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# RightMed® Gene Report

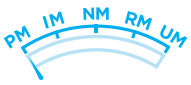
## Patient and report summary

Patient name: **Sample Patient**
Patient date of birth: **1985-03-04**
OneOme report date: **2023-03-06**

Ordering provider: **Sample Doctor**
Ordering facility: **Sample Clinic**
Report type: **Specialty**

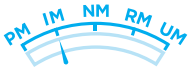
## Phenotype icon legend for CYP genes

CYP phenotype, or metabolizer status, is determined by the total predicted activity of the gene based on the genotype, and is represented by a gauge icon. Total predicted activity which falls between phenotypes will be reported as a range phenotype.



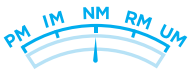

### Poor metabolizer

No to very low activity. Drugs converted to active metabolite(s) may have reduced efficacy. Active drugs converted to inactive metabolite(s) may cause side effects or toxicity.



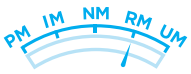

### Intermediate metabolizer

Decreased activity. Drugs converted to active metabolite(s) may have reduced efficacy. Active drugs converted to inactive metabolite(s) may cause side effects or toxicity.



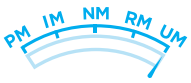

### Normal metabolizer

Normal level of activity. Drugs metabolized at a normal rate.




### Rapid metabolizer

Increased activity. Drugs converted to active metabolite(s) may cause side effects or toxicity. Active drugs converted to inactive metabolite(s) may lack efficacy.




### Ultrarapid metabolizer

Increased activity. Drugs converted to active metabolite(s) may cause side effects or toxicity. Active drugs converted to inactive metabolite(s) may lack efficacy.

## Phenotype icon legend for other genes

Phenotype icons for other genes represent the extent of impact of the genotype on protein activity, expression, or function, and/or observed clinical impact (e.g., adverse event risk).

### Atypical

Genotype indicates an absence of or major increase in protein activity, expression, or function.

### Atypical

Genotype indicates a moderate loss of or increase in protein activity, expression, or function.

### Typical

Genotype indicates normal or typical protein activity, expression, or function.

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# Report and laboratory comments

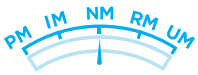
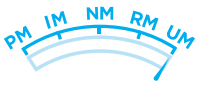
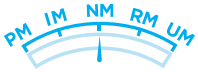
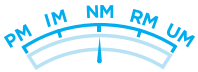
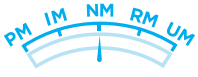
## Interpretive guidance

When two different decreased/no DPYD function variants are present, they are presumed to be on different gene copies. If available, a phenotyping test may further determine enzyme activity.

## Secondary findings

This patient is a carrier for one or more pathogenic or likely pathogenic variants in the following gene(s): DPYD. Please review the *Gene and phenotype summary* for additional information and consider genetic counseling as appropriate.

# Gene and phenotype summary

| Gene | Genotype | | Phenotype summary / Metabolic status |
|---|---|---|---|
| CYP1A2 | *1A/*1A |  | **Normal metabolizer**<br>Fully functional enzyme activity is likely based on the genotype results. Normal metabolism of the medication affected by this gene is predicted. |
| CYP2B6 | *22/*22 |  | **Ultrarapid metabolizer**<br>Increased enzyme activity is likely based on the genotype results. The metabolism of the medication affected by this gene is predicted to be increased. |
| CYP2C9 | *1/*1 |  | **Normal metabolizer**<br>Fully functional enzyme activity is likely based on the genotype results. Normal metabolism of the medication affected by this gene is predicted. |
| CYP2C19 | *1/*1 |  | **Normal metabolizer**<br>Fully functional enzyme activity is likely based on the genotype results. Normal metabolism of the medication affected by this gene is predicted. |
| CYP2C Cluster | rs12777823 GG |  | **Normal**<br>CYP2C rs12777823 homozygous wild-type genotype consistent with normal clearance of a certain medication, independent of the impact of CYP2C9*2 and *3. CYP2C rs12777823, together with CYP4F2, CYP2C9, and VKORC1, may affect treatment management of a certain medication. |
| CYP2D6 | *1/*1 |  | **Normal metabolizer**<br>Fully functional enzyme activity is likely based on the genotype results. Normal metabolism of the medication affected by this gene is predicted. |

