



**Rheumatology
Research
Foundation**

A woman with dark hair and glasses, wearing a white lab coat, is looking through a microscope in a laboratory setting. The image is overlaid with a blue tint. In the background, another person is partially visible, also working in the lab.

2020 Award Recipients

ADVANCING TREATMENTS, FINDING CURES

Creating a Brighter Future for Rheumatology



The mission of the Rheumatology Research Foundation is to advance research and training to improve the health of the more than 54 million Americans affected by arthritis or other forms of rheumatic and musculoskeletal disease. The Foundation is committed to expanding the workforce to increase patient access to professional rheumatology care and to funding innovative research that will lead to a future with improved options, enabling patients to live longer, healthier lives.

In Fiscal Year 2021, the Foundation is committing close to \$10.8 million to support awards fulfilling our mission priorities. A majority of this amount has been awarded to advance research projects that may lead to new treatment options and, hopefully, a cure for rheumatic diseases. The remainder of the funds will support efforts to recruit and train the next generation of professionals to treat rheumatology patients, which will reduce patient wait times and increase access to rheumatology care.

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

BRYCE A. BINSTADT, MD, PHD

Chair, Scientific Advisory Council
University of Minnesota

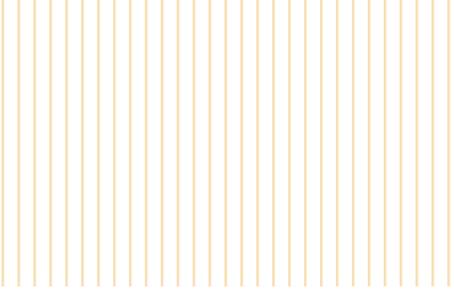


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Innovative Research Awards

The Innovative Research Award encourages independent investigators to conduct novel studies that generate new insights into the cause, progression, treatment, and outcomes of rheumatic diseases.



RICHARD BUCALA, MD, PHD

YALE UNIVERSITY

Defining Susceptibility to Lupus Inflammation

The morbidity and mortality of systemic lupus erythematosus (SLE) results from a severe and tissue-destructive inflammatory response. Macrophage Migration Inhibitory Factor (MIF) is an upstream cytokine and genetic determinant of disease severity in SLE. Caucasian and African-American SLE patients with high-expression MIF alleles have significantly increased serositis, nephritis, and CNS disease. A confluence of recent insights into MIF's mechanism of action, which include: 1) its activating role in NF- κ B and inflammasome activation, 2) identification of the unique transcription factor, ICBP90, that activates MIF's variant promoter microsatellite (-794 MIF CATT5-8), 3) the development of "humanized" MIF mice, and 4) the discovery of a small molecule inhibitor (CMFT) that blocks ICBP90 interaction with the CATT microsatellite, create an opportunity for developing a precision medicine approach to SLE treatment. We will pursue two Specific Aims:

1. Define the relationship between high-genotypic MIF expression and the innate immune response in human lupus monocytes. Our data indicate that MIF upregulates innate responses, including the NLRP3 inflammasome, in response to lupus immune complexes. We will apply sensitive multi-dimensional CyTOF and RNASeq transcriptional profiling to examine the activation responses of high- and low-genotypic MIF expressing human monocytes, and define quantitative relationships between MIF, its receptors, and downstream effector molecules.
2. Define the impact of high-genotypic MIF expression on lupus immunopathology in a novel humanized MIF mouse model. We created two humanized MIF mouse strains by recombinant replacement of the endogenous murine *Mif* gene with the low-expression MIF CATT5 and the high-expression MIF CATT7 human MIF alleles. We will define the impact of high- versus low-genotypic MIF expression on SLE immunopathology and test the ability of CMFT to reduce MIF-dependent innate responses in humanized *Sle1.Yaa* mice. The completion of these Aims will help delineate the mechanistic relationship between MIF genotype and tissue-damaging inflammatory responses, and provide proof-of-principle for precision-based inhibitors that target high-genotypic MIF expression in SLE.



CONG-QIU CHU, MD, PHD

OREGON HEALTH & SCIENCE UNIVERSITY

Novel Treatment Strategies Targeting Synovial Stroma
for Rheumatoid Arthritis

Therapy for rheumatoid arthritis (RA) has significantly improved the quality of life in these patients. However, even those most efficacious biological drugs are unable to cure the disease and have a therapeutic ceiling of response at 70%. The common mechanisms of action of these highly targeted and effective drugs are inhibition of inflammatory components and immune cells. Other mechanisms underlying the persistence of inflammation in RA have not been explored but open alternative avenues for targeted therapy. RA is primarily an inflammation of the synovium. RA synovium shares similarities to tumor tissue, namely, RA synovium proliferates and invades adjacent cartilage and bone, leading to joint destruction. The tumor like feature of RA synovium is largely contributed by fibroblast-like synoviocytes (FLS). In a healthy joint, synovium is a thin loosely organized connective tissue bordered by a lining layer which comprises resident FLS and cells of monocyte in origin. In RA, synovium grows enormously and invades into cartilage and bone. This is the result of expansion of FLS in the lining and sublining layers and infiltration of immune and inflammatory cells. FLS build a stromal network which harbors immune and inflammatory cells. Moreover, FLS actively interact with immune cells and inflammatory cells, leading to persistent inflammation of the synovium with new vessel formation and ectopic lymphoid follicles. In addition, RA FLS can also produce inflammatory cytokines that participate in the inflammatory process. Thus, RA FLS are a potential target for alternative therapy which may induce long-lasting therapeutic effect. Here in murine RA models, we propose two strategies to ablate FLS by targeting fibroblast activation protein (FAP) which is specifically expressed by FLS, thereby disrupting the stromal structure of the tumor-like synovium: 1) We will immunize arthritic mice with DNA based vaccines against FAP to generate cytotoxic T cell immunity; 2) We will use engineered chimeric antigen receptor (CAR) T cells against FAP to treat mice with arthritis. Both vaccines and CAR T cells are novel approaches to therapy of arthritis that target these non-immune cells. These strategies are highly translational into clinical trials for development of novel and potential long-lasting therapies for RA.



CARLA CUDA, PHD

NORTHWESTERN UNIVERSITY

Microglia-Specific Transcriptional Signatures in Neuropsychiatric Symptoms of SLE

Neuropsychiatric symptoms of systemic lupus erythematosus (NP-SLE), including headaches, cognitive dysfunction and psychiatric disorders, affect over 60% of SLE patients, may be among the earliest signs of SLE and often go undetected. Despite the impact of NP-SLE on health-related quality of life and although numerous mechanisms have been proposed, none can solely account for NP-SLE pathogenesis.

Microglia, the tissue resident macrophages of the brain, have recently gained more attention as contributors to disease. Microglia are comprised of at least two subsets: CD11chi disease-associated microglia (DAM), a subset of microglia thought to be instrumental in neurodegenerative diseases, and CD11clo microglia. We find that microglia from multiple NP-SLE-prone mouse models express a 'NP-SLE signature' as well as genes associated with DAM. Moreover, expression of 'NP-SLE' and 'DAM' signatures correlates with the severity of behavioral deficits in NP-SLE-prone mice. While previous studies in neurodegenerative disease models suggest that CD11chi DAM are a regulatory population, relatively little is known about microglia subsets in NP-SLE.

Thus, we will profile microglia subsets from multiple models of NP-SLE to determine the subset-specific penetrance of our newly discovered 'NP-SLE' and 'DAM' signatures as well as differences in transcriptional signatures indicative of their roles, and potential functional deficiencies, in disease. We will then compare these transcriptional profiles to that of microglia-like cells from cerebrospinal fluid of corresponding mice as well as SLE patients with central nervous system involvement to determine if our novel 'NP-SLE' and 'DAM' signatures are detectable in human disease. We will also evaluate circulating monocyte subsets in both mice and patients for NP-SLE-related signatures to address the utility of these populations as proxies for intrinsically defective microglia during NP-SLE disease.

Despite ongoing investigation into microglia subsets, in particular CD11chi DAM, in neurodegenerative disease models, we will be the first to examine the role of these populations in the pathogenesis of NP-SLE. Further, this study will be the first to determine the predictive value of our newly identified microglia-specific 'NP-SLE' and 'DAM' signatures as a surrogate for NP-SLE clinical outcomes. This information will be invaluable not only for downstream biomarker use but also targeted therapy development.



MARIA ANGELES LOPEZ-OLIVO, MD, PHD

THE UNIVERSITY OF TEXAS, MD ANDERSON CANCER CENTER

Improving Decision-making in Patients with Rheumatoid Arthritis and Concomitant Cancer Considering Immune Checkpoint Inhibition

National estimates suggest that about 40% of individuals will be diagnosed with cancer at any site at some point in their lifetime. Therefore, many patients with rheumatoid arthritis will develop a malignancy and will be treated with immune checkpoint inhibitors. Our study acknowledges the expanding impact of rheumatologists in the field of immune-related adverse events clinical care. The overall goal of this proposed study is to develop and test a decision support tool aimed at improving the decision-making process for healthcare providers and their patients with rheumatoid arthritis and melanoma who may benefit from immune checkpoint inhibition. The tool will help patients facing complicated barriers (uncertainty and decisional conflict) make decisions and will help providers deliver information and support and honor their patient's decision.



DAVID MARKOVITZ, MD

UNIVERSITY OF MICHIGAN

Centromeres and Scleroderma

Scleroderma is an often devastating disease that affects not only the skin but multiple other organs. Scleroderma is often broken down into two categories based on skin involvement: limited scleroderma and diffuse scleroderma. While scleroderma is generally considered a disease of autoimmunity, there have been indications of accompanying chromosomal dysfunction, and indeed patients with scleroderma have a higher incidence of cancer. A vital part of the chromosome is the centromere, which is key to accurate chromosomal partition during mitosis. Interestingly, most of the epigenetic marks involved in centromere biology were discovered because about half of the patients with limited scleroderma have antibodies to these proteins. Nevertheless, the concept that centromere dysfunction might play a role in scleroderma pathogenesis has not been much examined at either the epigenetic or genetic levels. The genetic study of centromeres has previously been greatly hindered by the lack of genetic information about these structures, whose tremendously repetitive DNA sequences make genomic annotation extremely difficult. We have developed PCR-based methods for assessing the status of centromeric DNA in a rapid fashion in almost all of the specific chromosomes. Using this methodology, we discovered that in diffuse scleroderma, but not in limited scleroderma, there is a profound loss of centromeric DNA accompanied by multiple chromosomal abnormalities. While patients with limited scleroderma do not exhibit defects in their centromeric DNA, in half of them, specifically those who have antibodies to centromeric proteins, we find kinetochore defects with a migration of the centromere/kinetochore out of the nucleus to a place in the cytoplasm. We now propose to more fully characterize the epigenetic defects seen in the centromeres of patients with scleroderma and to correlate these changes with defects in chromosomes. We will also examine the interplay between the epigenetic abnormalities of the centromere and the pro-fibrotic scleroderma phenotype. Further, we will ascertain whether the editing of centromere DNA can drive normal fibroblasts into the pro-fibrotic scleroderma phenotype. The proposed studies hold the potential to define a previously unexplored mechanism of scleroderma pathogenesis, centromeric dysfunction, and lead to new therapeutic approaches and management strategies for patients with scleroderma.



LAURA F. SU, MD, PHD

UNIVERSITY OF PENNSYLVANIA

Self-reactive CD4+ T Cells Drive Autoantibody Production in Ectopic Lymphoid Aggregates in Rheumatoid Arthritis

Rheumatoid arthritis (RA) is a debilitating disease that causes inflammation and deforming joint destruction. RA afflicts 1.5 million people in the United States and is becoming increasingly more common as the average age of the U.S. population increases. A hallmark of RA is the production of autoantibodies. Approximately 70% of RA patients generate rheumatoid factor (RF) and autoantibodies to cyclic citrullinated antigens (anti-CCP). While cognate interactions with the follicular helper subset of CD4+ T cells (Tfh) are broadly required for B cell differentiation and antibody affinity maturation, the specific mechanisms that promote autoreactive antibody formation in RA and other autoimmune diseases remain poorly understood. Recent studies have demonstrated an abnormal accumulation of autoantibody producing B cells with a distinct phenotypic profile in RA patients. These B cells belong to a broader effector B cell population generally referred to as age-associated B cells (ABC). ABCs arise with age and accumulate in the setting of autoimmunity and chronic infection. A dominant feature of ABCs is the expression of the transcription factor T-bet. Using HIV infection as a model to study chronic inflammation, we have observed an accumulation of T-bet+ B cells in inflamed primary human lymph nodes. Notably, we found T-bet expression in B cells correlated with the abundance of a distinct CXCR5- CD4+ T cell population characterized by up-regulation of activation markers and high PD-1 and ICOS expression. These CXCR5- CD4+ T cells that we identified in HIV-infected LNs phenotypically resemble a previously described circulating population of CXCR5- CD4+ T cells that has been implicated in the formation of ectopic lymphoid aggregates in the synovial tissues of RA patients. Whether CXCR5-PD-1+CD4+ T cells contribute to autoantibody production in RA is unknown. In the proposed study, we will use precise cellular tools and high dimensional imaging modalities to test the hypothesis that the CXCR5-PD-1+ phenotype is enriched for autoreactive CD4+ T cells that drive ectopic autoantibody production in inflamed synovium of RA patients.



