EXOSC3 gene

exosome component 3

Normal Function

The *EXOSC3* gene provides instructions for making a protein known as exosome component 3. As its name suggests, this protein forms one part (subunit) of a large, multi-protein complex known as the RNA exosome. Within cells, this complex helps to process multiple types of RNA, which are chemical cousins of DNA, by cutting (cleaving) RNA molecules in certain places. The RNA exosome also breaks down (degrades) molecules of RNA when they are no longer needed. Appropriate processing and breakdown of RNA molecules is essential for the normal functioning of all cells.

Studies suggest that the activity of exosome component 3 is necessary for the normal development and growth of certain areas of the brain, particularly the cerebellum, which is the part of the brain that coordinates movement. Exosome component 3 also appears to be important for the survival of specialized nerve cells in the spinal cord called motor neurons, which play an essential role in muscle movement.

Health Conditions Related to Genetic Changes

Pontocerebellar hypoplasia

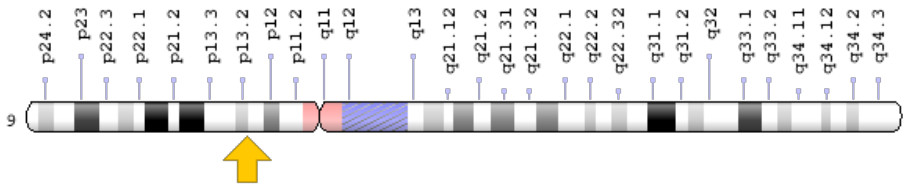
At least 16 mutations in the *EXOSC3* gene have been identified in people with a disorder of brain development called pontocerebellar hypoplasia. The major features of this condition include delayed development overall, an unusually small head size (microcephaly), and intellectual disability. *EXOSC3* gene mutations cause about half of all cases of a form of the disorder designated pontocerebellar hypoplasia type 1 (PCH1). When PCH1 results from *EXOSC3* gene mutations, it is sometimes categorized more specifically as PCH1B. In addition to the features listed above, PCH1B causes problems with muscle movement resulting from a loss of specialized nerve cells called motor neurons in the spinal cord.

The *EXOSC3* gene mutations that cause PCH1B result in an exosome component 3 protein with reduced or no function. The most common mutation alters a single protein building block (amino acid) in exosome component 3; it replaces the amino acid aspartic acid with the amino acid alanine at protein position 132 (written as Asp132Ala or D132A). People with this mutation tend to have somewhat less severe brain abnormalities than people with other *EXOSC3* gene mutations. Changes in this gene likely impair the activity of the RNA exosome, but it is unclear how these alterations lead to the problems with brain development and loss of motor neurons characteristic of PCH1B.

Chromosomal Location

Cytogenetic Location: 9p13.2, which is the short (p) arm of chromosome 9 at position 13.2

Molecular Location: base pairs 37,779,714 to 37,785,092 on chromosome 9 (Homo sapiens Annotation Release 109, GRCh38.p12) (NCBI)



Credit: Genome Decoration Page/NCBI

Other Names for This Gene

- bA3J10.7
- CGI-102
- exosome complex component RRP40
- exosome complex exonuclease RRP40
- hRrp-40
- hRrp40p
- p10
- PCH1B
- ribosomal RNA-processing protein 40
- RRP40
- Rrp40p

Additional Information & Resources

Educational Resources

- Genomes (second edition, 2002): Degradation of mRNAs https://www.ncbi.nlm.nih.gov/books/NBK21132/#A7399
- Marie Curie Bioscience Database: Structural Components and Architectures of RNA Exosomes https://www.ncbi.nlm.nih.gov/books/NBK45033/

Clinical Information from GeneReviews

- EXOSC3-Related Pontocerebellar Hypoplasia
  https://www.ncbi.nlm.nih.gov/books/NBK236968

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28EXOSC3%5BTIAB%5D%29+OR+%28%28hRrp40p%5BTIAB%5D%29+OR+%28RRP40%5BTIAB%5D%29+OR+%28Rrp40p%5BTIAB%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

- EXOSOME COMPONENT 3
  http://omim.org/entry/606489

Research Resources

- ClinVar
  https://www.ncbi.nlm.nih.gov/clinvar?term=EXOSC3%5Bgene%5D
- HGNC Gene Symbol Report
  https://www.genenames.org/data/gene-symbol-report/#!/hgnc_id/HGNC:17944
- Monarch Initiative
  https://monarchinitiative.org/gene/NCBIGene:51010
- NCBI Gene
  https://www.ncbi.nlm.nih.gov/gene/51010
- UniProt
  https://www.uniprot.org/uniprot/Q9NQT5

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