Simple, rapid, highly sensitive diagnostics at hand

NRAS$_3$

Idylla™
NRAS-BRAF-EGFR S492R Mutation Assay

BIOCARTIS

NRAS-BRAF-EGFR S492R

About 50% of all metastatic colorectal tumors harbor RAS mutations[1]. The frequency of NRAS mutations in exons 2, 3 and 4 is around 5%[1]. The frequency of BRAF mutations in mCRC is 8%[1]. Idylla™, Biocartis' fully automated, real-time PCR, offers fast and easy access to high quality biomarker data. The **Idylla™ NRAS-BRAF-EGFR S492R Mutation Assay** allows detection of NRAS, BRAF and EGFR 492 mutations directly from formalin-fixed paraffin-embedded (FFPE) tissue sections in approx. 2 hours with less than 2 minutes hands-on time. The Idylla™ NRAS-BRAF-EGFR S492R Mutation Assay is capable of detecting 25 relevant mutations: 8 NRAS mutations in codons 12 and 13 (exon 2), 6 NRAS mutations in codons 59 and 61 (exon 3), 4 NRAS mutations in codons 117 and 146 (exon 4), 5 BRAF mutations in codon 600 (exon 15) and 2 EGFR mutations in codon 492 (exon 12); at an average sensitivity of 1-5% based on research data. The game-changing real-time PCR based technology uses a unique combination of PlexPrime and PlexZyme technology, which allows very high sensitivity and specificity combined with high multiplexing capability.*

"Idylla's unique fully automated and on-demand process has proven to be accurate, reliable and fast"

Richard Colling
University of Oxford, UK

Outstanding ease of use

- Less than 2 minutes hands-on time
- Approx. 2 hours total turnaround time
- Directly from FFPE tissue sections

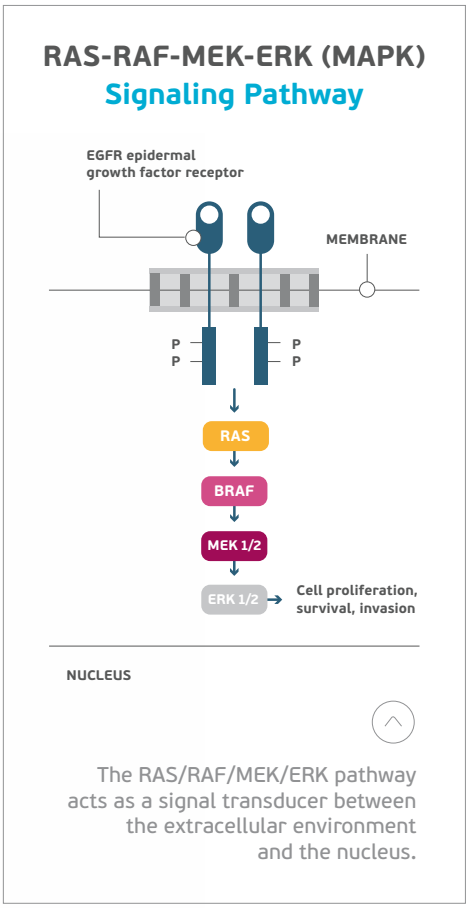
1 Scan sample and cartridge

2 Load sample into the cartridge

3 Insert the cartridge into the Idylla™ system

About NRAS, BRAF and EGFR S492R

- The RAS/RAF/MEK/ERK pathway acts as a signal transducer between the extracellular environment and the nucleus. Extracellular signals, such as hormones and growth factors, interact with their receptors to activate members of the RAS family. The NRAS gene codes for a protein involved in the Epidermal Growth Factor Receptor (EGFR) signaling cascade, which is important in cell proliferation, angiogenesis, migration, cell survival and cell adhesion. When NRAS is mutated, it leads to uncontrolled cell growth and division that may result in cancer.
- BRAF signals through MEK activate ERK, which in turn activates downstream transcription factors that induce processes like cell proliferation, growth and apoptosis.
- NRAS mutations have been detected in many tumors, including colorectal cancer. Mutations in exons 2, 3 and 4 of the NRAS gene are found in approximately 5% of colorectal cancers. In more than 55% of these cases, NRAS mutations are found in codon 61 [1,2].
- BRAF mutations are also detected in many tumors, including colorectal cancer. About 8% of CRC tumors are BRAF mutant. The presence of a BRAF V600E mutation in the setting of MLH1 absence would preclude a diagnosis of Lynch Syndrome[3].
- Recent data show that the EGFR S492R mutation may confer resistance to the anti-EGFR antibody cetuximab (Merck) and remains susceptible to panitumumab (Amgen). The prevalence of this mutation is 16% of patients treated with cetuximab[4,5].
- Tumor mutation status is usually assessed starting from FFPE tumor tissue material. Currently the process from sample to result is labor-intensive, requiring multiple steps. Most laboratories do not perform these tests in-house, but send them out to specialized centers, where samples are batched in order to optimize costs. This leads to long turnaround times from FFPE samples to results.