HENRI TIEDGE, PHD

SUNY DOWNSTATE MEDICAL CENTER

An RNA Mechanism in Systemic Lupus Erythematosus

Neuronal regulatory Brain Cytoplasmic (BC) RNAs are translational regulators that operate in synapto-dendritic neuronal domains. Lack of rodent BC1 RNA in BC1 knock-out (BC1 KO) animals causes cognitive impairment and epileptogenesis. BC RNAs are delivered to synapto-dendritic subdomains by heterogeneous nuclear ribonucleoprotein A2 (hnRNP A2), a trans-acting RNA transport factor. hnRNP A2 recognizes a noncanonical GA motif in the BC RNA dendritic targeting element (DTE) in interactions that are required for the dendritic delivery of these RNAs.

Systemic lupus erythematosus (SLE) is an autoimmune disease that often involves neurological or psychiatric impairments. We detected an autoimmune response to BC RNAs in a subset of SLE patients. SLE autoantibodies against BC RNAs (SLE anti-BC abs) belong to the IgG class of immunoglobulins and bind to the same DTE as dendritic transport factor hnRNP A2. SLE anti-BC abs compete with hnRNP A2 for access to the BC RNA dendritic targeting element, as a result impeding BC RNA synapto-dendritic delivery.

Here it is hypothesized that absence, or reduced presence, of regulatory BC RNAs in synapto-dendritic domains, caused by SLE autoimmune anti-BC ab competition with hnRNP A2, will cause phenotypic manifestations that are similar to those observed in BC1 KO animals and may include cognitive dysfunction and epileptogenesis. In the Innovative Research Award project proposed here, it is planned to investigate three key questions. (i) What is the molecular mechanism underlying the ability of autoimmune SLE anti-BC abs to compete with RNA transport factor hnRNP A2? (ii) Does such competition cause defects in the synapto-dendritic delivery of regulatory BC RNAs in neurons? (iii) Do autoimmune anti-BC abs give rise to cognitive impairment and epileptogenesis in vivo? Are serum levels of SLE anti-BC abs markers of disease status, i.e. of active disease, remission, and flares? There is confidence that investigating a novel RNA mechanism in SLE will in the long-term help address major gaps in our understanding of this complex disease.



BIN WANG, PHD

THOMAS JEFFERSON UNIVERSITY

MAGI-3 as a New Target for Therapy of Osteoarthritis

Osteoarthritis (OA) is a degenerative joint disease characterized by loss of articular cartilage and alterations in subchondral bone architecture. Parathyroid hormone-related protein (PTHrP) is a heterogeneous polypeptide with sequence homology to PTH. Both PTH and PTHrP bind to the type 1 PTH receptor (PTH1R). Signaling through the PTH1R maintains bone remodeling and regulates the articular chondrocyte phenotype under healthy conditions. PTH or PTHrP activates multiple signaling pathways, but not all of them are anabolic. Both published as well as our preliminary data demonstrate a Gs/cAMP signaling arm that is therapeutic and a Gq/phospholipase C (PLC) signaling arm that is pathogenic. Systemic or intra-articular daily injection of PTH or PTHrP is able to prevent and treat OA. PTHrP is normally secreted by articular chondrocytes in low levels and is increased in OA. An alternative and superior strategy is to “tune” PTH1R signaling to preferentially activate the PTH1R therapeutic signaling arm, while avoiding its pathogenic signaling arm. Our preliminary data show that MAGI-3 (membrane-associated guanylate kinase with inverted orientation 3) is a novel PTH1R-interacting PDZ protein, and MAGI-3 expression in articular cartilage is reduced in human OA and in a mouse OA model. Beta-catenin mediates canonical Wnt signaling pathway and promotes chondrocyte hypertrophy. Recent data from our group and others have demonstrated that beta-catenin interacts with the PTH1R and switches PTH1R signaling from Gs/cAMP to Gq/PLC activation. Importantly, our preliminary data indicate that MAGI-3 exhibits higher binding affinity with PTH1R than that of beta-catenin with PTH1R, and exogenous MAGI-3 enhances PTHrP stimulation of cAMP formation and reduces PLC activity in chondrocytes. Based on these findings, the central hypothesis of this proposal is that MAGI-3 competes with beta-catenin binding to the PTH1R to reverse the beta-catenin-mediated PTH1R signaling switch, and exogenous MAGI-3 can prevent/treat OA progression. Two specific aims will test this hypothesis. Aim 1 will characterize how MAGI-3 counteracts the beta-catenin-mediated PTH1R signaling switch and inhibits chondrocyte differentiation and apoptosis in vitro. Aim 2 will establish whether exogenous MAGI-3 protects against cartilage damage in an in vivo OA model. The predictive results are that external control of MAGI-3 expression will prevent cartilage lesions and increase cartilage repair via shifting the PTH1R signaling toward its therapeutic pathway. Successful completion of these studies therefore constitutes important preclinical findings that would facilitate advancement of this work toward clinical trials of OA and ultimate application in humans. The long-term goal of this project is to design cost-effective anabolic agents with less toxicity and convenient use for the treatment of OA.



Career Development Bridge Funding Awards

CAREER DEVELOPMENT BRIDGE FUNDING AWARD: R BRIDGE

The R Bridge Award encourages essential rheumatology research by supporting promising investigators who are revising outstanding NIH R01 or VA RCS/ORD award applications.

ALFRED H. KIM, MD, PHD

WASHINGTON UNIVERSITY IN ST. LOUIS

Complement Activation Signatures in Systemic Lupus Erythematosus

Clinicians assess complement activation through the components C3 and C4 in serum. Since complement activation occurs during systemic lupus erythematosus (SLE) flares, C3 and C4 levels should decrease. During systemic inflammation though, the liver increases C3 and C4 production. Thus, there is both consumption (due to their activation on cell surfaces) and production (by the liver) of C3 and C4 during SLE flares, leading to the underdetection of flares using these traditional biomarkers.

Complement activation generates products that are found in blood and on the surface of cells. The CASTLE (Complement Activation Signatures in sysTemic Lupus Erythematosus) study was started to understand the relationship between complement activation products (CAPs) and SLE disease activity. In the pilot phase of CASTLE, we showed that the CAP iC3b, when combined with C3 as a ratio (iC3b/C3 ratio), independently associated with SLE disease activity and outperformed C3 and C4. Leveraging the CASTLE cohort, this proposal will greatly expand the number of soluble and cell-bound CAPs analyzed, yielding the most comprehensive examination of the relationship of CAPs with SLE disease activity and damage.

Thus, we hypothesize that CAPs serve as biomarkers that associate with both SLE disease activity and improved future outcomes and induce pathogenic transcriptional pathways in immune cells. Three aims are proposed: 1) Do normal iC3b/C3 values lead to improved outcomes in SLE? 2) Do patients with SLE stratify into distinct CAP signatures that associate with SLE disease activity? 3) What is the function of activated C3 (hydrolyzed C3) in SLE PBMCs? We anticipate to 1) define the clinical utility of CAPs, 2) identify SLE patient stratifications based on CAP signatures, and 3) pioneer an understanding of how CAPs drive pathogenic responses in SLE immune cells using CITE-seq to delineate CAP-bearing cells.



CAREER DEVELOPMENT BRIDGE FUNDING AWARD: R BRIDGE

CARA L. LEWIS, PT, PHD

BOSTON UNIVERSITY

Etiology of cam morphology in adolescent athletes

Cam morphology is a variant shape of the proximal femur characterized by a nonspherical portion of the femoral head at the head-neck junction. Cam morphology can lead to femoroacetabular impingement (FAI) syndrome, chronic pain, and early onset osteoarthritis (OA). The primary treatment for FAI syndrome is hip arthroscopy to reshape the bone. Despite improvement in symptoms with this treatment, many individuals continue to have deficits that negatively impact their daily lives. For a vast majority of these individuals, prevention—rather than surgery—may be preferable. To make prevention possible, we need to determine the etiology of cam formation.



Currently, there is strong evidence that cam morphology develops during skeletal growth, rather than as an adaptation after skeletal maturity; however, it is not well established why cam morphology develops. A common assumption is that impact loading from high levels of activity during adolescence leads to changes in the proximal femoral growth plate and, subsequently, to the development of cam morphology. Yet no rigorous biomechanical study has characterized, longitudinally, the patterns of loading that contribute to growth plate reorientation in individuals who are at high risk for developing cam deformity, such as adolescent athletes who specialize in ice hockey or other “high-risk” sports.

The long-term goal of my research is to improve the lives of individuals with chronic musculoskeletal pain and prevent or slow the progression of musculoskeletal damage through improved knowledge of joint function, leading to advanced, targeted intervention strategies. For this study, we focus on understanding why the bone shape underlying FAI syndrome develops. We investigate the loading characteristics that contribute to the future development of cam morphology, and how changes in the three dimensional shape of the growth plate precede and contribute to cam morphology. By critically examining relationships between movement patterns, hip joint loading, and femoral growth plate morphology, these studies will advance our understanding of cam morphology etiology by identifying mechanism(s) that promote abnormal bone growth prior to skeletal maturity. Only by understanding the etiology of cam morphology itself can we design strategies to reduce or prevent the morphology, along with the subsequent FAI syndrome and OA.

CAREER DEVELOPMENT BRIDGE FUNDING AWARD: R BRIDGE

JEFFREY A. SPARKS, MD, MMSC

BRIGHAM & WOMEN'S HOSPITAL

Rheumatoid Arthritis-Related Autoantibodies, Articular Inflammation,
and RA-Associated Interstitial Lung Disease



Rheumatoid arthritis (RA) is a systemic autoimmune disease affecting 1% of adults characterized by serious consequences including chronic pain, disability, accumulation of morbidities, and excess mortality. Patients with RA are susceptible to developing interstitial lung disease (ILD), a devastating complication with high morbidity and mortality. Previous studies suggest that mucosal surfaces of the lung may be an initiating site for RA, where autoantibodies may be formed before joint symptoms develop. Aberrant post-translational modifications (PTM) to proteins may serve as neoantigens forming local inflammation in the lungs and production of autoantibodies related to PTM. Therefore, RA-related autoantibodies, articular inflammation, and RA-ILD may be linked throughout the disease course of RA.

The R01 investigations will study whether RA-related autoantibodies and articular inflammation predict subclinical and clinically apparent RA-ILD. In Aim 1, we will perform a case-control study using the Brigham RA Sequential Study (BRASS) and will replicate results in the Partners Biobank. The RRF R Bridge will support the identification of RA-ILD cases in the Partners Biobank and quantify the incidence of RA-ILD through the RA disease course. The R01 will support the measurement clinical and PTM RA-related autoantibodies. In Aim 2, we will perform a multi-site prospective study of patients with new-onset RA who will undergo chest high-resolution computed tomography imaging to investigate the relationship between articular inflammation and subclinical RA-ILD in early RA. The RRF R Bridge will support overall planning and initiation of recruitment at the BWH site. In Aim 3, we will analyze whether smokers in COPDGene with elevation of RA-related autoantibodies without articular RA are more likely to have interstitial lung abnormalities (ILA). COPDGene is a large US nationwide observational study that has already been phenotyped for presence or absence of ILA. The RRF R Bridge will support enhancement of the biostatistical analytic approach throughout the R01.

CAREER DEVELOPMENT BRIDGE FUNDING AWARD: K SUPPLEMENT

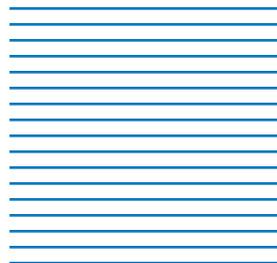
The K Supplement Award encourages junior investigators to expand promising research by providing additional support to cover research costs and help investigators become independent.

