

NUARS NEWSLETTER



INSIDE THIS ISSUE:

*Coverstory:
Autoimmunity and
Atherosclerosis at
Northwestern Uni-
versity*

1

*A Bone to Pick: A
Message from Dr.
Richard Pope, NU-*

2

*NUARS News-
flashes: Catch up
on the Latest News
at NUARS*

2

*MCRC Update:
The Latest Devel-
opments of NU's
Multidisciplinary
Clinical Research*

4

AUTOIMMUNITY AND ATHEROSCLEROSIS AT NORTHWESTERN UNIVERSITY



Dr. Darcy Majka, MD (center) author of the coverstory, meets with her mentors Dr. Kiang Liu, PhD (left) and Dr. Rowland Chang, MD, MPH (right) to discuss ongoing research strategies in autoimmunity and atherosclerosis.

Studies of Autoimmunity and

Atherosclerosis is a new research program within the Rheumatology Division. The primary aim of these studies is to examine whether autoantibody markers common to autoimmune connective tissue diseases (ACTDs) are associated with the presence of atherosclerosis. Dr. Darcy Majka joined the faculty of Rheumatology in 2003 in order to conduct these studies. She has joined forces with clinicians, epidemiologists, and biostatisticians from both Rheumatology and the Department of Preventive Medicine to examine the novel hypothesis that ACTD related autoantibody markers are related to atherosclerosis development.

Connective Tissue Diseases, Autoim-

munity, and Autoantibodies

Connective Tissue Diseases (CTDs) are a group of diseases that attack the collagen or other components of connective tissue. (Connective tissue is a term describing a group of tissues which bind and support other tissues. Connective tissues include collagen, fat, cartilage, tendons, ligaments, and bone, which are the tissues damaged in various rheumatic diseases.) CTDs include rheumatoid arthritis (RA) and systemic lupus erythematosus (lupus), and they usually have arthritis as a feature. CTDs are autoimmune in origin, which means that immune cells which normally function to fight off infection mistake the body's own tissues as invaders and attack them. Autoantibodies are made in this abnor-

mal immune response and are a characteristic component of most ACTDs. Autoantibodies can be measured for diagnostic purposes, and these studies will measure antibodies occurring in RA, lupus, and antiphospholipid antibody syndrome (APAS), a disorder often seen in lupus.

RA, Lupus, and APAS

RA is an ACTD manifest by inflammatory arthritis, bone erosions and mechanical dysfunction of the joints. Lung, cardiovascular, skin, and blood manifestations also occur in RA. Lupus is an autoimmune disease with a wide spectrum of clinical manifestations associated with circulating autoantibodies against components of the cell nucleus. Individuals with lupus (*cont'd on p3*)

NUARS NEWSFLASHES

We are pleased to announce that the Division of Rheumatology has once again been named one of the top rheumatology groups in the country by *US News and World Report*. This year we ranked 19th in the nation. Please visit the magazine's website for further information at <www.usnews.com>.

Welcome to **Diane Ecklund**, new laboratory technician working with Dr. Syamal Datta.

Diana, an Illinois native, plays both the piano and violin and enjoys collecting insects. She graduated from Johns Hopkins University and hopes to return to school in the coming years to develop a career in research and teaching. We look forward to working with Diane and she will be a great addition to our team!

Matthew Warner-Blakenship, new laboratory technician in Dr. John Varga's lab, joins us from a previous position at Notre Dame University. Matthew is an Iowa native and holds an MS degree in Neuroscience from the University of Iowa. He is an avid

traveler who has recently been to Costa Rica, Hawaii, and the desert of New Mexico. Eventually, he plans to return to school and earn his PhD.

Congratulations to **HeeKap Kang**, research assistant professor in Dr. Syamal Datta's laboratory, on his new grant award from the Arthritis Foundation, National Office. HeeKap's grant provides \$50,000 per year in salary and research support for one year.

The Karen Brown Scleroderma Foundation has awarded its very first research fellowship to rheumatology trainee **Dr. Monique Hinchcliff**. Dr. Hinchcliff is currently in her third year of training and is working under the mentorship of Drs. John Varga and Richard Pope. Congratulations to Dr. Hinchcliff on this tremendous honor.

We wish to bid farewell to **Gina Banks, Charmayne Dunlop-Thomas, Zaynab Kamal, Emily Yarrito, Jared Jarvis, ShuJen Chen, and Hongyan Ning**. We wish them all the best in their new positions. We will miss you!



