

Researchers identify gene behind rheumatoid arthritis

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University of Manchester researchers have identified a genetic variant in a region on chromosome 6 that is associated with rheumatoid arthritis (RA), the most common inflammatory arthritis affecting 387,000 people in the UK.

Professor Jane Worthington and her team at the Arthritis Research Campaign (arc) Epidemiology Unit at the University investigated 9 genetic regions identified earlier this year as potentially harbouring DNA variants determining susceptibility to rheumatoid arthritis. Association to one of the variants on chromosome 6 was unequivocally confirmed, reports this week's *Nature Genetics* (4 November 2007).

Although this variant is not located in a gene, Professor Worthington suggests that it may influence the behaviour of a nearby gene: tumour necrosis factor associated protein (TNFAIP3) as this is a gene that is known to be involved in inflammatory processes.

Rheumatoid arthritis, which affects up to 1% of the adult population, is a chronic inflammatory disease that can affect nearly all joints in the body, particularly the hands and feet. Complications such as lung disease can occur. In addition, patients with RA are more likely to die from cardiovascular disease and some cancers. Some people respond well to treatment, but most suffer a lifetime of disability.

Professor Worthington and her team, who are funded by the medical research charity arc, made their findings as part of the largest ever study

of the genetics behind common diseases, the £9M Wellcome Trust Case Control Consortium (WTCCC). The WTCCC study has given a major boost to the understanding of the genetics of seven common diseases, including RA. As well as providing insights into what leads some people to develop the diseases and offering new avenues for treatments, the success of the approach heralds exciting advances in the study of the genetics of disease.

The Manchester team is currently investigating several genomic regions which may be important in the development of RA but the locus near TNFAIP3 is the first to be fully validated. Until recently, only two other genes were known to explain 50% of genetically determined susceptibility. Now the Manchester researchers are working to understand how the variation within the chromosome 6q region influences the development of RA, the course of the disease and the response to treatment.

Professor Worthington said: “This is a very exciting result; the validation of this association takes us one step closer to understanding the genetic risk factors behind what is a debilitating disease for sufferers and an expensive disease for the NHS.

“We are indebted to the Arthritis Research Campaign (arc) for their longstanding support of this research and for recognizing the importance of establishing large well characterized cohorts of RA patients. This study was made possible by the fantastic collaboration of scientists from five other groups around the UK who helped us to assemble an impressive cohort of over 5,000 samples from RA patients for this experiment. Their continued collaboration will be significant in ensuring the continued progress of this research.”

Dr Anne Barton, a clinician on the team, said: “RA is a complex, heterogeneous disease with some people suffering inflammation of the

hands and feet which comes and goes whilst others develop a progressive form which can quite rapidly result in marked disability. We believe the genetic marker we have found may determine who develops RA or how severe the disease becomes.”

Source: University of Manchester

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