



TherapID™ KRAS

What is KRAS :

KRAS is a gene that encodes for protein RAS involved in the EGFR signaling pathway.

Why are KRAS mutations so important in cancer :

Mutated KRAS gene is constitutively active and bypasses blocking activity of anti-EGFR drugs.

Why testing KRAS mutations :

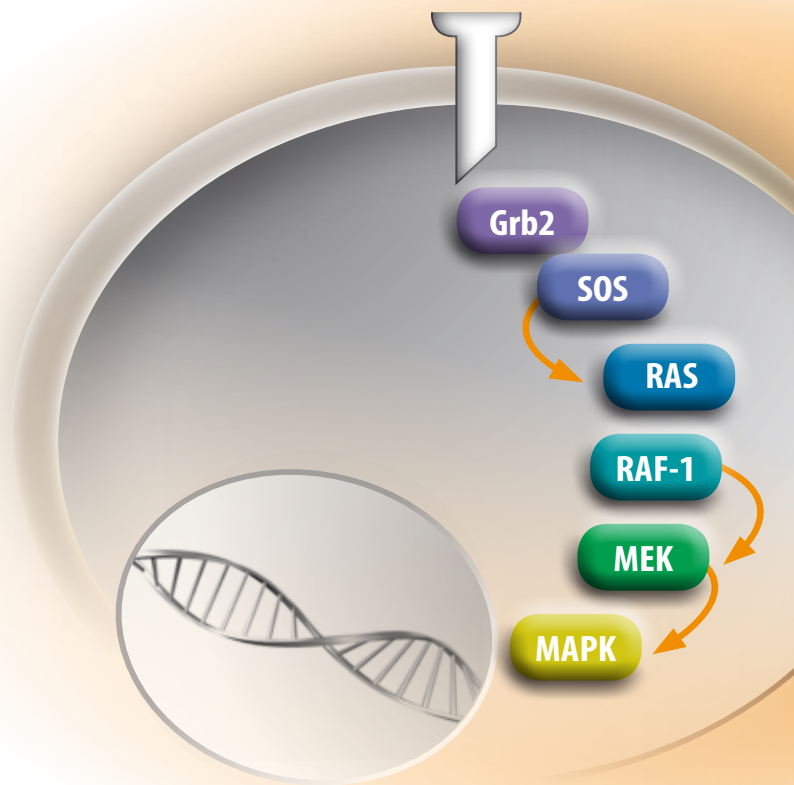
KRAS somatic mutations are found in 30-40% of colorectal cancers (CRC)^{1,2} and 10-30% of non-small cell lung carcinomas (NSCLC)³.

KRAS mutation can indicate prognosis and may also be predictive of drug response.

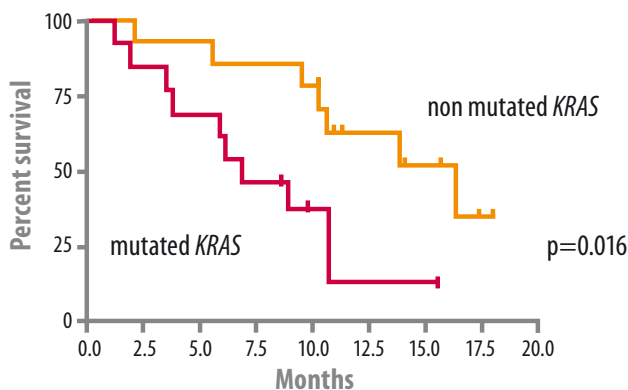
The American Society for Clinical Oncology (ASCO) has published⁴ a provisional clinical opinion (PCO) advising doctors to test patients with colorectal cancer for KRAS mutations before treating them with medicines that include Erbitux® (cetuximab) or Vectibix™ (panitumumab).

What is the EGFR pathway :

EGFR signaling pathway is involved in regulating genes that control cell cycle progression which gives rise to tumor survival, growth and proliferation.



EGFR signaling pathway



Overall survival according to KRAS mutation

From Lièvre A. et al, Cancer Res 2006

What does DNA Vision propose :

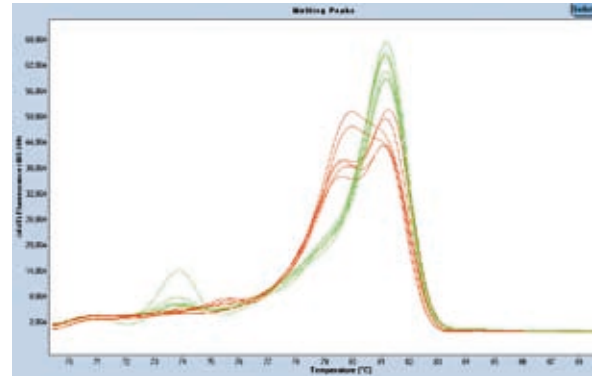
DNA Vision is now offering KRAS testing for mutation detection on DNA extracted from paraffin-embedded clinical material. **TherapID™ KRAS** is designed to detect every potentially activating mutations of the KRAS gene at codon 12 and 13 (which is not achievable with current commercially available kits).

