

2019

ANNUAL



REPORT

*Arthritis, Rheumatology and Autoimmune Diseases*

NEW STRIDES IN JOINT  
REPAIR AND **CARTILAGE  
REGENERATION**

**DIAGNOSTIC  
ADVANCEMENTS IN  
RHEUMATIC DISEASES**

GENETIC AND CELLULAR  
**RESEARCH IN  
AUTOIMMUNITY**



ANRF  
SCHOLARS  
2018/19

**INVESTING IN EXTRAORDINARY TALENT**  
*2018-19 AWARDEES*

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**\$18+ MILLION** IN RESEARCH FUNDING TO DATE  
**\$1.6 MILLION** IN GRANT AWARDS  
**250** SCIENTISTS FUNDED  
**82** COMMITTED PARTNER INSTITUTIONS

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**RUSH UNIVERSITY  
MEDICAL CENTER**

- 2. TIESHI LI, PhD  
OSTEOARTHRITIS
- 3. RACHEL MILLER, PhD  
OSTEOARTHRITIS

**Northwestern  
University**

- 4. DEBORAH R. WINTER, PhD  
RHEUMATOID ARTHRITIS

**VAN ANDEL  
RESEARCH INSTITUTE**

- 5. TAO YANG, PhD  
OSTEOARTHRITIS

**UNIVERSITY OF  
MICHIGAN**

- 6. RHIMA COLEMAN, PhD  
OSTEOARTHRITIS
- 7. ELIZA TSOU, PhD  
SCLERODERMA

**UNIVERSITY OF  
WASHINGTON**

- 1. ERIKA NOSS, MD,  
PhD  
RHEUMATOID ARTHRITIS

**UCSF**

University of California  
San Francisco

- 15. JUDITH ASHOURI-SINHA, MD  
RHEUMATOID ARTHRITIS
- 16. MICHAEL WATERFIELD, MD, PhD  
AUTOIMMUNE ARTHRITIS

**The UNIVERSITY of OKLAHOMA  
Health Sciences Center**

- 14. MATLOCK JEFFRIES, MD  
OSTEOARTHRITIS

**Baylor  
College of  
Medicine**

- 13. TIPHANIE VOGEL, MD, PhD  
JUVENILE ARTHRITIS



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- 8. PIERRE CUNIN, PharmD, PhD  
RHEUMATOID ARTHRITIS
- 9. ANNA HELENA JONSSON, MD, PhD  
RHEUMATOID ARTHRITIS



**Feinstein Institute for Medical Research  
Northwell Health**

- 10. TAM QUACH, PhD  
RHEUMATOID ARTHRITIS



**UNC | SCHOOL OF  
MEDICINE**

- 11. BRIAN DIEKMAN, PhD  
OSTEOARTHRITIS



**THE UNIVERSITY OF  
ALABAMA AT BIRMINGHAM**

- 12. MOHAMED KHASS, PhD  
OSTEOARTHRITIS





Throughout the year the #CureArthritis community hosts their own events to raise funds and awareness for research. We've highlighted a few below and encourage you to start your own project to help support this vital research!



Color Run | #CureArthritis Edition



Superstar JA Awareness Advocates



Blue Sky Cup | Skiing For A Cure



Facebook Fundraising Birthdays!



Racing for a cure

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ARTHRITIS NATIONAL RESEARCH FOUNDATION

## THANK YOU TO OUR FOUNDATION PARTNERS



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## A MESSAGE FROM OUR CHIEF EXECUTIVE OFFICER



Dear valued friend of ANRF,

Because of you, this year has been very transformative at the Foundation. Now more than ever, we are filling severe knowledge gaps, investing in innovative ideas, leading meaningful collaborations, partnering with patients for solutions and spreading much needed awareness about Arthritis, Rheumatology and Autoimmune diseases. I have the privilege of summarizing the highlights of the year below:

- We attracted and funded the largest number of scientific research projects in our 60+ year history, for greater impact. This year's cohort is comprised of eighteen outstanding scientists and physicians at the vanguard of innovation and technological advances. These original studies join more than 250 completed interdisciplinary projects at 75 prestigious research centers and universities across the United States supported by ANRF.
- We sponsored research travel grants to 40+ young scientists enabling them to present, share and publish their findings at major professional conferences. We also participated in and sponsored leading scientific conferences to foster collaboration.
- We modernized infrastructure across all the Foundation platforms. This includes new grant-making and communications systems for improved operation. Through these changes, we are ensuring the highest standards in data security, privacy and encryption.
- We tripled in size across the digital space and created a number of free tools and resources to serve our community better. This includes:
  - A digital newsletter, The ANRF Chronicle, that helps disseminate the latest scientific and medical information;
  - A downloadable Fact Sheet library of concise information about many conditions;
  - An upgraded Peer-to-Peer platform that bolsters community engagement; and
  - A new patient-centric platform, Arthritis Journeys, to amplify patients' voices and learn from shared experience.
- We maintained a top charity navigator status for the 11th year in a row and invested more than 90% of donations in research. Notably, we received our largest single individual donation in our history this year, underscoring the growing confidence in our work by our generous donors and supporters.

We are energized by this progress on many fronts, yet we know that we can do more - we left many meritorious grants behind this year due to limited resources. So in this season of giving, I hope that we can count on your financial support.

With much gratitude,

A handwritten signature in black ink that reads "Zaher Nahle". The signature is written in a cursive, flowing style.

Zaher Nahle, PhD, MPA

# FINANCIAL REPORT

2017, 2018 & 2019

AUDITED FINANCIAL STATEMENTS  
FISCAL YEARS ENDING MARCH 31st

## REVENUE AND EXPENSES

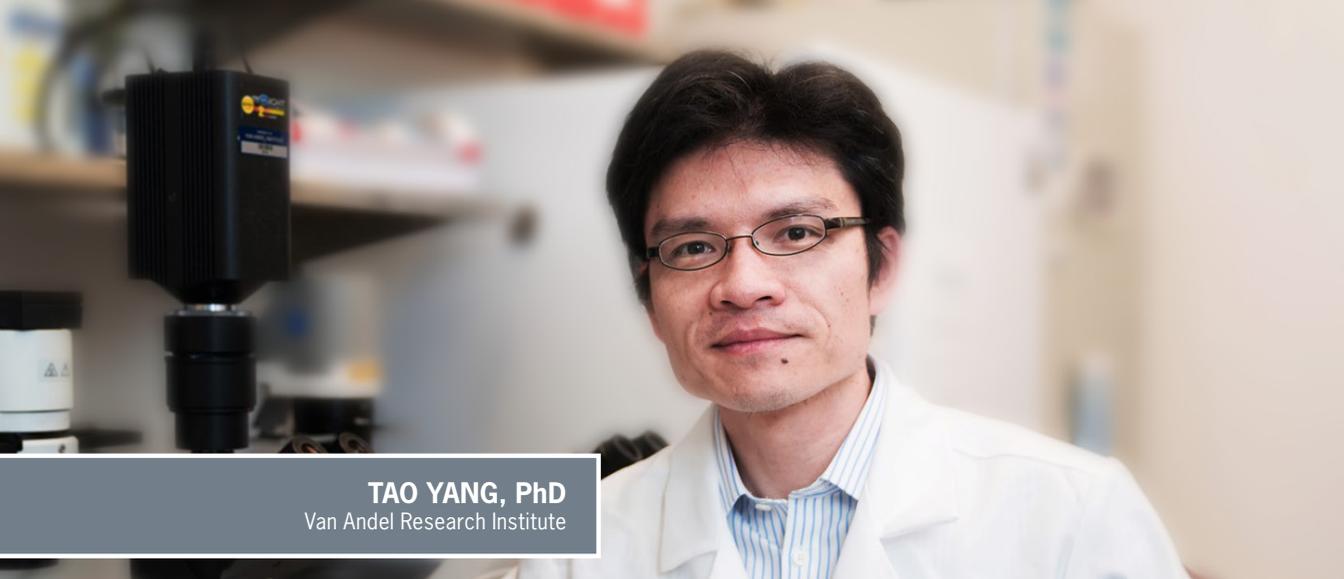
PUBLIC SUPPORT AND REVENUE	2017	2018	2019
Contributions and Bequests	877,844	2,564,271 <sup>A</sup>	1,391,531
Investment Income Net	383,106	378,310	224,639
Unrealized Gain (loss) on Investments	622,708	399,538	142,447
<b>TOTAL SUPPORT AND REVENUE</b>	<b>\$1,883,658</b>	<b>\$3,342,119</b>	<b>\$1,758,617</b>
<b>EXPENSES</b>			
Program Services			
Research	1,261,339	1,537,187	1,828,753
Education	243,640	236,428	250,165
Total Program Services	\$1,504,979	\$1,773,615	\$2,078,918
<b>SUPPORTING SERVICES</b>			
Management and General	107,364	115,912	144,304
Fund Development	37,554	120,016	111,029
Total Supporting Services	144,918	235,928	255,333
<b>TOTAL EXPENSES</b>	<b>\$1,649,897</b>	<b>\$2,009,543</b>	<b>\$2,334,251</b>
Change in Net Assets	233,761	1,332,576	(575,634)
Net Assets at Beginning of Year	7,975,728	8,209,489	9,542,065
<b>NET ASSETS AT END OF YEAR</b>	<b>8,209,489</b>	<b>9,542,065</b>	<b>8,966,431</b>

