

Overview

Useful For

Prediction of response to nicotine replacement therapy for smoking cessation

Investigation of inhibitor dosing for decreasing levodopa metabolism

Research use for assessing estrogen metabolism

Special Instructions

- [Informed Consent for Genetic Testing](#)
- [Multiple Genotype Test List](#)
- [Informed Consent for Genetic Testing \(Spanish\)](#)

Method Name

Real-Time Polymerase Chain Reaction (PCR) with Allelic Discrimination Analysis

NY State Available

Yes

Specimen

Specimen Type

Varies

Ordering Guidance

This test should not be ordered for pheochromocytoma or paraganglioma assessment. Instead, order 1 of the following:

- METAF / Metanephrines, Fractionated, 24 Hour, Urine
- PMET / Metanephrines, Fractionated, Free, Plasma
- CATU / Catecholamine Fractionation, Free, 24 Hour, Urine
- CATP / Catecholamine Fractionation, Free, Plasma

Testing is available as the single gene assay (this test) and as a part of a psychotropic pharmacogenomics panel. If genotype testing for psychotropic medications is desired, order PSYQP / Psychotropic Pharmacogenomics Gene Panel, Varies.

Specimen Required

Multiple genotype tests can be performed on a single specimen after a single extraction. See [Multiple Genotype Test List](#) in Special Instructions for a list of tests that can be ordered together.

Submit only 1 of the following specimens:**Specimen Type:** Whole blood**Container/Tube:** Lavender top (EDTA)**Specimen Volume:** 3 mL**Collection Instructions:**

1. Invert several times to mix blood.
2. Send specimen in original tube. **Do not** aliquot.

Specimen Stability Information: Ambient (preferred) 9 days/Refrigerated 30 days**Specimen Type:** Saliva**Patient Preparation:** Patient should not eat, drink, smoke, or chew gum 30 minutes prior to collection.**Supplies:** Saliva Swab Collection Kit (T786)**Specimen Volume:** 1 swab**Collection Instructions:** Collect and send specimen per kit instructions.**Specimen Stability Information:** Ambient 30 days**Specimen Type:** Extracted DNA**Container/Tube:** 2 mL screw top tube**Specimen Volume:** 100 µL (microliters)**Collection Instructions:**

1. The preferred volume is 100 µL at a concentration of 50 ng/µL.
2. Include concentration and volume on tube.

Specimen Stability Information: Frozen (preferred)/Ambient/Refrigerated**Forms**

1. **New York Clients-Informed consent is required.** Document on the request form or electronic order that a copy is on file. The following documents are available in Special Instructions:

-[Informed Consent for Genetic Testing](#) (T576)

-[Informed Consent for Genetic Testing-Spanish](#) (T826)

2. If not ordering electronically, complete, print, and send 1 of the following forms with the specimen:

-[Neurology Specialty Testing Client Test Request](#) (T732)

-[Therapeutics Test Request](#) (T831)

Specimen Minimum Volume

Blood: 0.4 mL

Saliva: 1 swab

Reject Due To

| |
|---|
| All specimens will be evaluated at Mayo Clinic Laboratories for test suitability. |
|---|

Specimen Stability Information

| Specimen Type | Temperature | Time | Special Container |
|---------------|-------------|------|-------------------|
| Varies | Varies | | |

Clinical & Interpretive

Clinical Information

Catechol-O-methyltransferase (COMT) is involved in phase II (conjugative) metabolism of catecholamines and catechol drugs, such as dopamine, as well as the catechol-estrogens. COMT transfers a donor methyl-group from S-adenosylmethionine to acceptor hydroxy groups on catechol structures (aromatic ring structures with vicinal hydroxy-groups).(1) Bioactive catecholamine metabolites are metabolized by COMT in conjunction with monoamine oxidase (MAO):

- Norepinephrine is methylated by COMT forming normetanephrine.
- Epinephrine is methylated by COMT forming metanephrine.
- Dopamine is converted to homovanillic acid through the combined action of MAO and COMT.

