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**FALL/WINTER 2008**

# DISCOVERY

## Forum for Discovery Conference 2008 Explores a Whole New Way of Looking at Lupus

*LRI Poised to Rapidly Accelerate Pace of Research through Science of Systems Biology*

There's a whole new way of looking at human lupus, and it's not through the standard-issue microscope.

It's through the lens of exciting new technologies that enable scientists to probe vast sets of data and generate comprehensive models more akin to what actually happens in the lupus immune system than was possible before.

The technologies, all of which have matured rapidly over the past few years, include powerful and dynamic imaging tools and data from the sequencing of the human genome. The biology of whole systems—not just small bits of them—are now at scientists' fingertips.

### Looking at the whole human system—not just splintered pieces

“Systems biology recognizes that individual humans and experimental animals are comprised of a complex set

of interacting elements,” said William E. Paul, MD, NIAID-NIH's chief of the Laboratory of Immunology and LRI Scientific Advisory Board chair, “and that to truly understand the biology of a whole organism in health and disease, we need to understand how these individual elements interact in a quantitative way.”

By appreciating the body's dynamic and massive interacting web of connections, systems biology not only produces far more realistic pictures of what happens in human lupus—it opens up a whole new spectrum of possibilities for ending the damage.

And it basically does this with a flick of a switch.

Ronald N. Germain, MD, PhD, head of the Laboratory of Immunology's Lymphocyte Biology Section and director of NIAID's new program in Systems

Immunology and Infectious Disease Modeling, explained how the recent explosion in the power of imaging technology could be harnessed to show “real time” moving pictures of the immune system in its normal state as well as in models of lupus.

He also showed how scientists can combine this new experimental insight with advances in computer simulation to eventually develop an ability to predict immune behavior.

Until recently, the best that scientists had to describe interactions in the immune system were static images (snapshots in time) or cartoons—those diagrams of action and reaction that many of us remember from biology textbooks.

“The older technologies gave us knowledge, but not understanding,” he said. “They didn't provide us the power to predict what would happen in a dynamic

immune system that includes time and space and quantity.”

The latest imaging and computational technologies put scientists in the driver’s seat, with an early stage capacity to simulate the behavior of biological systems of substantial complexity and actually make predictions about what happens in the immune system—from what goes wrong to response to therapies.

David Botstein, MD, director of the Leis-Sigler Institute for Integrative Genomics at Princeton University, sees a day coming soon when the information from the sequencing of the entire human genome produces answers about which genes are actually involved in diseases such as lupus.

Think of our genetic map as a railroad system, said the pioneer of the Human Genome Project. For years we have been looking at it on such a basic level—at how a locomotive moves along the track and how it starts and how it stops. But now “we can get into the control room down underneath...where you can see the connections about which trains go where.”


Forest M. White, PhD, associate professor at the Massachusetts Institute of Technology and a biological engineer, is busy using new technologies to nudge the static model we currently have of the human cell and its circuitry to a more realistic one with dynamic, fluid wiring.

By figuring out how information flows through human cells, his laboratory

aims to discover “what cells really care about.” The answers to this question will have implications for all kinds of illnesses, including lupus, in which cells end up making “bad choices.”

Virginia Pascual, MD, a pediatric rheumatologist and associate investigator at the Baylor Institute for Immunology



Research, graphically described the application of one of these systems approaches to human lupus and showed the great insights that could be achieved. One example: a description of the so-called “interferon signature” with, in some cases, as little as 1 milliliter of blood. 

## LRI Conference Industry Panel: Cutting-Edge Technologies in Systems Biology Promise to Fast-Forward Discovery in Human Lupus

Suggestions on how to harness the new technologies to move LRI discoveries from the laboratory to patient care—and quickly

- **First, explore!** Before an actual clinical trial, use the new technologies to do exploratory work to see if the proposed treatment agent is truly likely to work in patients—and which patients. Those with early disease? Late disease? Certain organ manifestations?
- **Economize** Design clinical trials that are smaller, faster, and more nimble with the help of new technologies that can reveal so much, so quickly, about what actually works. A good place to start: short proof-of-concept trials, some as brief as a week or two, in which an idea for a new agent can be tested in narrow, well-defined patient groups.
- **Strategize** Glean more precious data from completed clinical trials. Standardize and centralize collected samples that others might be able to use.
- **Reconsider!** Revamp what it means for a lupus drug to “work,” given the heterogeneity of the disease.