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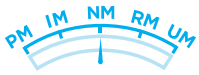
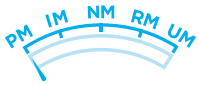
## Gene and phenotype summary (cont.)

| | | | |
|---|---|---|---|
| CYP3A4 | *1/*1 |  | **Normal metabolizer**<br>Fully functional enzyme activity is likely based on the genotype results. Normal metabolism of the medication affected by this gene is predicted. |
| CYP3A5 | *3/*3 |  | **Poor metabolizer**<br>This CYP3A5 genotype is associated with the phenotype most prevalent in studies used to define standard dosing guidelines. |
| CYP4F2 | *1/*1 |  | **Normal activity**<br>Genotype consistent with normal activity of the CYP4F2 enzyme, which catalyzes the metabolism of vitamin K, in counterpoint to the activity of VKORC1. CYP4F2, together with CYP2C9, VKORC1, and a variant in CYP2C Cluster, may affect treatment management of a certain medication. |
| COMT | rs4680 AA |  | **Low activity**<br>The COMT AA (Met/Met) genotype is predicted to yield lower COMT activity than the GG (Val/Val) or GA (Val/Met) genotypes at rs4680. |
| DPYD | Heterozygous for *2A and rs75017182 |  | **Poor metabolizer**<br>DPD activity score= 0.5. This genotype and activity score is consistent with a poor metabolizer phenotype. DPD deficiency is associated with an increased risk for severe or fatal drug toxicity when treated with fluoropyrimidine drugs. If available, a phenotyping test should be considered. |
| DRD2 | rs1799978 AA |  | **Normal receptor expression**<br>Homozygous wild-type dopamine receptor D2 (DRD2) rs1799978 AA genotype is consistent with normal receptor expression. |
| F2 | rs1799963 GG |  | **Normal risk**<br>Normal risk of thrombosis associated with Factor II (prothrombin). Other genetic and clinical factors contribute to the risk for thrombosis. |
| F5 | rs6025 GG |  | **Normal risk**<br>Normal risk of thrombosis associated with Factor V. Other genetic and clinical factors contribute to the risk for thrombosis. |
| GRIK4 | rs1954787 TT |  | **Altered receptor function**<br>Homozygous variant glutamate ionotropic receptor kainate type subunit 4 (GRIK4) genotype is consistent with altered receptor function. |

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## Gene and phenotype summary (cont.)