APRIL LYNN BARNADO, MD, MSCI

VANDERBILT UNIVERSITY MEDICAL CENTER

Using the electronic health record to risk stratify SLE nephritis patients and SLE pregnancies

My proposal will directly impact the management and treatment of the most vulnerable systemic lupus erythematosus (SLE) patients, SLE nephritis patients and pregnant SLE patients. My proposal aims to identify SLE nephritis and pregnant SLE patients that are at highest risk for severe adverse outcome such as dialysis, renal transplantation, preeclampsia, and preterm delivery by coupling genetic data with real-time clinical data in the electronic health record. By identifying SLE patients at highest risk for adverse outcomes, clinicians can then more aggressively target screening, resources, and treatments to the highest risk patients. Overall, this work will lay the foundation to leverage the electronic health record as part of a learning health system that 1) identifies SLE patients at highest risk for adverse outcomes and 2) informs precision-based approaches that tailor immunosuppressants. Accomplishing these goals will improve outcomes for SLE patients and reduce disease-related health disparities.



CAREER DEVELOPMENT BRIDGE FUNDING AWARD: K SUPPLEMENT

MILENA A. GIANFRANCESCO, PHD, MPH

UNIVERSITY OF CALIFORNIA, SAN FRANCISCO

Estimating and predicting the effect of biologics on disease activity in rheumatoid arthritis

While biologic medications have improved disease control and are associated with significant gains in quality of life, there is currently no established treatment strategy for patients beyond first-line treatment with methotrexate. Both patients and clinicians often juggle drug efficacy, cost, and concern about side effects in their decision making. How disease activity levels differ based on a variety of patient factors, such as age, race, and ethnicity is unknown, leading clinicians to have insufficient information to predict the probability of remission occurring in an individual patient who is prescribed a particular biologic.

This proposal will utilize national registry data (RISE) to examine over 100,000 individuals with RA to address two specific aims. In Aim 1, Dr. Gianfrancesco will use these databases to determine the longitudinal causal effect of biologics on disease activity. In Aim 2, a machine learning model to predict disease activity level at a patient's next clinic visit will be developed and validated. Findings from this study will further elucidate factors associated with disease activity for individuals prescribed biologics, thereby improving their effectiveness in the ambulatory settings.

Completing the proposed research will allow Dr. Gianfrancesco to gain experience in state-of-the-art computational methods using large datasets to better understand important patient outcomes. This award will provide the skills, mentorship, and experience necessary to propel her to independence and enable her to lead an independent multidisciplinary research program.



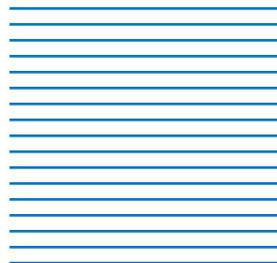
LAUREN A. HENDERSON, MD, MMSc

BOSTON CHILDREN'S HOSPITAL

Targeting T cell and B cell Interactions to Improve Outcomes
in Oligoarticular Juvenile Idiopathic Arthritis

Oligoarticular juvenile idiopathic arthritis (oligo JIA) is characterized by limited joint involvement (<5 joints) during the first 6 months of disease. The oligo JIA classification encompasses a cluster of patients defined by female sex, young age at disease onset, high rates of anterior uveitis, and ANA positivity. Unique HLA risk alleles and evidence of dysregulated humoral immunity distinguish this population from children who develop oligo JIA after 6 years of age. The disease mechanisms that drive chronic arthritis and uveitis in young, ANA positive, oligo JIA patients are not understood.

We hypothesize the pathogenic interactions between B cells and T cells may drive disease in patients with early onset and ANA positive oligo JIA. The proposed studies will test our hypothesis with human biosamples from the PIs repository and the LIMIT-JIA trial, which will evaluate abatacept (CTLA4-Ig) treatment in oligoJIA. Flow cytometry, transcriptomic studies, single cell RNA sequencing, and T-B cell functional assays will be employed to address these questions. This research will advance disease classification in JIA based on biology and may identify unique biomarkers and therapeutic approaches for children with oligo JIA.



DEEPAK A. RAO, MD, PHD

BRIGHAM AND WOMEN'S HOSPITAL

Regulation of T cell production of CXCL13

Many rheumatic diseases are characterized by pathologic T cell-B cell interactions and production of autoantibodies. The T cell populations that help B cells in autoimmune diseases vary in phenotype and include T follicular helper (Tfh) cells, which reside in follicles of secondary lymphoid organs, as well as T peripheral helper (Tph) cells, which are B cell-helper T cells that migrate to inflamed peripheral tissues such as the rheumatoid joint. Tph cells and Tfh cells share the ability to recruit B cells via production of the B cell chemoattractant CXCL13 and then promote B cell differentiation through both surface interactions and secreted cytokines. The signals that regulate development and function of Tph cells and Tfh cells in autoimmunity remain incompletely described, and particularly little is known about T cell production of CXCL13. Our project utilizes human primary T cells and patient samples to evaluate the factors that influence the development and function of Tph cells. This proposal builds upon ongoing work supported by the K08 award, now helping to pursue a new direction with a particular emphasis on identifying local factors in RA synovial fluid that may promote or alter the function or differentiation of Tph cells. We hypothesize that local signals within joints differ between different inflammatory arthritides, and that such signals may help to dictate the extent of synovial Tph cell accumulation. We expect that these studies will help to identify factors within synovial fluid that promote Tph cell accumulation in RA joints, and we anticipate that these efforts will bolster a promising R01 application that aims to develop new methods to manipulate Tph cells therapeutically.



CAREER DEVELOPMENT BRIDGE FUNDING AWARD: K BRIDGE

The K Bridge Award encourages junior investigators to continue conducting research into novel ideas while reapplying for an NIH or VA career development award.

ASHIRA D. BLAZER, MD, MSCI

NEW YORK UNIVERSITY

Macrophages, Apolipoprotein L1 Genotype, and Immunometabolic Challenges (MAGIC)

Dr. Blazer is an Assistant Professor in the New York University School of Medicine Division of Rheumatology. Her interests are in studying the biologic and genetic determinants of systemic lupus erythematosus severity in patients of African ancestry. Her current translational research project focuses on polymorphisms in the Apolipoprotein L1 (APOL1) gene, which are exceptionally common in those of West African heritage as they confer protection against African trypanosomiasis. APOL1, a major contributor to excess renal and cardiovascular risk in the African diaspora, is responsive to inflammatory cytokines and may be of heightened consequence in chronic inflammatory disease sufferers such as SLE patients. She has forged multiple international collaborations with rheumatology programs in West Africa and through this work has preliminarily shown that APOL1 variant carriers with SLE experience accelerated damage accrual, renal progression, and ultimately mortality. Further, beyond the clinical associations, Dr. Blazer is studying the mechanisms underpinning genetic toxicity through cultivating novel primary cell culture models. She has shown that metabolic disturbances in both endothelial and inflammatory cells render the candidate tissues vulnerable to chronic inflammatory stress. These data have furnished several funded grant awards including the Rheumatology Research Foundation's Scientist Development Award and the Pfizer Foundation's Medical and Academic Partnership fellowship. By studying the interplay between chronic inflammation, cellular function, and APOL1 gene expression, Dr. Blazer aims to provide personalized treatment options to the most vulnerable of patients.



CAREER DEVELOPMENT BRIDGE FUNDING AWARD: K BRIDGE

SARAH LYNN PATTERSON, MD

UNIVERSITY OF CALIFORNIA, SAN FRANCISCO

Relationship of Stress, Physical Activity, and Cell-Specific Gene Expression on Longitudinal Disease Activity in Rheumatoid Arthritis

Fluctuations in rheumatoid arthritis (RA) disease activity (i.e. flares) are thought to be multifactorial in origin, but the contributions from lifestyle and behavioral factors such as psychosocial stress and physical activity are poorly understood. Identification of lifestyle factors that affect RA disease activity, as well as novel biomarkers for measuring their effects, is needed to inform non-pharmacologic interventions that can, in combination with disease-modifying antimalarial drugs (DMARDs), improve clinical outcomes. The proposed study will generate preliminary data for my revised K23 proposal, which aims to test the following hypotheses: (a) RA patients with higher psychosocial stress will demonstrate a unique cell-specific gene expression signature assessed by droplet-based single cell RNA sequencing (dscRNAseq) and greater RA disease activity compared to patients with low stress; and (b) physical activity for at least 150 minutes per week (assessed objectively by actigraphy) independently and prospectively associates with less chronic psychological stress and lower symptom burden. I will leverage resources from an NIH-funded longitudinal RA cohort (RAZZ, N=150), including data from actigraphy, blood specimens, and patient-reported outcomes. My K23 proposal builds on RAZZ by adding objective physical activity data, physician-assessed disease activity assessments (Clinical Disease Activity Index and Disease Activity Score-28), and transcriptomic data. Additionally, a subset of participants will be enrolled in a qualitative assessment to identify barriers to physical activity and exercise modalities that are acceptable and feasible among people with RA. This will be the first longitudinal study to examine the interplay of perceived stress, cell-specific stress-responsive gene expression, and physical activity on disease outcomes in RA. Determining the impacts of psychological factors and modifiable lifestyle behaviors on molecular pathways and disease activity in RA will inform future studies to improve outcomes for this patient group.



CAREER DEVELOPMENT BRIDGE FUNDING AWARD: K BRIDGE

LIN SHEN, MD, PHD

UNIVERSITY OF CALIFORNIA, SAN FRANCISCO

The Impact of TCR Signaling Strength on Peripheral Tolerance and Autoimmunity

Autoimmune rheumatic diseases, which constitute a broad range of chronic illnesses, cause significant morbidity and mortality in the US and worldwide. The strong allelic association of major histocompatibility complex genes with rheumatoid arthritis and lupus in genome-wide association studies is compelling evidence that TCR recognition and signaling plays a critical role in pathogenetic processes leading to autoimmune diseases. However, how altered TCR signaling strength affects peripheral tolerance and promotes autoimmunity remains incompletely understood. Here we seek to understand how abnormal TCR signaling resulting from mutations in ZAP-70, including one from human patients with complex autoimmune syndrome, may alter T cell antigen sensitivity, affect T helper cell fate, and impair peripheral tolerance. We will test the central hypothesis that tuning TCR signaling strength can subvert mechanisms of peripheral tolerance to produce autoimmunity. The advance in understanding the mechanisms for peripheral tolerance, including regulation of T cell responsiveness and T helper cell fate, may have implications in preventing cancer immunotherapy related adverse events and identification of new therapeutic targets for autoimmune diseases.



CAREER DEVELOPMENT BRIDGE FUNDING AWARD: K BRIDGE

ELENI TINIAKOU, MD

JOHN HOPKINS UNIVERSITY

RNA Polymerase III specific CD8+ T cells: a mechanistic insight into cancer-induced autoimmunity in scleroderma

There is increasing evidence from human and animal studies suggesting an immunologic link between cancer and autoimmunity. The immune system is able to reject cancer through recognition of self and altered self-antigens; however, recognition of self-antigens in healthy tissues could lead to autoimmunity. Scleroderma (SSc) offers a unique opportunity to study this relationship since SSc patients with autoantibodies to RNA polymerase III (RPC1) have an increased risk of cancer coincident with SSc onset. Genetic alterations within the RNA polymerase III (POLR3A) locus were identified in cancers from anti-RPC1+ SSc patients and distinct populations of CD4+ T cells were detected that recognized normal and mutated versions of RPC1. Together, these observations suggest that antitumor immunity initiated against the mutated RPC1 protein could cross-react with the wild-type protein and lead to SSc. However, since cytotoxic CD8+ T cells play a critical role in the killing of tumor cells, and there is increasing evidence of involvement of CD8+ T cells in the pathogenesis of SSc, an important outstanding question is whether RPC1-specific cytotoxic T cells can be identified in patients with SSc and cancer. This proposal seeks to investigate RPC1-specific CD8+ T cells in the peripheral blood and target tissues of patients with SSc and cancer. Aim 1 will examine how the protein RPC1 is processed by antigen presenting cells and determine the repertoire of naturally presented MHC class I RPC1 peptides. In aim 2, the frequency, phenotype, and function of RPC1-specific CD8+T-cells will be studied in SSc patients with cancer. Aim 3 will examine RPC1-specific CD8+T-cells that are directly involved in both the antitumor response at the site of the cancer as well as autoimmune damage of affected skin tissue from SSc patients. The results of this study will lay the foundation for future studies exploring whether T cell responses to RPC1 could be used as targeted monitoring tools and antigen-specific immunotherapies for SSc, and inform the study of other cancer-associated rheumatic diseases.



