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Researchers identify genetic patterns that may predict osteoarthritis

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Scientists from University of North Carolina at Chapel Hill School of Medicine and Interleukin Genetics, Inc. announced today findings from a large clinical study to evaluate the role played by genetic factors in the worsening of osteoarthritis.

The study, which was part of the Johnston County Osteoarthritis Project, showed patients with X-ray evidence of knee osteoarthritis who inherited a specific pattern of genetic variations in the interleukin-1 receptor antagonist (IL-1Ra) gene were almost twice as likely to progress to severe disease as other patients. Results from the study, which followed 1,154 patients for up to 11 years, will be presented this week at the World Congress on Osteoarthritis in Brussels, Belgium.

The study, led by Joanne Jordan, MD, MPH, the Herman & Louise Smith Distinguished Professor of Medicine and Chief, Division of Rheumatology, Allergy, and Immunology at the Thurston Arthritis Research Center at University of North Carolina at Chapel Hill, is the first of its kind to include both African-Americans and Caucasians, as well as inclusion of genetic, radiographic, serologic, physical and functional examinations of its participants.

"The strong association shown in this study between progressive OA and the IL-1Ra gene variations, as well as the body of previous related published research, might suggest that this IL-1Ra genetic information could be tested as a tool to identify high-risk patients for participation in clinical trials for the development of a much-needed disease modifying

OA drug," Jordan said.

Interleukin Genetics previously reported variations in the gene for IL-1Ra are strongly associated with severe knee osteoarthritis and this clinical study validates the company's earlier findings and other previous studies that have implicated the anti-inflammatory protein IL-1Ra in progression to severe disease.

Although osteoarthritis (OA) is the greatest cause of physical disability in the U.S., there are currently no drugs approved that modify the disease progression. One of the challenges to development of new drugs in OA has been the lack of tools that predict which OA patients are more likely to progress to severe disease, thereby making clinical trials more complicated and expensive.

According to the U.S. Department of Health and Human Services, Osteoarthritis was ranked among the top 10 most expensive medical conditions to treat. In 2005 alone it cost $34 billion, with joint replacement surgery absorbing most of the cost.

"Drug development for OA has been challenging, in part due to the difficulty of enrolling patients who are likely to exhibit disease progression during the study. There appears to be strong potential to use the IL-1Ra genetic patterns to select for clinical trials patients who are more likely to benefit from an effective drug," said Ken Kornman, Chief Scientific Officer, Interleukin Genetics. "A genetic test also would have strong clinical utility for physicians to better manage patients who will more likely progress to a severe form of the disease and require surgery."

The 1,154 subjects in the Johnston County Osteoarthritis Projected, which is directed by Jordan, were monitored for a period between 4 and 11 years to study initiation or progression of osteoarthritis. Subjects at

the start of the study were analyzed for genetic markers that predicted those subjects who remained stable and those subjects who progressed to severe osteoarthritis, as measured radiographically. Nine genes were found to be associated with osteoarthritis progression, with the strongest prediction of progression from combinations of gene variations in the gene for IL-1Ra.

Iinterleukin-1 (IL-1) is one of the key chemicals involved in cartilage and bone destruction, and on specific genetic patterns in the naturally occurring inhibitors of that are predictive of IL-1 and of OA progression. The study demonstrated that three specific genetic patterns commonly found in the osteoarthritis population are strongly predictive of different risks for progression of osteoarthritis once it has been diagnosed.

Provided by University of North Carolina School of Medicine