# MSX2 gene

msh homeobox 2

## Normal Function

The *MSX2* gene provides instructions for producing a protein that is necessary for proper development of cells and tissues throughout the body. The MSX2 protein is a transcription factor, which means it attaches (binds) to specific regions of DNA and helps control the activity of certain genes. Specifically, the protein controls the activity of genes that regulate cell growth and division (proliferation), cell maturation and specialization (differentiation), and cell survival. The regulation of these functions ensures that cells start and stop growing at specific times and that they are positioned correctly during development.

The MSX2 protein is part of a chemical signaling pathway known as the bone morphogenic protein (BMP) pathway. This signaling pathway regulates various cellular processes and is involved in the growth of cells, including new bone cells. The MSX2 protein seems to be particularly critical for the development of the skull.

## Health Conditions Related to Genetic Changes

Enlarged parietal foramina

At least 10 mutations in the *MSX2* gene have been identified in people with enlarged parietal foramina type 1. This condition is characterized by enlarged openings (foramina) in the parietal bones, which are the two bones that form the top and sides of the skull. Openings in the parietal bones are normal during fetal development, but they usually close before birth. In people with this condition, the parietal foramina remain open throughout life.

The mutations that cause enlarged parietal foramina result in the production of an MSX2 protein that cannot bind to DNA, which alters the regulation of multiple genes. As a result, several cell processes are disrupted, including proliferation, differentiation, and survival. In early development, the skull seems to be particularly sensitive to changes in MSX2 protein activity and changes in cell function. Specifically, cells in the skull that are involved in bone formation (ossification) cannot function normally, leading to a lack of bone in areas of the skull and enlarged parietal foramina.

Other disorders

At least two mutations in the *MSX2* gene cause a condition called craniosynostosis type 2 (also known as Boston type craniosynostosis). Craniosynostosis involves premature closure of the bones of the skull, leading to a misshapen head. People with craniosynostosis type 2 can have skull malformations including a protruding forehead ( frontal bossing), a short wide head that is pointed at the top (turribrachycephaly), or a cloverleaf-shaped skull (Kleeblattschaedel deformity). Most affected people have vision problems, and a few have experienced seizures. Intelligence is typically normal.

It is unclear how changes in the MSX2 gene can cause premature closure of the skull bones in craniosynostosis type 2 and impaired bone formation in enlarged parietal foramina (described above).

## Other Names for This Gene

- CRS2
- FPP
- HOX8
- MSH
- msh homeobox homolog 2
- MSX2_HUMAN
- PFM
- PFM1

## Additional Information & Resources

Tests Listed in the Genetic Testing Registry

- Tests of MSX2 (https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=4488[geneid])

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28MSX2%5BTI%5D%29+OR+%28enlarged+parietal+foramina%5BTIAB%5D%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1800+days%22%5Bdp%5D)

Catalog of Genes and Diseases from OMIM

- MSH HOMEOBOX 2; MSX2 (https://omim.org/entry/123101)
- CRANIOSYNOSTOSIS 2; CRS2 (https://omim.org/entry/604757)

Gene and Variant Databases

- NCBI Gene (https://www.ncbi.nlm.nih.gov/gene/4488)
- ClinVar (https://www.ncbi.nlm.nih.gov/clinvar?term=MSX2[gene])

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## Genomic Location

The *MSX2* gene is found on chromosome 5 (https://medlineplus.gov/genetics/chromosome/5/).

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