CAREER DEVELOPMENT BRIDGE FUNDING AWARD: K BRIDGE

KAZUKI YOSHIDA, MD, MPH, SCD

BRIGHAM & WOMEN'S HOSPITAL

Gout and Cardiovascular Comorbidities: Disentangling the Interplay with Advanced Methods to Address Measurement Issues

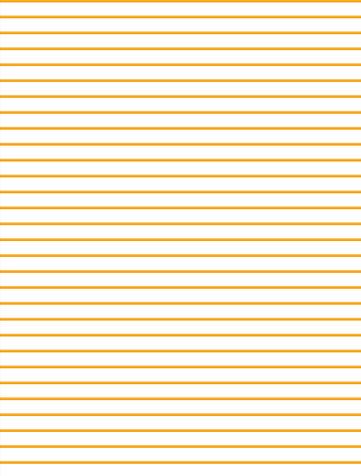
Gout is the most common inflammatory arthritis, afflicting an estimated 9.2 million Americans. Reflecting gout's chronic metabolic nature, patients with gout typically experience multimorbidity. For example, patients with gout – particularly women – have a 2-4 times higher cardiovascular (CV) comorbidity burden compared to those without gout.

However, measurement issues hamper our understanding of the true underlying link between gout and CV comorbidities. Low sensitivities of self-reported CV comorbidities suggest underestimation of comorbidity prevalence in existing reports. For example, only one-third of heart failure patients correctly self-report. Investigation of potential causal links between hyperuricemia/gout and CV comorbidities may benefit from consideration of mediating mechanisms such as chronic vascular inflammation and a heightened state of acute inflammation in gout flares. Nevertheless, self-report of gout flares does not fully coincide with physician assessment. Inflammatory biomarkers, although objective, are not free from measurement errors as evident from their varying levels of reliability. These measurement issues can obscure and hide causal links. Incorporating patients' perspectives is fundamental to the effective management of multimorbid patients. However, existing multimorbidity indices have not been validated against gout patients' lived experience. Despite such concerns, standard statistical analyses typically employed in clinical research ignore imperfect measurements, potentially introducing bias, reducing power, and masking important features – the so-called “triple whammy of mismeasurement.”

My long-term goal is to improve the management of gout patients with CV comorbidities by conducting high-quality clinical research through the application, development, and dissemination of advanced quantitative methods that account for measurement issues. The future K project on the interplay of gout and comorbidities will tackle important measurement issues in (1) cross-sectional prevalence estimation, (2) causal investigation, and (3) patient-centered consideration of disease burden. During the K Bridge period, I will develop preliminary data to demonstrate the feasibility of these aims and the significance of measurement issues.

Through this K-Bridge and future K award period, I will build practical skills in the assessment of measurements and robust quantitative methods to account for measurement issues in analyses. I aim to establish an independent research career as a patient-oriented researcher contributing to the methodological advancement of clinical research in rheumatic diseases.





Investigator Awards

The Investigator Award encourages junior investigators to continue conducting innovative research that will be competitive for more significant funding while they establish themselves as independent investigators.

KATHRYN LOUISE BACON, PHD, MPH

BOSTON UNIVERSITY

Machine-learning Analysis of Longitudinal Gait
Data in Osteoarthritis

Osteoarthritis (OA), the most common arthritis, is a leading cause of disability. In the U.S., the cost and number of people treated have both more than doubled since 1996 due to an increasingly obese, aging population. Effective treatments for preventing or delaying progression of OA are lacking, with end-stage disease often leading to joint replacement.

OA is a mechanically driven disease, and the altered gait of persons with knee OA may accelerate disease progression, worsen functional loss, and contribute to pathology in nearby joints. Gait changes may be subtle, especially in early OA. Understanding elements of gait that adversely affect OA outcomes may provide novel insights into managing OA and downstream consequences. Wearable gait sensors, used in or outside of labs, coupled with state-of-the-art machine learning (ML) analysis techniques, may offer fresh prospects for characterizing the relation of gait changes to OA outcomes. ML algorithms can “learn” connections within data using few assumptions. Currently used in Parkinson’s disease research, these approaches have not yet been systematically applied to gait in OA.

My hypothesis is that there are elements of OA gait that increase the risk of function loss, pain, and pathology in knees and nearby joints. We will leverage data from the Multicenter Osteoarthritis Study (MOST), a longitudinal study of individuals with or at risk of knee OA, which provides wearable sensor data on a large number of individuals plus data on OA outcomes. Two-year follow-up data will allow assessment of longitudinal outcomes.

Aims: (1) Use ML to identify gait features associated cross-sectionally and longitudinally with knee pain, radiographic OA, physical function and other lower extremity joints with frequent pain. We hypothesize different gait features will be associated with symptomatic vs. structural outcomes. (2) Compare the discriminant ability of ML models to more traditional analysis methods.

Using advanced machine learning strategies applied to spatio-temporal gait data, we hope to provide new insights into gait abnormalities and aid in identifying rehabilitation strategies to intervene in OA biomechanical processes. Sensors might also allow for clinical implementation of rehabilitation interventions that aim to alter gait for people with knee OA.



SABRINA G MUCA, MD, MSCE

CHILDREN'S HOSPITAL OF PHILADELPHIA

Exploring Resilience in Adolescent Chronic Musculoskeletal Pain

Long-term physical and psychosocial outcomes for adolescents with chronic musculoskeletal pain (CMP) are poor with increased healthcare utilization and psychological co-morbidities among affected adolescents. Additionally, current treatment regimens for adolescent CMP have limited accessibility and poor patient adherence. Resilience is a dynamic process of positive adaptation or development in the context of significant adversity such as living with excessive chronic pain. The overall objective of the proposed project is to evaluate key psychosocial factors, including resilience, associated with disease severity and treatment adherence in adolescent CMP as well as to apply a resilience-training intervention to this patient population. This will be accomplished through two specific aims, which are to 1) evaluate baseline psychosocial factors associated with disease severity and treatment adherence at 6 months after diagnosis among adolescents with CMP, 2) conduct a pilot trial of an existing, successful resilience training intervention for youth with chronic illnesses, PRISM (Promoting Resilience in Stress Management), using a mixed-methods approach to assess feasibility and acceptability as well as determine any potential adaptations. Findings from Aim 1 will identify modifiable psychosocial factors associated with treatment adherence and long-term prognosis. Findings from Aim 2 will serve as preliminary data for a future study to perform a multicenter RCT of PRISM for adolescent CMP. Overall, these studies will address how to improve access to and efficacy of non-pharmacologic treatments for adolescent CMP.



ANNA HELENA JONSSON, MD, PHD

BRIGHAM & WOMEN'S HOSPITAL

Roles of Granzyme K+ CD8 T Cell Subsets Expanded
in Rheumatoid Arthritis

CD8 T cells are enriched in synovium and synovial fluid of patients with rheumatoid arthritis (RA), yet little is known about their functions and subsets. We have found that synovial CD8 T cells make cytokines IFN γ and TNF at the same or higher frequency than CD4 T cells, indicating that CD8 T cells promote and perpetuate inflammation in RA synovium. Our goal is to investigate the subsets of CD8 T cells present in inflamed joints in RA, how they are activated, and what effects they have on other cells. The majority of CD8 T cells in the synovium express granzyme K (GzmK), a protein that, unlike the classic cytotoxic protein granzyme B (GzmB), cannot initiate apoptotic caspase cascades. This was a surprising finding, as terminal differentiation of CD8 T cells is usually associated with GzmB expression alone. In this Foundation-funded project, we will investigate the factors that govern the expansion and activation of GzmK+ cells in inflamed joints in RA. We will also assess the effect of GzmK molecules on synovial fibroblasts from patients with RA. These studies will provide insights into the role of CD8 T cells in RA and hopefully also identify new treatment targets.



CRISTINA MARIELLA LANATA, MD

UNIVERSITY OF CALIFORNIA, SAN FRANCISCO

The Methylome Across the Lifespan as a Biomarker for Systemic Lupus Erythematosus Outcomes and Disease Activity

The goal of the current study is to examine the role of DNA methylation as a biomarker for disease activity and progression by utilizing a multi-ethnic longitudinal cohort of SLE patients. Currently no reliable predictors of long-term outcomes and organ-specific involvement for SLE patients have been identified. Although substantial evidence links DNA methylation with specific SLE manifestations, its potential utility as a biomarker for outcomes has not been examined. This proposal utilizes the California Lupus Epidemiologic Study (CLUES), a CDC-funded multi-ethnic longitudinal cohort of SLE patients with detailed molecular and clinical data to address three specific aims. In Aim 1, I will develop a model of SLE outcomes based on previously generated DNA methylation profiles. In Aim 2, I will examine the dynamics of the methylome longitudinally in relationship to disease flares and remissions. In Aim 3, I will obtain newborn bloodspots from CLUES SLE participants to determine whether methylation differences associated with SLE are present at the time of birth in participants who subsequently develop SLE. Findings from this study will increase understanding of the DNA methylome's role as a biomarker for SLE outcomes.

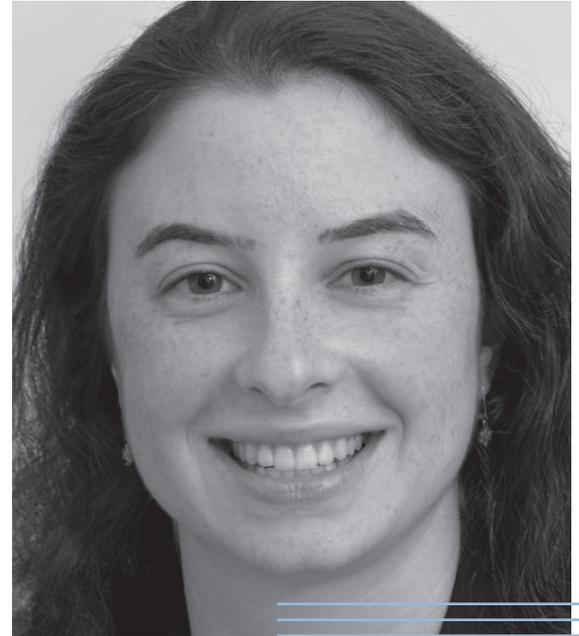


JULIA MANASSON, MD

NEW YORK UNIVERSITY

Genetic, Microbial and Immune Signatures of Psoriatic Disease Progression

Psoriasis (PsO) is an immune-mediated skin disease that in a third of cases evolves into psoriatic arthritis (PsA). The pathogenesis of this transition is poorly understood, and we lack the means to predict which individuals will progress from skin to synovio-entheseal inflammation. Importantly, PsO typically precedes PsA by 5-7 years, providing a rare opportunity to study mechanisms of disease progression. Genes play a role in the development of PsA as patients with PsO who have first-degree relatives with PsA are at the highest risk for progression. Apart from genes, immune system dysregulation, particularly the interleukin-23/T-helper 17 (IL-23/Th17) axis, and microbial perturbations have also been associated with psoriatic disease. We therefore propose to further elucidate the contribution of these factors to PsO-to-PsA progression in genetically similar populations: 1) PsO patients and their biologic first-degree relatives with PsA; and 2) monozygotic twins with discordant psoriatic disease. In Aim 1 we will identify Th17 immune cell phenotypes across the psoriatic disease spectrum by characterizing the gene expression profiles of circulating Th17 cells and building Th17 regulatory networks reflective of psoriatic disease. In Aim 2 we will identify the differentiating microbial features across the psoriatic disease spectrum by characterizing the intestinal and cutaneous bacterial microbiome. In Aim 3 we will integrate Th17 immune phenotypes with microbiome signatures to model PsO-to-PsA progression. We expect to find distinctive microbial-immune features in PsA compared to PsO and health, the interaction of which could be used to predict individuals who are at high-risk for disease progression.



