

## Major new study finds clues to the genetic causes of osteoarthritis (Update)

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(Medical Xpress) -- UK scientists have discovered more genetic regions associated with the cause of osteoarthritis. Researchers from nine institutions across the UK have described the findings as a significant breakthrough in understanding the genetic risk factors that cause the disease.

Publishing their findings in *The Lancet* today, the Arthritis Research UK-funded arcOGEN consortium has highlighted eight genetic regions linked to the development of osteoarthritis. Previously, only three osteoarthritis genetic regions had been identified.

Several of the genetic regions encompass genes that are known to regulate how joints are made and then maintained, making them excellent osteoarthritis candidate genes. Another genetic region contains a gene involved in the regulation of body weight, which is a strong risk factor for osteoarthritis.

The £2.2million project is the world's biggest ever-genome wide study into osteoarthritis, comparing the genetic differences of 7,400 patients with severe osteoarthritis with 11,000 healthy volunteers. The results were then replicated in over 7,000 OA individuals and 43,000 control individuals, from four European collaborating partners.

Osteoarthritis affects about 40 per cent of people over the age of 70, a total of 8 million people in the UK, causing pain and disability. There is currently no cure for the condition. Treatments for early osteoarthritis

are limited to non-surgical options such as pain killers and physiotherapy until joint replacement becomes a viable option. Osteoarthritis is a complex disorder with both environmental and genetic causes. It is estimated that about 50 per cent of an individual's risk of developing osteoarthritis is due to inherited genetic factors.

Professor Bill Ollier, from the University of Manchester's Centre for Integrated Medical Research (CIGMR), said: "Osteoarthritis is one the most common conditions affecting adults and is responsible for causing much pain and suffering for a large proportion of the population. Unfortunately, this is becoming a larger health problem as we live longer. We are only now just beginning to identify the genetic and lifestyle factors involved in OA and work out how they interact to allow the disease to develop. Only by doing this will we be able to develop treatments to tackle the disease at an early stage and avoid surgical replacements of joints. This landmark study, supported by the Alzheimer's Research UK, has brought together the major research groups working on OA in collaboration, rather than being in competition. This important study opens up a number of exciting new avenues for tackling this common condition."

Two of the novel regions are close to genes that immediately suggest clinical implications for osteoarthritis. One, CHST11, affects cartilage proteoglycan (proteins in the cartilage modified with sugar chemicals) and changes in proteoglycan are an active area of development of new treatments for osteoarthritis. A second gene, PTHLH, is the basis for recently developed parathyroid hormone-based treatments for osteoporosis. The research team suggest a next step would be to explore whether these compounds may also be effective in osteoarthritis.

Gillian Wallis, Professor of Genetics in Manchester's Wellcome Trust Centre for Cell-Matrix Research, said: "It is very exciting that many of the chromosomal regions associated with osteoarthritis contain genes

that are involved in the development, production and maintenance of healthy cartilage. This makes sense because cartilage is one of the tissues of the joint that is degraded by the osteoarthritic disease process. Knowing which genes contribute to osteoarthritis susceptibility provides a firm starting point for research into the causes of this complex disease which may identify new targets for drug development.”

Principal investigator of arcOGEN John Loughlin, Professor of Musculoskeletal Research at Newcastle University, said: “We know that osteoarthritis runs in families and that this is due to the genes that people pass on, rather than their shared environment. In this study we were able to say with a high degree of confidence which genetic regions are the major risk factors for developing osteoarthritis: the first time that this has been possible for this common yet complex disease. It’s an important first step.”

Medical director of Arthritis Research UK Professor Alan Silman added: “There is no cure for osteoarthritis yet it affects millions of people around the world. For 60 years we have known that you are twice as likely to have osteoarthritis if your parents have the disease, yet we haven’t known why.

“Until we understand the cause of this complex disease, we cannot hope to find a cure. This is a major breakthrough in our understanding of osteoarthritis which we hope will help us to unlock the genetic basis of the disease.”

Further work is now needed to pinpoint the actual DNA changes within the genetic regions to establish exactly how these changes lead to osteoarthritis.

Professor Loughlin said that they were not yet able to use their discoveries as a tool to predict who was more or less likely to develop

the disease, or to predict the degree of osteoarthritis severity, based on the genes they have inherited. Far more genes are involved in causing disease susceptibility than was previously thought, and there are still many left to find.

He added: “However, what we are able to do is to use our genetic discoveries to identify key biological pathways that can now be exploited to develop new treatments.”

Provided by University of Manchester

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