Advancing Treatments, Finding Cures

2019 Award Recipients

Rheumatology Research Foundation
Advancing Treatment | Finding Cures

Cultivating the Future of Rheumatology

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

The Foundation is fueling the future pipeline of rheumatology professionals by supporting them in a number of ways. We've recently implemented two new award mechanisms, the Fellowship Training Award for Workforce Expansion and the Rheumatology Future Physician Scientist Award. These awards aim to support the rheumatology workforce and ensure an adequate supply of highly-trained rheumatology providers is available to treat patients.

In Fiscal Year 2020, the Foundation committed to fund more than $10 million to rheumatology research and training. The majority of the funds will be awarded to advance innovative research projects that lead to breakthroughs in treating people with rheumatic diseases. The remainder of the funds support efforts to recruit and train the next generation of rheumatology professionals, which decreases patient wait times and increases 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 the people impacted by rheumatic disease.

Bryce A. Binstadt, MD, PhD

Chair, Scientific Advisory Council

Table of Contents

Innovative Research Award

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.

Felipe Andrade, MD, PhD

Johns Hopkins University

Rediscovering Ro52 in Systemic Lupus Erythematosus

Antibodies to self-antigens are considered to play a crucial role in the pathogenesis of systemic lupus erythematosus (SLE). Understanding the mechanisms that initiate immune responses to autoantigens may therefore provide opportunities for the discovery of novel biomarkers and disease mechanisms, which can lead to new tools for diagnosis and target-specific therapies. To better understand the source and mechanisms of autoantigen production in SLE, we focused on neutrophils and interferons (IFNs), two important players in SLE pathogenesis. Using biochemical and proteomic approaches to identify neutrophil-specific autoantigens linked to IFN activation in SLE, we found that neutrophils express at least four splicing variants of Ro52, which differ in structure, E3 ubiquitin ligase activity and immunogenicity. Interestingly, the expression of the distinct forms of Ro52 is strongly linked to interferogenic activation in patients with SLE, suggesting that these are IFN-induced autoantigens. Moreover, we identified a new set of autoantibodies in SLE patients, which target a unique sequence found in two novel Ro52 isoforms described for the first time in this proposal. Building on these results, we hypothesize that neutrophils are a major source of immunogenic isoforms of Ro52, which are linked to IFN-induced activation in SLE. In addition, we propose that Ro52 isoforms have unique regulatory functions on the production of type I IFNs (IFN-I), via ubiquitination-induced degradation of IFN regulatory factors (IRFs), which may be relevant for SLE pathogenesis. We will examine these hypotheses directly in the human model in two specific aims. In Aim 1, we will use in vitro and cellular assays to define the regulatory role of the Ro52 isoforms in the ubiquitination of IRFs and the activation of IFN-I genes. In Aim 2, we will study a prospective observational cohort of patients with SLE to define the clinical significance of the newly discovered antibodies to Ro52 isoforms. Together, these studies seek to elucidate the potential relevance of Ro52 isoforms expressed in the neutrophil to SLE pathogenesis. The final goal of this work is to identify novel tools to improve diagnosis and gain new insights into disease mechanisms, thus laying the foundation to explore novel therapies.

Ru L. Bryan, PhD

University of California, San Diego

Inhibition of CD38 and Supplementation with Nicotinamide Riboside as Novel Approaches for Osteoarthritis

Joint injury and aging are the major risk factors for development of osteoarthritis (OA). As OA progresses, failure of the synovial joint organ frequently develops, with degeneration of articular cartilage as a core disease feature. Chondrocytes, the sole cells in articular hyaline cartilage, are responsible for maintaining the homeostatic balance between extracellular matrix anabolism and catabolism. Dysfunction of chondrocytes in OA, amplified by local inflammatory processes, leads to cartilage degradation as a result of excessive chondrocyte catabolic activity.

Maintenance of proper intracellular levels of nicotinamide adenine dinucleotide (NAD+), a key intermediate metabolite, is critical for maintaining tissue homeostasis. NAD+ levels steadily decline with age, associated with increased expression of CD38, the main NADase in mammalian tissues. The changes in NAD content are reflected in altered activities of NAD-dependent enzymes such as sirtuins, thereby leading to changes in cellular metabolism, gene expression and protein function. Our preliminary studies reveal that NAD+ decline was associated with increased CD38 expression and activity in human knee chondrocyte and cartilage of OA and aged donors and in chondrocytes stimulated with IL-1b. Inhibition of CD38 by its inhibitor apigenin in human OA chondrocytes diminished NADase activity, raised NAD+ levels, improved mitochondrial function, prevented excessive oxidative stress, and attenuated chondrocyte and cartilage catabolic responses to IL-1b likely via SIRT1 and SIRT3 signaling. Treatment of human OA chondrocytes with NAD+ precursor nicotinamide riboside (NR) also led to increase in NAD+ levels and attenuation of chondrocyte and cartilage catabolic responses to IL-1b. These data suggest that maintaining a proper chondrocyte NAD+ content is critical for cartilage homeostasis.

In this translational project, we propose to test our central hypothesis that NAD+ decline contributes to cartilage degradation after joint injury and spontaneously during aging, and restoration of NAD+ levels limits OA development and progression in mice in vivo using experimental mouse models of both injury-induced OA through destabilization of medial meniscus (DMM) and age-related spontaneous OA. Completion of these studies will provide new insights into how critical NAD+ metabolism influences cartilage tissue integrity and a translational approach to help develop and test novel medical treatment for OA.

Erikah Darrah, PhD

Johns Hopkins University

The Role of Citrullination in the Processing and Presentation of Autoantigens in Rheumatoid Arthritis

Citrullinated proteins, generated via the post-translational deimination of arginine residues by the peptidylarginine deiminase enzymes (PADs), are hallmark targets of the autoimmune response in rheumatoid arthritis (RA). Despite the wide-spread acceptance of citrullinated antigens as key drivers of RA pathogenesis, it remains unknown how citrullinated antigens become immunologic targets. The strong association of anti-citrullinated protein immune responses with a specific group of MHC class II alleles called the “shared epitope” (SE) alleles suggests that CD4+ T cells specific for citrullinated peptides are critical for this process. A growing body of evidence suggests that even minor modifications to self-proteins may play a role in their targeting by the immune system through alteration of class II antigen processing. This supports a mechanism for how citrullination of self-proteins may lead to the generation of neo-epitopes. In addition, a newly described form of neutrophil death induced by host and bacterial pore-forming molecules, called leukotoxic hypercitrullination (LTH), has been shown to trigger widespread protein citrullination and may act as a pro-inflammatory source of citrullinated autoantigens in RA. This proposal aims to define the consequences of citrullination on antigen processing at the molecular level using proteolytic mapping and a novel cell-based natural antigen processing assay. This proposal will also determine if neutrophils dying by LTH are a pro-inflammatory source of RA autoantigens and will provide a cellular model to interrogate the efficacy of current and emerging therapeutics on this process. These studies have the potential to define fundamental mechanisms by which citrullinated proteins become immunogenic targets in patients with RA and elucidate some of the most proximal factors in RA initiation. This may inform the design of novel therapies aimed at blocking the generation of immunogenic peptides or selectively inhibiting antigen-specific immune responses.

Liana Fraenkel, MD, MPH

Berkshire Medical Center

Improving Treat-to-Target by Incorporating the Patient Perspective

Despite proven benefits and widespread endorsement, implementation of treat-to-target (T2T) strategies in rheumatoid arthritis (RA) is low, with most studies demonstrating appropriate escalation of treatment in less than 50% of patients with moderate to high disease activity. Documented reasons underlying poor adherence to T2T strategies include discordance between disease activity scores and rheumatologists' global impact scores, co-morbidities, medication lag, and patient reluctance. Of these, only the latter represents a missed opportunity to escalate treatment. Therefore, increasing T2T rates will require changing patients' decision-making.

We propose to gain in-depth understanding of patients' decision making using the mental models approach to risk communication (MMARC) derived from decision science. The objective of the MMARC is to develop interventions which address the critical discrepancies between experts' and end-users' mental models. In this context, mental models refer to rheumatologists' and patients' thought processes and beliefs about how T2T strategies work.

We hypothesize that patient reluctance to add or change medications does not represent a dichotomous perspective, but rather that patients can be clustered into distinct groups based on their mental models of T2T in RA. We will first create a rheumatologist mental model of T2T in RA. We will then conduct up to 30 in-depth mental model interviews with a purposeful sample of patients to create a RA patient mental model. We will field a large-scale survey to quantify the prevalence of the specific patient factors (e.g., illness perceptions, attitudes, and beliefs) related to T2T generated in the interviews, objective knowledge underlying implementation of T2T, and the relationships between key concepts. We will use Best Worst Scaling to quantify the relative importance of patients' beliefs. We will subsequently use latent class analysis to define distinct RA patient positions based on the BWS data. This effort will identify critical gaps between the rheumatologist and patient mental models and will identify the content to be targeted in interventions. Lastly, we will create a framework matching communication strategies to distinct RA patient positions towards T2T.