## BALANCE SHEET SUMMARY

<i>Total Unrestricted Assets*</i>			\$8,530,041
<i>Total Restricted Assets*</i>			\$436,390
<b>Total Assets</b>	<b>\$8,267,105</b>	<b>\$9,586,356</b>	<b>\$8,966,431</b>
<b>Total Liabilities</b>	<b>\$57,616</b>	<b>\$44,291</b>	<b>\$37,323</b>
<b>NET ASSETS AT END OF YEAR</b>	<b>\$8,209,489</b>	<b>\$9,542,065</b>	<b>\$8,966,431</b>

\*Beginning in 2019, new accounting regulations require reporting restricted and unrestricted assets as seen above.

<sup>A</sup> Bequests in 2018 totaled \$1,319,600.00



**TAO YANG, PhD**  
Van Andel Research Institute

## MAKING NO BONES ABOUT OA RESEARCH AND TREATMENT

Dr. Tao Yang, an assistant professor at the Van Andel Research Institute, is striving to reveal the underlying causes of osteoarthritis. Interest in this research field was inspired by his grandfather. He saw his grandfather, an avid sports enthusiast, decline both physically and emotionally after OA halted his participation in physical activities. It became clear to Dr. Yang that OA had far-reaching effects, extending much further than the physical pain and associated limited mobility.

His interest in science was ignited at a young age by his father; a mechanical engineer who often spoke about science and technology. A young Dr. Yang devoured books on the subjects as they were readily available in his family home. Early encouragement in his endeavours has helped Dr. Yang become a force in OA research.

Many of our biological processes are controlled by proteins our cells produce. Sumoylation is one of the mechanisms that modify these proteins. Stem, or progenitor, cells are those which act as a pool from which more specialized and differentiated cells will be developed.

Sumoylation has emerged as a key mechanism in maintaining the balance of these “starter” cells. If sumoylation occurs excessively it can drive cellular senescence, this is common in aging and results in cells that no longer divide but enter a state of permanent growth arrest without undergoing cell death.

Osteoblasts are the cells in charge of bone building whilst chondrocytes create and form part of our cartilage. The starter cells for osteoblasts and

chondrocytes are osteochondroprogenitors (OCP). The role of sumoylation in regulation of OCPs is unclear. Dr. Yang has been studying this process to better understand how our bone cells are modified and which changes lead to improper cellular responses and disease.

From this research the laboratory has been able to identify a key protein, (SENp6), involved in the sumoylation pathway. Postnatal loss of this protein in mice caused premature aging. Mice in which the gene that produces this protein had been turned off developed much smaller skeletons with higher levels of bone cell death as well as increased senescence in OCPs and mature chondrocytes.

It was found that in cells lacking SENp6, p53 (a protein that regulates cell cycle) signalling was elevated as were factors excreted by senescent cells. This indicated greater levels of senescence in these cells.

Understanding the role of these components in overall skeletal health is key to developing more effective treatment of skeletal disorders such as arthritis.

### OSTEOARTHRITIS RESEARCH

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**It became clear to Dr. Yang that OA had far-reaching effects, extending much further than the physical pain and associated limited mobility.**

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## ROGUE IMMUNE CELLS AND HOW TO STOP THEM

Microphages are the front line of our immune system. These white blood cells are responsible for capturing, engulfing and eliminating foreign threats. Starter cells called monocytes circulate in our blood stream. These transform into an army of macrophages when necessary. In a normal healthy immune system, these cells disappear once their job is done. In rheumatoid arthritis (RA) these cells can linger which leads to inflammation in joints.

Deborah R. Winter, PhD, is an Assistant Professor in the Division of Rheumatology at Northwestern University Feinberg School of Medicine. As an ANRF scholar, this researcher is exploring the role of macrophages in RA.

In RA the starter cells, monocytes, are predisposed to become inflamed and are directed straight to joints where they cause swelling, stiffness and pain.

In order to understand why monocytes and macrophages act inappropriately in RA, Dr. Winter is looking at the problem at the genomic level, investigating mechanisms behind how genes associated with immune cell development are regulated and expressed.

Dr. Winter's background in computational biology and immunology helps her to determine and decipher intricate patterns of gene expression. Macrophages are widespread throughout our bodies, but are programmed to carry out a variety of specific and

necessary functions. The challenge is finding a way to target only the cells that are going off script without disrupting those performing their necessary functions. Dr. Winter's research suggests that a potential RA treatment is to block the production of macrophages that boost joint inflammation.

## RHEUMATOID ARTHRITIS RESEARCH

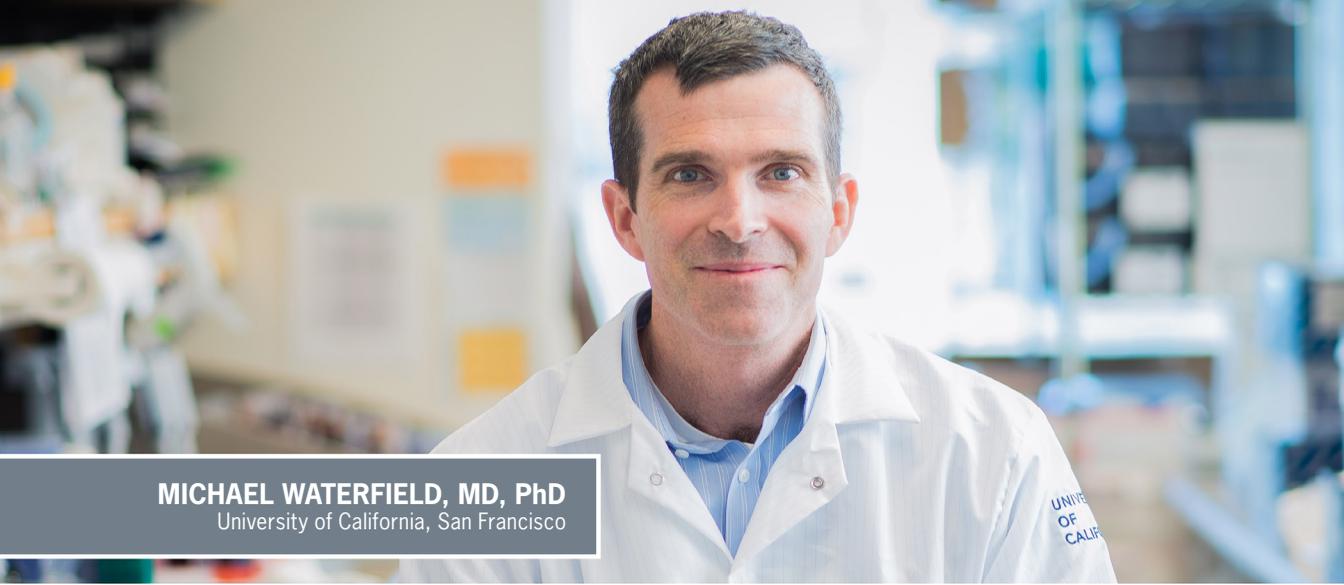
**“I am bringing my unique perspective to understanding how macrophages malfunction in RA. Genomic approaches offer really exciting potential targets for individuals who are suffering from this devastating disease.”**

Thanks to the Arthritis National Research Foundation, Dr. Winter was able to establish an independent lab.