JESSICA LEIGH TURNIER, MD, MS

UNIVERSITY OF MICHIGAN

Defining Cutaneous Gene Expression Signatures in Juvenile Dermatomyositis to Guide Treatment

Juvenile dermatomyositis (JDM) is a potentially life-threatening vasculopathy that commonly presents with skin inflammation, heralding onset of severe multi-organ disease. The disease presentation and course of JDM is highly heterogeneous, and we lack knowledge of underlying disease mechanisms and reliable biomarkers to predict patients who will have a severe disease course and poor response to standard therapies. Despite skin inflammation frequently persisting in the absence of active muscle disease and preventing complete disease remission, there exists uncertainty as to the relation of skin disease to systemic disease activity and the role of skin disease in directing treatment. Skin transcriptomic signatures hold the potential to delineate inflammatory pathways important for disease activity and chronicity and also to molecularly classify patients for individualized treatment. The global objectives of this project are to characterize cutaneous molecular signatures in JDM and begin to unravel their association with variable clinical disease phenotypes, disease activity, and chronicity. We hypothesize that cutaneous gene expression signatures will predict skin disease activity and chronicity and identify key genes important for disease development and progression that can be targeted for treatment. In our approach, we will collect clinical skin disease activity scores and perform non-invasive, serial tape stripping of skin for RNA-sequencing in current and newly diagnosed JDM patients at the University of Michigan. We will pursue the following specific aims, (1) To define cutaneous gene expression signatures and IFN scores in lesional and non-lesional skin of JDM patients, (2) To determine the association of molecular skin disease activity and chronicity scores with systemic disease activity and response to therapy. At the completion of this study, we expect to have established tape stripping as a non-invasive method to follow cutaneous gene expression signatures in JDM that can (1) aid in monitoring of disease activity, (2) provide a molecular classification of skin disease, and (3) lend insight into individualized treatment.



YU ZUO, MD, MSC

UNIVERSITY OF MICHIGAN

Anti-NET Autoantibodies and Thrombotic Risk
in Antiphospholipid Syndrome

Antiphospholipid Syndrome (APS) is a thromboinflammatory disorder that can have devastating effects on patients and their families. While it is well known from population studies that antiphospholipid antibodies (aPL) increase the risk of thrombosis, defining an individual patient's susceptibility is hindered by an incomplete understanding of APS pathophysiology. In the clinic, there are no biomarkers utilized in day-to-day practice, beyond the aPL themselves.

A potential breakthrough in recent years is the implication of neutrophils and their pro-clotting remnants (known as neutrophil extracellular traps or NETs) in the pathogenesis of APS. Somewhat unexpectedly, our preliminary studies have also revealed evidence of anti-NET autoantibodies in patients with primary APS. These autoantibodies do not appear to correlate with traditional aPL. We speculate that this anti-NET activity may interfere with NET degradation and thereby predict certain APS clinical manifestations. The overarching goal of this proposal is to comprehensively define autoantibodies recognizing NET-associated antigens in aPL-positive individuals and in doing so define both their clinical associations and pathogenic impact.

Our proposed research will leverage one of the largest APS biorepositories in the world and cutting-edge laboratory techniques (bioassays for NET degradation and thrombin generation, as well as a novel autoantigen microarray platform). These unique resources will be integrated to (1) evaluate the prevalence, specificities, and clinical association of anti-NET autoantibodies in aPL-positive individuals, (2) determine several potential aspects of autoantibody function, and (3) define the longitudinal relationship between aPL, NETs, and anti-NET autoantibodies as it relates to thrombin generation. Upon completion, this study will determine the extent to which anti-NET autoantibodies may be a new class of clinically-actionable biomarker that can inform personalized (and earlier) interventions.



NORMAN B. GAYLIS, MD CLINICAL RESEARCH AWARD

Established with a generous commitment to the Foundation from Dr. Gaylis, the Norman B. Gaylis, MD Clinical Research Award provides funding for research that will impact community practice. Studies may include, but are not limited to, international collaborations, health services research, outcomes studies, practice supply and demand, and/or clinician-patient communications.

MELISSA MANNION, MD, MSPH

UNIVERSITY OF ALABAMA AT BIRMINGHAM

Analysis of Current Target Clinical Measures in the Therapeutic Management of JIA

JIA is the most common rheumatic disease of childhood and is a life-long chronic disease that typically can be treated effectively. However, it is unclear if medications are being optimally used in clinical practice and if patient outcomes can be further improved with refinement of treatment strategies. Treat to target (T2T) strategies for adults with rheumatoid arthritis (RA) have demonstrated improved outcomes by establishing a disease activity target of inactive disease, or at least low disease activity, and changing therapy until that target is met. Recently published T2T guidelines for JIA state a similar goal, but there are no published data to support this approach. While remission is the stated medical goal of most pediatric rheumatologists, actual behavior in clinical practice is likely different and the actual treatment patterns in North America for JIA patients including the observed threshold for treatment escalation and physicians' and patients' beliefs about the relative benefits, harms, and potential unintended consequences of pursuing various targets are not known. Since T2T strategy recommends treatment intensification until the disease activity target is reached, we infer that at the time when no treatment escalation occurs the physician and the patient have agreed that the currently measured disease activity is tolerable or acceptable. The objectives of this project using the Childhood Arthritis and Rheumatology Research Alliance (CARRA) Registry are to (1) identify current usual care treatment patterns, (2) determine patient characteristics associated with those patterns, (3) establish short-term outcomes following tolerated disease activity, and (4) generate patient and provider preferences related to disease management that will become the attributes for future conjoint analysis. We will test the hypotheses that JIA patients have observed tolerated disease activity states higher than LDA, that short-term outcomes are better for patients who attain LDA over more active disease states, and that patients and parents will prioritize inactive disease as the treatment target. Understanding current practices, subsequent outcomes, and patient priorities will help to derive a T2T intervention protocol for use in future prospective studies to assess both short- and long-term outcomes of different treatment targets.



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

Established with a generous commitment from Mrs. Tobé and Dr. Stephen Malawista, this endowment ensures that physician scientists can continue their academic careers in vital rheumatic disease research. The Tobé and Stephen E. Malawista, MD Endowment in Academic Rheumatology provides a permanent source of support in basic science research career development for early career investigators.

ANDREEA MONICA BUJOR, MD, PHD

BOSTON UNIVERSITY

The Role of Myeloid Fli1 in Organ Fibrosis in Systemic Sclerosis

SSc (systemic sclerosis) is an autoimmune disease with high mortality, for which there is no cure or uniformly effective drug. Cardiac fibrosis is common, and when cardiomyopathy becomes clinically symptomatic, prognosis is very poor. Myeloid cell dysregulation has been implicated in the pathogenesis of SSc, but the mechanism remains unclear. We have recently found that the transcriptional factor Fli1 is downregulated in SSc monocytes. Fli1 expression is also reduced in fibroblasts and endothelial cells, where it promotes fibrosis and vasculopathy. Here, we seek to establish whether Fli1 deficiency in monocytes/macrophages contributes to SSc fibrosis and cardiomyopathy, thus qualifying this transcription factor for therapeutic intervention. To test this hypothesis, we will assess changes in monocyte/macrophage migration and secretion of cytokines in cells with low Fli1 and their ability to activate fibroblasts and endothelial cells. We expect that decreased Fli1 in monocytes/macrophages will result in enhanced migration and will promote the production of extracellular matrix. We will use our new mice with conditional deletion of Fli1 in myeloid cells, along with lineage tracing, to determine the contribution of monocytes/macrophages with low Fli1 to heart fibrosis. We anticipate that these mice will have enhanced inflammatory infiltrates, heart fibrosis and diastolic dysfunction. We expect to validate these changes in SSc patients, using an existing database of human samples. The proposed project will address an unanswered question in SSc heart fibrosis: whether monocytes/macrophages contribute to the disease pathogenesis. The study will address this knowledge gap by systematically examining the contribution of decreased Fli1 in monocytes/macrophages to fibrosis in vivo and in vitro. Our analysis will determine whether future treatments in SSc, including treatment for SSc cardiomyopathy, should target Fli1 and the myeloid system, thus providing the basis for potentially safer, more effective therapies.





Scientist Development Award

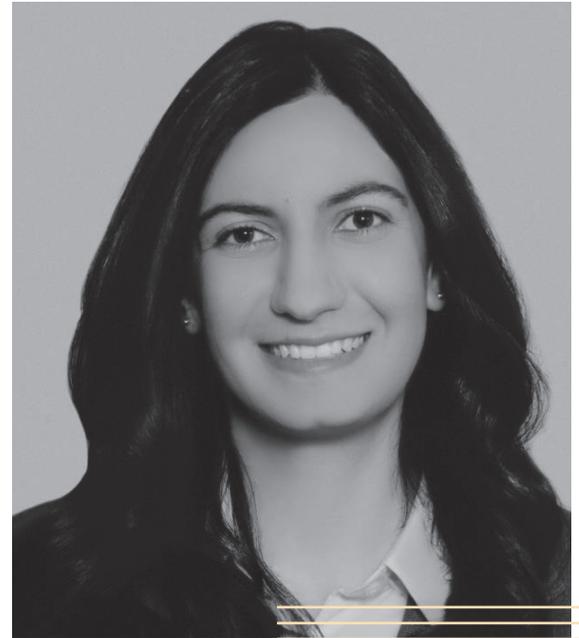
The Scientist Development Award encourages rheumatologists and rheumatology health professionals to pursue innovative research ideas.

CHRISTINE ANASTASIOU, MD

UNIVERSITY OF CALIFORNIA, SAN FRANCISCO

A National Investigation of Opioid Use and Its Consequences in Patients with Rheumatoid Arthritis and Systemic Lupus Erythematosus

Patients with rheumatic diseases, such as rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE), suffer from both acute and chronic pain. Early studies suggest rising opioid use among patients with RA. The national prevalence of opioid use in U.S. SLE patients has never been studied. Despite the likely high prevalence of opioid use in patients with RA and SLE, no information on important outcomes such as hospitalization and mortality from opioid overdoses in these patients is available, and the impact of recent state-level policies on individual rheumatologist prescribing patterns is unknown. The pivotal importance of these knowledge gaps becomes clear when we recognize that in the general US population opioid overdose hospitalizations are most common in women and opioid overdose deaths most frequently occur in 25-54 year-olds, the patient demographics in which the incidence of these autoimmune diseases is highest. Therefore, we hypothesize that the effects of the opioid epidemic are magnified in patients with RA and SLE, marking them as a critical population for which further relevant research is indicated. We will analyze time trends in the risk of opioid overdose-related hospitalizations among admitted patients with RA and SLE compared to the general population. We will also investigate opioid prescription patterns by rheumatologists nationally for individuals with both RA and SLE and assess the contributions of patient, provider-level and contextual factors including state-level legislation on observed levels of opioid prescriptions. Our timely research will help inform national policy and guide efforts to address the opioid epidemic in our patient population.

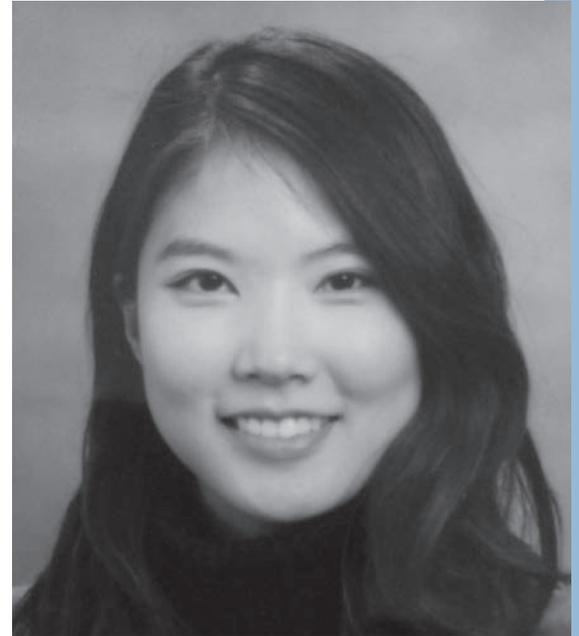


SANGMEE BAE, MD

UNIVERSITY OF CALIFORNIA, LOS ANGELES

Abnormal Anti-oxidant Function of High Density Lipoproteins in Patients with Idiopathic Inflammatory Myopathies

This proposal describes a two-year mentored research training program for the development of an academic career in rheumatology. The principal investigator has completed formal fellowship training in rheumatology at the University of California in Los Angeles (UCLA) and is currently finishing work for a master's degree in clinical research methodology. This career award will build upon the candidate's clinical science background, expanding her skills in areas of laboratory research, biostatistics and disease specific outcome measures in order to establish a strong foundation for her future career. The proposed research addresses a critical knowledge gap regarding the pathogenesis of microvascular injury in idiopathic inflammatory myopathies (IIM) and IIM associated interstitial lung disease (IIM-ILD). The current proposal will allow the candidate to address this knowledge gap by working with a team of mentors who will supervise and collaborate on the following training goals: (1) to attain proficiency and experience in advanced data analysis from a longitudinal cohort, (2) to develop an understanding of oxidative lipids and dysfunctional HDL, (3) to attain expertise in the application of IIM disease outcome measures. Dr. Christina Charles-Schoeman, an expert and leader in clinical investigation and idiopathic inflammatory myopathies; Dr. Srinivasa T. Reddy, co-director of the Center for Biomarker Discovery at UCLA and a recognized leader in atherosclerosis and lipoprotein research; and Dr. Goldin, Chief, Multi-Specialty Radiology Division, UCLA Radiological Sciences and a nationally recognized leader in quantitative lung imaging will co-mentor the principal investigator's scientific development. The candidate will attain these training goals with guidance from the mentorship team complemented by formal coursework and seminars. The research will focus on the functional role of lipoproteins in microvascular damage in IIM and IIM-ILD. Dr. Reddy's lab has suggested the proinflammatory HDL, and my preliminary work suggests that it is associated with increased disease activity. Specific aims of the current proposal are: (1) evaluate whether abnormal HDL function contributes to disease burden in patients with IIM and IIM-ILD; and (2) determine whether HDL-associated proteins and lipid hydroperoxides in IIM patients are associated with a) abnormal HDL function, b) IIM disease activity, and c) IIM-ILD severity.