The results from this study will inform interventions to improve T2T strategies both at the individual RA patient and population level.

Sarah L. Gaffen, PhD

University of Pittsburgh

Regulation of Renal IL-17 Signaling in Antibody-Mediated Kidney Diseases

Kidney is an immunologically distinct organ, due to poor regenerative capacity, accumulation of toxins (uremia), hypoxia and arterial blood pressure. Our understanding of the fundamental immune processes in the kidney lags behind that of other visceral organs such as the gut or liver. End organ damage is a major cause of morbidity and mortality in patients with rheumatic disease. Autoimmune glomerulonephritis (AGN) causes significant mortality and morbidity in auto-inflammatory kidney disorders, and lupus nephritis affects up to 60% of adults with systemic lupus erythematosus (SLE). Indeed, renal injury is the most important predictor of mortality in SLE patients. Given the urgent need to ameliorate responses in patients with kidney damage, the development of improved therapeutic approaches will require a more comprehensive understanding of fundamental inflammatory responses affecting AGN, including immune events occurring directly within renal specific cell types. The cytokine IL-17 contributes significantly to damage of glomerular and tubular epithelial cells during AGN, but its underlying signaling mechanisms remain poorly understood. One of the major genes induced by IL-17 signaling is a kidney-damaging factor known as Lipocalin 2 (Lcn2), which causes apoptosis of RTECs and is a hallmark biomarker of kidney disease. Expression of Lcn2 is controlled at multiple levels, requiring complex integration of both transcriptional and post-transcriptional mechanisms. The objective of this proposal is to dissect the regulation of IL-17 and Lcn2 signaling in the kidney by defining specific cellular targets and mechanistic interactions between regulation of transcription and control of mRNA. The premise of this project, and indeed of basic immunology research in general, is that defining the fundamental basis of inflammation can lay essential groundwork for the rational design of therapeutic interventions.

S. Reza Jafarzeda, DVM, MPVM, PhD

Boston University

Personalized Dynamic Regimens of Physical Activity for Persons with Knee Osteoarthritis

Limited understanding of factors affecting the course of osteoarthritis has hampered the development of strategies that would lessen pain and slow disease progression. Osteoarthritis is a mechanically-driven disease. There are important knowledge gaps regarding the effects of physical activity, the most common reason for mechanical stimulation of joint structures. Osteoarthritis-related pain is mainly activity-induced (e.g., stair climbing, walking), but paradoxically, walking regimens can reduce pain. It is uncertain what duration and intensity of activity could be beneficial for pain relief or function improvement without causing harm and accelerating disease progression. The long-term goal of this project is to facilitate decision making for clinicians and patients of a more optimal physical activity regimen for pain relief, maintaining functional performance, and decelerating structural damage in osteoarthritis. This proposal hypothesizes that physical activity's influence on osteoarthritis outcomes differs depending on individual characteristics and the stage of disease. Further, I hypothesize that the optimal activity regimen may evolve as the patient characteristics change. Therefore, a person-specific physical activity regimen that is adjustable and consistent with the patient's current characteristics is needed. I utilize data from Osteoarthritis Initiative (OAI) and Multicenter Osteoarthritis Study (MOST) cohorts, two large-scale longitudinal studies on osteoarthritis with extensive clinical, imaging, medication history, and physical activity data, measured objectively by accelerometer. My aims are: 1) to characterize the time-varying association of physical activity types with knee osteoarthritis structural progression, 2) to examine a person-specific and dynamic physical activity regimen for pain reduction in persons with knee osteoarthritis, and 3) to characterize a person-specific and dynamic physical activity regimen for performance-based physical function in persons with knee osteoarthritis. This work contributes to a better understanding of how physical activity duration and intensity may improve or worsen the outcomes of osteoarthritis. Unlike population-oriented approaches in trials that were indifferent to an individual's unique characteristics, this study develops a person-specific approach that allows adjustment to a physical activity regimen as the disease evolves. This work will provide new evidence about diverse durations and intensities of physical activity and could inform better osteoarthritis management.

Alessandra B. Pernis, MD

Hospital for Special Surgery

Signaling Pathways Regulating ABCs

ABCs (autoimmune/age-associated B cells) are an emerging B cell subset that has recently been implicated in autoimmunity. ABCs are the major producers of autoantibodies in SLE patients, and their peripheral expansion correlates with disease severity and specific clinical manifestations, including lupus nephritis. Formation of ABCs is promoted by toll-like receptors (TLR7 and TLR9) and cytokines (IFN-γ and IL-21). Although generation of ABCs requires T-bet (and hence these cells are also known as CD11c+T-bet+B cells), the molecular pathways that promote their generation, function, and differentiation in autoimmune settings are largely unknown. The SWEF family of proteins is comprised of only two members, SWAP-70 and DEF6, which have recently been identified as genetic risk factors for human SLE. The SWEF proteins are multifunctional proteins and play an important immunoregulatory role as demonstrated by the fact that the lack of SWEF proteins in mice leads to the development of a lupus syndrome, which preferentially affects females similarly to human lupus. We have recently found that the lupus syndrome that develops in female mice lacking the SWEF proteins is accompanied by a marked accumulation of ABCs. We have furthermore found that generation of ABCs in SWEF-deficient mice is associated with dysregulated activity of IRF5 whose variants are strongly associated with SLE. In this project, we will investigate the hypothesis that the SWEF proteins regulate ABC generation and function by a dual mechanism, which involves not only restraining IRF5 activity but also preventing the downregulation of inhibitory transcriptional complexes. We will also delineate the pathways controlling the differentiation of ABCs into plasma cells. Understanding the molecular mechanisms responsible for the regulation and differentiation of ABCs will provide critical information into SLE pathogenesis and help uncover novel therapeutic targets.

Sarah Ringold, MD, MS

Seattle Children's Hospital/Seattle Children's Research Institute

Disease Recapture after Drug Discontinuation and Flare in JIA

The use of conventional disease-modifying antirheumatic drugs (DMARDs) and biologic medications has significantly improved disease control for children with juvenile idiopathic arthritis (JIA), resulting in increasing numbers of children attaining remission. Ongoing treatment after achieving disease control comes with multiple downsides, including the considerable costs of biologic medications, missed school and work for infusions, toxicity risks, side effects, the psychological burdens of repeated injections, and the uncertain risks of future adverse drug effects, particularly malignancies. As a result, stopping medication for remission is a priority for many patients, families, and clinicians. An important part of the decision-making around stopping treatment is understanding whether restarting medications can promptly and fully control flares that follow medication discontinuation. Very few data regarding disease recapture for children with JIA have been published. This lack of data contributes to the uncertainty surrounding outcomes associated with medication discontinuation and makes decisions about medication discontinuation particularly challenging for patients, families, and providers.

This proposal will generate much needed information for providers and families to make more informed decisions about the risks and benefits of continued medication use versus discontinuation. The data collected during the study period will identify children with lower rates of successful recapture who may benefit from alternative management strategies, such as dose reduction instead of complete discontinuation. This study will lay the groundwork for future research on biologic predictors of recapture and facilitate the development of personalized regimens for both discontinuing and re-initiating treatment following flare once initial remission is achieved.

John Varga, MD

Northwestern University

Dysregulated Ciliogenesis in Scleroderma: Novel Pathogenic Mechanism?

Fibrosis, the defining feature of systemic sclerosis (SSc), is characterized by accumulation of activated myofibroblasts that originate from mesenchymal progenitors through fibroblast-myofibroblast transition (FMT) and endothelial cell-myofibroblast transition (EndoMT). However, there is a gap in understanding how in SSc fibrosis develops synchronously in multiple non-contiguous organs, as well as the mechanisms that drive and sustain the process. The objective of this application is to capitalize on our recent discoveries that implicate SPAG17 (sperm-associated antigen 17) and primary cilia in the pathogenesis of SSc. Using unbiased RNAseq technology, we found that expression of a little-known protein called SPAG17 was markedly reduced in SSc patients. We showed that SPAG17 regulates the formation, maintenance and function of primary cilia, which are ubiquitously expressed essential sensory antennae for hedgehog and related profibrotic morphogens (Wnt, TGF-ß). The premise of this proposal is that SPAG17 controls both ciliogenesis and fibrogenesis, and its reduced expression in SSc will result in aberrant profibrotic ciliary signaling and multiple organ fibrosis. Our proposal is highly innovative, since the mechanism and role of SPAG17 in fibrosis have never been studied, and the contribution of cilia to disease pathology in SSc is unknown. Our investigative research team with deep expertise and unique experimental tools in myofibroblast biology, fibrosis and ciliogenesis is poised for successful accomplishment of these aims. Understanding the contribution of SPAG17 and ciliogenesis in fibrosis will inform the development of entirely new approaches for fibrosis therapy.

