WINTER 2019

Arthritis Progress Report

News from the Russell/ Engleman Rheumatology Research Center

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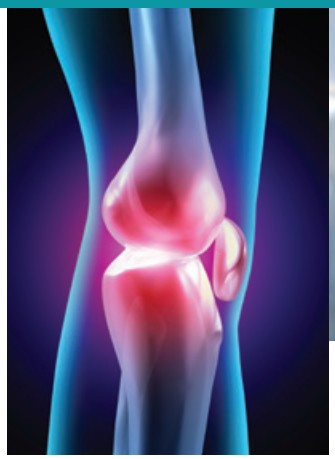

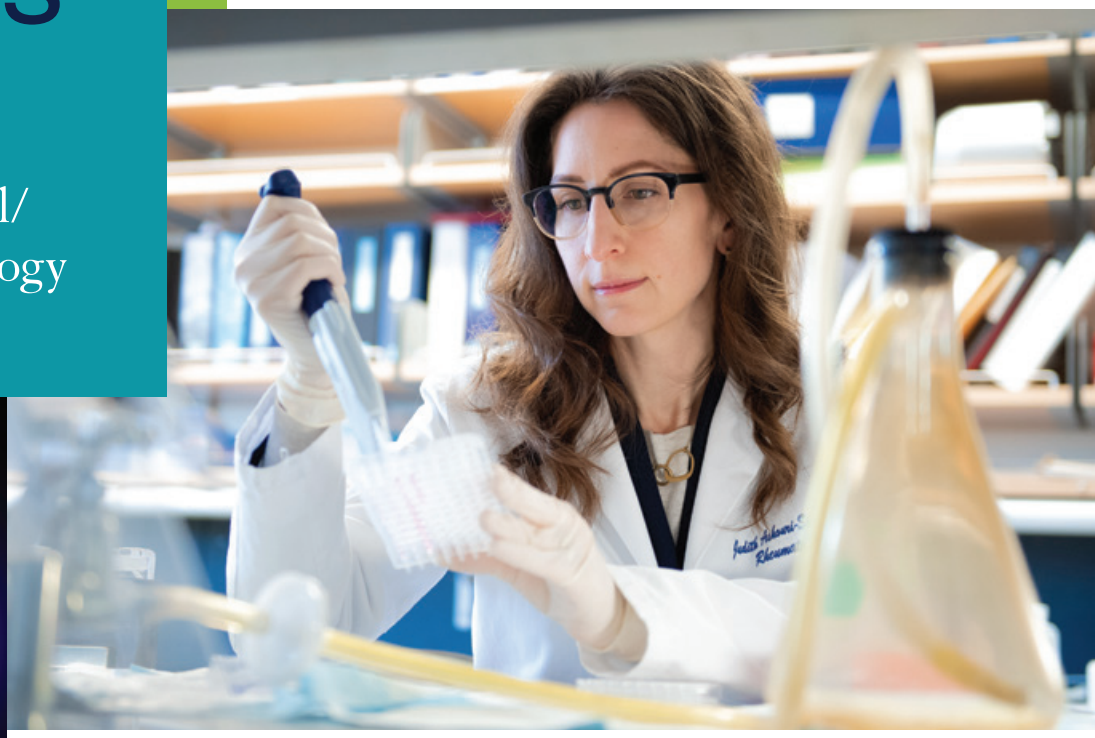

Judith Ashouri-Sinha, MD, works to find a breakthrough cure for rheumatoid arthritis.

Racing Toward a Cure for Rheumatoid Arthritis

Driven by her patients' concerns and memories of her mother becoming terminally ill from complications related to her advanced rheumatoid arthritis (RA), physician-scientist Judith Ashouri-Sinha, MD, is building a powerful research program aimed at unearthing a breakthrough cure for RA.

Ashouri-Sinha's work has already yielded important new knowledge. Now – by leveraging UCSF's emerging strategic research initiatives, cutting-edge technology and cross-disciplinary approach – her research is poised to accelerate and expand its contribution to a precision medicine approach for RA.