“This award was a big jump for a junior researcher in her first position as an investigator,” she said. “I am bringing my unique perspective to understanding how macrophages malfunction in RA. Genomic approaches offer really exciting potential targets for individuals who are suffering from this devastating disease.”



**DEBORAH R WINTER, PhD**  
Northwestern University



**MICHAEL WATERFIELD, MD, PhD**  
University of California, San Francisco

## A KNIGHT IN SHINING ARMOR FOR CHILDREN WITH JIA

Arthritis is not a disease of the elderly. Arthritis does not discriminate based on age and many do not know it is also a disease that affects children. Children suffering from Juvenile idiopathic arthritis (JIA) experience swollen and painful joints, limiting their ability to simply be children enjoying their childhood.

One researcher who has geared up to fight JIA is Dr. Michael Waterfield, a pediatric rheumatologist at UCSF Benioff Children's Hospital in San Francisco. Presently there are around 300,000 children in the US with JIA, and through his work Dr. Waterfield sees first-hand the devastating consequences of this disease.

“While we have many new drugs, we have not cured the disease and we do not understand why one child will respond to treatment and another will not,” says Dr. Waterfield. The aggressive inflammation that frequently accompanies JIA can lead to impaired growth and on-going joint problems. In around 50% of cases, this will persist throughout a patient's life. Assisted by an ANRF grant, Dr. Waterfield is attempting to demystify pathways involved in the progression of JIA.

T-cells are the stormtroopers that our body unleashes in order to fight disease-causing molecules. One such T cell, T-helper 17 (Th17), is seen in large numbers in patients with autoimmune conditions. Inhibiting Th17 is increasingly used as a therapeutic tool against these conditions. In order to fully be able to use this approach, it is necessary to understand how Th17 drives inflammation.

Using mice in which certain genes had been “turned off”, it was determined that the activating transcription factor 7 interacting protein (ATF7ip), a regulator of genes, was essential for the development of properly functioning Th17 cells.

Building on this, the team was able to identify ATF7ip as an inhibitor of interleukin 2 (IL-2) production. IL-2 is a molecule crucial for T-cell proliferation and other activities central to properly regulated immune responses.

Mice in which the ATF7ip gene was switched off had abnormal overproduction of IL-2 and in turn impaired Th17 differentiation. These results demonstrate a new epigenetic pathway by which IL-2 production is hampered, and this in turn may provide novel avenues for modulating its production and treating autoimmune conditions.

Dr. Waterfield is hopeful that by gaining insight into this pathway he will be able to slay the dragon that is JIA, becoming a knight and a hero to the young patients that mean so much to him.

### JUVENILE ARTHRITIS RESEARCH

**“While we have many new drugs, we have not cured the disease and we do not understand why one child will respond to treatment and another will not.”**



**TIPHANIE VOGEL, MD, PhD**

Baylor College of Medicine, Texas Children's Hospital

## INVESTIGATING THE ROLE OF STAT3 MUTATION IN JUVENILE ARTHRITIS

Dr. Vogel, an Assistant Professor of Pediatrics at Baylor College of Medicine, played a critical part in identifying a rare form of Juvenile Arthritis caused by a mutation affecting a specific gene, STAT3.

This specific form of JA results in an immense overreaction by a child's immune system, resulting in devastating symptoms and a number of autoimmune conditions. Symptoms can include enlarged and painful lymph nodes, decreased numbers of mature blood cells, increased incidence of infection, eczema and short stature to name a few. Working with a young patient with this condition fuelled the fire pushing this doctor to tackle this rare condition.

ANRF funding has allowed Dr. Vogel to try and pinpoint the exact region within the protein that leads to the overactivity of the STAT3 gene. "I believe that changes in a particular region of STAT3 are more likely to predispose children to JA as a complication," she explains. "Targeting that area may decrease the overactivity of the STAT3 molecule, which would presumably decrease the risk of autoimmunity."

The ultimate goal of drug discovery would be to design a new compound that blocks the specific region of the STAT3 molecule in order to effectively treat these young patients.

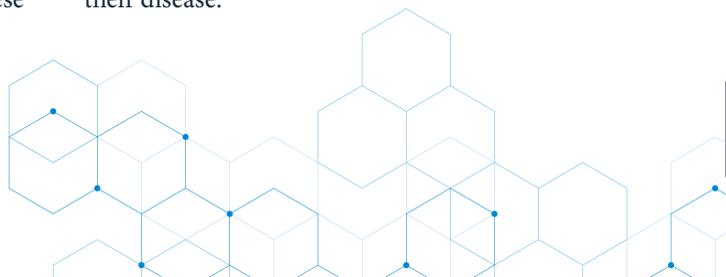
### JUVENILE ARTHRITIS RESEARCH

**"I work on understanding the causes and mechanisms of juvenile arthritis in my laboratory because I one day hope to be able to provide each of them with an arthritis treatment that uniquely targets and resolves their disease."**

Further down the road she is hopeful that treatment can occur in the form of a small molecule inhibitor. This class of drug can often be given orally, thus avoiding the need to give babies or toddlers repeated injections which can be physically and emotionally draining on patients and their parents.

She is also hopeful that molecule inhibitor treatment could slow progression of the disease whereas current treatment options only address symptom reduction.

"I work on understanding the causes and mechanisms of juvenile arthritis in my laboratory because I one day hope to be able to provide each of them with an arthritis treatment that uniquely targets and resolves their disease."



# EPIGENIC INSIGHTS INTO THE TREATMENT OF SCLERODERMA

Scleroderma, or systemic sclerosis, is a chronic connective tissue disease that can result in changes to the skin, blood vessels, muscles and internal organs. Symptoms may include thickening of the skin, stiffness, fatigue and poor blood flow to the fingers and toes with cold exposure.

Eliza Tsou, PhD, is a Research Assistant Professor and Research Fellow in the Division of Rheumatology at the University of Michigan with a sole focus on scleroderma research—in particular the role of epigenetics in scleroderma. Epigenetic factors are non-genetic factors which still influence how our genes are expressed.

## SCLERODERMA RESEARCH

**Therapeutic intervention to promote CYR61 levels or increase its activity could be extremely beneficial in the treatment of scleroderma.**

Each year Dr. Tsou participates in a patient education event held at the University of Michigan, this giving her a glimpse of the real-life impact of the disease she is researching.

“Interacting with the patients, knowing their stories, learning their daily struggles, motivates me

to work harder so that we better understand this disease and find a cure for it soon.”

Utilizing and comparing cells isolated from skin biopsies from healthy volunteers and scleroderma patients, Dr. Tsou is determining the key factors affecting the how this disease develops and progresses.

This approach allowed Dr. Tsou to identify areas of difference in the two different sample groups. One significant difference was in the level of a specific protein, CYR61 in skin cells and in fibroblasts. Fibroblasts have a key role in structural support of other cells and in the production of collagen.

When the levels of this protein were artificially increased in cells from scleroderma patients it demonstrated that CYR61 prevented excessive connective tissue production (anti-fibrotic), it promoted the formation of new blood vessels (pro-angiogenic), and it had immune modulatory properties.

This gives a very real insight into a novel therapeutic target. Therapeutic intervention to promote CYR61 levels or increase its activity could be extremely beneficial in the treatment of scleroderma. Attacking scleroderma on three fronts could hold the key to vastly improving treatment and reducing the symptoms associated with this disease.



**ELIZA TSOU, PhD**  
University of Michigan



**TAM QUACH, PhD**  
The Feinstein Institute for Medical Research

## DISRUPTION OF B CELL HOMEOSTASIS IN RHEUMATOID ARTHRITIS

An important cell in our immune response arsenal is the B cell, a white blood cell that fights infection by producing antibodies. However, if the B cell homeostasis (maintenance of internal stability) is disrupted some of the cells may produce auto-antibodies which attack our own tissue instead of foreign molecules.

Disruption of B cell homeostasis can occur as a result of the treatment of inflammatory arthritis with TNF inhibitors or biologic anti-inflammatory agents, this can lead to the development of secondary autoimmune conditions such as lupus.

