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FALL 2008

DISCOVERY

LRI Scientists Win \$60 Million from NIH to Expand Research *Innovation Drives Powerful New Research Model for Complex Disease*

A recent analysis shows that 65 percent of the LRI scientists completing their 3-year Novel Research grants have successfully proven their innovative hypotheses and gone on to secure nearly \$60 million at the National Institutes of Health (NIH) and other agencies to expand lupus research.

“The scope, speed, and consistent pace of this scientific discovery are unprecedented in private-sector lupus research,” said LRI President Margaret Dowd. “We began convinced that the path to a cure lay in freeing investigators to think creatively and imaginatively, so we asked

for outside-of-the-box thinking. LRI investigators have turned that box inside-out and upside-down.”

“The LRI strategy of funding novel scientific ideas in lupus has more than demonstrated its power,” adds William E. Paul, MD, chief of the Laboratory of Immunology at NIAID-NIH, and chair of the LRI’s Scientific Advisory Board. “The model strengthens the lupus research landscape by moving novel concepts forward to secure large-scale federal funding.”

The LRI invests \$300,000 each in grants for innovative projects at academic medical centers nationwide.

It’s the only organization pioneering lupus discovery through this bold, high-risk model.

At first, no one else would fund exploration of Dr. Betty Diamond’s novel idea that certain stress hormones might be responsible for allowing toxic antibodies to penetrate the brain in lupus and destroy nerve cells there, causing memory loss, confusion, and other cognitive problems. **Now the Feinstein Institute for Medical Research researcher has an LRI-generated NIH program grant for \$6.5 million** to build on more strategies for dealing with this devastating development.

STORY CONTINUED ON PAGES 2 AND 3

LRI Investigators Win \$60 Million from NIH to Expand Work

At first, no one else would fund exploration of Dr. Marcus Clark's novel idea that the kidneys of people with lupus may actually contain activated B cells that directly promote inflammation and damage in these critical organs. But in his LRI research, Dr. Clark examined small bits of tissue taken from inflamed lupus kidneys—and did in fact find activated B cells. **Now the University of Chicago researcher has an NIH grant for \$1.7 million** to further explore, explain, and expand on this major discovery. “This government grant was funded entirely based on research supported by the LRI,” Dr. Clark said.

At first, no one else would fund exploration of Dr. Elahna Paul's novel idea that a special mouse model could be used to identify and block pathways of kidney cell activation and associated inflammation and damage in lupus. **Now the Massachusetts General Hospital researcher has an NIH grant for**

\$1.6 million to continue this groundbreaking work.

At first, no one else would fund exploration of Dr. Greg Lemke's novel idea that a curious family of “TAM” receptors might function as a core ‘control switch’ over the immune system’s inflammatory response. But he was right. **Now the Salk Institute for Biological Studies researcher has grants of \$1.4 million from the NIH and others** to explore exciting new approaches to mastering this switch—shutting down the uncontrolled inflammation of lupus and other autoimmune illnesses by restoring immune system regulation. “Without the LRI...this fundamental discovery in immunology wouldn’t have happened,” Dr. Lemke said.

At first, no funding group except the LRI would back exploration of Drs. Bevera Hahn and Maureen McMahon's novel idea that a certain form of the normally “good” HDL cholesterol linked to

heart health might play a counterproductive role in lupus and actually promote atherosclerosis. **Now the University of California at Los Angeles researchers have various grants totaling over \$869,000** to find new ways to detect, prevent and treat lupus-related atherosclerosis.

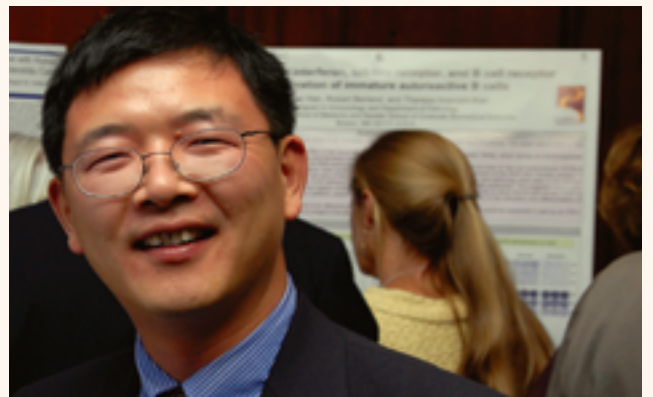
At first, no one else would fund exploration of Dr. Amy S. Major's novel model for accelerated atherosclerosis in lupus. Dr. Major believed the model held promise for explaining what immune system activities lead to premature atherosclerosis and heart enlargement (cardiomyopathy) in so many people with lupus, raising their risk for heart attack and stroke. **Now the Vanderbilt University School of Medicine researcher has an NIH grant for \$1.5 million** to further develop this animal model and generate techniques for early detection and prevention of lupus atherosclerosis. “I am thrilled that I could provide a great return on your investment in me!” Dr. Major said.

