

# Looking at Iron As a Trigger for Lupus Nephritis

As the provider of life-giving oxygen to organ systems through its role in red blood cell production – the health benefits of iron are tremendous. This essential element is vital for proper growth throughout the body and for robust cellular health.

## But what happens when a good thing goes bad, and iron makes cells die?

This process – *ferroptosis* – is the focus of a Lupus Research Alliance-funded investigation that is currently being conducted by **Erika Boesen, PhD**, at the University of Nebraska Medical Center in Omaha, NE. Dr. Boesen is studying iron and ferroptosis to gain a better understanding of lupus – particularly lupus nephritis and renal failure.

**The term *ferroptosis* is derived from the Greek word *ptosis*, meaning “a fall,” and *ferrum*, the Latin word for iron. It describes a form of regulated cell death in which iron appears to be a factor.**

Dr. Erika Boesen believes ferroptosis may play an important role in lupus nephritis.

*“Iron doesn’t just transport oxygen around in red blood cells – it can also promote free radical activity that can damage cells of the body,”* explains Dr. Boesen. *“Ferroptosis is a particular type of cell death that occurs when iron has generated free radicals that overwhelm the antioxidant defenses of the cells.”*

Connecting this back to lupus, Dr. Boesen is now building on the findings of her first Lupus Research Alliance grant to learn how much of a factor iron is to renal damage in lupus. In murine models, Dr. Boesen discovered an increase of iron in the kidneys. *“We found that iron did contribute to lupus nephritis,”* said Dr. Boesen. *“But we still need to understand how ... and I’m grateful for the additional support I have received from the Lupus Research Alliance to continue this work.”*

Ferroptosis is a relatively new field of study, and the tools to investigate it are few and far between at this stage. But a small number of chemicals have been identified that may stop this type of cellular death from happening.

*“The particular chemical that I am going to use is pretty specific to ferroptosis and this iron-mediated, free radical pathway,”* shared Dr. Boesen. *“So to block ferroptosis, my approach is pharmacological.”*



Dr. Erika Boesen

If Dr. Boesen can successfully block ferroptosis, she may have found a way to block certain types of kidney damage. But she also wants to know if the debris from these cells is recognized by the immune system and if it is responsible for provoking further inflammatory responses.

As a second-time grant awardee, Dr. Boesen has much enthusiasm for the Lupus Research Alliance. *“This amazing organization does a great job in bringing in investigators who may not have worked exclusively in lupus research,”* she said. *“The Lupus Research Alliance allows researchers like me to explore new ideas – and bringing a more diverse group of minds to the complexities of lupus has only proven to be a good thing.”*

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## NEW GRANTS ... NEW ANSWERS

Ingenuity, skill, and determination are the hallmarks of our **Target Identification in Lupus** program grantees.

The Lupus Research Alliance applauds each diverse quest to bring new understanding of lupus and ways to treat, prevent, and cure it.

### **Joseph Craft, MD**

*Targeting Follicular Helper T Cells in Lupus*  
Yale University

### **Keith Elkon, PhD**

*The Cyclic GAMO Pathway in SLE*  
University of Washington

### **David Levy, PhD**

*Targeting Interferon-Stimulated Transcription as a Novel Lupus Therapy*  
New York University School of Medicine

### **Eric Meffre, PhD**

*PTPN22 Function in Human B Cells and Inhibition to Reset Tolerance in SLE*  
Yale University

### **Deepak Rao, MD, PhD**

*Targeting Peripheral T Cell – B Cell Interactions in SLE*  
The Brigham and Women's Hospital, Inc.

### **Jillian Richmond, PhD**

*Targeting the CXCR3 Chemokine Axis in Cutaneous Lupus*  
University of Massachusetts Medical School

### **Nan Yan, PhD**

*Mammalian Free Glycan, Glycocalyx and Anti-glycan Antibody in Lupus*  
UT Southwestern Medical Center

## Studying Chemoattractants To Break Through in Lupus Research

Straightforward. Clear. Innovative.

These words aptly describe the research that **Jillian Richmond, PhD**, of the University of Massachusetts Medical School at Worcester, MA, is conducting with a grant from the Lupus Research Alliance.

She is looking for ways to stop lupus from damaging healthy tissue. But to attain a better picture of Dr. Richmond's investigation, we just need one more word: Promising.

Building on her vast experience in the field of autoimmune skin diseases, Dr. Richmond is seeking to understand the pathology of cutaneous lupus erythematosus (CLE). Her goal: better diagnostics and new treatment targets for both skin-limited and systemic lupus.

She started with a very basic – but critical – question: What drives white blood cells to travel around the body?

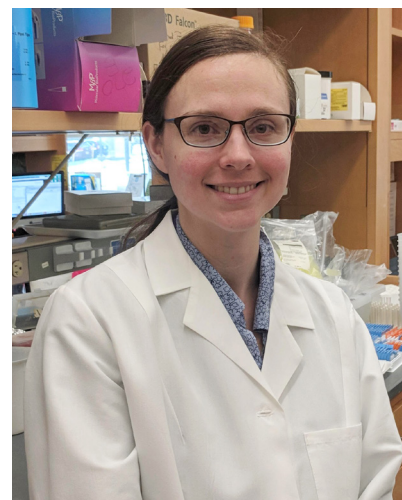
Dr. Richmond explains: *"Pertinent to both infection and to autoimmune diseases are proteins the body expresses that tell cells where to go. So if someone cuts himself, there are proteins that will say to his white blood cells, 'Hey there's a cut and you need to come clear out any infection and start the healing process' – but in lupus, those signals can get turned on inappropriately."*

Dr. Richmond and her team have found specific proteins highly expressed in the skin that are required for getting white blood cells there, and they are prominent in lupus.

