



2017



AWARD RECIPIENTS

ADVANCING TREATMENT
AND FINDING CURES



**Rheumatology
Research Foundation**
Advancing Treatment | Finding Cures



INVESTING IN THE FUTURE



The Rheumatology Research Foundation is committed to improving care for the more than 54 million Americans affected by arthritis or other forms of rheumatic disease. The Foundation's extensive awards program helps patients by increasing the number of rheumatology health professionals, while also funding research advancements that lead to new treatments and cures.

In the coming fiscal year (July 1, 2017 - June 30, 2018), the Foundation has committed to fund more than \$9.9 million to rheumatology research and training. About half of those awards will support efforts to recruit and train the next generation of rheumatology professionals, which decreases patient wait times and increases access to rheumatology care. The remaining funds will be awarded to advance research projects that lead to breakthroughs in treating people with rheumatic diseases. This year's innovative research awards were expanded to investigators studying *all* rheumatic diseases, so that progress can be made to find cures for the full spectrum of rheumatic diseases. In all, the Foundation has committed more than \$153 million to fund more than 3,400 awards since 1985, making it the largest private funding source of rheumatology research and training in the United States.

Congratulations to the Foundation's latest award recipients. Their work is vital to creating a brighter future for the field of rheumatology and for the people impacted by rheumatic disease.

TIMOTHY B. NIEWOLD, MD

CHAIR, SCIENTIFIC ADVISORY COUNCIL
RHEUMATOLOGY RESEARCH FOUNDATION

STEWART AND JUDITH COLTON PROFESSOR
OF MEDICINE AND PATHOLOGY
COLTON CENTER FOR AUTOIMMUNITY
NEW YORK UNIVERSITY

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2017 AWARDEES AT A GLANCE

THE FOUNDATION WILL FUND MORE THAN **63** NEW AWARDS
FOR RHEUMATOLOGY PROFESSIONALS IN **32** CITIES.

Birmingham, AL	Durham, NC
Little Rock, AR	Chapel Hill, NC
Los Angeles, CA	Omaha, NE
Stanford, CA	Lebanon, NH
San Diego, CA	New York, NY
San Francisco, CA	Rochester, NY
New Haven, CT	Madison, NY
Washington, D.C.	Buffalo, NY
Newark, DE	Cincinnati, OH
Orlando, FL	Cleveland, OH
Miami, FL	Oklahoma City, OK
Evanston, IL	Portland, OR
Chicago, IL	Philadelphia, PA
Boston, MA	Memphis, TN
Baltimore, MD	Houston, TX
Ann Arbor, MI	Milwaukee, WI





Research investigates factors that might cause or worsen rheumatic diseases, including

- Genetics
- Epigenetics
- Immune dysfunction
- Cell characteristics
- Joint features
- Gut microbiota
- Diet
- Chemical exposure
- Smoking
- Obesity
- Prior injuries



Studies could reduce the impact rheumatic diseases have on the

- Brain
- Eyes
- Mouth
- Shoulders
- Spine
- Lungs
- Heart
- Hips
- Knees
- Skin
- Joints
- Cardiovascular System



Discoveries could lead to new treatments and cures for

- Gout
- Inflammatory Arthritis
- Juvenile idiopathic arthritis
- Osteoarthritis
- Psoriatic arthritis
- Rheumatoid arthritis
- Scleroderma
- Sjögren's syndrome
- Spondyloarthritis
- Systemic Lupus Erythematosus
- Systemic Sclerosis

Awards recruit and train the next generation of rheumatology professionals by funding



24 Fellowship training opportunities for future rheumatologists

13 Preceptorship learning experiences for students, residents, and health professionals

2 Clinician Scholar Educator awards that revolutionize the way future health professionals are trained to diagnose and treat people with rheumatic diseases



INNOVATIVE RESEARCH AWARD

THE INNOVATIVE RESEARCH AWARD ALLOWS
INDEPENDENT INVESTIGATORS TO EXPLORE NEW IDEAS
THAT IMPROVE UNDERSTANDING OF ALL RHEUMATIC
DISEASES. THEIR BREAKTHROUGHS ARE THE FIRST
STEP IN DISCOVERING NEW TREATMENTS, CURES, AND
PREVENTION FOR RHEUMATIC DISEASES.

HYON CHOI, MD, DRPH

MASSACHUSETTS GENERAL HOSPITAL

EFFECT OF THE DASH DIET ON SERUM URIC ACID IN GOUT PATIENTS

Gout is the most common inflammatory arthritis in the US and is caused by hyperuricemia. Gout represents a metabolically-driven arthropathy that could be substantially controlled through dietary and lifestyle modifications; however, a compelling lack of dietary intervention trials exists in gout. Perpetuated by the “Western” lifestyle, the prevalence of gout has increased over the past few decades to 3.9% of US adults (8.3 million individuals). This gout disease burden is further complicated by a high level of cardiovascular (CV)-metabolic comorbidities (e.g., hypertension in 74%; metabolic syndrome in 63%) and their sequelae (e.g., increased future risk of myocardial infarction and premature death). The conventional low-purine dietary approach to gout offers limited efficacy, palatability, and sustainability, and promotes increased consumption of refined carbohydrates and unhealthy fats that can actually exacerbate CV-metabolic comorbidities by furthering insulin-resistance and increasing levels of plasma glucose, triglycerides, and LDL-C. Therefore, there is a key unmet need for an effective and novel dietary strategy to address both gout and its comorbidities. To that effect, there are several proven, effective dietary approaches for CV-metabolic conditions that could also lower serum uric acid (SUA) levels. In particular, the Dietary Approaches to Stop Hypertension (DASH) diet, which emphasizes fruits, vegetables, low-fat dairy foods, and reduced saturated and total fat, substantially reduces blood pressure and is also recommended to prevent cardiovascular disease (CVD). Furthermore, recent studies have found that the DASH diet also lowers SUA levels substantially among hyperuricemic non-gouty individuals (as compared to a control diet) and is associated with a lower risk of incident gout. Thus, the DASH diet carries remarkable promise in gout care by improving both SUA and CVD, particularly hypertension, which affects 74% of gout patients. With the central goal of holistically reducing the disease burden of both gout and its comorbidities, we plan on a randomized controlled trial to assess the efficacy of the DASH diet compared to a control diet on SUA levels. This trial holds the potential to revolutionize our non-pharmacological anti-gout approach by addressing both gout and its comorbidities and to fill this critical void in gout care.



A. DARISE FARRIS, PHD

OKLAHOMA MEDICAL RESEARCH FOUNDATION

CD4+ T CELLS IN ORAL PATHOGENESIS OF SJÖGREN'S SYNDROME

Sjögren's syndrome (SS) is a debilitating rheumatic disease characterized by severe dry eyes and mouth, infiltration of the moisture-producing exocrine glands by CD4+ T cells, and systemic complications including arthritis, fatigue, and B cell lymphoma. There are currently no approved, effective therapies for the disorder, and most treatments for dryness are designed to relieve symptoms but do not address drivers of immune dysfunction. This is because causes of SS, including target salivary and lacrimal gland antigens, are largely unknown. By evaluating T cell receptor (TCR) sequences of single CD4+ T cells isolated from the minor salivary glands of subjects with SS, we observed clonal expansions, which are evidence of T cells responding to proteins that their TCRs recognize. We also found that patients who have the highest percentages of clonally expanded CD4+ T cells in their salivary glands also have the lowest production of saliva and the highest degree of salivary gland damage. Thus, these T cells may be causing oral disease in SS. In this project, we will use these TCR sequences, as well as recombinant human monoclonal antibodies derived from salivary gland B cell plasmablasts of the same individuals, as tools to learn what salivary gland

proteins are driving autoimmune dysregulation leading to oral disease in these patients. Approaches include probing of human proteome arrays with SS salivary gland monoclonal antibodies and testing expressed TCRs from the same subjects for specificity to Ro, La and other monoclonal antibody-recognized salivary gland antigens. Other approaches include salivary gland TCR deep sequencing for confirmation of the relationship between low saliva production and salivary gland T cell clonal expansion, as well as single cell RNA sequencing to learn what genes are expressed by clonally expanded salivary gland T cells. Successful execution of these studies is expected to lead to the identification of new salivary gland antigens and new therapeutic targets for this debilitating condition.



