

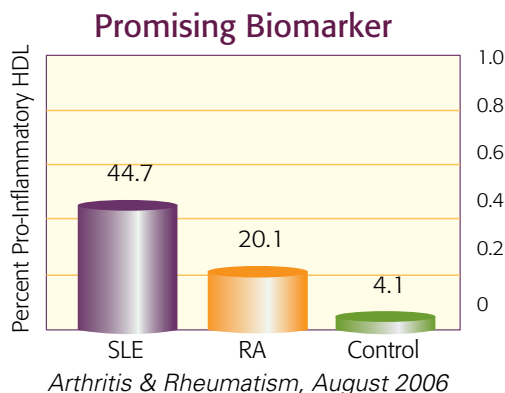
Surge in LRI Biomarker Research Signals New Hope for Diagnosing and Managing Lupus

In the year 2007, a life with the chronic and unpredictable multi-system disease that is lupus remains rife with uncertainty. "Will I get sicker?" the person with lupus asks. "Will my kidneys start to fail? My heart? Will my siblings or children get lupus? Will a new drug work for me? *Will I ever feel better?*"

Doctors asked these questions today can only give the vaguest of answers—estimations and educated guesses based on signs and symptoms that reflect damage already underway, the behavior of the disease to date, and what might happen to people in similar situations. Years of costly tests provide only a vague picture of what is going on inside the body of a person with lupus.

Biomarkers, in many cases simple blood or urine tests, could change all this, drastically minimizing the guesswork in diagnosing and treating the disease. Biomarkers provide tools with

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LRI-funded researchers Maureen McMahon, MD, and Bevra Hahn, MD, have found large amounts of damaging "pro-inflammatory" (piHDL) versions of the normally "good" HDL cholesterol in people with lupus that might explain the predisposition to atherosclerosis and help identify those at risk for heart disease. In one study (left), nearly 45% of people with lupus had the damaging piHDL as compared to 20% of people with RA (rheumatoid arthritis) and 4% of healthy controls.

LRI Leads the Lupus Biomarker Search

In its commitment to staying open to powerful new ideas in lupus research, the Lupus Research Institute has reaped a remarkable reward for the more than 1.5 million Americans and millions more worldwide with this devastating disease—a panel of candidate biomarkers that may have the potential to change the way that lupus affects their lives.

In just 6 years, the LRI has invested \$6 million in novel studies that are now generating findings on 20 potential lupus biomarkers. This research is taking place today in laboratories nationwide and is as varied and heterogeneous as the multi-system disease itself.

"Of the numerous highly promising biomarkers for lupus

currently under investigation," notes Hugh O. McDevitt, MD, professor of immunology at Stanford University School of Medicine and an LRI Scientific Advisory Board member, "several were generated by the high-risk, high-reward approach of the LRI. The Institute's contribution to lupus biomarkers has been immeasurable."

An independent outside assessment of the Institute's 3-year studies completed so far shows that seven have such potential as biomarkers that testing them in people and human tissue has already begun. And first glimpses of the many studies still underway indicate that six or more could lead to completely new candidate biomarkers.



LUPUS 2007
Shanghai China

LRI Sponsors Biomarker Session
8th International Congress on SLE

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Reasons for Giving – A Message from Our Co-Chairman

I can still clearly recall the winter day seven years ago that I and a group of other frustrated yet determined folks—patients and people with children and spouses waking daily to the unforgiving pain and struggles of lupus—

gathered together as a Board of Directors to write checks for the first round of Lupus Research Institute investigators.

What a distance in time and results we have traveled in those seven years!

More than ever, I am convinced that the research strategy to which the LRI has held fast—to solely fund novel and innovative ideas in lupus—largely explains how we’ve been able to so quickly spawn such dramatic advances in understanding this complicated disease. The tale of our biomarker findings alone, profiled on page 1, is just one example of the strategy’s strength.



