CRPPA gene

CDP-L-ribitol pyrophosphorylase A

Normal Function

The *CRPPA* gene provides instructions for making a protein that is involved in a process called glycosylation. Through this chemical process, sugar molecules are added to certain proteins. In particular, the CRPPA protein helps produce a molecule called ribitol 5-phosphate, which is an important component of the chain of sugar molecules added to a protein called alpha (α)-dystroglycan. Glycosylation is critical for the normal function of α-dystroglycan.

The α-dystroglycan protein helps anchor the structural framework inside each cell (cytoskeleton) to the lattice of proteins and other molecules outside the cell (extracellular matrix). In skeletal muscles, glycosylated α-dystroglycan helps stabilize and protect muscle fibers. In the brain, it helps direct the movement (migration) of nerve cells (neurons) during early development.

Health Conditions Related to Genetic Changes

Walker-Warburg syndrome

At least 17 mutations in the *CRPPA* gene have been found to cause Walker-Warburg syndrome, the most severe form of a group of disorders known as congenital muscular dystrophies. Walker-Warburg syndrome causes skeletal muscle weakness and abnormalities of the brain and eyes. Because of the severity of the problems caused by this condition, affected individuals usually do not survive past early childhood.

CRPPA gene mutations involved in Walker-Warburg syndrome prevent the normal glycosylation of α-dystroglycan. As a result, α-dystroglycan can no longer effectively anchor cells to the proteins and other molecules that surround them. Without functional α -dystroglycan to stabilize the muscle fibers, they become damaged as they repeatedly contract and relax with use. The damaged fibers weaken and die over time, which affects the development, structure, and function of skeletal muscles in people with Walker-Warburg syndrome.

Defective α-dystroglycan also affects the migration of neurons during the early development of the brain. Instead of stopping when they reach their intended destinations, some neurons migrate past the surface of the brain into the fluid-filled

space that surrounds it. Researchers believe that this problem with neuronal migration causes a brain abnormality called cobblestone lissencephaly, in which the surface of the brain lacks the normal folds and grooves and instead appears bumpy and irregular. Less is known about the effects of *CRPPA* gene mutations on other parts of the body.

Limb-girdle muscular dystrophy

MedlinePlus Genetics provides information about Limb-girdle muscular dystrophy

Other Names for This Gene

- 2-C-methyl-D-erythritol 4-phosphate cytidylyltransferase-like protein
- 4-diphosphocytidyl-2C-methyl-D-erythritol synthase homolog
- hCG_1745121
- isoprenoid synthase domain containing
- isoprenoid synthase domain-containing protein
- IspD
- ISPD
- ISPD_HUMAN
- MDDGA7
- Nip
- notch1-induced protein

Additional Information & Resources

Tests Listed in the Genetic Testing Registry

- Tests of CRPPA (https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=729920[geneid])

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28ISPD%5BTIAB%5D%29+OR+%28IspD%5BTIAB%5D%29+AND+%28%28Genes%5BMH%5D%29+OR+%28Genetic+Phenomena%5BMH%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

- CDP-L-RIBITOL PYROPHOSPHORYLASE A; CRPPA (https://omim.org/entry/614631)

Gene and Variant Databases

- NCBI Gene (https://www.ncbi.nlm.nih.gov/gene/729920)
- ClinVar (https://www.ncbi.nlm.nih.gov/clinvar?term=CRPPA[gene])

References

- Cirak S, Foley AR, Herrmann R, Willer T, Yau S, Stevens E, Torelli S, Brodd L, Kamynina A, Vondracek P, Roper H, Longman C, Korinthenberg R, Marrosu G, NurnbergP; UK10K Consortium; Michele DE, Plagnol V, Hurles M, Moore SA, Sewry CA,Campbell KP, Voit T, Muntoni F. ISPD gene mutations are a common cause ofcongenital and limb-girdle muscular dystrophies. Brain. 2013 Jan;136(Pt1):269-81. doi: 10.1093/brain/aws312. Epub 2013 Jan 3. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/23288328) or Free article on PubMed Central (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3562076/)
- Gerin I, Ury B, Breloy I, Bouchet-Seraphin C, Bolsee J, Halbout M, Graff J, Vertommen D, Muccioli GG, Seta N, Cuisset JM, Dabaj I, Quijano-Roy S, Grahn A, Van Schaftingen E, Bommer GT. ISPD produces CDP-ribitol used by FKTN and FKRP totransfer ribitol phosphate onto alpha-dystroglycan. Nat Commun. 2016 May 19;7:11534.doi: 10.1038/ncomms11534. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/27194101) or Free article on PubMed Central (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4873967/)
- Kanagawa M, Kobayashi K, Tajiri M, Manya H, Kuga A, Yamaguchi Y, Akasaka-ManyaK, Furukawa JI, Mizuno M, Kawakami H, Shinohara Y, Wada Y, Endo T, Toda T.Identification of a Post-translational Modification with Ribitol-Phosphate andIts Defect in Muscular Dystrophy. Cell Rep. 2016 Mar 8;14(9):2209-2223. doi:10.1016/j.celrep.2016.02.017. Epub 2016 Feb 25. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/26923585)
- Roscioli T, Kamsteeg EJ, Buysse K, Maystadt I, van Reeuwijk J, van den ElzenC, van Beusekom E, Riemersma M, Pfundt R, Vissers LE, Schraders M, Altunoglu U, Buckley MF, Brunner HG, Grisart B, Zhou H, Veltman JA, Gilissen C, Mancini GM, Delree P, Willemsen MA, Ramadza DP, Chitayat D, Bennett C, Sheridan E, PeetersEA, Tan-Sindhunata GM, de Die-Smulders CE, Devriendt K, Kayserili H, El-HashashOA, Stemple DL, Lefeber DJ, Lin YY, van Bokhoven H. Mutations in ISPD causeWalker-Warburg syndrome and defective glycosylation of alpha-dystroglycan. Nat Genet.2012 May;44(5):581-5. doi: 10.1038/ng.2253. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/22522421) or Free article on PubMed Central (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3378661/)
- Tasca G, Moro F, Aiello C, Cassandrini D, Fiorillo C, Bertini E, Bruno C,Santorelli FM, Ricci E. Limb-girdle muscular dystrophy with alpha-dystroglycandeficiency and mutations in the ISPD gene. Neurology. 2013 Mar 5;80(10):963-5.doi: 10.1212/WNL.0b013e3182840cbc. Epub 2013 Feb 6. No abstract available. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/23390185)
- Willer T, Lee H, Lommel M, Yoshida-Moriguchi T, de Bernabe DB, Venzke D, CirakS, Schachter H, Vajsar J, Voit T, Muntoni F, Loder AS, Dobyns WB, Winder TL, Strahl S, Mathews KD, Nelson SF, Moore SA, Campbell KP. ISPD loss-of-

functionmutations disrupt dystroglycan O-mannosylation and cause Walker-Warburg syndrome. Nat Genet. 2012 May;44(5):575-80. doi: 10.1038/ng.2252. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/22522420) or Free article on PubMed Central (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3371168/)

Genomic Location

The *CRPPA* gene is found on chromosome 7 (https://medlineplus.gov/genetics/chromosome/7/).

Last updated January 1, 2017