

# Health Connection

Your Good Health Newsletter

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## A Candidate Biomarker to Improve Treatment of Lupus Patients

by Mary K. Crow, MD, Attending Physician, Associate Chief, Division of Rheumatology,  
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HOSPITAL  
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SURGERY**



**A** chronic disease of the immune system, lupus affects approximately 1,500,000 women and men nationwide, according to the Lupus Foundation of America. The most prevalent and pervasive form of lupus is systemic lupus erythematosus (SLE). Characterized by the production of auto-antibodies throughout the body, SLE can cause problems ranging from a skin rash to joint pain and stiffness, organ damage, or heart failure. The wide range of disease symptoms among patients makes SLE difficult to diagnose and an ongoing challenge to manage.



A recent study allows investigators to better target trials of promising new lupus therapies and doctors to more effectively treat lupus patients most at risk for dire complications. Published in the May 2005 issue of *Arthritis & Rheumatism* ([www.interscience.wiley.com/journal/arthritis](http://www.interscience.wiley.com/journal/arthritis)), its findings shed important light on the role of interferon, a protein critical to immunity released into the bloodstream, in the progression of SLE.

Supported by the Alliance for Lupus Research, the Lupus Research Institute, the Mary Kirkland Center for Lupus Research, and the National Institutes of Health, the study was conducted by a team of researchers from the Kirkland Center, Hospital for Special Surgery, and Weill Medical College of Cornell University in New York City. Led by Kyriakos A. Kirou, MD and Mary K. Crow, MD, the team set out to test the hypothesis that activation of a particular interferon pathway—the type I interferon pathway—is most common among SLE patients with the most pronounced disease activity. Activation of this pathway is indicated by high levels of expression of interferon-inducible genes (IFIGs).

The team collected blood samples from 77 SLE patients, 22 disease controls (20 with rheumatoid arthritis, two with autoimmune uveitis—inflammation of a part of the eye called the uvea) and 28 healthy controls. Drs. Kirou and Crow and their associates made an effort to match SLE patients with both control groups with regard to sex (with women as the majority) and race (with progressively decreasing ratios of whites, African-Americans, Asians, and Hispanics).

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# Advances in Cartilage Repair at HSS

by Riley J. Williams III, MD, Associate Attending Orthopedic Surgeon, Director, Institute for Cartilage Repair

**A**rticular cartilage is the smooth, gristle-like surface at the ends of our bones. These pristine surfaces allow for near frictionless movement in many joints in the body including the knee, shoulder, hip, and ankle. Loss of the articular occurs following traumatic injury and in arthritic conditions. In these situations, joint function suffers as the smooth surfaces become rough and ultimately painful for affected individuals.

Unfortunately, articular cartilage has a very poor ability to heal itself. As a result, articular cartilage lesions have long been considered one of the most difficult clinical problems that orthopedic surgeons must address. For many years, relatively few methods of stimulating cartilage regeneration were available; in most cases, these techniques resulted in the formation of scar-like, poorly durable, fibrocartilage. However, in 1994, the *New England Journal of Medicine* published an article that described a then novel method of regenerating articular cartilage by harvesting, growing, and ultimately reimplanting one's own cartilage cells into a cartilage defect. The effect of this article and the availability of this method here in the United States was dramatic; the cartilage repair subspecialty was born.

Naturally, surgeons at HSS soon focused on this area and actively participated in applying this new technology. In 1997, the HSS Cartilage Study Group was formed.

This informal group of surgeons



and physicians met regularly to discuss these demanding articular cartilage repair cases. This informal group ultimately led to the formation of the Institute for Cartilage Repair. The Institute represents a cooperative effort between the Departments of Orthopedic Surgery and Radiology and the Foster Center for Outcomes Research. The goal of the Institute is to critically evaluate the clinical outcomes and surgical techniques of cartilage repair procedures. As such, every patient who is treated for a cartilage problem at HSS is entered into a registry for the purpose of tracking their outcome. To date, there are approximately 500 patients who have been entered into the registry. This registry has proven to be a powerful source of information and has resulted in the publication of three peer-reviewed publications and numerous presentations at national academic meetings. The group's members also interact routinely with industry partners in an effort to aid these commercial

entities in their efforts to provide better surgical options for repairing articular cartilage defects.

Surgeons with a focus on knee, shoulder, ankle, and hip problems currently participate in the Institute's activities. Cartilage repair techniques including microfracture, mosaicplasty, cartilage transplantation, autologous chondrocyte implantation, and synthetic cartilage grafting are applied routinely at HSS. Much has occurred in the last decade as the clinical offerings for cartilage repair have greatly expanded. The ICR and its members look forward to the availability of emerging technologies that may allow us to fill defects with a more durable, articular-like repair tissue, all without the technical challenges that are associated with many of the currently available methods. The emerging field of cartilage repair represents a fast growing subspecialty, and we are proud to continue the HSS tradition of having a strong academic and clinical presence in this important field.

