Congratulations to Dr. Leena Sharma, Solovy/Arthritis Research Society Research Professor of Medicine, who has just been awarded a new R01!

This prestigious grant from the National Institute of Health will support the study of early events in knee osteoarthritis (OA) development, helping to identify which of the early changes should become targets for treatments to delay or prevent the full-blown development of disease.

In this important work, 1226 persons from the Osteoarthritis Initiative (OAI) cohort who were at higher risk for developing knee OA but did not have it at entry to the OAI will be studied at a 10-year follow-up.

This study is among the longest-running of its kind, and integrates experts in epidemiology, rheumatology, imaging, and biostatistics.

Dr. Sharma is also the leader of our Multi-disciplinary Clinical Research Center (MCRC)! The MCRC operates as an integrated unit with other departments, such as Preventive Medicine, Physical Medicine and Rehabilitation, and the Institute for Public Health and Medicine, to address a broad range of clinical research endeavors.

The MCRC has been a critical part of the Division of Rheumatology for over 25 years, and Dr. Sharma is herself a product of the MCRC program. Her first grant for the knee OA research program, Mechanical Factors in Arthritis of the Knee (MAK) came from the MCRC; since then, she has had a project in four consecutive cycles. The findings from the MAK program led to the development of ancillary studies to the Multicenter Osteoarthritis Study (MOST) and the OAI. Her program represents an extremely successful, long-term outcome for an MCRC researcher.

In addition to her cutting-edge research with Northwestern, Dr. Sharma is active in the medical community. She has been a member of the American College of Rheumatology throughout her career, and also served on the board of the Osteoarthritis Research Society International (OARSI). She actively participates in grant reviews, and has served as chair of an NIH study section. She has been recognized for her work in the research community at large: she has received the NIH GCRC Clinical Associate Physician Award, and has been awarded the OARSI Clinical Research Award for “seminal work on the role of mechanical, neuromuscular, and psychosocial factors affecting individuals with OA and the onset of OA.”

“**It has been extraordinarily difficult to develop treatment that delays or prevents worsening of knee OA. A major barrier to its development is the nature of knee OA disease progression, which involves many tissues.**”

- Leena Sharma, MD
NUARS Newsflashes

Congrats on Grants

**PI: Rosalind Ramsey-Goldman**  
(MPI: Linda Ehrlich-Jones)  
Funding Source: NIH/NIAMS  
Project Title: Planning Activity and Nutrition Trial in Lupus to Energize and Renew  
Project Period: 05/02/2014 – 04/30/2016

**PI: Rosalind Ramsey-Goldman** (MPI: Bernatsky/Clarke/Ramsey-Goldman)  
Funding Source: Subcontract McGill University  
(via National Cancer Institute)  
Project Title: Cancer Risk: Advancing Knowledge in Systemic Rheumatic Disease  
Project Period: 07/02/13-06/30/15

**PI: John Varga**  
Funding Source: Biogen Idec, Inc.  
Project Title: Nrf2 Agonists as an Important Therapeutic Target for Tissue Injury and Fibrosis  
Project Period: 12/16/13-06/16/15

**PI: Leena Sharma**  
Funding Source: NIAMS  
Project Title: Long-term Significance of Pre-Radiographic Lesions in Persons at Risk for Knee OA  
Project Period: 06/01/14-05/31/19

**PI: Harris R. Perlman, PhD**  
Funding Source: American College of Rheumatology – Disease Targeted Innovative Research Award  
Project Title: The role of non-classical monocytes and resident synovial macrophages in RA  
Project Period: 07/01/14-06/30/16

**PI: Calvin Brown, MD**  
Funding Source: Abbvie, Inc.  
Project Title: Rheumatology Training Program (Fellowship Support)  
Project Period: 07/01/14-06/30/15

Jingle Bell Run 2014 Medical Honoree

As a division, we regularly participate in events that raise funds and awareness for foundations that support Rheumatologic disorders. Just as your donations help us continue research, we want to pay it forward to the foundations that promote patient education and advocacy.

We are extremely please to announce that the Chicago Chapter of the Arthritis Foundation asked our 2013 Northwestern Team to be the Medical Honoree for the 2014 Jingle Bell Run/Walk for Arthritis. Dr. Calvin R. Brown, Jr, led the team last year as our Fellowship Director. Focusing on the fellowship program, we nominated our second year fellow, Dr. Mary Mahieu, as our spotlight for this honor.

