2015 Update: Division of Rheumatology and Immunology
Dear Friends and Colleagues,

I am proud to share with you some of the many accomplishments from the Division of Rheumatology and Immunology here at The Ohio State University College of Medicine. It’s been a year of forging connections with rheumatologists and scientists from around the world, breakthroughs in research and patient care, and equipping residents and fellows to lead the future of our field.

The year 2014 is distinguished by building relationships internationally. You can read about our colleague, Joseph Flood, MD’s global outreach as president of the American College of Rheumatology. Several of us were able to be a part of a reception in his honor at the ACR annual meeting in Boston in November, capping off his tremendous year of service to our professional organization.

While Dr. Flood represented our specialty throughout the world, we had a number of international visitors here at Ohio State. I met with a delegation from Addis Ababa University College of Health Sciences in Ethiopia to explore how we can collaborate in helping them train rheumatologists. We have a great opportunity to train physicians from other countries to be better able to serve their populations and improve the outlook for many people with rheumatic conditions. Junfeng Jia, MD, joined us as a visiting professor from Xining Hospital, Fourth Military Medical University in Xi’an, China, where I had the privilege of visiting in 2013. Toshhide Mimura, MD, PhD, professor and chief, Division of Rheumatology and Applied Immunology at Saitama Medical School in Moroyama, Japan presented his research on Epigenetic Abnormalities in RA at our Everett D. Reese Immunology Seminar.

In this update, we’ve also featured Dr. Clark Anderson’s 40 years of NIH funding, our rheumatology clinic’s recognition as a patient-centered specialty practice, our research on the link between estrogen and lupus and membrane repair in myositis, insights into the anti-inflammatory benefits of curcumin, plus introduced our first combined adult and pediatric fellow.

For the seventh year in a row, we will be hosting our popular musculoskeletal ultrasound conference in 2015. This two-day continuing medical education workshop features experts from around the country with hands-on training. Our new faculty member, Hareth Madhoun, DO, will direct this year’s conference.

As you examine this update, I know you will agree that it’s a very exciting and promising time to be working in rheumatology and immunology. The influence and impact of our work here at Ohio State is growing stronger each year. This was apparent to me at the ACR annual conference. Stacy P. Ardoin, MD, MHS, presented her significant study on detecting early signs of myocardial damage in lupus patients using cardiac MRI. Ohio State was also well represented in poster and podium presentations by all levels of learners — a medical student, a graduate student, an internal medicine resident, pediatric and rheumatology fellows, and postdoctoral fellows.

Thank you for the chance to share our endeavors. I hope you find it enlightening and inspiring. I’d value the opportunity to hear your comments or questions. Please feel free to contact me at Wael.Jarjour@osumc.edu.
ACR President Raises the Understanding of Rheumatology Issues

Columbus and The Ohio State University were well represented to rheumatologists throughout the world during 2014. Joseph Flood, MD, adjunct professor with Ohio State’s Division of Rheumatology and Immunology and private practice rheumatologist in Columbus, completed his term as president of the American College of Rheumatology (ACR) in November.

Dr. Flood fulfilled the mission of the ACR — Advancing Rheumatology! — both in the United States and internationally.

**A Global Ambassador for American Rheumatology**

Dr. Flood and his wife, Jeanne, traveled to 11 countries on four continents, meeting with rheumatologists throughout the world. Everywhere they went — Uruguay, Philippines, India, France, Poland and elsewhere — they took the best wishes of American rheumatologists and rheumatology health professionals. They developed a deeper understanding of the practice of rheumatology worldwide.

“I visited some parts of the world where the need for rheumatologic care is so basic and fundamental and the need is so unmet, those of us from wealthy countries are astounded. There are places where the burden of rheumatic disease hasn’t even been assessed, where they lack funds just to count how many people may have gout in their country or how many children have rheumatoid arthritis,” says Dr. Flood.

“At the same time, I learned about great scientific endeavors happening all around the world, meeting enthusiastic young rheumatologists excited to share their science and their work.”

**Advocacy Efforts Pay Off**

In addition to connecting with rheumatologists internationally, Dr. Flood’s leadership in the ACR is marked by better awareness of rheumatology and influence in policies that affect patients.

Dr. Flood sees great dividends for the understanding of rheumatology through ACR’s “Simple Tasks” public awareness campaign (simpletasks.org) and ongoing lobbying work in Washington, D.C. He’s personally given away hundreds of the Simple Tasks lapel pins — a tiny bent fork — to remind people about the impact of rheumatic disease on 11 million Americans.

“Five years ago, when we walked into a congressman’s office, we’d need to spend the first five minutes explaining what we do. Now, they recognize the bent fork and know.”