# A Candidate Biomarker to Improve Treatment of Lupus Patients

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(continued from page 1)

In addition, the SLE patients and disease controls were well matched for age, disease duration, and daily prednisone dose. The team also gathered relevant clinical data on the SLE patients. Then, they analyzed and compared all the blood samples for levels of IFIG expression.

Overall, SLE patients scored higher than the other disease patients, as well as the healthy donors, for activation of the type I interferon pathway.

Among SLE patients, the highest scoring group was strongly associated with increased disease severity, increased disease activity, and certain autoantibodies known to react with proteins that bind to the important nucleic acid, RNA. SLE patients with high scores were also more likely to suffer from kidney disease.

“Our data have defined a subgroup of SLE patients who have more severe disease, with frequent kidney involvement, and more active disease,

as measured by complement activation, suggesting that determination of IFIG expression may prove a useful approach to selection of patients for clinical studies,” states Dr. Kirou. “We are currently conducting longitudinal clinical studies to validate the measurement of IFIG as a biomarker for active lupus.” Beyond its clinical applications, this study provides new clues to the underlying mechanisms that drive autoimmunity.

## From the Editor NEWS AND VIEWS



### Asking the Right Questions

It is well known that research has led to huge advances in medicine over the years (think of smallpox, polio, and influenza). Clinical research participation offers the unique opportunity to help others, the potential to improve health, and the possibility of better access to new medications and interventions. However, before taking part in a research study, it is always important to ask the right questions. Be prepared to ask these and any other questions you may have before agreeing to participate in a clinical research study:

- What is the goal of the study?
- What are the possible side effects?
- What tests or procedures will be done?

- Will I be told the results of the study?
- How long will the study last?
- Who will pay for any extra costs associated with the study?

### Research Terms Review

Sometimes the world of research can seem overwhelming and full of complex terms and concepts. Expand your knowledge with these frequently used research terms:

- **Control group** Clinical trial participants that receive the placebo or standard therapy for a condition, while another group is given the experimental treatment. The control group serves as a measuring stick to determine the effectiveness of the experimental treatment.
- **Double-blinded study** A clinical trial in which neither the subject nor the investigator is aware of which

participants are receiving the placebo or standard therapy and which participants are receiving the experimental treatment.

- **Pilot study** A study conducted to obtain information and work out the logistics and management necessary for further clinical trials.
- **Protocol** An outline of the clinical trial specifics, such as study qualifications, treatments, and procedures.
- **Therapeutic window** The difference between the minimum and maximum doses that may be given to subjects to obtain an adequate clinical response and avoid intolerable toxic effects. The greater the value calculated for the therapeutic window, the greater a medicine's margin of safety.

# What Does it Mean to Give Informed Consent?

by Pamela M. Sánchez, MPA, Assistant Director, Research Education & Training, Education Division

In simple terms, informed consent is the process of learning the key facts about a clinical research study before deciding to participate in the trial ([www.clinicaltrials.gov](http://www.clinicaltrials.gov)).

In actuality, “giving” informed consent is much more than that. The informed consent process is one by which an investigator and a potential research participant discuss the specifics of a research study, including the benefits and risks involved with participation. For instance, if you are approached by an investigator to participate in a clinical research study, your agreement to participate should be based on full disclosure of the facts by the investigator and you should agree to participate only when you have had the opportunity to get answers to all of your questions, so that you are ensured a solid understanding of

the research.

In addition, when an investigator presents a research study to you as a potential participant, you should be provided a sufficient amount of time to consider participation so you can make an informed and intelligent decision.

The question of what happens if you change your mind after giving informed consent deserves further

*The HSS website features a listing of current clinical trials being conducted at the hospital. To view this list, go to [www.hss.edu/Research/Clinical-Trials](http://www.hss.edu/Research/Clinical-Trials).*

explanation. Once you agree to enter into a study, it is vital that you understand that your participation is voluntary and withdrawing from the study or refusing to perform certain tasks can occur at any time.

In order for people from different

cultures who may speak different languages to be “informed,” it is important that investigators strive to minimize any potential language or cultural barriers so that when consenting, there is full understanding of the study. For example, if the primary language of a potential study participant is Spanish, the informed consent process should be done

with an authorized translator and/or an approved and translated informed consent document. With respect to cultural barriers, investigators should be familiar with the cultural norms of the study

population and be sensitive and accommodating.

