

## ZIC2 gene

Zic family member 2

### Normal Function

The *ZIC2* gene provides instructions for making a protein that plays an important role in the development of the front part of the brain (forebrain). This protein is a transcription factor, which means that it attaches (binds) to specific regions of DNA and helps control the activity of certain genes. The ZIC2 protein regulates genes involved in both early and late stages of forebrain development.

### Health Conditions Related to Genetic Changes

#### Nonsyndromic holoprosencephaly

More than 80 mutations in the *ZIC2* gene have been found to cause nonsyndromic holoprosencephaly. This condition occurs when the brain fails to divide into two halves (hemispheres) during early development. *ZIC2* gene mutations are the second most common cause of nonsyndromic holoprosencephaly. The facial features of individuals with *ZIC2* gene mutations are different from those with nonsyndromic holoprosencephaly caused by mutations in other genes. These distinctive facial features include a narrowing of the head at the temples, outside corners of the eyes that point upward (upslanting palpebral fissures), large ears, a short nose with upturned nostrils, and a broad and deep space between the nose and mouth (philtrum). It is unclear how mutations in the *ZIC2* gene lead to these facial features.

*ZIC2* gene mutations that cause nonsyndromic holoprosencephaly reduce or eliminate the activity of the ZIC2 protein. Without enough functional ZIC2 protein, the genes involved in normal forebrain development are not properly controlled. As a result, the brain does not separate into two hemispheres. The signs and symptoms of nonsyndromic holoprosencephaly are caused by abnormal development of the brain and face.

#### Coloboma

MedlinePlus Genetics provides information about Coloboma

## Other Names for This Gene

- HPE5
- Zic family member 2 (odd-paired Drosophila homolog)
- Zic family member 2 (odd-paired homolog, Drosophila)
- ZIC2\_HUMAN
- Zinc finger protein of the cerebellum 2
- zinc finger protein ZIC 2

## Additional Information & Resources

### Tests Listed in the Genetic Testing Registry

- Tests of ZIC2 ([https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=7546\[geneid\]](https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=7546[geneid]))

### Scientific Articles on PubMed

- PubMed (<https://pubmed.ncbi.nlm.nih.gov/?term=%28ZIC2%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+1800+days%22%5Bdp%5D>)

### Catalog of Genes and Diseases from OMIM

- ZIC FAMILY, MEMBER 2; ZIC2 (<https://omim.org/entry/603073>)

### Gene and Variant Databases

- NCBI Gene (<https://www.ncbi.nlm.nih.gov/gene/7546>)
- ClinVar ([https://www.ncbi.nlm.nih.gov/clinvar?term=ZIC2\[gene\]](https://www.ncbi.nlm.nih.gov/clinvar?term=ZIC2[gene]))

## References

- Brown LY, Odent S, David V, Blayau M, Dubourg C, Apacik C, Delgado MA, Hall BD, Reynolds JF, Sommer A, Wieczorek D, Brown SA, Muenke M. Holoprosencephaly due to mutations in ZIC2: alanine tract expansion mutations may be caused by parental somatic recombination. Hum Mol Genet. 2001 Apr 1;10(8):791-6. doi:10.1093/hmg/10.8.791. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/11285244>)
- Brown SA, Warburton D, Brown LY, Yu CY, Roeder ER, Stengel-Rutkowski S, Hennekam RC, Muenke M. Holoprosencephaly due to mutations in ZIC2, a homologue of Drosophila odd-paired. Nat Genet. 1998 Oct;20(2):180-3. doi: 10.1038/

2484. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/9771712>)

- Dubourg C, Bendavid C, Pasquier L, Henry C, Odent S, David V. Holoprosencephaly. *Orphanet J Rare Dis*. 2007 Feb 2;2:8. doi:10.1186/1750-1172-2-8. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/17274816>) or Free article on PubMed Central (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1802747/>)
- Roessler E, Lacbawan F, Dubourg C, Paulussen A, Herbergs J, Hehr U, Bendavid C, Zhou N, Ouspenskaia M, Bale S, Odent S, David V, Muenke M. The full spectrum of holoprosencephaly-associated mutations within the ZIC2 gene in humans predicts loss-of-function as the predominant disease mechanism. *Hum Mutat*. 2009 Apr;30(4):E541-54. doi: 10.1002/humu.20982. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/19177455>) or Free article on PubMed Central (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2674582/>)
- Roessler E, Muenke M. The molecular genetics of holoprosencephaly. *Am J Med Genet C Semin Med Genet*. 2010 Feb 15;154C(1):52-61. doi: 10.1002/ajmg.c.30236. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/20104595>) or Free article on PubMed Central (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2815021/>)
- Solomon BD, Lacbawan F, Mercier S, Clegg NJ, Delgado MR, Rosenbaum K, Dubourg C, David V, Olney AH, Wehner LE, Hehr U, Bale S, Paulussen A, Smeets HJ, Hardisty E, Tylki-Szymanska A, Pronicka E, Clemens M, McPherson E, Hennekam RC, Hahn J, Stashenko E, Levey E, Wieczorek D, Roeder E, Schell-Apacik CC, Booth CW, Thomas RL, Kenwrick S, Cummings DA, Bous SM, Keaton A, Balog JZ, Hadley D, Zhou N, Long R, Velez JI, Pineda-Alvarez DE, Odent S, Roessler E, Muenke M. Mutations in ZIC2 in human holoprosencephaly: description of a novel ZIC2 specific phenotype and comprehensive analysis of 157 individuals. *J Med Genet*. 2010 Aug;47(8):513-24. doi: 10.1136/jmg.2009.073049. Epub 2009 Dec 2. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/19955556>) or Free article on PubMed Central (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3208626/>)
- Solomon BD, Mercier S, Velez JI, Pineda-Alvarez DE, Wyllie A, Zhou N, Dubourg C, David V, Odent S, Roessler E, Muenke M. Analysis of genotype-phenotype correlations in human holoprosencephaly. *Am J Med Genet C Semin Med Genet*. 2010 Feb 15;154C(1):133-41. doi: 10.1002/ajmg.c.30240. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/20104608>) or Free article on PubMed Central (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2815217/>)
- Tekendo-Ngongang C, Muenke M, Kruszka P. Holoprosencephaly Overview. 2000 Dec 27 [updated 2020 Mar 5]. In: Adam MP, Feldman J, Mirzaa GM, Pagon RA, Wallace SE, Bean LJH, Gripp KW, Amemiya A, editors. *GeneReviews*(R) [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2024. Available from <http://www.ncbi.nlm.nih.gov/books/NBK1530/> Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/20301702>)
- Warr N, Powles-Glover N, Chappell A, Robson J, Norris D, Arkell RM. Zic2-associated holoprosencephaly is caused by a transient defect in the organizer region during gastrulation. *Hum Mol Genet*. 2008 Oct 1;17(19):2986-96. doi: 10.1093/hmg/ddn197. Epub 2008 Jul 9. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/18617531>)

## **Genomic Location**

The *Z/C2* gene is found on chromosome 13 (<https://medlineplus.gov/genetics/chromosome/13/>).

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