AWARD RECIPIENT

WILLIAM H. ROBINSON, MD, PhD

Stanford University School of Medicine

PROJECT

"PROTEOMIC ANALYSIS OF RHEUMATOID ARTHRITIS IN THE GERIATRIC POPULATION"

MENTORSHIP TEAM

C. GARRISON FATHMAN, MD   MARK C. GENOVESE, MD
MARY K. GOLDSTEIN, MD

Rheumatoid arthritis (RA) is an inflammatory synovitis affecting over 0.5 percent of the world population, yet the autoantigen targets and mechanisms underlying the initiation and progression of RA remain poorly understood. Further, in the elderly population the incidence of RA continues to rise until age 85.

We developed synovial protein microarrays and mass spectroscopy approaches to characterize the specificity of autoantibody responses in RA. Synovial microarray studies suggest differential targeting of candidate autoantigens in recent-onset RA in older (more than 60 years old) as compared to younger patients. We have also observed increased circulating (blood) immune complexes in patients with long-standing RA. For this award, we propose to use C1q capture assays to quantify and mass spectrometry to identify autoantigens bound in synovial fluid and circulating immune complexes. Synthetic peptides and recombinant proteins representing the identified antigens will be added to synovial arrays. We will apply synovial microarrays to identify autoantibody profiles associated with recent-onset RA in older patients (more than 60 years old) as well as long-standing RA (more than 10 years). We anticipate that:

1. High-throughput characterization of synovial fluid and circulating immune complexes will identify novel autoantigens that are targets of pathogenic autoimmune responses in RA.

2. Autoantibody responses in elderly patients with recent-onset RA target distinct subsets of antigens as compared to those in younger patients.

The proposed studies will provide insights into the specificity of the autoimmune responses and the mechanisms underlying autoimmune initiation and progression in the elderly RA patient population.

As part of the Geriatric Research, Education, and Clinical Center at the Palo Alto Veterans Administration Medical Center, my laboratory performs translational bench-to-bedside research with a focus on RA. We investigate the pathogenesis of RA, with the objective of rapidly converting discoveries at the bench into practical patient care tools and therapies. This American College of Rheumatology Research and Education Foundation-ASP Junior Career Development Award in Geriatric Medicine will further promote our investigations of RA and autoimmunity in the elderly population. Success of these studies would advance: (1) our understanding of the mechanisms underlying the loss of self-tolerance, and (2) the development of RA in the elderly and could lead to development of novel diagnostics and therapeutics.