Q: What made you choose Rheumatology?  
A: "I chose a career in Rheumatology because I was fascinated by the broad range of diseases that Rheumatologists encounter, but also because Rheumatologists can dramatically impact a patient’s quality of life and limit disability. I strive to become proficient in the diagnosis and treatment of both common and uncommon rheumatologic disorders. I also hope to be productive in clinical research, which I believe will enhance my patient care skills."

Q: What is your path for research in your second year of the fellowship?  
A: I have worked with Dr. Rosalind Ramsey-Goldman on a project investigating a potential serum biomarker for subclinical cardiovascular disease in patients with systemic lupus erythematosus (SLE), and the manuscript was recently accepted for publication. As a fellow, I will continue my research with Dr. Ramsey-Goldman first in a project evaluating the interplay between physical activity, physical function, and quality of life in patients with SLE. A second project is also planned to assess potential biomarkers for patient-reported health status in domains such as pain, fatigue, and physical function.

Q: Where do you hope to be in the next 5/10 years in your career?  
To supplement my research experience, I will concurrently work towards earning a Master of Science in Clinical Investigation degree through the Graduate School at Northwestern University, and I hope to continue research pursuits beyond my fellowship training. My long term career goal is to practice at an academic institution where I can be involved in both patient care and clinical research.
Early Diagnosis Key to Getting Rheumatoid Arthritis Patients to "Target," Leading Academic Physicians Agree

Plainsboro, N.J. (PRWEB) April 30, 2014

Two leading academic rheumatologists, who took part in a live discussion with A. Mark Fendrick, MD, co-editor-in-chief of The American Journal of Managed Care, agreed that getting an accurate early diagnosis of rheumatoid arthritis (RA) is key to getting the patient started on disease modifying therapy. Today’s goal, they said, is remission of the disease, not just managing symptoms.

Eric Ruderman, MD, Professor of Medicine, Rheumatology at the Feinberg School of Medicine at Northwestern University and James O’Dell, Professor of Internal Medicine, Division of Rheumatology, University of Nebraska College of Medicine, took part in the latest installment in the AJMCtv Panel Discussion series, which shares updates in clinical practice, therapies, and healthcare management featuring providers, payers, and formulary decision makers.

The full discussion will be published in the summer issue of Evidence-Based Immunology and Infectious Disease, one of four news publications of The American Journal of Managed Care. Important points in the discussion are:

- According to Dr. O’Dell, if therapeutic principles are followed, more than 50 percent of RA patients should be able to achieve remission.

- Despite the busy schedules of rheumatologists, most will find a way to work in a patient with suspicious symptoms to find out if the person has RA. Said Dr. Ruderman, “We want to get the patients before there’s damage that’s permanent.”

- Another error is being too reliant on tests or imaging to make a diagnosis. Primary care physicians shouldn’t hesitate to make referrals in borderline cases because the “test” is negative, Dr. Ruderman said.

- RA patients need to be treated by a rheumatologist, but the primary care physician plays a critical role in managing comorbidities, such as cardiovascular disease.

- Lifestyle modifications, especially quitting smoking, are important, but they do not replace disease modifying therapy, which almost always starts with methotrexate.

- Additional therapies, including biologics, are added after a rheumatologist evaluates a patient’s response to methotrexate. A critical error may be not waiting to let methotrexate work.

The final part of the discussion involved issues of insurance coverage for therapies. Both rheumatologists told Dr. Fendrick that issues of cost and coverage come up almost every day they spend in the clinic. Dr. Ruderman said it’s especially frustrating to see some patients go without their medication for a month at the beginning of each calendar while going through prior authorization. “It just can’t be good for care,” he said.

Dr. Fendrick said under healthcare reform, the goal of “value-based” medicine aims to eliminate these kinds of hurdles for doctors and patients who have already demonstrated the need and effectiveness of a therapy. Repeat prior authorizations should not occur just because a drug is expensive, he said.

About the Journal
The American Journal of Managed Care, now in its 20th year of publication, is the leading peer-reviewed journal dedicated to issues in managed care. In December 2013, AJMC launched The American Journal of Accountable Care, which publishes research and commentary devoted to understanding changes to the healthcare system due to the 2010 Affordable Care Act. CONTACT: Nicole Beagin
New Clues on Tissue Scarring in Scleroderma

by Roger Anderson on Apr 25, 2014

A discovery by Northwestern Medicine scientists could lead to potential new treatments for breaking the cycle of tissue scarring in people with scleroderma.