A BONE TO PICK:
RICHARD POPE, M.D.
 NUARS DIRECTOR &
 MABEL GREENE MYERS
 PROFESSOR OF
 MEDICINE

I hope this message finds you happy and healthy and that you are looking forward to an enjoyable holiday season.

Our faculty and research staff continue to work hard and pursue many avenues of cutting-edge research, but times are challenging. The tremendous success of research programs nation-wide has increased the competition for grant funding from the National Institutes of Health. Even veteran researchers are finding they must submit a grant application more than once to receive funding.

The current funding environment makes the support from our NUARS friends more important than ever. The support we receive from you is used to help bridge the gap between the costs of research and available grant funds. Over this past year, NUARS donations were used in the fights against scleroderma and rheumatoid arthritis, paying for research staff salaries and lab supplies. Some of the funds were also used to help support our fellowship program and to train new rheumatology physician/scientists. It is exciting to see the results of the generosity of our NUARS friends.

2007 is already shaping up to be an exciting year. We are in the process of expanding our faculty and have interviewed several very promising candidates. At this time of year, I wish to send a special greeting out to all of you, our NUARS friends. Thank you for your generous support over the past year. I wish you the very best in the upcoming holiday season and a very happy and healthy new year!

Warmest Holiday Wishes,

Richard Pope

AUTOIMMUNITY AND ATHEROSCLEROSIS (CONT'D)

(cont'd from p1) may have a variety of symptoms including rashes, kidney failure, anemia, blood clots, inflammatory arthritis, psychiatric disorders, neurological syndromes, and inflammation of the lungs and heart. APAS is a disorder characterized by autoantibodies causing blood clots in the arteries and veins, or pregnancy loss. APAS may exist as a primary disorder or as a secondary feature of lupus or other ACTDs.

Increased Risk of Atherosclerosis in RA, Lupus, and APAS

Cardiovascular disease (CVD), or atherosclerosis, is a disease of the arteries in which cholesterol is deposited in plaques on the arterial walls. The plaque narrows blood flow leading to tissue damage. CVD in the coronary arteries is called coronary artery disease (CAD), which can lead to a myocardial infarction (heart attack). CVD remains the leading cause of death in the USA. One in 3 Americans develop CVD and 910,000 die from CVD annually.

RA, lupus, and APAS are risk factors for CVD. Patients with RA and lupus have a high prevalence of CAD and are younger than expected when they develop CAD. It has been proposed that inflammation occurring in ACTDs is the cause for the increase in CAD. Furthermore, a few preliminary studies showed that individual autoantibodies were found in the circulating blood of patients with CVD, indicating that atherosclerosis may have autoimmune features. The Studies of Autoimmunity and Atherosclerosis were designed to further test

whether a broad range of ACTD related autoantibodies are present in atherosclerosis.

The CARDIA and MESA Studies

Dr. Majka is working with a team of experts in the study of rheumatic disease and cardiovascular disease epidemiology and basic science. She is conducting these studies with the assistance of her mentors, Drs. Rowland Chang MD, MPH, and Kiang Liu PhD, both from the Department of Preventive Medicine; and Dr. Richard Pope, MD, NUARS Director. In addition, she is taking advantage of two rich resources at Northwestern, the Coronary Artery Risk Development in Young Adults (CARDIA) study and the Multi-Ethnic Study of Atherosclerosis (MESA). These are two previously assembled NIH-funded studies examining cardiac risk. The CARDIA study is an ongoing prospective study initiated in 1985 with the goal of studying the evolution of CAD risk factors in young adults. Data have been collected at two- to five-year intervals for 5,108 participants aged 18-30 who were evenly balanced by sex, and race (African American/Caucasian).

The MESA study population is comprised of White, African-American, Hispanic and Chinese subjects. MESA was initiated in July 2000 in a population-based sample of 6814 men and women aged 45-84 years. Subjects are examined at 18-24 month time points and the 4th MESA exam is underway. Repeated CVD risk factor data collected by CARDIA and

MESA include blood pressure, blood tests for inflammatory markers, height and weight, medical histories, family histories, physical activity and smoking questionnaires, psychosocial data, and diet and alcohol histories.

