NYU Langone Health

Rheumatology

2019 HIGHLIGHTS

Gut Microbiome Forecasts RA Drug Responses

Utilizing individual microbial signatures

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Minimizing Risk of Eye-Damaging Toxicity

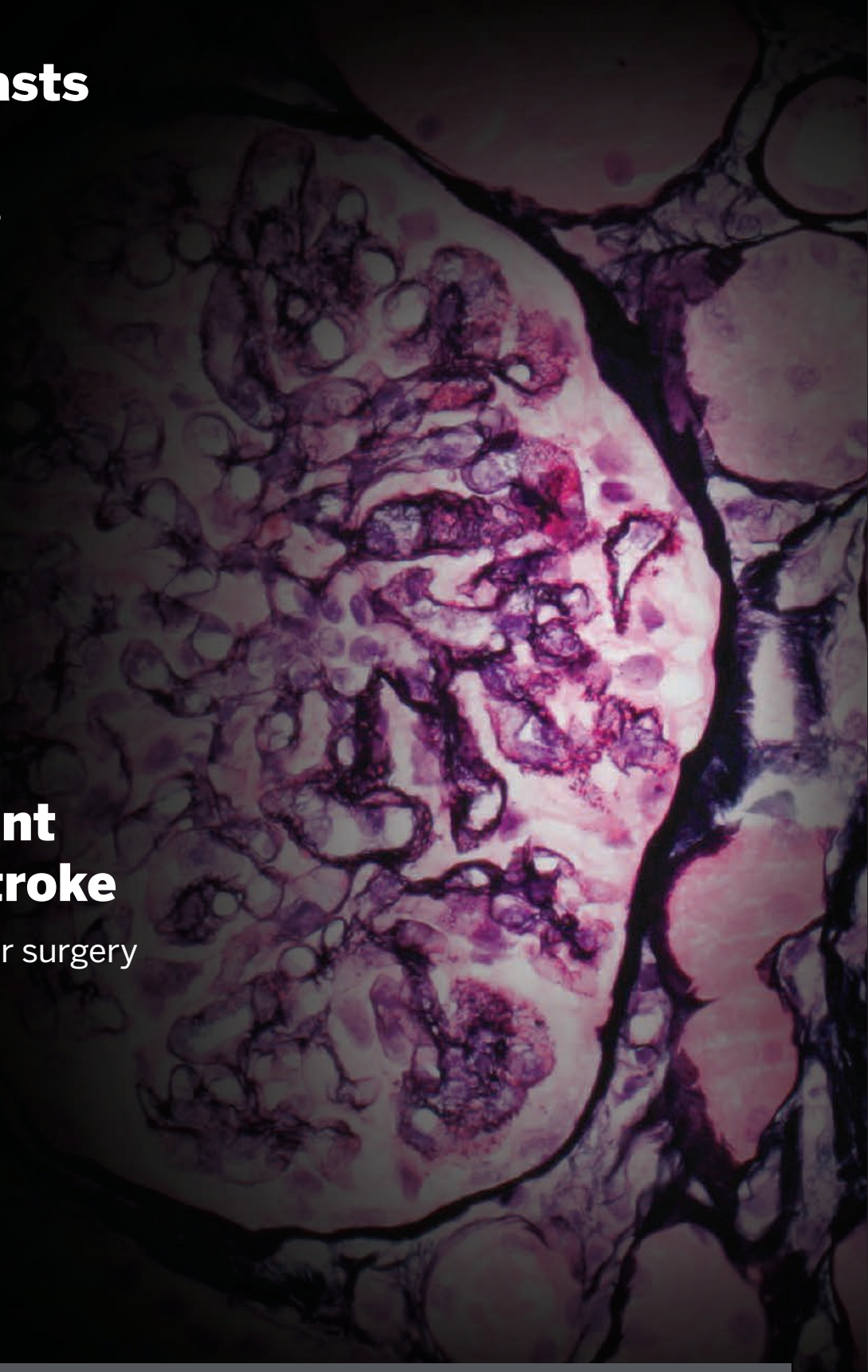
Withdrawing hydroxychloroquine in elderly lupus patients

→ page 3

Novel Solution for Antiphospholipid Patient Following Left-Brain Stroke

Anticoagulation therapy averts need for surgery

→ page 6

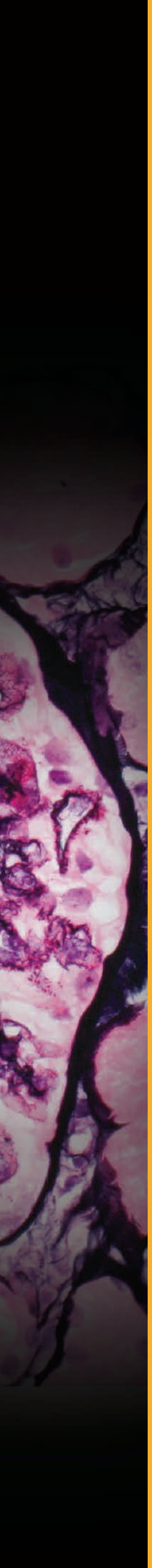


3,500+
Outpatient visits monthly

#8 in the Nation
In *U.S. News & World Report*

100+
Faculty members

61
Accepted ACR abstracts



MESSAGE FROM THE DIRECTOR

JILL P. BUYON, MD

Sir Deryck and Lady Va Maughan Professor of Rheumatology
Director, Division of Rheumatology
Director, Lupus Center

Dear Colleagues,

In 2019, NYU Langone Health's Division of Rheumatology extended our reach both at the bench and bedside, accelerating our progress toward more effective therapeutics and precision medicine, and reaffirming our ability to care for the most complex patients.

We applauded faculty promotions from assistant to full professor and received two new NIH grants, one on RA to identify how gut flora can alter autoimmune disease–targeting medications, and the other to evaluate the safety of withdrawing hydroxychloroquine in elderly patients with SLE. Our full thickness programs in SLE, PsA, RA, OA and Gout continue to thrive. Two newly launched programs, one focused on autoimmune related events following checkpoint inhibitors and the other on autoimmune eye disease, are quickly gaining stride. The merger between NYU Langone and NYU Winthrop Hospital has significantly enlarged our rheumatology footprint across the metropolitan region and bolstered our experience and expertise in conditions such as Sjögren's syndrome.

