

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.

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

Tests Listed in the Genetic Testing Registry

- Tests of EXOSC3 ([https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=51010\[geneid\]](https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=51010[geneid]))

Scientific Articles on PubMed

- PubMed (<https://pubmed.ncbi.nlm.nih.gov/?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%29>)

Catalog of Genes and Diseases from OMIM

- EXOSOME COMPONENT 3; EXOSC3 (<https://omim.org/entry/606489>)

Gene and Variant Databases

- NCBI Gene (<https://www.ncbi.nlm.nih.gov/gene/51010>)
- ClinVar ([https://www.ncbi.nlm.nih.gov/clinvar?term=EXOSC3\[gene\]](https://www.ncbi.nlm.nih.gov/clinvar?term=EXOSC3[gene]))

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Genomic Location

The *EXOSC3* gene is found on chromosome 9 (<https://medlineplus.gov/genetics/chromosome/9/>).

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