Dr. Tam Quach, an instructor in the Department of Autoimmune Diseases at The Feinstein Institute for Medical Research, is using an ANRF grant to research the mechanisms that lead to the disruption of B cell homeostasis. B cells mature at sites within the lymph and spleen – Germinal Centres (GCs). This is also where B cells alter their antibody production to create a specific response to threats.

TNF inhibitors, commonly used to treat arthritis, prevent GCs from forming thus preventing B cells from developing appropriate production of antibodies. Dr. Quach used a mouse model to investigate how TNF deficiency, as experienced when using TNF inhibitors, effected B cell homeostasis. It was found that a TNF deficiency led to a higher level of pro-inflammatory molecules causing disruption of B cell homeostasis.

Additionally, Dr. Quach was able to establish that immune responses to infections and a predisposition

to autoimmune conditions were other factors driving the formation of altered GCs.

### RHEUMATOID ARTHRITIS RESEARCH

**“We hope that by having a thorough understanding of the mechanism of action of this TNF deficiency/inhibition, we will be able to understand how TNF contributes to regulation of autoimmunity.”**

Having learned that dysregulated B cells in TNF deficient mice occurs via multiple pathways, it will be necessary for the team to study the detailed molecular pathways involved and translate results to a more clinical setting by recruiting RA patients who are starting TNF inhibitor treatment for a translational study.

**“We hope that by having a thorough understanding of the mechanism of action of this TNF deficiency/inhibition, we will be able to understand how TNF contributes to regulation of autoimmunity, to develop preventive therapies for patients being treated with TNF inhibition, and also to build predictive models to assess risk of using TNF inhibitors of each RA patient.”**



# FIBROBLAST REGULATION—A POTENTIAL UNIVERSAL RA TREATMENT

## RHEUMATOID ARTHRITIS RESEARCH

**“Maybe a cell that is not traditionally a drug target, like a fibroblast, will someday put people completely into remission.”**

Dr. Erika Noss is an assistant professor, division of rheumatology, Roosevelt Clinic, University Washington Medical Center. Despite the improvements in RA treatment that have been made in the last two decades there are still sizeable challenges facing rheumatologists today.

One critical challenge relates to selection of appropriate treatment option for their patients. Striving to treat patients, these difficulties come to the fore for Dr. Noss. “The hardest part about being a rheumatologist is starting patients on the right drug, with rheumatoid arthritis (RA), all you can do is give it your best shot. You’re simply rolling the dice.”

Around 80% of patients do find some level of relief after trying a number of different treatments. It is Dr. Noss’ ambition to improve this percentage and offer relief to a greater number of patients. Funding as an ANRF fellow and grant recipient has allowed Dr. Noss to rigorously pursue this goal.

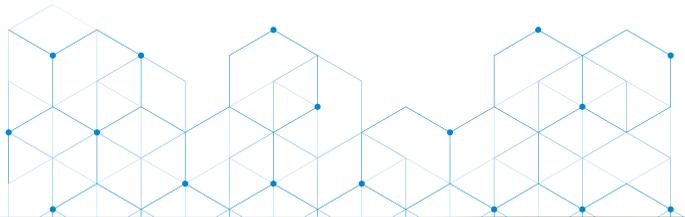
Fibroblasts are biological cells that are key in the synthesis of the extracellular matrix and collagen, necessary in providing structural support in our cells as well as being a component in wound healing. In patients with RA, these cells are produced at a vastly accelerated rate.

Dr. Noss is attempting to find mechanisms that can block these rogue fibroblasts.

Data has highlighted the role of a protein important for cellular adhesion, cadherin 11, as a marker and regulator of fibroblast function in our joints in inflammatory arthritis. It could be a means of fibroblast regulation, preventing over production of these cells. This, in turn, could prevent long-term joint destruction resulting from RA.

As fibroblasts are the most common cell in connective tissue, it may be effective for the majority of patients, eliminating the need to gamble with treatment options before patients feel relief.

Dr. Noss has high hopes for the implications of this potentially universal approach. In her words, “maybe a cell that’s not traditionally a drug target, like a fibroblast, will someday put people completely into remission.”



**ERIKA NOSS, MD, PhD**  
University of Washington



**RACHEL E MILLER, PhD**  
Rush University Medical Center

## OBSERVING NEURON RESPONSE TO ASCERTAIN THE ROUTE OF OA PAIN

The most significant symptom associated with osteoarthritis (OA) is pain, yet the source of this pain and the mechanisms driving it remain under-researched. A unique academic history, both in the medical and engineering fields, placed Dr. Miller in a prime position to contribute to the fight against osteoarthritis by directing her resources towards unravelling this mystery. In order to prevent traffic accidents, one must first understand the route a vehicle will take. One can only place safety measures, such as traffic lights, correctly if one understands the hazards along the road. The same is true for biological processes, it is necessary to understand how pain is created, and how it moves from the point A to point B in our bodies.

### OSTEOARTHRITIS RESEARCH

**Knowing whether arthritic pain travels along the highway or the back roads will provide much needed information that will hopefully stop it in its tracks.**

Dr. Miller focuses her research on tracking pain and creating a road map of its route from origin (such as sites of OA) to the central nervous system where it is processed. Using surgery, the team artificially created joints in mice that would result in pain similar to that resulting from OA. After mice began to develop joint damage and pain-related behaviors, stimuli were applied to the area to generate pain. Calcium

imaging was then used to quantify the number of nerve responses to these stimuli. The majority of responses in both groups of mice were in small to medium-sized neurons, consistent with the size of nociceptors.

Nociceptors are sensory neurons that respond to potentially damaging stimuli. Interestingly it was observed that in this situation this type of neuron recruited other nociceptors thereby reducing the level of stimulus necessary to generate a pain response. Basically, by increasing the number of nerves responding to a smaller stimulus, such as pressure applied to joint, the pain experienced was greater.

This could provide a unique way to test the effectiveness of drugs aimed at reducing OA pain as you can accurately detect increases or decreases in nerve responses. Simply put knowing whether arthritic pain travels along the highway or the back roads will provide much needed information that will hopefully stop it in its tracks.

Dr. Miller is taking this idea further using the same technique to study the effect of force applied to other cells important in the development of OA. Moving forward Dr. Miller hopes to build on the momentum she has achieved as an ANRF fellow, working to identify potential therapeutic targets that will help lead to treatments which restore a level of normality to movement with osteoarthritis, allowing patients to walk, run and dance pain free!



# CYTOKINE INHIBITION MAY PREVENT AND TREAT OSTEOARTHRITIS

Dr. Tieshi Li has an outstanding research and academic background. Currently he is an assistant professor in the Department of Pediatrics at Rush University.

## OSTEOARTHRITIS RESEARCH

**By inhibiting interleukin 36a the rate of OA progression was reduced as was the pain associated with it.**

As an avid soccer fan, Dr. Li didn't just watch from the side lines but enjoyed playing the game. Unfortunately, an injury to his right knee eleven years ago not only limited his participation but led to post-traumatic osteoarthritis (OA) progression.

The pain he experienced from this and the pain he saw in other family members with the same condition is a driving force inspiring this researcher to understand and treat OA.

Our immune cells secrete substances called cytokines. These cytokines elicit a response in other cells that help our body to fight off a foreign attack such as an infection. One such response is to promote inflammation. Inflammation is the body's attempt at self-protection to remove harmful stimuli and begin the healing process and as such is a necessary element in our immune responses.

Problems occur when this inflammation is not kept in careful balance. A particular cytokine that causes inflammation as a response is interleukin 36a. Dr. Li has focused his research on this cytokine and the part it may play in OA progression and the pain associated with it.

Using mice, Dr. Li discovered that treatment with interleukin 36a not only promoted the maturing chondrocytes (cells responsible for cartilage production) it induced the expression of a number of other substances involved in skeletal development and bone mineralization. It was also key in regulating chondrocyte homeostasis.

Further tests revealed that by inhibiting interleukin 36a the rate of OA progression was reduced as was the pain associated with it. If levels were artificially increased, the opposite was seen and OA progressed more rapidly. Therefore, maintaining appropriate levels of this cytokine could have a large role to play in preventing and treating OA.