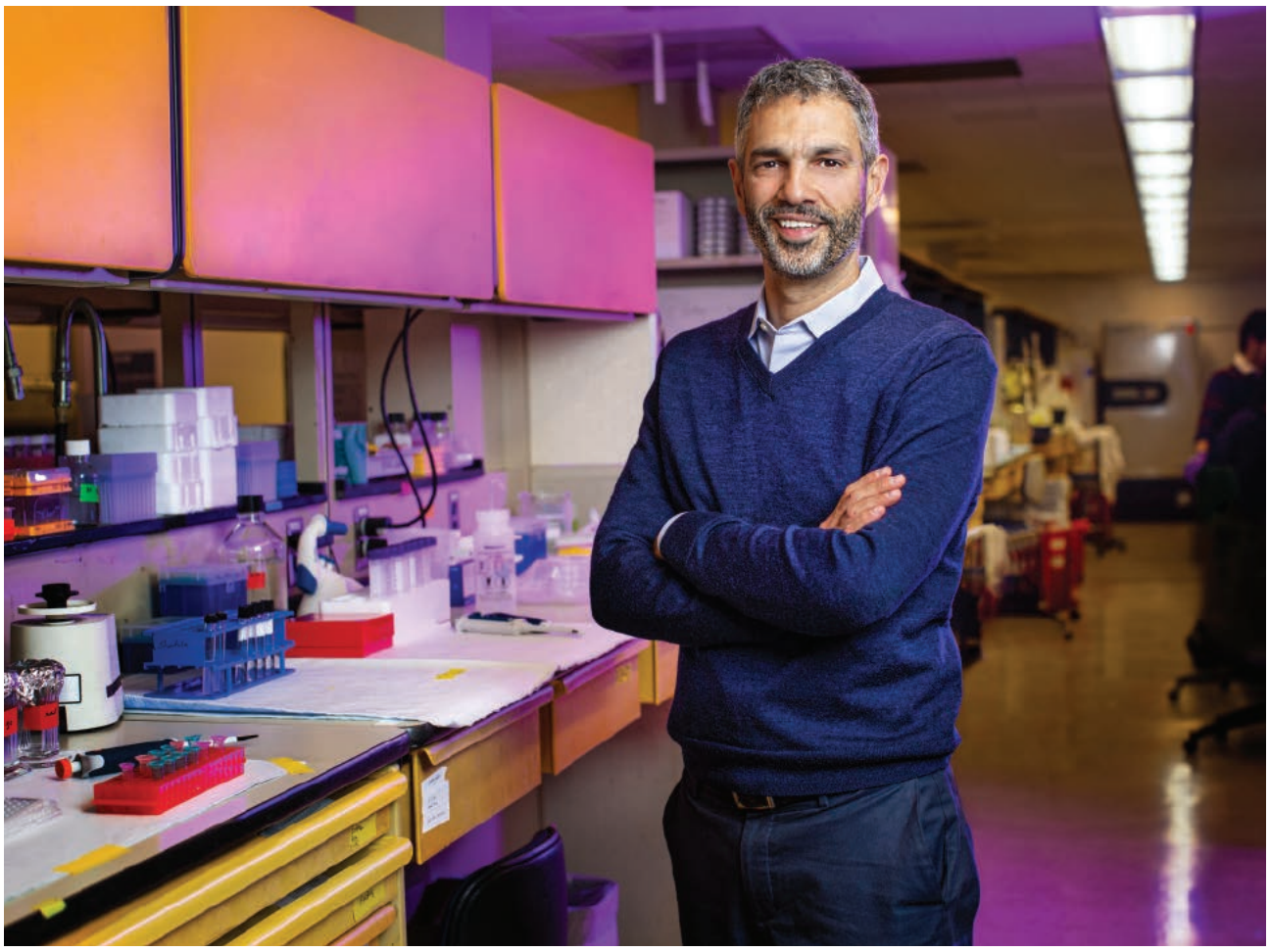
Our continued leadership in research was demonstrated with an unprecedented 20 oral presentations at ACR. In a plenary session, we shared results of a national study showing that hydroxychloroquine can reduce the rate of recurrent congenital heart block from 18 percent (historical rate) to 7.5 percent in fetuses exposed to maternal anti-SSA/Ro antibodies. Once again, we applauded a fellow standing at the podium honored among the nation's best. We welcomed in our new clinical footprint at Winthrop and continued to watch the amazing transformation on our Brooklyn campus. The Colton Center has brought our immunology community closer, together opening new doors for collaboration.

The division has made many contributions to the literature illustrating the reach across a spectrum of diseases. Our researchers have shown that an interleukin 1 receptor antagonist (IL1RN) gene variant predicts the radiographic severity of knee osteoarthritis and the risk of incident disease. Turning to spondyloarthritis, we have shown that IL-17 inhibition associates with subclinical perturbations of the gut microbiome and a distinctive, IL-25-driven type of intestinal inflammation that involves certain bacterial and fungal taxa. Moving from clinically silent autoimmunity to established lupus and severe disease, salivary dysbiosis may provide clues to why some mothers with anti-Ro antibodies remain asymptomatic for years and others progress to lupus. Mothers of children with congenital heart block can now be counseled on risk factors in fetal life such as male sex, black race, and lower fetal heart rates, which influence cardiac morbidity into adulthood. Fortunately, cardiac dysfunction in the first year often normalizes by later childhood.

Importantly, this year will forever be etched in our minds with the loss of Dr. Gerald Weissmann, the director of our Division from 1973 to 2000, and mentor to so many of us. We honored his contributions during an afternoon celebration symposium on December 22. We will always remember the purple pens, the ear cartilage, the puns upon puns, the colored black slides, the challenging questions, and the lasting inspirations.

Taken together, our experience, expertise, and close collaborations have helped us manage complicated diseases, improve patients' quality of life, and lead cutting-edge research. As we begin a new decade, we're better positioned than ever to build upon this legacy of excellence.

Cover image: Glomerulus in a patient with membranous LGN (Jones Silver stain, 400x).
PHOTO: COURTESY OF MING WU, MD, NYU LANGONE PATHOLOGY



Rheumatologist Dr. Jose U. Scher leads teams that study drug responses in rheumatoid arthritis patients, as well as predictions for psoriatic arthritis patients based on their symptom progression.

PHOTO: NYU LANGONE STAFF

Smarter Predictions for Rheumatoid Arthritis Drug Responses

With growing awareness of the gut microbiome's key role in mediating sickness and health, scientists are ramping up investigations of whether the pathogenic mechanisms of certain microbes may trigger rheumatoid arthritis (RA) and other autoimmune diseases. NYU Langone researchers are conducting a related but novel assessment of how gut flora may be altering the efficacy and toxicity of autoimmune disease–targeting medications. Additionally, a study is underway that could ultimately help clinicians predict the psoriasis patients at highest risk for psoriatic arthritis.