Why the Science Matters

RA is an autoimmune disorder that afflicts millions of people worldwide. It occurs when the body's immune system mistakenly attacks the joints, causing deformity, chronic pain and a diminished quality of life. The inflammation and, ironically, some of the treatments associated with RA can also lead to many adverse health outcomes, including kidney, heart and lung disease – and, ultimately, shortened life spans.

Despite RA's prevalence and the suffering it inflicts, scientists do not yet know what causes the disease. While effective therapies have emerged for many RA patients, "Others struggle to get relief because we frequently don't know what therapies work for each patient or because the side effects of existing therapies can be prohibitive," says Ashouri-Sinha, who understands all too well how desperate patients and families are for a cure.

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Also in This Issue

OUR MISSION: To provide outstanding clinical care while advancing the discipline of rheumatology through cutting-edge research and training of the next generation of academic rheumatologists. **https://rheumatology.ucsf.edu**

Message from the Director

Looking to the Future

This year I am celebrating my 40th year on the Rheumatology faculty at UCSF. Those years have taken us through a period of great discovery and progress, from a past when our patients often came to their appointments in wheelchairs, to a present in which our profession has transformed most rheumatologic diseases from disabling to manageable – and often to asymptomatic entirely. It is now becoming realistic to look to a future that will take us beyond successful management to the discovery of cures.

David Wofsy, MD

In this issue of *Arthritis Progress Report,* we focus on two areas of great importance, with pride in a new generation of scientists and leaders in our program. In our cover story, we feature a rising star in rheumatology research, Judith Ashouri-Sinha, MD, who is tackling the critical problem of identifying the molecular mechanisms underlying rheumatoid arthritis with the intent to eventually find a cure. Dr. Ashouri-Sinha represents a group of outstanding young scientists who recently joined our program and about whom you will hear more in future newsletters. This issue also features Professor Jinoos Yazdany, MD, MPH, the new chief of Rheumatology at Priscilla Chan and Mark Zuckerberg San Francisco General Hospital and Trauma Center (ZSFG). Dr. Yazdany was chosen through a national search to succeed the recently retired John Imboden, MD, and she is exceedingly well qualified to lead ZSFG, because of her proven commitment to studying and serving communities that are too often marginalized in the health care system.

My sincere thanks for your interest in our work and for your support.

David Wofsy, MD
Director, Russell/Engleman Rheumatology Research Center

Racing Toward a Cure

Continued from front page

Ashouri-Sinha's research program builds on the knowledge that immune cells, known as CD4 T cells, become activated by proteins through their T-cell receptor to cause RA. The goal is to discover the process that activates these cells to attack the joints, in order to find a therapeutic target that halts the process and minimizes any side effects.

In the lab, she has paired high-throughput, single-cell RNA sequencing with T-cell receptor (TCR) sequencing of both an animal model of arthritis and human synovial (joint) tissue to identify and characterize these activated T cells. She recently found that among the T cells that infiltrate an inflamed joint, a subset is enriched with a protein called Nur77 that marks T cells activated through their TCR (or antigen-activated T cells) as opposed to those activated by the surrounding inflammation. This important finding has given a promising focus to Ashouri-Sinha's efforts to trace the origins of the disease process.

"We are taking advantage of Nur77 to identify antigen-activated T cells and are working backwards to find out which T cells are driving disease and what they are responding to," she says. "I'm optimistic that this knowledge could enable us to identify a therapeutic target capable of efficiently shutting down the dysregulated immune system."

The next phase will get a significant boost from a large National Institutes of Health (NIH) program grant at UCSF and an increasingly efficient UCSF research infrastructure that includes a rich tissue bank, a database of related research and the latest high-throughput sequencing technologies. Moreover, Ashouri-Sinha believes that others can use the RA research platform she is creating to explore the roots of other rheumatologic diseases. "There are a lot of far-reaching implications," she says.