ADAM BERLINBERG, MD

UNIVERSITY OF COLORADO

Metabolic Regulation of Type 3 Innate Lymphoid Cells by Intestinal Bacteria-Derived Indoles in Ankylosing Spondylitis

Ongoing research in spondyloarthritis (SpA), and in particular ankylosing spondylitis (AS), has identified the Th17 pathway and gut dysbiosis to be important factors contributing to disease. However, how these are linked to each other and the development of AS remain unknown. Of the IL-17 producing cells contributing to AS, type 3 innate lymphoid cells (ILC3s) have been identified as being expanded in the gut, peripheral blood, synovium, and bone marrow of patients with AS. Additionally these cells often express the aryl hydrocarbon receptor (AhR), which has known ligands that are produced by intestinal bacterial metabolism of tryptophan. ILCs are a relatively recently discovered class of lymphoid cells involved in tissue homeostasis and inflammation; they are characterized by the lack of lineage-specific immune markers while mimicking their T cell counterparts (Th1/ILC1, Th2/ILC2, Th17/ILC3). Our unpublished data support an expansion of ILC3s in the intestinal tissue of individuals with AS as compared to healthy controls. Additionally, we found significantly increased tryptophan metabolites, indole-3 acetate (IAA) and indole-3-acetaldehyde (IAld), in the same subjects with AS compared to controls. In this proposal we hypothesize that bacterial dysbiosis in AS results in increased bacteria-derived indole metabolites in the gut that influence ILC3 expansion and function. In Aim 1 we will determine the effect of indole signaling on intestinal ILC3 function. In Aim 2 we will then evaluate the role of the microbiome in establishing the local gut metabolic environment by identifying relevant indole producing bacteria in AS using a shotgun metagenomics approach. If our hypothesis is correct, we expect to demonstrate that microbial dysbiosis in AS results in the production of indoles which drive ILC3 proliferation and activation. Such findings will begin to link microbial dysbiosis, Th17 immune responses, and the pathogenesis of AS.



ALI DUARTE GARCIA, MD

MAYO CLINIC

Multimorbidity and Lupus: Impact of Multiple Chronic Conditions on Outcomes

Patients with systemic lupus erythematosus (SLE) have a 3-fold increase in all-cause mortality, compared to the general population. Young patients with SLE are 40 and 60 times more likely to have cardiovascular disease and end-stage renal disease, respectively, and have at least twice the risk for psychiatric comorbidities, such as depression, than people of comparable age without SLE. These and other chronic conditions have emerged as factors contributing to the excess morbidity and shorter lifespan of patients with SLE. To date, characterization of age-, disease- and treatment-related comorbidities associated with SLE has relied almost exclusively on individual comorbidity assessment. The extent to which multiple chronic conditions (multimorbidity) predict adverse outcomes is unknown. Additionally, understanding the patient's "trajectory" or accumulation of multimorbidity may be helpful in predicting adverse outcomes.

By using novel data-driven analytic methods and leveraging the resources of a nationally representative database containing de-identified claims and clinical data of over 150 million persons, we will characterize the patterns of comorbidities and identify the longitudinal trajectories and consequences of multimorbidity among patients with SLE.

As the survival of patients with SLE has improved, the rise of chronic comorbid conditions has created different care needs. Identifying multimorbidity patterns that are most predictive of bad outcomes will allow future research to examine the best care delivery models that address the needs of those with the most serious disease combinations.

Findings from this novel research will provide the basis for subsequent development of rheumatologic care strategies to identify, manage, and prevent multimorbidity of patients with SLE.



ISAAC T.W. HARLEY, MD, PHD

**UNIVERSITY OF COLORADO ANSCHUTZ
MEDICAL CAMPUS**

MicroRNA Enforcement of Autoreactive B Cell Tolerance

Autoimmune diseases such as rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE) are characterized by autoreactive B cells. Curiously, more than 2-10% of naïve B-cells in healthy individuals are autoreactive, but remain incompetent to signal through their antigen receptor (BCR). While extensive data support the hypothesis that when dysregulated, these tolerant autoreactive cells become the autoantibody secreting B cells that fuel systemic autoimmune disease, the mechanisms regulating this loss of tolerance remain incompletely defined. However, phosphatase activity antagonizing the PI3K pathway downstream of the BCR is central to maintaining tolerance, as high expression of the PI3K-antagonizing phosphatase PTEN (phosphatase and tensin homolog) defines tolerant autoreactive human B cells. Recently microRNAs have been defined as key regulators of PTEN expression throughout B cell development. Further, microRNA changes upon receptor stimulus demonstrate kinetics that would be consistent with the rapid loss of B cell tolerance following autoantigen removal. These observations lead to three independent, but interrelated, questions that I aim to address:

1. Does chronic BCR stimulus lead to decay of PTEN-targeting microRNAs, increased PTEN expression and therefore tolerance?
2. Is BCR-driven microRNA decay a general mechanism enforcing tolerance in autoreactive B cells via PTEN-independent mechanisms?
3. Are tolerance inhibitory microRNAs dysregulated in RA and SLE B cells?

This proposal aims to answer these questions using genetic manipulation of microRNAs and target mRNAs, transcriptomic profiling and RNA-flow cytometry. I anticipate the revelation of mechanisms leading to maintenance of tolerance by autoreactive B cells in healthy individuals mediated by microRNAs. Validation that candidate tolerance inhibitory microRNAs are dysregulated within the formerly tolerant autoreactive B cell compartment will nominate novel approaches to RA and SLE therapy.

My long-term goal is to exploit the mechanistic understanding of the maintenance of B-cell self-tolerance to develop therapies that either reverse autoimmunity in RA and SLE or prevent disease development.

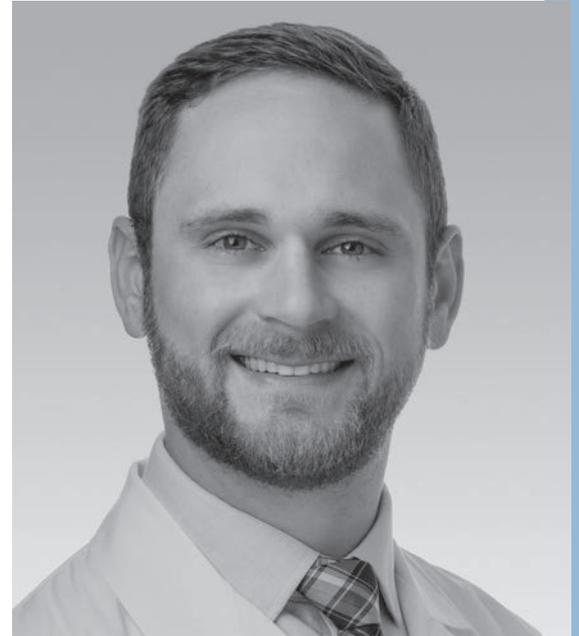


MICHAEL S. PUTMAN, MD

MEDICAL COLLEGE OF WISCONSIN

Macrophage Function and Topography in Giant Cell Arteritis

Patients with giant cell arteritis often experience delays in diagnosis, and current prognostic information does not allow for a tailored approach to therapy. To diagnose giant cell arteritis (GCA), patients frequently undergo temporal artery biopsy (TAB) with hematoxylin and eosin (H&E) staining, which is the pathologic standard of care. This approach has a low sensitivity, with a 60% rate of false negative pathologic interpretations. Even when present, classic pathologic findings do not reliably identify which patients will ultimately suffer vascular complications. This may be related to limitations of H&E staining, which does not identify the location or function of specific immune cell populations. We hypothesize that inflammatory macrophages in the adventitia drive early disease and that remodeling macrophages near the internal elastic lamina drive pathologic vascular remodeling. To test this hypothesis, we intend to use TAB specimens from 300 patients with GCA who are enrolled in the Vasculitis Clinical Research Consortium (VCRC) Longitudinal Study of GCA. This large international cohort of patients with GCA collected prospective longitudinal comprehensive clinical data as well as validated outcome measures. In Aim 1, we will determine whether identifying the location or functional profile of macrophages in TAB specimens improves the diagnostic sensitivity of TAB. In Aim 2, we will identify associations between the development of vascular damage on validated outcome measures and the location or functional profile of macrophages in TAB specimens. In an additional small pilot study, we will further investigate our hypothesis by using single cell RNA sequencing of macrophages from TAB specimens to determine their transcriptional profile. This project will be the only investigation of its kind on an international cohort, the first to assess associations between GCA pathology and validated clinical outcome measures, and the first to apply single cell RNA sequencing to TAB tissue from patients with GCA. Successful completion of this project may improve our ability to diagnose GCA at an early stage and may provide prognostic information that allows physicians to ultimately tailor therapeutic interventions.



CHIO YOKOSE, MD

MASSACHUSETTS GENERAL HOSPITAL/ HARVARD MEDICAL SCHOOL

Coronary Artery Calcium and Coronary Urate Deposits
in Patients with Gout

Gout patients have a high burden of comorbid atherosclerotic cardiovascular disease (ASCVD) and experience premature mortality, primarily driven by ASCVD deaths, which has remained unchanged in the last 16 years. Thus, improved strategies for ASCVD screening and management in gout patients are needed. Patients at borderline or intermediate 10-year ASCVD risk in whom treatment decisions (e.g., statin or aspirin initiation) remain uncertain may benefit from further risk stratification with coronary artery calcium (CAC) scores, which are obtained from ECG-gated coronary CT. CAC scores improve ASCVD risk classification and are strongly associated with future ASCVD events. Furthermore, studies suggest that knowing one's CAC score can motivate initiation and adherence to medications and lifestyle changes which benefit both ASCVD and gout. However, the utility of CAC scores as an ASCVD risk tool has not been studied among gout patients. Furthermore, in light of mounting evidence of monosodium urate (MSU) deposition in atherosclerotic plaque, there is surging interest in the novel application of dual-energy CT for the non-invasive identification of vascular MSU. Thus, this proposal leverages ECG-gated coronary CT performed in dual-energy mode for CAC scoring, obtained as part of routine care, to simultaneously compare CAC scores as well as coronary MSU prevalence between gout patients and age- and sex-matched patients without gout. We hypothesize that gout patients will have higher CAC scores which substantially upgrade their risk classification, as well as higher prevalence of coronary MSU, which will associate strongly with presence of gout and CAC scores. The anticipated findings will inform future studies to investigate the effect of CAC scoring on ASCVD morbidity and mortality, as well as initiation and adherence to ASCVD prevention strategies in gout patients. Furthermore, our coronary MSU findings will lead to future studies to elucidate the role of urate-lowering therapy as a cardioprotective intervention.





Education & Training Awards

CLINICIAN SCHOLAR EDUCATOR AWARD

The Clinician Scholar Educator Award supports educators dedicated to developing new and improved programs to enhance education in musculoskeletal and rheumatic diseases for future doctors and rheumatology health professionals.

MARCY B. BOLSTER, MD

MASSACHUSETTS GENERAL HOSPITAL

Extending Our Reach: Training Rheumatology Fellows in Telehealth to Provide Care to a United States (US) Underserved Patient Population

Telehealth, an all-encompassing term that includes the features of health care services, education, and delivery of clinical care with the use of interactive technologies, offers an ideal mechanism for health care delivery at a time when access to care is affected by many factors including workforce limitations and a maldistribution of US rheumatology care providers. Clinical medicine, through technology, is advancing beyond the bedside for providing patient care, making the skill set of “webside manner” a new priority. Formal telehealth education however is largely absent from the training environment and is specifically not yet included in the updated Rheumatology Core Curriculum Outline. As we train rheumatology fellows to develop the skills, knowledge, and attitudes to capably and competently provide care across the spectrum of the rheumatic diseases, we must also prepare them to be effective and competent practitioners in rheumatology telemedicine.