BACTERIAL ENZYMES MAY DECREASE METHOTREXATE ABSORPTION

In the first set of studies, a team led by Jose U. Scher, MD, associate professor of medicine and director of the Psoriatic Arthritis Center, is asking whether gut flora–produced enzymes may metabolize oral methotrexate and decrease its intestinal absorption, thereby reducing its effectiveness in RA patients. The question is critical for clinical care, given that methotrexate remains the anchor drug for treating RA. The problem is that more than half of patients with moderate or severe arthritis show either no symptom improvement in response to this medication or, at best, suboptimal improvement.

"What we're seeing is that for some patients, certain genes within the gut flora may predict whether or not they're going to respond to the methotrexate," Dr. Scher says.

Several National Institutes of Health (NIH) grants, including a prestigious new R01 award, are helping the researchers address this critical clinical question. For one set of ex vivo experiments, Dr. Scher's team took gut flora cultures from the baseline fecal samples of new-onset patients whose RA subsequently responded or failed to respond adequately to methotrexate.

When researchers added the cultures to Petri dishes containing the drug, they saw significant variability in the amount of methotrexate that remained in the dish two to three days later. Importantly, Dr. Scher says, "there is a correlation between the methotrexate that disappears, or gets metabolized, and the corresponding patient's response to the drug in the real world."

METABOLISM STUDY AND MACHINE LEARNING IMPLICATE MULTIPLE GENES

Dr. Scher and other researchers hypothesize that when more methotrexate is metabolized in a patient's intestinal lumen, less of it is absorbed and available to help fight the disease. Instead of specific microbes mediating the metabolism, he suspects that similar enzyme-encoding genes from multiple species may be collectively responsible. So far, his research has identified dozens of microbial genes, some of which have been directly implicated in methotrexate metabolism. The role of others remains unknown.

Simultaneously, Dr. Scher and collaborators are feeding clinical phenotypic, metagenomic, metabolomic, and other data into machine learning algorithms. The methods can help generate predictions about which genes and mechanisms are most relevant in driving in vivo drug alterations. Using an algorithm called "random forest," for example, the team identified 39 microbial genes that predict a methotrexate response.

ADVANCING TOWARD MICROBIOME-MEDIATED PRECISION MEDICINE

If supported by further research, Dr. Scher's finding might help advance precision medicine via analysis of individual patients' gut microbiomes: the relative abundance of specific microbial genes might yield a signature that warns rheumatologists that a different therapeutic strategy may be necessary. For patients whose gut flora are more adept at meta-

bolizing methotrexate, doctors might consider administering the drug subcutaneously or switching to a different medication.

Alternatively, ongoing research with collaborators at the University of California, San Francisco, is trying to optimize methotrexate through modification experiments in mice. "If you colonize the mice with different human microbiomes, can you modify them in such a way that they no longer metabolize methotrexate?" Dr. Scher asks. Adding various probiotics or prebiotics, for example, may decrease the efficiency with which a microbiome metabolizes the drug, thereby improving the drug's bioavailability for ameliorating RA symptoms.

Together, these lines of research could eventually lead to markedly improved outcomes for patients whose own gut flora may be thwarting an effective drug response.

For more on this story and other topics, visit
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> *"What we're seeing is that for some patients, certain genes within the gut flora may predict whether or not they're going to respond to the methotrexate."*
>
> **Jose U. Scher, MD**

The heat map shows bacterial gene orthologs from patients with RA that respond to methotrexate (MTX-R), which are different from those found in patients that do not respond (MTX-NR).

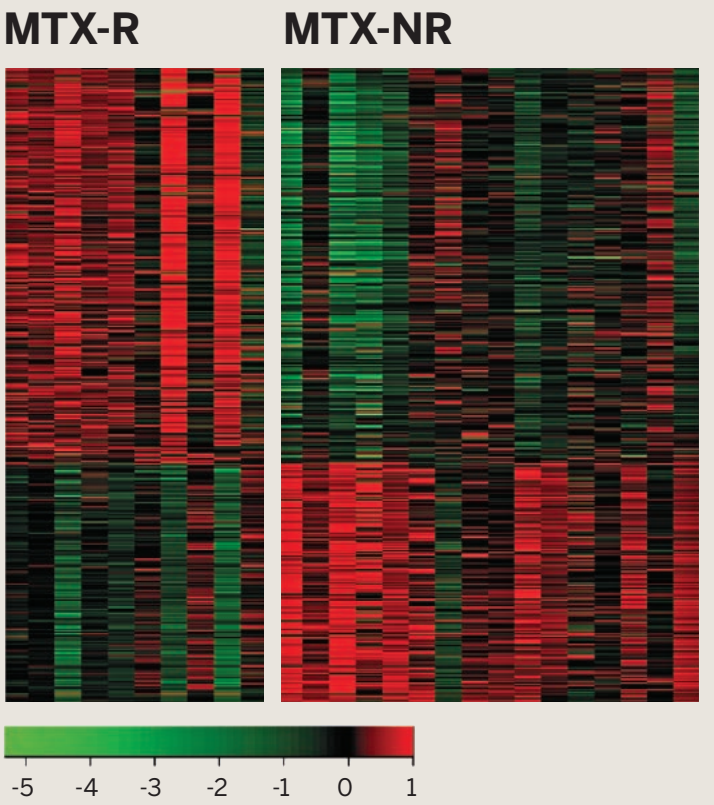


PHOTO: COURTESY OF JOSE U. SCHER, MD

From Psoriasis to Psoriatic Arthritis: Predicting the Progression

Rebecca Haberman, MD
PHOTO: NYU LANGONE STAFF

Nearly one third of patients with psoriasis will develop psoriatic arthritis. As a part of a suite of studies known as Preventing Psoriatic Arthritis, or PreP, Dr. Scher and colleagues have launched two new efforts to better predict disease progression in patients.

In July 2019, the National Psoriasis Foundation awarded Rebecca Haberman, MD, a clinical instructor of medicine, a prestigious early career research grant. Dr. Haberman, also one of NYU Langone's recipients of an NIH T32 training award, is leading a study to compare four patient populations at different stages and risk for psoriatic arthritis development. The goal is to determine the most relevant clinical, genetic, and microbiome-based risk factors of disease progression.