LIANA FRAENKEL, MD, MPH

YALE UNIVERSITY

DEVELOPMENT OF A GLOBAL OUTCOME MEASURE FOR RHEUMATOID ARTHRITIS CLINICAL TRIALS

Currently available outcome measures for patients with inflammatory arthritis do not provide patients with the information they need in order to make informed decisions. In the words of a patient with rheumatoid arthritis (RA): "Patients have no way to determine the potential net benefit of a treatment, much less to compare across treatments."

The results of randomized controlled trials are currently reported as either average improvement scores across study subjects, (e.g. DAS) or the percentage of patients attaining a specified amount of improvement (e.g., ACR 20, 50 and 70). The numbers of subjects experiencing specific adverse events (AEs) are reported separately. While based on sound scientific methods, this approach does not provide any information on the overall effect of treatment.

The aim of this project is to develop a new outcome measure that encompasses both benefits and harms of treatment at the individual patient level. The result will be a ranking of all trial subjects by the desirability of their overall outcome. The best possible global outcome, i.e., highest level, is "Remission without AEs" and the worst possible outcome is "No clinical improvement and a life threatening AE (or death)". Between these two extremes are mutually exclusive hierarchical levels of clinical outcomes ordered in terms of their desirability. Using this global outcome measure (which we will call G-PROM), randomized controlled trials could then report the percentage of patients classified into each level; thus, providing patients with a much clearer understanding of the range and likelihood of the total effects of treatment on their lives.

While the extreme levels for the outcome measure are set, the intermediate levels must be developed. We propose to use Trajectory Mapping – a non-metric scaling technique – to elicit patients' mental models of the differences between benefits and harms. We will subsequently obtain preliminary estimates of the validity of the G-PROM using the raw data from three completed randomized controlled trials comparing traditional disease modifying anti-rheumatic drugs to biologics.

We hope that a scale measuring desirability of patients' overall outcome will generate more informative comparative data than current approaches.



MONICA GUMA, MD, PHD

UNIVERSITY OF CALIFORNIA, SAN DIEGO

MITOCHONDRIA-BOUND HK2 AS A TARGET IN RHEUMATOID ARTHRITIS



Fibroblast-like synoviocytes (FLS) are a key component of rheumatoid arthritis (RA) invasive synovium and have a major role in the initiation and perpetuation of destructive joint inflammation. FLS from patients with RA display unique aggressive features, including increased migration and the ability to invade and 'metastasize' in vivo. FLS must adapt to changing environmental conditions in inflamed joints in which not only nutrients and oxygen might be limited, but also is enriched with apoptosis-inducing factors. An up-regulated glucose metabolism, mediated by glucose transporters (such as GLUT-1) and hexokinases (HK) is known to help activated cells to adapt to this microenvironment, to give them powerful growth advantage, which promotes proliferation and invasion. The inducible HK isoform, HK2, which is highly expressed in activated cells and restricted in normal adult tissue, is in part responsible for its accelerated glucose flux. HK2 localizes not only in the cytosol but also at mitochondria and protects mitochondria against apoptosis.

Our preliminary data demonstrates that expression of HK2 was observed only in RA synovial samples. Growth factors such as PDGF increased HK2, GLUT-1 and glycolysis rate in RA FLS. PEGF also induces HK2 translocation to mitochondria. Of interest, HK2 knockdown impaired FLS invasion and migration. Conversely, overexpression of HK2 increased FLS invasion and migration rate. Interestingly, a HK2 mutant that does not bind to the mitochondria reversed the invasive phenotype. Finally, in a mouse model of inflammatory arthritis, we observed an increase of glucose uptake in the stromal compartment in arthritic joints. Glycolytic inhibition by bromopyruvate and treatment with clotrimazole, which dissociated HK2 from mitochondria, significantly decreased arthritis severity. Thus, we will test the hypothesis that that mitochondrial HK2 is key regulator of glucose metabolism and FLS phenotype, which contributes to joint destruction in RA, and that selective HK2 inhibition is an attractive potential selective metabolic FLS target safer than global glycolysis and independent of systemic immunosuppression.

I-CHENG HO, MD, PHD

BRIGHAM AND WOMEN'S HOSPITAL

DEFINING A MOLECULAR TIMELINE OF PRECLINICAL RHEUMATOID ARTHRITIS

Rheumatoid arthritis (RA) affects up to 1-2% of the general population in North America. As more effective therapies for RA are emerging, the focus of RA care is shifting from controlling inflammation to early detection, prevention, and cure of this disease. A better understanding of early molecular events predating the onset of clinical symptoms will help us achieve these goals. One unique feature of RA is the presence of anti-citrullinated protein antibodies (ACPA). Citrullination is a form of post-translational modification of proteins, by which peptidyl arginines are converted to peptidyl citrullines. This process is mediated by the peptidyl arginine deiminases (PADs), including PAD1-4 and PAD6. Dysregulated citrullination probably contributes to the pathogenesis of RA. For example, cigarette smoking, a major risk factor of RA, can enhance citrullination in cells from bronchial lavage. In addition, a RA-prone genetic variation at PTPN22, a phosphatase that also suppresses citrullination independently of its phosphatase activity, interrupts its interaction with PAD4, rendering PTPN22 unable to suppress citrullination. Accordingly this genetic variation is associated with hypercitrullination in blood cells. This overarching goal of this project is to test two hypotheses: hypercitrullination is a precondition of RA; and hypercitrullination not only expands the pool of citrullinated RA antigens but also actively modulates the function of immune cells, thereby setting the disease process of RA into motion.



Dr. Ho's laboratory has recently discovered that healthy donors who are at high risk for developing RA have an abnormally high level of citrullinated proteins in their blood cells. Their blood cells also exhibit several abnormal features that are seen in RA patients, indicating that hypercitrullination and these abnormal features predate the clinical symptoms of RA. In the first aim, Dr. Ho's group will investigate the cause of hypercitrullination and to establish the causal relationship between hypercitrullination and the abnormal features of preclinical RA. The second aim of this project is to use both pharmacological and genetic approaches to determine the impact of attenuated citrullination on T lymphocytes. In summary, knowledge gained from this study will bring us one step closer to early detection, prevention, and cure of RA.