Chenchen Wang, MD, MSc

Tufts Medical Center

Neurobiological Mechanisms of Mind-body Therapy for Knee Osteoarthritis

This proposal aims to provide crucial knowledge of the neurobiological mechanisms underlying Tai Chi mind-body therapy for knee osteoarthritis. Knee osteoarthritis is a leading cause of long-term pain and disability for which no effective medical treatments currently exist. Our recent trials showed that Tai Chi mind-body exercise for knee osteoarthritis produced clinical improvements in pain and function after 12 weeks of intervention, with benefits maintained up to 12 months. However, limited knowledge of the underlying mechanisms has restricted the understanding and further development of this promising therapy.

The long-term objective of our research is to provide theoretical and empirical evidence to optimize the effects of Tai Chi for patients with knee osteoarthritis. The aim of this study is to investigate the central mechanism of knee osteoarthritis pain using brain imaging technology to evaluate how brain function and structure change in response to mind-body exercise over time. By combining multiple brain imaging modality measurements, we will examine the neural substrates of Tai Chi compared with wellness education in adults with knee osteoarthritis. We will randomize eligible individuals who meet the American College of Rheumatology criteria for knee osteoarthritis into Tai Chi mind-body practice or wellness education interventions. We will compare changes in resting state functional connectivity of the cognitive control network functional magnetic resonance imaging responses to pressure pain and brain morphometry, as well as their association with clinical outcomes. Results of this innovative mechanistic study will have important therapeutic implications and provide critical insight into the clinical, behavioral, and neurobiological mechanisms of the potential disease-modifying role of mind-body therapies for osteoarthritis. The findings will lead to the establishment of a new treatment paradigm in osteoarthritis and have broad application to the management of chronic musculoskeletal pain.

Innovative Research Award for Community Practitioners

The Innovative Research Award for Community Practitioners will help enable research that has the potential to improve treatment of rheumatic diseases, patient outcomes, and/or increase quality of care.

Norman B. Gaylis, MD, Research Award for Rheumatologists in Community Practice

Established with a generous commitment to the Foundation from Dr. Gaylis, the Norman B. Gaylis, MD, Research Award for Rheumatologists in Community Practice provides funding for rheumatologists in community-based practice who, in addition to taking care of patients, want to test their own observations through research.

Sou-Pan Wu, MD

HealthPartners

The Hmong Gout Project

It is well known that in the Twin Cities Minnesota area, ethnic Hmong patients often present with severe manifestations of gout. Compared to other ethnic groups, Hmong patients develop gout at an earlier age, often with very high urate levels, rapid progression to tophi, renal insufficiency, difficulty controlling inflammatory joint destruction, as well as poor response to traditional doses of urate lowering therapy. The complications of gout among the Hmong lead to decreased quality of life and early disability. This is often further exacerbated by distrust of Western medicine among the Hmong.

Based on genetic studies in other population cohorts, particularly the New Zealand Polynesians and Taiwanese aborigines, it is suspected that there are also genetic factors that play an important role in the development of hyperuricemia and intense inflammatory response in the Hmong. Some genetic variations in East Asians already known include the SLC2A9, ABCG2, and SLC22A12 genetic loci, among others. Many of these genes are important in urate transport.

This project seeks to identify these and other genetic factors specific to the Hmong, develop a genetically and clinically based statistical risk model, and to create a registry for this particular vulnerable population. An understanding of why gout is so common and severe for the Hmong can help medical providers provide earlier detection and better communication with these patients, which may lead to more timely treatment and prevention of subsequent morbidities that occur because of gout.

Career Development Research Awards

Career Development Bridge Funding Award: R Bridge

The R Bridge Award encourages essential rheumatology research by supporting promising investigators who are at risk of running out of research funding and are revising outstanding NIH R01 or VA RCS/ORD award applications.

Erika H. Noss, MD, PhD

University of Washington

Investigating How Platelet-derived Growth Factor Receptors Direct Synovial Fibroblast-Mediated Pathology in Inflammatory Arthritis

Even with our newest rheumatoid arthritis (RA) therapies, most patients do not achieve disease remission, suggesting new treatment approaches are needed. Since all currently approved drugs block components of the systemic immune response, the number of effective drug combinations is limited by the infection risk from long-term immunosuppression. One way to increase treatment efficacy while minimizing immunosuppression is to target the non-immune resident joint cells that also contribute to RA pathology. One such cell is activated synovial fibroblasts, which function both to amplify inflammation and directly erode cartilage. We have identified platelet-derived growth factor receptors (PDGFRs) as candidate molecules for targeting RA synovial fibroblasts. PDGFR expression is upregulated in RA, and their activation stimulates fibroblast proliferation, migration, and invasion, key pathologic pathways of RA fibroblasts. PDGFR blockade is particularly attractive as a candidate therapy, as new anti-PDGFR biologics have been developed in other diseases. As they are already used in other patient populations, these drugs may be more rapidly translated to autoimmune arthritis treatment. Our research objective is to determine how PDGFRs function in a pre-clinical arthritis mouse model and in synovial fibroblasts, assessing the translational potential of anti-PDGFR therapeutics and increasing our basic understanding of joint biology. This bridge award allows us to move forward these research efforts, supporting the revision of an NIH R01 application to further support this work.

Jose U. Scher, MD

New York University

Employing the Gut Microbiome to Accelerate Effective Initiation of Rheumatoid Arthritis Therapy

Rheumatoid arthritis (RA) – a complex, multifactorial, autoimmune disorder affecting ~1% of the worldwide population (~2 million adults in the US) – is characterized by chronic synovitis that, left untreated, can result in irreversible joint destruction and deformity, leading to increased morbidity and all-cause mortality. The last three decades have witnessed impressive advances in the understanding of disease pathogenesis and therapeutic outcomes. The use of methotrexate (MTX) first and subsequent incorporation of anti-TNF and other "biologics" have substantially improved RA clinical outcomes, enhancing quality of life for millions of patients. Nonetheless, a significant question remains unanswered: why do >50% of patients with moderate-to-severe RA fail to respond appropriately to these agents? Pharmacomicrobiomics – an emerging field that investigates the effect on drugs of human gut microbiome variations – promises to overcome these barriers and facilitate precision medicine approaches in autoimmune disease. MTX remains the anchor drug for RA treatment, but achieves significant results in <50% of patients and remission in only 25%. Its inter-individual bioavailability is extremely variable, ranging from 10-80%, for reasons that are presumably multifactorial. The intestinal microbiome and its enzymatic machinery are likely to play a significant role, based on our preliminary results and given that MTX metabolism differs significantly in animals treated with antibiotics or kept under germ-free conditions versus controls. Our multidisciplinary team will study: a) whether baseline intestinal microbiome, its genes, and associated metabolites can be used to predict the immunomodulatory responses to MTX in treatment-naïve, new-onset RA (NORA) patients; and b) the mechanisms through which specific gut bacterial communities modulate MTX biotransformation and bioavailability. We believe that the results of our highly translational, innovative studies will directly influence therapeutic approaches for the treatment of RA and offer a more personalized approach in which clinical response would be predicted early in any given patient and potentially discover novel treatment strategies based on gut microbial modulation.

CAREER DEVELOPMENT RESEARCH AWARD
Career Development Bridge Funding Award: R Bridge

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.