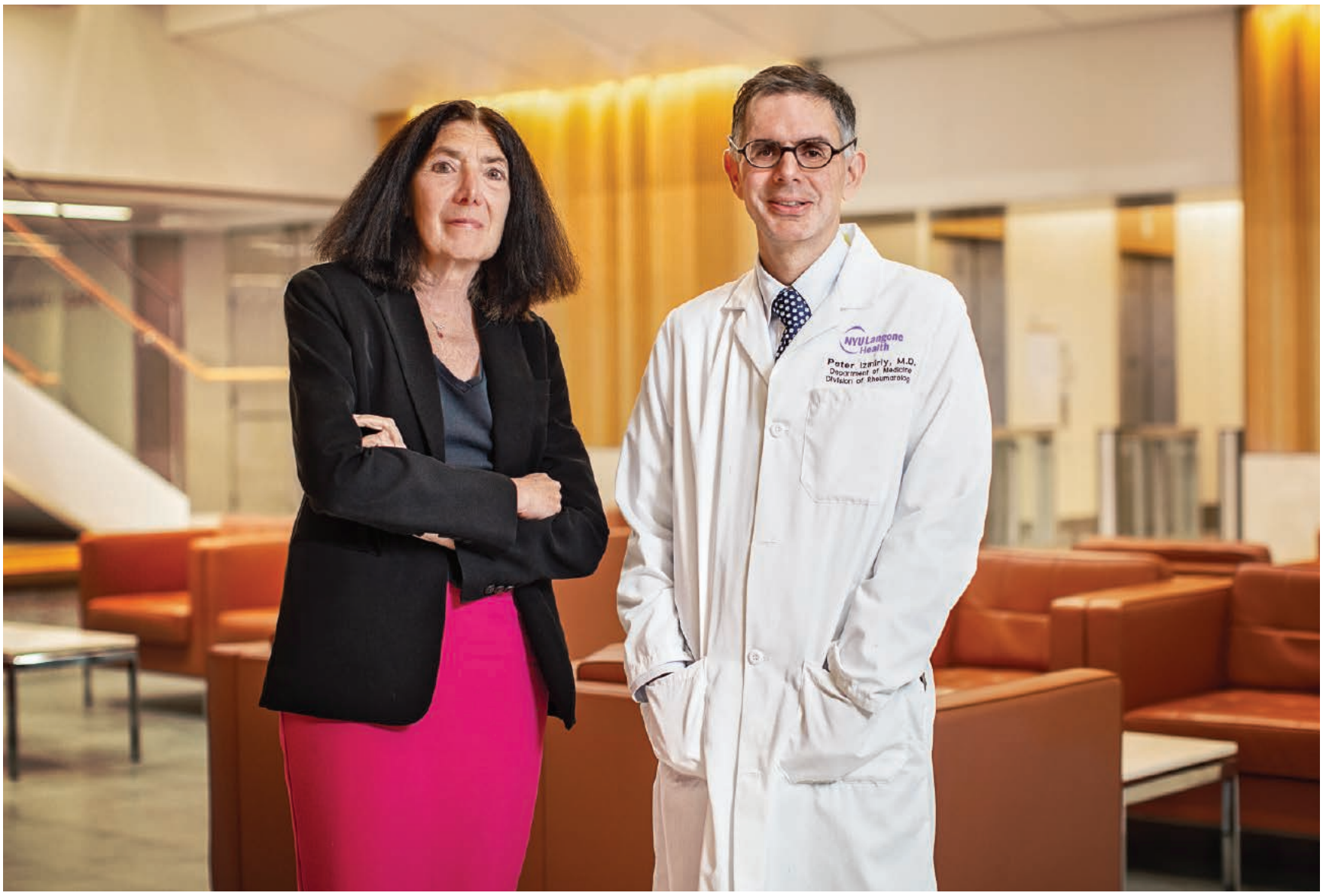
Dr. Haberman's aim is a predictive model that could help clinicians and scientists accurately assess the risk of psoriatic arthritis development in psoriasis patients. In turn, the work could accelerate early diagnoses and inform preventive clinical trials by identifying the patients at highest risk.

SPOTTING PSORIATIC ARTHRITIS SYMPTOMS WITH A SMARTPHONE APP

A separate multicenter collaboration called the Psorcast Study is aimed at developing digital biomarkers of psoriatic arthritis based on smartphone sensors. "Essentially, the study is asking how we can obtain data that is passively captured through gyroscopes and accelerometers that live in our smartphones," Dr. Scher says.

The researchers are asking psoriasis patients to pay attention to digital markers that may highlight telltale symptoms and provide a personalized forecast of psoriatic arthritis risk. For this proof-of-concept study, patients use a phone app to assess their joint function via gyroscope and accelerometer data, take photos of joint swelling and psoriasis plaques, and record other patient-reported outcomes.

The study, done in collaboration with Psoriasis and Psoriatic Arthritis Clinics Multicenter Advancement Network (PPACMAN) and Sage Bionetworks, could lead to an open-source repository of patient-captured data for future research and eventually to a multifaceted diagnostic test with the promise of detecting the earliest signs of disease.



Rheumatologists Dr. Jill P. Buyon and Dr. Peter M. Izmirly have teamed up to study the risks and benefits of hydroxychloroquine withdrawal in older patients with stable lupus.

PHOTO: NYU LANGONE STAFF

New Study Assesses Whether Hydroxychloroquine Withdrawal in Older Lupus Patients Can Preserve Benefits While Minimizing Risks

A new line of research led by scientists at NYU Langone Health is investigating whether it is safe to withdraw hydroxychloroquine (prescribed as Plaquenil®) therapy in older lupus patients with stable or quiescent disease, since the drug is associated with ocular toxicity over time.