#1 NIH Grant to LRI Researcher Zhixin Zhang, PhD

Dr. Zhixin (Jason) Zhang’s grant proposal was so strong that the National Institutes of Health (NIH) ranked it NUMBER ONE out of 500 applications.

At first, no one else would fund exploration of Dr. Zhixin (Jason) Zhang's novel idea that the normal immune system process that alters antibody genes—VH replacement—is what goes into overdrive in lupus, causing B cells to make damaging autoantibodies. But with LRI funding, he was able to show that 30 to 60 percent of these genes in people with lupus are in fact generated by this ‘VH replacement’ process, compared with less than 5 percent in healthy people. **Now the former University of Alabama researcher, currently at the University of Nebraska, has received two NIH grants totaling \$2.9 million** to further pursue this discovery and its potential to find an early marker for lupus diagnoses and organ involvement. He’ll also look at whether chronic viral or bacterial infections may actually trigger lupus.

Brilliant Idea, Dr. Zhang!



“Without the LRI we wouldn’t have been able to generate the preliminary data for the NIH grants,” Zhang said. **“LRI support made this happen.”**

Dramatic Impact on the Field of Lupus Research

At first, no one else would fund exploration of Dr. Chander Raman's novel idea that tinkering with a molecule known as CD5 might reprogram the immune system by sounding the death knell for auto-reactive B cells. Now the University of Alabama at Birmingham researcher has an NIH grant for \$1.8 million to examine this approach to shutting off the over-reactive immune system. The research may also help with treatments for other immune system illnesses such as MS and rheumatoid arthritis. "There is no way this [NIH] grant would have happened without the LRI," Dr. Raman said.

At first, no one else would fund exploration of Dr. Christopher Roman's novel idea that the damaging over-stimulation of the immune system in lupus could be mitigated by inactivating the gene regulatory proteins that his lab discovered control the molecule CD40L and others normally charged with fighting infections. Now the State University of New York Downstate Medical Center (Brooklyn) researcher has an NIH grant for \$1.35 million to look deeper into the link between CD40L gene regulation, infection, abnormal behavior in immune system cells, and lupus.

At first, no one else would fund exploration of Dr. Eric Greidinger's novel approach to predicting lupus organ damage. With LRI funds, he developed a special model to assess the potential of immune system "danger signal" sensors to indicate which organs and tissues in lupus were under imminent attack. Now the University of Miami Miller School of Medicine researcher has a Veterans Administration grant for \$650,000 to further study these immune response patterns and their potential for generating new therapies that could convert severe disease to mild disease. ○

LRI and NIAMS Director Update Congressman Young on Progress of NIH Lupus Research Plan

Congressman Bill Young (R, FL), LRI President Margaret Dowd, and NIAMS Director Stephen I. Katz, MD (pictured at right) met on Capitol Hill this summer to discuss progress of the NIH Lupus Research Plan and its scientific accomplishments in finding answers for the more than 1.5 million Americans with lupus.

The LRI worked closely with Congressman Young to develop this first-ever Trans-Institute Lupus Research Plan at the NIH, which was released in August 2007.

Dr. Katz, who chairs the Lupus Federal Working Group, headed the multi-Institute campaign to involve scientists and the lupus community in developing the official Lupus Research Plan.



LRI Talks about the Science with Families, Scientists, Physicians in Chicago, San Francisco, New York



Stimulating conversation at the University of Chicago

LupusResearchInstitute.org is Relaunching



Have ideas on things you'd like to see?
Email us at lupus@lupusny.org

Headlines from the Web:

Dedicated Dad Rides for a LifeWithoutLupus.org

Chris Paradysz, father to a teenage daughter with lupus, will ride his bike solo from New York City to Daytona International Speedway this Fall to raise critical funds for lupus research. Show you care and are behind what he's doing by donating now—\$500 to inscribe the name of your loved one with lupus on Chris' jersey, \$100 for a bike tune-up, \$25 to sponsor a mile—at LifeWithoutLupus.org

Gala in Los Angeles Sets Fundraising Record

See story and pictures at LupusLA.org

With Your Will, A Cure

Please consider including the Lupus Research Institute in your Will.

It is a gift that will sustain your support of our important mission—*pioneering discovery to prevent, treat and cure lupus.*

Help Secure the Future through Intelligent Estate Planning

Learn about making the Lupus Research Institute the beneficiary of a gift through trust agreements, life insurance, retirement accounts, and other forms of planned gifts.

► Contact Andrea O'Neill at 212-812-9881 or email aoneill@lupusny.org



Become an Ambassador for the Cure!

Call or email us for copies of the new LRI Annual Report. We ordered extras so that we could send you copies to pass along to friends and family!

Orders: 212-812-9881 or lupus@lupusny.org

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