Measures of Sub-clinical Atherosclerosis in CARDIA and MESA

Of interest to the Studies of Autoimmunity and Atherosclerosis, CARDIA and MESA have measured a variety of surrogates for early CVD. Electron Beam CT scanning is a noninvasive means of screening for coronary artery calcification (CAC) which is a marker of overall atherosclerotic burden. The intima media thickness (IMT) of the carotid arteries measured by ultrasound is also a noninvasive means of measuring generalized atherosclerosis. Ankle-brachial index (ABI), the ratio of arm blood pressure to leg blood pressure, is a simple and noninvasive measurement of peripheral arterial disease, and ABI is a useful addition to coronary risk assessment. CAC, IMT, and ABI are all measures of sub-clinical atherosclerosis which can be measured before any clinical symptoms of atherosclerosis occur. Dr. Majka's studies are testing CARDIA and MESA serum samples for autoantibodies and will then be able to determine whether subjects with positive measures of sub-clinical atherosclerosis have a higher prevalence of ACTD related autoantibodies.

Pre-clinical ACTD Related Autoantibodies and Sub-clinical Atherosclerosis

The presence of ACTD

related autoantibodies in asymptomatic individuals is a predictor of future clinical ACTD development. This indicates that the disease activity in RA and lupus is already present prior to disease diagnosis. Furthermore, some patients with RA already have CVD at the time of RA diagnosis, indicating that the CVD in ACTDs may begin before clinical ACTD development. Although the association between active ACTDs and CVD is established, an association between pre-clinical ACTD related autoantibodies and sub-clinical CVD has not been explored. Dr. Majka is conducting studies to examine this new area of research with the invaluable assistance of her NIH-funded grants, "Studies of Autoimmunity and Coronary Artery Disease" and "Studies of Autoimmunity and Atherosclerosis".

These studies offer innovation to the study of cardiac risk. If our findings prove that ACTD related autoantibodies are associated with sub-clinical atherosclerosis, then information gained from these studies may be used in the future to identify new risk factors for CVD so that prevention strategies can be implemented. What's more, these projects will provide a better understanding of an important complication of RA and lupus. While the association between ACTDs and atherosclerosis is well established, the cause for the association is not. Therefore, these studies from the Division of Rheumatology at Northwestern will allow us to further characterize the reason for the increased rate of CVD in patients with ACTDs.

Written by Dr. Darcy Majka, MD, Instructor of Medicine, Northwestern Univ

Northwestern University
Arthritis Research Society
Research Society

NU Division of Rheumatology
240 East Huron, McGaw M-300
Chicago, IL 60611
NUARS Director: Richard Pope, M.D.
NUARS Newsletter Editor: Chris Loertscher
Phone: 312-503-8003
Fax: 312-503-0994
Email: c-loertscher@northwestern.edu

We're on the Web!

www.medicine.northwestern.edu/divisions/rheumatology

Thank you for your
support!

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 Marci Price at 312.503.0766 or marciprice@northwestern.edu

NU Arthritis Research Society
McGaw M-300
240 East Huron Street
Chicago, IL 60611

Send all donations and
Subscription requests to:

NU Arthritis Research Society
McGaw Pavilion Suite M-300
240 East Huron Street
Chicago, IL 60611

MULTIDISCIPLINARY CLINICAL RESEARCH IN RHEUMATOLOGY (MCRC) UPDATE

Rodlescia Sneed, new lead coordinator for Dr. Rosalind Ramsey-Goldman's MCRC lupus research group, joins the NUARS team after working two and a half years in Miami. Rodlescia is a Detroit native who studied as an undergraduate in Molecular Biology at Princeton and later received her Master of Public Health degree from Columbia University. When not working on Dr. Goldman's lupus research, Rodlescia enjoys the performing arts, reading good books, and cooking. She hopes to one day develop her own independent research career in public health. Welcome Rodlescia!

Congratulations to Dr. Rosalind Ramsey-Goldman on receipt of a **Kirkland**

Scholar grant from the Mary Kirkland Center for Lupus Research at the Hospital for Special Surgery in New York. This grant provides funding for rheumatology training and will be used to support the research projects of the new investigators being mentored by Dr. Ramsey-Goldman.

Congratulations to **Dr. Dipali Kapoor** on receipt of her new F32 individual training grant from the NIH. You may recall our announcement in the previous NUARS newsletter about Dr. Kapoor's grant from the American College of Rheumatology. The accomplishment of receiving two grants of this nature is indicative of the successful, exciting projects in osteoarthritis that Dr. Kapoor and her mentor Dr. Sharma are developing. We look forward to her continued success.