JAMES N. JARVIS, MD

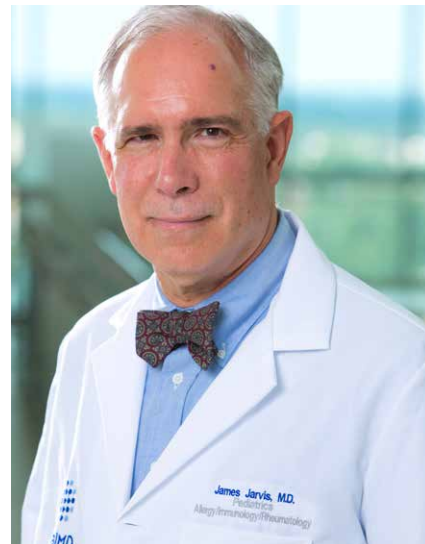
UNIVERSITY AT BUFFALO JACOBS SCHOOL OF MEDICINE & BIOMEDICAL SCIENCES

GENETICS AND EPIGENETICS IN JIA CD4+ T CELLS

The preponderance of data suggests that juvenile idiopathic arthritis (JIA) is a complex trait mediated by gene-environment interactions. Like most complex traits, however, most of the genetic risk for JIA resides in non-coding regions of the genome. These regions contain multiple functional elements that carry specific epigenetic signatures and whose primary function is to regulate and coordinate transcription on a genome-wide basis. a

Our overall goal is to understand how genetic variation and the epigenome interact to create disease risk and to regulate treatment response in JIA. In the current application, we will be examining CD4+ T cells. We will first obtain a global view of the functional elements within JIA CD4+ T cells using ATAC sequencing, a method for assessing all regions where chromatin is accessible and therefore likely to be functional. We will compare results from what we find in healthy age and sex matched children, and determine whether/how therapy for JIA alters these functional elements. Next, we will determine whether novel functional regions in JIA T cells are associated with genetic variation, using computational approaches that overlap novel, JIA-associated regions of open chromatin with genetic variation as observed from whole genome sequencing that we have recently finished. Finally, we will determine the functional significance of epigenetic and genetic variation by correlating them with gene/transcript expression using RNA sequencing.

The studies are the necessary first step toward our gaining a broad understanding of genetic and epigenetic risk in JIA and determining the molecular mechanisms of treatment response or non-response. We expect them to provide the foundation for future studies that will comprehensively survey the functional genome in JIA and develop testable models for disease pathogenesis and treatment response.



AMANDA E. NELSON, MD, MSCR

UNIVERSITY OF NORTH CAROLINA AT CHAPEL HILL

SONOGRAPHY OF OA BY RHEUMATOLOGISTS (SOAR): THE JOHNSTON COUNTY OA PROJECT

Knee osteoarthritis (KOA) is a common cause of disability and leads to the majority of knee replacements. Radiographic assessment is most frequently used in research studies of KOA but does not correlate well with symptoms and lacks information about soft tissue structures. Ultrasound (US) provides detailed information about multiple relevant joint pathologies (osteophytes, synovitis/effusion, meniscal and cartilage damage) in a similar fashion and with comparable reliability to MRI but in a more widely available, cost-effective manner, while avoiding some of the limitations of MRI including claustrophobia, weight restrictions, and issues with metal implants. To date, there is a lack of well-designed large studies evaluating US features of KOA in non-clinical populations; such studies are essential for expanding the use of US for KOA in both research and clinical settings. The Johnston County Osteoarthritis Project is a large population-based study of risk factors in OA, which in its next phase will include younger (35 and older) participants and Hispanics in addition

to African Americans and whites. These individuals, again not selected for OA or symptoms, will be extremely well-characterized for risk factors, symptoms, and function, in addition to US assessments, making this an ideal setting to add and evaluate US, which will provide valuable information regarding soft tissue features and inflammation in KOA. The aims of our project are: 1) to determine the feasibility and reliability of US assessment for features of KOA (i.e., cartilage and meniscal damage, synovitis, and osteophytes) in this cohort using a trained technologist and multiple expert rheumatologist readers and 2) to examine cross-sectional associations between US features of KOA and radiographic features and symptoms, considering the influence of sex, race, obesity, prior injury, multiple joint complaints, and medical comorbidities. This work will highlight the value of US in KOA care, with the potential to identify and treat KOA at an earlier, pre-radiographic stage; expanded use of US could increase the impact and value of rheumatologic care while improving access to care for patients with KOA.

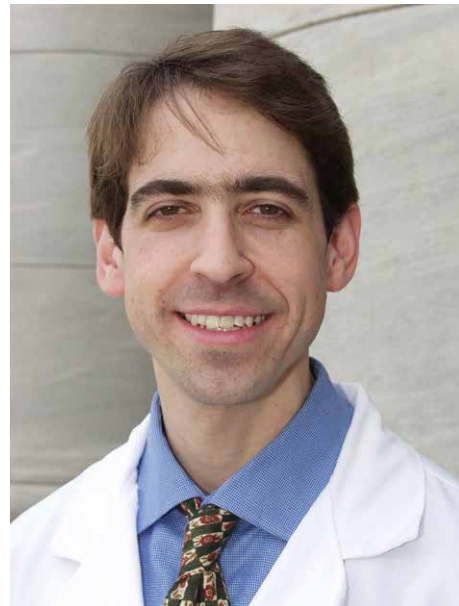


PETER A. NIGROVIC, MD

BRIGHAM AND WOMEN'S HOSPITAL

SYNOVIAL T RESIDENT MEMORY CELLS IN ARTHRITIS

Inflammatory arthritis in adults and children is often characterized by periods of quiescent activity followed by disease flares. Remarkably, in any individual patient, the same joints typically flare repeatedly, in a more or less asymmetric pattern that usually establishes itself early in disease and then persists for years or decades. The hypothesis of this proposal is that such "joint-specific memory" reflects the presence of T resident memory cells (TRM). TRM are a recently-described subset of long-lived T cells, of either CD8 and CD4 type, that develop in skin and other tissues as a response to tissue inflammation, persisting for years thereafter to provide long-lasting site-specific immunity. However, TRM have never been described in joints. Using a novel, highly-efficient 3-dimensional culture system, the Nigrovic and Fuhlbrigge labs employed cytometry by time of flight (CyTOF) to identify cells with TRM phenotype in rheumatoid synovium. Further, we adapted existing animal models to develop a novel murine system characterized by recurrent, joint-specific, T cell-dependent inflammatory arthritis characterized by synovial cells with TRM phenotype. Building upon these studies, we will both characterize TRM from human joint specimens and employ the animal model to confirm that TRM play a role in recurrent, site-specific disease.



