RESEARCH GRANTS LAY SUMMARIES

Name: Michelle Yau, MPH
Award Type: Doctoral Dissertation – DD
Amount: $30,000.00
Project Title: *Elucidating the genetic architecture of osteoarthritis progression*
Institution: University of Maryland, Baltimore
Mentors: Marc C. Hochberg, MD, MPH and Braxton D. Mitchell, PhD
Award Period: July 1, 2013 – June 30, 2015
Study Section: Genetics
Disease Focus: Osteoarthritis

Lay Language Summary: Osteoarthritis (OA) is the most common form of arthritis in the United States and is a major cause of disability among older adults. Genetics has been shown to play a role in whether individuals develop OA, but little is known about how genes affect the progression of OA after development of the condition. Some researchers believe that the risk factors for development of OA may be different from the risk factors for the progression of OA, speculating that the initiation of OA is often due to injury, while progression of OA is due to a problem with the process of cartilage repair. Therefore, better understanding of the genetic basis of OA progression will contribute to our understanding of the disease process and the biological mechanisms that may be involved. The overall goal of this study is to identify genetic risk factors for OA progression in the hip and knee. The study will use data from 1,271 participants from the Genetics of Generalized Osteoarthritis (GOGO) study who were examined at baseline and 4 years later. Individuals having evidence of OA at the initial visit and an increase in severity of OA at the follow-up visit were classified as having progression of OA. In a preliminary analysis, we found evidence that a region located on the X chromosome is likely to harbor genes related to the progression of OA. Genes identified within this region have not been found to be associated with development of OA, supporting the possibility that genes involved in progression of OA may be different from the genes involved in development of OA. To follow up this result, I will narrow down this previously identified region on the X chromosome to identify the specific gene(s) related to OA progression through analysis of already collected data – a set of 550,000 DNA markers blanketing the entire genome, including the X chromosome. After identifying specific DNA markers that are associated

with OA progression, I will then determine if these same DNA markers are associated with OA progression in two independent datasets (the Osteoarthritis Initiative and the Johnston County Osteoarthritis Project) and whether combining data from all three datasets yields additional interesting genetic variations. As an exploratory aim, I will also determine whether specific gene(s) are related to change in biomarkers for cartilage degradation, synthesis, and inflammation. The outcomes of this research will be essential to elucidating genes that may play a role in the trajectory of OA. By identifying potential genes and biochemical targets, interventions may be developed to slow or prevent the progression of OA, thereby improving quality of life and decreasing associated health care costs.