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

AWARD RECIPIENT

Kim M. Huffman, MD, PhD
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PROJECT

"Mechanisms of Insulin Resistance in Older Individuals with Rheumatoid Arthritis"

MENTORSHIP TEAM

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Rheumatoid arthritis (RA) is a chronic, inflammatory arthritis prevalent in approximately 2% of individuals over age 60. Recently, significant advances have been made in pharmacologic treatment for RA. However, persons with RA remain at increased risk of cardiovascular disease and insulin resistance. In individuals without RA, habitual physical activity improves insulin action and cardiovascular morbidity. The potential for exercise to confer similar health benefits in RA patients has not been explored. This award supports a research and career development plan that will provide the basis for developing specific interventions whereby physical activity can be used to modulate metabolic cardiovascular risk in older individuals with RA.

In this project, we will evaluate the role of skeletal muscle pathophysiology and altered body composition in promoting insulin resistance in older individuals with RA. The underlying hypothesis is that inflammation associated with RA mediates increased abdominal obesity and skeletal muscle atrophy. In turn, these body composition changes lead to mitochondrial dysfunction and eventual insulin resistance. This hypothesis will be tested using a cross-sectional comparison of older individuals with RA and sex, age, and body mass index-matched controls. In these individuals, we will compare visceral and subcutaneous adiposity, thigh skeletal muscle density and fiber type distribution, and insulin sensitivity between persons with RA and matched controls. To better understand the mechanisms underlying disrupted insulin action, we will evaluate pathways integral to skeletal muscle

atrophy and insulin-mediated glucose uptake by measuring expression of skeletal muscle proteins involved in the ubiquitin-dependent proteosomal degradation and insulin-mediated signaling. Additionally, we will relate measures of inflammation, fatty acid metabolism, and mitochondrial function to atrophy signaling, insulin-mediated signaling, and insulin sensitivity. In this fashion, we hope to deepen understanding of the mechanisms of musculoskeletal disease in aging persons and use this knowledge to develop exercise interventions to modulate metabolic cardiovascular risk in older individuals with RA.

In addition to these research goals, the American College of Rheumatology Research and Education Foundation-ASP Junior Career Development Award in Geriatric Medicine will support critical components of my career development. During this award, I will acquire research skills through coursework in exercise physiology, statistical analysis, clinical trial design, and clinical trial implementation. Additionally, this award will support the implementation of a career focused on geriatrics aspects of rheumatologic disease by supporting on-going training of geriatrics fellows in rheumatology. My career development and research program will be guided by an excellent mentoring team and advisory committee (Drs. Harvey Cohen, Miriam Morey, and Deborah Muoio). Specifically, this research project will allow me to move toward my long-term goals of investigating mechanisms of beneficial responses to physical activity and developing guidelines for the application of physical activity in older populations with rheumatologic disease.