Tamar B. Rubinstein, MD, MS

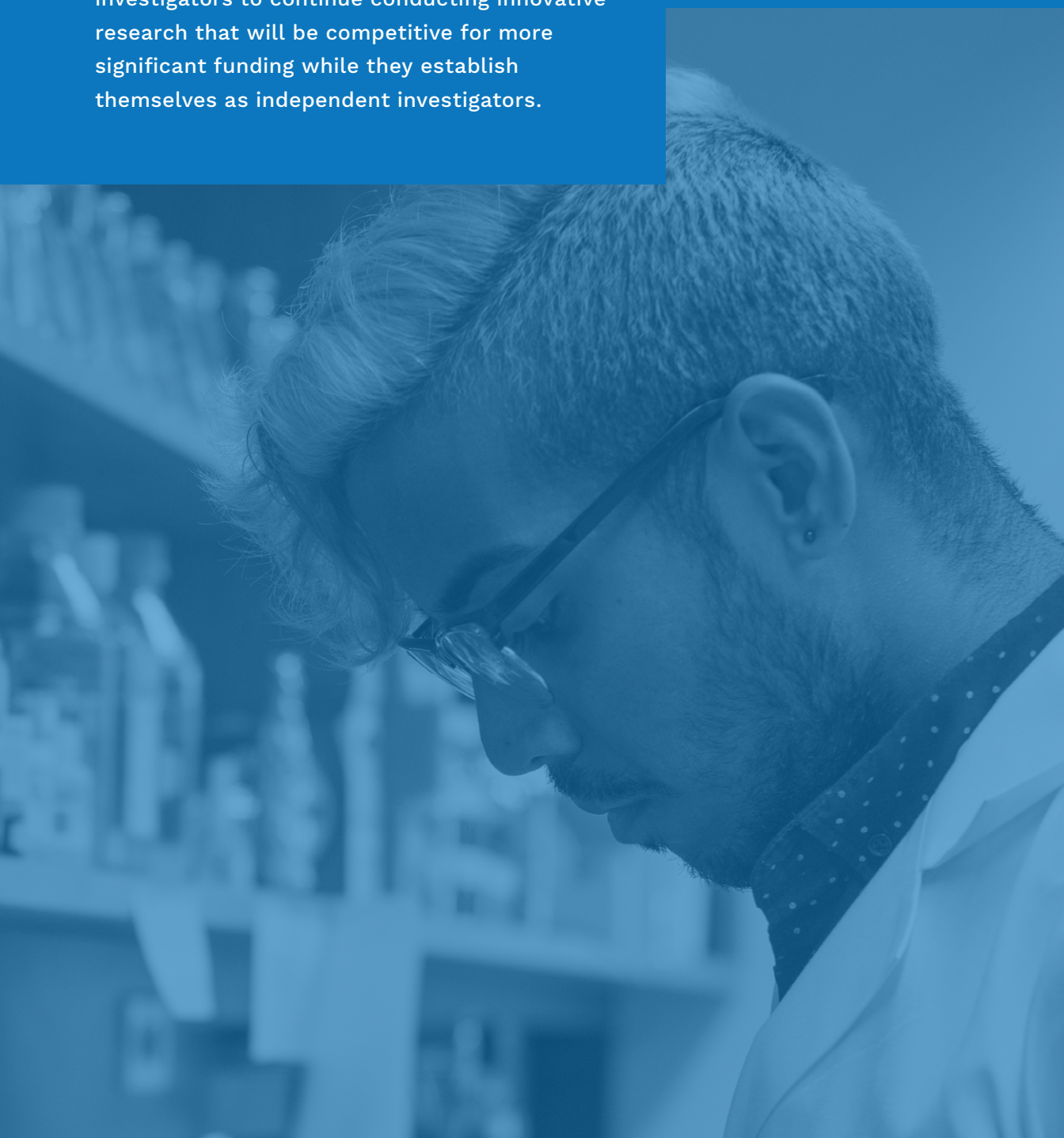
Albert Einstein College of Medicine

Investigating the Impact of Adverse Childhood Experiences in Youth with Lupus

Exposure to major life adversity may be associated with worse pediatric systemic lupus erythematosus (pSLE), a devastating multi-organ disease that can occur in childhood. Adverse Childhood Experiences (ACEs) are experiences of neglect, abuse, violence, and household dysfunction, and important examples of major life adversity for youth. This research will investigate the connection between adversity, psychological distress, and organ damage in youth with pSLE; explore epigenetic changes that may play a role; and aim to uncover targets for future interventions to improve the health of youth with pSLE.

Investigator Award

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.



Colleen K. Correll, MD, MPH

University of Minnesota

Assessment of Environmental Risk Factors and Metabolomic Profiles for Juvenile Idiopathic Arthritis Disease Flare and Progression

Juvenile idiopathic arthritis (JIA) is characterized by chronic arthritis affecting children, and encompasses seven subtypes based upon clinical phenotype. However, as more sophisticated genomic research has been conducted over the last decade, these phenotypical subtypes have come into question. Based upon genetic studies of JIA and adult rheumatoid arthritis (RA), four major clusters of arthritis have been identified based upon shared risk alleles: seropositive arthritis, seronegative arthritis, spondyloarthritis, and systemic arthritis. However, within these four large groups defined by genetic similarities, internal heterogeneity exists. It is theorized that much of this heterogeneity is secondary to environmental exposures and gene-environment interaction. Yet, while high technology and data-driven genomic studies continue to be conducted, similar high-technology studies to evaluate the role of environmental exposures in disease pathogenesis, such as metabolomics, are lacking. Metabolomics allows for the detection and quantification of a robust profile of small molecules in a biological specimen. It represents the portrait of exogenous and endogenous metabolites and can help identify novel disease associations and biochemical pathways in disease pathogenesis. The importance of metabolomics research has been gaining attention in many chronic diseases including RA. However, there is a substantial lack of metabolomics research in JIA. We have previously established the JaMINN Study (Juvenile Arthritis in Minnesota), a statewide population-based cohort of patients with JIA in Minnesota, to identify genetic and environmental factors associated with disease onset and progression. Through JaMINN, we are prospectively collecting environmental exposure data through questionnaires to identify exposures associated with JIA. We seek to expand upon the JaMINN Study by conducting a metabolomics profiling and case-control study to understand the role of exogenous metabolites associated with JIA disease onset. We hypothesize that patients with JIA will have a unique metabolic profile, which will lead to a better understanding of JIA pathogenesis and potential treatments.

Paul J. Hoover, MD, PhD

Brigham & Women's Hospital

Dissecting the Role of Myeloid Cells in Lupus Nephritis

Lupus nephritis (LN) is a devastating autoimmune disease with few therapies. Prior work has shown that myeloid cell infiltration is associated with pathologic tissue changes and reduced renal function. A deeper understanding of these cells could yield more accurate interpretation of histopathologic lesions, better disease predictors, and new therapeutic concepts. We propose the hypothesis that myeloid cells within LN kidney form a highly organized network that drives tissue remodeling and clinical outcome.

Preliminary support for this hypothesis derives from the Accelerating Medicines Partnership (AMP) consortium. Single-cell RNA seq (scRNA-seq) of LN tissue identified 21 immune cell types/states enriched in diseased compared to healthy kidneys, including 5 myeloid phenotypes: 1 resident macrophage, 1 dendritic cell, and 3 monocyte-like. Spatial localization of cells within different kidney compartments or their relation to damaged tissue and clinical outcome were not determined.

Therefore, we collected fixed kidney samples from 40 patients presenting with 3 major LN histological classes. Using markers defined by scRNA-seq, in class IV tissue, we mapped the 5 myeloid cell subsets to glomeruli and interstitial regions, defining the organization of myeloid cells in situ. We now propose 3 aims to build on these findings. In Aim 1, we will expand and confirm the definition of myeloid cells using scRNA-seq and in situ staining. In Aim 2, we will spatially map the distribution of each myeloid cell type and their immune cell neighbors in annotated LN tissue. These aims will localize and deconstruct myeloid and local immune cell neighborhoods for new insights into tissue damage. In Aim 3 we will identify associations between in situ myeloid organization, lesions, and clinical phenotypes. This proposal offers a powerful approach to identify mechanisms driving disease and would provide the basis for a new histological classification based on the immune response, more effective disease predictors, and drug targets.

Namrata Singh, MD, MSCI, FACP

University of Iowa

Impact of Early Therapy with Tumor Necrosis Factor Inhibitors on Lymphoma Risk in Patients with Rheumatoid Arthritis

Population studies conducted over the past decades have linked lymphoma and rheumatoid arthritis (RA). RA disease activity and duration are recognized risk factors for lymphomagenesis. Treatment of RA patients with tumor necrosis factor inhibitors (TNFi) and a “treat-to-target” approach has markedly improved outcomes and remission rates in RA, but the impact of this paradigm on incident lymphoma is not known. This career development application outlines a didactic and research training program with linked aims to address the hypothesis that the declining lymphoma incidence in veteran RA patients over recent time (as observed in our preliminary studies) is likely from an improved control of systemic inflammation by early intervention with biologic agents such as TNFi. Specific Aims will: (1) examine the effect of early intervention with bDMARDS (i.e., TNFi) on incidence of lymphoma in RA, (2) examine the contributions of intervention with TNFi and disease control in mediating risk of lymphoma in RA, and (3) evaluate the impact of TNFi intervention on lymphoma risk in specific patient sub-groups and lymphoma subtypes. The experimental approach will use a population-based retrospective cohort study design of patients treated at nationwide Department of Veterans Affairs’ (VA) Medical and a novel mediation analysis. The knowledge gained through this study can be used to inform RA treatment guidelines, as well as discussions of treatment options with patients in the clinic.

