Genetic Testing in Melanoma

Clinical Background and Genetics

BRAF, KIT, NRAS, GNA11 and GNAQ mutation analysis is available at BGL for melanoma patients to guide targeted inhibitor therapy, clinical trial eligibility and diagnosis.

BRAF
37-50% of melanomas harbour a mutation in the BRAF gene, with the p.(V600E) mutation (commonly known as V600E) accounting for 90% of BRAF variants in melanoma.

BRAF and MEK inhibitors are licensed and approved in the UK for patients with BRAF codon 600 mutation positive unresectable, advanced or metastatic melanoma. Clinical trials have shown near 50% response rate and improved overall survival with vemurafenib (BRAF inhibitor) treatment compared to dacarbazine chemotherapy. Furthermore, combinational therapy using trametinib (MEK inhibitor) plus dabrafenib (BRAF inhibitor) improved overall survival compared to dabrafenib plus placebo in a multicentre, double-blind, phase 3 randomised controlled trial.

KIT
Somatic KIT mutations have been found in 2–8% of all malignant melanoma. KIT mutations may be found in all melanoma subtypes but are the most common in acral melanomas (10–20%) and mucosal melanomas (15–20%). KIT mutated melanomas have been reported to respond to tyrosine kinase inhibitor (TKI) therapy such as imatinib.

NRAS
Somatic NRAS mutations are reported in 13-25% of malignant melanomas and are associated with resistance to BRAF inhibitors in BRAF mutated melanoma. Clinical trials investigating MEK Inhibitor therapy in NRAS mutated melanoma are ongoing.

GNA11 and GNAQ
34%-50% of primary uveal melanomas and 28%-63% of uveal melanoma metastases harbour a mutation in either the GNA11 or GNAQ genes. Testing can be used diagnostically to confirm an uveal primary in metastatic disease.

Service Offered
- Solid tumour Next Generation Sequencing (NGS) panel with analysis restricted to melanoma genes (Illumina TruSight Tumour 15 assay). Regions covered are: BRAF codons 581-605; KIT exons 8, 9, 10, 11, 13, 14, 17, 18; NRAS codons 1 to 22, codons 56 to 94, exon 4; GNA11 codons 203 to 230; GNAQ codons 203 to 243.
  - Urgent requests or requests for BRAF only are analysed by BRAF codon 600 pyrosequencing.
  - These assays can detect a mutation at minimum 5% allele frequency in a background of wild type DNA.

Referrals
- Referrals are accepted from Consultant Oncologists, Dermatologists or Histopathologists.
- For sample requirements please refer to the information on the left.

Target Reporting Times
14 days maximum. Urgent requests: 3 days.

Quality
BGL participates in the GENQA scheme for this service.

References
1) NICE guidance: TA269, TA321, TA396
   https://www.mycancergenome.org/content/disease/melanoma