MedicalXpress

Third genetic link to osteoarthritis discovered

August 25 2011

Researchers have today revealed a new gene associated with osteoarthritis. This is only the third gene to be identified for this painful and debilitating disease that affects more than 40 per cent of people aged more than 70 years.

The disease-associated variant, in the gene MCF2L, was discovered when Wellcome Trust Sanger Institute researchers used data from the 1000 Genomes Project to increase the power of their genome-wide association scan. The preliminary stage of the original arcOGEN study, funded by Arthritis Research UK, compared the genomes of 3,177 people with osteoarthritis with 4,894 people from the general population and looked at 600,000 variants.

At that level of detail, no new genes were identified (although the full study has yet to be published). By imputing the data from the 1000 Genomes Project, the new study was able to scan for 7.2 million variants and revealed the association of MCF2L with osteoarthritis without requiring any new sequencing to be carried out.

"By using the 1000 Genomes Project data to add value to our original genome-wide association scan for osteoarthritis, we have uncovered a disease-associated gene that had previously remained hidden," says Dr Eleftheria Zeggini, senior author from the Sanger Institute. "We were able to analyse our results in greater detail and zoom in on variants that we hadn't been able to identify before. We hope that this approach and our findings will help to improve our biological understanding of this very painful disease."

Osteoarthritis is a complex condition and researchers have found it difficult to identify its genes. Only two loci have been found so far in European populations – GDF5 and a signal from a region on chromosome 7.

The newly identified gene, MCF2L, is found on chromosome 13 and regulates a nerve growth factor (NGF). It has been reported that when people with osteoarthritis in the knee are treated with a humanized monoclonal antibody against NGF, they experience less pain and show improvement in their movement. This suggests that MCF2L is involved in the development of osteoarthritis and provides a new focus for future research.

To ensure that the variant of MCF2L is associated with the development of osteoarthritis, the team worked with international collaborators to investigate 19,041 people with arthritis and 25,504 people without the condition. A number of centres across Europe collaborated by screening people in Iceland, Estonia, the Netherlands and the UK for the newly identified variant to corroborate the association.

"The discovery of this MCF2L variant suggests a possible genetic link to the finding that regulating NGF is important in knee osteoarthritis, and is supported by the fact that the variant is more strongly associated with knee osteoarthritis than hip osteoarthritis in the study," says Aaron Day-Williams, first author of the study from the Sanger Institute. "We hope the identification of this variant will lead to further insights into the biological processes at work and offer potential treatment targets."

The study's findings are based on the work of the arcOGEN Consortium, which has been funded by Arthritis Research UK and is a vital supporter of research in this area.

"Osteoarthritis is a complex disease with many genetic causes. Yet it has

proved very difficult to find the genes involved and help us to identify potential areas of treatment," says Alan Silman, Medical Director of Arthritis Research UK. "We are delighted that researchers at the Sanger Institute have been able to identify a new gene associated with this painful condition and offer new lines of research for possible treatments. We are also excited that employing the technique of using the 1000 Genomes Project data to investigate genetic associations in far greater depth could reveal even greater insights into this debilitating disease."

More information: Day-Williams AG et al. (2011) A variant in MCF2L is associated with osteoarthritis. American Journal of Human Genetics, published online 25 August 2011 doi: 10.1016/j.ajhg.2011.08.001

Provided by Wellcome Trust Sanger Institute