

## **Breaking Through Uncovering a Probable Cause of Lupus:**

An innate – and lifelong – curiosity about the most complex, unresolved questions in medicine has served **John D. Mountz, MD, PhD**, from the University of Alabama at Birmingham, Division of Clinical Immunology and Rheumatology, well.

For the past three decades he has made significant strides in piecing together some of the most disparate aspects of lupus – greatly advancing the molecular understanding of this disease for the entire lupus community.

With so many fundamental gaps in our understanding of lupus, Dr. Mountz's current work aims high. He is looking to uncover a root cause of lupus with a major grant he received from the Lupus Research Alliance.

Dr. Mountz is pursuing an innovative research investigation that focuses on interferon-beta. He seeks to prove that it sets off a chain of events that triggers an inflammatory response and destructive mechanisms that can lead to advanced disease in patients.

*Why interferon beta?* It is the most potent of all 13 interferons, the class of protein molecules used to trigger the protective defenses of the immune system that help eradicate pathogens.

In his work, Dr. Mountz has found that patients with high levels of this molecule in the early development of B-cells are more likely to have higher levels of autoantibodies and kidney disease. He hopes his study of interferon-beta will explain how lupus develops and why some people are at greater risk for flares and kidney disease.

Another interesting fact about interferon-beta is that African-Americans with lupus have higher levels of it in their cells compared with Caucasians with lupus.

*"If we can figure out why interferon-beta is produced, why it is high in lupus patients, and what it does to promote B-cell tolerance loss and autoantibody production – we are going to have major clues. And, of course, if it is interferon-beta, well, the solution is obvious – block it,"* Dr. Mountz said with authoritative zest.

Going back to an earlier point, if interferon-beta is expressed in the early development of the B-cells, it does two things. *"There are B-cells that produce interferon beta and B-cells that respond to interferon beta,"* said Dr. Mountz. *"So the ones that produce it probably produce it both for themselves and for other B-cells in the environment. But interferon-beta also has an effect on itself, due to the interferon signaling pathway in the DNA of the B-cell."*

In this scenario, if a patient produces a B-cell or a group of B-cells that have a lot of interferon, the trajectory of those B-cells is changed forever. Because it imprints on the chromatin, those B-cells are more susceptible to interferon. The chromatin is a complex of macromolecules found in cells, consisting of DNA, protein, and RNA.

*"Inhibiting interferon-beta at the right time and with the right people might inhibit disease progression and even induce tolerance,"* he continued. *"The patient might not have to receive the therapy forever – just long enough to cause tolerance, to re-stabilize or normalize their immune system that went off track."*

The Lupus Research Alliance is eager to see the outcome of this investigation. If Dr. Mountz is correct in his assumption, doctors may finally have the ability to keep lupus at bay for a large percentage of people who have the disease.



*Dr. John D. Mountz*

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## Bold Initiatives ... Tremendous Strides Breaking Through on Lupus Research

In 2018 the Lupus Research Alliance has taken daring chances, pursued bold initiatives, and made tremendous strides! We truly are breaking through on many pioneering fronts of lupus research – thanks to the unwavering generosity of donors at all levels of support.

Throughout the year, the brilliant scientists we brought to the table ushered in discovery after discovery. These minds – the world’s best and brightest – have helped the Lupus Research Alliance break through in directions that once were considered impossible.

But battling lupus takes more than fostering the most innovative lupus research. That’s why we advocated –from the halls of Congress to the homes of average

Americans – for greater lupus awareness and funding. We proved that everyone could become powerful catalysts for change.

Our groundbreaking discoveries helped to broaden the basic knowledge of this disease for the entire lupus community, illuminating multiple paths to new treatments. And we made important gains toward our ultimate aim: Finding a cure for the millions living with lupus worldwide.

Second only to the National Institutes of Health in funding, the Lupus Research Alliance has invested more than \$200 million in lupus research programs and delivered breakthroughs that are speeding up the development of new treatments.

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### Breaking Through ... Investing in Trailblazing Research

As the world’s largest private funder of lupus research, the Lupus Research Alliance funded 15 scientists to conduct promising investigations in three critical areas:

- 7 scientists received \$4.2 million in grants through our two-year **Target Identification in Lupus** grant program. Supporting highly meritorious research, this program aims to discover molecular pathways and therapeutic targets that will lead to new treatments.
- Our **Novel Research Grant Program** awarded \$1.8 million for 6 high-risk, high-reward, original research projects relevant to basic, translational, and clinical investigations in lupus.
- The **Dr. William E. Paul Distinguished Innovator Award in Lupus and Autoimmunity** challenged 2 extraordinary scientists to pursue innovative, hypothesis- or discovery-driven projects with \$1 million in grants.

### Breaking Through ... Accelerating Drug Development

Comprised of leading lupus experts at academic research centers throughout North America, our **Lupus Clinical Investigators Network (LuCIN)** program provides an invaluable framework to test potential new treatments.

The scope of the eight clinical trials currently underway is wide ranging – from evaluating a new app

aiming to help patients report their symptoms more accurately in real time, to testing new and existing drugs as potential treatments for lupus.