The RAS/RAF/MEK/ERK pathway acts as a signal transducer between the extracellular environment and the nucleus.

Highly standardized

The **Idylla™ NRAS-BRAF-EGFR S492R Mutation Assay**, performed on the Biocartis Idylla™ System, is a molecular assay for the qualitative detection of mutations in codons 12, 13, 59, 61, 117, 146 of the NRAS oncogene, codon 600 of the BRAF oncogene and codon 492 of the EGFR gene. The Idylla™ NRAS-BRAF-EGFR S492R Mutation Assay, from sample to result, starts with formalin-fixed, paraffin-embedded (FFPE) human tissue to liberate DNA for subsequent real-time PCR amplification and detection.

Allele detection - NRAS	Codon 12 (exon 2)	G12C (c.34G>T)
		G12S (c.34G>A)
		G12D (c.35G>A)
		G12A (c.35G>C) G12V (c.35G>T)
	Codon 13 (exon 2)	G13D (c.38G>A)
		G13V (c.38G>T) G13R (c.37G>C)
	Codon 59 (exon 3)	A59T (c.175G>A)
	Codon 61 (exon 3)	Q61K (c.181C>A)
		Q61L (c.182A>T)
		Q61R (c.182A>G)
		Q61H (c.183A>C; c.183A>T)
	Codon 117 (exon 4)	K117N (c.351G>C; c.351G>T)
	Codon 146 (exon 4)	A146T (c.436G>A) A146V (c.437C>T)
	NRAS Total (acting as Sample Processing Control)	
Allele detection - BRAF	Codon 600 (exon 15)	V600E (c.1799T>A; c.1799_1800TG>AA) V600D (c.1799_1800TG>AC)
		V600K (c.1798_1799GT>AA) V600R (c.1798_1799GT>AG)
	BRAF Total (acting as Sample Processing Control)	
Allele detection - EGFR	Codon 492 (exon 12)	S492R (c.1476C>A; c.1474A>C)
	EGFR Total (acting as Sample Processing Control)	
Sample type	FFPE tissue sections (5µm to 10µm glass mounted FFPE slides or FFPE slices)	
Total turnaround time	approx. 2 hours	

References

1 Jean-Yves Douillard, M.D., Ph.D., Kelly S. Oliner, Ph.D., Salvatore Siena, M.D., et al. Panitumumab–FOLFOX4 Treatment and RAS Mutations in Colorectal Cancer. N Engl J Med 2013;369:1023-34.

2 Peeters M. et al., Prevalence of RAS mutations and individual variation patterns among patients with metastatic colorectal cancer: A pooled analysis of randomised controlled trials. Eur J Cancer 2015, http://dx.doi.org/10.1016/j.ejca.2015.05.017

3 Clinical Practice Guidelines in Oncology (NCCN Guidelines®) - Colon Cancer. Version 1.2016.

4 Montagut C. et al., Identification of a mutation in the extracellular domain of the Epidermal Growth Factor Receptor conferring cetuximab resistance in colorectal cancer. Nature Medicine 2012

5 Newhall K. et al., Frequency of S492R Mutations in the Epidermal Growth Factor Receptor: Analysis of Plasma DNA from Metastatic Colorectal Cancer Patients Treated with Panitumumab or Cetuximab Monotherapy. 16th World Congress on Gastrointestinal Cancer, Barcelona, Spain 2014

About Idylla™

Biocartis' fully automated, real-time PCR-based molecular system offers fast and easy access to high-quality biomarker data.

- FFPE tissue 'sample to result' in approx. 2 hours
- Less than 2 minutes hands-on time
- All reagents integrated within the cartridge
- Contamination-controlled design
- No manual deparaffinization required
- Sample processing controls in all PCR chambers
- High specificity and high average sensitivity of 1-5% based on research data

Order information

Idylla™ NRAS-BRAF-EGFR S492R Mutation Assay RUO	6 cartridges/box	Catalog# A0031/6
Idylla™ Instrument CE-IVD	1 unit	Catalog# P0010
Idylla™ Console CE-IVD	1 unit	Catalog# P1010

NOTICE TO PURCHASER

This Idylla™ NRAS-BRAF-EGFR S492R Mutation Assay contains PlexZyme and PlexPrime technology covered by patents granted and pending in certain jurisdictions, which are supplied under licence of SpeeDx Pty Ltd.

Idylla™ NRAS-BRAF-EGFR S492R Mutation Assay is intended for Research Use Only.

Not for sale in the USA and Canada.

BIOCARTIS

NRAS20151117

Distributed by Abacus dx

1800 ABACUS (AUS) 0800 222 170 (NZ) | info@abacusdx.com | www.abacusdx.com

abacus dx