Fibrosis, or scarring, is a hallmark of the disease, and progressive tightening of the skin and lungs can lead to serious organ damage and, in some cases, death.

The concept for new therapeutic options centers on findings made by Swati Bhattacharyya, PhD, Research Assistant Professor in Medicine-Rheumatology, who identified the role that a specific protein plays in promoting fibrosis.

“Our results show how a damage-associated protein called fibronectin ( FnEDA ) might trigger immune responses that convert normal tissue repair into chronic fibrosis in people with scleroderma,” Bhattacharyya said. “We also found that FnEDA, which is undetectable in healthy adults, was markedly increased in the skin biopsies of patients with scleroderma.” The study was published April 16 in Science Translational Medicine.

Scleroderma remains a disease with high mortality and no effective treatment. The factors responsible for fibrosis in scleroderma are largely unknown. Working with John Varga, MD, John and Nancy Hughes Distinguished Professor of Rheumatology and director of the Northwestern Scleroderma Program, Bhattacharyya and colleagues previously showed that innate immunity is persistently activated in scleroderma patients.

To investigate the connection between immunity and fibrosis in the disease, the scientists looked at skin biopsies of scleroderma patients to identify factors responsible for persistent scarring. They discovered that FnEDA was highly elevated.

To test the theory that FnEDA was needed for the scarring to occur, Bhattacharyya used a genetically engineered mouse lacking the protein and discovered these mice did not develop skin fibrosis.

On a cellular level, FnEDA triggered an immune response in skin cells, leading to fibrosis. Moreover a small molecule which specifically blocks the cellular immune response triggered by FnEDA was able to prevent skin fibrosis in mice.

While the current study focused on scleroderma, the mechanisms uncovered might also underlie more common forms of fibrosis, such as pulmonary fibrosis and liver cirrhosis.

“This pioneering study using state of the art experimental approaches is the first to identify an innate immune pathway for scleroderma fibrosis,” Dr. Varga said. “We expect that the results will shift our thinking about the disease, and hopefully open new avenues for its treatment.”

“We have raised the possibility for developing novel therapeutic approaches,” Bhattacharyya said. “We are also developing novel small molecules to selectively block the receptor for FnEDA as a potential anti-fibrotic therapy in humans.”

The multi-disciplinary scleroderma research team included scientists at Northwestern University Feinberg School of Medicine and the University of Michigan. The study was supported by National Institute of Arthritis and Musculoskeletal and Skin Diseases grants AR42309 and AR057216.

Graduating Fellows

Congratulations to our two new graduates as of June 30th, 2014, from the Northwestern Rheumatology Fellowship Program

Benjamin Korman, MD
&
Diana Sandler, MD
Light Activity Every Day Keeps Disability At Bay

Good news for those who struggle to increase the intensity of their physical activities

by Erin White

CHICAGO --- Pushing a shopping cart or a vacuum doesn’t take a lot of effort, but
enough of this sort of light physical activity every day can help people with or at risk of
knee arthritis avoid developing disabilities as they age, according to a new Northwestern
Medicine study.

It is known that the more time people spend in moderate or vigorous activities, the less
likely they are to develop disability, but this is the first study to show that spending
more time in light activities can help prevent disability, too.

“Our findings provide encouragement for adults who may not be candidates to increase
physical activity intensity due to health limitations,” said Dorothy Dunlop, Professor of
Medicine at Northwestern University Feinberg School of Medicine and lead author of
the study. “Even among those who did almost no moderate activity, the more light ac-
tivity they did, the less likely they were to develop disability.”

Results of the study were published April 29 in the *British Medical Journal*. **

The scientists identified a group of almost 1,700 adults, ages 45 to 79, from the Osteoarthritis Initiative study who were
free of disability but were at elevated risk for developing it because they had knee osteoarthritis or other risk factors for
knee osteoarthritis, such as obesity.

Knee osteoarthritis commonly leads to disability, preventing people from engaging in activities essential to independent
living and quality of life, such as dressing, bathing, walking across a room or making telephone calls, managing money
and grocery shopping. Two-thirds of obese adults are expected to develop knee osteoarthritis during their lifetime.

To track the amount and intensity of physical activity these at-risk people engaged in every day, scientists had them wear
an accelerometer during waking hours for about a week. The device is worn around the hip and measures the intensity of
movement. The data collected reveals how much time is spent in vigorous, moderate or light activities.

