SUCLA2-related mitochondrial DNA depletion syndrome

Description

SUCLA2-related mitochondrial DNA (mtDNA) depletion syndrome is an inherited disorder that affects the early development of the brain. Affected infants typically develop weak muscle tone (hypotonia) in the first few months of life. In these infants, hypotonia can delay the development of motor skills such as lifting the head and rolling over. Children with *SUCLA2*-related mtDNA depletion syndrome typically have difficulty eating and may require a feeding tube; as a result, they have difficulty growing and gaining weight as expected (failure to thrive).

Additional features of *SUCLA2*-related mtDNA depletion syndrome can include uncontrolled movements (dystonia), hearing loss, muscle wasting (atrophy), and intellectual disabilities. In most affected children, a substance called methylmalonic acid builds up in the blood.

People with *SUCLA2*-related mtDNA depletion syndrome typically have a shortened lifespan. Approximately 30 percent of individuals with *SUCLA2*-related mtDNA depletion syndrome do not survive past childhood.

Frequency

Approximately 60 people with *SUCLA2*-related mtDNA depletion syndrome have been reported in the medical literature. This condition occurs more frequently among people from the Faroe Islands in the North Atlantic Ocean.

Causes

SUCLA2-related mtDNA depletion syndrome is caused by variants (also called mutations) in the *SUCLA2* gene. The *SUCLA2* gene provides instructions for making one part (the beta subunit) of an enzyme called succinyl-CoA ligase. This enzyme plays an important role in mitochondria, which are the energy-producing centers inside the cell. Succinyl-CoA ligase is involved in producing and maintaining the molecules that make up mtDNA, which is essential for the normal function of mitochondria.

Variants in the *SUCLA2* gene lead to the production of an altered version of the beta subunit, which disrupts the normal function of succinyl-CoA ligase. A shortage (deficiency) of the normal enzyme leads to problems with the production and maintenance of mtDNA. A reduction in the amount of mtDNA (known as mtDNA

depletion) impairs energy production in many of the body's cells and tissues. These problems lead to the characteristic features of *SUCLA2*-related mtDNA depletion syndrome.

Learn more about the gene associated with SUCLA2-related mitochondrial DNA depletion syndrome

- SUCLA2

Inheritance

This condition is inherited in an autosomal recessive pattern, which means both copies of the gene in each cell must have a variant to cause the disorder. The parents of an individual with an autosomal recessive condition each carry one copy of the altered gene, but they typically do not show signs and symptoms of the condition.

Other Names for This Condition

- Mitochondrial DNA depletion syndrome 5 (encephalomyopathic with or without methylmalonic aciduria)
- Mitochondrial DNA depletion syndrome, encephalomyopathic form with or without methylmalonic aciduria, autosomal recessive, SUCLA2-related
- MTDPS5
- Succinate-CoA ligase deficiency
- SUCLA2 deficiency
- SUCLA2-related mitochondrial DNA depletion syndrome, encephalomyopathic form with methylmalonic aciduria

Additional Information & Resources

Genetic Testing Information

- Genetic Testing Registry: Mitochondrial DNA depletion syndrome, encephalomyopathic form with methylmalonic aciduria (https://www.ncbi.nlm.nih.gov/gtr/conditions/C2749864/)

Genetic and Rare Diseases Information Center

- Mitochondrial DNA depletion syndrome (https://rarediseases.info.nih.gov/diseases/13643/index)

Patient Support and Advocacy Resources

- National Organization for Rare Disorders (NORD) (https://rarediseases.org/)

Catalog of Genes and Diseases from OMIM

- MITOCHONDRIAL DNA DEPLETION SYNDROME 5 (ENCEPHALOMYOPATHIC WITH OR WITHOUT METHYLMALONIC ACIDURIA); MTDPS5 (https://omim.org/entry/612073)

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=SUCLA2-Related+Mitochondrial+DNA+Depletion+Syndrome+OR+Succinate-CoA+ligase+deficiency&filter=lang.english&filter=hum_ani.humans&sort=date)