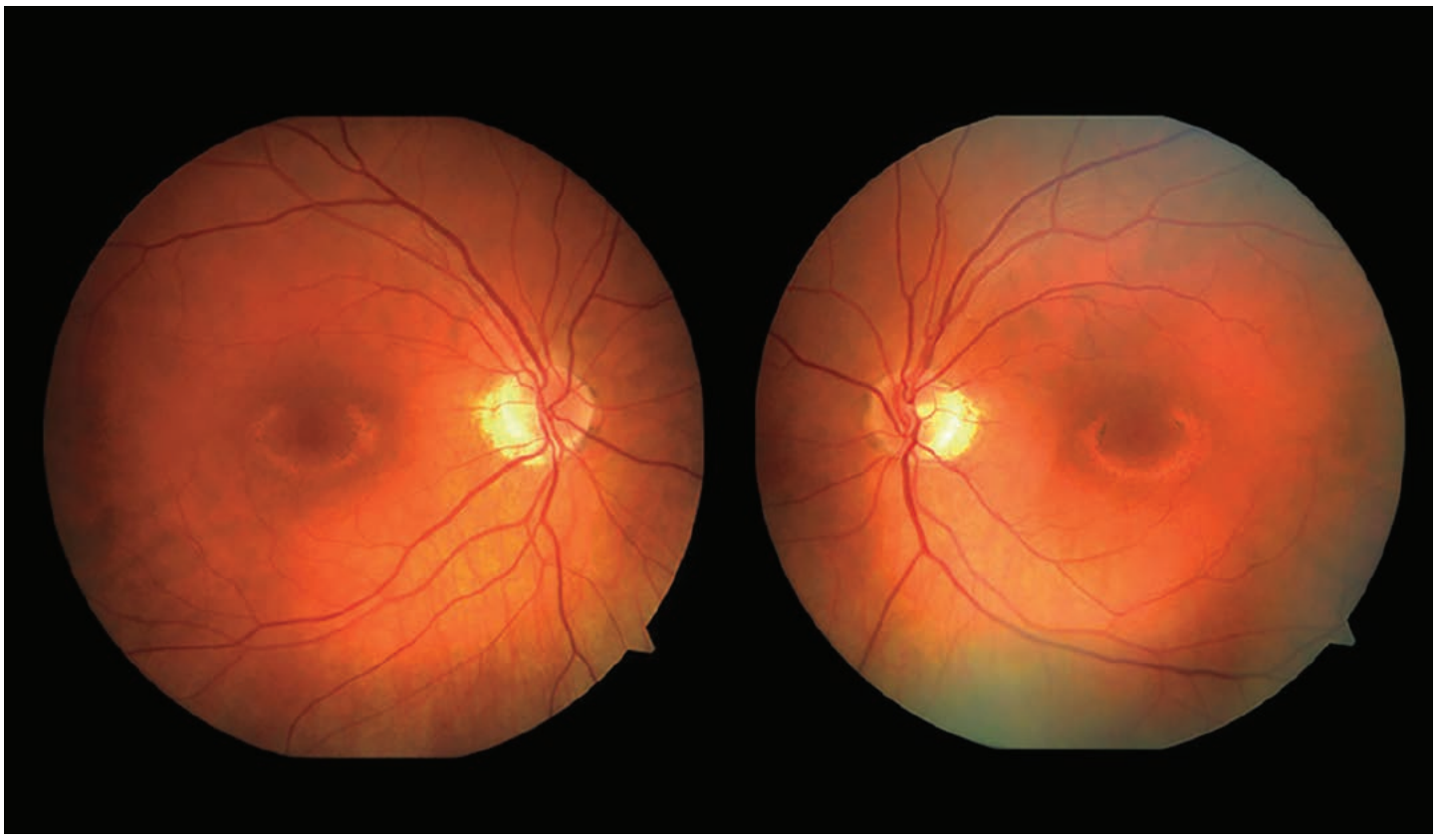
A GROWING FOCUS ON LONG-TERM SAFETY CONCERNS

Hydroxychloroquine (HCQ) is considered the mainstay of systemic lupus erythematosus (SLE) treatments. Studies have suggested that HCQ can prevent or forestall organ damage such as kidney involvement, possibly have beneficial cardiovascular effects, and maybe even lower mortality rates. Among older SLE patients, however, accumulating evidence has fueled concern over the risk of ocular toxicity that can lead to blindness if not addressed. A drug withdrawal study is one of the best ways to evaluate how beneficial a drug really is and whether its continued use is warranted, says Jill Buyon, MD, the Sir Deryck and Lady Va Maughan Professor of Rheumatology and director of the Division of Rheumatology.

"There are virtually no studies that have looked at this population of older lupus patients," Dr. Buyon says. "Knowledge is power, and as we achieve our goal of having patients live longer, we must now consider the potential toxicities of medications in aging populations."

Research on other immunosuppressive drugs, like those for rheumatoid arthritis, suggests that toxicities can indeed build up over time.

"Although traditionally thought to be a relatively safe medication, HCQ has been shown to have an ophthalmologic toxicity," says Peter Izmirly, MD, associate professor of medicine. At first, doctors thought the toxicity was



Retinal examination shows a bull's-eye pattern of hypopigmentation in both the right and left eye.

PHOTO: COURTESY OF YASHA S. MODI, MD, NYU LANGONE OPHTHALMOLOGY

relatively rare and of concern mainly in patients taking the medication on a long-term basis, he says, but more sensitive testing has suggested that the risk is much higher than previously thought. Evidence of increased cardiomyopathy risk has begun to accrue as well, though the rate remains unknown for patients on HCQ therapy.

RETROSPECTIVE STUDY SUGGESTS HCQ WITHDRAWAL IS SAFE IN OLDER PATIENTS

After encountering both eye and heart toxicities in patients, Dr. Izmirly says, "I began to wonder if maybe the benefits of the drug that we see in younger, more active lupus patients aren't there as much in older quiescent patients." Multiple discussions with Dr. Buyon ensued, and the researchers teamed up to study the risks and benefits of HCQ withdrawal in older patients with stable disease.

In an initial retrospective study, the researchers assessed the outcomes of 27 lupus patients who had been on HCQ for at least five years before discontinuing it for a variety of reasons. The patients were at least 55 years old at the point of withdrawal, and nearly half stopped taking the drug after developing maculopathy.

Compared to a control group of 39 patients who remained on HCQ and were matched for age, gender, and race/ethnicity, the researchers showed that stopping the drug had no effect on the risk of moderate or severe lupus flares within one year of withdrawal. "These data suggested that it was relatively safe to withdraw the medication in this stable older population," Dr. Izmirly says.

LARGE PROSPECTIVE STUDY PLANNED TO FURTHER ASSESS HCQ SAFETY

With the aid of an NIH planning grant, the researchers hope to expand their safety assessment through a prospective, multi-center trial that will enroll about 330 patients who are at least 60 years old. "We will take older, non-active lupus patients and randomize half to stop the medication and the other half to continue the medication," Dr. Izmirly says. "We will follow them for a year and see if this older population has any increased risk of flares."

Both Dr. Izmirly and Dr. Buyon caution that they wouldn't stop prescribing HCQ in young patients with active lupus unless forced to do so due to significant side effects. "But in older patients who've been on it for a long time, maybe the risk-benefit ratio is tilting more toward the risk than we previously thought," Dr. Izmirly says. By carefully following patients after HCQ withdrawal, the team can begin to address that question.

"Accordingly, we're addressing a very timely and critical consideration that is increasingly facing clinicians caring for older adults with SLE: can HCQ be safely withdrawn?" Dr. Buyon says. "This question has even more relevance given the minimal attention that has been focused on managing SLE in the aging patient population. Just as physicians are seeking new therapies in an ever-expanding landscape of biologics, we see the need to adjust medications and address withdrawal as critical components of patient care."