Parkinsonism patients receiving levodopa (L-Dopa) therapy are frequently also prescribed a COMT inhibitor to minimize metabolism of L-Dopa by COMT, thereby prolonging L-Dopa action.

COMT is also involved in the inactivation of estrogens. Estradiol can be hydroxylated forming the catechol estrogens 2-hydroxyestradiol and 4-hydroxyestradiol.(2) These hydroxylated estradiols are methylated by COMT, forming the corresponding methoxyestradiols. The gene encoding COMT is transcribed from alternative promoters to produce 2 forms of the enzyme, a soluble short form of the enzyme and a membrane-bound long form. Variants in the *COMT* gene are therefore designated in the literature by the position of the amino acid change in both the short and long form of the enzyme. A single nucleotide variant (SNV) in exon 4 of the gene produces an amino acid change from valine to methionine (Val108/158Met). The presence of methionine at this position reduces the maximum activity of the variant enzyme by 25% and also results in significantly less immunoreactive COMT protein, resulting in a 3-fold to 4-fold decrease in activity compared to wild type (valine at this position). This variant has been associated with prediction of response and risk of relapse when using nicotine replacement therapy for smoking cessation.(3)

The following information outlines the relationship between the polymorphism detected in this assay and the effect on the activity of the enzyme produced by that allele:

| Amino acid change | cDNA nucleotide change (NM_000754.3) | Effect on enzyme activity/metabolism |
|-------------------------------------|---|--------------------------------------|
| None (wild-type) | None (wild type) | Normal activity |
| p.Val158Met (known as Val108Met) | c.472G>A | Reduced activity |

Reference Values

An interpretive report will be provided.

Interpretation

An interpretive report will be provided.

Cautions

Samples may contain donor DNA if obtained from patients who received non-leukoreduced blood transfusions or allogeneic hematopoietic stem cell transplantation. Results from samples obtained under these circumstances may not accurately reflect the recipient's genotype. For individuals who have received blood transfusions, the genotype usually reverts to that of the recipient within 6 weeks. For individuals who have received allogeneic hematopoietic stem cell transplantation, a pretransplant DNA specimen is recommended for testing.

COMT genetic test results in patients who have undergone liver transplantation may not accurately reflect the patient's catechol-O-methyltransferase (COMT) status.

This test does not detect variants other than those listed. Variants in primer binding may affect test results and ultimately the genotyping calls made.

Absence of a detectable variant does not rule out the possibility that a patient has an intermediate or poor metabolizer phenotype. Patients with a normal (extensive) or intermediate metabolizer genotype may have COMT enzyme activity inhibited by a variety of medications, or their metabolites. The following is a partial listing of drugs known to affect COMT activity.

Drugs that undergo metabolism by COMT:

- Alpha-methyl DOPA
- Apomorphine
- Benserazide
- Bitolterol
- Dihydroxyphenylserine
- Dobutamine
- Dopamine
- Epinephrine
- 2-Hydroxyestrogens
- 4-Hydroxyestrogens
- Isoetherine
- Isoprenaline
- Isoproterenol
- Norepinephrine
- Rimiterol

Coadministration may decrease the rate of elimination of other drugs metabolized by COMT.

Drugs that undergo structural modification but are not metabolized by COMT:

- Albuterol
- Metaproterenol

-Methoxamine
-Phenylephrine
-Perbuterol
-Terbutaline

Coadministration will not decrease the rate of elimination metabolism of other drugs metabolized by COMT.

Drugs known to inhibit COMT activity:

-Entacapone
-Tolcapone
-Nitecapone

Dietary components that inhibit COMT activity:

-Quercetin
-Tea catechins

Coadministration will decrease the rate of metabolism of COMT metabolized drugs, increasing the possibility of toxicity, including in heterozygous individuals.