| | | | |
|---|---|---|---|
| HLA-A | Negative |  | **Normal risk**<br>Negative for the presence of the HLA-A*31:01 allele. Normal risk of hypersensitivity induced by certain medications, and possibly others of structural similarity. Hypersensitivity and severe cutaneous reactions may occur regardless of the presence of the HLA-A*31:01 allele, in particular the presence of the HLA-B*15:02 allele is associated with severe cutaneous reactions induced by certain medications. |
| HLA-B | Negative |  | **Normal risk**<br>Negative for presence of the HLA-B*15:02, HLA-B*57:01, and HLA-B*58:01 alleles. Normal risk of hypersensitivity, severe cutaneous reactions, and severe hepatotoxicity induced by certain medications. Hypersensitivity, severe cutaneous reactions, and severe hepatotoxicity may occur regardless of the presence of HLA-B*15:02, HLA-B*57:01, or HLA-B*58:01 alleles. In particular, the presence of the HLA-A*31:01 allele is associated with hypersensitivity reactions induced by a certain medication, and possibly other medications of structural similarity. |
| HTR2A | rs7997012 AA |  | **Intron 2 genotype AA**<br>Homozygous wild-type HTR2A (5-hydroxytryptamine receptor 2A) genotype is consistent with normal HTR2A receptor function. |
| HTR2C | rs3813929 CC |  | **Increased risk**<br>This genotype predicts an increased risk of weight gain with clozapine or olanzapine treatment when compared to other genotypes. Other clinical and/or genetic factors may influence response. The HTR2C gene is located on the X chromosome. In patients with only one X chromosome (typically, biologically male individuals), results are hemizygous for rs3813929 (C;-). However, due to testing limitations with X chromosome number determination, patients with only one X chromosome will be reported as homozygous (CC) instead of hemizygous (C;-). |
| IFNL4 | rs12979860 CC |  | **Normal**<br>Genotype consistent with a normal likelihood of hepatitis C sustained virologic response (SVR) with certain treatment options. |
| NUDT15 | *1/*1 |  | **Normal metabolizer**<br>NUDT15 genotype is consistent with normal enzyme activity and is not associated with an increased risk of thiopurine-induced toxicities. Toxicities with thiopurines can occur due to impaired TPMT activity independently from the NUDT15 activity. |

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## Gene and phenotype summary (cont.)

| | | | |
|---|---|---|---|
| OPRM1 | rs1799971 AA |  | **Asn/Asn isoform**<br>OPRM1 Asn/Asn (AA) genotype consistent with normal mu-1 opioid receptor function, and normal to increased sensitivity to the effects of certain substrates has been observed when compared to OPRM1 Asn/Asp (AG) or Asp/Asp (GG) genotypes at rs1799971. Normal to increased sensitivity has not been consistently observed in this genotype for all substrates that activate the mu-1 receptor. |
| SLC6A4 | L/L (La/La) |  | **Typical to increased expression**<br>Genotype consistent with a typical to increased expression of the SLC6A4 transporter compared to other genotypes. This genotype was shown to exhibit different phenotypes in East Asian populations, as opposite outcomes were observed for this genotype in East Asian populations when compared to Caucasian populations. |
| SLCO1B1 | *1A/*1A |  | **Normal function**<br>SLCO1B1 genotype consistent with normal function of the OATP1B1 transporter. |
| TPMT | *1/*1 |  | **Normal metabolizer**<br>TPMT genotype is consistent with a normal metabolizer phenotype and is not associated with an increased risk of thiopurine-induced toxicities. Toxicities with thiopurines can occur due to impaired NUDT15 activity independently from the TPMT activity. |
| UGT1A1 | *1/*1 |  | **Normal metabolizer**<br>Genotype consistent with fully functional UGT1A1 enzyme activity, or a normal metabolizer phenotype. |
| VKORC1 | rs9923231 GG |  | **Normal activity**<br>Genotype consistent with normal activity of the vitamin K epoxide reductase enzyme, associated with c.-1639GG (rs9923231). VKORC1, together with CYP2C9, CYP4F2, and a variant in CYP2C Cluster, may affect treatment management of a certain medication. |

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## Test information

Specimen ID: **9038360527371**
Specimen type: **Buccal swab**
Collection date: **2023-03-05**
Receive date: **2023-03-06**

Clinical testing performed by:
**OneOme**
**807 Broadway St. NE Suite 100**
**Minneapolis, MN 55412, United States**

Reported by: **Cathryn Jennissen**
CLIA: **24D2109855**
CAP: **9432670**
NY PFI: **9226**

## Test results

The following analytical results were interpreted by OneOme to produce the pharmacogenomic interpretations and annotations described in the *Gene and phenotype summary*. Method-specific analytical limitations or inferred haplotypes may limit the ability to produce a definitive phenotype interpretation. See *Methodology and limitations* and/or the *Report and laboratory comments* sections for additional information.

