MECP2 Gene

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Contributor: Lily Guo

methyl-CpG binding protein 2

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1. Introduction

The *MECP2* gene provides instructions for making a protein called MeCP2. This protein helps regulate gene activity (expression) by modifying chromatin, the complex of DNA and protein that packages DNA into chromosomes. The MeCP2 protein is present in cells throughout the body, although it is particularly abundant in brain cells.

In the brain, the MeCP2 protein is important for the function of several types of cells, including nerve cells (neurons). The protein likely plays a role in maintaining connections (synapses) between neurons, where cell-to-cell communication occurs. Many of the genes that are known to be regulated by the MeCP2 protein play a role in normal brain function, particularly the maintenance of synapses.

Researchers believe that the MeCP2 protein may also be involved in processing molecules called messenger RNA (mRNA), which serve as genetic blueprints for making proteins. By cutting and rearranging mRNA molecules in different ways, the MeCP2 protein controls the production of different versions of certain proteins. This process is known as alternative splicing. In the brain, the alternative splicing of proteins is critical for normal communication between neurons and may also be necessary for the function of other types of brain cells.

2. Health Conditions Related to Genetic Changes

2.1. MECP2 duplication syndrome

An extra copy (duplication) of the *MECP2* gene in each cell causes *MECP2* duplication syndrome, a condition characterized by intellectual disability, delayed development, and seizures. This condition affects males more often than females. When females are affected, they tend to have milder features. The duplication occurs on the long (q) arm of the X chromosome and includes the *MECP2* gene; other genes may also be involved, depending on the size of the duplicated segment. The size of the duplication varies from 100,000 to a few million DNA building blocks (base pairs).

Duplication of the *MECP2* gene leads to the production of extra MeCP2 protein and an increase in protein function. The resulting changes in gene regulation and protein production in the brain lead to abnormal neuronal function. These neuronal changes disrupt normal brain activity, causing the signs and symptoms of *MECP2* duplication syndrome.

2.2. MECP2-related severe neonatal encephalopathy

At least 19 mutations in the *MECP2* gene cause *MECP2*-related severe neonatal encephalopathy. This condition almost exclusively affects males and is characterized by small head size (microcephaly), movement disorders, breathing problems, and seizures. Many of the *MECP2* gene mutations that cause this condition in males cause a similar disorder called Rett syndrome (described below) in females. Most of these mutations change single base pairs, insert or delete base pairs in the gene, or change how protein is produced from the gene. These changes in DNA alter the structure of the MeCP2 protein or reduce the amount of protein that is produced. As a result, cells do not have enough MeCP2 protein to bind to DNA and regulate other genes. A shortage of MeCP2 alters the activity of genes that are normally controlled by this protein. Mutations in the *MECP2* gene may also disrupt alternative splicing of proteins critical for communication between neurons. Although these defects disrupt normal brain development, it remains unclear how *MECP2* gene mutations lead to the signs and symptoms of *MECP2*-related severe neonatal encephalopathy.

2.3. PPM-X syndrome

Mutations in the *MECP2* gene have been found to cause PPM-X syndrome. This disorder is characterized by mild to severe intellectual disability, bipolar disorder, and a pattern of movement abnormalities known as parkinsonism. This condition affects males more often than females; when females are affected, they tend to have only mild intellectual disability.

Eight particular mutations are responsible for approximately half of all cases of PPM-X syndrome. These mutations either change single protein building blocks (amino acids) in the MeCP2 protein or create a premature stop signal in the instructions for making the protein. Mutations that cause PPM-X syndrome lead to the production of a MeCP2 protein that cannot properly interact with DNA or other proteins and so cannot control the expression of genes. It is unclear how *MECP2* gene mutations lead to the signs and symptoms of PPM-X syndrome, but misregulation of genes in the brain likely play a role in the development of intellectual disability and movement and mood disorders in affected individuals.

2.4. Rett syndrome

More than 620 mutations in the *MECP2* gene have been identified in females with Rett syndrome, a brain disorder that causes problems with communication, learning, and coordination. These mutations include changes in single base pairs, insertions or deletions of DNA in the gene, and changes that affect how the information carried by the gene is used to produce proteins. *MECP2* gene mutations alter the structure of the MeCP2 protein or reduce the amount of protein that is produced. The resulting shortage of functional MeCP2 likely impairs the regulation of gene expression in brain cells and may also disrupt alternative splicing of proteins critical for communication between neurons. Studies suggest that these changes may reduce the activity of certain neurons and impact their ability to communicate with one another. It is unclear how these changes lead to the specific features of Rett syndrome.

2.5. Other disorders

Mutations in the *MECP2* gene have also been identified in people with several other disorders that affect the brain. For example, *MECP2* gene mutations are associated with some cases of moderate to severe X-linked intellectual disability without other features of the syndromes described above. In addition, several people with both the features of Rett syndrome and signs and symptoms similar to Angelman syndrome (a condition characterized by intellectual disability, problems with movement, and inappropriate laughter and excitability) have mutations in the *MECP2* gene. *MECP2* gene mutations or changes in the gene's activity have been reported in some cases of autism spectrum disorder, which affects communication and social interaction.

3. Other Names for This Gene

- MeCP2 protein
- MECP2_HUMAN
- methyl CpG binding protein 2
- methyl CpG binding protein 2 (Rett syndrome)
- MRX16
- MRX79
- PPMX
- RTS
- RTT

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