BRIGHAM AND WOMEN'S HOSPITAL

Life. Giving. Breakthroughs.

The Rheumatology Fund for Discovery and Innovation

SUPPORTING EMERGING LEADERS IN RHEUMATIC DISEASE STUDY AND CARE

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A Case for Philanthropic Support

In recent decades we have witnessed a revolution in the study and treatment of rheumatoid arthritis, lupus and a host of other immune and inflammatory disorders. The mapping of the human genome, the advent of computer-enhanced medical technologies and other powerful investigative tools are enabling researchers to probe the root causes, risk factors, outcomes and biological mechanisms that underlie these intractable diseases.

The Division of Rheumatology, Immunology and Allergy at Brigham and Women's Hospital (BWH) is proud to announce the creation of the *Rheumatology Fund for Discovery and Innovation*. The Fund is being spearheaded by Michael E. Weinblatt, MD, a BWH rheumatologist who is passionate about advancing the academic careers of early- and mid-career faculty and trainees. This mission has become especially challenging in recent years, when the National Institutes of Health – our nation's primary source of support for medical research and training – has been forced to significantly reduce its funding levels. These cuts are having a marked negative effect on the careers of future leaders in the field, and in doing so are hindering progress in finding new ways to treat and prevent rheumatic diseases.

However, now is the time to accelerate the pace of discovery, not slow it. Rheumatic disease research has led to new forms of treatment such as TNF inhibitors (e.g., enbrel, humira, remicade), IL-6 blockade (actemra), co-stimulatory blockade (orencia), and B-cell depletion therapy (rituxan). These drugs have fundamentally changed the practice of rheumatology and the quality of life for patients with rheumatic disease. Today, promising studies at BWH are focusing on a range of topics, including the identification of genetic and lifestyle risk factors, outcomes of rheumatic diseases, the causes and treatments for joint pain, the biological basis of bone disease and the mechanisms that drive arthritis in adults and children. Our investigators are making progress every day in these multiple lines of attack, setting the stage for other exciting breakthroughs.

We are poised to build on our work, but decreasing support from the NIH is a major obstacle that even threatens our ability to retain our most gifted physician-scientists. To sustain momentum and promote the next wave of big ideas, philanthropy must step up to take a front-and-center role in supporting our research effort. This is why we are creating the Rheumatology Fund for Discovery and Innovation, and we are asking patients and friends to help make it a success. Our goal for the Fund's 3-year start up period is $2 million.

BRIGHAM AND WOMEN'S HOSPITAL: AN IDEAL SETTING, A WEALTH OF TALENT

With a long history of medical firsts, BWH is a clinical, scientific, and academic powerhouse dedicated to delivering life-giving breakthroughs. Discovery and innovation have always been at the heart of what we do. From the compassionate, expert clinicians providing new hope for our patients today, to the brilliant scientists working in close collaboration to quickly translate their research findings into better, more personalized patient care, to the devoted educators who are shaping the next generation of medical pioneers, BWH is redefining the future of medicine in Boston and beyond.

With so many breakthroughs within our reach, we know that the time to confront the world's toughest medical challenges is now. That is why we embarked on *Life. Giving. Breakthroughs.*, a comprehensive $1 billion campaign dedicated to sustaining and fueling the quality patient care, innovative training, and life-changing discoveries that will benefit current and future patients—including those suffering from painful rheumatic diseases.

BWH is one of a small number of institutions in our nation with the intellectual assets, record of achievement, commitment to innovation and pipeline of talent necessary to sustain an all-out effort to conquer rheumatic diseases. The hospital's Rheumatology, Immunology and Allergy Division is perennially ranked among the top ten programs of its type in our country and supports the largest research enterprise of any similar program in the nation. Our physicians collaborate with other BWH experts in a broad spectrum of specialties, and last year we had over 33,000 patient visits to our rheumatology service. The Division's training programs are among the most competitive anywhere.

