SUMF1 Gene

Subjects: Genetics & Heredity
Contributor: Rui Liu

Sulfatase modifying factor 1: The SUMF1 gene provides instructions for making an enzyme called formylglycine-generating enzyme (FGE).

Keywords: genes

1. Normal Function

The *SUMF1* gene provides instructions for making an enzyme called formylglycine-generating enzyme (FGE). This enzyme is found in a cell structure called the endoplasmic reticulum, which is involved in protein processing and transport. The FGE enzyme modifies other enzymes called sulfatases, which aid in breaking down substances that contain chemical groups known as sulfates. These substances include a variety of sugars, fats, and hormones. Specifically, FGE converts a protein building block (amino acid) within sulfatases called cysteine into a molecule called C-alpha-formylglycine.

2. Health Conditions Related to Genetic Changes

2.1. Multiple sulfatase deficiency

At least 35 mutations in the *SUMF1* gene have been found to cause multiple sulfatase deficiency. This condition is apparent at birth or early childhood and is characterized by neurological decline, scaly skin (ichthyosis), and skeletal abnormalities. Most *SUMF1* gene mutations that cause multiple sulfatase deficiency change single amino acids in the FGE enzyme. These changes severely reduce enzyme function or produce an unstable enzyme that is quickly broken down. The activity of multiple sulfatases is impaired because the FGE enzyme modifies all known sulfatase enzymes. Sulfate-containing molecules that are not broken down build up in cells, often resulting in cell death. The death of cells in particular tissues, specifically the brain, skeleton, and skin, cause many of the signs and symptoms of multiple sulfatase deficiency. Research indicates that mutations that lead to reduced FGE enzyme function are associated with the less severe cases of the condition, whereas mutations that lead to the production an of unstable FGE enzyme tend to be associated with the more severe cases of multiple sulfatase deficiency.

3. Other Names for This Gene

- AAPA3037
- C-alpha-formylglycine-generating enzyme 1
- FGE
- FGly-generating enzyme
- sulfatase-modifying factor 1
- UNQ3037

References

1. Annunziata I, Bouchè V, Lombardi A, Settembre C, Ballabio A. Multiplesulfatase deficiency is due to hypomorphic mutations of the SUMF1 gene. HumMutat. 2007 Sep;28(9):928.
2. Cosma MP, Pepe S, Annunziata I, Newbold RF, Grompe M, Parenti G, Ballabio A.The multiple sulfatase deficiency gene encodes an essential and limiting factorfor the activity of sulfatases. Cell. 2003 May 16;113(4):445-56.

3. Cosma MP, Pepe S, Parenti G, Settembre C, Annunziata I, Wade-Martins R, DiDomenico C, Di Natale P, Mankad A, Cox B, Uziel G, Mancini GM, Zammarchi E,Donati MA, Kleijer WJ, Filocamo M, Carrozzo R, Carella M, Ballabio A. Molecularand functional analysis of SUMF1 mutations in multiple sulfatase deficiency. Hum Mutat. 2004 Jun;23(6):576-81.
4. Dierks T, Dickmanns A, Preusser-Kunze A, Schmidt B, Mariappan M, von Figura K,Ficner R, Rudolph MG. Molecular basis for multiple sulfatase deficiency andmechanism for formylglycine generation of the human formylglycine-generatingenzyme. Cell. 2005 May 20;121(4):541-552. doi: 10.1016/j.cell.2005.03.001.
5. Dierks T, Schmidt B, Borissenko LV, Peng J, Preusser A, Mariappan M, vonFigura K. Multiple sulfatase deficiency is caused by mutations in the geneencoding the human C(alpha)-formylglycine generating enzyme. Cell. 2003 May16;113(4):435-44.
6. Schlotawa L, Ennemann EC, Radhakrishnan K, Schmidt B, Chakrapani A, ChristenHJ, Moser H, Steinmann B, Dierks T, Gärtner J. SUMF1 mutations affectingstability and activity of formylglycine generating enzyme predict clinicaloutcome in multiple sulfatase deficiency. Eur J Hum Genet. 2011 Mar;19(3):253-61.doi: 10.1038/ejhg.2010.219.
7. Schlotawa L, Radhakrishnan K, Baumgartner M, Schmid R, Schmidt B, Dierks T,Gärtner J. Rapid degradation of an active formylglycine generating enzyme variantleads to a late infantile severe form of multiple sulfatase deficiency. Eur J HumGenet. 2013 Sep;21(9):1020-3. doi: 10.1038/ejhg.2012.291.
8. Schlotawa L, Steinfeld R, von Figura K, Dierks T, Gärtner J. Molecularanalysis of SUMF1 mutations: stability and residual activity of mutantformylglycine-generating enzyme determine disease severity in multiple sulfatase deficiency. Hum Mutat. 2008 Jan;29(1):205.
