Numerous factors contribute to OA development and progression but mechanical stress and trauma, aging, and genetic predisposition are among the primary factors. In addition to genetic factors which predispose us to OA, modifications in chromatin structure are also present in OA. Chromatin is the complex of proteins (histones) and DNA that is tightly packed to fit into the cell nucleus. Some proteins modify the chromatin structure; among these, histone deacetylases (HDACs) are responsible for modifications of histones. A number of HDACs were found increased in chondrocytes isolated from OA patients. Mechanical injury of cartilage is also known to lead to cartilage degradation. However, no studies have investigated the collaboration between mechanical stress and chromatin remodeling changes in OA. This project aims to analyze the changes in the levels of HDAC proteins between normal and OA cartilage samples in addition to the effect of mechanical stimulation. Better understanding of the role of chromatin changes in OA and the connection with mechanical stress and cartilage remodeling changes in OA. We will also analyze the mechanical changes in the chromatin structure; among these, histone deacetylases (HDACs) are responsible for modifications of histones. A number of HDACs are known to lead to cartilage degradation. However, no studies have investigated the collaboration between mechanical stress and chromatin remodeling changes in OA. This project aims to analyze the interaction between these two potential causative factors of OA and how aging cartilage responds to this interaction. We will analyze the changes in the levels of HDAC proteins between normal and OA cartilage samples in addition to the effect of mechanical stimulation. Better understanding of the role of chromatin changes in OA and the connection with mechanical stress and cartilage remodeling changes in OA. We will also analyze the mechanical changes in the chromatin structure; among these, histone deacetylases (HDACs) are responsible for modifications of histones. A number of HDACs are known to lead to cartilage degradation. However, no studies have investigated the collaboration between mechanical stress and chromatin remodeling changes in OA. This project aims to analyze the interaction between these two potential causative factors of OA and how aging cartilage responds to this interaction. We will analyze the changes in the levels of HDAC proteins between normal and OA cartilage samples in addition to the effect of mechanical stimulation. Better understanding of the role of chromatin changes in OA and the connection with mechanical stress and cartilage remodeling changes in OA.
in articular cartilage degeneration and maintain it through life. Research is expected to reveal the mechanisms by which mesenchymal cells differentiate into cartilage, however, currently limiting their therapeutic use. It is important to identify the genetic and environmental factors that influence the specific maintenance and development. The results of this study will help orient the focus of basic research and clinical trials towards identifying efficient ways to use mesenchymal cells in therapeutic strategies to repair cartilage in osteoarthritics.

Emily C. Somers, PhD, ScM
Senior Investigator, Brigham and Women's Hospital, Harvard, Cambridge, MA
New Investigator Grant
Epidemiologic Insights related to RA and SLE: Role of X Chromosome Factors
Rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE) are both autoimmune diseases that are characterized by the chronic inflammation of joints and other tissues. RA affects more women than men, while SLE affects more women than men as well. RA affects the joints, particularly in the hands, wrists, knees, and fingers, while SLE can affect any part of the body, including the skin, joints, kidneys, and brain. The inflammation in RA and SLE causes pain, swelling, and damage to these structures.

Lydia Li, PhD, MSW
University of Michigan, Ann Arbor
Innovative Research Grant
Acupressure for Older Adults with Symptomatic Knee Osteoarthritis
Knee osteoarthritis is a leading cause of disability in the elderly population. Current treatments for knee pain are only modestly effective and some treatments like non-steroidal anti-inflammatory drugs (NSAIDs) have adverse long-term effects. Acupressure is an inexpensive and non-invasive treatment that has the potential to be a useful long-term self-management strategy for knee pain. This study will randomize older adults with symptomatic knee osteoarthritis to treatment with acupressure or to a sham intervention. The primary outcomes of this trial will be to determine if acupressure is an effective and feasible self-management strategy for older adults with symptomatic knee osteoarthritis.

Michelle Rosan Abelson, PhD
University of Pittsburgh, Postdoctoral Fellow
C/EBPbeta: Signaling and Response in Arthritis
Rheumatoid arthritis (RA) is a chronic, systemic inflammatory autoimmune disease. RA primarily affects joints but can target other organs and tissues. This disease is associated with a significant disability, estimated to be worth $9 billion in 2005 and significant socioeconomic costs. Drugs that target “cytokines” such as tumor necrosis factor (TNF) have improved treatment options in RA. Despite these advances, however, a significant number of patients either do not respond or stop responding to available anti-cytokine therapies. Interleukin-17 (IL-17) is a cytokine implicated in RA. Many RA patients have elevated levels of IL-17 in the blood and affected joints. Patients in early clinical trials testing IL-17 blocking antibodies have shown clinical improvements, indicating that IL-17 is likely to be a valuable target to treat RA and other autoimmune diseases. Little is known about IL-17 mechanisms or how this cytokine contributes to the pathogenesis of RA, yet understanding the biological signaling events mediated by cytokines such as IL-17 can be used to provide new avenues for intervention or identification of biomarkers that can be used to track disease course and drug efficacy. We have shown that IL-17 activates its effects via the CCAAT enhancer binding protein (C/EBPbeta) transcription factor. A person with RA has shown that C/EBPbeta plays an important role in the susceptibility of mice to an autoimmune disease model of multiple sclerosis. Finding from multiple sclerosis are frequently translatable to arthritis, suggesting a potential role for C/EBPbeta in driving arthritis. Despite the importance of C/EBPbeta in the IL-17 molecular pathway, the role of IL-17 in the development of C/EBPbeta has not been investigated in RA. This proposal investigates two aspects of the IL-17/C/EBPbeta signaling pathway - to assess molecular mechanisms that regulate expression of the different protein forms of C/EBPbeta, and to determine the biological significance of certain C/EBPbeta isoforms in a collagen-induced arthritis model of RA. Understanding the mechanism by which IL-17 mediates signaling, particularly in the context of arthritis, may aid in the development of new drugs, vaccines or treatments in diseases affected by IL-17.

A FEW FACTS...
- The Arthritis Foundation is the largest, private funder of arthritis research in the world and has contributed nearly $4.25 billion to an array of projects since 1948.
- In 2013, the Foundation is funding 138 researchers, working on studies related to rheumatoid arthritis, osteoarthritis and juvenile arthritis, as well as other rheumatic diseases.
- The Arthritis Foundation targeted $9 million for research funding in 2012 and projects an additional $9 million in funding during 2013, in support of New Investigator and Innovative Research grants and Postdoctoral Fellowships.