The strength of BWH's rheumatology program also reflects the creativity and energy of a new generation of gifted physician-scientists who are emerging leaders in their respective areas of study. BWH is committed to providing these faculty with the resources necessary to mount high risk, high reward research attacks on rheumatic diseases that go beyond conventional investigative efforts. However, a significant funding obstacle – cutbacks in NIH support – is pressuring our capacity to meet this commitment.

The work of five exceptional faculty illustrates the importance of developing new resources that can help lessen the impact of federal budget cuts, accelerate our current research effort and encourage innovation. All of these gifted physician-scientists – profiled below – exhibit a shared set of qualities that epitomizes BWH's approach to finding solutions to our most challenging health problems:

- They are driven by a desire to be at the forefront of innovation, to advance the field and be the "go to" person in their respective areas of expertise.
- They were attracted to rheumatology, in part, because of the opportunity it provides to care for patients over an extended period of time.
- They appreciate the Division's highly collegial and collaborative work environment.
- They are proud to be part of one of our nation's largest and most accomplished rheumatic disease research enterprises. This includes the Division's Section for Clinical Sciences, one of the world's oldest and best-organized groups devoted to epidemiological studies of rheumatic disease.

These gifted physician-scientists are:

Karen H. Costenbader, MD, MPH

Director, Rheumatology Clinical Research Fellowship Training Program
Co-Director, Lupus Center
Associate Professor of Medicine, Harvard Medical School

Risk Factors and Outcomes in Rheumatoid Arthritis and Lupus

Dr. Karen Costenbader's research is focused on risk factors and health effects associated with rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE). These diseases disproportionately strike women and disadvantaged and minority populations. As an investigator in the Section for Clinical Science, she and her colleagues design innovative study tools to gather and analyze data that measure the impact of everyday lifestyle choices (e.g., cigarette smoking, contraceptive use, vitamin intake, sunlight exposure) and biological factors (e.g., early menarche, postmenopausal hormones) that may increase the risk of developing RA or SLE. For example, studies have shown that smoking increases a woman's risk of developing either RA, while early menarche, contraceptive use and postmenopausal hormones raise a woman's risk of SLE. Dr. Costenbader's team is also working to identify predictors of health outcomes in RA and SLE, including heart disease, cancer and kidney disease.

A foundational strength of this research is a number of landmark clinical trials and unique patient registries initiated and maintained at BWH. These include the Nurses' Health Study, Women's Health Study, the Vitamin D and Omega-3 (VITAL) Trial, the BWH Lupus Registry and the BWH Rheumatoid Arthritis Sequential Study (BRASS). These databases and registries provide Dr. Costenbader and her colleagues with unparalleled resources and tools for understanding the risks for developing RA and SLE or for being stricken by serious chronic diseases as an outcome of these rheumatic disorders.

Yvonne Claire Lee, MD, MMSc

Director, Pain Research, BWH Division of Rheumatology, Immunology and Allergy
Assistant Professor of Medicine, Harvard Medical School

Causes and Treatments for Pain in Rheumatic Diseases

Dr. Yvonne Lee is investigating the causes and treatments for pain in patients suffering from RA and related conditions. Pain is the primary reason these patients see their physician, yet the underlying causes and the best treatments for pain are poorly understood. The challenge is made more difficult by variations in how patients experience and report pain. It has long been believed that the pain associated with rheumatic disease is caused mainly by inflammation, so the traditional pain-reducing strategy has been to squelch the inflammatory process. However, even when strong anti-inflammatory drugs are used, many patients continue to experience pain.

As Director of Pain Research in the Division of Rheumatology, Immunology and Allergy and a member of the Division's Section for Clinical Sciences, Dr. Lee and her colleagues are conducting a number of studies aimed at evaluating inflammation as well as other factors that contribute to pain, e.g., defects in pain modulation by the central nervous system. Using technologies such as magnetic resonance imaging (MRI) and state-of-the-art tests to gauge patients' pain sensitivity, they are assessing how patients with RA process pain in comparison to healthy controls, how effectively different types of drugs control pain and how physicians can determine in advance which recently-diagnosed patients with RA are more likely to develop chronic pain.