> *"Knowledge is power, and as we achieve our goal of having patients live longer, we must now consider the potential toxicities of medications in aging populations."*
>
> **Jill P. Buyon, MD**

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Expanded Footprint Offers Broader Opportunities Across Patient Care, Research, and Education

The 2019 merger between NYU Langone and NYU Winthrop Hospital in Mineola, New York, is yielding a significantly expanded rheumatology presence in clinical research, patient care, and medical education across the New York metropolitan region.

CLINICAL TRIAL POINTS TOWARD FIRST-EVER SJÖGREN'S SYNDROME THERAPY

One new research initiative is aimed at addressing the lack of therapeutic options for Sjögren's syndrome. "There's a tremendous unmet need for a definitive therapy for the disease," says Steven E. Carsons, MD, chief of NYU Winthrop Hospital's Division of Rheumatology, Allergy, and Immunology. "Practically all of the current successful biologics in rheumatic diseases have been tried in Sjögren's and have failed."

As part of its clinical research portfolio, NYU Winthrop Hospital is participating in an exciting multicenter trial evaluating the CD-40 antibody, recently named iscalimab, in treating Sjögren's syndrome. Preliminary data suggest that iscalimab has a beneficial effect on systemic manifestations of the disease. Based on the European Sjögren's syndrome disease activity index (ESSDAI), treatment with the antibody resulted in a mean reduction of 5.2 ESSDAI units over 24 weeks. "If the results hold up, this could represent the first biologic therapy ever approved for the disease," Dr. Carsons says.

Based on promising results from the phase II study, researchers are expanding the trial's patient cohort, and NYU Winthrop Hospital is actively seeking more patient referrals from across the New York region for potential enrollment.

NYU WINTHROP HOSPITAL LAUNCHES WOMEN'S HEALTH IN AUTOIMMUNITY PROGRAM

NYU Langone's Manhattan and Mineola locations have further strengthened their research and clinical ties through the recruitment of Julie Nusbaum, MD, clinical assistant professor of medicine and a former research fellow at NYU Langone. In her new role, Dr. Nusbaum is building a special Women's Health in Autoimmunity Program.

During her three-year research fellowship at NYU Langone, Dr. Nusbaum collaborated with the Department of Population Health in studying the health of women with lupus. At NYU Winthrop Hospital, she is continuing that collaboration while forging new partnerships with the NYU Winthrop Hospital Research Institute and NYU Winthrop Hospital's Division of Maternal–Fetal Medicine.

"We see an unmet need to reach out, identify, and proactively manage women patients with all forms of autoimmune disease," Dr. Carsons says. Lupus is among the most prominent, and the new program will help women manage their health risks during conception and child bearing, as well as their maternal health during pregnancy.

NYU LONG ISLAND SCHOOL OF MEDICINE WELCOMES FIRST CLASS

In a major expansion of NYU Langone's educational mission, the Division of Rheumatology, Allergy, and Immunology at NYU Winthrop Hospital is also playing a key role at NYU Long Island School of Medicine, where Dr. Carsons is serving as senior associate dean for translational science integration. The unique school, which offers full-tuition scholarships, welcomed its first class of 24 students in July 2019.

"The school is designed to be an accelerated three-year program aimed at producing primary care physicians who hopefully will stay in the health system and increase the primary care presence both on Long Island and throughout the region," Dr. Carsons says. As a stand-alone three-year program with an integrated curriculum emphasizing primary care, he adds, the school represents an exciting new model for medical education in the United States.

The curriculum, with a year of preclinical sciences and two years of clinical rotations, is focusing on internal and community medicine, pediatrics, and obstetrics and gynecology, as well as general surgery. Given that proficiency in musculoskeletal medicine is of paramount importance for primary care physicians, the Division of Rheumatology, Allergy, and Immunology developed an integrated five-week block on musculoskeletal medicine, rheumatology, and dermatology. Elise Belilos, MD, clinical assistant professor of medicine, is serving as the course director.

Dr. Steven E. Carsons leads research and education initiatives for Rheumatology at NYU Winthrop.

PHOTO: NYU LANGONE STAFF

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Partnering closely with experts at NYU Langone, Dr. H. Michael Belmont used a novel approach to treat a stroke patient with antiphospholipid syndrome.

PHOTO: NYU LANGONE STAFF

Anticoagulation Therapy Averts Valve Surgery for Antiphospholipid Syndrome Patient After Stroke

NYU Langone clinicians utilized expertise and knowledge of the medical literature to avoid surgery and successfully treat a patient with antiphospholipid syndrome, whose left-brain stroke had been triggered by a large thrombotic valvular vegetation.

INFORMED TESTING REVEALS A DIAGNOSIS OF NONBACTERIAL THROMBOTIC ENDOCARDITIS

A 36-year-old man living in New York City who had been previously diagnosed with primary antiphospholipid syndrome (PAPS) and rejected first-line treatment with warfarin was treated with rivaroxaban due to personal preference. His medical history included a prior deep vein thrombosis as well as hypertension and asthma. The patient presented to the Ronald O. Perelman Center for Emergency Services, located within NYU Langone's Tisch Hospital, with a left-brain stroke characterized by aphasia in March 2018. A brain MRI revealed evidence of multiple cerebral emboli and a transthoracic echocardiogram demonstrated a large, 2.7-centimeter vegetation on his aortic valve.

H. Michael Belmont, MD, professor of medicine and co-director of NYU Langone's Lupus Center, says several aspects of the case influenced how the medical team responded. Test results revealed a triple positive antiphospholipid (aPL) antibody profile, which is associated with a high risk for arterial and venous thrombotic antiphospholipid syndrome (APS) as well as non-criteria manifestations of APS, which includes cardiac valvulopathy. Dr. Belmont notes that the lupus anticoagulant (LAC) test result could have been a false positive given the patient's use of rivaroxaban, a Factor Xa inhibitor, at the time of the test. Assay for antiphosphatidylserine-prothrombin can be useful in this circumstance as the presence of this aPL associates with a true LAC but is insensitive to anticoagulation.

Based on the patient's negative blood cultures and lack of fever or leukocytosis, as well as prior PAPS, Dr. Belmont made a clinical diagnosis of nonbacterial thrombotic endocarditis or marantic endocarditis.

