RRM2B gene

ribonucleotide reductase regulatory TP53 inducible subunit M2B

Normal Function

The *RRM2B* gene provides instructions for making one piece, called the p53 inducible small subunit (p53R2), of a protein called ribonucleotide reductase (RNR). Two copies of the p53R2 subunit are attached to two copies of another protein called R1 to form RNR. (R1 can also attach to another small subunit, called R2, to make another form of RNR). Whether made with p53R2 or R2, RNR helps produce DNA building blocks (nucleotides), which are joined to one another in a particular order to form DNA.

RNRs containing p53R2 make nucleotides that are used for the formation of DNA in specialized cell structures called mitochondria. Although most DNA is packaged in chromosomes within the cell's nucleus (nuclear DNA), mitochondria also have a small amount of their own DNA (mitochondrial DNA or mtDNA). Mitochondria are the energy-producing centers in cells, and the DNA in these structures contains genes essential for the process of energy production (called oxidative phosphorylation). The production of nucleotides by p53R2 also helps maintain a normal amount of mtDNA in cells.

Health Conditions Related to Genetic Changes

Mitochondrial neurogastrointestinal encephalopathy disease

MedlinePlus Genetics provides information about Mitochondrial neurogastrointestinal encephalopathy disease

Progressive external ophthalmoplegia

At least 17 mutations in the *RRM2B* gene have been identified in people with an eye condition called progressive external ophthalmoplegia. This disorder weakens the muscles that control eye movement and causes the eyelids to droop (ptosis). Some affected individuals have additional signs and symptoms, such as weakness of other muscles, extreme tiredness (fatigue), hearing loss caused by problems with the inner ear (sensorineural hearing loss), and digestive problems.

Typically, mutations that cause progressive external ophthalmoplegia occur in one copy of the *RRM2B* gene, although rarely both copies of the gene are altered. *RRM2B* gene mutations associated with progressive external ophthalmoplegia lead to impaired RNR

activity. These mutations result in large deletions of genetic material from mtDNA in muscle tissue, possibly because impairment of RNR activity leads to a shortage of nucleotides, although the mechanism is unclear. Researchers have not determined how deletions of mtDNA lead to the specific signs and symptoms of progressive external ophthalmoplegia, although the features of the condition may be related to impaired oxidative phosphorylation. It has been suggested that eye muscles are commonly affected by mitochondrial defects because they are especially dependent on oxidative phosphorylation for energy.

RRM2B-related mitochondrial DNA depletion syndrome, encephalomyopathic form with renal tubulopathy

More than a dozen mutations in the *RRM2B* gene can cause *RRM2B*-related mitochondrial DNA depletion syndrome, encephalomyopathic form with renal tubulopathy (*RRM2B*-MDS), a severe condition that affects multiple body systems. It typically leads to brain dysfunction combined with muscle weakness (encephalomyopathy) and a problem with kidney function known as renal tubulopathy. The mutations that cause this disorder occur in both copies of the *RRM2B* gene. They reduce the activity or amount of RNR, which likely impairs production of mtDNA nucleotides. A shortage of nucleotides available for the production of mtDNA molecules leads to a reduction in the amount of mtDNA (known as mtDNA depletion) and impairs mitochondrial function in many different types of cells.

Impairment of oxidative phosphorylation is thought to underlie the signs and symptoms of mitochondrial DNA depletion syndrome. It is unclear why some *RRM2B* gene mutations result in deletions of genetic material from mtDNA (as in progressive external ophthalmoplegia, described above) and others reduce the overall amount of mtDNA (as in *RRM2B*-MDS).

Other Names for This Gene

- MTDPS8A
- MTDPS8B
- p53-inducible ribonucleotide reductase small subunit 2 homolog
- p53-inducible ribonucleotide reductase small subunit 2 short form beta
- p53-inducible ribonucleotide reductase small subunit 2-like protein
- P53R2
- ribonucleoside-diphosphate reductase subunit M2 B isoform 1
- ribonucleoside-diphosphate reductase subunit M2 B isoform 2
- ribonucleoside-diphosphate reductase subunit M2 B isoform 3
- ribonucleotide reductase M2 B (TP53 inducible)
- TP53-inducible ribonucleotide reductase M2 B

Additional Information & Resources

Tests Listed in the Genetic Testing Registry

- Tests of RRM2B (https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=50484[geneid])

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28%28RRM2B%5BTIAB%5D%29+OR+%28ribonucleotide+reductase+regulatory+TP53+inducible+subunit+M2B%5BTIAB%5D%29%29+AND+%28%28Genes%5BMH%5D%29+OR+%28Genetic+Phenomena%5BMH%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1800+days%22%5Bdp%5D)

Catalog of Genes and Diseases from OMIM

- RIBONUCLEOTIDE REDUCTASE REGULATORY TP53 INDUCIBLE SUBUNIT M2B; RRM2B (https://omim.org/entry/604712)

Gene and Variant Databases

- NCBI Gene (https://www.ncbi.nlm.nih.gov/gene/50484)
- ClinVar (https://www.ncbi.nlm.nih.gov/clinvar?term=RRM2B[gene])

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Genomic Location

The *RRM2B* gene is found on chromosome 8 (https://medlineplus.gov/genetics/chromosome/8/).

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