As a potential research study participant, bear in mind that informed consent is based on two very important concepts: informed decision making and voluntary participation.

## Federal regulations require that the informed consent process provide a potential research participant answers to the following questions:

- Why is this research being done?
- What are the requirements involved with participation?
- What are the anticipated risks or discomforts associated with participation?
- What are the benefits of participation?
- How will the investigator and institution maintain confidentiality of my records?
- Are there alternative treatments or procedures that would be beneficial?
- What happens if I am injured as a result of participation in the research protocol? Who should I contact?
- What will I be asked to do?
- Who can I contact for further information about the study or my rights as a research participant?
- What happens if I change my mind after I give informed consent?

# Atherosclerosis & RA: New Research Insights

by Silvia Heidi Norbis, Project Coordinator, Division of Rheumatology

A recent study published in the *Annals of Internal Medicine* sheds light on the relationship between cardiovascular disease and Rheumatoid Arthritis (RA).

## What is RA?

RA is a chronic disease characterized by inflammation of the synovium, or lining of the joints. It can lead to long-term joint damage, resulting in chronic pain, swelling, and deformed joints. RA affects 1 percent of the U.S. population or 2.1 million Americans.<sup>1</sup> Currently, there is no cure for RA, but early and aggressive treatment helps to reduce symptoms and joint damage. Much about the condition remains unknown. For example, although we know that women are more likely to get RA, the exact causes and mechanisms by which people get RA are unknown. It is thought that people with RA have a higher risk of heart attack and stroke than people without the disease.

## What is Atherosclerosis?

Atherosclerosis describes the process in which deposits of fatty substances, cholesterol, cellular waste products, calcium, and other substances build up in the inner lining of an artery. This buildup is called plaque. Plaque is a systemic disease. It develops in arteries throughout the body. Plaque can obstruct the blood's flow through an artery. Of most concern is the fact that plaque can become fragile and rupture. This can cause blood clots to form near

the plaque that can obstruct blood flow and prevent needed oxygen transport to organs. If this happens and it blocks a blood vessel that feeds the heart, it causes a heart attack. If it blocks a blood vessel that feeds the brain, it causes a stroke.<sup>2</sup>

**RA affects 1 percent of the U.S. population or 2.1 million Americans.<sup>1</sup> Currently, there is no cure for RA, but early and aggressive treatment helps to reduce symptoms and joint damage.**

## *Annals of Internal Medicine* Article

Researchers at Hospital for Special Surgery were involved in a study published in the *Annals of Internal Medicine* that attempted to determine whether people with RA have accelerated and more prevalent early atherosclerosis even though they do not have symptoms of cardiovascular disease yet. This is important because identifying factors associated with early atherosclerosis in people with RA might lead to a better understanding of cardiovascular disease in this and other conditions. 98 patients with RA who did not have symptoms of cardiovascular disease and 98 people without RA participated in the study—the control group. Researchers collected cardiovascular

disease risk factor information (such as blood pressure, diabetes, smoking, and cholesterol levels). The researchers also analyzed carotid ultrasounds (a test to measure atherosclerosis in the carotid artery) from all participants to determine the percentage of patients from the RA group, compared to the control group, that had pre-clinical cardiovascular disease.

Despite the fact that participants in the control group were more likely to have traditional cardiovascular disease risk factors such as high blood pressure and elevated cholesterol levels, 44 percent of patients in the RA group had carotid atherosclerosis compared to 15 percent of participants in the control group. From this information the authors conclude that traditional cardiovascular disease risk factors do not explain the increased risk for atherosclerosis in patients with RA. Instead, they propose that systemic inflammation seen in patients with RA may contribute to the development of atherosclerosis.<sup>3</sup> The authors recommend that in patients with RA, in addition to management of traditional cardiovascular risk factors, there should also be aggressive control of disease activity.

1. Arthritis Foundation. Overview of Rheumatoid Arthritis. Available at: [http://www.arthritis.org/conditions/DiseaseCenter/RA/ra\\_overview.asp](http://www.arthritis.org/conditions/DiseaseCenter/RA/ra_overview.asp)

2. American Heart Association. Atherosclerosis. Available at: <http://www.americanheart.org/presenter.jhtml?identifier=4440>

3. Roman MJ et al. Preclinical "Carotid Atherosclerosis in Patients with Rheumatoid Arthritis." *Annals of Internal Medicine* (2006); 144(4):249-256.

# Minimally Invasive Knee Surgery: HSS Leads the Way

by Steven B. Haas, MD, Associate Attending Orthopedic Surgeon, Associate Chief, Knee Service

The first successful total knee replacements were developed at HSS in the 1970's. Continuing this legacy of breakthroughs in knee surgery, HSS has led the way in developing minimally invasive knee replacement.

