We have over 20,000 different genes in the body, and those genes are located in our DNA. These genes are like instruction manuals for how to build a protein, and each protein has an important function that helps to keep our body working how it should. The *MECP2* gene makes a protein called methyl-CpG binding protein 2 (MeCp2). MeCp2 helps to control the expression (activity) of several genes, particularly those which have a role in normal brain function and allow for communication between nerve cells (neurons).

If someone has a harmful change (called a pathogenic variant) in one of their *MECP2* genes, they will have decreased amounts of MeCp2. This may result in decreased gene expression in the brain and may also disrupt the communication between neurons leading to a variety of symptoms, including but not limited to, intellectual disability, problems with coordination, and seizures.

Pathogenic variants in *MECP2* are inherited in an X-linked pattern, although most of the time, a pathogenic variant in *MECP2* is new (or *de novo*) and discovered in an affected individual without any family history of the disorder. Rarely, a pathogenic variant may be inherited from a carrier mother who is mildly affected or healthy. When a mother is a known carrier of a pathogenic variant in *MECP2*, the risk of occurrence in her offspring is 50%. Unfortunately, most males with a *MECP2* pathogenic variant have a shortened life expectancy and pass away during infancy. Females with a *MECP2* pathogenic variant can present with classic Rett syndrome, variant Rett syndrome, or mild learning disabilities (also referred to as *MECP2*-related disorders).

GENETIC TESTING FOR *MECP2*

Genetic testing for pathogenic variants in *MECP2* is currently available, but there are a few different ways to approach testing:

- *Single site analysis*: Testing specific to a known pathogenic variant in the family
- Full gene sequencing and deletion/duplication analysis: Comprehensive testing to search for all currently detectable pathogenic variants in the gene
- Gene panels: Newer, more broadly based gene tests that would include not only the *MECP2* gene, but other genes known or suspected to be associated with similar health complications described in *MECP2*-related disorders.