(Above) Paul Brunetta, MD, Genentech; Matthew D. Linnik, PhD, Biogen Idec; Gregory Dennis, MD, Human Genome Sciences; Marcus Clark, MD, University of Chicago; (below) moderator Mark Shlomchik, MD, PhD, Yale University



**“Using systems modeling to predict immunological responses is fascinating. It suggests that one day it might be possible to perform more informative proof-of-concept studies to assess immune targets prior to initiating clinical trials.”**

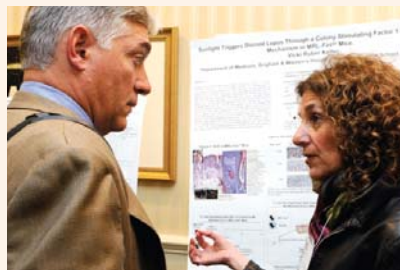
**– Gregory Dennis, MD, Human Genome Sciences**

**“It’s an incredibly exciting time.”**

**– Paul Brunetta, MD, Genentech**

8th Annual Forum for Discovery in Manhattan

# LRI Conference Merges Scientific Innovation and New Technologies, Advancing Discoveries and Accelerating Pace of Lupus Research



## 2-DAY CONFERENCE – A SCIENTIFIC SHOWCASE OF NEW IDEAS

The 39 scientists currently working on LRI Novel Research Grants presented findings in panels and posters on such topics as:

- progress and breakthroughs in understanding organ damage
  - clues to the cause and development of the disease
- new insights into the regulation of the immune system
- discoveries of biomarkers—key early markers that can measure disease activity and help accelerate development of new therapies

## BOLD THINKERS

*“The LRI has really managed to assemble some of the most outstanding researchers.”*

- Matthias Wabl, PhD, University of California at San Francisco

## CROSS-FERTILIZATION OF IDEAS AND PERSPECTIVES

Presentations were from some of the nation’s most dynamic thinkers in systems biology, NIH representatives, scientists, clinicians, pharmaceutical and biotechnology experts, and technology innovators.

*“The meeting is a place to forge new collaborations.”*

- Chandra Mohan, MD, PhD, University of Texas Southwestern Medical Center

*“Seeing and learning about the incredible range, depth, and quality of the science presented by the participants...it is energizing and sparks creative thinking.”*

- Christopher A.J. Roman, PhD, SUNY-Downstate Medical Center

## Compelling Implications for LRI’s New Human Lupus Biology Program

The technologies of systems biology supply rocket fuel to the LRI’s recently launched program to spur investigation of the biology of human lupus.

This initiative will use tiny amounts of human material (cells, blood, tissue), rather than material from animals, to generate new answers applicable to the human disease.

It’s a vital approach because “what works in the mouse with lupus just doesn’t always work in the person with lupus—including what may first appear to be promising drug treatments,” explained Michel Nussenzweig, MD, PhD, of Rockefeller University and a member of the LRI’s Scientific Advisory Board.

“The potential now to leap-frog rapidly from animal models to understanding human systems is nothing less than stunning,” said LRI President Margaret Dowd.

*“Provocative and inspiring.”*

- David S. Pisetsky, MD, PhD, Duke University Medical Center and an LRI Novel Research Task Force co-chair

## THANK YOU!

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| Human Genome Sciences | ZymoGenetics            |

# Dinner Speaker at LRI Forum for Discovery 2008, NIAMS Director, Stephen I. Katz, MD, PhD



LRI Approach to Leveraging NIH Millions for Lupus Research is a “Wonderful Partnership” and a “Paradigm” to Model Nationwide

*“I can’t emphasize enough the importance of collaboration among government, industry, academic institutions, and private foundations like the LRI. I think we have an enormous number of scientific opportunities in lupus.”*

## MEETING THE CHAMPIONS FOR DISCOVERY

Patients and families get a chance to meet the scientists at the leading edge of finding better treatments and a cure for lupus.

*“I think it is especially important for the scientists to meet the relatives of the patients, and if possible the patients. At least for those of us who do not treat patients, this drives home in a more personal way the importance of understanding this mysterious disease.”* - Vicki Rubin Kelley, PhD, Brigham and Women’s Hospital

### Did You Know?

IRA Charitable Rollover Is Now an Option for Giving to the LRI in 2008 + 2009

#### Please Help us Pioneer Discovery to Prevent, Treat and Cure Lupus!

A newly extended IRA rollover provision—passed in Fall 2008 along with the Emergency Economic Stabilization Act of 2008—permits use of an IRA to help accomplish your philanthropic goals with no federal tax impact.

If you are 70 ½ or older, you may make a gift up to \$100,000 per year to the Lupus Research Institute from your IRA; your gift will be counted towards your required minimum distribution.

Instruct your IRA administrator to transfer funds directly to the Lupus Research Institute. Check with your professional advisor before you make a charitable IRA rollover gift, and call or email Andrea O’Neill with any questions at (212) 812-9881 or [aoneill@lupusny.org](mailto:aoneill@lupusny.org).

### With Your Will, A Cure!

Please remember the Lupus Research Institute in your Will.

Our legal title is: Lupus Research Institute, 330 Seventh Avenue, Suite 1701, New York, NY 10001. Tax ID #06-1565950.



L - R: Hope Hetherington (CT); NIAMS Director Stephen I. Katz, MD, PhD; Betsey and Arthur Selkowitz (CT)



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