BOLA3 gene

bolA family member 3

Normal Function

The *BOLA3* gene provides instructions for making a protein whose function is not well understood. The BOLA3 protein is thought to be involved in the formation of molecules called iron-sulfur (Fe-S) clusters or in the attachment of these clusters to other proteins. Certain proteins require attachment of Fe-S clusters to function properly.

Two versions (isoforms) of the BOLA3 protein are produced from the *BOLA3* gene. One version is found in cellular structures called mitochondria. Mitochondria are the energy-producing centers of cells. In these structures, several proteins carry out a series of chemical steps to convert the energy in food into a form that cells can use. Many of the proteins involved in this process require Fe-S clusters to function, including protein complexes called complex I, complex II, and complex III.

Fe-S clusters are also required for another mitochondrial protein to function; this protein is involved in the modification of additional proteins that aid in energy production in mitochondria, including the pyruvate dehydrogenase complex and the alpha-ketoglutarate dehydrogenase complex. This modification is also critical to the function of the glycine cleavage system, a set of proteins that breaks down a protein building block (amino acid) called glycine when levels become too high.

The other version of the BOLA3 protein is found in the fluid-filled space inside the cell (the cytoplasm). While this protein is likely involved in Fe-S cluster formation in the cytoplasm, the role of this isoform is not well understood.

Health Conditions Related to Genetic Changes

Multiple mitochondrial dysfunctions syndrome

At least three mutations in the *BOLA3* gene have been found to cause multiple mitochondrial dysfunctions syndrome. This severe condition is characterized by impairment of more than one mitochondrial function, such as reduced activity of complex I, II, or III, pyruvate dehydrogenase, alpha-ketoglutarate dehydrogenase, or the glycine cleavage system. Affected infants often have severe brain dysfunction (encephalopathy) and elevated levels of a chemical called lactic acid in the body (lactic acidosis). These babies usually do not survive past infancy.

BOLA3 gene mutations lead to production of an altered protein that is likely broken down quickly. Although some mutations affect both isoforms of the BOLA3 protein, loss of the mitochondrial version appears to be responsible for the condition. The lack of mitochondrial BOLA3 protein impairs Fe-S cluster formation. Consequently, proteins affected by the presence of Fe-S clusters, including those involved in energy production and glycine breakdown, cannot function normally. Reduced activity of complex I, II, or III, pyruvate dehydrogenase, or alpha-ketoglutarate dehydrogenase leads to potentially fatal lactic acidosis, encephalopathy, and other signs and symptoms of multiple mitochondrial dysfunctions syndrome. In some affected individuals, impairment of the glycine cleavage system leads to a buildup of glycine (hyperglycinemia).

Other Names for This Gene

- bolA homolog 3
- bolA-like protein 3
- bolA-like protein 3 isoform 1
- bolA-like protein 3 isoform 2
- BOLA3_HUMAN
- MMDS2

Additional Information & Resources

Tests Listed in the Genetic Testing Registry

- Tests of BOLA3 (https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=388962[geneid])

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28BOLA3%5BTIAB%5D%29+AND+%28%28Genes%5BMH%5D%29+OR+%28Genetic+Phenomena%5BMH%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+3600+days%22%5Bdp%5D)

Catalog of Genes and Diseases from OMIM

- BOLA FAMILY MEMBER 3; BOLA3 (https://omim.org/entry/613183)

Gene and Variant Databases

- NCBI Gene (https://www.ncbi.nlm.nih.gov/gene/388962)
- ClinVar (https://www.ncbi.nlm.nih.gov/clinvar?term=BOLA3[gene])

References

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Genomic Location

The *BOLA3* gene is found on chromosome 2 (https://medlineplus.gov/genetics/chromosome/2/).

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