I propose the integration of specific and comprehensive telehealth training into rheumatology fellowship training. This will be accomplished through a comprehensive didactic curriculum that includes simulated telehealth patient encounters, direct observation in a precepted environment for synchronous patient care visits, development of a broad set of assessment tools including pre- and post-surveys of fellows’ confidence and skills, evaluations of simulated and clinical performance, and measures of clinical data to assess improvements in patient outcomes. Through collaboration with primary care providers, the Indian Health Service (IHS), and Rosebud Indian Reservation, precepted patient care using telemedicine and direct observation will extend the reach of rheumatology care to one underserved patient population. To disseminate this project, a comprehensive train-the-trainer module will be developed to permit full incorporation of telemedicine rheumatology curriculum into any rheumatology fellowship program. This template will enhance rheumatology fellowship training and facilitate extending our reach by providing rheumatology care to populations served by the IHS or other underserved rheumatology populations.



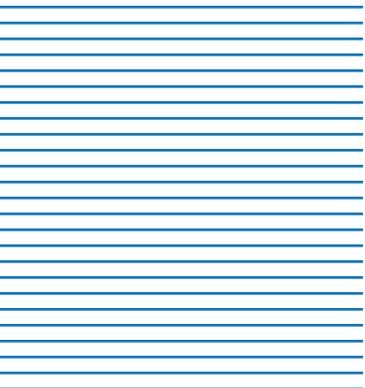
CLINICIAN SCHOLAR EDUCATOR AWARD

DAVID L. LEVERENZ, MD

DUKE UNIVERSITY

RheumMadness: An Online Community of Inquiry for Rheumatology Trainees

The goal of this project is to utilize social constructivist learning theory and the Community of Inquiry (CoI) framework to develop a community of rheumatology trainees from multiple institutions engaged in collaborative discussion, reflection, and application of core rheumatology concepts. This will be accomplished through the creation of RheumMadness, an online tournament of rheumatology topics modeled after NephMadness, an existing collaborative activity in the nephrology community that has engaged approximately 1,000 nephrology practitioners from over 30 countries. RheumMadness will expand the impact of rheumatology by connecting rheumatology trainees from diverse educational settings and will inspire the co-creation of knowledge, generating opportunities for fellows to make new insights into rheumatologic disorders.



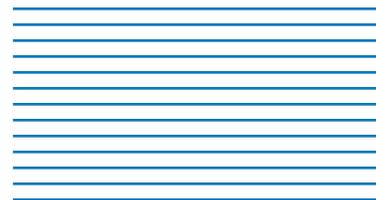
CLINICIAN SCHOLAR EDUCATOR AWARD

ANGELA B. ROBINSON, MD, MPH

CLEVELAND CLINIC FOUNDATION

Using Online Simulation to Teach High-Value Care of Pediatric Musculoskeletal Complaints: Assessing Cost of Care and Diagnostic Decision-Making

Musculoskeletal pain is a frequent complaint in childhood and makes up about 6-15% of general pediatric visits. In their daily practice, general pediatricians need to know how to properly evaluate a variety of musculoskeletal complaints, put forth a reasonable differential diagnosis using standard evaluation techniques, laboratory and imaging workup, and understand when referral to a subspecialist is required. We hypothesize that an online musculoskeletal complaint simulation game can be used to teach high value care and proper musculoskeletal evaluation to medical students and pediatric residents and hopefully increase correct diagnosis of pediatric musculoskeletal and potentially rheumatic complaints. This project aligns with IOM recommendations in the development of tools to teach high value care to reduce per capita cost of care.



Health Professional Online Education Grant

The Health Professional Online Education Grant covers the cost of registration for either the Fundamentals of Rheumatology Course or the Advanced Rheumatology Course in order to increase the knowledge and skills of rheumatology health professionals so that they are better equipped to meet the needs of a growing rheumatology patient population.

Ava Afshar, PharmD, BCPS, BS

Emory University Hospital Midtown

Kelly Caruso, MMS, BS

Southland Rheumatology Center LLC

Jill Cryder, MSN

Southland Rheumatology Center LLC

Elizabeth Dassow, MPAS, MSOT

UnityPoint Health

Michelle Morales, PharmD

Emory University Hospital Midtown

Tisa M. Parsons, MSN, CRNP, FNP-C

Princess Anne Family Practice

Lindsay Tapia, MSN

UnityPoint Clinic – Multi-Specialty – Rheumatology

Yvonne M. Waters, MSN

University of New Mexico Hospital

Fellowship Training Award for Workforce Expansion

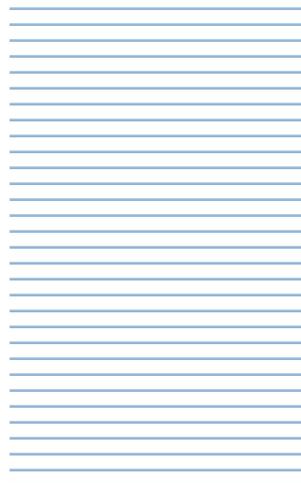
The Fellowship Training Award for Workforce Expansion supports the training of a rheumatology fellow at an institution that has previously been unable to fill all of their ACGME-approved slots due to funding constraints, in order to ensure an adequate supply of rheumatology providers in all areas of the country.

Children's Hospital of Pittsburgh*

University of North Carolina

University of Rochester

**Funding for this award was provided in part
by the Andrejeski Fund for Fellowship Training.*



Fellowship Training Awards

These Fellowship Training Awards support the training of a rheumatology fellow to provide a more robust and highly trained workforce to care for people with rheumatic disease.

Baylor College of Medicine

Amgen Fellowship Training Award

Beth Israel Deaconess Medical Center

Fellowship Training Award

Children's Hospital of Philadelphia

Fellowship Training Award

Duke University

Fellowship Training Award

Georgetown University

Amgen Fellowship Training Award

Johns Hopkins University

Amgen Fellowship Training Award

Massachusetts General Hospital

Amgen Fellowship Training Award

Northwestern University

Fellowship Training Award

Oregon Health & Science University

Amgen Fellowship Training Award

Stanford University

Fellowship Training Award

Tufts Medical Center

Fellowship Training Award

University of Alabama at Birmingham

Amgen Fellowship Training Award

University of California, Los Angeles

Amgen Fellowship Training Award

University of California, San Diego

Fellowship Training Award

University of California, San Francisco

Amgen Fellowship Training Award

University of Chicago

Fellowship Training Award

University of Michigan

Fellowship Training Award

University of Minnesota (Adult)

Fellowship Training Award

University of Minnesota (Pediatric)

Fellowship Training Award

University of Nebraska Medical Center

Amgen Fellowship Training Award

University of Pennsylvania

Fellowship Training Award

Funding for these awards was provided in part by Amgen, Inc.

Paula De Merieux Fellowship Training Award

The Paula de Merieux Fellowship Training Award provides support for the training of a promising rheumatology fellow who is an under-represented minority or a woman.

New York University School of Medicine

Audrey M. Nelson, MD Pediatric Rheumatology Fellowship Endowment in Training

Dr. Nelson's exceptional support of the Foundation enabled the establishment of the Audrey M. Nelson, MD Pediatric Rheumatology Fellowship Endowment in Training. The endowment supports awards aimed at providing robust education and training opportunities for pediatric rheumatologists and addresses the growing demand for pediatric rheumatologists to ensure that children with rheumatic diseases have access to the care they need.

Cincinnati Children's Hospital Medical Center

Mentored Nurse Practitioner/ Physician Assistant Awards for Workforce Expansion

The Mentored Nurse Practitioner/Physician Assistant Award for Workforce Expansion provides tailored training for nurse practitioners or physician assistants who are new to the field of rheumatology and who are in geographically underserved areas.

Advanced Rheumatology of Houston

Tamar Brionez, MD
Amanda Zuber, APRN, AGNP

Comprehensive Orthopaedic Global

Rebecca Manno, MD, MHS
Jennifer Blake Arizu, MS

Crystal Arthritis Center, Inc.

David E. Bacha, MD
Margaret A. Pullin, MSN

Crystal Arthritis Center, Inc.

Carlos E. Zevallos, DO
Michelle L. Bacha, MSN, CNP

Idaho Arthritis & Osteoporosis Center PC

Mikael D. Lagwinski, MD
Colette Weber, PA-C

Idaho Arthritis & Osteoporosis Center PC

Eric J. Palfreyman, MD
Megan George, PA-C

Loma Linda University

Karina D. Torralba, MD, MACM
Gergette Sacay, NP-C

Olive View-UCLA Medical Center

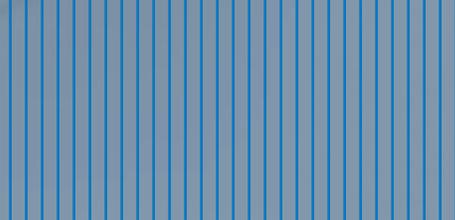
Andrew L. Wong, MD
Karla J. Otero-Vo, FNP-C, MSN, RN

Phillip A. Waller, MD, PA

Phillip A. Waller, MD
Pedro Ambriz, PA-C

Washington University in St. Louis

Alfred H. Kim, MD, PhD
Sara Ranae Kellahan, MSN, APRN,
AGPCNP-C



Preceptorships

RHEUMATOLOGY FUTURE PHYSICIAN SCIENTIST AWARD

This award supports MD/PhD students who demonstrate outstanding potential and significant commitment to a career in rheumatology research, in order to support the nation's top emerging physician-scientists in the field of rheumatology.

JULIA ANNE RIEDL, BBME

UNIVERSITY OF MINNESOTA

Interferonopathies are a group of monogenic disorders defined by persistent type 1 interferon (IFN α,β,γ) signaling and have varying phenotypes, including inflammation of the skin, vasculature, eyes, lung, gut and joints. We recently identified a patient with a novel interferonopathy inflammatory skin disease and mutations in a gene encoding a protein expressed in sebaceous glands, hair follicle-associated structures that are immunologically active and protect the skin by secreting lipid sebum. This work seeks to understand how these mutations disrupt the normal function of this protein and of sebaceous glands to drive a type I IFN response "interferonopathy" and skin inflammation.



RHEUMATOLOGY FUTURE PHYSICIAN SCIENTIST AWARD

PHILIP JOHN TITCOMBE, BA

UNIVERSITY OF MINNESOTA

B cells are critical for defense against pathogens, but can also pose a threat to host tissues in the case of autoimmunity. The specificity of an individual B cell is governed by the antibody molecules that are expressed on the cell surface as the B cell receptor (BCR). Despite processes to select against dangerous BCRs with self-antigen reactivity, rare B cell clones still sometimes manage to escape self-tolerance and mediate autoimmune damage. The self-antigens and cellular events that initiate B cell self-tolerance breakdown are still not known. Current understanding of self-antigens that are relevant to a given autoimmune disease relies on inference from the antibody specificities that can be observed in late disease. While these autoantibody profiles have been useful for establishing distinct diagnostic criteria for each autoimmune disease, they provide minimal information about actual pathogenesis. This is because the diversity of self-antigens and accompanying autoantibody specificities greatly expands by the time that autoimmune disease is detected. The aims proposed in this project are therefore designed to clarify the specificity and genetic features of autoreactive B cells before extensive diversification has occurred. This will be accomplished by studying the predicted ancestors of many related self-specific B cell clones. Aim 1 will use a post-translationally modified peptide microarray to determine early antigenic drivers of rheumatoid arthritis (RA), an autoimmune disease with well-characterized late autoantibody targets. Aim 2 will investigate transcriptome changes that are unique to the clonal evolution of self-specific B cells. Collectively, the data will contribute important new insights into B cell specificities and genes underlying early RA pathogenesis.



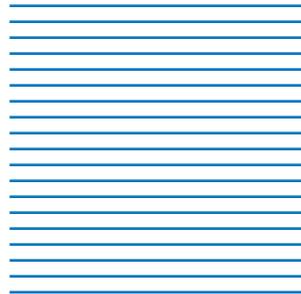
RHEUMATOLOGY FUTURE PHYSICIAN SCIENTIST AWARD

NANCY WAREING, BS

**UNIVERSITY OF TEXAS HEALTH SCIENCE
CENTER AT HOUSTON**

The most common clinical feature of systemic sclerosis (SSc; scleroderma) is skin thickening and tightening, caused by deposition of excess extracellular matrix material in the skin. There are no FDA-approved drugs for skin involvement in SSc, primarily due to the fragmented understanding of its driving pathophysiologic mechanisms. This underscores the urgent need to identify novel targeted therapies for the treatment of SSc.

