American College of Rheumatology Research and Education Foundation–ASP Junior Career Development Award in Geriatric Medicine

AWARD RECIPIENT

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PROJECT

"Age-Associated Matrix Alteration and Inflammation in Idiopathic Knee Osteoarthritis"

MENTORSHIP TEAM

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Osteoarthritis (OA) is the most common joint disease worldwide and is a major public health problem in the United States. Increasing age is a primary risk factor for developing OA as many age-related changes in joint cartilage matrix have been identified. Several specific matrix products that can be altered during aging, including fibronectin fragments and advanced-glycation end-products, have the capacity to induce an immune response. Although traditionally categorized as a non-inflammatory disease, OA can exhibit inflammation within the synovial membrane lining the joint. This inflammation may be a source of pain and may contribute to disease progression. However, the stimulus for the recruitment of the inflammatory cells to synovium is not yet known. Current thinking suggests that OA synovitis is secondary to the effects of matrix degradation products released from the articular cartilage, but the specific factors responsible for the synovial response have not been defined.

We propose to investigate the hypothesis that age-associated alterations in cartilage matrix products contribute to the development of inflammation in OA by inducing synthesis of cytokines and chemokines involved in leukocyte recruitment. Furthermore, we hypothesize that the immunostimulatory matrix components act via a toll-like receptor (TLR) mediated pathway. We plan to test this hypothesis using in vitro approaches to demonstrate the presence of TLR ligands released from cartilage and present in synovial fluid from patients with both early and advanced OA. Furthermore, we will characterize the ability of specific age-related matrix alterations to act as immunostimulants in these in vitro systems. We anticipate that the proposed research will identify mechanisms leading to synovial inflammation in OA and, ultimately, lead to the development of improved therapeutic strategies for this debilitating disease.

The support of the American College of Rheumatology Research and Education Foundation–ASP Junior Career Development Award in Geriatric Medicine is crucial to my goal of becoming an independent investigator. As I pursue a career in academic rheumatology, I hope to apply my clinical and research training to the understanding of the pathobiology of OA, the most common rheumatologic condition affecting older adults. Specifically, I plan to focus my studies on the interplay between aging and inflammatory pathway activation in relation to disease phenotypes and prognosis. This award will support my research and education during the early years of my first faculty appointment, a time when I will pursue further training in specific research methods and focus my clinical practice on geriatric rheumatology. I hope to use the knowledge and data gained from this project in support of future independent research funding in this field.