A tool for effective drug prescription

A Doctor’s guide to:
Cytochrome P450 Genetic Analysis

What is Cytochrome P450?
Cytochrome P450 represents a major set of drug-metabolising enzymes. Although there are many P450 genes, three (2C9, 2D6 and 2C19) are responsible for the metabolism of most commonly used drugs. They are highly polymorphic and vary between individuals. This can lead to variability in response to drug therapy.

What is the test?
The test can help you predict how a patient is likely to respond to a particular drug and guides you to prescribe the best medication for each patient based on that patient’s Cytochrome P450 profile.

How is the test performed?
The genotyping of Cytochrome P450 is performed on a mucosal sample collected by a buccal swab. The results are evaluated algorithmically using clinical and genetic parameters to provide a personalised patient report known as the ‘Signature Genetics Report’.

Why chose the Cytochrome P450 test?
Variability in drug response between individuals is a major problem leading to therapeutic failure or adverse effects in a significant number of patients. The Cytochrome P450 test will guide you to:
- which medications will work most effectively and at what dosage
- which treatments might cause adverse reactions and/or react with other concurrent treatments

What data is used to generate the report?
- Data evaluated and summarised in the Signature Genetics™ reports are primarily from peer-reviewed publications.
- Case reports and other recognised public domain sources such as product information monographs are also evaluated.
- The analysis of CYP450 genotype information derived from the medical science literature is carried out by a team of postdoctoral scientists.
- The knowledge base is continuously updated according to rigorous and established criteria.

Which patients should be tested?
The following may benefit:
- patients who have previously experienced adverse drug reactions
- patients who show no improvement to existing drug therapy
- patients receiving multiple medications
- patients initiated on therapies for chronic conditions
- cancer and psychiatric patients where ‘trial and error’ drug prescribing is high risk

What does the report say?
There are two types of report which can be requested:
- All Inclusive Report – provides a comprehensive gene panel analysis for an in-depth evaluation of the patient’s drug regimen as well as a prospective review of approximately 300 drugs based specifically on the patient’s genetic results.

The main aspects of the reports are summarised below:
1. Executive Summary – containing key patient-specific drug metabolism information including dosage adjustments and/or considerations for selected drugs.
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2. General and patient specific drug metabolism – containing detailed supporting information for dosage adjustments and/or considerations.
4. Prospective Assessment identifies potentially problematic drugs based on patient genotype. More detailed information on these drugs can be obtained in the form of an updated report. This is provided free of charge for the first year.

To view a sample Drug-Gene report please click here

Which medications can be influenced by genetic mutations?
There are approximately 300 medications that are known to be influenced by genetic mutations, a few of the more common ones are:

<table>
<thead>
<tr>
<th>DRUG CLASS NAME</th>
<th>BRAND</th>
<th>GENERIC</th>
</tr>
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<tbody>
<tr>
<td>Antipsychotics</td>
<td>Abilify®</td>
<td>Aripiprazole</td>
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<tr>
<td></td>
<td>Risperdal®</td>
<td>Risperidone</td>
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<tr>
<td></td>
<td>Various</td>
<td>Haloperidol</td>
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<tr>
<td>CNS stimulants</td>
<td>Strattera®</td>
<td>Atomoxetine</td>
</tr>
<tr>
<td>Antidiabetics</td>
<td>Amaryl®</td>
<td>Glimepiride</td>
</tr>
<tr>
<td>Cardiovascular drugs</td>
<td>Aprovel®</td>
<td>Ibesartan</td>
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<tr>
<td></td>
<td>Various</td>
<td>Warfarin</td>
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<tr>
<td></td>
<td>Cozaar®</td>
<td>Losartan</td>
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<td></td>
<td>Lescol®</td>
<td>Fluvastatin</td>
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<tr>
<td>Non-steroidal anti-inflammatory drugs</td>
<td>Celebrex®</td>
<td>Celecoxib</td>
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<tr>
<td>Antidepressants</td>
<td>Cipramil®</td>
<td>Citalopram</td>
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<tr>
<td></td>
<td>Efexor®</td>
<td>Venlafaxine</td>
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<td></td>
<td>Faverin</td>
<td>Fluvoxamine</td>
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<td></td>
<td>Sexstat®</td>
<td>Paroxetine</td>
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<td></td>
<td>Prozac®</td>
<td>Fluoxetine</td>
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<td></td>
<td>Levitra®</td>
<td>Sertaline</td>
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<tr>
<td></td>
<td>Various</td>
<td>Amitriptyline</td>
</tr>
<tr>
<td>Analgesic drugs</td>
<td>Arthritis</td>
<td>Codeine</td>
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<tr>
<td></td>
<td>Tramadol</td>
<td></td>
</tr>
<tr>
<td>Hypnotics and anxiolytics drugs</td>
<td>Various</td>
<td>Diazepam</td>
</tr>
<tr>
<td>Antiepileptics</td>
<td>Epanutin®</td>
<td>Phenytoin</td>
</tr>
<tr>
<td>Gastrointestinal drugs</td>
<td>Zoton®</td>
<td>Lansoprazole</td>
</tr>
<tr>
<td></td>
<td>Losec®</td>
<td>Omeprazole</td>
</tr>
</tbody>
</table>

How long will it take to receive patient results?
From receipt of samples at our testing laboratory, a report will be sent within 15 working days.

How is the patient’s information kept safe?
Patient confidentiality is maintained throughout the testing process. The information received is referenced through personal identification numbers (PINs). Only you will have access to your patient’s identity and their genetic results. All the communications between you and the company providing the test take place securely.

Will the patient have to have the test done more than once?
No. Your patient’s genetic profile on which the test is based never changes and the results are always valid.

Will the patient receive an updated report if their medication is changed in the future?
Yes. An updated report can be requested to advise which medications are most suitable for your patient. This report is free of charge for the first year.

Is there further scientific support?
A team of staff scientists will be able to answer questions and provide assistance to you for any matter related to a Signature Genetics™ report.

The support team can be contacted directly by email physicianinfo@signaturegenetics.com or alternatively you can contact them on 0845 6777 110 (local call charges UK only) or +44 (0) 1489 898610 to receive a call back at a time that suits you.

Is there separate patient material available?
Yes. Please contact us at info@lab-21.com to request this material.

Case Study
Dr. Jones has a patient that is not responding to either antidepressant nortriptyline or desipramine. P450 testing and analysis may help to determine whether there is an issue with compliance or if this lack of response is a result of the patient’s drug metabolism.

- The Drug-Gene report has been chosen since both nortriptyline and desipramine are drugs specifically covered on this report.
- For both desipramine and nortriptyline, the report identifies CYP2D6 as a key metabolic pathway.
- Dr. Jones has decided to include CYP2C19 testing to analyse alternative treatment options.
- The patient’s genetic test reveals that he is an ultra-rapid metaboliser for CYP2D6 (UM) and an extensive or standard metaboliser (EM) for CYP2C19.
- The scientific literature demonstrates that ultra-rapid metabolisers for CYP2D6 can eliminate these two antidepressants from their bodies before they can provide any therapeutic benefit. Non-responding patients are sometimes categorised as non-compliant, when in fact they have issues metabolising drugs.
- Signature Genetics™ can help rule out the metabolism component of drug therapy to better address a compliance issue, should it exist.

For more case studies please click here

How to order the test?
Contact us either through your healthcare team or directly by telephone, fax or email referring to the product codes SER 01 (Drug-Gene report) or SER 02 (All-Inclusive report).

Tel: 0845 6777 100 (local call charges UK only) or +44 (0) 1489 898 600
Fax: +44 (0) 1489 582 327
Email: info@lab-21.com
Website: www.lab-21.com