

# SPOTLIGHT ON RESEARCH

## Funded Projects



SPRING 2014

## Northeast Researchers Earn AF Awards

**T**he Arthritis Foundation (AF) has a long and distinguished history of supporting research on diseases affecting the joints. This year four investigators from the Northeast Region received major Arthritis Foundation research awards. Three of the projects support research into the physical basis of, and potential treatments for osteoarthritis, the most common form of arthritis affecting an estimated 27 million adults in the U.S.; and the fourth project is in the area of rheumatoid arthritis, an autoimmune form of arthritis affecting 1.5 million Americans.

The addition of these four 2014 awards brings the total number of active arthritis-related projects funded by the Arthritis Foundation in the Northeast Region (NY, NJ and Eastern PA) to 20, including investigations underway at many of the area's major institutions.

“All AF-funded investigators, by focusing on understanding a specific part of the disease process, are making significant contributions to the collective knowledge of how arthritis develops and the mechanisms that promote joint destruction—an understanding that will ultimately help to discover a cure. At the same time, these investigations are uncovering new ways to mediate, or retard, disease progression. The more treatments we have in our arsenal of weapons against arthritis, the better equipped we are to offer viable options to the many arthritis patients who respond differently to therapies.”

—Bruce N. Cronstein, MD

### 2014 Support for Regional Investigators

Arthritis Foundation awards, totaling more than \$3.2 million, range from \$100,000 - \$500,000, providing support over 2-5 years to investigators from the following institutions:

- Albert Einstein College of Medicine of Yeshiva University
- Children's Hospital of Philadelphia
- Columbia University
- The Feinstein Institute for Medical Research
- Hospital for Special Surgery
- Mount Sinai School of Medicine
- New York University School of Medicine
- University of Pennsylvania Medical Center
- The Research Foundation for SUNY
- The Rockefeller University

## PROJECTS FUNDED IN 2014

**Bruce Neil Cronstein, MD**, from the New York University School of Medicine received an Arthritis Foundation Investigator Award which provides \$500,000 over five years for his study: *The Role of Adenosine Receptors in Osteoarthritis*. In addition, Innovative Research Grants which provide \$200,000 over two years were awarded to: **Carl P. Blobel, MD, PhD** from the Hospital for Special Surgery in New York, for his study: *The Role of *iRhom2* and *ADAM17* in Osteoarthritis*; **Motomi Enomoto-Iwamoto, PhD** from The Children's Hospital of Philadelphia Institute, for her study: *Protection of Articular Cartilage by Blocking Alpha 5 Integrin*; and to **Jose U. Scher, MD** from NYU-Langone Hospital for Joint Diseases for his study: *Pan-Microbiome in At-Risk Subjects and New-Onset Rheumatoid Arthritis*.

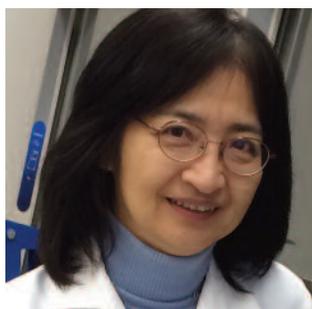


### **Bruce N. Cronstein, MD**

*Paul R. Esserman Professor of Medicine  
Director, NYU-HHC Clinical and  
Translational Science Institute  
Associate Chairman for Research, Department of Medicine  
New York University School of Medicine*

**B**ruce N. Cronstein is studying the role of adenosine receptors in the development of osteoarthritis. While breeding mice lacking adenosine A2A receptors, Dr. Cronstein and his group observed that these mice had some difficulty moving around as they aged, although still relatively young. When Dr. Cronstein and his group examined these

mice more closely they found that, even at a young age, these mice had signs of osteoarthritis. The team will show how a lack of adenosine and its receptors promote the development of osteoarthritis. Findings from this study could lead to development of novel agents or repurposing of established drugs for the treatment of osteoarthritis.



### **Motomi Enomoto-Iwamoto, DDS, PhD**

*Division of Orthopedic Surgery  
Department of Surgery  
Children's Hospital of Philadelphia*

**M**otomi Enomoto-Iwamoto from the Children's Hospital of Philadelphia Research Institute received Arthritis Foundation funding for a project entitled: "Protection of Articular Cartilage by Blocking Alpha 5 Integrin." Osteoarthritis is characterized by the progressive loss of chondrocyte (the cells that make and maintain cartilage) function and cartilage matrix; and in this project Dr. Enomoto-

Iwamoto will investigate the role of Alpha 5 Integrin, a protein present in the matrix, in preventing chondrocyte death and dysfunction. Dr. Enomoto-Iwamoto suspects that this protein can prevent the death of cartilage cells and inhibit the degeneration that occurs in cartilage. If this hypothesis is correct, then it may be possible to devise an approach to replacing this molecule in affected joints to treat osteoarthritis.