Robert J. Ravitz

And with the LRI’s audited 2006 financials now in hand, I see yet another explanation for our success: that nearly all of every dollar we’ve raised—an incredible 93 cents of each—is sent straight to the research program with scientists in their laboratories searching for the answers that so many desperately need. A mere 7 cents of every dollar raised goes to the expense of management, overhead, and fundraising.

Of course, every Board Member and donor has his or her own reason for writing out a check to the LRI. For my wife Francine and me, the reason is our daughter Annie. For Tania and Jose Fano, the reason is apparent in the ‘Why I Give to the LRI’ column on this page. Whatever reason you may have for giving, we can all do so with confidence that the LRI not only has a winning strategy for finding answers to lupus, but that its stewardship of donated funds is prudent and sound.

Sincerely,

Robert J. Ravitz
Co-Chairman
Lupus Research Institute

‘Why I Give to the LRI’

The LRI only works because of the contributions it gets, large and small, from donors around the country and the world. In this ongoing column, we get glimpses of this committed community.

Jose and Tania Fano, Independent Construction Managers, Miami area

Jose Fano: “For the longest time, I didn’t know I had lupus. I do a lot of fishing here in Miami, and for years I thought the sun was causing these little red spots on my arms and hands. But I also knew that something more was happening—that something was really wrong.

I’m going to be 58 this year, and four or five years ago my dermatologist finally insisted that I get blood tests. Well, I’ve never really been one for doctors, but I listened. The tests showed that I had antiphospholipid antibodies, and that my blood cell counts were low.

I went to see a local doctor here in Miami. He was absolutely fantastic. But he also said to me, ‘What you have is bad. Get a second opinion.’ So the next time I went to visit my son in New York City, I also went to see Dr. Michael Lockshin at New York-Presbyterian/Weill Cornell Hospital. I’ve been seeing him ever since.

I know I am very lucky. My lupus is quiet now. But dealing with it and sitting in the doctor’s office in New York, I see people who are not as lucky, and who really need help. I asked about places that were doing something about lupus and Dr. Lockshin told us about the work of the LRI.

Luckily, my wife and I can help, and we give regularly to the LRI. We also try to do what we can here in Miami. My friends know that I am not a great promoter of myself. I’d rather just give and not ask. It’s always a struggle, asking others to give. Not everybody is willing.

But it’s also important just to talk about the disease. *It bothers me a lot that we don’t think of lupus as a severe disease, and therefore it isn’t in the public eye like some other sicknesses are.*

When we do talk about lupus, more people are aware and know that this horrible disease is out there. We’ve even made interesting connections to other people. I remember a few years ago, a friend of mine didn’t know I had lupus until we talked to him about giving to the LRI. Well it turns out his sister had lupus. It’s all around us.”

*LRI Chicago
has launched!*

Visit us at:
www.LRIchicago.org

Chicago Lupus Study Group Lectures



*Darby N. Tio
LRI Chicago
Executive Director*

In a push to expand knowledge of current advances in lupus research, the LRI Chicago is partnering with the Greater Chicago Chapter of the Arthritis Foundation to present a lupus research lecture series for physicians and other health professionals involved in caring for people with lupus.

Attendance at the scientific lectures, in which an expert will speak on an aspect of basic or clinical research into lupus, qualifies the professional for continuing medical education (CME) credits. University of Chicago rheumatologist Tammy Utset, MD, MPH, will moderate the events.

The inaugural program on January 24th—"An Update on the Role of Genes in Systemic Lupus Erythematosus"—was presented by Betty P. Tsao, PhD, of the division of rheumatology at UCLA's David Geffen School of Medicine.

The next lecture will take place on the evening of May 2nd at Lloyd's Chicago and will feature Boston University's Ian Rifkin, MD, PhD, on "An Update on the Role of Toll-like Receptors in Systemic Lupus Erythematosus." The program is open to Greater Chicago-area rheumatologists, rheumatology fellows and their guests. Please RSVP by April 25th. For more information on this and other lectures in the series, and to RSVP, call the Arthritis Foundation at 312-372-2080, ext. 27. LRI Chicago Executive Director Darby N. Tio can be reached at DTio@LRIchicago.org.

