The ALR Attends Annual American College of Rheumatology Meeting

The Alliance for Lupus Research (ALR) once again had a presence at the annual meeting of the American College of Rheumatology (ACR). At this year's meeting in San Diego on October 26-27, ALR staff and members of the ALR Scientific Advisory Board heard presentations by some of the most brilliant minds in the field of rheumatology and lupus.

The ACR is the leading national organization of and for physicians, health professionals, and scientists who have made it their mission to discover advance the science of rheumatology. This medical society represents more than 8,500 rheumatologists, scientists, and other health professionals from around the world. And at this annual meeting, attendees had the opportunity to learn about the most up-to-date investigations by attending an array of informative presentations by worldwide experts and viewing posters in the exhibition hall.

Among the many participants was the Hospital for Special Surgery (HSS), which has a close relationship with the ALR. Physician in Chief and Chair of the Division of Rheumatology at HHS, Dr. Mary Crow, is also Chair of the ALR's Scientific Advisory Board.

"HSS had a strong presence at this scientific meeting — with more than 60 accepted studies," said Dr. Crow. *"Our researchers highlighted discoveries helping to elucidate the underlying mechanisms of rheumatic disease and presented findings regarding best practices. These investigations may one day change the face of how we diagnose and treat these potentially devastating conditions."*

To review a summary of one of these presentations — *the pioneering work being done by Dr. Jane Salmon to eliminate the risks for pregnant women with lupus* — please see the article that follows. Throughout her career, Dr. Salmon's work has been greatly advanced through funding from the ALR.

Since it's inception in 1999, the ALR has attended every annual meeting of the ACR because the two fields of scientific inquiry — lupus and rheumatology — are so closely related.

But how exactly are they related? A rheumatologist treats diseases of the joints *and* of the muscles and bones — such as osteoporosis and a number of autoimmune diseases, such as lupus. Many of the diseases that a rheumatologist treats involve — as in lupus — multiple organ damage caused by inflammation. Most often, rheumatologists are the principal physicians for people with lupus.

In summing up the ACR's pivotal work, Dr. Crow said: *"On behalf of the HSS and the ALR, I commend the American College of Rheumatology for the extraordinary role it plays in creating this important forum to share the most crucial ideas in research today. For those of us who remain steadfast in our dedication to discovering new approaches for prevention, diagnosis, and treatment to improve the lives of our patients — the ACR is essential."*

The American College of Rheumatology's mission is advancing rheumatology. The organization represents over 8,500 rheumatologists and rheumatology health professionals around the world.

The ACR offers its members the support they need to ensure that they are able to continue their innovative work by providing programs of education, research, advocacy, and practice support. It also organizes scientific meetings, publishes two medical journals "Arthritis & Rheumatism" and Arthritis Care & Research" — and promotes research into rheumatologic conditions, including the formulation of diagnostic criteria for diseases.

Reducing Risk of Adverse Outcomes In Lupus Pregnancies

Leading world experts in rheumatology and lupus gathered at the American College of Rheumatology (ACR) annual Fall 2013 meeting in San Diego, CA, to propel scientific discovery through the sharing of ideas. Jane Salmon, MD — Attending Physician at the Hospital for Special Surgery and former ALR grantee and current member of the ALR's Scientific Advisory Board— was among the presenters.

Dr. Salmon led an informative presentation on her critical work to understand why pregnant women with lupus are at a greater risk of poor pregnancy outcomes than women without the disease. She and her team have found an answer. An imbalance of angiogenic factor — *proteins required for the development of the placenta and the health of blood vessels* — is at play.

Specifically, increased levels of the anti-angiogenic protein called sFlt1 in pregnant lupus patients place them at increased risk of placental insufficiency and preeclampsia, a potentially life-threatening complication.

In the study, titled "Angiogenic Factor Dysregulation and Risk of Adverse Pregnancy Outcomes in Lupus Pregnancies," Dr. Salmon determined that higher levels of sFlt1 reduce the activity of other angiogenic proteins that are necessary for growth of placenta and the mother's blood vessels.

"Pregnant women with lupus or antiphospholipid syndrome are at increased risk for adverse outcomes, particularly preeclampsia, yet identification of those destined for complications has been elusive," said Dr. Salmon. *"We prospectively studied patients to see if we could find a biomarker early in pregnancy that would predict a poor outcome."*

The study is part of an ongoing, multi-center lupus/pregnancy-research initiative led by Dr. Salmon known as PROMISSE. In the current phase of PROMISSE, scientists enrolled 384 pregnant women with lupus and 153 healthy pregnant controls. Subjects were evaluated and monthly blood draws began at 12 weeks into pregnancy. Poor pregnancy outcomes were defined

as preeclampsia, fetal death, neonatal death, preterm delivery before 36 weeks because of placental insufficiency, or intrauterine growth restriction (IUGR), which refers to poor growth rate of the baby in the womb. Levels of sFlt1 and other angiogenic proteins were measured and compared in women with lupus versus control subjects.

