FMO3 Gene

Subjects: Genetics & Heredity
Contributor: Vivi Li

Flavin containing monooxygenase 3

genes

1. Normal Function

The *FMO3* gene provides instructions for making an enzyme that is part of a larger enzyme family called flavin-containing monooxygenases (FMOs). These enzymes break down compounds that contain nitrogen, sulfur, or phosphorus. The FMO3 enzyme, which is made chiefly in the liver, is responsible for breaking down nitrogen-containing compounds derived from the diet. One of these compounds is trimethylamine, which is the molecule that gives fish their fishy smell. Trimethylamine is produced as bacteria in the intestine help digest certain proteins obtained from eggs, liver, legumes (such as soybeans and peas), certain kinds of fish, and other foods. The FMO3 enzyme normally converts fishy-smelling trimethylamine into another compound, trimethylamine-N-oxide, which has no odor. Trimethylamine-N-oxide is then excreted from the body in urine.

Researchers believe that the FMO3 enzyme also plays a role in processing some types of drugs. For example, this enzyme is likely needed to break down the anticancer drug tamoxifen, the pain medication codeine, the antifungal drug ketoconazole, and certain medications used to treat depression (antidepressants). The FMO3 enzyme may also be involved in processing nicotine, an addictive chemical found in tobacco. Normal variations (polymorphisms) in the *FMO3* gene may affect the enzyme's ability to break down these substances. Researchers are working to determine whether *FMO3* polymorphisms can help explain why people respond differently to certain drugs.

2. Health Conditions Related to Genetic Changes

2.1 Trimethylaminuria

More than 25 mutations in the *FMO3* gene have been identified in people with trimethylaminuria. Most of these mutations lead to the production of a small, nonfunctional version of the FMO3 enzyme. Other mutations change single building blocks (amino acids) used to build the enzyme, which alters its shape and disrupts its function. Without enough functional FMO3 enzyme, the body is unable to convert trimethylamine into trimethylamine-N-oxide effectively. As a result, trimethylamine builds up in the body and is released in an affected person's sweat, urine, and breath. The excretion of this compound is responsible for the strong body odor characteristic of

trimethylaminuria. Studies suggest that diet and stress also play a role in determining the intensity of the fish-like odor.

3. Other Names for This Gene

- Dimethylaniline monooxygenase [N-oxide-forming] 3
- Dimethylaniline oxidase 3
- FMO3_HUMAN
- FMOII

References

1. Bain MA, Fornasini G, Evans AM. Trimethylamine: metabolic, pharmacokinetic andsafety aspects. Curr Drug Metab. 2005 Jun;6(3):227-40. Review.
2. Dolphin CT, Janmohamed A, Smith RL, Shephard EA, Phillips IR. Missensemutation in flavin-containing mono-oxygenase 3 gene, FMO3, underlies fish-odoursyndrome. Nat Genet. 1997 Dec;17(4):491-4.
3. Hernandez D, Addou S, Lee D, Orengo C, Shephard EA, Phillips IR.Trimethylaminuria and a human FMO3 mutation database. Hum Mutat. 2003Sep;22(3):209-13. Review.
4. Koukouritaki SB, Poch MT, Henderson MC, Siddens LK, Krueger SK, VanDyke JE,Williams DE, Pajewski NM, Wang T, Hines RN. Identification and functionalanalysis of common human flavin-containing monooxygenase 3 genetic variants. JPharmacol Exp Ther. 2007 Jan;320(1):266-73.
5. Krueger SK, Vandyke JE, Williams DE, Hines RN. The role of flavin-containingmonooxygenase (FMO) in the metabolism of tamoxifen and other tertiary amines.Drug Metab Rev. 2006;38(1-2):139-47. Review.
6. Mitchell SC. Trimethylaminuria: susceptibility of heterozygotes. Lancet. 1999 Dec 18-25;354(9196):2164-5.
7. Zhang J, Tran Q, Lattard V, Cashman JR. Deleterious mutations in theflavin-containing monooxygenase 3 (FMO3) gene causing trimethylaminuria.Pharmacogenetics. 2003 Aug;13(8):495-500.
8. Zhou J, Shephard EA. Mutation, polymorphism and perspectives for the future ofhuman flavin-containing monooxygenase 3. Mutat Res. 2006 Jun;612(3):165-171. doi:10.1016/j.mrrev.2005.09.001.

9. Zschocke J, Kohlmueller D, Quak E, Meissner T, Hoffmann GF, Mayatepek E. Mild trimethylaminuria caused by common variants in FMO3 gene. Lancet. 1999 Sep4;354(9181):834-5.