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RAS-RAF-SEQ

Ultra-sensitive liquid biopsy test for the detection of genomic alterations in the RAS-RAF and PI3K pathways

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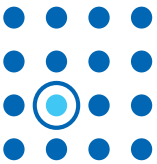
RAS-RAF-SEQ

Understanding genomic alterations along the RAS-RAF and PI3K pathways

Genetic mutations along the RAS-RAF pathway (KRAS, NRAS, BRAF) are common across numerous cancer types, and often play a significant role in cancer development and progression, as well as treatment resistance. Following initial diagnosis, understanding a patient's specific genomic alterations along the RAS-RAF pathway can help inform therapy selection, monitor treatment response, and identify emerging resistance. Moreover, mutations in the PI3K pathway (PIK3CA, AKT1) are known to modulate signaling through the RAS-RAF pathway, and may provide additional information to guide therapeutic decision-making.

Plasma-Safe-SeqS RAS-RAF pathway assay (RAS-RAF-SEQ)

RAS-RAF-SEQ is a clinical grade, CLIA-validated liquid biopsy test for the identification of gene mutations in KRAS, NRAS, BRAF, as well as PIK3CA and AKT1, to inform therapy selection by detecting established and emerging predictive markers, resistance mutations, and frequently occurring genetic alterations associated with various cancers.



Therapeutic selection:

Applying ultra-sensitive Plasma-Safe-SeqS technology to identify mutant molecules at low levels, RAS-RAF-SEQ increases clinical trial efficiency by streamlining the identification of patients that may be eligible for novel therapies, including combination treatments.

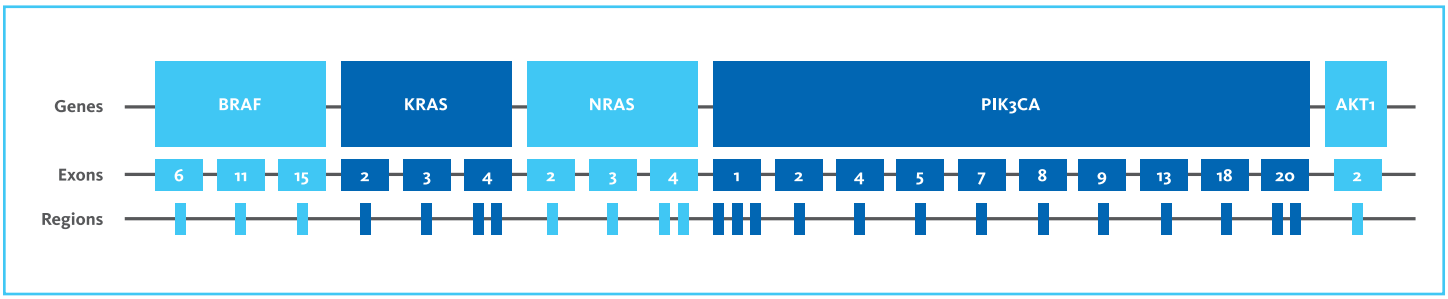
Monitoring therapeutic efficacy and disease dynamics:

RAS-RAF-SEQ provides the ability to identify and monitor molecular alterations, including those that may evolve during the course of certain therapies. By accurately monitoring disease response and clonal dynamics, RAS-RAF-SEQ facilitates the informed adaptation of therapeutic strategies.

Sensitivity matters

Plasma-Safe-SeqS technology is expertly designed to preserve all input molecules for analysis, leading to ultra-sensitive detection of low-level genomic mutations. In contrast, other NGS pan-cancer assays are known to lose up to 40% of all input DNA during sample prep, which decreases reliable detection of ctDNA.[1]

FIG 1. RAS-RAF-SEQ TARGET REGION OVERVIEW



RAS-RAF-SEQ test specifications

RAS-RAF-SEQ identifies key actionable mutations in exons within KRAS, NRAS, BRAF, PIK3CA, and AKT1 genes (Fig 1). These genes regions are known to contain the actionable mutations, for example V600E, for targeted therapy applications of cancer patients (Table 1).

TABLE 1: RAS-RAF-SEQ REGIONS AND REPRESENTATIVE MUTATIONS

GENE	EXONS	EXAMPLES FOR COVERED ALTERATIONS WITH KNOWN CLINICAL RELEVANCE
AKTI	2	E17K [c.49 G>A]
BRAF	6, 11, 15	V600X [c.1799T>A/C/G, c.1798_1799delinsAA, c.1798G>A/C/T and others]
KRAS	2, 3, 4	G12X [c.35G>A/C/T, c.34G>A/C/T, c.34_35delinsTT and others] G13X [c.38G>A/C/T, c.37G>A/C/T, c.38_39delinsAT and others] G61X [c.183A>C/G/T, c.182A>C/G/T, c.181C>A/G and others]
NRAS	2, 3, 4	G12X [c.35G>A/C/T, c.34G>A/C/T, c.34_35delinsAA and others] G13X [c.38G>A/C/T, c.37G>A/C/T, c.37_38delinsAA and others] G61X [c.183A>C/G/T, c.182A>C/G/T, c.181C>A/G and others]
PIK3CA	1, 2, 4, 5, 7, 8, 9, 13, 18, 20	C420R [c.1258T>C] E545X [c.1635G>A/C/T, c.1634A>C/G/T, c.1633G>A/C] M1043I [c.3129G>T] H1047X>[c.3140A>G/T, c.3139G>T]