Two years after collecting the results from the accelerometer, participants were surveyed and asked about the develop-
ment of disabilities. As expected, more time spent in moderate or vigorous activity was associated with lower reports of
disabilities, but researchers were pleased to find that greater time spent in light intensity activities also was related to
fewer disabilities, even after accounting for time spent in moderate activities.

Those who spent more than four hours per day doing light physical activity had more than a 30 percent reduction in the
risk for developing disability compared to those spending only three hours a day in light activity (the least average num-
ber of hours collected in the study).

The findings controlled for time spent in moderate or vigorous physical activity and other predictors of disability, both
demographic and health factors.

“We were delighted to see that more time spent during the day, simply moving your body, even at a light intensity, may
reduce disability,” Dunlop said. “Now people with health problems or physical limitations, who cannot increase the in-
tensity of their activity, have a starting place in the effort to stay independent.”

This study is funded in part by National Institute for Arthritis and Musculoskeletal Diseases of the National Institutes of Health (grant no. R01-
AR054155, R21-AR059412, P60-AR48098 and P60-AR64464) and by the Falk Medical Trust. The publicly released Osteoarthritis Initiative data
were funded through a public-private partnership comprised of five contracts (N01-AR-2-2258; N01-AR-2-2259; N01-AR-2-2260; N01-AR-2-2261;
N01-AR-2-2262) awarded by the NIH.

**To Note:**

Dr. Dulop’s article picked up 1.6 billion media views/impressions by being featured in several sources including:
MCRC Project 1: Physical Activity Changes & Thresholds: Quality of Life and Outcomes in Knee OA

Dr. Dorothy Dunlop’s MCRC study focuses on the public health and clinical practice paradigm to promote better health for adults with osteoarthritis, especially those not doing recommended levels of physical activity. We know regular physical activity is good for health, especially moderate activity like taking a brisk walk. We know a sedentary lifestyle leads to health problems. What we do not know is whether health problems from a sedentary lifestyle only reflect inadequate physical activity or if being sedentary is a separate and distinct risk factor for health problems.

This physical activity research group (Dunlop along with Jing Song, Drs. Rowland Chang, Jungwha (Julia) Lee, and Pamela Semanik) collaborated with Dr. Jennifer Hootman of the Centers for Disease Control and Prevention to better understand this question. What they found was a smoking gun which received international attention. Sitting and being sedentary was not just a synonym for inadequate physical activity. They found evidence sedentary behavior was its own separate risk factor for the presence of disability, using national US data from adults age 60 or older surveyed by the National Health and Nutrition Examination Survey (NHANES). Each additional hour spent being sedentary increased the chance by 50% a person belonged to the pool of disabled people in this study. The strong relationship of sedentary behavior to disability was not explained by a lack of moderate activity. Because the findings were based on survey data, it is not known the extent being sedentary caused disability and vice versa. However, it does represent another piece of evidence stacked against sitting and being sedentary.

Their study “Sedentary Time in U.S. Older Adults Associated with Disability in Activities of Daily Living Independent of Physical Activity” was published in the February 2013 issue of the Journal of Physical Activity and Health.

What can you do to decrease the time you spend sitting and being sedentary? Here are some ideas:

1) Walk for short errands instead of taking the car
2) When you watch television, stand up and walk around during commercial breaks
3) When you get for a cup of coffee or water, take a walk around the house or office
4) When you go to grocery store or mall, park in a space farthest away.
5) Take the stairs instead of the elevator, if you are able.
6) Stand up when you talk on the phone or during a work meeting.
7) Instead of emailing your co-worker down the hall, walk over there to talk face-to-face

MCRC Project 1: The MAK-3 (Mechanical Factors in Arthritis of the Knee)