ANALYSIS OF VALVULAR VEGETATION POINTS TO HEPARIN THERAPY IN LIEU OF SURGERY

The existing medical literature, relying principally on acute or chronic bacterial endocarditis, argues that a vegetation in excess of one centimeter, with evidence of clinical embolization, should be surgically managed with a thrombectomy or aortic valve replacement. However, based on

NIH Grants Awarded in 2019

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

Identifying how gut flora can be employed to predict response to autoimmune disease-targeting medications

Grant Recipient:
Jose Scher, MD: R01

Funded by:
National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS)

Withdrawal of Hydroxychloroquine in Elderly Lupus Patients

Evaluating the safety of withdrawing hydroxychloroquine in elderly patients with SLE

Grant Recipients:
Jill Buyon, MD, and Peter Izmirly, MD (mPIs): R34

Funded by:
National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS)

New Programs Launched in 2019 Include:

Immunotoxicity Program

Focusing on autoimmune-related events following checkpoint inhibitors

Behçet's Syndrome & Autoimmune Eye Diseases Program

Focusing on autoimmune eye diseases

Selected Publications

Attur M, Zhou H, Samuels J, Krasnokutsky S, Yau M, Scher JU, Doherty M, Wilson AG, Bencardino J, Hochberg M, Jordan JM, Mitchell B, Kraus VB, Abramson SB. Interleukin 1 receptor antagonist (IL1RN) gene variants predict radiographic severity of knee osteoarthritis and risk of incident disease. *Annals of the Rheumatic Diseases*. December 18, 2019; epub ahead of print.

Azzouz D, Omarbekova A, Heguy A, Schwudke D, Gisch N, Rovin BH, Caricchio R, Buyon JP, Alekseyenko AV, Silverman, GJ. Lupus nephritis is linked to disease-activity associated expansions and immunity to a gut commensal. *Annals of the Rheumatic Diseases*. July 2019; 78: 947–956.

Der E, Suryawanshi H, Morozov P, Kustagi M, Goilav B, Ranabathou S, Izmirly P, Clancy R, Belmont HM, Koenigsberg M, Mokrzycki M, Rominieki H, Graham JA, Rocca JP, Bornkamp N, Jordan N, Schulte E, Wu M, Pullman J, Slowikowski K, Raychaudhuri S, Guthridge J, James J, Buyon JP, Tuschl T, Putterman C. Tubular cell and keratinocyte singlecell transcriptomics applied to lupus nephritis reveal type I IFN and fibrosis relevant pathways. *Nature Immunology*. July 2019; 20: 915–927.

Clancy RM, Marion MC, Ainsworth HC, Blaser MJ, Chang M, Howard TD, Izmirly PM, Lacher C, Masson M, Robins K, Buyon JP, Langefeld CD. Salivary dysbiosis and the clinical spectrum in anti-Ro positive mothers of children with neonatal lupus. *Journal of Autoimmunity*. October 31, 2019; epub ahead of print.

Ghodke-Puranik Y, Imgruet M, Dorschner JM, Shrestha P, McCoy K, Kelly JA, Marion M, Guthridge JM, Langefeld CD, Harley JB, James JA, Sivils KL, Niewold TB. Novel genetic associations with interferon in systemic lupus erythematosus identified by replication and fine-mapping of trait-stratified genome-wide screen. *Cytokine*. January 23, 2019; pii: S1043–4666(19)30002-X.

Izmirly PM, Buyon JP, Wan I, Belmont HM, Sahl S, Salmon JE, Askanase A, Bathon JM, Geraldino-Pardilla L, Ali Y, Ginzler EM, Putterman C, Gordon C, Helmick CG, Parton H. The incidence and prevalence of adult primary Sjögren's syndrome in New York county. *Arthritis Care & Research*. July 7, 2019; 71(7): 949–960.

Manasson J, Wallach DS, Guggino G, Stapylton M, Badri MH, Solomon G, Reddy SM, Coras R, Aksenov AA, Jones DR, Girija PV, Neimann AL, Heguy A, Segal LN, Dorrestein PC, Bonneau R, Guma M, Ciccia F, Ubeda C, Clemente JC, Scher JU. IL-17 Inhibition in spondyloarthritis associates with subclinical gut microbiome perturbations and a distinctive IL-25-driven intestinal inflammation. *Arthritis & Rheumatology*. November 14, 2019; epub ahead of print.

Saxena A, Izmirly PM, Bomar RP, Golpanian RS, Friedman DM, Eisenberg R, Kim MY, Buyon JP. Factors associated with long-term cardiac dysfunction in neonatal lupus. *Annals of the Rheumatic Diseases*. 2020; 79: 217–224.

Suryawanshi H, Clancy R, Morozov P, Halushka MK, Buyon JP, Tuschl T. Cell atlas of the fetal human heart and implications for autoimmune-mediated congenital heart block. *Cardiovascular Research*. October 7, 2019; epub ahead of print.

Wang S, Pillinger MH, Krasnokutsky S, Barbour KE. The association between asymptomatic hyperuricemia and knee osteoarthritis: data from the third National Health and Nutrition Examination Survey. *Osteoarthritis Cartilage*. September 2019; 27(9):1301–1308.

confidence that the vegetation was neither infectious nor inflammatory, with no clinical or serological systemic lupus erythematosus (SLE) to suggest a Libman-Sacks valvular lesion, the rheumatology team recommended that surgery be deferred and the patient instead be treated with a continuous therapeutic heparin infusion.

That decision not only spared the patient from major cardiovascular surgery but also resulted in a rapid and complete response of his marantic endocarditis. "In a series of 3 echocardiograms over 10 days, the large vegetation completely disappeared," Dr. Belmont says. The patient subsequently agreed to warfarin anticoagulation therapy with a target international normalized ratio (INR) of 3.

For more on this story and other topics, visit
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Bariatric Surgery & Knee Arthroplasty Combine for a Life-Changing Outcome for Morbidly Obese Patient

Careful coordination of bariatric and knee replacement surgeries coupled with continuous rheumatologic care at NYU Langone helped a morbidly obese osteoarthritic patient overcome a worsening pattern of pain, diminished mobility, and decreased quality of life.

CAUGHT IN A VICIOUS CYCLE

In 2010, Jonathan Samuels, MD, associate professor of medicine and recently appointed associate director, clinical initiatives, began treating a morbidly obese 51-year-old woman who had been previously diagnosed with tricompartmental osteoarthritis (OA) in both knees. Since the 2004 onset of pain in her left knee and subsequent involvement of her right knee two years later, the patient faced increasing difficulty walking from the train station to her office during her daily commute to work. Despite Tylenol®, nonsteroidal anti-inflammatory drugs (NSAIDs), physical therapy, and injections into the joints with corticosteroids or hyaluronic acid viscosupplementation, the growing pain eventually forced her to use a cane to walk.

By 2010, the patient couldn't walk two blocks at a time and had considerable difficulty climbing stairs. "She was struggling," says Dr. Samuels. "You could see her progression from having trouble walking fully on her own from the subway, to needing a cane, to at times needing painkillers and narcotics because the pain was so bad."