### CYP1A2 *1A/*1A

| | | |
|---|---|---|
| rs762551 | NM_000761.4:c.-9-154C>A | CC |
| rs2069514 | NG_008431.2:g.28338G>A | GG |
| rs2069526 | NM_000761.4:c.-10+103T>G | TT |
| rs12720461 | NM_000761.4:c.-10+113C>T | CC |
| rs35694136 | NM_000761.4:c.-1635delT | TT |

### CYP2B6 *22/*22

| | | |
|---|---|---|
| rs3745274 | NM_000767.4:c.516G>T | GG |
| rs2279343 | NM_000767.4:c.785A>G | AA |
| rs34223104 | NM_000767.5:c.-82T>C | CC |
| rs3211371 | NM_000767.4:c.1459C>T | CC |
| rs36079186 | NM_000767.5:c.593T>C | TT |
| rs28399499 | NM_000767.4:c.983T>C | TT |

### CYP2C9 *1/*1

| | | |
|---|---|---|
| rs7900194 | NM_000771.3:c.449G>A | GG |
| rs1799853 | NM_000771.3:c.430C>T | CC |
| rs1057910 | NM_000771.3:c.1075A>C | AA |
| rs28371686 | NM_000771.3:c.1080C>G | CC |
| rs56165452 | NM_000771.3:c.1076T>C | TT |
| rs28371685 | NM_000771.3:c.1003C>T | CC |
| rs9332131 | NM_000771.3:c.817delA | AA |

### CYP2C19 *1/*1

| | | |
|---|---|---|
| rs12248560 | NM_000769.2:c.-806C>T | CC |
| rs4244285 | NM_000769.2:c.681G>A | GG |
| rs4986893 | NM_000769.2:c.636G>A | GG |
| rs6413438 | NM_000769.2:c.680C>T | CC |
| rs28399504 | NM_000769.2:c.1A>G | AA |

### CYP2C Cluster rs12777823 GG

| | | |
|---|---|---|
| rs12777823 | NC_000010.10:g.96405502G>A | GG |

### CYP2D6 *1/*1

| | | |
|---|---|---|
| rs28371706 | NM_000106.5:c.320C>T | CC |
| rs267608319 | NM_000106.5:c.1319G>A | GG |
| rs16947 | NM_000106.5:c.886C>T | CC |
| rs79292917 | NM_000106.5:c.975G>A | GG |
| rs1065852 | NM_000106.5:c.100C>T | CC |
| rs1135840 | NM_000106.5:c.1457G>C | GG |
| rs3892097 | NM_000106.5:c.506-1G>A | GG |
| rs769258 | NM_000106.5:c.31G>A | GG |
| rs5030862 | NM_000106.5:c.124G>A | GG |
| rs201377835 | NM_000106.5:c.181-1G>C | GG |
| rs5030867 | NM_000106.5:c.971A>C | AA |
| rs765776661 | NM_000106.5:c.1411_1412insTGCCCACTG | GTGCCCACGTGCCCAC |
| rs5030656 | NM_000106.5:c.841_843delAAG | AAGAAG |
| rs35742686 | NM_000106.5:c.775delA | AA |
| rs72549353 | NM_000106.5:c.765_768delAACT | AACTAACT |
| rs5030655 | NM_000106.5:c.454delT | TT |
| rs774671100 | NM_000106.5:c.137_138insT | -- |
| rs1080985 | NM_000106.5:c.-1584C>G | CC |
| rs59421388 | NM_000106.5:c.1012G>A | GG |
| rs28371725 | NM_000106.5:c.985+39G>A | GG |
| rs72549346 | NM_000106.5:c.1088_1089insGT | -- |
| rs5030865 | NM_000106.5:c.505G>[A,T] | GG |

### CYP3A4 *1/*1

| | | |
|---|---|---|
| rs2740574 | NM_017460.5:c.-392G>A | AA |
| rs35599367 | NM_017460.5:c.522-191C>T | CC |