The MAK-3 (Mechanical Factors in Arthritis of the Knee) study team, led by Dr. Leena Sharma, is immersed in statistical analyses of data collected from the completed baseline and follow-up evaluations within the third cycle of their natural history study of knee osteoarthritis. The shortage of approaches to modify the course of knee osteoarthritis by delaying either disease progression or disability is due in large part to a critical barrier: factors that bear major responsibility for these outcomes and that might become targets for novel therapy are not well understood. With the renewed funding for our Multidisciplinary Clinical Research Center, these investigators will be able to evaluate the study participants five years after their baseline evaluation, a crucial opportunity given the usual slow pace of change in osteoarthritis. The team will apply quantitative gait analysis, to evaluate the role of key forces and joint motion measured during ambulation, and state-of-the-art measures of cartilage loss, function, disability, and stage of pain outcomes. This study will uniquely position the MAK-3 team to identify intervention and prevention targets: the longitudinal design and meaningful duration; strategic assessment, using quantitative gait analysis, of key mechanical factors under the dynamic conditions of the most common human weight bearing activity, coupled with direct, state-of-the-art measurement of cartilage loss and dynamic assessment of critical elements of knee-level joint function coupled with person-level function and disability outcomes. These findings will inform the knee osteoarthritis natural history paradigm as well as identify as yet untapped targets for novel strategies to prevent cartilage loss, function decline, and disability progression.

Dr. Sharma and the MAK team deeply appreciate the involvement of the participants who make this work possible!!!
A Bone To Pick
By Richard Pope, MD
Mabel Greene Myers
Professor of Medicine
Rheumatology

After a long, cold winter, it looks like summer has finally arrived! The Division of Rheumatology is gearing up for a busy summer. As July approaches, we congratulate our graduating fellows, Benjamin Korman, MD, and Diana Sandler, MD. Dr. Sandler will be entering a private practice this summer in Hinsdale, while Dr. Korman will stay in the division as we welcome him as our newest faculty member! He has recently received a junior faculty award to study the pathogenesis of fibrosis and its link to metabolism in the laboratory of Dr. John Varga. We congratulate them both as the venture on to their next steps in the field of Rheumatology.

We are also excited to welcome our two new fellows into the program: Zineb Aouhab, MD, and Hussein Bhikhapurwala, MD. Dr. Aouhab is finishing her residency at John H. Stroger Hospital here in Chicago and is looking forward to continuing to learn more about lupus and patient care during her time with us. Dr. Bhikhapurwala is currently finishing his residency at the Atlanta Medical Center and is also excited to not only be part of the program, but to return home, since he is originally from Chicago. He is very interested in continuing down a research path and has a lot of enthusiasm towards being part of the team. Welcome Drs. Aouhab and Bhikhapurwala!

Thank you to all of our donors for your continued philanthropic support of the division. The value of each gift is multiplied many times over as it allows us to grow our research enterprise, furthering our knowledge, and better positioning us to vie for competitive research grants in our fight against rheumatic diseases. If you have not yet supported the division, please consider making a gift. If you like more information on areas or projects to support, please contact Maureen Mizwicki at 312.503.1090 or m-mizwicki@northwestern.edu.

From all of us at NUARS, we wish you and your family a safe and enjoyable summer!

Sincerely,

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Introducing ANTLER

Rosalind Ramsey-Goldman, MD

“Activity and Nutrition Trial in Lupus to Energize and Renew”

The ANTLER study focuses on management of patients with SLE by identifying effective strategies to decrease fatigue.

Systemic lupus erythematosus (SLE) is a systemic autoimmune disease characterized by pronounced inflammation that affects up to 1.5 million persons in the US. One of the major issues people with lupus face is chronic, debilitating fatigue that significantly decreases quality of life, and increases work disability and associated health care costs. Fatigue is a frequent and widely heard complaint with limited treatment options.

We focus on physical activity and nutrition to help control weight and reduce fatigue in patients with SLE. This study was modeled after the successful Diabetes Prevention Program. To address this management gap for patients with lupus, our recently funded planning grant, ANTLER will help us design the intervention and plan a clinical trial to test the intervention.

Sunday June 22:
Stepping Out to Cure Scleroderma Walk

The Northwestern Scleroderma Program is again hosting a team for the 12th Annual Scleroderma Walk.

As a division we continue to support and cheer them on in their participation.
Your support of the Arthritis Research Society has allowed Northwestern to establish and advance its standing in the field of rheumatologic and autoimmune disease research. Because of the tremendous progress the Division has made, the Feinberg School of Medicine as a whole continues to benefit, ascending national rankings, gaining accolades, and securing vital research grants as a result.

While the Division of Rheumatology continues to rank among the nation’s best, private donor support remains paramount to our continued success. For those lives affected by disease, both patients and their families, the importance of research to improve treatment options and advance progress toward cures cannot be overstated.

For further information about giving opportunities, please contact Maureen Mizwicki at 312.503.1090 or m-mizwicki@northwestern.edu.