One could definitely say Dr. Li has scored a winning goal on his new playing field.



**TIESHI LI, PhD**  
Rush University, relocated to University of Nebraska Medical Center

# ANRF | GIVING GUIDE

*Suggestions to Support our Foundation*

\$

## EVERYTHING GIFT

Every donation to the ANRF, regardless of size, supports advancing research through a combination of the programs listed below. If you wish to donate to a specific area, please note the suggested contribution amounts. We are grateful for the generosity of the community and thank you for your support.

100K

## BIOMEDICAL RESEARCH GRANTS

Fund groundbreaking research in Arthritis, Rheumatology and Autoimmune Diseases conducted by talented MD and PhD professionals at prestigious institutions. This is critical for filling knowledge gaps, identifying new therapies and finding longlasting cures.

50K

## SCIENTIFIC SYMPOSIUMS

Convene top minds in scientific research and clinical care to collaborate and cross-pollinate. Information sharing is a key component in accelerating the discovery process and improving the quality of research and clinical care.

25K

## MEDICAL EDUCATION & AWARENESS

Disseminate the latest news in Arthritis, Rheumatology and Autoimmune Diseases through credible and FREE newsletters, webinars, fact sheets and other digital and print mediums. Access to accurate and concise information to stay up-to-date is needed in a constantly changing medical field.

10K

## RESEARCH TRAVEL GRANTS

Facilitate the direct access of young trainees and scientists with limited resources to participate in professional meetings and publish their work. This is indispensable for sharing ideas, receiving feedback and sustaining the pipeline of new talent entering the field of Arthritis and Rheumatology.

5K

## INFRASTRUCTURE & READINESS

Keep our grantmaking systems, research platforms and Medical Education channels up-to-date for optimal impact. This will enable us to perform our functions effectively and remain competitive as a leading Medical Foundation.

## LEAVE A LEGACY

*Make a planned gift or donation today to leave a lasting impact in the search to cure arthritis!*

- Give Online at [CureArthritis.org](http://CureArthritis.org)
- Leave a gift in your will
- Give through your workplace
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- Donate your car
- Make monthly or annual gifts
- Give through the Combined Federal Campaign (CFC)
- Give us a call at 800.588.2873 or email us at [donate@curearthritis.org](mailto:donate@curearthritis.org)



Use the enclosed envelope or go to  
**[CUREARTHRTIS.ORG/DONATION](http://CUREARTHRTIS.ORG/DONATION)**

## THE SURROGATE LIGHT CHAIN AS A DETERMINANT OF BONE HEALTH

Mohamed Khass, PhD, was a post-doctoral fellow in the Division of Clinical Immunology and Rheumatology at the University of Alabama when he received his research grant from ANRF. A strong research background in numerous areas including pharmacology, biochemistry, genetics, microbiology and immunology has created a researcher capable of unique insights from a multidisciplinary perspective and set Dr. Khass apart as a researcher to watch. Recently, he proudly added ANRF scholar to his growing list of achievements. He firmly believes that the ANRF grant facilitated his promotion at the University of Alabama to assistant professor.

Increasing interested in the field of immunology, Dr. Khass had his eureka! moment when he noted an fascinating phenomenon. B cells are white blood cells responsible for secreting antibodies when they realize the body is under attack. In order for this happen, B cells need to be able to recognize when there are harmful foreign bodies present. A molecule on the surface of these cells is responsible for allowing this recognition. Dr. Khass noted that if B cells lacked this signaling molecule, patients experienced bone fragility.

These signaling molecules are known as B cell receptors (BCRs). An antigen is the part of a cell that that a BCR binds to resulting in an immune response. If a B cell has a defective BCR the body will be alerted and the cell won't survive as it cannot perform its

function.

During early B cell development, one of the first check points to test whether it will work correctly is the development of a functioning pre-BCR. Dr. Khass determined that a specific portion of this pre-BCR, the surrogate light chain, was a key component affecting bone health. If this pre-BCR is absent or malfunctions our bones are simply not as strong. So ironically, we need a light chain to make our bones heavy enough!

Dr. Khass hopes that with continued support from ANRF and his home institution he can shed light on the mechanisms by which early B cells affect joint and bone homeostasis, which will in turn help in the development of preventive and therapeutic tools for the management and treatment of bone diseases including arthritis - helping those with arthritis to move and live lighter.

### OSTEOARTHRITIS RESEARCH

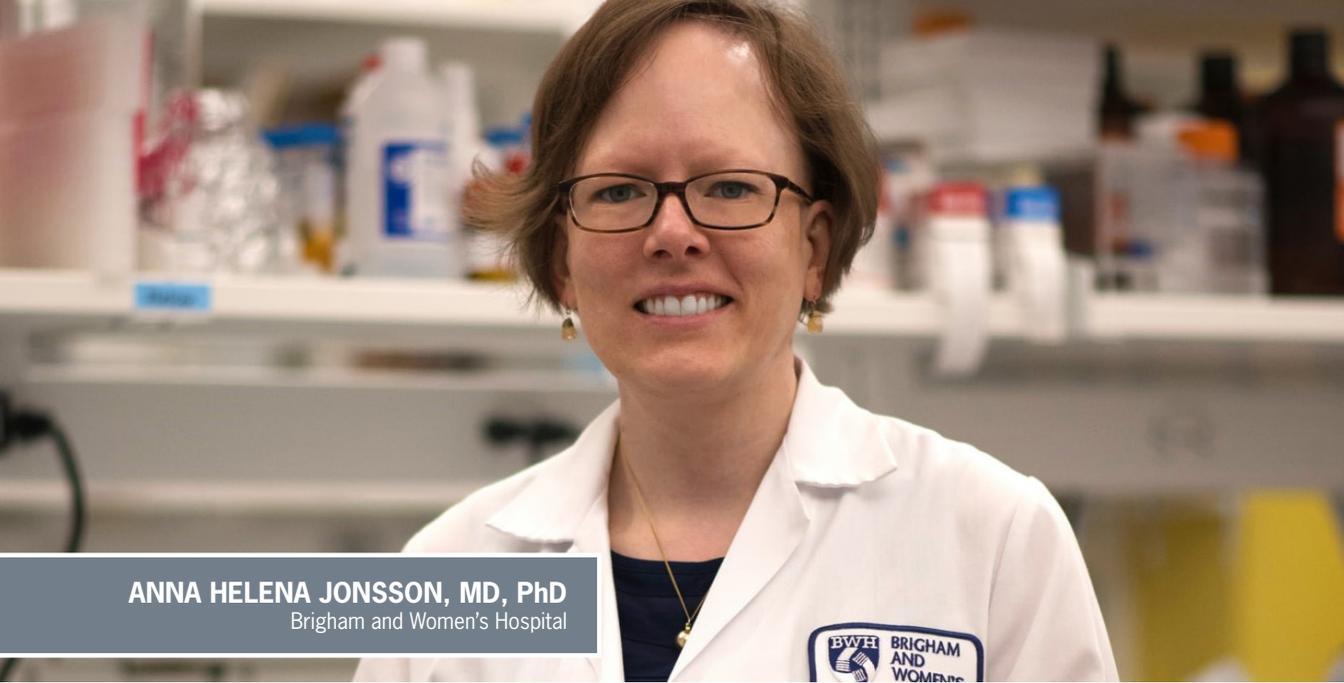
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**Dr. Khass determined that...the surrogate light chain was a key component affecting bone health. If this factor is absent or malfunctions, our bones are simply not as strong.**

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**MOHAMED KHASS, PhD**  
University of Alabama at Birmingham



**ANNA HELENA JONSSON, MD, PhD**  
Brigham and Women's Hospital

## NEW INSIGHTS INTO THE DETAILS OF RA AND INFLAMMATION

Dr. Anna Helena Jonsson is currently an Instructor in Medicine at Harvard Medical School and an associate physician at Brigham and Women's Hospital in Boston. The transition from post-doctoral work to faculty is critical in a researcher's career path. Without adequate funding at this pivotal career milestone, many researchers are forced to leave academia.

Dr. Jonsson believes that the support she received by being awarded an ANRF grant early on in her research career allowed her to continue to contribute to this field of research in a very meaningful way. "Receiving the grant felt like a big vote of confidence from a team of established arthritis researchers. Their support showed me that I am on the right track and will successfully navigate through this transition."