References

- Alberio S, Mineri R, Tiranti V, Zeviani M. Depletion of mtDNA: syndromes andgenes. Mitochondrion. 2007 Feb-Apr;7(1-2):6-12. doi: 10.1016/j.mito.2006.11.010.Epub 2006 Dec 5. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/17280874)
- Carrozzo R, Dionisi-Vici C, Steuerwald U, Lucioli S, Deodato F, DiGiandomenico S, Bertini E, Franke B, Kluijtmans LA, Meschini MC, Rizzo C,Piemonte F, Rodenburg R, Santer R, Santorelli FM, van Rooij A, Vermunt-de KoningD, Morava E, Wevers RA. SUCLA2 mutations are associated with mild methylmalonicaciduria, Leigh-like encephalomyopathy, dystonia and deafness. Brain. 2007Mar;130(Pt 3):862-74. doi: 10.1093/brain/awl389. Epub 2007 Feb 14. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/17301081)
- Carrozzo R, Verrigni D, Rasmussen M, de Coo R, Amartino H, Bianchi M, Buhas D, Mesli S, Naess K, Born AP, Woldseth B, Prontera P, Batbayli M, Ravn K, Joensen F, Cordelli DM, Santorelli FM, Tulinius M, Darin N, Duno M, Jouvencel P, Burlina A, Stangoni G, Bertini E, Redonnet-Vernhet I, Wibrand F, Dionisi-Vici C, Uusimaa J, Vieira P, Osorio AN, McFarland R, Taylor RW, Holme E, Ostergaard E. Succinate-CoAligase deficiency due to mutations in SUCLA2 and SUCLG1: phenotype and genotypecorrelations in 71 patients. J Inherit Metab Dis. 2016 Mar;39(2):243-52. doi: 10.1007/s10545-015-9894-9. Epub 2015 Oct 16. Citation on PubMed (https://www.ncbi.nlm.nih.gov/pubmed/26475597)
- El-Hattab AW, Scaglia F. SUCLA2-Related Mitochondrial DNA DepletionSyndrome, Encephalomyopathic Form with Methylmalonic Aciduria. 2009 May 26[updated 2023 Sep 28]. In: Adam MP, Feldman J, Mirzaa GM, Pagon RA, Wallace SE,Amemiya A, editors. GeneReviews(R) [Internet]. Seattle (WA): Universityof Washington, Seattle; 1993-2025. Available fromhttp://www.ncbi.nlm.nih.gov/books/NBK6803/ Citation on PubMed (https://www.ncbi.nlm.nih.gov/pubmed/20301762)
- Elpeleg O, Miller C, Hershkovitz E, Bitner-Glindzicz M, Bondi-Rubinstein G,Rahman S, Pagnamenta A, Eshhar S, Saada A. Deficiency of the ADP-formingsuccinyl-CoA synthase activity is associated with encephalomyopathy andmitochondrial DNA depletion. Am J Hum Genet. 2005 Jun;76(6):1081-6. doi:10.1086/430843. Epub

2005 Apr 22. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/15877282) or Free article on PubMed Central (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1196446/)

- Ostergaard E, Hansen FJ, Sorensen N, Duno M, Vissing J, Larsen PL, Faeroe O, Thorgrimsson S, Wibrand F, Christensen E, Schwartz M. Mitochondrialencephalomyopathy with elevated methylmalonic acid is caused by SUCLA2 mutations.Brain. 2007 Mar;130(Pt 3):853-61. doi: 10.1093/brain/awl383. Epub 2007 Feb 7. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/17287286)
- Ostergaard E. Disorders caused by deficiency of succinate-CoA ligase. JInherit Metab Dis. 2008 Apr;31(2):226-9. doi: 10.1007/s10545-008-0828-7. Epub2008 Apr 4. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/18392745)
- Spinazzola A, Invernizzi F, Carrara F, Lamantea E, Donati A, Dirocco M,Giordano I, Meznaric-Petrusa M, Baruffini E, Ferrero I, Zeviani M. Clinical andmolecular features of mitochondrial DNA depletion syndromes. J Inherit Metab Dis.2009 Apr;32(2):143-58. doi: 10.1007/s10545-008-1038-z. Epub 2008 Dec 27. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/19125351)

Last updated July 19, 2024