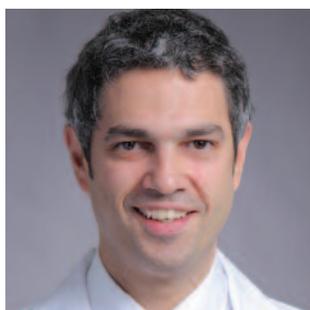
## **Carl P. Blobel, MD, PhD**

*Professor of Medicine and of Physiology & Biophysics  
V. F. and W. R. Salomon Chair in Musculoskeletal Research  
Director, Arthritis and Tissue Degeneration Program  
Hospital for Special Surgery*

**C**arl Blobel received funding for a study entitled: “The Role of iRhom2 and ADAM17 in Osteoarthritis.” During the course of osteoarthritis, inflammatory cells and chondrocytes release a variety of substances, including growth factors and pro-inflammatory cytokines, which in turn are thought to promote the destruction of cartilage. Because it is now clear that the cell surface metalloproteinase ADAM17 plays an important role in the release of these growth factors and cytokines, Dr. Blobel will study the potential role of ADAM17 and its newly discovered regulator, iRhom2, in the development of osteoarthritis. Further exploration of these molecules could lead to the development of agents that might halt both cartilage degradation and the inflammation that promotes further progression of osteoarthritis.



**Dr. Coline Haxaire (left) and Dr. Carl Blobel (right) evaluate osteoarthritic damage in mouse knee joints at their lab at the Hospital for Special Surgery.**



## **Jose U. Scher, MD**

*Assistant Professor of Medicine  
NYU Division of Rheumatology  
Director, Arthritis Clinic  
NYU-Langone Hospital for Joint Diseases*

**J**ose Scher has previously reported on changes in the composition of intestinal bacteria (microbiome) in the development of rheumatoid arthritis. In his study, *Pan-Microbiome in At-Risk Subjects and New-Onset Rheumatoid Arthritis*, Dr. Scher and co-investigators, Drs. Leo Segal (NYU-HJD) and Kevin Deane (University of Colorado), propose to further

define the intestinal and airways microbiome of patients with RA at various stages in their disease, from pre-clinical to later stages. By better understanding the composition of the microbiome in patients with rheumatoid arthritis, we may be able to determine specific factors involved in the development of this disease that can be targeted by new therapies.

## **You Can Participate in Discovery**

Clinical trials and disease registries are part of medical research and are at the heart of medical advances. By enrolling in a disease registry or by volunteering for a clinical trial, you and your loved ones can help find better treatments for others in the future. See the back page of this newsletter for more information on the Arthritis Internet Registry developed by the Arthritis Foundation. Find out more by visiting <http://www.arthritis.org/research/participate-in-research/> or <https://www.researchmatch.org/>.

## REACHING FOR A CURE

*The Arthritis Foundation Research Program*

### Accelerated Medicines Partnership

The Arthritis Foundation has joined the Accelerated Medicines Partnership (AMP), an alliance between the National Institutes of Health, biopharmaceutical companies and nonprofit organizations with a common goal of earlier drug discovery and development for diseases, including rheumatoid arthritis and lupus. The partnership will work to make data and analyses publicly available to the biomedical community, resulting in better and faster ways to detect and treat diseases. The Arthritis Foundation has given \$100,000 to the partnership, and currently serves on the partnership's steering committee. Read the NIH press release here, <http://www.nih.gov/news/health/feb2014/od-04.htm>.

### Impact of Foundation Support

Over the past 50 years, the Arthritis Foundation has invested more than \$450 million in research to support over 2,200 scientists, physicians and health professionals, resulting in major treatment advances for the more than 100 forms of arthritis.

### The Arthritis Internet Registry

Using the power of the Internet to create a community of arthritis patients, particularly those with rheumatoid arthritis (RA), the Arthritis Internet Registry (AIR) facilitates research discovery and social networking. The data patients provide can help researchers better understand and potentially cure this disease. Go to <http://www.arthritis.org/research/participate-in-research/arthritis-internet-registry/> to learn more or to join now.

### ACL Study Update

As reported in a special November 2013 Research Brief, the Anterior Cruciate Ligament (ACL) Intervention Feasibility Study, with the potential to revolutionize the future treatment of osteoarthritis (OA), is underway with researchers at these prestigious medical centers: the Hospital for Special Surgery in New York, the Mayo Clinic in Rochester, and the University of California in San Francisco.

Although the study is still at a very early stage, when recent MRI data in published literature is combined with what we are learning in the present study, a picture of progression from initial ACL tear to OA is already beginning to emerge. It looks like this:

- The initial injury damages the outside compartment of the knee primarily as detected by conventional MRI and T1 MRI.
- This lesion slowly heals, but during the next year a new lesion appears in the medial compartment indicating new breakdown of cartilage.
- Sometime soon thereafter features of early OA then emerge in a substantial portion of patients.

One hypothesis is that the ACL tear alters knee mechanics so that greater stress is placed on the medial compartment and begins to drive the OA disease process. Another hypothesis is that metabolic alterations resulting from tissue injury and inflammation alter cartilage metabolism to make it less resilient to mechanical stress. In either case finding ways to stabilize the cartilage immediately after an ACL tear has a good prospect to lessen the impact of later OA.