

**This fact sheet talks about the field of pharmacogenomics or pharmacogenetics. This is where a person's genetic make-up is used to predict the likely response or possible side effects from the use of particular drugs/medication.**



### IN SUMMARY

- The terms pharmacogenomics and pharmacogenetics are often used interchangeably. In this fact sheet we will refer to both fields as pharmacogenomics
- Pharmacogenomics looks at how a number of genetic variants in a person's DNA can influence their response to drugs or medications
- There are a number of benefits of pharmacogenomics. There is, however, still debate about its everyday use in healthcare
- To date there are only a few approved pharmacogenomics tests in Australia.

Findings from the Human Genome Project have shown that 99.9% of the information in over 20,000 human genes is identical from one person to the next. The differences in the remaining 0.1% of genetic information present in human cells are unique to each person.

Usually these differences do not cause any problem with how our body grows, develops or works.

These variations may, however, influence a person's susceptibility to certain health problems. Sometimes they may also predict how a person's body reacts to, or metabolises (breaks down) different treatments or medications.

### PHARMACOGENOMICS

The term **pharmacogenomics** comes from the combination of two words: **pharmacology** and **genomics**.

- **Pharmacology** is the study of how drugs or medications work in the body and **genomics** is the study of how genes may act together to influence health, development or how the body works. These changes or variation may be inherited.
- Therefore, **pharmacogenomics** is the study of genetic factors that influence how a drug works in the body.

Factors that influence how a person responds to medication includes their external and internal environments, overall health, as well as their genetic make-up.

The goal of pharmacogenomics is to understand the role that a person's genetic make-up plays in how well a medicine works, as well as what side effects are likely to happen. Understanding this can help tailor drugs for that person (personalised medicine) or for a group of people.

Some potential benefits of pharmacogenomics:

- **More powerful medicines:** Drugs may be developed to act on specific health problems so that benefits are increased, but damage to nearby healthy cells is limited.
- **Safer drugs the first time:** Doctors may be able to find out which drug to use for a person based on their genetic profile instead of trying many drugs on a person to find the right one. This reduces the chance of reactions that may be harmful.

- **More accurate methods of determining dosages:** Doctors may be able to choose the right dose of certain drugs using a person's genetic profile rather than, for example, being based only on body weight and age. This may decrease the chance of an under-dose or overdose.
- **Better vaccines:** Vaccines made of genetic material (DNA) could activate the right immune response with all the benefits of other vaccines.

Some potential limitations of pharmacogenomics:

- **Many genes are likely to be involved** in how someone reacts to a drug, so choosing the right drug may be complex.
- **It is time-consuming and difficult** to find the variations in a person's genes that may influence how a condition develops, or a drug is metabolised.
- **The interactions with other drugs a person is taking**, their general health and environmental factors will need to be assessed before conclusions can be made about the genetic influence on how the drug is working.

## PHARMACOGENOMICS IN PRACTICE

### Drug response

Common variations in a person's DNA code usually cause no direct problem. In some people, however, such changes may have an impact on their response to a drug. Differences in the DNA code that influence a response to certain drugs are more common in certain population groups than others.

For example, the right dose of warfarin, a blood thinning medication, may be different for each person. Certain genetic variants of *CYP2C9* and *VKORC1* genes affect the warfarin dose needed for a person and time to stabilisation. The overall value of genetic testing still remains uncertain. This is due to the effect of other factors which can also affect the warfarin dose e.g., interacting drugs, diet, advanced age, and the reason for needing warfarin therapy.

### Drug targets

Some drugs work by binding to specific chemicals, called receptor sites, on the body cells. Variation in the genes that code for the receptors may mean that some people may make receptors that do not interact well with the drug. Genetic information may also control how many receptors are made so that some people make more receptors than others.

Examples of targeted treatments include those for cancer. Cancer is a genetic disease where variants in DNA cause cells to grow and divide out of control, forming tumours. Trastuzumab is a drug used in the treatment of breast cancer. A genetic test for the *HER2* gene in the tumour cells from someone with breast cancer is needed before trastuzumab is given. This is because the drug works by binding to the *HER2* protein receptor made by the *HER2* gene and this slows the growth of tumour cells.

### Drug metabolism

How people absorb, break down (metabolise) and eliminate drugs in the body can also be influenced by their genetic information.

For example, some medications for pain relief such as codeine need an enzyme made in the liver named *CYP2D6*, for the drug to be used properly by the body. Variations in the gene coding for the enzyme can change how much enzyme is made in the liver.

People who have low levels of the enzyme metabolise codeine slowly, which can lead to reduced pain relief while still causing side effects. Codeine use is not recommended in these people.

### Drug adverse effects

Here are examples of pharmacogenomic tests, for identifying people who have a higher chance of having severe side effects from certain drugs:

- The human leukocyte antigen *HLA-B\*5701* allele (version of the gene) is linked with people who may develop a severe skin reaction to abacavir therapy. This is used to treat human immunodeficiency virus (HIV)

- The thiopurine S-methyltransferase (TPMT) gene test is for finding people who have a higher chance of developing severe side effects from thiopurine drugs (e.g. azathioprine, mercaptopurine and tioguanine).
- Testing specifically for the *HLA-B\*1502* allele may be considered before giving carbamazepine in certain populations, as this may be linked with severe reactions involving the skin and mucous membranes (tissue layers that produce mucus secretions).

### Drug development

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Knowledge of genetics is being used in research for new medications.

If researchers have the ability to exclude people whose genetic make-up would make a drug being tested harmful or ineffective for them, the more likely that the drug will be targeted to the right groups of people.

Pre-genetic screening of those participants taking part in a research trial may also make the research easier, faster, and therefore less expensive.

### ETHICAL ISSUES

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The idea of individually targeted drug therapy is very attractive but it raises a number of ethical concerns. Firstly, a person will only benefit from pharmacogenomics if they are willing to undergo genetic testing. This in itself can raise concerns about who should have access to that genetic information, particularly as electronic health records become more widely used, and there is greater potential for data sharing.

Pharmacogenomic testing may be expensive and sometimes difficult to interpret. Genetic test results can provide information about other family members and many genetic variants are involved in a number of different conditions.

### REGULATIONS

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The Therapeutic Goods Administration (TGA) has adopted the [European Medicines Agency Guidelines for the use of pharmacogenomics methods](#) in the evaluation of medications where the guidelines correspond to the Australian Product Information. There are a number of [pharmacogenomic tests available commercially](#). Regulation will be needed if the techniques are to be widely used including prescription guidelines, testing and usage labels. In Australia, there is a [Medicare rebate](#) for a small number of pharmacogenomics tests. For more about how useful a particular pharmacogenomic test may be, visit the [PharmGKB website](#).