Dr. Flood says the ACR is one of the most respected medical organizations of its size on Capitol Hill, with the ability to influence Congress on issues that affect patients, the specialty and sometimes all medical practices. The ACR’s efforts were instrumental in the delay of switching from ICD9 to ICD10. The impact of changing the disease coding system to ICD10 — when ICD11 will be required in a couple years — would have been very costly to every medical practice.

Another notable achievement in Washington — Medicare approved the ACR’s data-connecting initiative RISE, the Rheumatology Informatics System for Effectiveness Network, as a certified registry. This acceptance makes required Medicare reporting more efficient for all rheumatologic practices.

In addition to government, Dr. Flood is proud that the ACR has improved relationships with insurance companies. This year, the ACR worked with a major insurer to allow stable patients to remain on their current effective medication, instead of requiring a change to the company’s preferred biologic.

Get Involved

Dr. Flood has a long history of service in the ACR, including membership on the rheumatologic care committee, government affairs committees, the board and executive committees. He encourages his colleagues to get involved through committee membership, contributions to the ACR’s political action committee and ACR’s Foundation supporting scholarship and research, and by participation in advocacy.
Research Harnesses Curcumin’s Power

Researchers with Ohio State's Division of Rheumatology and Immunology have discovered how to spread the anti-inflammatory benefits of curcumin throughout the body and identified, for the first time, the compound's effect on a specific immune cell's activity.

The study results — published on November 4, 2014, by PLOS ONE — unveil how to take advantage of curcumin’s anti-inflammatory power. Senior co-authors are Wael Jarjour, MD, division director, and Lai-Chu Wu, D. Phil., associate professor from the Department of Molecular and Cellular Biochemistry, with Nicholas Young, PhD, postdoctoral researcher in the division, as the lead author.

Curcumin, a primary compound in the spice turmeric, has been used for centuries in Eastern medicine as an anti-inflammatory agent, but its therapeutic usefulness and molecular mechanisms of its activity are just now being explored. Curcumin is available in supplements and in food, but it is not well absorbed by the body. It is not water-soluble and stays in the gastrointestinal tract without entering the bloodstream and tissues.

To spread curcumin’s anti-inflammatory power throughout the body, the Ohio State research team mixed curcumin powder with castor oil and polyethylene glycol to create a nano-emulsion to increase the compound’s solubility and bioavailability. This formulation enabled the curcumin to dissolve and be absorbed better by the intestinal tract. Previous research established that the concentration of emulsified curcumin in blood is over 10 times higher than the curcumin powder in water after oral consumption.

Feeding mice this formulation of curcumin, the researchers found that it shut down an acute inflammatory reaction by blocking activation of a key protein (NF-κB) that triggers the immune response. The researchers were also the first to show that curcumin stops recruitment of specific immune cells or macrophages that, when overactive, are linked to such problems as Crohn’s disease, rheumatoid arthritis, lupus, inflammatory bowel disease, heart disease and obesity.
Career Marks 40 Years of NIH Support

Ohio State physician-scientist and professor, Clark L. Anderson, MD, has reached a milestone that few can claim. The National Institutes of Health (NIH) has continuously funded Dr. Anderson’s research for 40 years with R01 grants.

**Working at the Frontier of Receptors for Antibody Immune Complexes**

His early career produced breakthroughs in the understanding of the biology of receptors for immune complexes, now part of clinical practice, textbooks and pharmaceuticals. His fascination with how antibody-antigen complexes interact with cells led him to become a pioneer in the structure and function of the receptors that bind these complexes. The first part of his research produced discoveries about how antibodies work, while the next phase filled in gaps in that understanding. Those breakthroughs included how a different antibody receptor (FcRn) regulates IgG and albumin metabolism. Currently, his basic science laboratory is studying how liver sinusoidal endothelial cells remove and destroy blood-borne viruses and small immune complexes.

**Staying Focused on Challenging Questions**

Dr. Anderson credits his long and successful research career to his decision to stay focused on hard but solvable fundamental questions.

“I’m proud of my career. I didn’t allow myself to be seduced in other directions but stayed on the path to answer questions that couldn’t have been answered in a quick and easy way.”

He avoids collaborations outside of his own research direction. He publishes only what moves the field forward, producing a relatively short list of publications that have garnered a very high citation index, with other authors frequently citing his work.

The ability to write successful grant proposals is a key to Dr. Anderson’s continuous NIH funding. He attributes his writing skills to an ongoing interest in reading and language, especially a love of the works of Marcel Proust and Henry James that have helped develop the clear, concise writing style that he uses in his proposals.

Dr. Anderson joined Ohio State’s Division of Rheumatology and Immunology in 1985 from the University of Rochester, following his wife, Carole, to Columbus when she became dean of Ohio State’s College of Nursing. In 1994, he was honored with the University Distinguished Scholar Award, Ohio State’s highest accolade for research accomplishments.

