This fact sheet describes the field of pharmacogenomics (pharmacogenetics), where a person’s genetic make-up is used to determine a 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; however there is 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 the estimated 20,000 human genes is identical from one person to the next. The small differences in the remaining 0.1% of genes present in human cells are unique to each individual.

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

These variations however may influence an individual’s susceptibility to certain health problems or determine how an individual’s body reacts to different treatments, in particular, how different medicines are metabolised.

PHARMACOGENOMICS

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

- **Pharmacology** is the study of how drugs work in the body and **genetics** is the study of how characteristics that result from the action of a single gene or of several genes acting together are inherited and how they work in the cells of the body.
- Therefore, **pharmacogenomics** is the study of genetic factors that influence how a drug works in the body.

Factors that influence how an individual responds to medication include their external and internal environments and overall health, as well as their genetic make-up.

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

Some potential benefits of pharmacogenomics:

- **More powerful medicines**: Drugs may be developed targeting specific health problems that will maximise therapeutic effects but decrease damage to nearby healthy cells.
- **Safer drugs the first time**: Doctors may be able to find out which drug to use based on a genetic profile versus trial and error, reducing the likelihood of adverse reactions.
- **More accurate methods of determining dosages**: Instead of dosages being based on body weight and age, it may be based on an individual’s genetics. This would decrease the likelihood of an overdose.
- **Better vaccines**: Vaccines made of genetic material could activate the immune system to have all the benefits of existing vaccines but with reduced risks of infections.
Some potential limitations of pharmacogenomics:

- **Many genes are likely to be involved** in how someone reacts to a drug, making targeting different drugs very complex.

- **It's time consuming and difficult** to identify the small variations in everyone’s genes that may influence drug metabolism or how the condition develops.

- **The interactions with other drugs a person is taking, their general health and environmental factors will need to be determined before any conclusions are made about the genetic influence on how the drug is working.**

**PHARMACOGENOMICS IN PRACTICE**

**Drug response**

Common variations in the genetic information include changes to a single letter of the four letters of the DNA code – A, T, C and G. For example, the DNA letter ‘A’ may be changed to a ‘C’ so that the message in the gene has been slightly changed.

These variations usually cause no direct problem. However, in some people it can impact on their response to a drug. Small differences in the DNA code that influence a response to certain drugs are more common in certain population groups than others.

For example, the dose of warfarin, a blood thinning medication, is different for each person. Certain genetic variants of CYP2C9 and VKORC1 genes affect warfarin dose requirements and time to stabilisation, however, the clinical value of testing for these remains uncertain. This is due to the effect of other factors which can also affect the warfarin dose e.g., interacting drugs, individual patient characteristics, diet and the reason for having to have warfarin therapy.

**Drug targets**

Genes may also determine how many of the receptors are produced on or within cells and genetic variation may mean that some people produce more of these sites than others.

Examples of targeted drug therapy can be found in cancer therapy. 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 of the tumour cells for the HER2 gene is required before Trastuzumab is given. This is because the drug works by binding to the HER2 gene and reduces the growth of tumour cells.

**Drug metabolism**

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

For example, some pain relief medications such as codeine require a protein produced in the liver called CYP2D6 for the drug to be used by the body, break it down and remove it. Variations in the information contained in the CYP2D6 gene determine how much of this enzyme is produced 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 recommended to be avoided in these people.

**Drug adverse effects**

In Australia, there are some pharmacogenomic tests for identifying people who are at risk of having severe side effects from certain drugs:

- The human leukocyte antigen HLA-B*5701 gene test as people with this variant may develop a severe skin reaction to abacavir therapy which is used to treat human immunodeficiency virus (HIV). Available on Medicare

- The thiopurine S-methyltransferase (TPMT) gene test to identify people who are at risk of developing severe side effects from thiopurine drugs (e.g., azathioprine, mercaptopurine and tioguanine). Available on Medicare

- Consider testing for HLA-B*1502 allele in certain populations before giving carbamazepine in certain populations as it may cause and severe skin reactions.
Drug development
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 the drug being tested harmful or ineffective for them, there may be an increase in the chance that a drug may be useful to a particular population group.

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

ETHICAL ISSUES
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.

Pharmacogenomic testing may be expensive and 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. Very few medical professionals have formal training in genetics to help them understand the meaning of these results for their patient, or for the family.

REGULATIONS
The Therapeutic Goods Administration (TGA) have 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:

Many pharmacogenomic tests are 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.