Immune Dysregulation Seen in Autistic Children

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BUDAPEST, HUNGARY — Children with autism spectrum disorders appear to have immune responses different from those of healthy children, according to data presented at the 4th International Congress on Autoimmunity.

"There is evidence now for an immune dysregulation in children with autism, compared with children in the general population," said Paul Ashwood, Ph.D., of the University of California, Davis.

In a study of 31 children with autism spectrum disorders (ASD) and 19 typically developing control children aged 2-5 years, the children with ASD had abnormal levels of several cytokines in response to stimulation with three antigens, compared with the control children.

The study adds weight to the idea that autism has an immune component. There are several previous reports of both increased autoimmunity and immune response deficits in children with ASD. "However, a lot of these reports are conflicting, and there is no consensus so far," Dr. Ashwood said.

In this study, Dr. Ashwood and colleagues isolated and stimulated peripheral blood mononuclear cells for 48 hours with phytohemagglutinin, lipopolysaccharide, and vaccine antigens from tetanus and MMR. Analysis was performed for 18 cytokines. At baseline, cytokine levels were similar in the children with ASD and the control children.

Following stimulation with phytohemagglutinin, the children with ASD had statistically significantly lower levels of IL-2, IL-6, IL-10, and IL-12 than the control children. There was also a trend toward higher levels of IL-13 and granulocyte macrophage-colony stimulating factor—which stimulates the precursor cells of granulocytes, macrophages, and eosinophils—among the children with ASD than the control children.

A similar pattern was seen after stimulation with lipopolysaccharide. Children with ASD had lower levels of IL-12 and a slight increase in granulocyte macrophage-colony stimulating factor, compared with the control children.

Stimulation with tetanus antigens resulted in lower levels of IFN-ν, IL-1-η, IL-12, and granulocyte macrophage-colony stimulating factor in the children with ASD, compared to the control children.

Although there was no difference after stimulation with MMR vaccine antigens the researchers are planning to investigate the response to individual components of the MMR vaccine. ■

Coalition Starts Autism Genetics Research Plan

Federal health agencies have teamed up with private organizations and government health agencies in Canada and Ireland to provide funding for research into the genetic basis of susceptibility to autistic spectrum disorders.

The coalition, headed by the National Institute of Mental Health, has made $21 million available to researchers and requested grant applications that focus on using large data sets of more than 1,000 pedigrees that already have been assembled. These data sets should have adequate statistical power to detect autism susceptibility loci, according to the NIMH.

Studies have located several chromosomal regions associated with autism, but few specific genes have been identified. This project asks investigators to determine the functional significance of any genes or gene variants that are identified during the analysis of the large data sets.

The identification of new genes or gene variants may help researchers to subdivide the autism spectrum disorders into distinct disorders with different molecular mechanisms.

Some of the grant applications also may address the possibility that not all heritable traits of autism directly involve alterations in the genetic code. Heritable changes that do not alter the DNA sequence include epigenetic mechanisms such as imprinting, DNA methylation, and changes in chromatin or protein conformations; they could potentially regulate gene expression and play an important etiologic role in the disorder.

—Jeff Evans