FCRL3: A possible genetic link for rheumatoid arthritis

An organism’s inherent complexity can often generate self-destructive diseases that are hard to treat and difficult to understand. In rheumatoid arthritis, the body’s immune system turns against itself and attacks connecting tissue and joints. This constricts movement and causes pain. Precisely why this happens is unknown, but a complex mix of environmental and genetic factors are implicated. On the latter side, more genomic information is now available, helping to forge a link between a collection of genetic components and rheumatoid arthritis susceptibility. Researchers at RIKEN Yokohama Institute identified a single genetic variation that strengthens the genetic causal chain of this disease. Their findings were reported in the May 2005 issue of *Nature Genetics*.

Rheumatoid arthritis is a chronic, progressive illness that affects approximately 1% of the global population. Its onset, symptoms, and duration vary, but swollen joints, stiffness, fatigue and pain are common. It strikes women more than men, usually in the fourth decade. It is the most common of the autoimmune diseases, in which T- and B-cells turn on the synovial tissue that surrounds a jelly-like joint capsule causing inflammation. When the tissue swells, movement becomes painful and laborious. Treatment relies primarily on anti-inflammatory drugs to reduce pain and swelling, but the progressive nature of the disease eventually renders afflicted people immobile.

Results from earlier studies of autoimmune diseases suggested that RIKEN's researchers seek an explanation for the inflammation seen in rheumatoid arthritis in genetic ties with autoimmunity. Several haplotype genes were already identified for rheumatoid arthritis, but these alone are insufficient explanations. As a complex disease, rheumatoid arthritis is most likely the product of a combination of disease-related genes. Finding these genes within the entire genome was time consuming process, but whole genome linkage studies eventually honed in on one specific locus, Cytoband 1q21-23,
which is associated with several autoimmune disorders in search of those that might contribute to rheumatoid arthritis.

After the standard battery of genetic association tests, the researchers identified one mutation, a signal nucleotide polymorphism (SNP 169C → T), in the FCRL3 gene on that band, that was strongly associated with rheumatoid arthritis. Cell studies showed that the SNP -169C allele significantly increased FCRL3 gene expression which affected one of the two key cells in the immune system, B-cells. This affected immune response and led to rheumatoid arthritis. More than this, the team found that a higher susceptibility for other autoimmune disorders, like lupus, with this mutation.

Having demonstrated a possible genetic basis for B-cell abnormalities the researchers may have explained why a B-cell reduction therapy now in clinical trials might work. They have also significantly narrowed the investigative area that needs to be combed over in pursuit of clues that explain how rheumatoid arthritis develops and how it and other autoimmune disorders might be better treated.

This research was published in the May 2005 edition of Nature Genetics (Vol.37, pp.478-485).

http://www.wrongdiagnosis.com/r/rheumatoid_arthritis/stats-country.htm

For more information, please contact:

RIKEN Public Relations Office
Email: koho@riken.jp