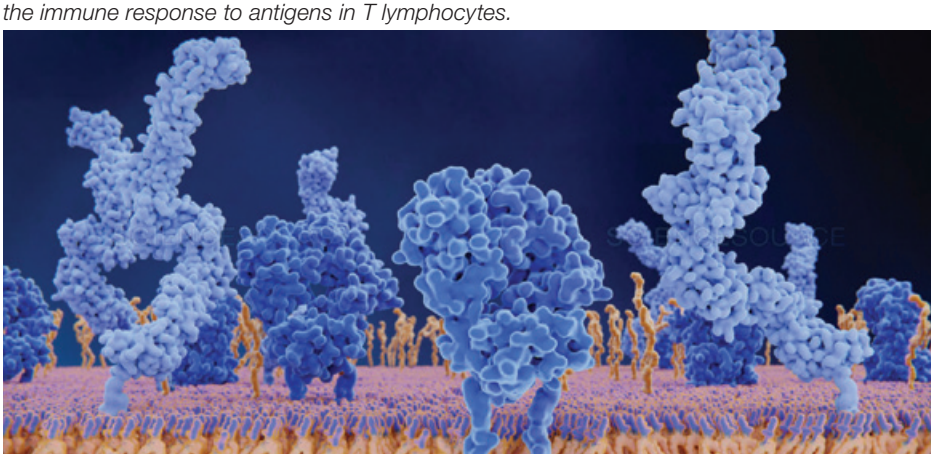
Getting Patients Involved

Because she maintains an active clinical practice, Ashouri-Sinha also identifies unmet clinical needs and research priorities directly from her patients. "For example, many patients ask if there are dietary changes that could help with their disease," she says. Because there is promising yet limited scientific evidence that certain diets can calm immune cells and affect disease progression, Ashouri-Sinha has begun assembling a team of other physician-researchers at UCSF to create a study to examine how diet might enhance existing RA therapies.

"As a referral center, we see many patients who struggle to find a therapy that works for them – and it's devastating," she says. "If we succeed in creating a precision medicine approach for rheumatologic disease, we can not only make existing therapies more effective, but also identify additional promising therapeutic targets to improve outcomes, life expectancy and quality of life for our patients." ■

"This knowledge could enable us to identify a therapeutic target capable of efficiently shutting down the dysregulated immune system." – Judith Ashouri-Sinha, MD

T-cell receptors (dark blue) on CD4 molecules (light blue). The T-cell receptor activates the immune response to antigens in T lymphocytes.



Jinoos Yazdany, MD, MPH

New ZSFG Chief a Boon for Rheumatologic Care

In July 2019, Jinoos Yazdany, MD, MPH, became chief of Rheumatology at Priscilla Chan and Mark Zuckerberg San Francisco General Hospital and Trauma Center (ZSFG). Her appointment recognizes decades of leadership aimed at extending expert rheumatologic care to traditionally underserved and vulnerable populations.

An integrated program of clinical care, research, service and education at ZSFG reflects her commitment to – and has important implications for – improving the care of *any* individual with a rheumatological disease.

A Family's Challenges Enhance a Specialty

In 1978, Yazdany's scientist parents were completing a sabbatical at UCLA when the Iranian revolution broke out, essentially stranding the family in the United States. The difficult challenges they would overcome wound up having enormous benefits for individuals with rheumatologic disease.

Raised in Southern California, Yazdany attended Stanford as an undergraduate, medical school at UCLA – during which time she also earned a master's degree in public health from Harvard – and UCSF for her residency and rheumatology fellowship. Witnessing her aunt's years of suffering from rheumatoid arthritis (RA) was an important factor in her choice of specialty.

"Rheumatology also just suits me," says Yazdany. "I love the patients, love the science and love the medical detective aspect of it."

Integrated, Patient-Centered Program Extends, Improves Care

The ZSFG rheumatology clinic sees over 3,000 patients a year, many with the most severe diagnoses, including RA, vasculitis and lupus. ZSFG rheumatologists also train and consult with primary care physicians who treat those with less complicated rheumatologic conditions.

Cultural competency, deep understanding of the social determinants of health and close collaboration with social and behavioral service providers from the San Francisco Department of Public Health characterize all of this care. In addition, ZSFG's quality improvement programs have enhanced care in multiple ways, including dramatically increasing vaccination rates for patients whose medications often require immunosuppression.

"Many have multiple comorbidities and are one paycheck away from homelessness – or don't have any stable housing at all," says Yazdany. "We work hard to help them stay healthy, because a case of pneumonia can ruin their lives."