Elizabeth Wellsandt, PhD, DPT

University of Nebraska Medical Center

Role of Biomarkers in the Osteoarthritis Pathway After Joint Injury

Posttraumatic osteoarthritis (PTOA) is rapidly becoming a major rheumatology concern in younger adults. Within ten years, 50% of individuals with an anterior cruciate ligament (ACL) injury develop PTOA, which is directly contributing to a 76% increase in recent total knee replacement surgeries among Americans aged 20-49 years. Younger adults with PTOA will live with this chronic disease for much longer than previous generations, resulting in substantial societal and personal burden. However, evidence-based interventions to prevent PTOA do not exist, and no prognostic clinical markers are available to identify patients most at risk for PTOA development. Our long-term goal is to prevent PTOA after knee injury before irreversible degenerative processes occur. We know that within months of ACL injury, a cascade of changes in biochemical markers and articular cartilage microstructure (such as T2 relaxation) indicate negative joint alterations. Therefore, the purpose of this study is to determine associations between knee joint loading after ACL injury with biochemical and structural signs of joint degeneration. Our central hypothesis is that lower levels of joint loading after ACL injury are associated with markers of joint breakdown. Our first aim will determine the range of healthy knee joint loading after ACL injury by correlating physical activity levels and gait biomechanics with serum and synovial fluid biomarkers of cartilage degeneration, bone resorption, and joint inflammation. Our second aim will develop a prognostic model of PTOA for future clinical application by correlating demographic, biochemical, physical activity, biomechanical, and clinical measures with increased T2 relaxation time (as a marker of future PTOA). The prognostic factors that emerge from this study will inform the development of a future clinical tool to identify patients at high risk for PTOA who may benefit from novel rehabilitation approaches that optimize total daily joint loading to prevent or delay PTOA after knee injury.

Scientist Development Award

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

April M. Jorge, MD

Massachusetts General Hospital

Investigation into the Potential Impact of Hydroxychloroquine Dose-Reduction on the Risks of Systemic Lupus Erythematosus Disease Flare and Mortality

Hydroxychloroquine (HCQ) is a cornerstone of SLE care and has been shown to reduce disease flares, improve survival, and lower the risks of certain comorbidities including venous thromboembolism (VTE). However, its major dose-limiting toxicity is vision-threatening HCQ retinopathy, and recent data describing increased retinopathy risk led to revised ophthalmology weight-based dosing guidelines, recommending HCQ dosing <5mg/kg/day. These guidelines now effectively recommend a lower dose of HCQ for many patients, as the prior commonly prescribed 400mg/day exceeds 5mg/kg for over 50% of women and 25% of men. Thus, in recent years, low-dose HCQ is increasingly prescribed. However, it is unknown whether lower HCQ dosing, per the latest guidelines, maintains the same benefits of prior dosing or whether it leads to worse outcomes for patients with SLE. To address this key issue, we will investigate the potential impact of lower HCQ dosing, per the guidelines, on SLE disease activity, mortality, and the comorbidity VTE. We will utilize two established lupus cohorts to achieve these goals, the Partners Healthcare Lupus Cohort and the Kaiser Permanente Northern California (KPNC) lupus cohort. We will examine the impact of HCQ dose reduction on SLE hospitalizations using both datasets. We will additionally examine the impact on overall SLE flares using detailed medical record review within the Partners cohort, and we will examine the impact on less frequent outcomes including mortality and VTE using the large KPNC cohort. We will use inverse probability of treatment weighting in our analyses to overcome potential confounding by indication. The proposed work is expected to provide critically important evidence regarding the potential loss of efficacy of low-dose HCQ in the treatment of SLE.

Sahar Lotfi-Emran, MD, PhD

University of Minnesota

Murine Exposure to Natural Infectious Process Generates Robust Antigen and Collagen Induced Arthritis that Requires Resident Memory Cd8+ T Cells

Progress in understanding of both preclinical and clinical rheumatoid arthritis (RA) and an enlarged arsenal of target specific biologic disease modifying agents highlight that RA is not a monolithic disease but a common clinical phenotype with diverse pathophysiological pathways. Significant questions remain and fundamental hurdles in RA treatment require further understanding of both humoral and cell mediated mechanisms of disease, a goal which in turn requires disease models that better reflect the human immune system and response. The contribution of site specific, peripheral tissue immune networks and immunosurveillance mechanisms to what is often an individual-joint specific disease process has had little exploration. Our lab has demonstrated the importance of mouse pathogen exposure (“dirty” mice) to establish a basal immune network comparable to that of an adult human. Like adult humans, dirty mice have established resident memory CD8+ T cell populations and generate more immunoglobulin of all subclasses in comparison to specific antigen free (spf) mice. These aspects of “dirty mice” are key for modeling RA, a disease with both cell mediated and humoral immune mechanisms and a compelling role for intestinal dysbiosis. The goal of this project is to generate a “dirty” RA mouse model and evaluate the contribution of resident memory immune networks to disease expression. Ultimately, this proposal and the data generated herein will advance our understanding of the pathophysiology of RA and will be used to identify immune signals to appropriately select optimum biologic disease modifying anti-inflammatory therapy and develop local resident memory cell targeted therapies.

Lindsey A. MacFarlane, MD, MPH

Brigham & Women's Hospital

Association Between Adiposity and Inflammation in Knee Osteoarthritis

Symptomatic knee osteoarthritis (OA) is prevalent and disabling. Obesity affects over 30% of U.S. adults and increases the risk of knee OA. The biomechanical consequences of excess weight do not fully explain the link between obesity and risk of knee OA, prompting interest in obesity-related inflammation as a disease mechanism. Indeed, adipose tissue elaborates pro-inflammatory cytokines, but it is unclear whether obese individuals are more prone to an inflammatory OA phenotype, as characterized by evidence of inflammation on MRI, ultrasound or synovial white blood cell count.

Intra-articular inflammation manifesting as synovitis is a frequent finding in knee OA and is associated with accelerated cartilage damage and pain. Synovitis is commonly identified on MRI, but there has been little research on whether synovial fluid white blood cell (WBC) count or ultrasound offer clinically available and less costly methods of identifying synovitis. Synovitis may also have treatment implications, as it is associated with response to corticosteroids and inhibitors of pro-inflammatory cytokines. Body mass index (BMI) is positively associated with synovitis in knee OA on MRI. While BMI is widely used to assess obesity, it does not distinguish lean from fat mass. In comparison to BMI, measures of central obesity, such as waist circumference, are better predictors of cardiovascular risk factors. Whether measurements that more directly assess fat distribution are more closely associated with the presence of synovitis and pain in knee OA is unknown.

I propose to recruit a prospective cohort of 136 patients with symptomatic knee OA. I will assess performance characteristics of synovial fluid WBC count and ultrasound-identified synovitis in comparison to MRI-identified synovitis. I aim to investigate whether BMI or measures of central obesity associate with an inflammatory OA phenotype, and whether this subset with inflammatory knee OA have a favorable response to anti-inflammatory therapy.

Mazen N. Nasrallah, MD, MSc

Massachusetts General Hospital

Clinical and Translational Dissection of Inflammatory Arthritis Related to Immune Checkpoint Inhibitor Therapies

Harnessing the power of the immune system to treat solid cancer has been met with great success. By antagonizing molecular checkpoints that function to negatively regulate immune cell activation, checkpoint inhibitor therapies can potently augment anti-tumor immunity. However, these therapies are often limited by immune related adverse events (irAEs) that have the potential to affect nearly every organ system. Inflammatory arthritis that can mimic rheumatoid arthritis, seronegative spondyloarthropathies and polymyalgia rheumatica is a well-recognized irAE; however, the full clinical spectrum and natural evolution of these presentations is poorly characterized. These toxicities often necessitate interruption or cessation of immunotherapy as well as the initiation of immunosuppressive treatments with potential untoward effects on anti-tumor immunity. As such, there is a critical need to better study these events both clinically and translationally to enable earlier recognition of these toxicities, allow targeted treatment of immune-toxicity without affecting anti-tumor response, and gain insights into classical autoimmune diseases that these irAEs resemble. To study these irAEs we have established a specialty clinic that provides comprehensive clinical evaluation and long-term follow up and enables sample collection for translational studies. We propose to leverage the power of single-cell genomic analyses to profile the immune-cell phenotypic and molecular changes that occur as a result of immune checkpoint inhibitor therapy in patients who develop inflammatory arthritis. By analyzing blood and synovial tissue samples collected pre-immunotherapy and serially from patients with irAEs, we will be able to define changes occurring as a result of immunotherapy and identify specific cellular populations expanded in autoimmune lesions. Because these toxicities provide a model to study mechanisms of immune-tolerance and breakdown, we believe that this is a unique opportunity to study proximate events leading to autoimmunity in humans.