### RHEUMATOID ARTHRITIS RESEARCH

**Dr. Jonsson believes that her ANRF award allowed her to continue to contribute to this field in a meaningful way.**

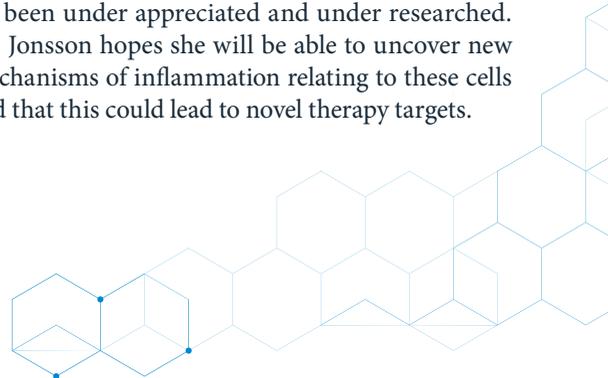
Much of the research surrounding rheumatoid arthritis (RA) focuses on CD4 T cells, a type of white blood cell that helps coordinate the immune system's response to infections and other attacks. Much less research has looked at the potential role of CD8 T cells, another immune cell, in RA. CD8 T cells are found in large quantities in inflamed joints in RA and

produce many of the same molecules that increase inflammation as CD4 T cells.

Analyzing blood samples showed that a protein, CCR2, found on the surface of immune cells was elevated in CD8 T cell populations of RA patients compared to samples from people without RA. This protein is responsible for directing immune cells to areas requiring an immune response. Synovial fluid in healthy individuals acts to reduce friction between the articular cartilage in joints during movement.

Dr. Jonsson's research revealed that in synovial fluid from RA patient's, CD 8 T cells in inflamed joints were more likely to be CCR2 positive. CCR2 positive cells in the blood and synovial fluid RA samples produce a protein, granzyme K, that activates the production of inflammatory molecules.

The role of CD8 T cells and the associated protein, granzyme K, in autoimmune arthritis has thus far been under appreciated and under researched. Dr. Jonsson hopes she will be able to uncover new mechanisms of inflammation relating to these cells and that this could lead to novel therapy targets.





**MATLOCK JEFFRIES, MD**  
University of Oklahoma

## COULD A CURE FOR OA BE AS SIMPLE AS FLICKING A SWITCH?

Epigenetics, to put it simply, is the study of biological mechanisms that turn our genes on and off. Epigenetic factors control when and how much protein a gene makes. These proteins in turn control many of the biological processes in our bodies.

Epigenetic factors are everywhere: your diet, where you live, who you interact with, when you sleep, how you exercise, even your age – all of these can ultimately cause chemical modifications around the genes that will turn genes on or off over time.

Dr. Matlock Jefferies is a physician and researcher who is delving into the world of epigenetics in order to find new osteoarthritis (OA) treatments. He used his ANRF grant to create a large-scale epigenetics study hoping to tease out which epigenetic differences are related to the most common risk factors for OA.

Using mice that had OA surgically induced in their knees, the team introduced risk factors associated with OA and then looked at any epigenetic changes within the knee cartilage. Most studies only look at specific genes whereas the large-scale nature of Dr. Jefferies' study examines epigenetic changes throughout the mouse genome (all of their DNA and genes). "By performing the first large-scale whole-genome epigenetic study, I hope that we will find additional drug targets which undergo epigenetic changes that

have been missed by previous studies using only parts of the genome."

Taking it a step further, the risk factors for OA can be separated into those over which the patient has control (such as weight and activity levels) and those which patients have no control over (such as injury or aging). Therapies can then be geared towards targets that cannot be addressed by any actions of the patients themselves. This would amount to a dual treatment approach. Patients would address the risk factors that are reversible through lifestyle changes while therapies become focused on blocking or activating genes and pathways patients cannot control. This dual approach, it is thought, could greatly improve treatment outcomes.

The fight against OA can be successful, particularly if we fight the disease at all levels.

### OSTEOARTHRITIS RESEARCH

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**"By performing the first large-scale whole-genome epigenetic study, I hope that we will find additional drug targets which undergo epigenetic changes that have been missed by previous studies using only parts of the genome."**

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## TREATING AGING IS NOT SKIN DEEP

Brian Diekman is an assistant professor of biomedical engineering at the University of North Carolina School of Medicine. Dr. Diekman and his team are working to identify the relationship between aging and osteoarthritis (OA). This is of paramount importance as medical advances are helping us live longer, resulting in a larger aging population: a population that is at greater risk for the development of OA.

By 2045, the CDC estimates there will be 78 million people living with diagnosed arthritis. It is important to note that although aging and OA are closely linked, they are still distinct processes. Understanding the interaction between the two is central to developing improved treatment options.

A hallmark of aging is the deterioration of cells. Most of us see this on the surface manifested as grey hairs and deepening wrinkles. However, this deterioration is also occurring in the cells below the surface. The deterioration of our cells as we age is known as cellular senescence. This deterioration drives the decline in aging tissues in two ways: by limiting cells ability to regenerate by replicating, and by producing molecules (known as SASP molecules) that increase inflammation. Chondrocytes are the cells responsible for the production and maintenance of cartilage. Chondrocytes display many of the features of senescent cells during aging. It has been observed that OA catalyzes the development of senescent cells and that

the resulting cellular stress intensifies the development of the pro-inflammatory SASP molecules. It is not yet clear which cells are responsible for the release of substances that cause SASP molecules to occur. Unraveling how chondrocytes enter senescence may be instrumental in developing therapies that address the heightened inflammation that comes with OA. The team also found a marker that indicates dysfunctional chondrocytes. Using this marker, they were able to determine that effect of senescent chondrocytes on OA is likely due to the production of the SASP molecules and the resultant inflammation rather than because the cells have lost the ability to reproduce.