Breaking new ground and attracting new researchers are part of LuCIN’s aim to advance quality research. LuCIN is administered by Lupus Therapeutics, an affiliate of the Lupus Research Alliance.

## Breaking Through ... In the Community

Launched in 2018, our new online **Lupus Community Forum** is helping lupus patients and their loved ones make stronger connections with the greater lupus community.

Participants learn what others are saying about matters that are critical to their lives. It is a place to give and

receive support ... and provide and gain new perspectives.

Community is a destination for discussion. Join the conversation and discover information on important matters that are a part of your life.

## Breaking Through ... Celebrating Outstanding Efforts

The achievements of lupus research giant, **John D. Mountz, MD, PhD**, to accelerate the development of new treatment options (see cover story) were recognized by the Lupus Research Alliance. Dr. Mountz is the recipient of the Dr. William E. Paul Distinguished Innovator Award in Lupus and Autoimmunity.

Dr. Mountz explains what this grant means to lupus research:

*"The Lupus Research Alliance allows for more novel approaches – such as the investigation I am*

*conducting – which is far from mainstream. The thing is – if we see evidence for something – we have to take a chance. And this is exactly what the Lupus Research Alliance allows researchers like me to do.*

*We have to build on new ideas, on new data, on new discussions. With the backing of this incredible organization, I am confident that my colleagues and I will break through to new treatment options and a cure for lupus."*

## Breaking Through ... Transforming Goodwill into Research

If there is one thing that the Lupus Research Alliance has learned, it's that there is power in numbers – and we need no greater proof than our **Walk with Us to Cure Lupus** events.

Walkers are passionate about ending lupus because many of them are personally affected. They may walk because a sister, mother, daughter, wife, or colleague

has lupus – or they may walk because they have lupus themselves.

Such passion has generated nearly \$3 million in 2018. Even more remarkable is the fact that since this grassroots fundraiser began, a cumulative total of nearly \$39 million has been raised for critical lupus initiatives from these supporters.

## Breaking Through ... Advocating for Lupus Research

When the Lupus Research Alliance speaks out and advocates for greater funds for lupus research ... people listen. The effort we lead at the House and Senate level has resulted in a \$5 million budget for the **Lupus Research Program** administered by the Department of Defense. An additional \$2 billion was

granted by the NIH to advance medical research, including lupus research.

To date we have secured \$15 million to fund the Lupus Research Program within the Department of Defense, and 13 exciting scientific projects are underway.

## Breaking Through ... Uniting the Global Community

TV newscaster and Lupus Research Alliance Board Member **Brenda Blackmon** is the first spokesperson for our **Breaking Through Social Media Campaign**.

In a series of short videos, Ms. Blackmon highlights how the Lupus Research Alliance is uniting the global community to break through the complexities of lupus by raising awareness, advancing new treatments,

advocating for more federal research dollars, and funding discoveries that will lead to the prevention and a cure.

*"As the parent of a daughter with lupus, this initiative gives me hope that better treatments and a cure for lupus are on their way,"* said Ms. Blackmon.

## Lupus News Corner



2018 Breaking through Lupus Gala

### Gala Brings Out Heavy Hitters

With **The Honorable Michael R. Bloomberg**, **Lady Gaga**, and **Selena Gomez** as honorary chairs, the success of our annual gala on November 19, 2018 – **Breaking through Lupus** was practically guaranteed. It was an unforgettable, spectacular evening, which brought in \$3.5 million for lupus research studies.

These big names came together to support our organization and to help us recognize the outstanding efforts that **William J. Wolfe**, Chairman and Chief Executive Officer of First Washington Realty, Inc. has made to end lupus. A leader in lupus research and highly active member of our Board, Bill is motivated by a father's love. His daughter has courageously battled the disease since she was a child.

**Willie Geist**, Host of *Sunday TODAY* and Co-Host of *Morning Joe*, was on board to share his warmth and humor as our emcee, while trumpeter **Brian Newman** and Tony Award Nominee **Norm Lewis** entertained with music and song.

This not-to-miss annual event has been a red-circled night on NYC's social calendar for decades. Annually, it draws over 600 members of the nation's lupus community and raises millions, with every dollar going directly to fund lupus research programs.

*"With such an impressive roster of celebrities and movers and shakers behind our annual gala, it is easy to see how this event has become the largest single lupus fundraiser in the world,"* said **Kenneth M. Farber**, President and CEO of the Lupus Research Alliance.

### Donor Dollars Fuel Lupus Research

The Lupus Research Alliance has an ambitiously tall order: Fund the most promising scientific investigations that will transform the lives of people with lupus. That's why we need the renewed commitment of great donors like you. Please make your generous gift today.

But act quickly while there is still time to receive a full tax credit for 2018.

With your year-end gift, the Lupus Research Alliance will speed the pace of scientific discovery ... bring greater understanding about this disease ... break through with better treatment options and ultimately a cure for lupus.

**Be part of the next big lupus research breakthrough in 2019!**

Visit [lupusresearch.org](http://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.



**walk** WITH US  
**TO CURE LUPUS**

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 information about lupus you can join our online community on:



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