Michael A. Paley, MD, PhD

Washington University in Saint Louis

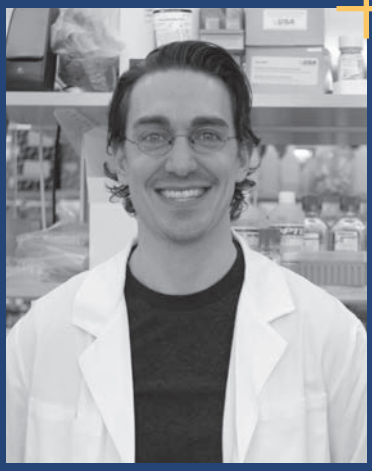
Eye-Antigen-Specific T Cell Responses in Uveitis

Eye inflammation such as uveitis occurs in multiple rheumatologic disorders and can lead to permanent vision loss. How immune cells contribute to ocular inflammation, however, is poorly understood. We hypothesize that relapsing or chronic human uveitis is driven by autoreactive T cells responding to eye antigens. To determine whether ocular T cells participate in an antigen-driven process, we have created a biorepository of ocular and blood samples from patients with active uveitis to be analyzed with single-cell RNA sequencing (scRNAseq) and single-cell T cell receptor (TCR) sequencing (scTCRseq). We plan to compare T cells isolated from the inflamed eye to T cells from the blood to assess antigen-specific responses. Preliminarily, we have performed scRNAseq and scTCRseq on cells isolated from the anterior chamber of a subject with granulomatous uveitis. Consistent with prior reports of sarcoid-associated uveitis, the majority of immune cells were CD4 T cells, with a smaller contribution of monocytes, B cells, and CD8 T cells. scTCRseq revealed that the CD4 T cell population was oligoclonal, supporting the hypothesis that antigens within the eye may contribute to chronic uveitis in humans. This patient demonstrates the feasibility of using scRNAseq and scTCRseq to interrogate antigen-specific responses in ocular inflammatory disease. Further biospecimen collection and data analysis is ongoing. We anticipate that the combined scRNAseq and scTCRseq datasets will offer a platform to interrogate pathogenic cells and their respective cytokines in order to improve the selection of targeted therapies in ocular inflammatory disease.

Cory A. Perugino, DO

Massachusetts General Hospital

The Identification of Auto-Antigens Driving B and T Cell Responses in Igg4-Related Disease: A Path to Studying the Mechanism of Fibrosis in Human Disease



The long-term objective of this proposal is to eventually establish an in vitro platform to study the mechanism of fibrosis in a human disease state. The overarching hypothesis is that, in the context of IgG4-related disease, B cell responses to self-antigens, such as galectin-3, drive the activation of CD4+ cytotoxic T lymphocytes through antigen presentation, which, in turn, contribute to fibrosis. Because CD4+ cytotoxic T lymphocytes are strongly associated with multiple human fibrotic diseases including IgG4-related disease, systemic sclerosis, and idiopathic pulmonary fibrosis, we hypothesize that this cell type plays an important biologic role in the development of fibrosis and may provide a novel direction for future targeted therapies.

In this proposal, we specifically aim to first, identify the repertoire of auto-antigens to which B cell responses are directed in IgG4-related disease, and second, to demonstrate a paired B- and T-cell response against the same antigen. We will be leveraging our established antigen discovery platform to address Aim 1, and our discovery of galectin-3 as an auto-antigen in IgG4-related disease using this platform to address Aim 2. We expect to find a diverse collection of auto-antigen responses among patients with IgG4-related disease. These auto-antigens may correspond with clinical sequestering by disease phenotype and may be specific to IgG4-related disease, thereby providing diagnostic utility. Because we propose to identify auto-antigens through a biologically meaningful approach (i.e., using dominantly-expanded plasmablast clones), we anticipate that the antigens identified will be capable of inducing a paired T cell response within the respective subjects.

Zheni Stavre, MD

University of Massachusetts Medical School

A Novel Nucleotide Based Nanoparticle Therapy in Treatment of Osteoporosis and Healing of Erosions in Rheumatoid Arthritis

Rheumatoid arthritis (RA) results in joint erosions/destruction and disability and an earlier development of systemic bone loss (osteopenia and osteoporosis). Osteoporosis leads to an increased risk of hip fracture and is associated with significant morbidity. There is currently no cure or therapy that will reverse joint destruction once it occurs, nor is there good therapy for the associated systemic bone loss. Most available therapies for osteoporosis target osteoclasts (bone resorbing cells) and consequently are associated with significant side effects such as osteonecrosis of the jaw and atypical femur fractures. An agent targeting osteoblasts (the bone forming cells), teriparatide is available in impractical daily injections and is limited in its use to only two years due to a fear of cancer. A newer agent, the anti-sclerostin antibody, also targets osteoblasts but has been found to have a negative impact in TNF-driven inflammatory arthritis in mice, making its use in RA patients precarious. Previously, we identified a protein called Schnurri-3 as a negative regulator of bone formation. We have recently discovered a novel association between Schnurri-3 and pro-inflammatory cytokines (IL17 and TNF), making this protein a promising target in inflammatory arthritis. With experienced collaborators, Schnurri-3 siRNA has been embedded in gold nanoparticles (SHN-3 NP) also coated with peptides that direct the nanoparticles specifically to bone after intravenous delivery. This presents a novel therapeutic strategy to address both joint erosions and systemic bone loss in RA. We hypothesize that SHN-3 NP will improve systemic bone loss and may improve joint erosions in a TNF-driven mouse model of inflammatory arthritis. If results prove fruitful, this project will pave the way to a cost effective, targeted and highly effective therapeutic delivery that is predicted to have little systemic side effects and excellent tolerability on inflammation.

Tobé and Stephen E. Malawista, MD, Endowment in Academic Rhematology

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

Kentaro Yomogida, MD

Washington University in Saint Louis

Plasticity of Innate Lymphoid Cells and Their Potential Pathological Roles in Juvenile Idiopathic Arthritis

My project is to delineate the contributions of innate lymphoid cells (ILCs) to the pathogenesis of juvenile idiopathic arthritis (JIA). ILCs are recently discovered lymphocytes without rearranged antigen receptors and are classified into three groups based on cytokine response, cytokine production and master transcription factors; T-bet+ILC1s secrete IFN-γ; GATA3+ ILC2s produce IL-5 and IL-13; and RORγt +ILC3s produce IL-17 and IL-22 as well as GM-CSF and TNF-α. While each group of ILCs has distinct phenotypic features, past reports have demonstrated their plasticity. ILC2 is known to produce IL-17 and IFN-γ in inflammatory conditions, and ILC3 can acquire phenotypes resembling ILC1 (ex-ILC3). Although ILC3 is known to convert to ILC1, the mechanisms and biological impact of ILC3 plasticity remain to be elucidated. In humans, ILC3 plasticity has been demonstrated only in vitro, and its presence has not yet been validated in vivo. Recent study revealed abundance of ILC3s in synovial fluid from patients with spondyloarthritis and psoriatic arthritis suggesting potential pathological roles of ILC3s in inflammatory arthritis. However, little is known about the mechanisms by which ILC3s may cause pathology: they could mediate damage through secretion of IL-17, IL-22, TNF-α or GM-CSF. Alternatively, ILC3 is known to acquire phenotypical features of ILC1 (ex-ILC3), and conversion into ILC1s may exacerbate pathology. Our preliminary studies demonstrate that activated ILC3s become ex-ILC3 in both human and mouse and that murine ILC3 conversion is strongly enhanced in models of autoimmunity. In addition, we identified the cell surface markers that profile ILC3s, converting ILC3s and ILC1s in human for the first time. Here, my project is divided into three parts: first, I am examining the mechanisms regulating ILC3 plasticity and generating mouse models in which plasticity is blocked. Second, I am establishing the impact of ILC3s and their plasticity in mouse models of arthritis. Finally, I am investigating the impact of ILC3s and their plasticity on JIA patients.

CAREER DEVELOPMENT RESEARCH AWARD
Tobé and Stephen E. Malawista, MD, Endowment in Academic Rhematology

Education and 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.

Jonathan S. Hausmann, MD

Beth Israel Deaconess Medical Center

Accelerating Learning and Enhancing Knowledge: Preparing Rheumatology Fellows to Succeed in a Rapidly Changing World

The future rheumatology workforce will need the skills to learn quickly and adapt to a rapidly changing medical environment. Preparing rheumatology fellows to thrive in this new environment will require changes to the way that rheumatology education is delivered: it will be necessary to be explicit about the science of learning, providing fellows with the skills and knowledge to accelerate their learning. It will also be essential to provide fellows with a solid basis in basic science and immunology from which they can direct future research and generate new knowledge.

With these goals in mind, I will develop an online “Science of Learning” curriculum for rheumatology fellows that leverages effective learning techniques. I will assess engagement of fellows with this novel curriculum and evaluate the success of the program in improving knowledge and changing fellows’ studying and learning behaviors.

I will also augment the learning impact of Rheum4Science modules by creating a complementary learning platform that incorporates distributive practice, peer teaching, and higher-order thinking questions with open-ended responses. I will assess fellow engagement with this novel learning platform and evaluate improvement in knowledge of basic science and immunology.

This project may have a significant impact on how medical education is delivered and how trainees become prepared to lead in a rapidly changing medical environment.