Research at ZSFG complements the clinical focus on vulnerable populations. "Over the last 20 years, we've been asking hard questions about whether advances we are making as a field benefit the entire population," says Yazdany. Their efforts include the following:

- Studying the impact of language, health literacy and socioeconomic status on treatment and access for patients with RA and lupus.
- Participating in StopRA, the first prevention research study for RA in the U.S. "We are one of the few centers enrolling a patient population that reflects the general population," says Yazdany.
- With colleagues at UCSF Helen Diller Medical Center at Parnassus Heights, participating in a Centers for Disease Control and Prevention (CDC)-funded study that documents, for the first time, the epidemiology and outcomes of lupus.
- Creating the Rheumatology Informatics System for Effectiveness (RISE) Registry with the American College of Rheumatology (ACR) to improve the quality and safety of rheumatologic care and advance research. Yazdany chairs the ACR committee that oversees this effort. She says, "We're seeing steady improvement that has a huge impact on the health of populations."

The research intersects with Yazdany's interest in increasing access to care by bringing rheumatology expertise from academic health centers to the local community. Consider her participation in two programs that exemplify ZSFG's service efforts.

"I love the patients, love the science and love the medical detective aspect of [rheumatology]."

— Jinoos Yazdany, MD, MPH (top photo)

- Volunteers to Expand Rheumatology Access (VERA) is an ACR-led effort to help address a nationwide shortage of rheumatologists by sending volunteer rheumatologists to regions experiencing a shortage.
- ZSFG will serve as a site for Project ECHO (Extension for Community Healthcare Outcomes), a national program that uses webinars, phone advice and case-based training to educate clinicians in areas that lack access to rheumatologists.

Finally, alongside expert clinician educators, rheumatology fellows at ZSFG learn how to treat severe rheumatologic disease using patient-centered care that incorporates an in-depth understanding of how to address the social determinants of health. Those social determinants affect the course of disease for all patients who must navigate a life burdened by rheumatologic disease – not just the most vulnerable.

Yazdany's commitment to these efforts is deeply personal. In addition to her connection to her patients, her 84-year-old father was recently diagnosed with RA. Medical advances enable him to continue with his regular 20-mile bicycle rides. From her new post as chief, Yazdany is well positioned to extend the advances her father benefits from to the many patients she serves. ■

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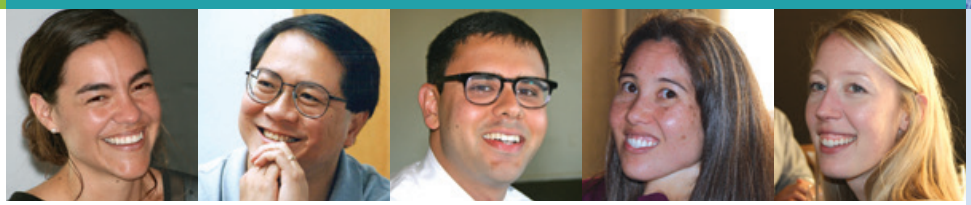

Past UCSF Rheumatology fellows at retreat.

Fellowship Program

Endowment Initiative Launched

Inspired by very generous contributions from two graduates of our Rheumatology Fellowship Program, the Russell/Engleman Rheumatology Research Center (R/ERRC) has launched a major fundraising initiative designed to substantially increase our capacity to train clinicians and scientists.

Over the past five years, the scope of the overall clinical enterprise at UCSF has grown dramatically. As a result, our traditional cadre of three new fellows per year is no longer sufficient to meet the clinical demand in rheumatology. To address this challenge, R/ERRC has made a commitment to provide the support necessary to increase the size of the program from three to four trainees per year, so that we can continue to provide an outstanding educational experience for our fellows and the highest quality of care for our patients.

The goal of this campaign is to generate a $2.5 million endowment. We anticipate that half of the endowment will be generated through donations from grateful former fellows, which will be matched by R/ERRC. We are already 40 percent of the way to our goal and are confident that we will succeed and maintain our stature as the premier rheumatology training program in the country. ■

UCSF Rheumatology
Department of Medicine

Arthritis Progress Report is produced by the Russell/Engleman Rheumatology Research Center (R/ERRC) in the Department of Medicine at UC San Francisco.

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