The LRI currently funds \$1.2 million in novel lupus research in Chicago.



Surge in Biomarker Research Signals New Hope

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which to peer into the immune system and witness the earliest indications of problems.

From its beginnings in the year 2000, the LRI recognized that biomarkers have the potential to illuminate the body's "control panel" and even guide treatment to change the outcome of disease.

"Because lupus is so unpredictable, managing the disease is a great challenge," explains LRI Scientific Board Chairman William E. Paul, MD, chief of the laboratory of Immunology at the NIH's National Institute of Allergy and Infectious Diseases. "Biomarkers can take the guesswork out of treating lupus and

help in creating a meaningful plan of action tailored to each person."

"Am I likely to get lupus? Will I probably have mild or severe disease?"

LRI-Funded Researchers Discover Potential Biomarkers of Risk and Flare

Most scientists point to a likely mix of genes and triggers in the environment as the cause for lupus. Biomarkers may help to untangle the mix.

► **Edward K. Wakeland, PhD**, at the University of Texas Southwestern Medical Center in Dallas, discovered that the SLAM family Ly108 gene causes susceptibility to lupus

in mice. Now he is searching for the human equivalent of this gene to determine if it can identify human beings susceptible to the disease.

► **Mary K. Crow, MD**, at the Hospital for Special Surgery in New York, and her colleagues are working to validate two promising novel markers of lupus flare—interleukin-8 (IL-8) and an unnamed gene product that emerged repeatedly in their preliminary data.

► **Timothy W. Behrens, MD**, began work at the University of Minnesota Medical School in Minneapolis that similarly aims to uncover very early indicators of an impending flare or remission. Researchers at the University now are testing approximately 1,500 blood samples from 300 people with lupus using sophisticated technology tools. The goal: to identify shifts in certain protein levels that point to lupus activity.

► **Chaim Putterman, MD**, at the Albert Einstein College of Medicine in the Bronx, and Martin Weigert, PhD, at the University of Chicago, have discovered two potential new **autoantibody biomarkers**, reversing a recent trend away from tracking auto-antibodies that attack genes inside cells to determine disease activity. Dr. Putterman identified x-actinin reactive auto-antibodies as potential biomarkers of disease activity; Dr. Weigert discovered "editor" auto-antibodies that might signal the earliest stages of the disease.



LRI to Sponsor Session on Biomarkers at May International Conference on Lupus in Shanghai, May 23rd–27th, 2007

Key session on biomarkers will cover such topics as:

- pro-inflammatory HDL as a novel biomarker for carotid artery plaque in women with lupus
- the clinical significance and prevalence of antibodies against coagulation factors in people with antiphospholipid antibody syndrome
- the use of certain red blood cell (erythrocyte) levels for monitoring disease activity
- insights into lupus via autoantibody profiles
- biomarkers for differentiating between disease flare and infection in people with lupus

Co-Chair: Bevra Hahn, MD, chief of rheumatology and arthritis at UCLA Medical Center in Los Angeles

Co-Chair: Michael Weisman, MD, director of the division of rheumatology at Cedars-Sinai in Los Angeles

“Are my kidneys all right?”

LRI-Funded Researchers Discover Possible Kidney Biomarkers

Because no single blood or urine test can signal the first signs of kidney disease—a common lupus complication—people with lupus often undergo frequent biopsies. Now LRI researchers are making headway in finding biomarkers for rendering these uncomfortable, costly, and sometimes risky biopsies obsolete.

- ▶ **Anne Davidson, MD**, at the North Shore-Long Island Jewish Health System in New York, has found that proteins made in the kidneys of mice during the earliest stages of the disease can be detected in their urine and blood as well. She now plans to investigate the appearance of these proteins in people and determine whether they signal the first stages of kidney involvement.