Philip Seo, MD, MHS

Johns Hopkins University

Rheum4Vasculitis: A Flipped-Classroom Approach to Vasculitis Education for Rheumatology Trainees

As a trainee, the systemic vasculitides can be particularly difficult to grasp. Because they are relatively uncommon, most trainees will not directly care for more than a handful of patients who have some form of vasculitis. Moreover, because of their rarity, it is difficult to devote a large amount of time to teaching trainees how to approach these diseases. Many trainees will, therefore, learn about the management of the systemic vasculitides by reading the published guidelines. It can be challenging, however, to translate these guidelines into the management of individual patients.

This project proposes a novel approach, using a "flipped classroom technique", in which the learner reads about the systemic vasculitides and then tests his comprehension by working through modules designed to simulate patients with small, medium, or large-vessel vasculitis. Each of the case-based modules will be interactive, soliciting input from the learner at crucial decision points, which will allow the learner to play out a variety of scenarios.

For each disease, cases will be selected that illustrate major branchpoints in the management of patients with systemic vasculitis, including the initial diagnosis, remission induction, remission maintenance, relapse management, and management of complications. A pre-test and a post-test will be used to assess the immediate impact of this project, and there are plans to explore the use of the American College of Rheumatology's In Training Examination to examine the impact of these modules across a broader cross-section of learners.

The modules will be programmed using the Articulate360 platform, which is already used by the American College of Rheumatology to disseminate the popular Rheum4Science modules, and will add to a growing database of learning tools that can be used by rheumatology training programs across the country.

These modules could be used as part of a longitudinal curriculum to teach post-doctoral rheumatology fellows about the diagnosis and management of the systemic vasculitides, but could also be used by more advanced learners. In addition to reading materials in advance of the modules, group discussion of the material and the cases will also be helpful to solidify the key points made by each module.

Fellowship Training Award for Workforce Expansion Recipients

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 bof the country.

University of Alabama at Birmingham

Louisiana State University Shreveport

Fellowship Training Award

The Fellowship Training Award supports the training of a rheumatology fellow to provide a more robust and highly trained workforce to care for people with rheumatic diseases.

Baylor College of Medicine
Fellowship Training Award

Children's Hospital of Los Angeles
Fellowship Training Award

Cincinnati Children's Hospital Medical Center
Amgen Fellowship Training Award

Duke University
Fellowship Training Award

Johns Hopkins University
Paula de Merieux Fellowship Training Award

Massachusetts General Hospital
Fellowship Training Award

Medstar Georgetown University Hospital
Fellowship Training Award

New York University
Amgen Fellowship Training Award

Oregon Health & Science University
Fellowship Training Award

Stanford University
Fellowship Training Award

The University of Chicago
Amgen Fellowship Training Award

Tufts Medical Center
Amgen Fellowship Training Award

University of California, San Diego
Amgen Fellowship Training Award

University of California, San Francisco
Fellowship Training Award

University of California, Los Angeles
Fellowship Training Award

University of Michigan
Amgen Fellowship Training Award

University of Minnesota
Amgen Fellowship Training Award

University of Nebraska Medical Center
Amgen Fellowship Training Award

University of North Carolina at Chapel Hill
Fellowship Training Award

University of Pennsylvania
Fellowship Training Award

University of Washington/Seattle Children's Hospital
Fellowship Training Award

Washington University in St. Louis
Amgen Fellowship Training Award

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

Dr. Nelson's exceptional support of the Foundation allowed for 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 children with rheumatic diseases have access to the care they need.

The Children's Hospital of Philadelphia

FELLOWSHIP TRAINING AWARD

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

Mentored Nurse Practitioner/Physician Assistant Award for Workforce Expansion

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

COLUMBIA UNIVERSITY MEDICAL CENTER
ANCA D. ASKANASE, MD, MPH
Leila Khalili, MSN

ARTICULARIS HEALTHCARE
COLIN C. EDGERTON, MD
Kaitlyn L. Horner, PA-C

ST. LUKE'S ADULT AND CHILDREN'S RHEUMATOLOGY
WILLIAM P. KNIBBE, MD
Teri Meadows, DNP, FNP-BC

SSK PHYSICIAN ASSOCIATES, PA
SWATI KUMAR, MD
Courtney M. Phillips, FNP-C

IDAHO ARTHRITIS CENTER
MIKAEL D. LAGWINSKI, MD
Megan M. Lane, PA-C

OREGON RHEUMATOLOGY
SHAWN MACALESTER, DO
Caitlyn Erickson, PA

THE PENNSYLVANIA STATE UNIVERSITY
NANCY OLSEN, MD
Jennifer Merris, MS, PA

DARTMOUTH HITCHCOCK MEDICAL CENTER
NICOLE M. ORZECHOWSKI, DO
Molly Keady, MSc, FNP

SOUTHWEST FLORIDA RHEUMATOLOGY
SHANMUGAPRIYA REDDY, MD
Joanne Hollingsworth, BS, MSc

MASSACHUSETTS GENERAL HOSPITAL
SARA R. SCHOENFELD, MD
Brianne L. Johnsen, MMSc, PA

UT SOUTHWESTERN MEDICAL CENTER
TRACEY B. WRIGHT, MD
Stephanie Armendariz, MSN, APRN, FNP-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.

Meagan Chriswell, BS

University of Colorado, Anschutz Medical Campus

Natural history studies in rheumatoid arthritis (RA) reveal the presence of a pre-disease "at-risk" state in first-degree relatives (FDRs) of RA probands characterized by antibodies to citrullinated protein antigens (ACPA). At-risk subjects have expanded circulating IgA+ plasmablasts as well as serum ACPA of the IgA isotype, suggesting a mucosal trigger for autoantibodies. We find that at-risk subjects have increased ACPA IgA in the feces as compared to healthy controls, further strengthening the connection between preclinical RA and the gut. My project seeks to better understand and characterize the preclinical stage of rheumatoid arthritis. I aim to do this through better investigating the mucosal triggers for disease, including inciting factors for mucosal ACPA development.

Lawren H. Daltroy Health Professional Preceptorship

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

Jesse C. Christensen, CPT, PhD

Preceptor: Jennifer E. Stevens-Lapsley, PT, PhD

University of Colorado, Denver/Veterans Affairs Eastern Colorado Health Care System

Movement Compensation and Hip Joint Loading in Patients Following Total Hip Arthroplasty: Can Movement Retraining and Wearable Technology Influence Joint Mechanics?

Total hip arthroplasty (THA) is the most common and effective elective treatment for end-stage hip arthritis in aging adults, with a projected 529,000 procedures being performed annually by 2030 in the United States. While most patients with THA self-report reductions in hip pain and functional limitations, more objective findings indicate persistent gait compensation, muscular weakness and reduced physical function outcomes continue to remain. Movement compensations are common in patients with THA and most commonly defined as increased lateral trunk lean during stance phase of gait on the surgical limb. This movement compensation is likely adopted prior to surgery to reduce pain and hip muscular demand; however, it continues to remain despite reductions in hip pain postoperatively. Over time, this movement compensation has been shown to provide excessive stress on the contralateral joints and trunk, leading to reduced physical function and likely accelerated arthritic changes.

Movement compensations are best assessed in gait laboratories, which require expense equipment and added travel to a research facility for evaluation. More importantly, this environment does not reflect daily life activities and potentially masks actual movement compensations. Alternatively, the detection of movement compensation with tools like inertial measurement units (IMUs) may allow for more real-world assessments of physical function in patients following surgery, especially for patients post-THA. Inertial measurement units are comprised of a wireless network each containing a gyroscope (detect positional change) and accelerometer (detect velocity change) that provide three-dimensional movement of the patient. Our research goal is to conduct a feasibility study to determine if cost-effective and quantitative IMUs can be integrated into real-world daily activities to detect movement compensation relative to the goal standard gait laboratory in patients undergoing unilateral THA. This will provide clinicians with important information on how patients are functioning and could inform plan of care decision making, while providing data to pursue novel treatment interventions in future grant applications.

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.

Sarah Bayefsky, MD

Preceptor: Cecilia Chung, MD, MPH

Vanderbilt University Medical Center

Genna Braverman, MD

Preceptor: Jon Giles, MD, MPH

Columbia University Medical Center

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.

