

Colorectal cancer – RAS Mutation Testing on ctDNA

Background

Mutations in the *KRAS* oncogene (OMIM 190070) and *NRAS* oncogene (OMIM 164790) are frequently found in a number of human cancers. Clinical data has established that 51% of metastatic colorectal tumours may carry a mutated *RAS* gene. An activating mutation indicates that drugs which target the Epidermal Growth Factor Receptor (EGFR) (such as Cetuximab and Panitumumab) will be ineffective in terms of control of tumour proliferation.

The recent development of circulating tumour DNA (ctDNA) technologies has presented us with new opportunities to improve the stratification of colorectal patients for treatment. ctDNA is shed into the patient's blood stream from the tumour. The ctDNA is representative of the tumour and therefore presents a viable alternative to an invasive procedure for molecular analysis for *RAS* mutations.

Recommended Clinical Referral Criteria

Patients with metastatic colorectal cancer, suitable for treatment with Cetuximab, where either no biopsy sample is possible, or where the biopsy sample has been exhausted or has failed molecular analysis.

Molecular Analysis

Mutation hotspot screen: Droplet digital PCR analysis of the most common *RAS* mutations in *KRAS* codons 12, 13 and 61 and *NRAS* codon 61 (covers 96% of known *KRAS* mutations and 47% of known *NRAS* mutations in colorectal cancer). The analysis will detect ~0.5%-1% of mutant in a background of wild-type genomic DNA

Prices* & Turnaround Times (TAT)

*Prices available on request

Test	TAT (calendar days)
Analysis for <i>KRAS</i> codons 12, 13 and 61 and <i>NRAS</i> codon 61	7

Contact Details	Sample Requirements
<p>All Wales Genomics Laboratory, Institute of Medical Genetics, University Hospital of Wales, Heath Park, Cardiff CF14 4XW Tel: 029 2074 2641 Fax: 029 2074 4043 lab.genetics.CAV@wales.nhs.uk www.medicalgenomicswales.co.uk</p>	<p>10-20ml blood in either CellSave© or Streck© tube to reach the laboratory within 24 hours; it is recommended that samples are not taken whilst patient is receiving chemotherapy. 20ml blood preferred to maximise test sensitivity.</p> <p>Please label samples with three identifiers and date of collection.</p> <p>All samples must be accompanied by request form. Consent for testing & DNA storage is assumed when request for test received</p> <p>Websites for tubes: www.streck.com www.janssen.com</p>