Study of genetic polymorphisms in autism spectrum disorder

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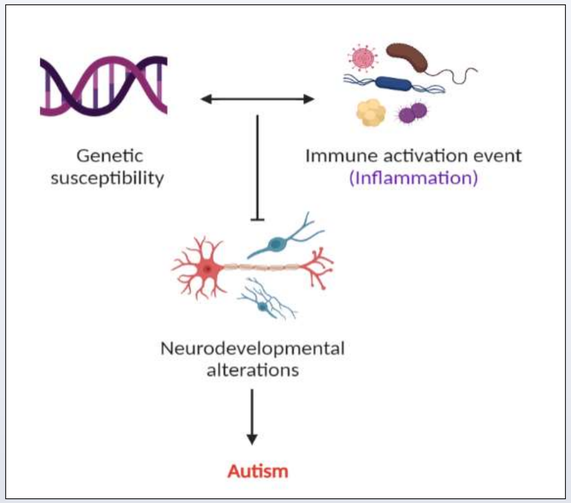
Abstract

Autism spectrum disorder (ASD) is a neurodevelopmental condition marked by stereotyped behavior and poor social interaction. There is no known underlying cause of this illness, but genetic research confirms it has a genetic basis due to a complex inheritance pattern. There are approximately 52 million people worldwide who suffer from this disease. ASD has several risk factors in common with other neurodevelopmental diseases, with symptoms developing at varying stages. A literature review included gene identifications from articles in databases including Web of Science, PubMed, Google Scholar, Embase, and others published over the previous 30 years. Candidate genes associated with ASD are CHD8, SHANK3, SLC6A4, RELN, DISC1, and ITGB3. It is known that a number of prenatal risk factors increase the chances of developing autism and other neurodevelopmental disorders in children. During the last decade, genomic research has led to the discovery of a number of genes related to ASD risk. Some genetic mutations and modifications may serve as useful biological markers, risk indicators, and therapeutic targets for diseases because of recent technological advances. High-throughput next-generation sequencing uncovers new risk genes in large cohorts that are highly individualized. To understand disease development better, more studies are needed on environmental variables. The clinical evidence supporting ASD's function is limited at present. The prevailing evidence suggests that many new candidate genes for ASD may be associated with its etiology. Therefore, they may be useful in developing an early diagnostic marker.

Introduction

Autism spectrum disorders (ASDs) are a set of neurodevelopmental illnesses characterized by three primary behavioral impairments. Limited interests, repetitive activity, inability to participate in reciprocal social relationships, and language and communication difficulties are characteristics of behavioral disorders. ASD is frequently associated with neurological diseases such as epilepsy, schizophrenia, intellectual impairment, and clinical symptoms such as dysmorphic features, gastrointestinal issues, and sleep difficulties. Autistic behaviours can also be a symptom of genetic syndromes, such as monogenic diseases (e.g., Fragile X syndrome, Rett syndrome) or chromosomal abnormality-related syndromes. Autism is caused by genetic risk factors that alter early brain development and function, including synaptic transmission. Advanced paternal age is considered to raise the risk of autism by raising the rate of de novo mutations and epigenetic changes. It is also linked to immune system sensitivity in pregnant women, hypothesized to combine with genetic factors to enhance susceptibility. A family history of autoimmune illness, maternal infection during pregnancy, and maternal autoimmune disease is all known risk factors for autism.

Causes of ASD



Biological pathways in ASD

- CHD8, an ATP–dependent chromodomain helicase that regulates the CTNNB1 and p53 pathways.
- Using whole-genome analysis of mRNA levels and CNVs to detect aberrant brain gene expression patterns in autistic brains, researchers discovered that the adenosine A2A receptor-signaling pathway was substantially dysregulated in young autistic people.
- In addition, researchers discovered unusual and harmful variations in the SHANK3, TSC1, and TSC2 genes in non-syndromic autistic people during an ASD inquiry that revealed distinct changes in the mGLUR signaling pathway.
- Differences in fMRI activation and deactivation patterns in response to social stimuli and structural and functional connectivity in the temporal-parietal region of the brain in ASD patients indicated abnormalities in the gene-brain pathway depending.
- The protein-protein interaction (PPIs) network is the foundation for cellular signaling circuitry, which directs cellular responses to environmental and genetic inputs. Understanding how ASD–related quantitative aspects affect fetal and adult cortex PPIs could lead to identifying pathways that regulate cortical development and ASD risk.

Genes involved in ASD

It is possible to have multiple genetic networks involved in a genetic predisposition to ASD. These genetic networks include neurological development, neuron migrating, synaptogenesis, axon pathfinding, and regionalization of neurons or glial cells. The study of association based on a candidate gene is known as a function-targeted study. CHD8, SHANK3, SLC6A4, RELN, DISC1, and ITGITGB3 have been identified as strongly associated with ASD by researchers. These genes are listed in Table 1.

Table 1: Genes associated with autism spectrum disorder

Gene symbol	Gene name	Location	Function	SNP
CHD-8	Chromodomain helicase DNA- binding protein-8	14q11.2	By regulating beta catenin activity, it acts as a negative regulator of the Wnt signalling pathway	c.4984C>T, P.Arg1662Ter
SHANK-3	SH3 and multiple ankyrin repeat domains 3	22q13.33	Plays a role in the functioning of synapses, which are the connections between nerve cells where cell-to-cells communication occurs	rs9616915
SLC6A4	Human serotonin transporter	17q11.2	Plays an important function in regulating the availability of serotonin to other serotonergic receptors	c.86A>G(p.Asp29Gly), c.978 T>G (p.Asp326Glu), c.Ala138Thr)
RELN	Reelin	7q22.1	Microtubule function in neurons and neuronal migration are regulated by this protein	g.504742G>A
DISC-1	DISC-1 scaffold protein	1q42.2	Neuronal proliferation, differentiation, migration, cAMP signaling, cytoskeletal modulation, and translational control are all mechanisms that regulate neural development and brain maturation via diverse signaling pathways	rs1322784
ITGB-3	Integrin subunit beta 3	17q21.32	Provides instructions for making the beta 3 subunit of a receptor protein called integrin protein called integrin alpha IIb/beta3	rs15908, rs12603582

Conclusion

Autism is a disorder caused by the environment when it was first identified. In recent decades, researchers have revealed that it is a highly complex genetic disorder. Epigenetics, sex-linked modifiers, CNVs, double-hit mutations, and environmental influences are examples of such modifiers. In order to gain a solid understanding of how these modulators influence autism, decades of study may be needed. To determine what is causing the problem, a simplified genetic testing methodology involving known risk loci, such as a microarray, may be a rapid and low-cost solution. The results of this research will ultimately lead to a more in-depth understanding of how genetic components interact with disease modifiers to cause autism spectrum disorders Individuals with ASD at risk can be identified using biomarkers before diagnostic behaviors emerge. In terms of prenatal biomarkers, maternal-fetal brain autoantibodies seem to be the most promising as they can predict autism in offspring with a high degree of accuracy. Despite the promise of postnatal presymptomatic neuroimaging, further research is required to prove its effectiveness. To improve personalized treatment regimens and result in a specialized precision medicine approach, biomarkers that predict treatment response might be used to identify how an individual will respond to ASD therapy.

References

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