Modern knee replacement surgery is a resurfacing procedure where the arthritic knee is resurfaced with artificial materials called implants. Knee replacement has had outstanding long-term results and many can last for over 20 years. Focusing on the whole patient experience, HSS surgeons have been working on ways to reduce the recovery time after surgery and allow patients to return to normal lives faster. They have been able to accomplish these goals through the development of

minimally invasive knee replacement.

Minimally invasive knee replacement surgery uses small, anatomically shaped instruments which were designed by surgeons at HSS. Because these surgical instruments are significantly smaller than those used in the past, skin incisions are smaller by about 40 to 50 percent. In addition, the resurfacing implants are placed in the knee with less cutting, and cutting of the main tendon (quadriceps) is avoided or minimized. The other major improvement to the surgery is that twisting, or inverting, the knee cap is no longer necessary.

Since 2001, over 1,000 minimally invasive knee replacements have been performed at HSS. Several studies on the results, published by HSS physicians, show faster recovery,



less pain, and improved early range of motion. These studies also show that the accuracy of the new instruments is just as good as with the traditional ones.

Not all patients are candidates for minimally invasive knee replacement. Only your surgeon can tell you if this is the best technique for your knee.

## LIBRARIAN

### CORNER

#### A Guide to Healthy Web Surfing

by Timothy Roberts, MLS  
Medical Librarian,  
Education Division



This is a new feature for *Health-Connection* newsletter. In each issue we will highlight a reliable website for consumer health information. Remember that a partnership with your health care provider leads to the best medical

decisions, so bring the information you find on these sites to your health care professional. It can be a great way to start a dialog and learn more about your health.

Hospital for Special Surgery's staff and other experts developed all the medical content on the HSS website. To ensure that patients receive the latest and most comprehensive musculoskeletal information, they regularly review and update the material. Hundreds of conditions and treatments are described, and many of the descriptions include audio and video clips.

To learn about a particular condition,

diagnostic test, or procedure in the area of orthopedics or rheumatology you might want to check out the *Conditions & Treatments* section of Hospital for Special Surgery's web page at [www.hss.edu/conditions](http://www.hss.edu/conditions).



## Computer Assisted Surgery (CAS) Center: *Where Technology and Medicine Meet*

Introduced in Europe in the late 1990's, computer assisted surgery permits real-time 3D visualization of surgical implants and tools during operative procedures. Like a GPS system for the operating room, these systems allow surgeons to track their surgical gestures and hardware positioning on a virtual image of the patient's anatomy. Combined with minimally invasive surgical techniques, these technologies have the potential to increase precision and decreased pain and disability for patients. Hospital for Special Surgery's CAS Center was established to further the development of surgical navigation and medical robotics in orthopedic surgery. In addition to providing an environment for research and development, the center's design allows for the study of actual operating room workflow. The specific goals of the Center are to:

- Promote and facilitate the adoption of CAS technologies



into the operating room

- Conduct pioneering research in CAS technologies, focusing on the integration of surgical navigation and robotics with arthroscopy, arthroplasty, and spine procedures
- Participate in product development with navigation and robotic companies
- Provide training for surgeons in the principles and utilization of CAS techniques
- Establish strategies to assimilate data generated from CAS systems into electronic medical records and clinical research databases

"Our goal is to explore and understand the potential of these technologies so that surgeons can use

them to solve difficult clinical problems," says Dr. Andrew Pearle, Assistant Attending Orthopedic Surgeon and Clinical Director of the CAS lab. "In addition to using the tools to make standard procedures more reproducible and minimally invasive, we hope to use these technologies to develop innovative surgical solutions that are customized to each individual patient."

The CAS Center is just one of the many ways HSS remains at the forefront of medical technology. For more information about the Center, call **212.774.2420**.

### Answers to Your FAQ's

The Education Division, in collaboration with expert speakers, compiles the answers to frequently asked questions taken from actual public and patient education lecture question and answer sessions. Learn more about a variety of orthopedics and rheumatology related topics, from minimally invasive hip and knee surgery and anesthesiology to lupus and nutrition. To view the latest FAQ's online, go to:

**[www.hss.edu/Education/Public-and-Patient-Education/FAQs](http://www.hss.edu/Education/Public-and-Patient-Education/FAQs)**



## From the Studio

“The instructor is very knowledgeable and patient. I really found the sessions helpful. I wish the sessions were longer!”

- Yoga-lates Participant



For more information about ongoing exercise/wellness programs at HSS, call 212.606.1057.



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lems related to different types of arthritis or  
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today, so that everyone can have a healthier  
tomorrow.

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*Musculoskeletal Health  
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