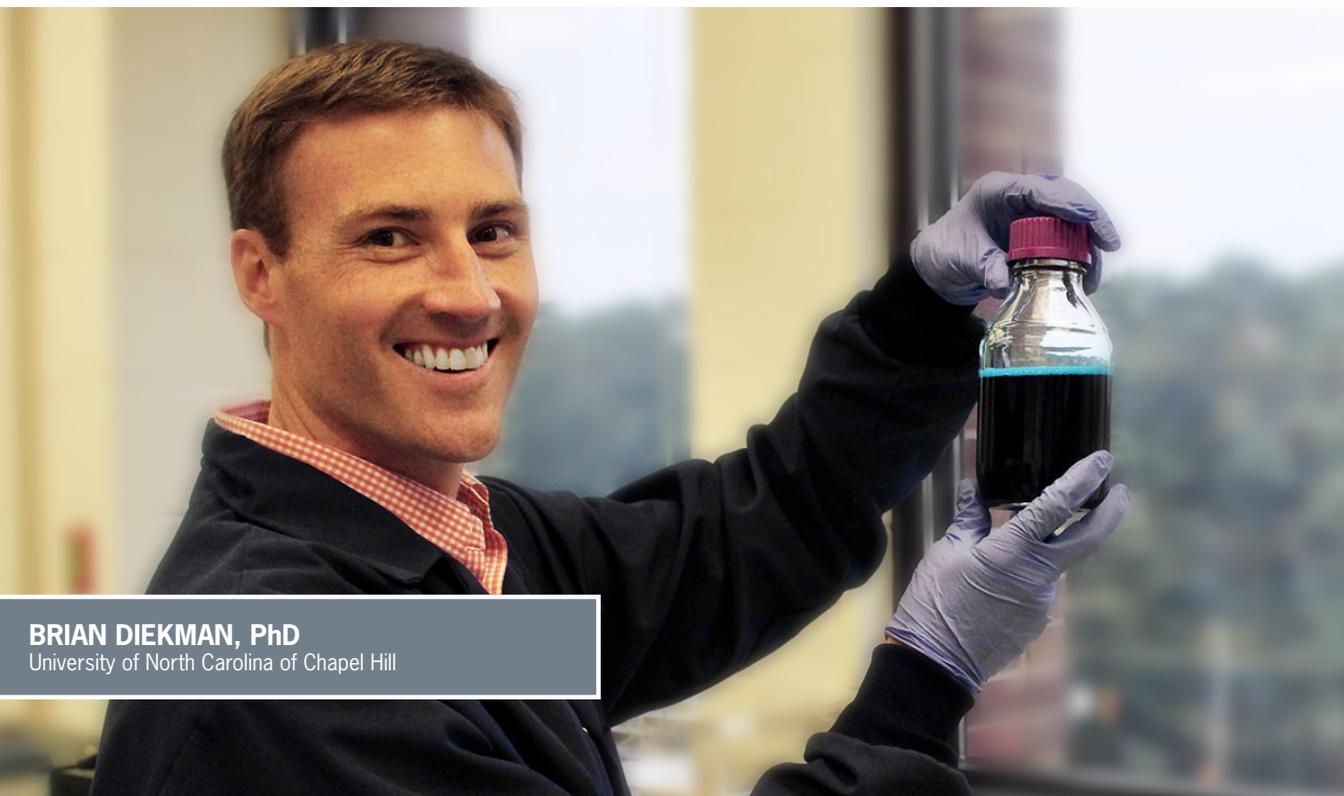
### AGING AND ARTHRITIS

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**Unraveling how chondrocytes enter senescence may be instrumental in developing therapies that address the heightened inflammation that comes with OA.**

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Identifying traceable markers of senescence in vivo, could be key to identifying and eliminating senescent cells from tissue that drive age-related disease, reducing inflammation and pain in OA patients.



**BRIAN DIEKMAN, PhD**  
University of North Carolina of Chapel Hill

# THE INS AND OUTS OF INCREASED INFLAMMATION IN ARTHRITIS

Rheumatoid arthritis remains an inadequately understood disease, with many knowledge gaps regarding how progression of the disease occurs. There are numerous and varied cells involved in the development of arthritis: macrophages, B and T lymphocytes, mast cells, neutrophils, and most recently platelets and megakaryocytes have all been found to be contributors. Understanding the roles of these cell types in joint injury and how the immune cells interact and communicate, aggravating the condition, will undoubtedly offer opportunities to discover new drug targets.

## RHEUMATOID ARTHRITIS RESEARCH

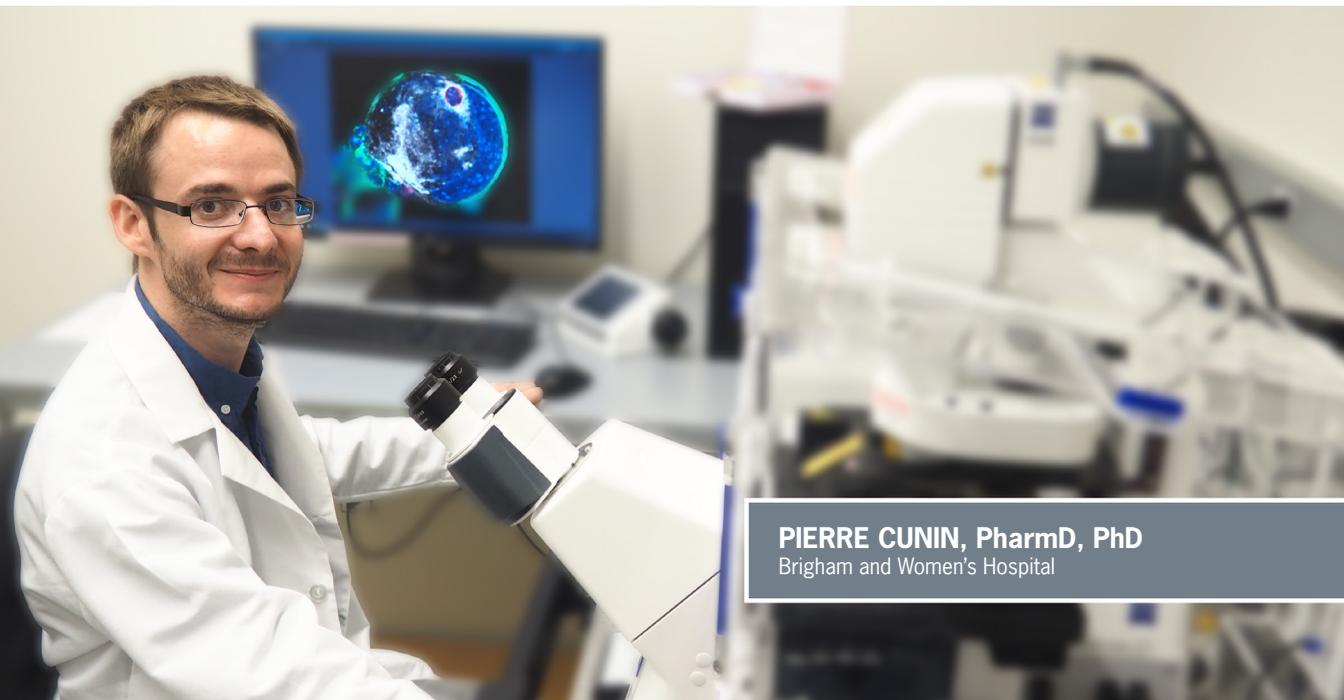
**Dr Cunin hopes that the ANRF grant will contribute to a fundamental change in our understanding of megakaryocytes as participants in immunity, and potentially open new avenues for intervention in inflammation.**

Dr. Cunin is an instructor in medicine at Harvard Medical School and has undertaken several training posts in research laboratories, including the Curie Institute and the University of Bath. Based on a great need to fill in knowledge gaps, Dr. Cunin focused his research on unravelling the roles certain cell types have in the development and progression of inflammatory arthritis. The ANRF grant gave Dr.

Cunin the opportunity to investigate an interesting phenomenon involving interactions between neutrophils (white blood cells that fight infections) and megakaryocytes (large bone marrow cells). The phenomenon is known as emperipolesis and it involves a neutrophil cell entering and existing a megakaryocyte cell. This research found that during emperipolesis, the megakaryocyte transfers biological material to the neutrophil which it takes with it when it exits. This transfer of biological material resulted in enhanced inflammatory responses.

By comparing samples from arthritis patients and those without the disease it was found that this interaction and transfer of biological material was heightened in arthritis patients. Therefore, pharmacological manipulation of emperipolesis may have significant implications for arthritis and other neutrophil-driven inflammatory disorder treatment strategies. This research has also been elemental in defining a new role for megakaryocytes as immune cells in their own right as well providing insights into the overlap of hematology and immunology, both areas of research critical to the study of arthritis.

Based on this data, Dr. Cunin has published two peer reviewed journal articles as an ANRF scholar and has a third under review. He hopes that the ANRF grant will contribute to a fundamental change in our understanding of megakaryocytes as participants in immunity, and potentially open new avenues for intervention in inflammation.



**PIERRE CUNIN, PharmD, PhD**  
Brigham and Women's Hospital



**RHIMA COLEMAN, PhD**  
University of Michigan

## ENGINEERING A NEW APPROACH TO REPAIR DAMAGED CARTILAGE

Dr. Coleman is an assistant professor of biomedical and mechanical engineering at the University of Michigan. At that institution, she formed the Cartilage Healing and Regeneration Laboratory where she is working to develop a replacement for cartilage damaged by injury or disease. Her goal: that recipients become able to use their joints normally, allowing improved movement.

### TISSUE REPAIR AND OSTEOARTHRITIS

**In an effort to improve how grafting cells could be used in situations with higher risk patients, Dr. Coleman is seeking to genetically re-program faulty chondrocytes.**

As an ANRF grant recipient, Dr. Coleman has been able to focus her research on early osteoarthritic cartilage cells, changing their genetic programming to increase their ability to repair any defects that lead to cartilage damage. To achieve this, Dr. Coleman uses an adaptation of a state-of-the-art technique known as autologous chondrocyte implantation (ACI).

Chondrocytes are the cells in our bodies responsible for producing new cartilage. A patient that undergoes ACI will require two procedures. First, a small piece of cartilage is surgically removed from the patient.

Chondrocytes are isolated from the sample and are then grown, expanding the number of cells greatly. After 6-8 weeks these cells are returned to the surgeon to allow for reimplantation.