The source of the primary effector cell in skin fibrosis, the dermal myofibroblast, is poorly understood. Epithelial cells have been shown to acquire characteristics of myofibroblasts and deposit excess fibrotic material, a process known as epithelial-to-mesenchymal transition (EMT). The contribution of epithelial cells to the myofibroblast population via EMT has been demonstrated in various fibrotic disorders, but remains largely under-investigated in SSc. Developmental genes, normally only expressed during embryogenesis, become activated in many disease states. Intriguingly, I identified the upregulation of a novel developmental transcription factor, *Sine Oculis Homeobox Homolog 1* (SIX1), in the skin of persons with SSc but not age- gender- race-matched healthy persons, and localized this protein to keratinocytes, the primary epithelial cell in the epidermis. SIX1 has been shown to drive EMT in development and numerous disease states. I demonstrated that SIX1 correlates with markers of EMT and fibrosis in SSc skin biopsies, supporting a driving role of SIX1 in skin fibrosis by promoting EMT. My project seeks to identify a novel pathogenic role of an unknown developmental transcription factor, SIX1 in skin fibrosis, which may represent a new therapeutic target for this potentially devastating disease.



Lawren H. Daltroy Health Professional Preceptorship

The Lawren H. Daltroy Health Professional Preceptorship 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.*

JERIK LEUNG, BA

PRECEPTOR: ELIZABETH BAKER, PHD, MPH

Saint Louis University, College for Public Health and Social Justice

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.

BRETT DOLINER, MD, MS

PRECEPTOR: ZACHARY WALLACE, MD, MS

Massachusetts General Hospital

Resident Research Preceptorship

The Resident Research Preceptorship introduces residents to the specialty of rheumatology and attracts promising physician scientists to the field by supporting a full-time research experience.

BRETT DOLINER, MD, MS

PRECEPTOR: ZACHARY WALLACE, MD, MS

Massachusetts General Hospital

RYAN D. STULTZ, MD, PHD

PRECEPTOR: CHRISTIAN LOOD, PHD

University of Washington



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.

Alexander J. Alexander, BA

PRECEPTOR: TIPHANIE VOGEL MD, PHD

Texas Children's Hospital

Courtney Bell, BS, MS

PRECEPTOR: SHAZIA BEG, MD

University of Central Florida College of Medicine

Thomas Bye, BS, MS

PRECEPTOR: DANIEL WHITE, PT, SCD, MSC

University of Delaware

Casey Cai

PRECEPTOR: KATIE STEWART, MD

University of Texas Southwestern Medical Center

Gabrielle Elizabeth Capone, BS

PRECEPTOR: RABHEH ABDUL AZIZ, MD, MS

Jacobs School of Medicine and Biomedical Sciences

Michael F. Cassidy, BA

PRECEPTOR: VAISHALI MOULTON, MD, PHD

Beth Israel Deaconess Medical Center,
Harvard Medical School

Alyssa Choi, BA

PRECEPTOR: VANESSA MALCARNE, PHD

San Diego State University

Grace E. Coleman

PRECEPTOR: DANIEL K. WHITE, PT, SCD, MSC

University of Delaware

Megan P. Connor, BS, BA

PRECEPTOR: MEGAN KRAUSE, MD

Kansas University School of Medicine

Gregory A. Demirjian, BS

PRECEPTOR: KOREY ULLRICH, MD

Rheumatology Associates of South Florida

Kristin Deneen, BS

PRECEPTOR: EMILY SMITHERMAN, MD, MS

University of Alabama at Birmingham School
of Medicine

Joshay Ford, BS, MS

PRECEPTOR: JENNIFER STICHMAN, MD

University of Colorado Hospital, Denver Health
Medical Center, and Children's Hospital Colorado

Nirupa Gadi, BA

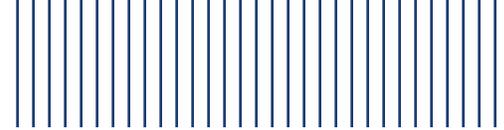
**PRECEPTOR: JENNIFER STEVENS-LAPSLEY,
MPT, PHD**

University of Colorado Denver

Jeremy Graber, BS, DPT

PRECEPTOR: VAISHALI MOULTON, MD, PHD

Beth Israel Deaconess Medical Center,
Harvard Medical School



Nora Hajnoczky, BS

PRECEPTOR: CHRIS DERK, MD, MS

University of Pennsylvania

Mahamudul Haque

PRECEPTOR: SALAHUDDIN AHMED, PHD

Washington State University

Lauren Hinrichs, PT, DPT, OCS

**PRECEPTOR: JENNIFER STEVENS-LAPSLEY,
PT, PHD, FAPTA**

University of Colorado School of Medicine

Seneca Hutson, BS

PRECEPTOR: CHICHI LAU, MD

University of Vermont Larner College
of Medicine

Khara A. James, MS

PRECEPTOR: JOSHUA STEFANIK, MSPT, PHD

Northeastern University

Jessica M. Jones, BS

PRECEPTOR: TRINE JORGENSEN, PHD

Cleveland Clinic Lerner Research Institute

Caroline Lojaco, BS

PRECEPTOR: RABHEH ABDUL AZIZ, MD, MS

Conventus Center for Collaborative Medicine

Andrea Marshall, DPT

PRECEPTOR: MICHAEL BADE, PHD, DPT

University of Colorado Denver, Anschutz Medical
Campus

Daniel O'Connell

PRECEPTOR: YVONNE GOLIGHTLY, PHD

University of North Carolina at Chapel Hill

Ani Oganesyan, BA

PRECEPTOR: SUSAN A. BOACKLE, MD

University of Colorado School of Medicine

Paul M. Panipinto, BSc

**PRECEPTOR: SALAH-UDDIN AHMED, PHD,
MSC, BSC**

Washington State University

Jessica M. Phan, BA

PRECEPTOR: ELENA WEINSTEIN, MD, FACR

University of Colorado

Jenna J. Port, BA

PRECEPTOR: ROBERT KALISH, MD

Tufts University School of Medicine

David Quammen, MEd, BATR

**PRECEPTOR: JESSE CHRISTENSEN,
DPT, PHD**

Salt Lake City Veterans Affairs

Aardra Rajendran

PRECEPTOR: MEGAN E. CLOWSE, MD, MPH

Duke University

Joseph Singer, BA

PRECEPTOR: ROCHELLA OSTROWSKI, MD

Loyola University Medical Center

Allison Spihlman, BS

PRECEPTOR: VAISHALI MOULTON, MD, PHD

Beth Israel Deaconess Medical Center,
Harvard Medical School

Daneka Stryker, MSc

PRECEPTOR: SABRINA GMUCA, MD, MSCE

Children's Hospital of Philadelphia

Tiffany Taylor, BA, MPH

PRECEPTOR: JINOOS YAZDANY, MD, MPH

University of California, San Francisco

Maria Tukis

PRECEPTOR: DANIEL WHITE, PT, SCD, MSC

University of Delaware

Thomas J. Vazquez, BS

PRECEPTOR: VICTORIA P. WERTH, MD

University of Pennsylvania Perelman School
of Medicine

Alexis Wilsey, BS

PRECEPTOR: HEATHER VAN MATER, MD, MS

Duke University

Samantha Wu, BA

PRECEPTOR: VAISHALI MOULTON, MD, PHD

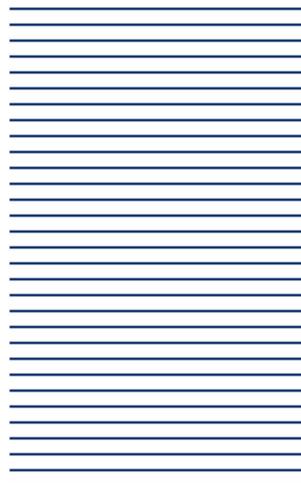
Beth Israel Deaconess Medical Center,
Harvard Medical School

Leta Yi

**PRECEPTOR: CANDACE FELDMAN, MD, MPH,
SCD**

Brigham and Women's Hospital

*Funding for recruitment awards was provided in part by
the Thasia G. Woodworth, MD Fund in Recruitment and
the Charles Christian, MD Education and Training Fund.*





Annual Meeting **Awards**

Student and Resident Pediatric Rheumatology Symposium (PRYSM) Scholarship

The purpose of the Student and Resident PRSYM Scholarship is to provide outstanding students and residents currently enrolled at institutions with no pediatric rheumatology program the opportunity to attend the 2020 Pediatric Rheumatology Symposium.

Dori Abel, MD

New York Presbyterian - Columbia University

Dahima Cintron, MD, MSc

University of Puerto Rico - Medical Sciences Campus

Tejaswi Dittakavi, DO

Advocate Healthcare

Esraa Elouseily, MBBCH, MRCPCH

University of Florida/Sacred Heart Children's Hospital

Sharanya Joginpalli, MD

Texas Tech University Health Sciences Center - Lubbock

Nicholas McClellan, DO

Marshfield Clinic

Amanda Moyer, MD

University of Oklahoma

Zachary Pettigrew, MD

University of North Carolina

Daphne Porat, MD

University of Illinois at Chicago

Leigh Stubbs, MD, MPH

University of Texas Houston McGovern Medical School Department of Pediatrics

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 2020. To learn more about all of the awards offered by the Foundation, visit www.rheumresearch.org.

Abstract Awards

These awards recognize scholarship among aspiring Rheumatology professionals and provide them the opportunity to attend the premiere scientific meeting in the field.

MARSHALL J. SCHIFF, MD MEMORIAL FELLOW RESEARCH AWARD

The Marshall J. Schiff, MD, Memorial Fellow Research Award encourages fellows to continue rheumatology research by providing an opportunity for them to present an abstract at the ACR Convergence. Funding for this award is made possible through an endowment from Dr. and Mrs. Michael H. Schiff and friends.

Priyanka Ballal, MBBS

Boston University Medical Center

Rayan Najjar, MBChB, MPH

University of Washington

Amy Cunningham-Bussel, MD, PhD

Brigham and Women's Hospital

MEDICAL AND PEDIATRIC RESIDENT RESEARCH AWARD

The Medical and Pediatric Resident Research Award motivates residents to pursue subspecialty training in rheumatology by providing an opportunity to experience the field firsthand and present an abstract at the ACR Convergence.

Ann Cameron Barr, MD

Duke University

Vijay Kannuthurai, MD

Washington University in St. Louis

Lena Eder, MD

Duke University Hospital

Tara Skorupa, MD

Beth Israel Deaconess Medical Center

Jennifer L. Simon Hanberg, MD

Massachusetts General Hospital

Surabhi S. Vinod, MD

Baylor College of Medicine

Mehmet Hocaoglu, MD

University of Maryland Medical Center
Midtown Campus

Jeong Min Yu, MD

Cedars-Sinai Medical Center

PEDIATRIC RHEUMATOLOGY SYMPOSIUM (PRYSM) ABSTRACT AWARD

The purpose of the Pediatric Rheumatology Symposium Abstract Award is to provide outstanding students, residents and fellows the opportunity to attend and present an abstract at the 2020 Pediatric Rheumatology Symposium.

Erin Balay, MD

University of Minnesota

Megan Colwell, MD

Children's Hospital at Montefiore

Vy K. Do, DO, MPH

University of Texas Southwestern
Medical Center

Yike Jiang, MD, PhD

Baylor College of Medicine

Sarah T. Kodama, BS

Virginia Commonwealth University School
of Medicine

Jacqueline A. Madison, MD

University of Michigan

Shawn Mahmud, MD, PhD

University of Minnesota

Christina Schutt, DO

University of Pittsburgh Medical Center

Matthew A. Sherman, MD

Children's National Medical Center

Alexis L. Wilsey

Duke University School of Medicine

STUDENT ACHIEVEMENT AWARD

The Student Achievement Award encourages medical and graduate students to consider a career in rheumatology by recognizing promising work and providing an opportunity to present an abstract at the ACR Convergence.

Philip Carlucci, BS

NYU Grossman School of Medicine

Kevin M. Gao, BSc

University of Massachusetts Medical School

K. Bates Gribbons, BS

McGovern Medical School

Maria Schletzbaum, BA

University of Wisconsin School of Medicine
and Public Health

Madison G. Wolfe, BS

University of Nebraska Medical Center

Memorial Lectureships

Memorial lectureships honor rheumatology professionals who have made significant contributions to the field during his or her lifetime. The lectureships are presented each year at the ACR Convergence and features outstanding investigators in various areas of rheumatology research.

PAUL KLEMPERER, MD MEMORIAL LECTURESHIP

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