The NIH funding has given Dr. Anderson the freedom to focus on basic science; he’s been a part of a revolution in the understanding of fundamental mechanisms of inflammation where interesting questions remain.

**Recognizing Fellow Faculty Contributions**

Dr. Anderson says his concentrated efforts in the laboratory have been possible only because of the dedication and talent of fellow faculty members focused on the teaching of students and the care of patients. The shared responsibility for research, teaching, and clinical practice in the Division of Rheumatology and Immunology created the environment for Dr. Anderson’s exceptional body of work.

In a specialized imaging machine, genetically engineered transgenic mice received nano-emulsified curcumin before being injected with components of bacteria (lipopolysaccharide) to stimulate an immune reaction. These mice showed minimal signs that the NF-kB protein had been activated at all.

Knowing that curcumin delivered in this way could shut down NF-kB activation throughout the animals’ bodies, researchers looked for further details about the compound's effects on inflammation. They found that nano-emulsified curcumin halted the recruitment of macrophages that “eat” invading pathogens, but also contributed to inflammation by secreting chemicals. In human cell cultures, the emulsified curcumin stopped the macrophages in their tracks.

Dr. Wu says, “Understanding more about how curcumin acts to reduce inflammation and especially its macrophage effect has exciting implications for a host of diseases. By creating a formulation that is more effective in suppressing inflammation throughout the body in an animal model, there is an opportunity to examine its effectiveness in preventing and treating a host of human diseases — at a fraction of the cost of developing a new drug.”

Latha P. Ganesan PhD, Alana Cheplowitz, Lindsay P. Hammer, Jessica M. Mates, PhD of the Anderson laboratory
Investigating Membrane Repair in Myositis May Impact Diagnosis and Treatment Options

Noah Weisleder, PhD, associate professor and researcher with Ohio State’s Department of Physiology and Cell Biology, in partnership with Wael Jarjour, MD, director of the Division of Rheumatology and Immunology, is exploring novel biomarkers and cellular pathways that may contribute to the development and exacerbation of myositis. Ohio State’s Center for Clinical and Translational Science (CCTS) awarded Dr. Weisleder and his team a Collaborative/Partnership Pilot grant to conduct the study.

In myositis, skeletal muscle tissue is chronically inflamed in response to unknown triggers. Dr. Jarjour’s work has linked the pathobiology of myositis to the compromised repair of skeletal muscle cell membranes. Dr. Weisleder’s previous research identified novel members of the tripartite motif (TRIM) family of proteins that regulate membrane repair capacity in muscle cells. In mouse models with myositis, he has identified the presence and activity of these specific TRIM proteins. This study will examine whether the findings in mouse models can translate to clinical relevance. The team, in collaboration with Dr. Chester Oddis, professor of Medicine, University of Pittsburgh, will determine if these TRIM proteins or autoantibodies against TRIM proteins, can be used as biomarkers for myositis in human patients. Further experiments will establish novel targets for the development of therapeutic approaches for treatment of myositis, which is currently limited to immunosuppressive drug regimes.

The study will test the hypothesis that TRIM proteins contribute to the progression of myositis by the development of autoantibodies against these proteins leading to the loss of membrane repair capacity in skeletal muscle. The study has three objectives. First, researchers will examine serum samples from patients with myositis looking for autoantibodies against TRIM proteins linked to membrane repair. Second, they will test serum samples added to human myocytes to determine if the autoantibodies compromise membrane cell repair. Third, researchers will measure the levels of TRIM proteins in muscle biopsies from patients to establish if the changes observed in mouse models correspond to human pathology.

The results of this study have significant potential for clinical impact in the diagnosis and treatment of myositis, but also for furthering the understanding of cell membrane repair processes in all tissues.

Study Links Estrogen and Immune-Regulating Genes in Lupus

In the U.S. and throughout the world, women are less likely to die from infectious diseases than men. The beneficial effects of estrogen on the immune system are credited. On the other hand, premenopausal women are much more likely to develop an autoimmune disorder. Many scientists believe estrogen plays a significant role in the pathobiology of these diseases.

Wael Jarjour, MD, director of Ohio State’s Division of Rheumatology and Immunology, and his team now have evidence to support the theory and insight into how estrogen’s normally protective effects could go awry.

Dr. Jarjour and his team examined a family of immune-regulating genes called toll-like receptors (TLRs) and demonstrated that estrogen can up-regulate the expression of a subgroup of these proteins called endosomal TLRs.

Dr. Jarjour’s lab is one of the few in the nation focused on sex bias in autoimmune disease. To test their theory that estrogen stimulates TLR signaling, they triggered an immune response in cells from men and women with and without lupus. Then, they added estrogen to see if gene expression changed, honing in on TLR8, an X chromosome-linked gene already suspected in the development of lupus.

