

Clinical-grade, affordable genetic testing

Pharmacogenomics (PGx) is the study of how genes might impact an individual's response to medications. This information can be considered along with non-genetic patient information to help optimize a medication's dose and reduce the likelihood of adverse reactions.

Color's Medication Response Genetic Test analyzes 14 genes for genetic variations that can affect how the body processes certain medications. Such variations can influence the absorption, transport, and/or metabolism of certain medications, which may help determine their effectiveness (efficacy) and tolerability (toxicity/side effects) for patients. Knowing which variants an individual has in these genes may be useful in determining whether or not to use a particular medication, as well as provide guidance for appropriate dosing. Non-genetic factors such as health history (e.g., liver and kidney function), body size, and other medications a patient is taking should also be considered to make informed decisions on current and future prescriptions. Genetics alone do not determine whether a medication is appropriate.

Color offers complimentary access to a team of clinical pharmacists to answer both provider and patient questions.

Actionable, evidenced-based results

The genes on Color's Medication Response Genetic Test were selected based on evaluation of Food and Drug Administration (FDA) labeling, as well as guidelines from the Clinical Pharmacogenetics Implementation Consortium (CPIC) and/or the Dutch Pharmacogenetics Working Group (DPWG).^{1,2} Using an evidence based-approach, these groups have established guidelines and recommendations for medications with known pharmacogenomics implications.

Knowing which variants an individual has may help determine how they respond to a specific medication. For example:

- **Ultra-Rapid Metabolizer:** Increased enzyme activity compared to rapid metabolizers. Medication may not be effective at the standard dose or may be more likely to cause side effects.
- **Rapid Metabolizer:** Increased enzyme activity (activity between ultra-rapid and normal metabolizer). Medication may not be effective at the standard dose or may be more likely to cause side effects.
- **Normal Metabolizer:** Fully functional enzyme activity. Medication is likely to be effective at the standard dose.
- **Intermediate Metabolizer:** Decreased enzyme activity (activity between normal and poor metabolizer). Medication may not be effective at the standard dose or may be more likely to cause side effects.
- **Poor Metabolizer:** Little to no enzyme activity. Medication may not be effective at the standard dose or may be more likely to cause side effects.
- **Indeterminate:** Allele contains a variant that has not yet been characterized.

Coverage and accuracy

Color performed a validation study and all genetic variants were detected for >99% sensitivity and >99% accuracy.

Specifications:

- Analysis of single nucleotide variants, small insertions/deletions, and copy number variants*
- Minimum read depth: 20X (>99% at >50X)
- Median read depth: 400-700X

Variant classification

- Reported variants are confirmed by alternate technologies, including Sanger sequencing, MLPA or aCGH according to Color's internal protocols.**
- Star alleles and variants analyzed are re-reviewed every six months as available medical literature and scientific knowledge are updated. We will update you and your patient if there is a reclassification.

*CYP2D6 only

**Certain exceptions apply. Variants will not be confirmed if, after testing, there is insufficient DNA available for secondary confirmation. Variants called at high confidence (color.com/variantconfidence) will be reported without secondary confirmation if the variant has been confirmed at least three times in previous carriers.

| Gene | Star alleles and variants analyzed |
|----------------|--|
| <i>CYP2D6</i> | *2, *3, *4, *5, *6, *7, *8, *9, *10, *11, *12, *14A, *14B, *15, *17, *19, *29, *35, *41, *xN |
| <i>CYP2C19</i> | *2, *3, *4A, *4B, *10, *17 |
| <i>CYP1A2</i> | *1F, *1J, *1K |
| <i>CYP2C9</i> | *2, *3, *4, *5, *6, *8, *11 |
| <i>CYP3A4</i> | *1B, *22 |
| <i>CYP3A5</i> | *3, *6, *7 |
| <i>CYP4F2</i> | *3 |
| <i>DPYD</i> | *2A, *13 |
| <i>F5</i> | rs6025 (Leiden) |
| <i>IFNL3</i> | rs12979860 |
| <i>NUDT15</i> | rs116855232 |
| <i>SLCO1B1</i> | rs4149056 |
| <i>TPMT</i> | *2, *3A, *3C, *4 |
| <i>VKORC1</i> | rs9923231 |

*** Results for 2 genes (CYP2D6 and CYP2C19) will be returned initially, and results for the remaining 12 genes will be returned within six (6) months of when we receive your patient's sample.

¹ Hicks JK, Bishop JR, Sangkuhl K, et al. Clinical Pharmacogenetics Implementation Consortium (CPIC) Guideline for CYP2D6 and CYP2C19 Genotypes and Dosing of Selective Serotonin Reuptake Inhibitors. *Clin Pharmacol Ther.* 2015;98(2):127-134.

² Center for Drug Evaluation, Research. Science & Research (Drugs) - Table of Pharmacogenomic Biomarkers in Drug Labeling. <https://www.fda.gov/Drugs/ScienceResearch/ucm572698.htm>. Accessed August 24, 2018.