

Pediatric researchers find possible 'master switch' gene in juvenile arthritis

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Researchers have found that a gene region known to play a role in some varieties of adult rheumatoid arthritis is also present in all types of childhood arthritis. The researchers say the responsible gene may be a "master switch" that helps turn on the debilitating disease.

Researchers at The Children's Hospital of Philadelphia reported on the link between the gene region and juvenile idiopathic arthritis (JIA), formerly called juvenile rheumatoid arthritis. The genetic variant is on chromosome 9 in a region housing two genes, TRAF1 and C5. The TRAF1 gene codes for a protein that regulates tumor necrosis factor, a chemical strongly associated with JIA. However, the researchers say further study is needed to determine whether the TRAF1 gene or the C5 gene is altered in the disease.

The study appears in the July 2008 issue of *Arthritis & Rheumatism*. Lead authors are Terri H. Finkel, M.D., Ph.D.; Hakon Hakonarson, M.D. Ph.D., director of the Center for Applied Genomics; and Edward M. Behrens, M.D., all of Children's Hospital.

"There are only a few genes that may act as master switches like this to regulate autoimmune diseases," said Finkel, the chief of Rheumatology at Children's Hospital. "This switch we discovered probably has to be an 'ON' gene and when it interacts with other genes and environmental triggers, a child may get juvenile arthritis."

The study compared 67 Caucasian patients being treated for JIA to

1,952 healthy Caucasian control subjects recruited within the hospital's patient network. While the cause of JIA is unknown, results from this study back up past research that shows arthritis arises in a genetically susceptible individual due to environmental factors.

About 300,000 children in the U.S. have JIA, of which about 1,500 children are seen at Children's Hospital. JIA is the inflammation of the lining tissues of a joint and often causes stiffness and pain. While there is no cure for JIA, medicines and physical therapy can help maintain movement and reduce swelling and pain. Researchers have previously identified seven subtypes of JIA.

"We think this finding may be a clue to the specific disease pathway that leads to arthritis," said Behrens, a pediatric rheumatologist at Children's Hospital. "We currently use medicines called tumor necrosis factor blockers to treat children with JIA. However, not all children respond to these drugs, and other children may develop severe allergic reactions and other side effects. If we can fully identify all the genes that interact with environmental risk factors, we might develop more targeted treatments with fewer side effects."

"The high-resolution genome-wide association approach has very markedly enhanced our ability to identify disease genes in complex disorders such as JIA, and what is remarkable about this discovery is that it appears there may be a common genetic factor predisposing to all seven forms of the disease," said Dr. Hakonarson.

Source: Children's Hospital of Philadelphia

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