HARRIS R. PERLMAN, PHD

NORTHWESTERN UNIVERSITY

UNDERSTANDING THE ROLE OF MACROPHAGES IN THE PATHOGENESIS OF RHEUMATOID ARTHRITIS



Metchnikoff described macrophages in the early 1900s, yet synovial macrophages were identified nearly 60 years later. The most well-known and reproducible biomarker for response to rheumatoid arthritis (RA), an autoimmune disease that greatly impacts morbidity and mortality, therapy is the reduction in the number of sublining synovial macrophages. We were the first to show that synovial macrophages exist as a heterogeneous population comprised of tissue-resident and monocyte-derived cells in both mice and humans. However, the contribution of each population to the pathogenesis, persistence and resolution of RA is still unknown. Based on our recent data, the current paradigm describing the role that cells play in the pathogenesis of RA-like disease in mice has been revised. We demonstrated that non-classical monocytes are required for the initiation and progression of a mouse model of RA-like disease that resembles its effector phase. Additionally, we showed that non-classical monocytes are sufficient to give rise to activated macrophages during joint inflammation. However, synovial macrophages exhibit plasticity during the development and persistence of RA-like disease and can

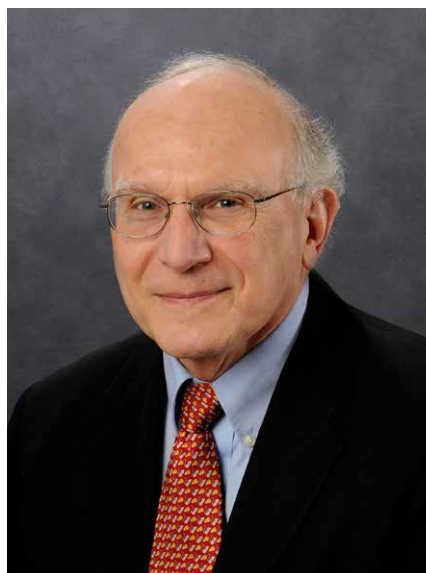
assume the cell surface phenotype of one another other (i.e. MHC II+ vs. MHC II-). Thus, it is clear that a more defined method is required to understand the differential roles that these populations play during the various phases of RA. We are the first to identify transcriptional signatures that are specific to each population of synovial macrophages during the peak of inflammatory arthritis in mice. Moreover, our group is the first to be trained and perform minimally invasive synovial tissue biopsies on RA patients with active disease. We already performed over 11 minimally invasive ultrasound guided synovial tissue biopsies on RA patients with active disease over the past 7 months, extracted RNA from whole tissue and from FACSsorted macrophages via single cell suspensions and performed RNA sequence (RNAseq) analysis. Thus we hypothesize that there is a distinct transcriptional signature corresponding to a specific synovial macrophage subpopulation that delineates its role during the multiple phases of RA.

JAMES T. ROSENBAUM, MD

OREGON HEALTH & SCIENCE UNIVERSITY

THE MICROBIOME, IGA COATED BACTERIA, AND JOINT INFLAMMATION

The microbiome is strongly implicated in immune-mediated diseases including rheumatoid arthritis (RA), spondyloarthritis (SpA), and psoriatic arthritis (PsA). Although the microbiome is immensely complex, IgA coating of bacteria in the bowel identifies bacteria which are most recognized by the immune system and arguably most pathogenic. Segmented filamentous bacteria are highly arthritogenic in a murine arthritis model and are markedly IgA-coated in the HLA B27+ rat model of spondyloarthropathy based on our own unpublished data. We hypothesize that IgA coated bacteria increase bowel permeability which allows bacterial translocation to the joint, a critical component in inflammatory joint disease. Our aims are 1) to compare and contrast IgA coated bacteria from saliva, urine, skin, and feces from patients with RA, SpA, PsA, osteoarthritis (OA), and healthy controls; 2) to measure bowel permeability in patients with these diseases and to correlate that permeability with the quantity and identity of IgA coated bacteria in the gut; and 3) to identify bacterial DNA in synovial fluid from patients with these diseases and to compare and contrast the results for each disease; to test the hypothesis that the gut is the source of these bacteria; to determine if bacteria in synovial fluid are IgA coated; and to correlate the bacterial load in the fluid with bowel permeability. These studies are likely to identify specific bacterial species which can be targeted to prevent and/or treat RA, SpA, and PsA.





CAREER DEVELOPMENT BRIDGE FUNDING AWARD: R BRIDGE

THE R BRIDGE AWARD PROVIDES ESSENTIAL FUNDING FOR
PROMISING INVESTIGATORS TO CONTINUE THEIR WORK
STUDYING RHEUMATIC DISEASES. SUPPORT KEEPS RESEARCH
ADVANCEMENTS MOVING, WHILE INVESTIGATORS REVISE
OUTSTANDING NIH R01 OR VA RCS/ORD AWARD APPLICATIONS.

CHRISTIE M. BARTELS, MD, MS

UNIVERSITY OF WISCONSIN

PREPARING TO PRIORITIZE CVD STRATEGIES IN RHEUMATOID ARTHRITIS AND LUPUS: P2P-CVD

Patients with rheumatoid arthritis (RA) and systemic lupus erythematosus (lupus) experience early cardiovascular disease (CVD) and death, and 75% of their visits occur in rheumatology clinics making these 4 million annual visits vital opportunities to address modifiable risk factors. We submitted a clinical observational R01 study proposing to determine which risk factors are most responsible for early CVD events and deaths across RA and lupus populations. That study, to be conducted at three diverse centers, aims to prioritize risk factor targets for future staff interventions. Our research team previously showed that rheumatology staff interventions can double timely primary care follow-up after high blood pressures and significantly increase tobacco quit line referrals. The objective of our proposed observational R01 is to inform priorities and the design of a future trial to test staff-intervention strategies to control the most important risk factors, to improve CVD risk

factor control, health, and longevity in RA and lupus populations. To demonstrate feasibility of our clinical observational R01 study that will prioritize risk factors, in this RRF bridge award we propose three specific aims: (1) Create validated lupus and RA cohorts using electronic health record data from two centers to (2) examine the prevalence and predictors of smoking in RA and lupus including the role of health disparities, and (3) test feasibility of collecting data using potential measures for future clinic staff intervention studies. Successful completion of the proposed bridge award aims will build multicenter RA and lupus cohorts, a data platform supporting successful resubmission and completion of the R01 study, and partnerships and methods for a future trial testing staff-interventions for CVD risk factors--advancing the Rheumatology Research Foundation's mission to improve health for people with rheumatic disease.





INVESTIGATOR AWARD

THE INVESTIGATOR AWARD HELPS DEVELOP
TOMORROW'S TOP INVESTIGATORS. FUNDING
ALLOWS JUNIOR INVESTIGATORS TO CONDUCT
INNOVATIVE RESEARCH AND ESTABLISH
THEMSELVES IN THE FIELD, SO THEY CAN LATER
COMPETE FOR MORE SIGNIFICANT FUNDING.

JAMIE E. COLLINS, PHD

BRIGHAM AND WOMEN'S HOSPITAL

DEFINING FAST PROGRESSORS IN KNEE OSTEOARTHRITIS

Knee osteoarthritis (OA) affects 250 million adults worldwide; with an aging population and the growing obesity epidemic, the prevalence is increasing. The disease is associated with lower quality of life and increased healthcare utilization, leading to health expenditures in the United States alone exceeding \$27 billion annually. While traditionally considered a disease of aging, recent estimates find that over 8 million of those affected in the US are under the age of 65 and 2 million are under age 45. Current treatments for knee OA are limited to symptom control. There are no currently approved disease-modifying osteoarthritis drugs (DMOADs) that modify disease onset or slow structural progression. Clinical trials of knee OA treatments are complicated by the heterogeneity of subjects enrolled in trials, as different patient phenotypes may have a differential treatment response. Understanding this heterogeneity has been identified as a top research priority in OA.

Traditional approaches to longitudinal data analysis may not be suitable in the presence of heterogeneous outcomes. We propose to use novel statistical methods to identify a subgroup of rapid progressors in knee OA. We hypothesize that progression patterns differ among patients with knee OA, with at least one group experiencing rapid progression and that we will identify a subgroup experiencing concurrent rapid symptomatic and structural progression. Finally, we will utilize a novel approach to assess semi-quantitative imaging data to define the most robust measure of disease activity. We will identify which specific joint features are most predictive of rapid disease progression.

