Lack of specific gene plays role in autism

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It is estimated that three to six out of every 1,000 children in the United States have autism - and the number of diagnosed cases is rising. Autism is one of a group of series developmental problems called autism spectrum disorders (ASD) that appear in early childhood, usually before age 3. Through symptoms and severity vary, all autism disorders affect a child's ability to communicate and interact with others.

It's not clear whether this is due to better detection and reporting of autism, a real increase in the number of cases, or both.

That's why researchers at Case Western Reserve University, led by Gary Landreth, a professor of neurosciences and neurology at the School of Medicine, have pulled together a number of recent findings that link a common genetic pathway with a number of human syndromes and a newly-recognized genetic form of autism, publishing them in the January 29, 2009, issue of the prestigious journal *Neuron*.

Landreth, whose research team is made up of partners from the Cole Eye Institute at the Cleveland Clinic, the Louis Stokes Cleveland VA Medical Center and the University of Pennsylvania, says his lab in particular has been researching the class of enzymes called ERKs (extracellular signal regulated kinase), which are the central elements of a major intracellular signal transduction pathway. His research team has found that in animal models the ERKs - known as ERK 1 and ERK 2 - are required for normal brain, heart and facial development.

This common genetic pathway that acts to regulate the ERK signaling

cascade is particularly important in brain development, learning, memory and cognition. It has been recently reported that mutation or deletion of elements within this signaling pathway leads to developmental syndromes in humans that are associated with impaired cognitive function and autism.

According to Landreth, these syndromes, called neuro-craniofacial-cardiac syndromes (NCFCs), encompass a group of syndromes also typified by cardiac, craniofacial and neurological defects. Current research has found that they arise from mutations in the intracellular signaling pathway that regulates ERKs.

"Very recently it was discovered that 1 percent of autistic children have either a loss or duplication in a region of Chromosome 16 that encompasses the gene for ERK 1," said Landreth, who also serves as director of the School of Medicine's Alzheimer's Research Laboratory. "What no one else realized is that the autistic children also have craniofacial and cardiac defects just like those children with NCFC syndromes."

Thus, Landreth says, mutations within the ERK signaling pathway appears to be a common cause for NCFC syndromes and those children with autism due to genetic changes in chromosome 16.

"Unexplained is why loss of ERK 1 is associated with autism and other ERK pathway mutations cause mental retardation and similar diseases," he said. "Our contribution to the autism story is that we recognized it was just like the NCFC syndromes and we are hypothesizing that they all arise from defects within a single genetic pathway."

Source: Case Western Reserve University