The genes below were analyzed to understand how they may impact the body's processing of certain medications. Please see the test methodology and limitations section for additional information.

CYP1A2, CYP2C19, CYP2C9, CYP2D6, CYP3A4, CYP3A5, CYP4F2, DPYD, F5, IFNL3, NUDT15, SLCO1B1, TPMT, VKORC1

<table>
<thead>
<tr>
<th>GENE</th>
<th>GENETIC RESULT</th>
<th>GENETIC INTERPRETATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>CYP1A2</td>
<td>*1/*1</td>
<td>normal metabolizer</td>
</tr>
<tr>
<td>CYP2C19</td>
<td>*1/*1</td>
<td>normal metabolizer</td>
</tr>
<tr>
<td>CYP2C9</td>
<td>*1/*15</td>
<td>intermediate metabolizer</td>
</tr>
<tr>
<td>CYP2D6</td>
<td>*1/*1</td>
<td>normal metabolizer</td>
</tr>
<tr>
<td>CYP3A4</td>
<td>*1/*1</td>
<td>normal metabolizer</td>
</tr>
<tr>
<td>CYP3A5</td>
<td>*3/*3</td>
<td>poor metabolizer</td>
</tr>
<tr>
<td>CYP4F2</td>
<td>*1/*1</td>
<td>normal metabolizer</td>
</tr>
<tr>
<td>DPYD</td>
<td>*1/*1</td>
<td>normal metabolizer</td>
</tr>
<tr>
<td>F5</td>
<td>rs6025 GG</td>
<td>variant absent</td>
</tr>
<tr>
<td>IFNL3</td>
<td>rs12979860 TT</td>
<td>unfavorable response</td>
</tr>
<tr>
<td>NUDT15</td>
<td>rs116855232 TT</td>
<td>poor metabolizer</td>
</tr>
<tr>
<td>SLCO1B1</td>
<td>rs4149056 CC</td>
<td>poor function</td>
</tr>
<tr>
<td>TPMT</td>
<td>*1/*1</td>
<td>normal metabolizer</td>
</tr>
<tr>
<td>VKORC1</td>
<td>rs9923231 GG</td>
<td>normal function</td>
</tr>
</tbody>
</table>
How do genes impact the processing of medications?
Genetic changes in genes can influence how fast the body breaks down a medication, how well the body absorbs a medication, or how quickly a medication gets to where it needs to work. This relationship between genetic changes and medication response is known as pharmacogenomics. Genetics is just one of many factors that can affect how the body responds to a medication.

What else besides genetics impacts the processing of a medication?
Your health history (age, weight, liver or kidney disease, other medical conditions), your lifestyle (smoking, drinking alcohol, diet), and other medications you are taking all influence how your body responds to a medication. It is the combination of genetics and these other factors that will determine how well a medication will work for you and if it will cause side effects.

What should I do with these genetic results?
Talk to your doctor about available resources related to specific medications. Additionally, you and your doctor are welcome to speak to one of Color's clinical pharmacists at no charge.

How will my doctor use this information?
Your doctor can use this genetic information, along with the other information they have about your medical history, to help select medications and starting doses. Share your results by fax or by printing your report and bringing it to your next visit.

What if my doctor is not familiar with using these genetic results?
Color's service includes access to clinical pharmacists to help answer questions about results.

Why does this report not include information about specific medications?
The Food and Drug Administration (FDA) has released guidance suggesting concern with some publicly available pharmacogenomics information relating to certain medications. Out of an overabundance of caution and in response to that guidance, Color is not currently providing summaries of medication information in our reports. The genetic results continue to be accurate and potentially useful for prescribing doctors.

Where can I go to learn more about how genes influence medications?

Methodology
Genomic DNA is extracted from the submitted sample, enriched for select regions using a hybridization protocol, and sequenced using Illumina Next Generation Sequencing. Sequence data is aligned to a reference genome, and variants are identified using a suite of bioinformatic tools designed to detect single nucleotide variants, small insertions/deletions, copy number variants, insertions and inversions, and to infer diplotypes. Reported variants may be confirmed by alternate technologies, including Sanger sequencing, MLPA, aCGH or probe-based genotyping. Analysis, variant calling and reporting focus on the complete coding sequence and adjacent intronic sequence of the primary transcript(s), unless otherwise indicated in the limitations section.