We must identify patients who are likely to experience rapid disease progression to help to establish DMOADs' efficacy. Successful completion of this work will identify prognostic factors for rapid disease progression, which will ultimately lead to more efficient design of clinical trials and the development and implementation of more effective therapies.



ANDREA KNIGHT, MD, MSCE

CHILDREN'S HOSPITAL OF PHILADELPHIA

MULTIMODAL IMAGING IN PEDIATRIC NEUROPSYCHIATRIC LUPUS

Neuropsychiatric SLE (NPSLE) affects 30-50% of youth with pSLE, but management remains a significant challenge due to poor understanding of the underlying pathophysiology. Enhanced characterization of underlying neural mechanisms is enabled through integration of multimodal neuroimaging techniques such as structural magnetic resonance imaging (sMRI), diffusion tensor imaging (DTI), and functional MRI (fMRI). This project applies these multimodal imaging techniques to study brain structure, function and development in pSLE. Leveraging existing normative imaging, cognitive and psychiatric data from typically developing youth in the large Philadelphia Neurodevelopmental Cohort, we will evaluate structural brain injury, calculate a newly developed measure of brain development, and examine structure-function relationships between imaging metrics and clinical features in pSLE. Specifically, we will: 1) quantify the effect of pSLE on brain integrity and function utilizing multimodal neuroimaging (sMRI, DTI, and resting state fMRI) in cross-sectional comparison to age and sex-matched typically developing youth, and 2) correlate cross-sectional multimodal imaging metrics in pSLE with longitudinal assessment of cognitive and affective function. The results of this study are anticipated to lead to further examination of neuroimaging biomarkers for early detection and targeted treatment of neuropsychiatric disorders in pSLE.



PUI Y. LEE, MD, PHD

BOSTON CHILDREN'S HOSPITAL

BRIDGING MONOCYTE DEVELOPMENT AND INFLAMMATION THROUGH AMINO ACID SENSING

Monocytes are essential to innate immunity but also propagate the inflammatory response in autoimmune arthritis and other rheumatologic diseases. Understanding the basic biology of monocyte development is therefore central to unraveling disease pathogenesis and to identifying new therapeutic targets. Our previous work have established an essential role of the central metabolic integrator mechanistic target of rapamycin complex 1 (mTORC1) as a master regulator of monocyte development. Monocytes displayed prominent mTOR signaling at baseline and mTOR inhibitors disrupted their differentiation from myeloid progenitors. The signal responsible for mTORC1 activation during myeloid development, however, remains undefined as mTORC1 integrates a broad array of biological input including cytokine signaling and nutrient sensing.



We show that sensing of amino acids via Ras-related GTP binding protein A (RagA) provides the key signal for mTORC1 activation that licenses monocyte development. Deficiency of RagA phenocopies the features of mTORC1-deficient mice. These preliminary results establish an unrecognized connection between nutrient sensing and myeloid development. We will characterize individual amino acids that provide input to the RagA-mTORC1 pathway to signal monocyte development in mice, with parallel studies in humanized mice. We will define targets of the amino acid sensing / metabolic pathway to inhibit myelopoiesis. Furthermore, we will address the impact of amino acid sensing on monocyte / macrophage polarization and functions in vitro and in murine models of inflammatory disease including arthritis, peritonitis and obesity. Together, these studies will provide novel insights into metabolic regulation of monocytes and help identify new targets for monocyte mediated inflammatory diseases.

SCIENTIST DEVELOPMENT AWARD



THE SCIENTIST DEVELOPMENT AWARD
PROVIDES AN OPPORTUNITY FOR EARLY CAREER
RHEUMATOLOGY HEALTH PROFESSIONALS TO
PURSUE INNOVATIVE RESEARCH IDEAS.

MATTHEW C. BAKER, MD

STANFORD UNIVERSITY

SEQUENCING THE PLASMABLAST REPERTOIRE TO IDENTIFY AUTOANTIGENS IN ANCA VASCULITIS

ANCA-associated vasculitis (AAV) is a life threatening disease. Its pathogenesis is poorly understood and there is an unmet need for highly efficacious, well-tolerated, targeted therapies. In granulomatosis with polyangiitis (GPA), a specific AAV subset, anti-neutrophil cytoplasmic antibodies (ANCAs) against proteinase-3 (anti-PR3 antibodies) are present in roughly 80% of patients. Although an important diagnostic marker of disease, the extent to which anti-PR3 antibodies play a role in disease pathogenesis is unclear. We believe novel autoantibodies may play a more primary role in PR3+ ANCA-vasculitis. Cell-barcode-enabled antibody repertoire sequencing was performed on plasmablasts from five PR3+ ANCA-vasculitis patients treated with rituximab in the RAVE trial. Plasmablasts are the antibody-producing cells formed during an immune response from naïve or memory B cells specific for the target antigen, which disseminate through the blood to populate in secondary lymphoid organs. Thus, the plasmablasts found in the blood of RAVE trial patients during baseline flare or post-rituximab flare represent flare-associated antibodies generated by germinal center B cell responses, which we anticipate are the antibodies relevant to disease pathogenesis. All five PR3+ ANCA-vasculitis patients sequenced from the RAVE trial achieved complete remission but subsequently flared. PR3 ELISA analysis was performed and none of the 24 antibodies bound to wild-type PR3, MPO, or elastase. Notably, a subset of clonal families is shared across patients during flares, suggesting a common antigen specificity, and this antigen does not appear to be PR3. Thus, we hypothesize that non-PR3 antigens are the targets of the plasmablast response during flare, and that these non-PR3 antigens may represent novel autoantigens associated with disease pathogenesis in ANCA-associated vasculitis. This project is to identify the human protein targets of the non-PR3-reactive recombinant antibodies and to test their association with disease. We expect to identify novel autoantigens that can be used as both biomarkers and therapeutic targets.



CRISTINA M. LANATA, MD

UNIVERSITY OF CALIFORNIA, SAN FRANCISCO

ENVIRONMENTAL ORGANIC CHEMICALS AND RISK OF SLE



Genetic, epigenetic and environmental risk factors have been implicated as causes for SLE. DNA methylation is an epigenetic mechanism that has been shown to be altered in immune cells in SLE. The field of epigenetics is evolving rapidly, in part because it provides a molecular link between environmental exposures and host susceptibility through alterations of gene expression. Studies linking environmental exposures with SLE have been largely epidemiologic/observational and not mechanistic. Very few studies have measured exposures in biological samples of SLE patients. Newer technologies such as liquid chromatography-quadrupole time of flight mass spectrometry (LC-QTOF/MS) allow for a non-targeted interrogation of hundreds of chemicals in an unbiased manner. We hypothesize that patients with SLE will have a distinct spectrum of circulating environmental organic chemicals compared to healthy controls, and that these compounds will be associated with specific epigenetic signatures. For the current application we will study 400 SLE patients and 200 matched healthy controls for exposure to environmental organic chemicals (EOCs) using LC-QTOF/MS in order to identify EOCs that may influence the risk of developing SLE. All study participants will also be characterized for genome-wide genetic and epigenetic (DNA methylation) profiles to support exploratory analyses that seek to identify interactions between EOC exposure and genetic and/or epigenetic factors. This will be the first study to apply this novel methodology for assessing environmental exposures, DNA methylation and risk of SLE.

