Scientists perform first Asian genome-wide association study on spine disease

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Singapore and China scientists, headed by Dr Liu Jianjun, Senior Group Leader and Associate Director of Human Genetics at the Genome Institute of Singapore (GIS) and Dr Gu Jieruo, a rheumatologist at the 3rd Affiliated Hospital of the Sun Yat-Sen University, have identified new genes that are associated with the spine disease ankylosing spondylitis (AS). This discovery, reported in the advanced online issue of *Nature Genetics* on 4 December 2011, brings scientists closer to understanding the disease and work towards its cure.

AS is a progressive autoimmune disease. It is characterized by the inflammatory low back pain, partly accompanied by peripheral arthritis, enthesis and iritis, and even spinal deformity and ankylosis. It can cause eventual fusion of the spine, a condition known as "bamboo spine". Its prevalence is 2.4 per 1,000 in the Chinese population, similar to that in populations of European ancestry. Genetic factors play an important role in the pathogenesis of AS and the estimated heritability is over 90%.

The gene HLA-B27 had previously been shown to be strongly associated with AS susceptibility, but it confers only 20-30% of the overall genetic risk. In order to identify other genetic susceptibility genes for AS, Drs Liu and Gu and their collaborators carried out a large genome-wide association study of AS in Chinese Han population. Initially, they performed a comprehensive genome-wide analysis of common genetic variants in 1,837 AS patients and 4,231 controls. Subsequently, they selected 30 genes for a validation study in an additional 2,100 patients and 3,496 controls. The researchers discovered two novel susceptibility

genes, EDIL3-HAPLN1 on 5q14.3 and ANO6 on 12q12. The newly discovered susceptibility loci implicate the genes related to bone formation and cartilage development, suggesting their potential involvement in the development of AS.

Their study also confirmed the previously reported association with HLA-B*27 variants, and the susceptibility locus on 2p15 in European population.

Dr Liu said: "AS is an autoimmune disease, and the association of HLA-B*27 is not surprising. Our study confirms the important role of the immunity, but more importantly, it indicates that other mechanisms, such as bone formation and cartilage development also play an important role in AS."

More information: The research findings described in the press release can be found in the 4 December 2011 advanced online issue of *Nature Genetics* under the title "A genome-wide association study in Han Chinese identifies new susceptibility loci for ankylosing spondylitis".

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