This test was developed and its performance characteristics determined by Color Genomics, Inc. (“Color”), a clinical laboratory accredited by the College of American Pathologists (CAP) and certified under the Clinical Laboratory Improvement Amendments (CLIA) to perform high-complexity testing (CAP #8975161 - CLIA #05D2081492). This
laboratory developed test has not been cleared or approved by the United States Food and Drug Administration (FDA). The FDA does not require this laboratory developed test to go through premarket FDA review. This test is used for clinical purposes. It should not be regarded as investigational or for research.

Variants, alleles and diplotypes are classified and described using recommended star-allele and metabolizer-effect nomenclature, where appropriate (PMID: 26479518).

Genes
CYP1A2, CYP2C19, CYP2C9, CYP2D6, CYP3A4, CYP3A5, CYP4F2, DPYD, F5, IFNL3, NUDT15, SLCO1B1, TPMT, VKORC1

Limitations
This analysis aims to detect the presence or absence of any of the following alleles, or genotypes at the specified positions:
CYP1A2: *1F, *1J, *1K
CYP3A4: *1B, *22
CYP3A5: *3, *6, *7
CYP4F2: *3
DPYD: *2A, *13
F5: rs6025C, rs6025T
IFNL3: rs12979860C, rs12979860T
NUDT15: rs116855232C, rs116855232T
SLCO1B1: rs4149056C, rs4149056T
VKORC1: rs9923231C, rs9923231T

This analysis does not detect all possible variations in the tested genes; in some cases the reported result may be refined as new alleles are added to the analysis. When *1 is reported, it indicates that none of the alleles listed above were identified; it does not rule out the presence of an allele not analyzed by this test, and does not rule out the possibility that a non-normal allele is present. In some cases, observed data can be consistent with more than one possible diplotype, and in these cases the diplotype may be reported as “indeterminate”. CYP2D6 copy number is inferred from read depth at representative regions, but does not allow differentiation between partial and whole gene deletions and/or multiplications. Hybrid alleles in CYP2D6 are not detected.

Color only reports findings within the genes that are on the ordered panel. There may be variations in those genes that current technology is not able to detect, and there may be additional relevant genes that are not included in this test.

This test is not designed to detect chromosomal aneuploidies, and sex chromosome aneuploidies, if detected, will not be reported. This test does not reliably detect mosaicism or complex rearrangements such as translocations. Sensitivity may be reduced to detect deletions and insertions in the range of 40-250bp, or larger events that do not overlap more than 250bp of contiguous coding sequence. Inversions including at least one coding exon will be detected only if the breakpoints are covered by the Color test. Sensitivity to detect variants may be reduced in regions of low/high GC content, and in the vicinity of homopolymers and simple sequence repeats.

In very rare cases, such as allogeneic bone marrow transplant, or recent blood transfusion (within 7 days of testing), the results of germline DNA analysis may be complicated by donor mutations. DNA quality may be affected if a
participant has received chemotherapy within the last 120 days. In addition, certain organ transplants or diseases (liver, kidney, heart) may limit the relevance of the results.

Disclaimers
Color implements several safeguards to avoid technical errors, such as automated sample handling and barcode scanning at several steps throughout the sequencing process. Color is not responsible for errors in specimen collection, transportation, and activation or other errors made prior to receipt at our laboratory. Due to the complexity of genetic testing, diagnostic errors, although rare, may occur due to sample mix-up, DNA contamination, or other laboratory operational errors (including, without limitation, equipment or reagent failure, or upstream supplier errors). In addition, poor sample DNA quality and certain characteristics inherent to specific regions of an individual’s genomic DNA may limit the accuracy of results in those regions.

All classifications are based on review, interpretation, and/or analysis of evidence available at the time of reporting, including without limitation medical literature and scientific databases, and may change as new evidence becomes available.