

## **Newly Discovered Gene Mutation Explains Cognitive Deficits Associated with Autism**

Autism is a genetically induced malfunction in the development of the brain, in which at least three, possibly up to 100 genes are involved. Researchers of the **Division of Molecular Genome Analysis headed by Professor Annemarie Poustka at the German Cancer Research Center (Deutsches Krebsforschungszentrum, DKFZ)**, jointly with colleagues of the Universities of Frankfurt and Salzburg, have identified mutations on the X chromosome that help to explain the cognitive deficits of autistic persons.

Since boys are affected four times more often by autism than girls, scientists believe that the genetic causes of the disease are located, among other sites, on the X chromosome. Several marker genes for autism were already identified on the X chromosome in the past. Scientists have now taken a closer look at further, yet uncharacterized regions on the X chromosome and have subjected 345 persons with autism to a molecular-genetic screening. In two male siblings from different families they found mutations in a region that is responsible for the production of ribosomes, the protein factories of the cell.

Although the mutations found in the two brother pairs were not identical, they were spatially located very close to each other and were not detectable in healthy control persons. They affected a sequence in the genome that codes for the L10 (RPL10) ribosomal protein. This protein is a member of a family of ribosomal proteins which has been highly conserved by evolution and is found from bacteria to humans. It is indispensable for the translation of genetic information into proteins.

Expression of RPL10 in the brain is particularly strong in areas such as the hippocampus where learning, memory, social and affective functions are located. "A malfunctioning RPL10 may be responsible for the lack of differentiation of nerve cells and insufficient formation of nerve cell connections during brain development that can be detected in autistic persons using imaging technologies and that are considered to be key to the disorder", says first author Dr. Sabine Klauck. Mutations in genes that play a role in synaptic connections in the hippocampus were already identified in autistic persons several times before.

The new findings support a disease model in which the genetic defect, via a disruption of translation, leads to insufficient development and connection of nerve cells in specific brain regions. These defects later manifest themselves in the typical cognitive deficits and perceptual abnormalities associated with autism.

S.M. Klauck, B. Felder, A. Kolb-Kokocinski, C. Schuster, A. Chiocchetti, I. Schupp, R. Wellenreuther, G. Schmötzer, F. Poustka, L. Breitenbach-Koller, A. Poustka: Mutations in the ribosomal protein gene RPL10 suggest a novel modulating disease mechanism for autism; *Molecular Psychiatry.*, doi:10.1038/sj.mp.4001883

The task of the Deutsches Krebsforschungszentrum in Heidelberg (German Cancer Research Center, DKFZ) is to systematically investigate the mechanisms of cancer development and to identify cancer risk factors. The results of this basic research are expected to lead to new approaches in the prevention, diagnosis and treatment of cancer. The Center is financed to 90 percent by the Federal Ministry of Education and Research and to 10 percent by the State of Baden-Wuerttemberg. It is a member of the Helmholtz Association of National Research Centers (Helmholtz-Gemeinschaft Deutscher Forschungszentren e.V., HGF).

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