Grafting cells in this way has proven to be an effective treatment for damaged joints. Unfortunately, many patients have joint damage as a result of an underlying condition such as osteoarthritis (OA). The same level of success has not been achieved with ACI in these patients because the bone from which the initial sample is taken is not as healthy.

In an effort to improve how this technique could be used in situations with higher risk patients, Dr. Coleman is seeking to genetically re-program these faulty chondrocytes. To do this, she inserts DNA (in the form of a gene circuit) into the cells before they are implanted back into the patients. This directs the cells to initiate repair processes.

She hopes that by creating sound repair options before such cells are implanted back into the patients exhibiting early OA that this will delay and slow their progression to late-stage OA.

Future work will involve modifying the DNA inserted into the cells in order to further boost the level of success of ACI in the patients that need it the most, reducing pain and improving mobility.

# ABNORMAL T CELL RECEPTORS IN THE DEVELOPMENT OF RA

Dr. Ashouri-Sinha's personal connection to Rheumatoid Arthritis (RA) has been the driving force behind her motivation to work in this research area. As a child, she experienced the impact of RA in her own home; witnessing the struggles her mother had to endure as a sufferer of severe and debilitating RA, eventually leading to her death due to RA-related complications. Instead of allowing these experiences to hamper her efforts, she used them as the foundation from which to begin her fight against this devastating disease.

During her medical studies it became clear that effectively fighting RA it would require unravelling the processes by which cells communicate with their environment and respond to external cues. Of particular interest in autoimmune conditions are CD4 T cells. These cells help suppress or regulate immune responses and it is generally accepted that they contribute to the progression of RA. With support received as an ANRF scholar, Dr. Ashouri-Sinha has used mouse and human models to investigate these CD4 T cells in the context of arthritis development.

T-cell receptors (TCR) are proteins on the surface of T cells, which take part in the activation of CD4 T cells, allowing them to respond appropriately when a foreign body is detected. Dr. Ashouri-Sinha's research concentrates on how abnormal and defective TCRs can lead to the development of disorders such as RA. In order to induce cell division of CD4 T cells to ensure there are enough soldiers to fight the foreign cells,

## RHEUMATOID ARTHRITIS RESEARCH

**With support received as an ANRF scholar, Dr. Ashouri-Sinha has used mouse and human models to investigate CD4 T cells in the context of arthritis development.**

the TCRs signal must reach a critical threshold. In cells with improperly functioning TCRs, this level of signalling may not be reached and the body can not elicit a strong enough immune response.

Determining the contribution of these activated cells to the development of RA could lead to the discovery of alternative therapeutic targets. During this research, a novel way to monitor TCR signalling (a reporter) was also developed. This was a key step in understanding these intricate communication pathways.

Despite what she has already achieved, Dr. Ashouri-Sinha has higher ambitions for herself and her research. She plans to advance her skillset in translational immunology by undertaking training in advanced human immune phenotyping to further her ultimate goal of identifying targets through which to mitigate early events in the development of RA.

ANRF is delighted to have played a part in assisting to achieve this goal and wish Dr. Ashouri-Sinha well as she continues to wage war against RA.



**JUDITH ASHOURI-SINHA, MD, PhD**  
University of California, San Francisco

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## A MESSAGE FROM THE CHAIR OF THE BOARD OF DIRECTORS



Dear Friend,

In 2019, I was honored to serve as Chair of the Board of the ANRF. For the second year in this role, I have witnessed the unprecedented growth of our supporter base, disease awareness platforms, education tools and, most importantly, ANRF-funded investigators in the fields of arthritis and related autoimmune diseases. Funding research is the cornerstone of the work we do at the ANRF. We work with the understanding that it is innovation through medical research that will lead to better treatments for patients and to cures that will bring relief to millions. To ensure that we contribute to the most advanced and promising studies, grant applications are selected following a rigorous peer-review process. This means that as our ability to fund more promising investigators grow, the potential for significant and innovative discoveries increases considerably.

The ANRF Board of Directors is comprised of respected professionals from diverse disciplines who volunteer their time because of a core belief in the importance of the organization's mission. I am delighted to have the opportunity to work with such a dedicated group of individuals. Within board committees and in regular meetings of the board as a whole, we ensure that supporters of ANRF continue to see their generous donations put to efficient use. Our role in this is amplified by the capable leadership of our CEO, Dr. Nahle, and the work of a small but committed staff.

As always, I am deeply moved by the generous support that we have received this year. Contributions to the ANRF are a vote of confidence in our mission and in the responsible operation as an organization. In this season of giving, I give my sincere thanks to those who make our work possible. I wish the best to you and your family and hope that you will continue to support our efforts as we continue to forge ahead towards a cure.

With gratitude,

A handwritten signature in black ink that reads "Debra Sampson".

Debra Sampson  
*Board Chair*

## ALL SMILES AT ANRF EVENTS

Throughout the year, ANRF engages in important events in the scientific community. Some highlights include:

- Participating in numerous symposiums, conferences, and events around the country and abroad to promote collaboration and advance the field.
- Providing travel scholarships to young scientists so that they may gain the benefits of collaboration and present their own work to colleagues in the field.
- Hosting events where ANRF grant recipients and members of the board of directors have the opportunity to network with ANRF supporters.



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### ANRF at work around the world.

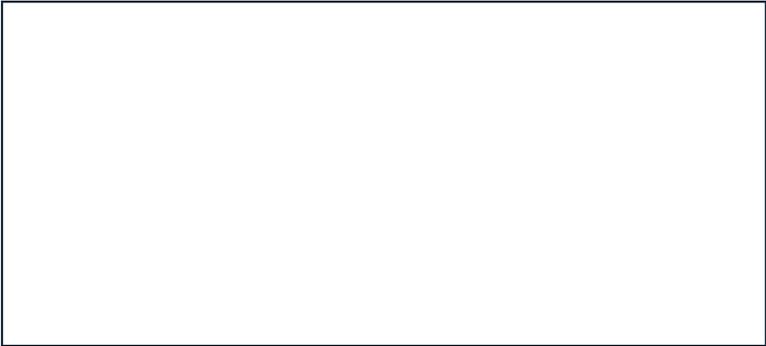
1. TNF Superfamily Conference, Pacific Grove, CA. 2-3. Autumn Immunology Conference & ANRF certificate award ceremony, Chicago, IL. 4. Dr. Nahle, ANRF CEO, announcing awardees at a conference in Stockholm, Sweden. 5-7. ANRF SAB Chair, Dr. Carl Ware, and team at SBP Insights lecture series on Autoimmunity and panel discussion, La Jolla, CA. 8. ANRF Social event at the American College of Rheumatology, Chicago, IL. 9. Collaboration visit and tour with USC, Los Angeles, CA. 10-11. ANRF Grant Review reception and Scientific Advisory Board review, Newport Beach, CA.







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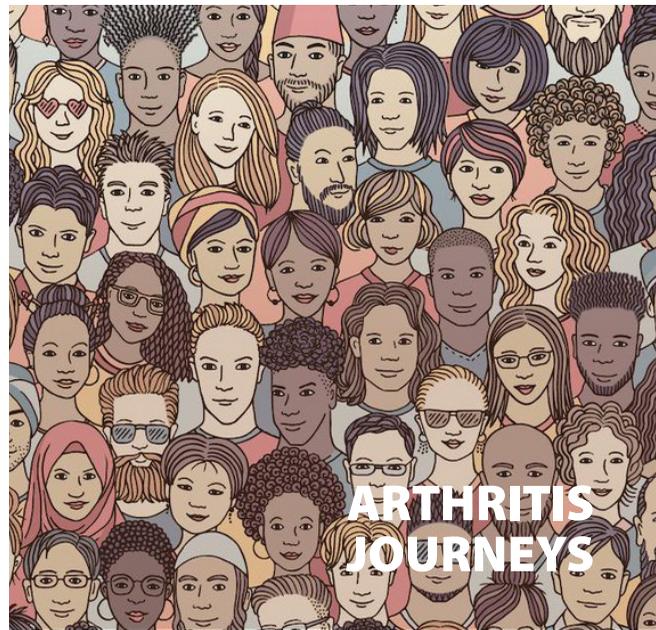


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