X-rays taken in 2011 revealed a worsening of the tricompartmental OA that was particularly prominent in the patient's left knee, with a significant loss of the joint space and near bone-on-bone contact of the left medial femoral condyle and medial tibial plateau. She had no viable medication options other than pain control with anti-inflammatories and narcotics.

Unfortunately, with a body mass index (BMI) that exceeded 45, the patient was a poor candidate for knee replacement surgery since a BMI above 40 increases risk for postoperative infections and additional complications. Because the patient was obese, she was caught in a spiral in which she had increased pain, trouble exercising, resultant weakening of her muscles, and ultimately, further weight gain.

The natural progression of OA cannot be stopped once it has begun to develop since there are no proven disease-modifying drugs. This is in contrast to the biologics and other immunosuppressives that revolutionized the treatment of rheumatoid arthritis and psoriatic arthritis 20 years ago. Cutting-edge research on halting OA progression centers on the interleukin-1 pathway, which has been a key focus of the lab of Steven B. Abramson, MD, the Frederick H. King Professor of Internal Medicine and chair of medicine at NYU Langone. In collaboration with Dr. Samuels and other researchers, Dr. Abramson's recent publication in *Annals of the Rheumatic Diseases* describes how the IL1RN TTG haplotype, a cluster set of variations of the IL1RN gene, which encodes for the interleukin-1 receptor antagonist, predicted radiographic severity of knee OA and risk of incident disease. Even if this haplotype proves to be a viable molecular target, however, it could still take many years for successful drug development and validation in the OA clinic.

Dr. Jonathan Samuels utilizes ultrasound imaging technology in treatment of patients with osteoarthritis.

PHOTO: NYU LANGONE STAFF

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Referenced Publications

Attur M, Zhou H, Samuels J, Krasnokutsky S, Yau M, Scher JU, Doherty M, Wilson AG, Bencardino J, Hochberg M, Jordan JM, Mitchell B, Kraus VB, Abramson SB. Interleukin 1 receptor antagonist (IL1RN) gene variants predict radiographic severity of knee osteoarthritis and risk of incident disease. *Annals of the Rheumatic Diseases*. December 18, 2019; epub ahead of print.

Ordi-Ros J, Sáez-Comet L, Pérez-Conesa M, Vidal X, Riera-Mestre A, Castro-Salomó A, Cuquet-Pedragosa J, Ortiz-Santamaria V, Mauri-Plana M, Solé C, Cortés-Hernández J. Rivaroxaban versus vitamin K antagonist in antiphospholipid syndrome: a randomized noninferiority trial. *Annals of Internal Medicine*. October 15, 2019; epub ahead of print.

Pengo V, Denas G, Zoppellaro G, Jose SP, Hoxha A, Ruffatti A, Andreoli L, Tincani A, Cenci C, Prisco D, Fierro T, Gresele P, Cafolla A, De Micheli V, Ghirarduzzi A, Tosetto A, Falanga A, Martinelli I, Testa S, Barcellona D, Gerosa M, Banzato A. Rivaroxaban versus warfarin in high-risk patients with antiphospholipid syndrome. *Blood*. September 27, 2018; 132(13): 1365–1371.

Wainwright B, Bahn R, Trad C, Cohen R, Saxena A, Buyon J, Izmirly P. Autoimmune-mediated congenital heart block. *Best Practice & Research Clinical Obstetrics & Gynaecology*. October 8, 2019; epub ahead of print.

Awards & Recognition

Ashira Blazer, MD, Rheumatology Research Foundation (RRF) Bridge Funding Award

Rebecca Haberman, MD, National Psoriasis Foundation Early Career Research Grant

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Jose Scher, MD, and Sergei Koralov, PhD (MPIs), National Psoriasis Foundation 2019 PsA Diagnostic Test Grant

Jill Buyon, MD, and Peter Izmirly, MD (MPIs), R34, National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS)

Jose Scher, MD, R01, National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS)

Ashira Blazer, MD, R01, Diversity Supplement, National Heart, Lung, and Blood Institute (NHLBI)

Julia Manasson, MD, Rheumatology Research Foundation (RRF) Investigator Award

Bruce N. Cronstein, MD, 2019 American College of Rheumatology Distinguished Basic Science Investigator Award

Rebecca Haberman, MD, 2019 American College of Rheumatology Distinguished Fellow Award

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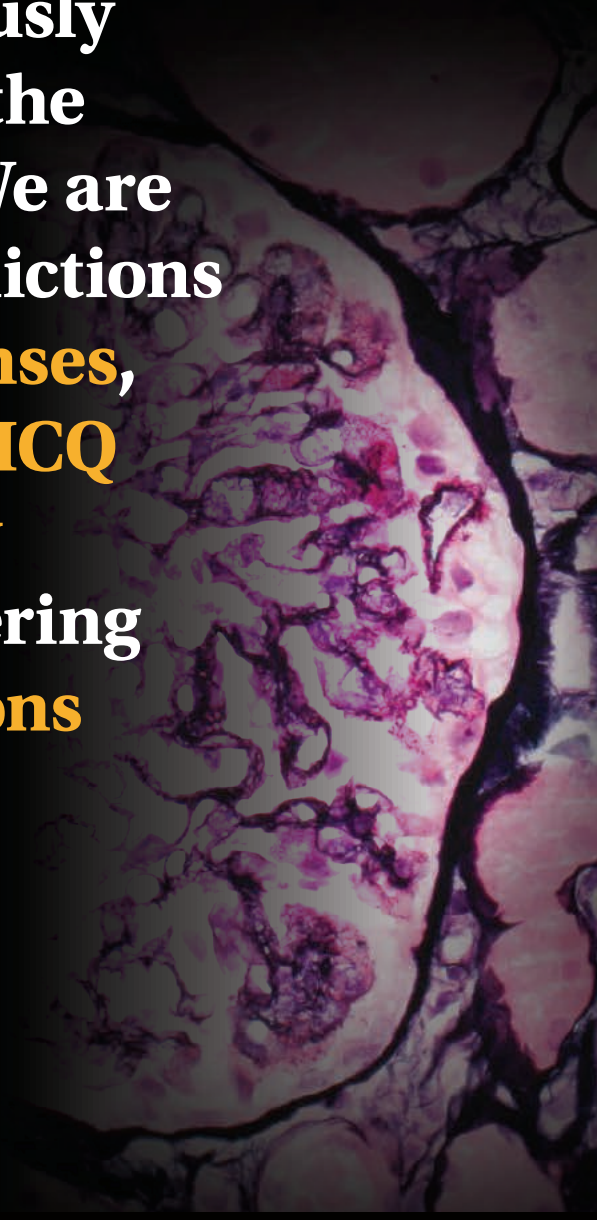

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