- ▶ **Elahna Paul, MD, PhD**, at the Massachusetts General Hospital in Boston, hopes to find new treatments that block kidney failure in lupus by identifying which pathways of kidney cell activation contribute to the damage.

- ▶ **Robert Winchester, MD**, at Columbia University College of Physicians and Surgeons in New York, is making headway in confirming the presence of certain genes expressed in white blood cells in cases of early kidney injury.

“A simple urine test that could tell us what’s going on with my kidneys?” asks the patient. “That makes a difference in the way I live.”

The Power of Biomarkers

For lupus—so difficult to diagnose, manage, and treat—the stakes and hopes for finding reliable “early predictors” for the disease and its complications are high indeed. The LRI actively participates in the public-private **SLE Biomarkers Working Group**, pooling biomarker findings and lupus resources.

Experts point out that biomarkers can also speed the development and approval

of more effective and less toxic drugs, which are desperately needed. “If proven valid, the potential new biomarkers will stimulate drug companies to get in the game,” explained Mary K. Crow, MD.

“Eliminating the uncertainties of lupus—that’s the power and hope of biomarkers,” said LRI President Margaret Dowd. “We can make this happen.”

“In the simplest terms, biomarkers are lab tests. You want to know what is going on with the person’s illness—whether they’re doing well, whether they’re going to flare, whether they are responding to treatment.”

—LRI Grant Recipient Elahna Paul, MD, PhD
Massachusetts General Hospital

“How Is My Heart?”

LRI-Funded Researchers Discover Possible Cardiovascular Biomarkers

Heart disease is a serious and potentially fatal complication that along with stroke develops in as many as a third of all women with lupus. Having biomarkers to signal which people are developing the first signs of atherosclerosis would enable doctors to be aggressive about trying to stop the process and prevent long-lasting damage.

- ▶ **Bevra Hahn, MD**, and colleagues at the University of California in Los Angeles are testing whether an abnormal plaque-promoting molecule in the blood called pIHDL (pro-inflammatory HDL) can be used as a biomarker to help predict the risk for atherosclerosis in people with lupus.

- ▶ **Mariana Kaplan, MD**, at the University of Michigan in Ann Arbor is examining whether a blood-based test that measures the level and type of dying endothelial cells could be used to identify people with lupus at particular risk for cardiovascular disease. Endothelial cells line the body’s blood vessels and other tissues.

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2nd Annual Shady Ladies Luncheon Reflects Hope for Lupus Research

March 10th Event Raises Over \$80,000



Dani and Allie Paradysz show off their newly acquired celebrity sunglasses



Event Chair Mark Badgley with rider Arianna Boardman and design partner James Mischka



Guests admire the many pairs of celebrity sunglasses up for auction



CNN's Lou Dobbs and his wife Debi stay cool in the Florida sun

The more than 150 guests gathered at the Palm Beach Polo Equestrian Club not only enjoyed the competitions of the annual Winter Equestrian Festival but took part in a hugely successful auction of celebrity sunglasses.

The luncheon's "shades" theme reflects a common symptom of lupus: extreme sensitivity to the sun. People with lupus are advised to stay out of direct sunlight, apply sun block daily, and wear hats—and sunglasses, of which there were many remarkable pairs at the club that afternoon.

The exciting live and silent auction of autographed celebrity sunglasses included pairs from Bruce Springsteen, Michael J. Fox, Kevin Kline, Sharon Stone, Jennifer Lopez, Jason Alexander, Christina Aguilera, Lou Dobbs, Mariska Hargitay, Eva Longoria and Teri Hatcher.

Famed New York fashion designer, Mark Badgley—himself an equestrian—chaired the event with the help of honorary chairs Marley Goodman of Palm Beach, Clara Lindner of Cincinnati, and presenting sponsor Paradysz Farms.

