ORC6 gene

origin recognition complex subunit 6

Normal Function

The *ORC6* gene provides instructions for making a protein that is important in the copying of a cell's DNA before the cell divides (a process known as DNA replication). The protein produced from this gene is one of a group of proteins known as the origin recognition complex (ORC). (The complex is made up of the proteins ORC1 to ORC6, which are produced from different genes.) ORC attaches (binds) to certain regions of DNA known as origins of replication (or origins), where the process of DNA copying begins. This complex attracts additional proteins to bind to it, forming a larger group of proteins called the pre-replication complex. When the pre-replication complex is attached to the origin, replication is able to begin at that location. This tightly controlled process, called replication licensing, helps ensure that DNA replication occurs only once per cell division and is required for cells to divide.

ORC also attaches to a form of DNA called heterochromatin. Heterochromatin is densely packed DNA that contains few functional genes, but it is important for controlling gene activity and maintaining the structure of chromosomes. It is unclear what effect ORC binding has on heterochromatin.

In addition to its roles as part of ORC, the ORC6 protein is involved in the process by which the dividing cells separate from one another (cytokinesis).

Health Conditions Related to Genetic Changes

Meier-Gorlin syndrome

At least two mutations in the *ORC6* gene have been found to cause Meier-Gorlin syndrome, a condition characterized by short stature, underdeveloped kneecaps, and small ears. One mutation changes a single protein building block (amino acid) in the ORC6 protein, replacing the amino acid tyrosine at protein position 232 with the amino acid serine (written as Tyr232Ser). The other gene mutation leads to production of an abnormally short protein. These changes impair assembly of the pre-replication complex, disrupting replication licensing; however, it is not clear how a reduction in replication licensing leads to Meier-Gorlin syndrome. Researchers speculate that such a reduction delays the cell division process, which slows growth of the bones and other tissues during development. Some studies suggest that alterations of ORC6 impair

cytokinesis, which may also delay cell division. It is not known why development of the kneecaps and ears is particularly delayed.

Other Names for This Gene

- ORC6_HUMAN
- ORC6L
- origin recognition complex, subunit 6

Additional Information & Resources

Tests Listed in the Genetic Testing Registry

- Tests of ORC6 (https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=23594[geneid])

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28ORC6%5BTIAB%5D%29+OR+%28ORC6L%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

- ORIGIN RECOGNITION COMPLEX, SUBUNIT 6; ORC6 (https://omim.org/entry/607213)

Gene and Variant Databases

- NCBI Gene (https://www.ncbi.nlm.nih.gov/gene/23594)
- ClinVar (https://www.ncbi.nlm.nih.gov/clinvar?term=ORC6[gene])

References

- Bicknell LS, Bongers EM, Leitch A, Brown S, Schoots J, Harley ME, Aftimos S,Al-Aama JY, Bober M, Brown PA, van Bokhoven H, Dean J, Edrees AY, Feingold M, Fryer A, Hoefsloot LH, Kau N, Knoers NV, Mackenzie J, Opitz JM, Sarda P, Ross A, Temple IK, Toutain A, Wise CA, Wright M, Jackson AP. Mutations in thepre-replication complex cause Meier-Gorlin syndrome. Nat Genet. 2011 Feb27;43(4): 356-9. doi: 10.1038/ng.775. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/21358632) or Free article on PubMed Central (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3068194/)
- Bleichert F, Balasov M, Chesnokov I, Nogales E, Botchan MR, Berger JM. AMeier-

Gorlin syndrome mutation in a conserved C-terminal helix of Orc6 impedesorigin recognition complex formation. Elife. 2013 Oct 8;2:e00882. doi:10.7554/eLife.00882. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/24137536) or Free article on PubMed Central (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3791464/)

- Chen S, de Vries MA, Bell SP. Orc6 is required for dynamic recruitment of Cdt1during repeated Mcm2-7 loading. Genes Dev. 2007 Nov 15;21(22):2897-907. doi:10.1101/gad.1596807. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/18006685) or Free article on PubMed Central (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2049192/)
- Niida H, Kitagawa M. Regulation of DNA replication licensing. Curr DrugTargets. 2012 Dec;13(13):1588-92. doi: 10.2174/138945012803529965. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/22998185)
- Prasanth SG, Prasanth KV, Stillman B. Orc6 involved in DNA replication, chromosome segregation, and cytokinesis. Science. 2002 Aug 9;297(5583):1026-31. doi: 10.1126/science.1072802. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/12169736)
- Prasanth SG, Shen Z, Prasanth KV, Stillman B. Human origin recognition complexis essential for HP1 binding to chromatin and heterochromatin organization. ProcNatl Acad Sci U S A. 2010 Aug 24;107(34):15093-8. doi: 10.1073/pnas.1009945107. Epub 2010 Aug 5. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/20689044) or Free article on PubMed Central (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2930523/)

Genomic Location

The *ORC6* gene is found on chromosome 16 (https://medlineplus.gov/genetics/chromosome/16/).

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