Among those enrolled in the study, 10 percent developed preeclampsia and another 10 percent had poor outcomes. Levels of sFlt1 protein, an anti-angiogenic factor, were significantly higher in patients destined for complications compared to lupus patients whose pregnancies were uncomplicated. In contrast, levels of PlGF, an angiogenic factor, were lower. Alteration in the balance of angiogenic factors was evident as early as 12 to 15 weeks into the pregnancy and persisted throughout pregnancy in women who experienced preeclampsia or other complications.

What will this data mean? Dr. Salmon's ultimate goal is to develop a risk profile to guide patients and physicians. *"Measurement of sFlt1 and PlGF provide a powerful tool to identify pregnant lupus patients at high risk for poor pregnancy outcomes sufficiently early to intervene,"* Dr. Salmon said. *"Hopefully, this will facilitate trials of novel treatments to prevent these devastating complications."*

In her long and fruitful relationship with the ALR, Dr. Salmon has received more than $XX from the organization to advance her lupus investigations. "*By funding researchers like me, the ALR is opening up critical pathways that look at the disease through a variety of avenues,"* said Dr. Salmon. *"I'm grateful to the organization for being the catalyst behind my work to take away the risks that pregnant women with lupus confront."*

Dr. Jane Salmon is Director of the Lupus and APS Center of Excellence at Hospital for Special Surgery and lead author of "Angiogenic Factor Dysregulation and Risk of Adverse Pregnancy Outcomes in Lupus Pregnancies." For the past xx years, Dr. Salmon's research has focused on elucidating mechanisms of tissue injury in lupus and other autoimmune diseases. Her basic and clinical studies have expanded our understanding of pregnancy loss and organ damage in lupus and the determinants of disease outcome in lupus patients with nephritis, pregnancy, and cardiovascular disease.

Looking at Lupus Nephritis Through a Fresh Lens

Lupus nephritis, or inflammation of the kidneys, is one of the most dangerous manifestations of lupus — which is why David Wofsy, MD from the University of California, San Francisco, is looking at ways to alter its course.

Focusing his current research on finding new agents for the treatment of lupus, Dr. Wofsy presented: "Treatment of Lupus Nephritis with Abatacept Plus Low-Dose Cyclophosphamide Followed by Azathioprine (the Euro-Lupus Regimen): 24-Week Data from a Double-Blind Controlled Trial" at this year's ACR conference in San Diego.

This study benefits from a quick review of Dr. Wofsy's prior work. For many years, his research focused on lupus in murine models. Based on this body of work, Dr. Wofsy shifted his emphasis to clinical trials of novel therapies for people with autoimmune diseases.

Several of these therapies arose out of Dr. Wofsy's pioneering work in murine models, including particular studies which demonstrated that inhibition of T cell co-stimulation could suppress autoimmunity in murine models for several human autoimmune diseases. This work contributed directly to the development of a novel agent, abatacept, which was recently approved for the treatment of rheumatoid arthritis.

As the title of his presentation indicates, Dr. Wofsy is looking to determine whether abatacept is also effective in people with life-threatening manifestations of SLE — namely lupus nephritis.

This was a 1:1 randomized, double-blind, controlled phase II multicenter trial involving individuals with lupus nephritis. The experimental group received a course of abatacept (at weeks 0, 2 and 4, then every 4 weeks until week 24), plus low dose cyclophosphamide every 2 weeks for 12 weeks, followed by azathioprine for 16 weeks. Participants randomized to the control group received abatacept placebo and cyclophosphamide followed by azathioprine as described for the experimental group. All participants also received a prednisone regimen.

While the trial did not achieve the primary goal of demonstrating enhanced benefit of this combination of therapies, it provided the first systematic examination of the Euro-Lupus Regimen in a racially and ethnically diverse North American population — suggesting that it may have broad applicability. Subjects in the trial are still undergoing blinded evaluation to determine later outcomes.

Dr. Wofsy is committed to improving and simplifying the assessment of new therapies while conducting clinical trials designed to prevent chronic kidney disease and end-stage kidney failure. In the United States, lupus nephritis is especially common among Black and Hispanic patients, occurring in up to 60 percent of adults with lupus.

Dr. David Wofsy received his undergraduate degree from Harvard in1968, his MD from the University of California, San Diego in 1974, and his medical residency training and rheumatology fellowship training from the University of California, San Francisco. He joined the UCSF faculty in 1980. He is currently Professor of Medicine and Microbiology/Immunology at UCSF. Dr. Wofsy also serves as Associate Dean for Admissions for the UCSF School of Medicine. He has served on numerous NIH study sections and is a past-President of the American College of Rheumatology.

Dr. Wofsy is the founder and leader of the Lupus Nephritis Trials Network, an international network of clinicians and investigators who perform collaborative studies to improve the lives of people with the most severe forms of SLE.