NADIA D. MORGAN, MBBS

JOHNS HOPKINS UNIVERSITY

INTERLEUKIN-13 AND SCLERODERMA IN AFRICAN AMERICANS

Scleroderma is characterized by pervasive fibrosis and exhibits a highly variable clinical course. Compared to other racial groups, African American patients with scleroderma have demonstrated an increased burden of disease with higher mortality. The African American race has been established as an independent predictor of scleroderma associated interstitial lung disease, and patients exhibit a predilection for severe fibrotic clinical manifestations. While there is mounting evidence suggesting genetic susceptibility to scleroderma in African Americans, the exact cause remains elusive. Interleukin-13 (IL-13) is a crucial pro-fibrotic cytokine produced by CD4+ Th2 cells as well as cytotoxic CD8+ T lymphocytes. Elevated levels of IL-13 have been demonstrated in the blood and skin of patients with scleroderma. The long-term goal of this study is to evaluate the association between IL-13 and the fibrotic manifestations of scleroderma in African Americans. We hypothesize that IL13 genetic variants and/or enhanced IL-13 production, are associated with a higher fibrotic burden, thereby contributing to the increased severity of cutaneous and pulmonary fibrosis noted in African Americans with scleroderma. Accordingly, our proposed research will seek to address whether (1) IL13 genetic variants and (2) elevated serum IL-13 levels, are associated with the severity of fibrosis among African American patients with scleroderma. We expect to identify clinically relevant IL13 genetic variants which are associated with attendant fibrotic outcomes in scleroderma. In addition, we expect to find that IL-13 cytokine levels are significantly elevated in the serum of African American scleroderma patients with severe interstitial lung disease and severe cutaneous fibrosis.



ALAN M. RATHBUN, PHD, MPH

UNIVERSITY OF MARYLAND, SCHOOL OF MEDICINE

CHARACTERIZING THE ETIOLOGY AND ROLE OF DEPRESSION IN OSTEOARTHRITIS



Depressive symptoms are two to three times more common in persons with osteoarthritis (OA) than in the general population. Depression is also dynamic and clinically heterogeneous, with variability in expression and severity, which may account for why this comorbidity is under-recognized and under-treated by practicing rheumatologists. The relationship between OA disease severity and depression is unclear, but there are bidirectional effects, such that OA disease severity affects the onset and severity of depressive symptoms and depression impacts OA disease progression, and ultimately, analgesic treatment outcomes. However, depressive symptom heterogeneity and the specific components of OA disease severity that contribute to depression and that are influenced by depression have not been definitively identified and evaluated in the context of analgesic treatments for OA that are commonly used in routine clinical practice. Existing research is limited in its ability to examine these relationships because it has operationalized OA disease severity and depressive symptoms as static unidirectional determinants and not considered the potential effects on

analgesic treatments for OA. An innovative causal framework and data from the Osteoarthritis Initiative will be used to accomplish the following specific aims: 1) to identify depression subtypes among individuals with knee OA and describe how they change over time; 2) to evaluate the dynamic effect of OA disease severity on depressive symptoms; 3) to assess the dynamic effect of depressive symptoms on OA disease severity; and 4) to determine whether depressive symptoms modify the effect of dynamic analgesic treatments on OA disease severity. The new knowledge generated by the proposed research will provide insight in to the variation and progression of depression in persons with OA and the dynamic relationships between OA disease severity, depressive symptoms, and analgesic treatments. The study findings will facilitate the identification and evaluation of depression treatment strategies that are tailored to individuals, where the type of intervention or intensity of treatment changes over time depending on the needs of the OA patient.

SARA R. SCHOENFELD, MD

MASSACHUSETTS GENERAL HOSPITAL

LYSOPHOSPHATIDIC ACID AS A BIOMARKER IN SYSTEMIC SCLEROSIS

Systemic sclerosis (SSc) is an autoimmune disease with substantial clinical and molecular heterogeneity. Despite advances in understanding disease pathogenesis, effective treatment options are lacking, and morbidity and mortality remain high. Novel biomarkers and treatment strategies are needed. Our laboratory demonstrated that the lipid mediator lysophosphatidic acid (LPA) and its receptor LPA1 are crucial in the development of bleomycin induced dermal fibrosis in mice. As a result of this work, a phase II trial of an LPA1 antagonist was completed in SSc patients, and demonstrated an excellent safety profile and promising clinical efficacy. My preliminary results indicate that LPA levels differ in subsets of patients with SSc, suggesting that LPA may be a biomarkers for particular disease phenotypes. The underlying hypothesis of my project is that LPA is both a biomarker and disease mediator in SSc. LPA levels will differ in subsets of SSc patients and predict cutaneous and visceral organ involvement. Furthermore, I anticipate that an



LPA-responsive gene signature exists in certain patients with SSc and that dysregulation of this pathway plays an important role in disease progression and response to treatment. The translational studies in my project will investigate the role of LPA in SSc using skin and blood samples from SSc patients. I will measure LPA levels in patients with dcSSc, lcSSc and healthy controls and correlate these levels with visceral organ involvement, mRSS and SSc specific auto-antibodies. I will also determine an LPA-responsive gene signature, investigate the prevalence of this signature in patients with SSc, and examine this gene signature in four previously identified molecular subsets of scleroderma skin. I anticipate that LPA levels will be increased in patients with dcSSc and with certain visceral organ involvement, including ILD. I expect that an LPA-responsive gene signature will be present in the inflammatory and/or diffuse-proliferation subset of SSc.

ELIZABETH R. VOLKMANN, MD, MS

UNIVERSITY OF CALIFORNIA, LOS ANGELES

DISCOVERING PREDICTORS OF TREATMENT RESPONSE IN SCLERODERMA LUNG DISEASE



Interstitial lung disease (ILD) occurs in the majority of patients with systemic sclerosis (SSc) and is the leading cause of death in SSc. While immunosuppressive therapy is often prescribed for patients with SSc-ILD, the results of previous SSc-ILD randomized controlled trials suggest that distinct clinical phenotypes exist within SSc-ILD, as some patients in these trials experienced a progressive deterioration in lung function despite treatment with immunosuppression, while others experienced an improvement in lung function with immunosuppression. Understanding the clinical and biological characteristics of these SSc-ILD treatment responsive/resistant phenotypes is central to identifying patients with SSc-ILD who are likely to derive the greatest benefit from immunosuppression and who may preferentially respond to specific ILD therapies (i.e. cyclophosphamide versus mycophenolate). This proposal aims to investigate baseline features of SSc-ILD patients as predictors of treatment response to immunosuppressive therapy, and in doing so, take the first steps towards developing a precision medicine model for managing patients with this disabling and often fatal

disease. Using data from the Scleroderma Lung Study (SLS) II, a 14-center, randomized controlled trial comparing cyclophosphamide and mycophenolate for SSc-ILD, this study seeks to investigate whether specific baseline clinical and imaging features predict treatment response as defined by the course of the FVC measured at multiple time points over one year (Aim 1). Importantly, all patients in this study had well-characterized SSc-ILD, uniform follow up measurements, equal access to health care and a standard treatment approach. The proposed study will use innovative strategies to define ILD severity (i.e. high-resolution computed tomography (HRCT)-based quantitative imaging analysis) and to select and combine variables for inclusion in the prediction model. This study will also explore whether a focused group of select peripheral proteins, measured at different time points, can predict severity of SSc-ILD (Aim 2) and whether the addition of these peripheral proteins to the treatment response model developed in Aim 1 can improve the predictive power of this model (Aim 3). An external, prospective cohort of SSc-ILD patients treated and followed in a similar manner as those in SLS II will be used to validate the model.

