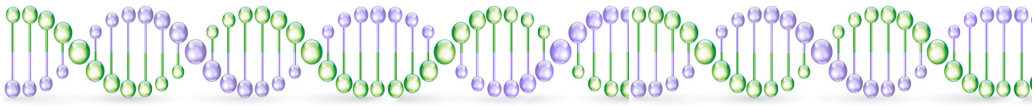
# Information Sheet



# Malignant Melanoma and the CDKN2A gene

In Australia, melanoma is the 3rd most common cancer. It affects 1 in18 people, mainly over age 60.

When 2 or more first degree relatives (close relatives such as your parents, brothers and sisters or children) have had a melanoma, it is referred to as Familial Malignant Melanoma syndrome.

**What are the risk factors for Melanoma?**

Increased risk of melanoma can be caused by genes that affect how someone looks (their "phenotype") and how their skin reacts to sun exposure. These features include:

- fair or red hair
- pale skin
- blue or green eyes
- naevi ("moles")

What colour your skin is and how it reacts to UV radiation is determined by multiple different genes interacting together. Genetic testing is not normally performed in this situation and standard sun sense guidelines should be followed.

**What is Familial Atypical Multiple Mole Melanoma syndrome**

In some families, the risk is also increased because of a mutation in a particular gene, such as CDKN2A . This syndrome is sometimes referred to as Familial Atypical Multiple Mole Melanoma syndrome. Other genes that can increase the risk of melanoma included CDK4, BAP1, POT1, ACD, TERF2IP and TERT.

These kind of inherited gene mutations are rare. For example, the average Australian diagnosed with a melanoma has only a 2% chance that it was caused by an inherited CDKN2A mutation. However, if you do carry a CDKN2A mutation, your risk of melanoma is very high.

**What is GenoMEL?**

To determine the chance of carrying an inherited a mutation in CDKN2A, GenoMEL, an International Melanoma Genetics Consortium, created an online risk assessment tool. One third of the data used to create it were Australian families with multiple melanomas.

The GenoMelPREDICT model uses information including the age of diagnosis, the number of melanoma, how many family members have also had melanoma and whether there is any personal or family history of pancreatic cancer to determine the likelihood of a CDKN2A mutation in you or your relative. (There is a link to GenoMelPREDICT on our website).

If the 4-factor GenoMELPREDICT model suggests a 20% or higher probability of carrying A CDKN2A mutation associated with Familial Atypical Multiple Mole Melanoma syndrome, genetic testing would be recommended.

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Clinics in Sydney. Telehealth throughout Australia including to rural and regional areas
All Correspondence: PO Box 845, Broadway, NSW, 2007
All appointments: (+61 2) 9304 0438 Fax: (+61 2) 9304 0468 E:info@SydneyCancerGenetics.com.au
www.SydneyCancerGenetics.com.au
Hereditary Health and Hope

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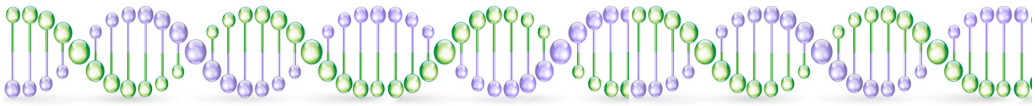

**Who Should Have Genetic Testing for Hereditary Melanoma?**
Australian guidelines recommended genetic testing, usually via a panel of high risk genes, if:

- the GenoMel score is >20%, suggesting a mutation in CDKN2A
- there is a loss of staining for BAP1 on IHC testing
- diagnosis of the melanoma was at a young age (eg before 30)
- there are 3 closely related relatives with melanoma
- there is a history of mesothelioma and/or uveal melanoma
- there are Atypical Spitz tumours
- there is personal or family history of pancreatic cancer

**What is BAP1 Tumour Predisposition syndrome?**
BAP1 Tumour Predisposition syndrome is associated with melanoma including melanomas of the eye (uveal melanoma), malignant mesothelioma, renal cell carcinoma, a type of meningioma called a rhabdoid meningioma and atypical Spitz tumours. You can read more about this hereditary cancer syndrome on the BAP1 gene page on our website.

**How is Familial Atypical Multiple Mole Melanoma syndrome Managed?**
If a germline mutation is detected in a high risk melanoma gene such as CDKN2A then the risk of melanoma is more than 50%. To reduce the risk and catch any melanoma while they are still small and easy to treat screening starts at age 18 and is performed every 6 months. It includes:

- dermoscopy and/or sequential digital dermoscopy imaging, performed every 6 months.
- total-body photography
- sequential digital dermoscopy imaging
- An individual with a CDKN2A mutation is also at increased risk of pancreatic and kidney cancer risk, particularly if they smoke.

**Is Melanoma Risk Inherited?**
Yes. It is associated with genes affecting skin, eye and hair colour and is some families it is due to the hereditary cancer syndrome Familial Atypical Multiple Mole Melanoma syndrome caused by a mutation in the CDKN2A gene.

There is a 50% chance of a person who carries a germline CDKN2A mutation, whether male or female, passing the mutation to their son or daughter. If a mutation were identified, then predictive testing would be available for adult blood relatives. This allows screening of at risk relatives to start early.

**Does this sound like you or your family?**
Have you or your relatives had multiple melanomas? Has mutation been detected in the CDKN2A or other high risk gene in a blood relative? Genetic testing is available.
Make an appointment with Dr Hilda High at Sydney Cancer Genetics. It is a confidential opportunity to discuss your personal and family history of cancer and genetic testing can be organised, if needed.

More information is available on our website, including links to the following:

- The Melanoma Institute Australia and Melanoma Patients Australia
- The Cancer Genetics section of the Cancer Institute's eviQ website provides up-to-date Australian-based management guidelines as well as the lifetime risk of tumours and cancers for individuals with CDKN2A and BAP1 mutations.

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