** or email info@lupusresearch.org.