Estrogen boosted the level of immune response in all the study samples, but the reactivity of cells from women was almost two times greater than cells from men. The results demonstrate that estrogen regulates TLR8 and other endosomal TLRs in ways that increase the inflammatory response with female cells even more sensitive to this response.

The TLR8 study, conducted in partnership with researchers at the University of Virginia, was published in the March issue of Clinical Immunology and discussed in the April 16, 2014, edition of Science Daily.

Dr. Jarjour plans to work on identifying more immune pathways that are activated by estrogen. He hopes that the findings prompt research to explore novel treatment options for lupus, which is nine times more common in women than men.
A new combined pediatric and adult rheumatology fellowship at Ohio State fills a unique niche in the specialty. The fellowship is a collaboration between Ohio State’s Division of Rheumatology and Immunology and Nationwide Children’s Hospital in Columbus.

Paul Jensen, MD, the first fellow in the new four-year program, started in July of 2014. Dr. Jensen became interested in rheumatology during his internal medicine and pediatric combined residency at Ohio State. He says, “I didn’t want to give up either area of my training. The two areas complement each other. Pediatrics makes me a better adult physician, and internal medicine makes me a better pediatrician.”

Ohio State faculty member Stacy Ardoin, MD, modeled the path Dr. Jensen wanted to follow. Dr. Ardoin is board certified in both adult and pediatric rheumatology. After medical school and a dual pediatric/internal medicine residency with Ohio State, she completed a combined fellowship at Duke University. She joined the Ohio State faculty and now sees pediatric patients at Nationwide Children’s and adult patients at Ohio State’s rheumatology and lupus clinics.

With an interested candidate, Kevin Hackshaw, MD, rheumatology fellowship director at Ohio State teamed with Charles Spencer, MD, chief of rheumatology at Nationwide Children’s. Both fellowship programs had to seek separate accreditation to create a combined program.

**What’s the Value of Both Adult and Pediatric?**

It takes a tremendous commitment — eight years of training after medical school — to complete the combined residency and fellowship and become board eligible in both adult and pediatric rheumatology. Only a handful, an estimated 40 physicians in the United States, are dual certified.

Dr. Hackshaw and Dr. Spencer believe that the combined fellowship can fill important gaps in rheumatology practice, providing the individual completing the fellowship with several potential career paths.

The transition from childhood to adulthood for patients with any chronic condition is a very challenging time. A teenager with juvenile rheumatoid arthritis or lupus moving from pediatric to adult care is at high risk for non-compliance, may disregard the long-term consequences of the condition and have trouble adjusting to a different approach to care.

Dr. Jensen’s research during the first year of his fellowship is focusing on best practices to care for patients in transition to adult care. His training in both adult and pediatrics gives him a unique perspective to help these patients and to serve as a resource for other rheumatologists.

The dual adult/pediatric rheumatologist can also fill a valuable role in serving areas that aren’t heavily populated enough to support a pediatric rheumatologist. Fewer than 300 pediatric rheumatologists are practicing in the U.S. Several states — and 20 percent of medical schools — don’t have access to that specialized expertise in their academic medical centers. An adult/pediatric rheumatologist can train medical students to diagnose pediatric rheumatologic conditions early in their young patients so they can benefit from quick referral and treatment. In addition, the dual specialist can provide access to the highest level of care for both children and adults.

With about 100 medical programs now offering dual residencies in pediatric and internal medicine, the candidate pool for combined pediatric/adult fellowships is growing.

**Continuing Medical Education Annual Conference:**

**Clinical Applications of Musculoskeletal Ultrasound**

Hareth Madhoun, DO will lead this two-day, intensive workshop in summer of 2015 featuring experts in musculoskeletal ultrasound from academic medical centers across the country, who will review ultrasound scanning techniques, normal extremity anatomy and common pathology in inflammatory arthritis. More than 10 hours of hands-on training in small groups include learning ultrasound-guided injections on cadavers; understanding and incorporating the role and use of musculoskeletal ultrasound in the care of patients with inflammatory arthritis; and recognizing on ultrasound common pathology of the musculoskeletal system.

Registration will open in early 2015. For information or to register, please visit cme.osu.edu or contact mikelle.powers@osumc.edu. You can also visit our website at internalmedicine.osu.edu/rheumatology.
A selection of journal articles from the impressive list of publications authored or co-authored by our faculty:


Mavrogeni S, Dimitroulas T, Buccarrell-Ducci C, Ardoir SP, Sfikakis PP, Kolovou G, Kitas GD. Rheumatoid Arthritis: an Autoimmune Disease with Female Preponderance and Cardiovascular Risk Equivalent to Diabetes Mellitus: Role of Cardiovascular Magnetic Resonance. *Inflamm Allergy Drug Targets.* 2014 May; 13(2): 81-93