ABHIMANYU AMARNANI, PHD
Preceptor: Olga Dvorkina, MD
SUNY Downstate Medical Center

EMMA ASTRIKE-DAVIS, BS
Preceptor: Rebecca Cleveland, PhD, MPH
University of North Carolina

ASHANK BAINS, MS
Preceptor: Fadi Badlissi, MD
Beth Israel Deaconess Medical Center

EMILY BAKAJ, BA
Preceptor: Ellen Ginzler, MD, MPH
SUNY Downstate Medical Center

RONALD BASS
Preceptor: Virginia Steen, MD
MedStar Georgetown University Hospital

PHILIP CARLUCCI
Preceptor: Robert Clancy, PhD
New York University School of Medicine

MATTHEW DIER, BS
Preceptor: ChiChi Lau, MD
Larner College of Medicine, University of Vermont

HANNAH ELSINGHORST, BS
Preceptor: Rabheh Aziz, MD, MS
John R Oishei Children's Hospital

ZUHAYR HAQ, BS
Preceptor: Arundathi Jayatilleke, MD
Department of Medicine, Drexel University College of Medicine

MELISSA JOHNSON
Preceptor: Jennifer Stichman, MD
Denver Health Medical Center & U Colorado SOM

EMILY KAIN, BS
Preceptor: Brandi Stevens, MD, MSCR
Riley Hospital for Children at Indiana University Health

LINH (JASON) NGO KHANH
Preceptor: John Varga, MD
Northwestern University Feinberg School of Medicine

MICAH LEFTON
Preceptor: Joerg Ermann, MD
Brigham and Women's Hospital

DEE LUO, BS
Preceptor: Alexis Ogdie, MD, MSCE
University of Pennsylvania

RAVYN NJAGU, BS
Preceptor: Megan Clowse, MD
Duke University

Medical and Graduate Student Preceptorship Cont.

HIRAL PATEL
Preceptor: Laura Carbone, MD
Medical College of Georgia

SHREYA PATEL, BS
Preceptor: Candace Feldman, MD, MPH, ScD
Brigham and Women's Hospital

CLAIRE SCHAFER, BS
Preceptor: Arundathi Jayatilleke, MD
Department of Medicine, Drexel University College of Medicine

KESHARI SHRESTHA
Preceptor: Joel Hirsh, MD
Denver Health

OLIVIA SOLOMON, BA
Preceptor: Lindsey Criswell, MD, MPH, DSc
University of California, San Francisco

ROBERTO VALDOVINOS, BS
Preceptor: Tamar Rubinstein, MD, MS
Albert Einstein College of Medicine/Montefiore Medical Center

VICTORIA WICKENHEISSER, BS
Preceptor: Teresa Tarrant, MD
Duke University Medical Center

NADIYA YERICH, BS
Preceptor: Amanda Nelson, MD, MSCR, RhMSUS
University of North Carolina

Other Awards for Students, Residents, and Health Professionals

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

Foundation Leadership

2019 Board of Directors

Abby Abelson, MD
President
Cleveland Clinic Foundation

S. Louis Bridges Jr., MD, PhD
Vice President
The University of Alabama at Birmingham

Kenneth Saag, MD, MSc
Secretary
The University of Alabama at Birmingham

David R. Karp, MD, PhD
Treasurer
UT Southwestern Medical Center

Bryce Binstadt, MD, PhD
Chair, Scientific Advisory Council
University of Minnesota

Stuart Kassan, MD
Chair, Development Advisory Council
Colorado Arthritis Associates

Erin Arnold, MD
Member-at-Large
Orthopedics and Rheumatology of the N. Shore

Norman B. Gaylis, MD
Member-at-Large
Arthritis & Rheumatic Disease Specialties

Jon Giles, MD, MPH
Member-at-Large
Columbia University

Beverly Guin
Member-at-Large

Elizabeth McKelvey
Member-at-Large

William Rigby, MD
Member-at-Large
Dartmouth-Hitchcock Medical Center

Steve Russell, MBA
Member-at-Large

Teresa Tarrant, MD
Member-at-Large
Duke University Medical Center

Beth Jonas, MD
ACR Workforce and Training Representative
University of North Carolina, Chapel Hill

Anne-Marie Malfait, MD, PhD
ACR Research Representative
Rush University Medical Center

Jay Mehta, MD
ACR Pediatric Special Committee
Children's Hospital of Philadelphia

Alysia Kwiatkowski, DO
Fellow-In-Training
Rush University Medical Center

Daniel White, PT, ScD, MSc
ARP Representative
University of Delaware

William Reiss, PharmD
CRT Representative
Genentech, Inc.

Ex Officio Members

Paula Marchetta, MD, MBA
ACR President
Concorde Medical Group, PLLC

Ellen Gravallese, MD
ACR President-Elect
University of Massachusetts Medical School

Hazel Breland, PhD, OTR/L, FAOTA, CLA
ARP President
Medical University of South Carolina

Mary Wheatley, IOM, CAE
Executive Director, Rheumatology Research Foundation

Development Advisory Council

Stuart Kassan, MD
Chair

Norman Gaylis, MD

Alieen Pangan, MD

Vikas Majithia, MD

Kamala M. Nola, PharmD, MS

Steve Russell, MBA

Leo Wegemer, JD and Terry Wegemer, MS

Scientific Advisory Council

Bryce A. Binstadt, MD, PhD
Chair

Leigh Callahan, PhD

Randy Q. Cron, MD, PhD

Liana Frankel, MD

Beth Jonas, MD

Patti Katz, PhD

Vanessa Malcarne, PhD

Anne-Marie Malfait, MD, PhD

Elena Myasoedova, MD, PhD

Alexis Ogdie-Beatty, MD, MSCE

Eric Ruderman, MD

Anthony Shum, MD

Judith Smith, MD, PhD

Honorary Board of Advisors

Mark Andrejeski

Stanley B. Cohen, MD

Mary K. Crow, MD

Ephraim P. Engleman, MD*

Norman B. Gaylis, MD

Stephen E. Malawista, MD* and Tobé Malawista

Audrey Nelson, MD

James R. O'Dell, MD

Arthur L. Weaver, MD

*Deceased

Foundation Staff

Administration and Governance:

Mary Wheatley, IOM, CAE, Executive Director

Heather Morgan, Coordinator

Awards and Grants:

Eryn Marchiolo, MPH, Senior Director, Research and Training

Damian Smalls, Director

Sarah Barksdale, Senior Specialist

Justin Lundstrom, Coordinator

Impact:

Shelley Malcolm, Director

Bonny Senkbeil, Specialist

Corporate Relations:

Amy B. Miller, Director

Development:

Charlie Goldsmith, Senior Director

Faith McGown, Senior Development Officer

Lauren Kenyon, Director

Andrea Sharper, Senior Specialist

Kristen Cothran, Coordinator

Ruben Cordoba, Coordinator

Operations and Finance:

Colleen Merkel, CPA, Vice President

Rhonda Armstrong, CPA, CMA, Senior Director

Grace Castillo, MAFM, Senior Specialist

Remembering Dr. Nadia Dominique Morgan

Nadia Dominique Morgan, MBBS, was an instructor in medicine at the Johns Hopkins University School of Medicine, Baltimore, and a faculty member of the Johns Hopkins Scleroderma Center. Dr. Morgan was an award recipient of the ACR and the Foundation. On December 15, 2018, the rheumatology community suffered a great loss when her life was cut short.

Dr. Morgan attended medical school at the University of the West Indies in Kingston Jamaica, where she received both medical and surgical honors. She was recruited by the State University of New York Downstate Medical Center, where she completed her training in internal medicine and subsequently served as chief resident. During her chief residency, the Eastern Seaboard was hit by Hurricane Sandy, which forced many New York Hospitals to close. As chief resident, Dr. Morgan was responsible for triaging and accommodating many of the patients who were displaced by the storm.

Dr. Morgan was then recruited by Johns Hopkins to complete her fellowship training in rheumatology, where she developed a strong interest in the impact of race on rheumatic disease. She was an investigator for the multi-center cohort GRASP, which is the largest study ever conducted of African Americans with scleroderma. In November 2016, she received the Distinguished Fellow Award from the ACR, which is the highest honor offered by the ACR to a trainee. In 2017, she received a Scientist Development Award from the Foundation in support of her work examining the role of IL-13 in the pathogenesis of lung disease among patients with scleroderma. In 2018, the Foundation also awarded her a Career Development Award in support of her work in this area.

She was in her third year as a member of the ACR's Standing Committee on Patient Registries and was the first Afro-Caribbean woman to serve on this committee. She has also served on the ACR's Fellows-in-Training Subcommittee's roundtables on obtaining independent grant funding. In 2017, she was appointed to Alpha Omega Alpha in recognition of her tremendous accomplishments, and she was about to be promoted to the position of assistant professor at Johns Hopkins University.

In 2016, Dr. Morgan became a U.S. citizen. However, she remained tremendously proud of her Jamaican heritage. She often quoted the Jamaican motto, "out of many, one." She used this as a way of reminding us that the aspects of life that draw us together are far more important than the quirks that pull us apart. She had a fierce, independent streak and a drive to succeed. This was complemented by her tremendous compassion for others, which she shared with patients and colleagues alike. The Foundation also awarded her an Investigator Award to begin in 2019.

Image: Dr. Nadia Morgan, with Dr. Ami Shah (L) and Dr. Fred Wigley (R), following her receipt of the 2017 Scientist Development Award