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- ▶ **Robert M. Clancy, PhD**, at the Hospital for Joint Diseases in New York, discovered that concentrations of endothelial protein C receptor are increased in people with lupus who are developing atherosclerosis but haven't yet shown any signs or symptoms—another possible tool for diagnosing this problem early, before damage sets in.
- ▶ **Joan Von Feldt, MD**, at the University of Pennsylvania in Philadelphia, is researching

imaging techniques for detecting heart disease in people with APS (anti-phospholipid antibody syndrome) and who have already suffered a blood clot.

- ▶ **Robert Roubey, MD**, at the University of North Carolina, Chapel Hill, is examining various blood clotting proteins as indicators of risk for blood clots in people with APS (anti-phospholipid antibody syndrome) and who have already suffered a blood clot.

Roy J. Wilson Joins LRI Board of Directors

The Institute is pleased to welcome Roy J. Wilson of Dallas to the Board of Directors. Mr. Wilson is a director for the technology sector division of the international executive search firm, Russell Reynolds Associates. He was previously the Executive Vice President of Human Resources and Information Technology for Allergan, Inc., a global healthcare company that develops and commercializes specialty pharmaceutical products.

Mr. Wilson has also held positions with Texas Instruments, Schlumberger Ltd., Pearle Vision, where he served as senior vice president and chief administrative officer, Compaq Computer, as vice president of human resources, and BMC Software, as senior vice president of human resources and administration. He is a graduate of Syracuse University.

Mary Even Joins LRI Staff as Manager of Corporate and Foundation Relations

In this newly created position, Mary Even will manage corporate and foundation outreach for the LRI and state and regional members of the Institute's National Coalition. The S.L.E. Lupus Foundation's New York and Los Angeles offices will also benefit from her work.

Mary has nearly 13 years of fundraising experience in a variety of settings, including Women In Need (a homeless-serving organization), the NAACP Legal Defense and Educational Fund, and the United Negro College Fund. Most recently she served as Director of Corporate and Foundation Relations at NYU Medical Center. Mary is a *magna cum laude* graduate of Rosary College in River Forest, Illinois, and holds an MA from NYU.



LUPUS RESEARCH INSTITUTE



The Patient Voice for Lupus Research

“Our hope is that the next 10 years will be the golden age for the development of new lupus drugs. Science is ready. But for success, the lupus community must band together. We have the experts to conduct the trials. We have the Institute and others to get the word out. But to get results, we need lupus patients to show interest. This is for them. They need to do their part.”

—Richard Furie, MD
North Shore-Long Island Jewish
Health System
Program Co-Chair, Clinical Trials Day

The LRI National Coalition Comes Together

*In D.C. to Sound the Patient Voice for
Lupus Research and New Treatments*

Clinical Trials Day, April 24

LRI National Coalition Brings Lupus Community Together to Advance New Lupus Treatments

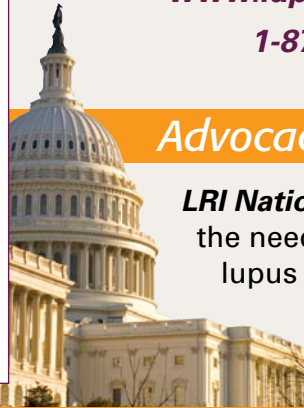
There is no known cause of lupus, few medicines, and no cure.

The time for people with lupus, doctors, drug developers, scientists, and advocates to change this is now—together.

On April 24th, experts in lupus science will orient patient advocates and leaders in the National Coalition on the state of clinical trials in America today.

The event kicks off a national year-long campaign to educate patients about lupus clinical trials.

Launching April 24th:
www.lupustrials.org
1-877-95-TRIAL



Advocacy Day, April 25

LRI National Coalition converges on Capitol Hill to sound the need for funding of lupus research. The message: lupus cuts short the lives of young women across this nation and around the world.

Please join us if you can. Call 212-812-9881.



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