UAE International Annual Conference & Exhibition
Abu Dhabi 2023

DOI 10.14293/ACS.2023.418
Available at www.emiratesscholar.com

Role of Genes in Pathogenesis of Autism

Nagwa Abdel Meguid, Ph.D
Professor of Human Genetics, Head of the DNA Research Laboratory in Genetic Behavioral Disorders, founder of the Autism Research Study Group, former Head of the Human Genetics Unit at the National Research Center, Egypt

Abstract

Despite extensive studies, however, the genetic basis for ASD is still not clear. Gene expression patterns differ geographically between populations and within populations. Identifying those panels of genes will help in developing reliable biomarkers for the early diagnostic and therapeutic purposes. In this study, we developed an analysing pipeline to search for de novo mutations, and possible pathways be related to ASD. Whole-exome sequencing was performed to screen de novo mutations and candidate genes in 80 ASD children together with their parents (trios). Roughly one-quarter of patients with autism suffer from epilepsy. Catalyses the phosphorylation and inactivation of the branched-chain alpha-ketoacid dehydrogenase complex (BCKDH), the key regulatory enzyme of the branched chain amino acid (BCAA) catabolic pathways. The branched-chain alpha-ketoacid dehydrogenase complex (BCKD) is an important regulator of the valine, leucine, and isoleucine catabolic pathways. Mutations in BCKDH lead to increased branched chain amino acids. We studied a line of mice engineered with a mutation in the same gene, which showed that the condition was both inducible by lowering the dietary intake of the BCAAs and reversible by raising the dietary intake. In addition, examined cultured neural stem cells from these patients found that they behaved normally in the presence of BCAAs, suggesting the condition might be treatable with nutritional supplementation. On the other hand, we investigate the main changes in RNA gene expression patterns of the reactive oxygen metabolism in autistic children and correlate changes with degrees of disease severity. The process of oxidative stress may be an objective target for therapeutic interventions. PCR Array profiles the expression of 84 genes related to oxidative stress was done. We have validated the altered mRNA abundance of five key signalling molecules in a larger number of patients by quantitative real time PCR (qRT-PCR). Only FTH1 gene exhibited downregulation in severe autistic patients compared to mild/moderate group which is unique in our population and may be considered as biomarker for severity. This suggests iron deficiency and impaired detoxification of toxic ferrous ions which in turn increases the severity of the autistic symptoms. This finding can also account for the sleep fragmentations in some of the severely studied cases. Nutrient levels affect the status of glutathione and antioxidant enzymes. If oxidative stress proves important in autism, then the nutritional management of autism, because it modulates oxidative stress, presumably gains importance.