MESP2 Gene

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mesoderm posterior bHLH transcription factor 2

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1. Introdcution

The *MESP2* gene provides instructions for making a transcription factor, which is a protein that attaches (binds) to specific regions of DNA and helps control the activity of particular genes. The MESP2 protein controls the activity of genes in the Notch pathway, an important pathway in embryonic development. The Notch pathway plays a critical role in the development of the bones of the spine (vertebrae). Specifically, the MESP2 protein and the Notch pathway are involved in separating future vertebrae from one another during early development, in a complex process called somite segmentation. Although the exact mechanism of somite segmentation is unclear, it appears to require the activity of several proteins in the Notch pathway, including the NOTCH1 protein and the MESP2 protein, to be turned on and off (oscillate) in a specific pattern.

The MESP2 protein regulates Notch activity by turning on (activating) genes in the Notch pathway, which ultimately block (repress) the activity of the NOTCH1 protein. Additionally, through unknown mechanisms, the MESP2 protein seems to mark the boundary separating future vertebrae from one another.

2. Health Conditions Related to Genetic Changes

2.1. Spondylothoracic dysostosis

At least three mutations in the *MESP2* gene have been found to cause spondylothoracic dysostosis, a condition characterized by abnormal development of bones in the spine and ribs. All of the known mutations replace one protein building block (amino acid) in the protein sequence. The most common mutation replaces the amino acid glutamate with a premature stop signal at position 103 (written as Glu103Ter or E103X). A similar mutation occurs at amino acid position 230 (written as Glu230Ter or E230X). The third mutation replaces the amino acid leucine with the amino acid valine at position 125 (written as Leu125Val or L125V). Most affected individuals have the Glu103Ter mutation in both copies of the *MESP2* gene. However, a few people with spondylothoracic dysostosis have the Glu103Ter mutation in one copy of the *MESP2* gene and either the Leu125Val or the Glu230Ter mutation in the other copy.

Mutations in the *MESP2* gene prevent the production of any protein or lead to the production of an abnormally short, nonfunctional protein. When the MESP2 protein is nonfunctional or absent, the NOTCH1 protein is abnormally active and the boundary separating future vertebrae from one another does not form. This results in the malformation and fusion of the bones of the spine and ribs seen in spondylothoracic dysostosis.

3. Other Names for This Gene

- bHLHc6
- class C basic helix-loop-helix protein 6
- mesoderm posterior 2 homolog (mouse)
- mesoderm posterior basic helix-loop-helix transcription factor 2
- mesoderm posterior protein 2
- MESP2_HUMAN
- SCDO2

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