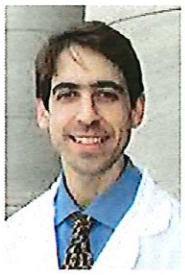
Katherine P. Liao, MD, MPH

Co-Director, Rheumatology, Cardiovascular Clinic in Rheumatology, BWH Arthritis Ctr.
Assistant Professor of Medicine, Harvard Medical School

Risk Factors for Cardiovascular Disease in Rheumatoid Arthritis

Dr. Katherine Liao is employing state-of-the-art data mining initiatives and genetic studies to expose the factors contributing to increased risk of cardiovascular disease (CVD) and joint destruction in RA. While scientists know that inflammation plays a central role in CVD among patients with RA, a precise inflammatory pathway linking the two diseases has not yet been identified. One source of untapped information is each patient's electronic medical record (EMR), a treasure trove of data that includes information in a narrative format, e.g., a physician's notes and dictation that now can be accessed and analyzed exclusively for research purposes with sophisticated biostatistical and bioinformatics methods. Using the Partners Healthcare EMR, Dr. Liao has identified a population of RA patients who offer an exciting opportunity to dovetail the study of known risks for CVD in RA with genetic factors and biomarkers associated with inflammatory processes.

Dr. Liao's research portfolio also addresses a series of key issues and questions regarding RA treatment and disease course, such as developing the capacity to quantify the burden of RA inflammation, which waxes and wanes; pinpointing genetic factors that increase risk of CV, e.g., an RA patient's lipid profile; determining why some patients respond to treatment while others are resistant; diagnosing RA earlier, when it can be treated more readily; and studying patients at the extremes of the disease to identify genetic factors that differentiate the two groups. Dr. Liao is a member of the Section for Clinical Sciences research team.



Peter Andrija Nigrovic, MD

Director, Center for Adults with Pediatric Rheumatic Illness at BWH
Assistant Professor of Medicine, Harvard Medical School

Arthritis Triggers in Adults and Children

Dr. Peter Nigrovic is interested in the ways the immune system prompts the body to attack its own joints and sustain the damaging process over time. By studying immune cells, animals (mice) and human tissue samples, he is working to unravel the biological triggers for both adult RA and its potentially devastating pediatric counterpart, juvenile idiopathic arthritis (JIA). In one series of studies, Dr. Nigrovic used a drug to shut down JIA during a critical onset period (ages 1–4), when JIA most often initiates an attack. His group also found that the drug is ineffective after the onset period. A current line of investigation is seeking the mechanism that sets up the resistance to the drug, with the hope that neutralizing this barrier will allow the drug to work beyond the onset period. If successful, this would be a major breakthrough in the treatment of JIA.

Dr. Nigrovic is also committed to developing innovative mentoring opportunities to help advance the field. For example, he founded the nation's first inter-institutional mentoring program in a sub-specialty. Called AMIGO, the program matches pediatric rheumatologists-in-training with experienced specialists at other institutions.

Julia F. Charles, MD, PhD

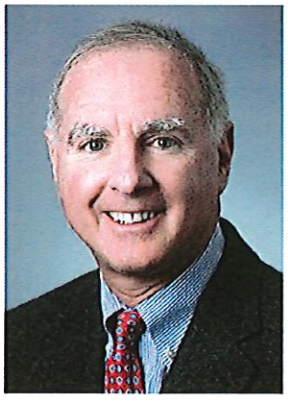
Associate Physician, BWH Department of Medicine
Instructor of Medicine, Harvard Medical School

Biological Basis of Bone Health and Disease

Dr. Julia Charles's research focuses on ways that the immune system and skeletal system interact – a newly emerging field called osteoimmunology. Most people believe, incorrectly, that an adult's bones are inert and unchanging when in fact they are dynamic and constantly recreating themselves to maintain good health. Dr. Charles conducts research on two major types of bone cells, one that forms bone (called *osteoblasts*) and another that breaks down bone (called *osteoclasts*). These two types of cells communicate with one another to maintain a balance needed for healthy bones. In RA, excessive osteoclasts are produced and contribute to joint erosion.

