Opioid Receptor, mu OPRM1 Genotype, 1 Variant

Opioid agonists (eg, morphine, fentanyl) are typically administered for pain control and opioid antagonists (eg, naltrexone) are often prescribed for the treatment of alcohol and/or opioid dependency. Pharmacogenetic variation may affect pharmacokinetics or pharmacodynamics of a drug which may contribute to toxicity and risk for adverse drug reactions, including reduced therapeutic benefit.

The *OPRM1* gene is associated with the pharmacodynamics of opioids. Variants in *OPRM1* can result in different binding affinities to and clinical effects of opioids. The association of *OPRM1* and drug sensitivity is not definitive and may be different for individual opioids. Testing should be performed for pretherapeutic identification of individuals who may require higher or lower doses of opioid drugs to achieve adequate pain control or have a better response to naltrexone for the treatment of alcohol and/or opioid dependency.

Tests to Consider

Opioid Receptor, mu OPRM1 Genotype, 1 Variant 2008767

Method: Polymerase Chain Reaction/Fluorescence Monitoring

Predicts response to opioid agents

Related Tests

Cytochrome P450 Genotyping Panel 3001524

Method: Polymerase Chain Reaction/Fluorescence Monitoring

- Assesses genetic risk of abnormal drug metabolism for drugs metabolized by *CYP2D6*, *CYP2C9*, *CYP2C19*, and *CYP3A5*
- May aid in drug selection and dose planning for many drugs
- Single tests for *CYP2D6*, *CYP2C9*, *CYP2C19*, and *CYP3A5* are available separately

Genetics

Gene

OPRM1

Inheritance

Autosomal codominant

Penetrance

Drug dependent

Structure/Function

OPRM1 encodes the μ-opioid receptor 1 protein and is the primary binding site of action for various synthetic and endogenous opioids, including both agonists and antagonists. One of three opioid receptors is involved in this process.[1]

Alleles

The OPRM1 c.118A>G variant has an overall frequency of ~10.5% but varies by ethnicity[2]:

- African Americans: 1.5-4%[3,4]
- Whites: 11-14%[3,4]
- Hispanics: 14-24%[3,4]
- Asians: 49-60%[5]

The c.118A>G variant results in[1]

- Loss of a putative N-glycosylation site in the extracellular receptor region

- Lower cell-surface receptor binding site availability compared to the A allele receptors
- Thought to decrease mRNA and receptor protein concentrations
- Lower sensitivity to opioid receptor agonists prescribed for pain control (eg, morphine)

- Higher sensitivity to opioid receptor antagonists used in the treatment of alcohol and drug dependency (eg, naltrexone)

Test Interpretation

Sensitivity/Specificity

- Clinical sensitivity/specificity: drug dependent
- Analytical sensitivity/specificity: >99%

Results

Result	Variant Detected	Clinical Significance
Homozygous G/G	Two copies of *OPRM1* c.118A>G variant detected	Genotype is consistent with decreased sensitivity to opioid agonists and increased sensitivity to opioid antagonists Individual may require higher or more frequent doses of opioid agonists to achieve adequate pain control and may be more likely to respond to opioid antagonists in treatment of alcohol and/or opioid dependency
Heterozygous G/A	One copy of *OPRM1* c.118A>G variant detected	Further studies are needed to determine clinical significance of this genotype, but it is possible that individual may require higher or more frequent doses of opioid receptor agonists to achieve adequate pain control and be more likely to respond to opioid antagonists in treatment of alcohol and/or opioid dependency
Homozygous A/A	No copies of *OPRM1* c.118A>G variant detected	Further studies are needed to determine clinical significance of this genotype, but it is possible that individual may require higher or more frequent doses of opioid receptor agonists to achieve adequate pain control and may be more likely to respond to opioid antagonists in treatment of alcohol and/or opioid dependency

Limitations

- *OPRM1* variants other than c.118A>G are not evaluated by this test
- Diagnostic errors can occur due to rare sequence variations
- Risk of therapeutic failure or adverse reactions with opioids may be affected by genetic and nongenetic factors that are not detected by this test
- Genetic testing does not replace the need for therapeutic or clinical monitoring

References

1. National Institutes of Health, U.S. National Library of Medicine. Genetics Home Reference: OPRM1 gene. [Reviewed: Nov 2017; Accessed: Apr 2020]

2. Online Mendelian Inheritance in Man (OMIM).Opioid receptor, mu-1; OPRM1. [Edited: Jan 2017; Accessed: Apr 2020]

3. Bond C, LaForge KS, Tian M, et al. Single-nucleotide polymorphism in the human mu opioid receptor gene alters beta-endorphin binding and activity: possible implications for opiate addiction. Proc Natl Acad Sci USA. 1998;95(16):9608-9613. PubMed

4. LaForge KS, Yuferov V, Kreek MJ. Opioid receptor and peptide gene polymorphisms: potential implications for addictions [published correction appears in Eur J Pharmacol 2001 Aug 24;426(1-2):145]. Eur J Pharmacol. 2000;410(2-3):249-268. PubMed

5. Mague SD, Isiegas C, Huang P, et al. Mouse model of OPRM1 (A118G) polymorphism has sex-specific effects on drug-mediated behavior. Proc Natl Acad Sci USA. 2009;106(26):10847-10852. PubMed

Related Information

ARUP Drug Testing Algorithm
ARUP Drug Testing (Unexpected Results) Algorithm

ARUP Laboratories is a nonprofit enterprise of the University of Utah and its Department of Pathology. 500 Chipeta Way, Salt Lake City, UT 84108
(800) 522-2787 | (801) 583-2787 | aruplab.com | arupconsult.com
Content Review April 2020 | Last Update August 2020