RPGR Gene

Subjects: Genetics & Heredity
Contributor: Karina Chen

retinitis pigmentosa GTPase regulator

Keywords: genes

1. Normal Function

The *RPGR* gene provides instructions for making a protein that is essential for normal vision. Although the protein's function is not well understood, studies suggest that it plays an important role in cell structures called cilia. Cilia are microscopic, finger-like projections that stick out from the surface of many types of cells. They are involved in cell movement and many different chemical signaling pathways. Cilia are also necessary for the perception of sensory input, including hearing, smell, and vision.

Several different versions (isoforms) of the RPGR protein are produced from the *RPGR* gene. One version contains a segment known as the ORF15 exon. This version of the RPGR protein is active (expressed) predominantly in the retina, which is the light-sensitive tissue at the back of the eye. Specifically, the ORF15-containing isoform is found in the retina's specialized light receptor cells (photoreceptors). Researchers suspect that this isoform may help maintain photoreceptors by regulating the function of cilia. Other isoforms of the RPGR protein are expressed in other parts of the body, where they are probably also involved in cilia function.

2. Health Conditions Related to Genetic Changes

2.1. Retinitis pigmentosa

More than 300 mutations in the *RPGR* gene have been found to cause the X-linked form of retinitis pigmentosa. This condition primarily affects males, causing night blindness in early childhood followed by progressive daytime vision loss. *RPGR* gene mutations account for about 70 percent of all cases of X-linked retinitis pigmentosa.

Most of the mutations responsible for X-linked retinitis pigmentosa occur in the ORF15 exon of the RPGR protein. These mutations usually result in an abnormally short, malfunctioning protein. Changes in the structure of the RPGR protein likely disrupt the normal function of cilia in photoreceptor cells. However, it is unclear how these changes lead to the gradual loss of photoreceptors and resulting vision problems that are characteristic of retinitis pigmentosa.

2.2. Other disorders

Although most *RPGR* gene mutations cause X-linked retinitis pigmentosa, a few mutations in the ORF15 exon have been found in people with other retinal disorders. These include cone-rod dystrophy, cone dystrophy, and atrophic macular degeneration. These retinal disorders are characterized by progressive vision abnormalities, although their signs and symptoms are distinct from retinitis pigmentosa.

Several additional *RPGR* gene mutations have been reported in people with a combination of retinitis pigmentosa and signs and symptoms affecting other parts of the body. In addition to progressive vision loss, affected individuals have had chronic respiratory and sinus infections, recurrent ear infections (otitis media), and hearing loss.

It is unclear why mutations in the *RPGR* gene can cause a variety of disorders. Studies suggest that certain mutations may disrupt the function of cilia in multiple tissues, including the inner ear and respiratory tract. Malfunctioning cilia in these tissues may underlie the hearing loss and respiratory abnormalities seen in some affected individuals. However, researchers are still working to determine how *RPGR* gene mutations cause specific abnormalities involving the retina and other parts of the body.

Other Names for This Gene

- COD1
- CORDX1
- CRD
- PCDX
- retinitis pigmentosa 15
- retinitis pigmentosa 3 GTPase regulator
- RP15
- RP3
- RPGR_HUMAN
- X-linked retinitis pigmentosa GTPase regulator
- XLRP3

References

1. Ayyagari R, Demirci FY, Liu J, Bingham EL, Stringham H, Kakuk LE, Boehnke M,Gorin MB, Richards JE, Sieving PA. X-linked recessive atrophic maculardegeneration from RPGR mutation. Genomics. 2002 Aug;80(2):166-71.
2. Demirci FY, Rigatti BW, Wen G, Radak AL, Mah TS, Baic CL, Traboulsi EI,Alitalo T, Ramser J, Gorin MB. X-linked cone-rod dystrophy (locus COD1):identification of mutations in RPGR exon ORF15. Am J Hum Genet. 2002Apr;70(4):1049-53.
3. Ebenezer ND, Michaelides M, Jenkins SA, Audo I, Webster AR, Cheetham ME,Stockman A, Maher ER, Ainsworth JR, Yates JR, Bradshaw K, Holder GE, Moore AT,Hardcastle AJ. Identification of novel RPGR ORF15 mutations in X-linked progressive cone-rod dystrophy (XLCORD) families. Invest Ophthalmol Vis Sci. 2005Jun;46(6):1891-8.
4. Iannaccone A, Breuer DK, Wang XF, Kuo SF, Normando EM, Filippova E, Baldi A,Hiriyanna S, MacDonald CB, Baldi F, Cosgrove D, Morton CC, Swaroop A, JablonskiMM. Clinical and immunohistochemical evidence for an X linked retinitis pigmentosa syndrome with recurrent infections and hearing loss in associationwith an RPGR mutation. J Med Genet. 2003 Nov;40(11):e118.
5. Moore A, Escudier E, Roger G, Tamalet A, Pelosse B, Marlin S, Clément A,Geremek M, Delaisi B, Bridoux AM, Coste A, Witt M, Duriez B, Amselem S. RPGR ismutated in patients with a complex X linked phenotype combining primary cili arydyskinesia and retinitis pigmentosa. J Med Genet. 2006 Apr;43(4):326-33.
6. Murga-Zamalloa C, Swaroop A, Khanna H. Multiprotein complexes of RetinitisPigmentosa GTPase regulator (RPGR), a ciliary protein mutated in X-linkedRetinitis Pigmentosa (XLRP). Adv Exp Med Biol. 2010;664:105-14. doi:10.1007/978-1-4419-1399-9_13. Review.
7. Pelletier V, Jambou M, Delphin N, Zinovieva E, Stum M, Gigarel N, Dollfus H,Hamel C, Toutain A, Dufier JL, Roche O, Munnich A, Bonnefont JP, Kaplan J, Rozet JM. Comprehensive survey of mutations in RP2 and RPGR in patients affected withdistinct retinal dystrophies: genotype-phenotype correlations and impact ongenetic counseling. Hum Mutat. 2007 Jan;28(1):81-91.
8. Shu X, Black GC, Rice JM, Hart-Holden N, Jones A, O'Grady A, Ramsden S, WrightAF. RPGR mutation analysis and disease: an update. Hum Mutat. 2007Apr;28(4):322-8.
9. Vervoort R, Lennon A, Bird AC, Tulloch B, Axton R, Miano MG, Meindl A,Meitinger T, Ciccodicola A, Wright AF. Mutational hot spot within a new RPGR exonin X-linked retinitis pigmentosa. Nat Genet. 2000 Aug;25(4):462-6.
10. Wright AF, Shu X. Focus on Molecules: RPGR. Exp Eye Res. 2007 Jul;85(1):1-2.
11. Yang Z, Peachey NS, Moshfeghi DM, Thirumalaichary S, Chorich L, Shugart YY,Fan K, Zhang K. Mutations in the RPGR gene cause X-linked cone dystrophy. Hum MolGenet. 2002 Mar 1;11(5):605-11.
12. Zito I, Downes SM, Patel RJ, Cheetham ME, Ebenezer ND, Jenkins SA,Bhattacharya SS, Webster AR, Holder GE, Bird AC, Bamiou DE, Hardcastle AJ. RPGRmutation associated with retinitis pigmentosa, impaired hearing, andsinorespiratory infections. J Med Genet. 2003 Aug;40(8):609-15.