Patient Information Sheet: Paired tumour / germline DNA testing in patients with cancer.

1. What are genes?

Genes are instructions within the cells of our body which tell our cells how to grow, develop and function. We all inherit two copies of every gene, one from our mother and one from our father.

2. What role do genes play in the development of cancer?

As we live, lifestyle and environmental factors can cause faults (mutations) in our genes. Over time, if enough mutations develop, a cancer can form. These mutations that occur as a process of living are called **somatic** mutations. Somatic mutations are only in the cells of the cancer and they cannot be passed on from parent to child. Therefore, other family members are not at risk of having inherited these mutations.

In some rare families, a person can be born with (inherit) a gene mutation that increases their chance of developing cancer. These mutations are called **germline** mutations. Germline mutations are present in every cell of our body. Not everyone with a germline mutation will develop a cancer. In most cases, germline mutations are inherited from our mother or our father. However, sometimes, they can occur in a person for the first time (a ***de novo*** mutation). If a person has a germline mutation, they can pass it on to their children (boy or girl).

In some cases, a germline mutation may be present in some but not all the cells of our body. This is known as **mosaicism**. If the mutation is present in the egg or the sperm (known as **gonadal mosaicism**) it can be passed on from parent to child.

3. The role of tumour and germline DNA testing in patients with cancer

When genetic testing is performed on a sample of a person's cancer it is known as somatic gene testing. There are a number of reasons why somatic testing might be performed, including:

- to confirm the cancer type
- to provide information about how the cancer may respond to treatment
- to assist with treatment decisions (including whether a person is eligible for government funded anti-cancer treatments)
- to decide if the patient is eligible for a clinical trial or the testing may be performed as part of a clinical trial
- to allow monitoring of the cancer's response to treatment and to detect early relapse (most commonly in haematological (blood) cancers)
- to assess the chance of a person having a heritable predisposition to cancer.

Somatic gene testing may involve testing of one or more genes. When multiple genes are tested, this is known as panel gene testing. Somatic gene testing is performed on a stored sample of a person's cancer. Therefore, no further biopsies or surgeries are needed.

Sometimes, somatic gene testing is paired with germline gene testing. Germline testing often requires a person to provide a blood sample. However, in a person where the cancer involves the blood, another sample, such as hair can be used. When gene testing involves the germline, it has the potential to provide information about a person's wider family.

4. What might be detected by germline gene testing?

There are three possible outcomes of germling genetic testing:

- no mutations are identified in any of the tested genes
- a change is found in one of the tested genes, but the significance of this change is not known (called a variant of uncertain significance or VUS)
- a pathogenic (disease-causing) mutation is identified in a gene which may change your and/or your family's management (a clinically actional result)

It is your choice whether you undergo germline gene testing or not. If you decide to undertake testing, you will be asked to provide written consent. As part of your consent, you will be asked whether you wish to be advised of any clinically actionable germline results. You can change your mind about receiving clinically actionable results at any time.

Patients undergoing paired somatic and germline testing at Pathology Queensland will only be notified of germline genetic test results when a pathogenic mutation is identified in a gene which may change their and/or their family's management.

There are a number of important factors to consider before undertaking germline genetic testing. These include:

- a negative result does not always exclude a familial predisposition to cancer
- the result of your testing may have implications for other family members, including children
- the possibility of an unexpected result. While these results may provide useful information for you and your family, they may initially cause some distress

5. Referral to a cancer genetics service

Genetic services employ experts (geneticists and genetic counsellors) who can provide further information, advice and support. You may be referred to a genetic service if:

- a familial predisposition to cancer is suspected on the basis of family history or tumour characteristics, regardless of the genetic test result
- with the patient's consent, a clinically-actionable mutation in a cancer predisposition gene is identified after germline testing.