RMRP Gene

Subjects: Genetics & Heredity

Contributor: Karina Chen

RNA component of mitochondrial RNA processing endoribonuclease

genes

1. Normal Function

Unlike many genes, the *RMRP* gene does not contain instructions for making a protein. Instead, a molecule called a noncoding RNA, a chemical cousin of DNA, is produced from the *RMRP* gene. Several proteins attach (bind) to this RNA molecule, forming an enzyme called mitochondrial RNA-processing endoribonuclease, or RNase MRP.

The RNase MRP enzyme is thought to be involved in several important processes in the cell. For example, it likely helps copy (replicate) the DNA found in the energy-producing centers of cells (mitochondria). The RNase MRP enzyme also processes ribosomal RNA, which is required for assembling protein building blocks (amino acids) into functioning proteins. In addition, this enzyme helps control the cell cycle, which is the cell's way of replicating itself in an organized, step-by-step fashion.

2. Health Conditions Related to Genetic Changes

2.1. Anauxetic dysplasia

At least four *RMRP* gene mutations have been identified in people with anauxetic dysplasia, a disorder characterized by severe short stature (dwarfism) and other skeletal abnormalities. The *RMRP* gene mutations that cause anauxetic dysplasia alter the noncoding RNA produced from the gene, and the RNase MRP enzyme containing the altered noncoding RNA is impaired in its ribosomal RNA processing function. Although the specific mechanism is unknown, impairment of this function likely disrupts skeletal development, leading to the signs and symptoms of anauxetic dysplasia.

2.2. Cartilage-hair hypoplasia

More than 100 mutations that cause cartilage-hair hypoplasia have been identified in the *RMRP* gene. Approximately 90 percent of cases of this disorder result from a mutation in which the DNA building block (nucleotide) guanine is substituted for the nucleotide adenine at position 70 in the *RMRP* gene (written as 70A>G). This mutation is found in almost all known affected individuals in the Amish population, approximately 92 percent of affected individuals of Finnish descent, and about half of affected individuals in other populations.

Mutations in the *RMRP* gene likely result in the production of a noncoding RNA that cannot bind to some of the proteins that are normally part of the RNase MRP enzyme complex. These changes are believed to affect the activity of the enzyme, which interferes with its important functions within cells. Impaired RNase MRP enzyme complex causes dwarfism, skeletal abnormalities, abnormal immune system function (immune deficiency), elevated cancer risk, sparse hair growth (hypotrichosis), and other signs and symptoms of cartilage-hair hypoplasia.

2.3. Other disorders

RMRP gene mutations, including some of the same mutations that cause cartilage-hair hypoplasia (described above), may result in a similar disorder known as metaphyseal dysplasia without hypotrichosis. This condition is characterized by short stature and skeletal abnormalities that are usually less severe than those seen in cartilage-hair hypoplasia. Individuals with metaphyseal dysplasia without hypotrichosis do not have any changes in the structure or appearance of their hair, but they may have immune deficiency and an increased risk of developing cancer. It is unknown why the same mutations may cause both of these conditions. Together with anauxetic dysplasia, they are often referred to as cartilage-hair hypoplasia spectrum disorders, with anauxetic dysplasia as the most severe form and metaphyseal dysplasia without hypertrichosis on the mild end of the spectrum.

3. Other Names for This Gene

- CHH
- NME1
- RMRPR
- RRP2

References

1. Hermanns P, Bertuch AA, Bertin TK, Dawson B, Schmitt ME, Shaw C, Zabel B, Lee B. Consequences of mutations in the non-coding RMRP RNA in cartilage-hairhypoplasia. Hum Mol Genet. 2005 Dec 1;14(23):3723-40.
2. Hermanns P, Tran A, Munivez E, Carter S, Zabel B, Lee B, Leroy JG. RMRPmutations in cartilage-hair hypoplasia. Am J Med Genet A. 2006 Oct1;140(19):2121-30.
3. Hirose Y, Nakashima E, Ohashi H, Mochizuki H, Bando Y, Ogata T, Adachi M, TobaE, Nishimura G, Ikegawa S. Identification of novel RMRP mutations and specificfounder haplotypes in

Japanese patients with cartilage-hair hypoplasia. J HumGenet. 2006;51(8):706-710. doi: 10.1007/s10038-006-0015-3.

4. Martin AN, Li Y. RNase MRP RNA and human genetic diseases. Cell Res. 2007Mar;17(3):219-26. Review.
5. Ridanpää M, Sistonen P, Rockas S, Rimoin DL, Mäkitie O, Kaitila I. Worldwidemutation spectrum in cartilage-hair hypoplasia: ancient founder origin of themajor70A-->G mutation of the untranslated RMRP. Eur J Hum Genet. 2002Jul;10(7):439-47.
6. Ridanpää M, van Eenennaam H, Pelin K, Chadwick R, Johnson C, Yuan B,vanVenrooij W, Pruijn G, Salmela R, Rockas S, Mäkitie O, Kaitila I, de laChapelle A. Mutations in the RNA component of RNase MRP cause a pleiotropic humandisease, cartilage-hair hypoplasia. Cell. 2001 Jan 26;104(2):195-203.
7. Thiel CT, Horn D, Zabel B, Ekici AB, Salinas K, Gebhart E, Rüschendorf F,Sticht H, Spranger J, Müller D, Zweier C, Schmitt ME, Reis A, Rauch A. Severelyincapacitating mutations in patients with extreme short stature identifyRNA-processing endoribonuclease RMRP as an essential cell growth regulator. Am J Hum Genet. 2005 Nov;77(5):795-806.
8. Thiel CT, Mortier G, Kaitila I, Reis A, Rauch A. Type and level of RMRPfunctional impairment predicts phenotype in the cartilage hairhypoplasia-anauxetic dysplasia spectrum. Am J Hum Genet. 2007 Sep;81(3):519-29.
9. Thiel CT, Rauch A. The molecular basis of the cartilage-hairhypoplasia-anauxetic dysplasia spectrum. Best Pract Res Clin Endocrinol Metab.2011 Feb;25(1):131-42. doi: 10.1016/j.beem.2010.08.004. Review.