Dr. Charles is working to isolate the source of osteoclasts in patients with RA. In mice, she identified an enlarged population of cells that originate in bone marrow and develop into joint-eroding cells. She also found that these cells not only break down bone but also suppress immune system activity – a groundbreaking discovery that has generated additional funding and has attracted increased attention and recognition from the nation's scientific community.

Each of these investigators is poised to take their research to the next level and develop new, out-of-the-box ideas. At the same time, colleagues working in their labs are anxious to advance their own careers by launching independent branches of investigation, while other researchers in the Division are seeking new rounds of funding to transition from one avenue of study to another. Unfortunately, NIH cuts are hindering all of these hopes and expectations, an unacceptable reality that must be addressed if we are to continue moving the field forward and providing patients with state-of-the-art care. The Rheumatology Fund for Discovery and Innovation is our answer.



INVESTING IN PROGRESS

The Rheumatology Fund for Discovery and Innovation was conceived by **Dr. Michael E. Weinblatt**, who is the R. Bruce and Joan M. Mickey Distinguished Chair in Rheumatology at Brigham and Women's Hospital and the John R. and Eileen K. Riedman Professor of Medicine at Harvard Medical School. A prolific investigator in new therapies for rheumatoid arthritis, Dr. Weinblatt wants to create a dedicated pool of funds that can help offset some of the most deleterious consequences of federal budget cuts, especially for early-to-mid-career faculty in the Division. He cites several reasons why creating the Fund is so important:

1. **Accelerating Progress** — After five years of healthy growth in the late 1990s and early 2000s, NIH funding began stagnating and then eroding as a result of Congressional budget cuts. They have had two immediate effects on medical research: far fewer deserving proposals are funded, and those that receive grant support tend to be "safe" studies that remain within conventional boundaries of thinking. As a result, real progress and momentum are slowing. The Fund will support the work of BWH's most creative and imaginative investigators – such as those profiled above – who are a font of new and bold ideas.

2. **Promoting Careers** — Early-career investigators need to establish their independence by securing multi-year research grants that can support their respective labs. However, in order to submit a competitive proposal to the NIH they first need to generate data that demonstrates the validity of their hypotheses and can pass a rigorous peer review process. The Fund will help advance new ideas and pilot studies that can produce this critical data. Often, a modest expenditure of seed funds can leverage millions of dollars in NIH support down the road.

3. **Bridging Gaps** — Early- and mid-career researchers who are completing work funded by a grant often need "bridge funding" while they make the transition from their current work to securing support for their next initiative. Timing issues and unpredictable events can delay or disrupt a project schedule, and the Fund can offer a safety net when necessary. Also, it may take up to ten years for a young faculty member to receive independent funding given the current NIH funding crisis. Because we lack the resources to support our physician-scientists over such a lengthy period, we risk losing outstanding rheumatology researchers to other institutions or to pharmaceutical or biotech firms. The Fund will help alleviate these problems.

4. **Sustaining Academic Research** — Academic centers such as BWH have traditionally served the nation and the world as engines of discovery and innovation, often performing basic and costly research that lacks a profit motive and is therefore unattractive to industry. With federal grant monies shrinking, many of our best and brightest young physician-scientists are being lured away from academic settings to seek more lucrative jobs in the private sector. The Fund can help keep future leaders at BWH.

Our goal is to raise $2 million over three years to launch the Fund. While we welcome gifts of all magnitudes, the Fund will grow and flourish only through exceptionally generous donations. Therefore, we are asking grateful patients and friends to consider creating named, endowed funds or making major gifts that can be allocated when and where they will have the greatest impact. Dr. Weinblatt and selected senior colleagues will choose award recipients and will work with donors to accommodate any interests or preferences.

The Rheumatology Fund for Discovery and Innovation will give a boost to gifted people who are committed to improving the health and quality of life for BWH patients and countless others affected by rheumatic diseases. The potential impact of their work is profound, and investing in the Fund will pay health dividends for years and decades to come.