PCBD1 Gene

Subjects: Genetics & Heredity
Contributor: Lily Guo

pterin-4 alpha-carbinolamine dehydratase 1

genes

1. Introduction

The *PCBD1* gene provides instructions for making an enzyme called pterin-4 alpha-carbinolamine dehydratase. This enzyme helps carry out one step in the chemical pathway that recycles a molecule called tetrahydrobiopterin (BH4).

Tetrahydrobiopterin plays a critical role in processing several protein building blocks (amino acids) in the body. For example, it works with the enzyme phenylalanine hydroxylase to convert an amino acid called phenylalanine into another amino acid, tyrosine. Tetrahydrobiopterin is also involved in reactions that produce chemicals called neurotransmitters, which transmit signals between nerve cells in the brain. Because it helps enzymes carry out chemical reactions, tetrahydrobiopterin is known as a cofactor.

When tetrahydrobiopterin interacts with enzymes during chemical reactions, the cofactor is altered and must be recycled to a usable form. Pterin-4 alpha-carbinolamine dehydratase is one of two enzymes that help recycle tetrahydrobiopterin in the body.

2. Health Conditions Related to Genetic Changes

2.1. Tetrahydrobiopterin deficiency

At least nine mutations in the *PCBD1* gene have been found to cause tetrahydrobiopterin deficiency. When this condition results from *PCBD1* gene mutations, it is known as pterin-4 alpha-carbinolamine dehydratase (PCD) deficiency. PCD deficiency accounts for about 5 percent of all cases of tetrahydrobiopterin deficiency.

Some mutations in the *PCBD1* gene change single amino acids in pterin-4 alpha-carbinolamine dehydratase, while other mutations introduce a premature stop signal in the instructions for making this enzyme. Changes in pterin-4 alpha-carbinolamine dehydratase reduce the enzyme's activity, which affects the body's ability to recycle tetrahydrobiopterin. As a result, less of this cofactor is available to participate in chemical reactions such as the

conversion of phenylalanine to tyrosine. If phenylalanine is not converted to tyrosine, the excess can build up in the bloodstream and other tissues.

Although people with PCD deficiency usually have elevated levels of phenylalanine in the blood, this form of tetrahydrobiopterin deficiency rarely causes significant medical problems. Researchers believe that other enzymes may compensate for the reduced activity of pterin-4 alpha-carbinolamine dehydratase in people with *PCBD1* gene mutations.

3. Other Names for This Gene

- 4-alpha-hydroxy-tetrahydropterin dehydratase
- 6-pyruvoyl-tetrahydropterin synthase/dimerization cofactor of hepatocyte nuclear factor 1 alpha (TCF1)
- Carbinolamine-4a-dehydratase
- DCOH
- Dimerization cofactor of hepatocyte nuclear factor 1-alpha
- Dimerization cofactor of HNF1
- PCBD
- PCD
- Phenylalanine hydroxylase-stimulating protein
- PHS_HUMAN
- Pterin carbinolamine dehydratase
- pterin-4 alpha-carbinolamine dehydratase/dimerization cofactor of hepatocyte nuclear factor 1 alpha
- pterin-4 alpha-carbinolamine dehydratase/dimerization cofactor of hepatocyte nuclear factor 1 alpha (TCF1)
- Pterin-4-alpha-carbinolamine dehydratase
- Pterin-4a-carbinolamine dehydratase (dimerization cofactor of hepatic nuclear factor 1-alpha)

References

1. Citron BA, Kaufman S, Milstien S, Naylor EW, Greene CL, Davis MD. Mutation in the 4a-carbinolamine dehydratase gene leads to mild hyperphenylalaninemia withdefective cofactor metabolism. Am J Hum Genet. 1993 Sep;53(3):768-74.
2. Longo N. Disorders of biopterin metabolism. J Inherit Metab Dis. 2009Jun;32(3):333-42. doi: 10.1007/s10545-009-1067-2.Erratum in: J Inherit Metab Dis. 2009 Jun;32(3):457.
3. Shintaku H. Disorders of tetrahydrobiopterin metabolism and their treatment.Curr Drug Metab. 2002 Apr;3(2):123-31. Review.
4. Thöny B, Auerbach G, Blau N. Tetrahydrobiopterin biosynthesis, regenerationand functions. Biochem J. 2000 Apr 1;347 Pt 1:1-16. Review.

5. Thöny B, Blau N. Mutations in the BH4-metabolizing genes GTP cyclohydrolase I,6-pyruvoyl-tetrahydropterin synthase, sepiapterin reductase,carbinolamine-4a-dehydratase, and dihydropteridine reductase. Hum Mutat. 2006Sep;27(9):870-8.
6. Thöny B, Neuheiser F, Kierat L, Rolland MO, Guibaud P, Schlüter T, Germann R, Heidenreich RA, Duran M, de Klerk JB, Ayling JE, Blau N. Mutations in thepterin-4alpha-carbinolamine dehydratase (PCBD) gene cause a benign form ofhyperphenylalaninemia. Hum Genet. 1998 Aug;103(2):162-7.