Familial Melanoma (R254)

Background

Melanomas are one of the most common cancers in the UK. Familial melanoma can be characterised in families where either two first-degree relatives or three or more family members on the same side are diagnosed with melanoma. Approximately 3-15% of melanoma cases are familial. Susceptibility to familial melanoma has been associated with pathogenic variants in various melanoma predisposition genes. The AWMGS laboratory currently offer screening of the high-penetrance melanoma susceptibility genes *CDKN2A (*600160), *CDK4* (123829) and *BAP1 (*603089). If a pathogenic variant is found in one of these genes then other family members can be tested. Heritability in these families is consistent with an autosomal dominant inheritance pattern with incomplete penetrance. Therefore there is a 50% chance of an affected adult passing the disease allele onto his/her child.

Recommended Clinical Referral Criteria

Requests for testing will only be accepted from the clinical genetics service. These referrals will likely be for affected individuals from families with the following criteria:

- Three or more cases of melanoma
- 2 cases of melanoma in first degree relatives with multiple primary melanoma in at least one case
- At least one invasive melanoma and two or more other diagnoses of invasive melanoma and/or pancreatic cancer among first- or second-degree relatives

Individuals with a personal or family history of melanoma that fulfils the testing criteria above can be referred to the All Wales Medical Genomics Service for familial cancer risk assessment and genetic testing. Individuals with a significant personal or family history of melanoma that does *not* fulfil the genetic testing criteria *may* still benefit from a familial cancer risk assessment and can be referred to the All Wales Medical Genomics Service.

Information on making a cancer genetics referral is available here.

Molecular Analysis and Turnaround Times (TATs)
Prices available on request, please contact the laboratory using details below.

Test	Details	TAT (calendar days)
Next generation sequencing (NGS) and dosage analysis	*CDKN2A*, *CDK4* and *BAP1* are enriched using an Illumina TruSight Cancer assay and sequenced on an Illumina NextSeq. Common gaps will be filled using Sanger sequencing, where gaps remain coverage will be reported. Dosage analysis will be carried out by NGS.	42 CD
Familial follow-up	Testing for known familial pathogenic variants in *CDKN2A*, *CDK4* and *BAP1* for parental and variant investigations.	42 CD
Pre-symptomatic testing	Pre-symptomatic testing for known familial pathogenic variants in *CDKN2A*, *CDK4* and *BAP1*.	28 CD

Sample requirements
Blood: 5ml in EDTA. Please label samples with three identifiers and date of collection. Please contact lab prior to sending a prenatal sample. All samples must be accompanied by a request form. Consent for testing & DNA storage is assumed when request for test received.

Contact Details
All Wales Genomics Laboratory,
Institute of Medical Genetics,
University Hospital of Wales,
Heath Park,
Cardiff, CF14 4XW
Tel: 029 2184 4023
Fax: 029 2184 4043
lab.genetics.cav@wales.nhs.uk
https://medicalgenomicswales.co.uk
Accredited to ISO 15189:2012 (8988)

Links and Support
Orphanet: http://www.orpha.net/
OMIM: http://www.omim.org/
Genetic Test Registry: http://www.ncbi.nlm.nih.gov/gtr/
Support: https://www.melanomauk.org.uk/