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The Genetic Role of Autism

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What is Autism?

Autism spectrum disorder (ASD) is a neurodevelopment disorder that affects social interaction, communication skills, and cognitive learning. The symptoms are usually present in early childhood and affect daily activities. Some of the symptoms present in a patient with autism are; no response to their name by 12 months of age, avoid eye contact and want to be alone, have trouble understanding other people's feeling and talking about their own, have delayed speech and language skills, repeat words and phrases, get upset over minor changes and have obsessive interest (1). Research has shown that genetic variation plays a huge role in the development of Autism, it has been shown that *De novo* mutations are changes in the sequences of deoxyribonucleic acid or DNA, the hereditary material in humans, which can occur in a parent's sperm or egg cell during fertilization. The mutation then occurs in each cell as the fertilized egg divides (2).

These mutations may affect a single gene or change the number of copies which stretches the DNA containing multiple genes that can be deleted or duplicated due to the number variation. Cytogenetic abnormalities found at the 15q11-q13 locus are reported most frequently in patients with autism, up to 1% to 4%.83,93–96 Various population studies and case reports have described duplications,93,96–99 deletions,93,95 and inversions100,101 at this locus (3). ASD has also increased in children born to older parents. There have been many different cases regarding the disorder but there hasn't been any case disclosing the potential role environmental factors could have on spontaneous mutations and how it can influence the risk of ASD. ASD occurs in every racial and ethnic group and across all socioeconomic levels. However, men are significantly more likely to develop ASD than women. The latest analysis from the Centers of Disease Control and Prevention estimates that 1 in 68 children have ASD (2). This project is going to present the different types of gene mutations within Autism.

Genes Associated with Autism and their Affects.

Gene FOXP2 : A protein which is reported to be mutated in patients with a severe speech and language disorder. FOXP2 was located on chromosome 7p31 which is one of the loci involved in autism. Autism and specific language impairment share some of the same clinical phenotypes. In addition, based on the graph below we can see that FOXP2 expresses itself abundantly in the brain (4).

Figure 1: Chromosomal location of FOXP2

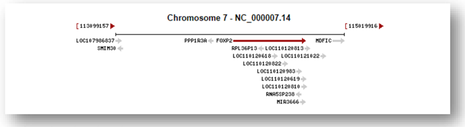
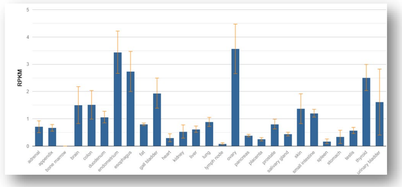


Figure 2: Gene expression in the body



Gene RELN: This gene encodes large secreted extracellular matrix protein to control cell-cell interaction and its critical for cell positioning and neuronal migration during brain development (5). This protein may be involved in schizophrenia, autism, bipolar disorder, major depression and epilepsy.

Figure 3: Chromosomal location of RELN

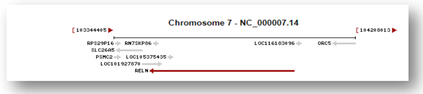
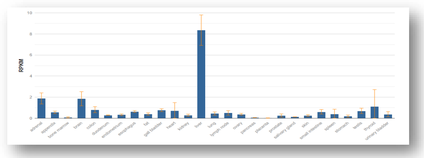


Figure 4: Gene expression in the body



Gene GABRB3: A major inhibitory neurotransmitter of mammalian nervous system, the gene is in the long arm of chromosome 15. This gene is associated with several disorders including Angelman syndrome, Prader-Willi syndrome, nonsyndromic orofacial clefts, epilepsy and autism (6).

Figure 5: Chromosomal location of GABRB3

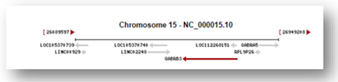
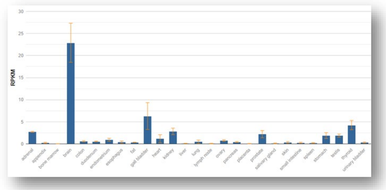


Figure 6: Gene Expression in the body



What happens if those genes are mutated?

FOXP2 gene is one of the biggest factors involved with cognitive functions in humans and non-human mammals. Heterozygous mutations of human FOXP2 gene causes a monogenic speech and language disorder (7). A reduced functional dosage causes deficient synaptic plasticity and impairs motor-skill learning. Its critical for vocal learning and developing the central nervous system. FOXP2 impacts the growth of primary neurons and neurological cells which is why when mutations occur, they usually result in syndromes such as autism or any form of delayed speech.

RELN is gene that provides instructions for making a protein called reelin, the protein is produced in the brain before and after birth. Reelin is released by the brain cells; then binds to specific receptor proteins, during the development of the brain this binding turns on a signal activating the pathway that triggers nerve cells to migrate to their proper locations (8). If any change or disturbance occurs during this process health conditions occur such as Lissencephaly with cerebellar hypoplasia, ASD, Myoclonus-dystonia and more due to the mutation within the gene.

GABRB3 gene also known as Gamma-aminobutyric acid has been identified with autism. GABRB3 is responsible for protein coding and can be associated to many different diseases due to improper coding. The gene encodes the subunits of a multi-subunit chloride channel that serves as a receptor for the gamma-aminobutyric acid a major inhibitory neurotransmitter for the mammalian nervous system (8).

Epigenetics is the study of the factors that control gene expression, this control involves the chemicals that surround a gene's DNA . Autism is often the result from a combination of genetic susceptibility and environmental triggers. Normal epigenetics marks modifiable by both genetic and environmental exposures can result in epigenetic alterations that disrupt the regulation of gene expression, negatively impacting biological pathways important for brain development (9). Which is why epigenetics plays an important role in the molecular mechanism of ASD.

What is a possible course of treatment?

After doing all this research and realizing what genes affect ASD we can go in and fix the problem. The biggest threat that lies within ASD is the mutations of genes that weren't properly coded, I believe by going in and fixing the mutation of FOXP2 for instance we can minimize the symptoms of ASD. CRISPR is a tool that can be used to tweak almost any gene in any plant or animal. Researches already have used it to fix genetic diseases in animals, to combat viruses (10). If CRISPR was used to go in and alter the genes that influence autism such as FOXP2, RELN, and GARBB3 I believe the syndrome could be eliminated or become more manageable for patients with ASD to interact, communicate and learn. Like stated above these genes affect motor skills which would make it difficult for a patient with ASD to form healthy relationships, this course of treatment could change that.

Contact

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