TOBÉ AND STEPHEN E. MALAWISTA, MD, ENDOWMENT IN ACADEMIC RHEUMATOLOGY

The largest named endowment at the Rheumatology Research Foundation, established by a past president and member of the American College of Rheumatology, provides a permanent source of support in basic science research career development of early career investigators. Established in 2014 with a generous commitment from Mrs. Tobé and Dr. Stephen E. Malawista, who served his entire career at Yale University, this endowment ensures that physician scientists are able to continue their academic careers in vital rheumatic disease research. Annually, the Foundation's Scientific Advisory Council chooses an outstanding recipient of the Scientist Development or Investigator Awards to receive the Malawista designation.

KEVIN WEI, MD

BRIGHAM AND WOMEN'S HOSPITAL

DECONSTRUCT SYNOVIAL FIBROBLAST HETEROGENEITY IN RA

In rheumatoid arthritis (RA) synovium, accumulation of leukocytes and fibroblasts lead to pannus formation which causes irreversible joint destruction. Successful therapeutic targeting of synovial fibroblasts in RA could prevent joint damage while minimizing immunosuppression. However, complex heterogeneity of fibroblasts in RA synovium poses a major challenge towards identifying a therapeutic target. In the Brenner lab, we approached this challenge by applying cytometric cell sorting to subdivide fresh synovial fibroblasts into putative subpopulations based on surface markers. Next, we applied low input RNA-seq to generate transcriptomic profiles for each subtype. Using hierarchical clustering, we identified 3 major fibroblast subtypes with distinct transcriptomes. Classification of synovial fibroblast by single cell RNA-seq validated these 3 populations as the major fibroblast subtypes in synovium. Next, we surveyed 17 synovial samples with established RA and uncovered striking expansion of CD34negThy1pos fibroblasts. Our findings raise intriguing questions regarding the role of CD34negThy1pos fibroblasts in RA pathogenesis. Furthermore, improved understanding of their functions in RA could lead to a new therapeutic target in RA. In pursuit of our preliminary findings, we propose to validate and expand our hypothesis that CD34neg Thy1pos fibroblasts are expanded in early RA and correlate with specific synovial histological type (Aim 1). Next, we will identify unique synovial fibroblast subtype functions after TNF-stimulation (Aim 2). Our approach to deconstruct heterogeneity with fibroblast could shed light on their contribution to pathogenic expansion in RA.



A man with a mustache, wearing a white lab coat, is shown in profile, gesturing with his hands as if speaking or presenting. He is wearing a black wristwatch on his left wrist. The background is a blurred lecture hall with rows of seats.

CLINICIAN SCHOLAR EDUCATOR AWARD

THE CLINICIAN SCHOLAR EDUCATOR AWARD
SUPPORTS EDUCATORS AS THEY DEVELOP NEW
PROGRAMS AND TOOLS TO TRAIN THE NEXT
GENERATION OF HEALTH PROFESSIONALS WHO WILL
CARE FOR PATIENTS WITH RHEUMATIC DISEASES.

IRENE BLANCO, MD, MS

ALBERT EINSTEIN COLLEGE OF MEDICINE

A RHEUMATOLOGY FELLOWSHIP CURRICULUM ADDRESSING HEALTH DISPARITIES

Many factors contribute to the health disparities seen in racial and ethnic minority groups in the US. These include poverty, access to care, differences in response to treatment as well as differences in both patient and provider behaviors. These disparities span the spectrum of human disease affecting all subspecialties, including rheumatology. We know that Black and Hispanic patients tend to do worse when affected with lupus nephritis, having a higher risk of developing end stage renal disease. Black patients are less likely to undergo joint replacement for their osteoarthritis. Less educated and poorer patients are less likely to get biologic DMARDS for rheumatoid arthritis. While health disparities affect all specialties, few residency and fellowship training programs have formal curricula addressing disparities, although this training is mandated by the ACGME. Given these issues, we propose to establish a health disparities curriculum for rheumatology fellowship programs. The aims of this proposal are to: 1. Develop a needs assessment of both rheumatology fellows and programs directors to assess baseline knowledge centered on health disparities and to assess what is currently being taught in fellowships across the country. 2. Design, implement, and rigorously evaluate a health disparities curriculum giving fellows knowledge of health disparities and the social determinants of health; how they pertain to the rheumatic diseases, and arm them with the attitudes and skills to affect change as providers to mitigate these disparities. 3. Evaluate the curriculum developed under Aims 1 and 2, revise as indicated, and disseminate effective components across rheumatology fellowship programs. The goal of these three aims is to produce a rheumatology workforce armed with the tools to combat health disparities in our subspecialty, and ultimately contribute to achieving health equity for all of our patients.

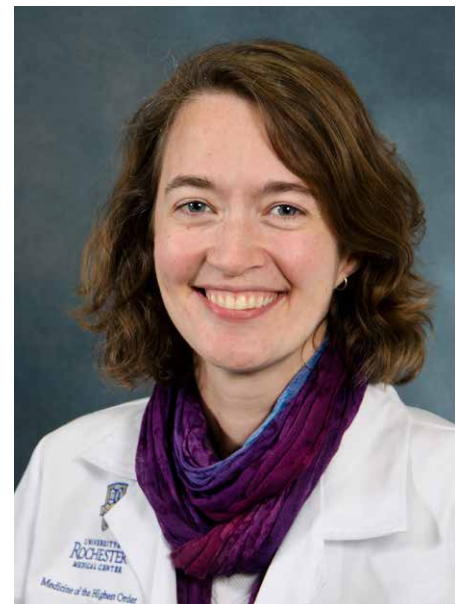


BETHANY A. MARSTON, MD

UNIVERSITY OF ROCHESTER

RHEUM4SCIENCE: AN INTERACTIVE ONLINE TUTORIAL FOR RHEUMATOLOGY FELLOWS

Rheumatology fellows are expected to understand an increasing complex body of science that informs clinical practice. Program directors surveyed in 2014 endorsed the development by the ACR of web-based modules as a resource to help teach both basic science and clinical research methodology, which some programs lacked the necessary resources to teach locally. Online learning strategies are increasingly being used to meet the needs of adult learners with different backgrounds, diverse geographic and time constraints, and individual learning goals. The availability of powerful authoring tools and learning management systems has made the creation of robust interactive teaching modules a more practical option than it was in the past. The Rheum4Science initiative was designed to create such a durable curricular resource, has identified topics of interest and content experts as authors, and is now in the process of developing a series of interactive web-based tutorials to supplement resources that may already be available to fellows and programs locally.



The aims of this project are to support and study the implementation of the Rheum4Science curriculum, ensuring that content written by scientific experts is converted into high quality interactive modules that appropriately reinforce key objectives, and evaluating the implementation of this curriculum using a framework of self-determination theory. Self-determination theory posits that increasing a learner's sense of competency, autonomy, and relatedness will increase intrinsic motivation to learn, which is associated with better educational outcomes. The inclusion of interactive elements with immediate feedback, the format of brief modular lessons framed by clinical cases, and the inclusion of an online discussion group may support these needs. Using a mix of qualitative and quantitative methods including written feedback, focus groups, online discussions, and survey results, we hope to study how this curriculum is implemented and what elements affect learning and motivation. In doing so, we hope to continuously improve the efficacy and impact of this resource, and help to ensure that graduates have the foundational knowledge and skills needed to understand research results and apply these to practice in an increasingly complex environment.