Here's what's going on at the molecular level: CXCL9 and CXCL10 are protein ligands – or chemoattractants – that are made in the skin and bind to CXCR3 on white blood cells in order to direct the cells into the tissue where they can wreak havoc.

Dr. Richmond helps her students to understand this complex process by asking them to imagine finding a bottle of perfume when they are blindfolded. *"In this example, your nose is CXCR3 and the perfume is CXCL9 and 10. Following the scent to the strongest area is how the cells find their way into the skin tissue,"* she explains. *"So it is highest at the site of injury or, in the case of lupus, the site of disease activity. And that is how the cells are finding their way there."*

The next step for Dr. Richmond is to understand the functional



*Dr. Jillian Richmond*

significance of her findings in murine models and, eventually, to find a way to disrupt the course of lupus by blocking CXCR3 or its ligands.

Dr. Richmond is quick to acknowledge the pivotal influence of her mentors – Drs. John Harris and Ann Rothstein – on her successful investigative work. She’s also grateful to the Lupus Research Alliance. *“I absolutely would not have been able to do this research without this incredible organization,”* she said. *“We scientists need these types of grants to take lupus research to the next level, and I am thrilled to be part of the Lupus Research Alliance team!”*

## FACES OF LUPUS

### **Patient Involvement: Let Your Story Become Part of Community**

The Lupus Research Alliance is pleased to invite you to join our new **Lupus Community Forum** – a place to unite with others who face many of the same struggles you may have experienced.

The Lupus Community Forum is where you can discover what others are saying about critical issues that matter in your life. It’s the ideal place to share your trials and triumphs – as well as your questions and suggestions.

By participating, you can both give and receive support ... exchange ideas ... provide perspectives. And you’ll also help to direct science – Kenneth M. Farber, President and CEO of the Lupus Research Alliance, explains:

*“As the premier private organization devoted to scientific exploration that seeks new ways to treat, prevent, and cure lupus, we must reflect the priorities of the people we aim to help.*

*The Forum is a giant step in the right direction in helping the lupus community aid in the realization of this vision.”*

Please visit [lupusresearch.org/community](http://lupusresearch.org/community) and join the conversation today.

Don’t hold back! This is your chance to share your story – and touch the lives of people just like you!

**LUPUS**  
community



### **PROMISING NOVEL GRANT AWARDS**

The Lupus Research Alliance supports game-changing lupus research, and our **Novel Research Grant** program is exploring lupus from many perspectives.

The following awardees of this grant mechanism are testing new theories about what causes lupus and why it has such a varied and widespread effect in the body.

#### **Erika Boesen, PhD**

*Ferroptosis as a Novel Driver of Inflammation in Lupus Nephritis*  
University of Nebraska  
Medical Center

#### **Theresa Lu, PhD**

*Lymphatic Regulation and Photosensitivity*  
Hospital for Special Surgery

#### **Kevin Nickerson, PhD**

*Age-Associated B cells in Autoimmune Lupus*  
University of Pittsburgh

#### **Joshua Ooi, PhD**

*Genetically Engineering Regulatory T cells to Treat SLE*  
Monash University

#### **Jeremy Tilstra, MD, PhD**

*Examining the Role of T cell Exhaustion in Lupus Pathogenesis*  
University of Pittsburgh

#### **Michael Waterfield, MD, PhD**

*Epigenetic Regulation of Il2 by ATF7ip – Implications for SLE*  
University of California,  
San Francisco

# Lupus News Corner



18th Annual Jets Kickoff Luncheon

## Jets Tackle Lupus at Kickoff Luncheon

The New York Jets hosted their 18<sup>th</sup> Annual **Jets Kickoff Luncheon** at Cipriani Wall Street on August 28, 2018 – and raised over \$750,000 to benefit the New York Jets Foundation and the Lupus Research Alliance. They also gave cheering fans – nearly 800 generous supporters – a glimpse of the upcoming year.

**Neil Glat**, President of the New York Jets, spoke about giving back:

*"We firmly believe it is our responsibility. Our community activities include efforts to eradicate bullying, promote youth football, fight child obesity, work with the military and first responders, and, of course, to actively support lupus research. We especially thank our players because we could not do this important philanthropic work without them."*

With the backing of incredible supporters like the Jets, the Lupus Research Alliance is able to enlist the world's top researchers.

## LUPUS RESEARCH ALLIANCE BREAKING THROUGH GALA 2018

## Breaking Through Gala ... Save the Date!

The 2018 **Breaking Through Gala** will take place on Monday, November 19, 2018, at the Ziegfeld Ballroom in New York City.

This year, we proudly honor **William J. Wolfe**, Chairman and Chief Executive Officer of First Washington Realty, Inc. A leader in the lupus community and a highly active member of our Board of Directors, Bill ardently supports the Lupus Research Alliance on behalf of his daughter, who has courageously battled the disease for many years.

**Willie Geist**, Host of *NBC's Sunday Today with Willie Geist* and Co-Host of *Morning Joe*, will share his warmth and humor as our emcee, and Broadway star and Tony Award Nominee, **Norm Lewis**, will perform Broadway classics. The event will open with jazz musician **Brian Newman**. And our honorary co-chairs are none other than The Honorable **Michael R. Bloomberg**, **Lady Gaga**, and **Selena Gomez**.







For more information, please call 212.888.7003 or visit [lupusresearch.org](http://lupusresearch.org).

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.



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](https://facebook.com/lupusresearchalliance)
-  [twitter.com/lupusresearch](https://twitter.com/lupusresearch)
-  [youtube.com/lupusresearchorg](https://youtube.com/lupusresearchorg)
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