### CYP3A5 *3/*3

| | | |
|---|---|---|
| rs776746 | NM_000777.4:c.219-237G>A | GG |
| rs10264272 | NM_000777.4:c.624G>A | GG |
| rs41303343 | NM_000777.4:c.1035_1036insT | -- |

### CYP4F2 *1/*1

| | | |
|---|---|---|
| rs2108622 | NM_001082.4:c.1297G>A | GG |

### COMT rs4680 AA

| | | |
|---|---|---|
| rs4680 | NM_000754.3:c.472G>A | AA |

### DPYD Heterozygous for *2A and rs75017182

| | | |
|---|---|---|
| rs75017182 | NM_000110.4:c.1129-5923C>G | CG |
| rs55886062 | NM_000110.3:c.1679T>G | TT |
| rs67376798 | NM_000110.3:c.2846A>T | TT |
| rs3918290 | NM_000110.3:c.1905+1G>A | GA |
| rs115232898 | NM_000110.4:c.557A>G | AA |

### DRD2 rs1799978 AA

| | | |
|---|---|---|
| rs1799978 | NM_000795.3:c.-585A>G | AA |

### F2 rs1799963 GG

| | | |
|---|---|---|
| rs1799963 | NM_000506.4:c.*97G>A | GG |

### F5 rs6025 GG

| | | |
|---|---|---|
| rs6025 | NM_000130.4:c.1601G>A | GG |

### GRIK4 rs1954787 TT

| | | |
|---|---|---|
| rs1954787 | NM_001282470.2:c.83-10039T>C | TT |

### HLA-A Negative

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## Test results (cont.)

| | | |
|---|---|---|
| HLA00097 | NM_002116 (interrogated at exon 2) | Negative |

### HLA-B Negative

| | | |
|---|---|---|
| rs144012689 | NM_005514.7:c.1012+104A>T | TT |
| HLA00386 | NM_005514 (interrogated at exon 2 and intron 2) | Negative |
| HLA00381 | NM_005514 (interrogated at exon 3) | Negative |

### HTR2A rs7997012 AA

| | | |
|---|---|---|
| rs7997012 | NM_000621.4:c.614-2211T>C | TT |

### HTR2C rs3813929 CC

| | | |
|---|---|---|
| rs3813929 | NM_000868.3:c.-759C>T | CC |

### IFNL4 rs12979860 CC

| | | |
|---|---|---|
| rs12979860 | NM_001276254.2:c.151-152G>A | CC |

### NUDT15 *1/*1

| | | |
|---|---|---|
| rs116855232 | NM_018283.3:c.415C>T | CC |

### OPRM1 rs1799971 AA

| | | |
|---|---|---|
| rs1799971 | NM_000914.4:c.118A>G | AA |

### SLC6A4 L/L (La/La)

| | | |
|---|---|---|
| rs25531 | NM_001045.5:c.-1936A>G | AA |
| rs774676466 | NM_001045.5:c.-1917_-1875del43 | LL |

### SLCO1B1 *1A/*1A

| | | |
|---|---|---|
| rs2306283 | NM_006446.4:c.388A>G | AA |
| rs4149056 | NM_006446.4:c.521T>C | TT |
| rs4149015 | NM_006446.4:c.-910G>A | GG |

### TPMT *1/*1

| | | |
|---|---|---|
| rs1142345 | NM_000367.3:c.719A>G | AA |
| rs1800584 | NM_000367.3:c.626-1G>A | CC |
| rs1800462 | NM_000367.3:c.238G>C | GG |
| rs1800460 | NM_000367.3:c.460G>A | GG |

### UGT1A1 *1/*1

| | | |
|---|---|---|
| rs4148323 | NM_001072.3:c.862-6536G>A | GG |
| rs1976391 | NM_001072.3:c.862-9697A>G | AA |