FELLOWSHIP TRAINING AWARD RECIPIENTS

The Fellowship Training Award supports the training of future rheumatologists, so they are prepared to diagnose and treat people with rheumatic diseases.

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A woman with blonde hair and glasses, wearing a white lab coat, stands on the left. A man with a mustache, wearing a blue button-down shirt and khaki pants, stands on the right. They are in a brightly lit hospital hallway with a yellowish tint. The background shows a long corridor with doors and lights.

PRECEPTORSHIPS

PRECEPTORSHIPS ENCOURAGE STUDENTS
AND RESIDENTS TO LEARN MORE ABOUT
RHEUMATOLOGY AND PURSUE CAREERS IN THE
FIELD BY SUPPORTING A ONE-ON-ONE, REAL-
WORLD LEARNING EXPERIENCE.

EPHRAIM P. ENGLEMAN ENDOWED RESIDENT RESEARCH PRECEPTORSHIP

The Ephraim P. Engleman Endowed Resident Research Preceptorship encourages residents to consider a career in rheumatology research by supporting a full-time, in-depth research experience with an established rheumatology professional. Funding for this award is made possible through an endowment from Dr. Ephraim P. Engleman.

THOMAS DORAN GARVEY, MD

PRECEPTOR: ANN K. ROSENTHAL, MD

MEDICAL COLLEGE OF WISCONSIN

ELEVATED ADENOSINE LEVELS IN AGING TISSUES CONTRIBUTE TO POLYMYALGIA RHEUMATICA

Polymyalgia rheumatic (PMR) is a common idiopathic inflammatory process preferentially affecting elderly patients. Management of PMR often requires long-term treatment with corticosteroids and their concomitant risks. Better and more targeted therapies for PMR are needed.

One therapeutic target under investigation is interleukin-6 (IL-6). This is an inflammatory cytokine which is elevated in many inflammatory syndromes including PMR. In PMR – in contrast to the other inflammatory diseases with IL-6 elevation – inflammation primarily affects large tendons and proximal muscles around the hips and shoulders. Recent work suggests that IL-6 may be locally produced in and around these tissues in patients with PMR.

Correlations between extracellular adenosine levels and IL-6 production have been noted in connective tissue cells. Furthermore, extracellular adenosine levels dramatically increase with age in some tissues. This is related to ineffective adenosine re-uptake through decreased activity of transporters such as ectonucleoside transporter 1 (ENT1).

Studies have shown that circulating IL-6 levels decrease with corticosteroid therapy and – in recent work – with IL-6 receptor blockade. Unfortunately, in PMR both symptoms and elevation in IL-6 levels recur after withdrawal of therapy, suggesting that some other upstream process is driving IL-6 elevation in PMR.

IL-6 has important roles in tendon pathology but little is known about its regulation in this tissue. The interesting connection between local IL-6 production, tendon, and high levels of adenosine with aging led us to hypothesize that an age-associated decrease in adenosine re-uptake leads to elevated adenosine levels in tendon, thereby promoting IL-6 release and facilitating the development of PMR. In this proposal, using primary porcine tenocytes from adult pigs, we will determine if extracellular adenosine increases IL-6 production in normal adult tenocytes, and if inhibition of ENT1 increases IL-6 production by tenocytes.

This project will ultimately implicate a role for adenosine in PMR and provide further support for a role for local IL-6 production in PMR. It will explain some of the characteristic pattern of tissue involvement in this disease, and lead to a larger project which may provide a pathophysiologic rationale for PMR's predilection for aging patients.



LAWREN H. DALTROY HEALTH PROFESSIONAL PRECEPTORSHIP

The Lawren H. Daltroy Award was designed to improve patient-clinician interactions through the development of a more qualified and trained health professional workforce. Funding for this award is made possible in part through the Rheumatology Research Foundation, and through an endowment from Rheuminations, Inc.

MILENA GIANFRANCESCO, PHD, MPH

PRECEPTOR: PATRICIA KATZ, PHD

UNIVERSITY OF CALIFORNIA, SAN FRANCISCO

PATIENT-CENTERED SAFETY OUTCOMES IN INDIVIDUALS PRESCRIBED HYDROXYCHLOROQUINE

Long-term use of hydroxychloroquine (HCQ) may lead to irreversible and potentially vision-threatening retinal toxicity. Guidelines were issued by the American Academy of Ophthalmology (AAO) in 2011 and 2016 to suggest that dosage of HCQ be based on an individual's body weight, and recommend how and when screening for toxicity should take place. The objective of this study is to characterize prescription patterns of HCQ according to AAO Guidelines, identify factors that may be associated with high dose prescriptions, and create a patient-clinician interface to monitor prescription dose.

The project will consist of three aims: 1) examine prescription patterns of HCQ using electronic medical records collected at the University of California, San Francisco and determine factors associated with increased dosage recommendations in order to identify individuals at risk; 2) create a feature called "HCQ Monitoring" in the patient synopsis report within an existing provider performance dashboard with the intent to increase patient-clinician interaction, and conduct preliminary analyses to measure whether this feature has a direct impact on prescription patterns. We hope that visibility of current dosage will serve as a tool to stimulate patient-physician communication around safe prescribing of HCQ.

Adverse side effects of medications, such as retinopathy, can be experienced in patients with rheumatic disease and may be more common than previously reported. By focusing on an important patient-centered safety outcome, this study hopes to encourage clinicians to properly assess their dosing patterns for patients on HCQ in order to minimize the risk of retinal toxicity and improve patient-clinician communication. Results will be informative to other potential protocols to improve patient safety outcomes. A full understanding of factors associated with high dosage of HCQ will help lead to personalized, targeted patient safety outcomes for individuals with chronic, rheumatic diseases.



MEDICAL AND GRADUATE STUDENT PRECEPTORSHIP

The Medical and Graduate Student Preceptorship encourages medical and graduate students to consider a career in rheumatology by supporting a clinical or research mentorship with an established rheumatology professional.

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Drexel University College of Medicine

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Preceptor: Arundathi Jayatilleke, MD
Drexel University College of Medicine

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Dartmouth Hitchcock Medical Center

TEERA CRAWFORD, M4

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University of Tennessee
Health Science Center

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Cleveland Clinic

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Drexel University College of Medicine

JENNIFER HERINGTON

Preceptor: Leigh F. Callahan, PhD
University of North Carolina, Thurston
Arthritis Research Center

MICHAEL RAMADA

Preceptor: Arundathi Jayatilleke, MD, MS
Drexel University College of Medicine

PEDIATRIC RHEUMATOLOGY SYMPOSIUM ABSTRACT AWARD

The Pediatric Rheumatology Symposium Abstract Award provides outstanding medical students, residents and fellows with the opportunity to attend the 2017 Pediatric Rheumatology Symposium.

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Children's Hospital of Philadelphia

EMILY A. SMITHERMAN, MD

Cincinnati Children's Hospital Medical Center

OTHER AWARDS FOR STUDENTS, RESIDENTS AND HEALTH PROFESSIONALS

The Foundation also offers a variety of awards for students, residents and health professionals beyond those currently listed here. Recipients of those awards will be announced in November. To learn more about all the awards offered by the Foundation, visit www.rheumresearch.org.

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