Clinical Reference

1. Weinshilboum RM, Otterness DM, Szumlanski CL. Methylation pharmacogenetics: catechol O-methyltransferase, thiopurine methyltransferase, and histamine N-methyltransferase. *Annu Rev Pharmacol Toxicol.* 1999;39:19-52. doi: 10.1146/annurev.pharmtox.39.1.19
2. Sun H, Guo S, Chen D, et al: Association of functional COMT Val108/Met polymorphism with smoking cessation in a nicotine replacement therapy. *J Neural Transm (Vienna).* 2012;119(12):1491-1498. doi: 10.1007/s00702-012-0841-8
3. Herman AI, Jatlow PI, Gelernter J, Listman JB, Sofuoglu M: COMT Val158Met modulates subjective responses to intravenous nicotine and cognitive performance in abstinent smokers. *Pharmacogenomics J.* 2013;13(6):490-497. doi: 10.1038/tpj.2013.1
4. Worda C, Sator MO, Schneeberger C, Jantschev T, Ferlitsch K, Huber JC: Influence of the catechol-O-methyltransferase (COMT) codon 158 polymorphism on estrogen levels in women. *Hum Reprod.* 2003;18(2):262-266. doi: 10.1093/humrep/deg059
5. Shield AJ, Thomae BA, Eckloff BW, Wieben ED, Weinshilboum RM: Human catechol O-methyltransferase genetic variation: gene resequencing and functional characterization of variant allozymes. *Mol Psychiatry.* 2004;9(2):151-160. doi: 10.1038/sj.mp.4001386
6. Crews KR, Monte AA, Huddart R, et al: Clinical Pharmacogenetics Implementation Consortium Guideline for CYP2D6, OPRM1, and COMT Genotypes and Select Opioid Therapy. *Clin Pharmacol Ther.* 2021 Jan 2. doi: 10.1002/cpt.2149. Epub ahead of print

Performance

Method Description

Genomic DNA is extracted from whole blood or saliva. Genotyping for *COMT* alleles is performed using a polymerase chain reaction (PCR)-based 5'-nuclease assay. Fluorescently labeled detection probes anneal to the target DNA. PCR is used to amplify the section of DNA that contains the variant. If the detection probe is an exact match to the target DNA,

the 5'-nuclease polymerase degrades the probe, the reporter dye is released from the effects of the quencher dye, and a fluorescent signal is detected. Genotypes are assigned based on the allele-specific fluorescent signals that are detected. (Unpublished Mayo method)

PDF Report

No

Day(s) Performed

Monday through Friday

Report Available

3 to 8 days

Specimen Retention Time

Whole Blood/Saliva swab: 2 weeks Extracted DNA: 2 months

Performing Laboratory Location

Rochester

Fees & Codes**Fees**

- Authorized users can sign in to [Test Prices](#) for detailed fee information.
- Clients without access to Test Prices can contact [Customer Service](#) 24 hours a day, seven days a week.
- Prospective clients should contact their account representative. For assistance, contact [Customer Service](#).

Test Classification

This test was developed and its performance characteristics determined by Mayo Clinic in a manner consistent with CLIA requirements. It has not been cleared or approved by the US Food and Drug Administration.

CPT Code Information

0032U

LOINC® Information

| Test ID | Test Order Name | Order LOINC® Value |
|---------|------------------|--------------------|
| COMTQ | COMT Genotype, V | 74511-7 |

| Result ID | Test Result Name | Result LOINC® Value |
|-----------|------------------------|---------------------|
| 610124 | COMT Genotype | 74511-7 |
| 610125 | COMT Phenotype | 93411-7 |
| 610126 | Interpretation | 69047-9 |
| 610127 | Additional Information | 48767-8 |

Test Definition: COMTQ

Catechol-O-Methyltransferase (COMT)

Genotype, Varies

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|--------|-------------|---------|
| 610128 | Method | 85069-3 |
| 610129 | Disclaimer | 62364-5 |
| 610130 | Reviewed by | 18771-6 |