### VKORC1 rs9923231 GG

| | | |
|---|---|---|
| rs7200749 | NM_024006.5:c.358C>T | GG |
| rs9923231 | NM_001311311.1:c.-1639G>A | GG |

**Electronically signed by:**
Cathryn Jennissen
2023-03-06

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## Methodology and limitations

This test was developed and its performance characteristics determined by OneOme, LLC, a clinical laboratory located at 807 Broadway Street NE Suite 100, Minneapolis, MN 55413. These tests have not been cleared or approved by the U.S. Food and Drug Administration. The FDA does not require this test to go through premarket FDA review. OneOme is certified under CLIA-88 and accredited by the College of American Pathologists as qualified to perform high-complexity testing. This test is used for clinical purposes and should not be regarded as investigational or for research.

Genomic DNA was analyzed by PCR using Thermo Fisher TaqMan® and/or LGC Biosearch BHQ® probe-based methods to interrogate the variant locations listed in the *Test results* table above. In addition, CYP2D6 copy number status was assessed at sites within the promoter, intron 2, intron 6, and exon 9. The test detects CYP2D6 deletions, duplications/multiplications, and hybrid alleles, but cannot differentiate duplications in the presence of a deletion.

Haplotypes, or combinations of inherited variants on a chromosome, are annotated according to legacy nomenclature for the genes and alleles in the table below.

| | |
|---|---|
| CYP1A2 | *1C, *1D, *1E, *1F, *1J, *1K, *1L, *1V, *1W |
| CYP2B6 | *4, *5, *6, *7, *9, *18, *22, *35, *36 |
| CYP2C9 | *2, *3, *4, *5, *6, *8, *11 |
| CYP2C19 | *2, *3, *4, *4B, *10, *17 |
| CYP2D6 | *2, *2A, *3, *4, *4M, *4N, *5, *6, *6C, *7, *8, *9, *10, *11, *12, *13, *14, *15, *17, *18, *19, *20, *29, *31, *34, *35, *36, *39, *41, *42, *59, *63, *64, *68, *69, *70, *91, *109, *114 |
| CYP3A4 | *1B, *22 |
| CYP3A5 | *3, *6, *7 |
| CYP4F2 | *3 |
| DPYD | *2A, Asp949Val, *13, HapB3, Tyr186Cys |
| SLCO1B1 | *1B, *5, *15, *17, *21 |
| TPMT | *2, *3A, *3B, *3C, *4 |
| UGT1A1 | *6, *28 |

The test does not detect all known and unknown variations in the gene(s) tested, nor does absence of a detectable variant (designated as *1 for genes encoding drug metabolizing enzymes) rule out the presence of other, non-detected variants.

As with other common SNP genotyping techniques, these assays cannot differentiate between the maternal and paternal chromosomes. In cases where observed variants are associated with more than one haplotype, OneOme infers and reports the most likely diplotype based on published allele frequency and/or ethnicity data. Inferences with potential clinical impact are reported in the *Report and laboratory comments* section.

The variant detection methods validated by OneOme provide >99.9% accuracy; however, PCR may be subject to general interference by factors such as reaction inhibitors and low quality or quantity of extracted DNA. When present, these interferents typically yield no result rather than an inaccurate one. Very infrequent variants or polymorphisms occurring in primer- or probe-binding regions may also affect testing and could produce an erroneous result or assay failure. Variant locations tested by the assay but not assigned a genotype call are reported as “No Call.” Test results and clinical interpretation may be inaccurate for individuals who have undergone or are receiving non-autologous blood transfusions, tissue, and/or organ transplant therapies. Although extremely rare, results could also be impacted by other factors not addressed above, such as laboratory error.

Due to the complexity of interpreting some genetic test results, such as those that may carry a probabilistic risk of disease, patients and providers should consider the benefits of consulting with a trained genetic counseling professional, physician, or pharmacogenomic specialist. For additional support, contact OneOme through the website or by calling 844-663-6635.

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## OneOme liability disclaimer

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