DOK7 gene

docking protein 7

Normal Function

The *DOK7* gene provides instructions for making a protein that helps form connections between nerve cells and muscle cells at the neuromuscular junction. The neuromuscular junction is the area between nerve cells and muscle cells where signals are passed on to trigger muscle movement.

The Dok-7 protein participates in turning on (activating) a protein called MuSK that helps organize the various proteins that are important for developing and maintaining the neuromuscular junction. In particular, MuSK is involved in gathering a protein called the acetylcholine receptor (AChR) on the surface of the muscle cells at the neuromuscular junction. The AChR protein is critical for signaling between nerve and muscle cells.

Health Conditions Related to Genetic Changes

Congenital myasthenic syndromes

Many variants (also called mutations) in the *DOK7* gene have been found to cause congenital myasthenic syndromes. These are a group of conditions that are characterized by weak muscles that tire easily (myasthenia). The myasthenia in people with these conditions typically begins shortly after birth or during early childhood.

Variants in the *DOK7* gene can cause cells to produce an altered version of the Dok-7 protein that cannot activate the MuSK protein. As a result, less AChR is present in the neuromuscular junction, which reduces signaling between nerve and muscle cells. These signaling abnormalities lead to decreased muscle movement and the muscle weakness that is characteristic of congenital myasthenic syndromes.

Other disorders

In rare cases, variants in the *DOK7* gene have been found to cause a condition called fetal akinesia deformation sequence. This severe condition is characterized by a lack of movement before birth (fetal akinesia) and multiple physical abnormalities. The lack of fetal movement results in joint stiffness (arthrogryposis). Affected individuals often have slow growth before birth, underdevelopment of the lungs (pulmonary hypoplasia), and

an opening in the roof of the mouth (cleft palate).

Fetal akinesia deformation sequence caused by *DOK7* gene variants is typically fatal before birth. The *DOK7* gene variants that cause fetal akinesia deformation sequence often cause cells to produce a nonfunctional version of the Dok-7 protein. This likely impairs the signaling between nerve and muscle cells, leading to fetal akinesia.

Other Names for This Gene

- C4orf25
- CMS1B
- Dok-7
- DOK7_HUMAN
- downstream of tyrosine kinase 7

Additional Information & Resources

Tests Listed in the Genetic Testing Registry

- Tests of DOK7 (https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=285489[geneid])

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=(DOK7%5BTIAB%5D)+OR+(Dok-7%5BTIAB%5D)+AND+((Genes%5BMH%5D)+OR+(Genetic+Phenomena%5BMH%5D))+AND+english%5Bla%5D+AND+human%5Bmh%5D)

Catalog of Genes and Diseases from OMIM

- DOWNSTREAM OF TYROSINE KINASE 7; DOK7 (https://omim.org/entry/610285)

Gene and Variant Databases

- NCBI Gene (https://www.ncbi.nlm.nih.gov/gene/285489)
- ClinVar (https://www.ncbi.nlm.nih.gov/clinvar?term=DOK7[gene])

References

- Abicht A, Muller JS, Lochmuller H. Congenital Myasthenic Syndromes Overview. 2003 May 9 [updated 2021 Dec 23]. In: Adam MP, Bick S, Mirzaa GM, Pagon RA, Wallace SE, Amemiya A, editors. GeneReviews(R) [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2026. Available fromhttp://www.ncbi.nlm.nih.

gov/books/NBK1168/ Citation on PubMed (https://www.ncbi.nlm.nih.gov/pubmed/20301347)

- Beeson D, Webster R, Cossins J, Lashley D, Spearman H, Maxwell S, Slater CR, Newsom-Davis J, Palace J, Vincent A. Congenital myasthenic syndromes and theformation of the neuromuscular junction. Ann N Y Acad Sci. 2008;1132:99-103. doi:10.1196/annals.1405.049. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/18567858)
- Engel AG, Shen XM, Selcen D, Sine SM. What have we learned from the congenitalmyasthenic syndromes. J Mol Neurosci. 2010 Jan;40(1-2):143-53. doi:10.1007/s12031-009-9229-0. Epub 2009 Aug 18. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/19688192) or Free article on PubMed Central (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3050586/)
- Engel AG. Current status of the congenital myasthenic syndromes. NeuromusculDisord. 2012 Feb;22(2):99-111. doi: 10.1016/j.nmd.2011.10.009. Epub 2011 Nov 21. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/22104196) or Free article on PubMed Central (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3269564/)
- Kinali M, Beeson D, Pitt MC, Jungbluth H, Simonds AK, Aloysius A, Cockerill H, Davis T, Palace J, Manzur AY, Jimenez-Mallebrera C, Sewry C, Muntoni F, Robb SA.Congenital myasthenic syndromes in childhood: diagnostic and managementchallenges. J Neuroimmunol. 2008 Sep 15;201-202:6-12. doi:10.1016/j.jneuroim.2008.06.026. Epub 2008 Aug 15. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/18707767)
- Muller JS, Herczegfalvi A, Vilchez JJ, Colomer J, Bachinski LL, Mihaylova V,Santos M, Schara U, Deschauer M, Shevell M, Poulin C, Dias A, Soudo A, Hietala M, Aarimaa T, Krahe R, Karcagi V, Huebner A, Beeson D, Abicht A, Lochmuller H. Phenotypical spectrum of DOK7 mutations in congenital myasthenic syndromes. Brain. 2007 Jun;130(Pt 6):1497-506. doi: 10.1093/brain/awm068. Epub 2007 Apr 17. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/17439981)
- Radhakrishnan P, Shukla A, Girisha KM, Nayak SS. Biallelic c.1263dupC in DOK7results in fetal akinesia deformation sequence. Am J Med Genet A. 2020Apr;182(4):804-807. doi: 10.1002/ajmg.a.61473. Epub 2019 Dec 27. Citation on PubMed (https://www.ncbi.nlm.nih.gov/pubmed/31880392)
- Selcen D, Milone M, Shen XM, Harper CM, Stans AA, Wieben ED, Engel AG. Dok-7myasthenia: phenotypic and molecular genetic studies in 16 patients. Ann Neurol. 2008 Jul;64(1):71-87. doi: 10.1002/ana.21408. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/18626973) or Free article on PubMed Central (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2570015/)

Genomic Location

The *DOK7* gene is found on chromosome 4 (https://medlineplus.gov/genetics/chromosome/4/).

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