

EIF2AK4 gene

eukaryotic translation initiation factor 2 alpha kinase 4

Normal Function

The *EIF2AK4* gene provides instructions for making a protein that helps direct a cell's response to changes that could damage the cell. This protein is found in several tissues throughout the body, including blood vessel walls. The EIF2AK4 protein can turn on (activate) another protein called eIF2 alpha (eIF2 α), which helps control protein production. When cells are under stress, for example when the level of protein building blocks (amino acids) is too low, EIF2AK4 activates eIF2 α . When turned on, eIF2 α stimulates processes that reduce protein production, which helps conserve amino acids. In addition, activated eIF2 α can trigger production of certain proteins called transcription factors, which control gene activity. The transcription factors regulated by eIF2 α control the activity of genes involved in processes that help reduce the stress on the cell.

Health Conditions Related to Genetic Changes

Pulmonary veno-occlusive disease

Mutations in the *EIF2AK4* gene are the primary genetic cause of a condition called pulmonary veno-occlusive disease (PVOD); at least 22 mutations in this gene have been found in affected individuals. In PVOD, excess fibrous tissue builds up in the small vessels in the lungs that carry oxygenated blood from the lungs to the heart (the pulmonary veins). This buildup narrows (occludes) the vessels and impairs blood flow. Because blood flow through the lungs is difficult, pressure rises in the vessels that carry blood that needs to be oxygenated to the lungs from the heart (pulmonary arteries). Increased pressure in these vessels is known as pulmonary arterial hypertension.

The *EIF2AK4* gene mutations involved in PVOD likely lead to a complete loss of functional protein. It is not known how absence of EIF2AK4 protein function leads to the pulmonary vein abnormalities characteristic of PVOD.

Pulmonary arterial hypertension

MedlinePlus Genetics provides information about Pulmonary arterial hypertension

Other Names for This Gene

- E2AK4_HUMAN
- eukaryotic translation initiation factor 2-alpha kinase 4
- GCN2
- GCN2 eIF2alpha kinase
- GCN2-like protein
- general control nonderepressible 2
- KIAA1338
- PVOD2

Additional Information & Resources

Tests Listed in the Genetic Testing Registry

- Tests of EIF2AK4 ([https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=440275\[geneid\]](https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=440275[geneid]))

Scientific Articles on PubMed

- PubMed (<https://pubmed.ncbi.nlm.nih.gov/?term=%28%28EIF2AK4%5BTIAB%5D%29+OR+%28eukaryotic+translation+initiation+factor+2+alpha+kinase+4%5BTIAB%5D%29%29+OR+%28%28GCN2+eIF2alpha+kinase%5BTIAB%5D%29+OR+%28GCN2%5BTIAB%5D%29+OR+%28eukaryotic+translation+initiation+factor+2-alpha+kinase+4%5BTIAB%5D%29+OR+%28general+control+nonderepressible+2%5BTIAB%5D%29%29+AND+%28%28Genes%5BMH%5D%29+OR+%28Genetic+Phenomena%5BMH%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1080+days%22%5Bdp%5D%29>)

Catalog of Genes and Diseases from OMIM

- EUKARYOTIC TRANSLATION INITIATION FACTOR 2-ALPHA KINASE 4; EIF2AK4 (<https://omim.org/entry/609280>)

Gene and Variant Databases

- NCBI Gene (<https://www.ncbi.nlm.nih.gov/gene/440275>)
- ClinVar ([https://www.ncbi.nlm.nih.gov/clinvar?term=EIF2AK4\[gene\]](https://www.ncbi.nlm.nih.gov/clinvar?term=EIF2AK4[gene]))

References

- Deval C, Chaveroux C, Maurin AC, Cherasse Y, Parry L, Carraro V, Milenkovic D, Ferrara M, Bruhat A, Jousse C, Fafournoux P. Amino acid limitation regulates the expression of genes involved in several specific biological processes through GCN2-dependent and GCN2-independent pathways. *FEBS J.* 2009 Feb;276(3):707-18. doi: 10.1111/j.1742-4658.2008.06818.x. Epub 2008 Dec 19. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/19120448>)
- Donnelly N, Gorman AM, Gupta S, Samali A. The eIF2alpha kinases: their structures and functions. *Cell Mol Life Sci.* 2013 Oct;70(19):3493-511. doi:10.1007/s00018-012-1252-6. Epub 2013 Jan 26. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/23354059>)
- Eyries M, Montani D, Girerd B, Perret C, Leroy A, Lonjou C, Chelghoum N, Coulet F, Bonnet D, Dorfmueller P, Fadel E, Sitbon O, Simonneau G, Tregouet DA, Humbert M, Soubrier F. EIF2AK4 mutations cause pulmonary veno-occlusive disease, a recessive form of pulmonary hypertension. *Nat Genet.* 2014 Jan;46(1):65-9. doi:10.1038/ng.2844. Epub 2013 Dec 1. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/24292273>)
- Murguia JR, Serrano R. New functions of protein kinase Gcn2 in yeast and mammals. *IUBMB Life.* 2012 Dec;64(12):971-4. doi: 10.1002/iub.1090. Epub 2012 Nov 5. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/23129244>)

Genomic Location

The *EIF2AK4* gene is found on chromosome 15 (<https://medlineplus.gov/genetics/chromosome/15/>).

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