1. Lièvre, A. et al., (2008) J Clin Oncol; 26:374-9
2. Amado, R. G. et al., (2007) Eur J of Can Supp (5):6

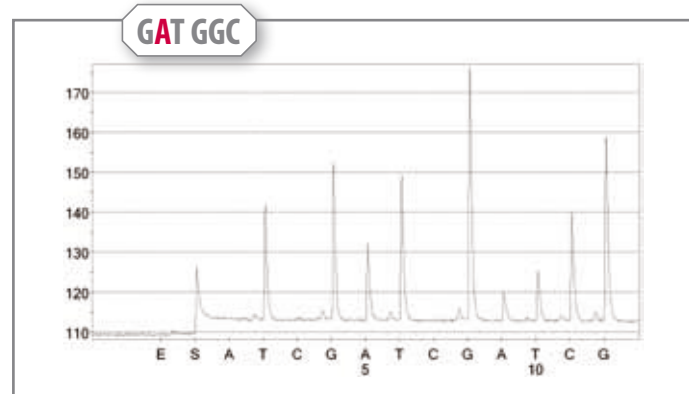
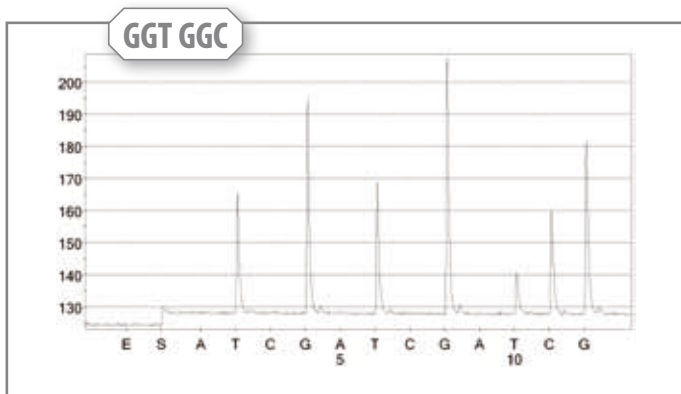
3. Eberhard et al. (2005) J Clin Oncol; 23:5900-9
4. Allegra, C. J. et al (2009). J Clin Oncol 27:2091-2096

TherapID™ KRAS testing overview :

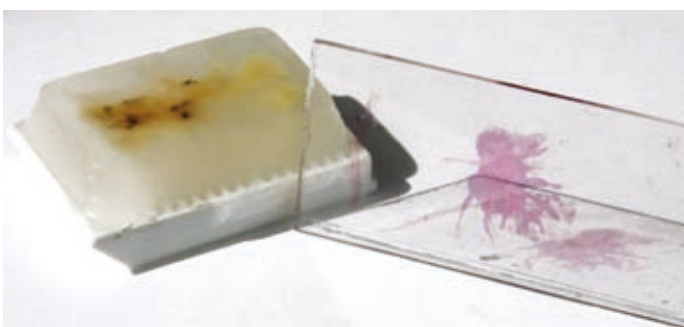
- Step 1.** Tumor sample reception and processing : if needed, paraffin embedding, sections cutting, H&E staining.
- Step 2.** Histopathology review of the sample to ensure tumor tissue is present and analyse healthy/tumor tissue proportion.
- Step 3.** DNA extraction from selected tumor.
- Step 4.** First screening by High-resolution melting analysis (HRMA).
- Step 5.** Further mutation identification by Pyrosequencing™ assay.



High-resolution melting analysis of KRAS. Green curves indicate wild-type (wt) control and red curves colorectal cancer samples with somatic mutations.



Step 6. Mutated/non mutated genotype reporting



Specimen Requirements :

- A.** Formalin-fixed paraffin embedded tissue block with corresponding H&E
- B.** Unstained slides (Min. 9 slides (w/ 1 H&E) or 10 slides (w/o H&E), 7 micron section, Formalin-fixed, air dry)
- C.** Tumor genomic DNA extracted by Qiagen DNA extraction kit (or equivalent).
 - a) and b) will be transported at room temperature. c) will be transported frozen.