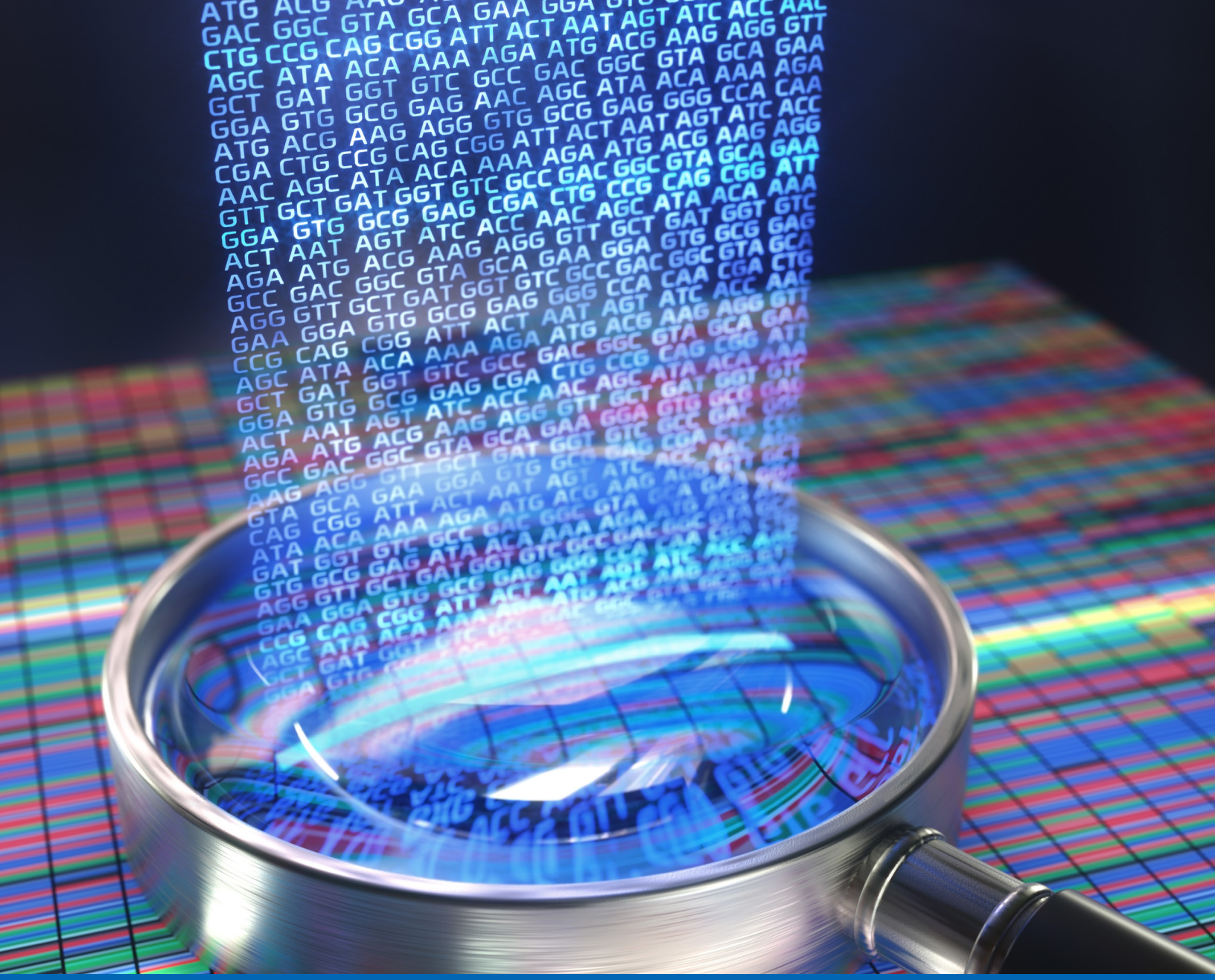
RAS-RAF-SEQ performance specifications

The RAS-RAF-SEQ assay achieves ultra-sensitivity, while maintaining robust specificity (Table 2).

TABLE 2: RAS-RAF-SEQ TEST PERFORMANCE

ALTERATION TYPE	ALLELIC FRACTION*	# OF ctDNA MOLECULES	ANALYTICAL SENSITIVITY	REPORTING THRESHOLD*	ANALYTICAL SPECIFICITY
SNV/Indels	0.10%	20	100%	≥7 ctDNA molecules	100%
	0.05%	10	99.7%		
	0.03%	5	98.1%		
	0.01%	3	84.8%		

*Based on cell-free DNA input of 66ng in patient samples. Analytical sensitivity cited above is for targeted, clinically important regions. Reporting threshold is set above LoD95.



RAS-RAF-SEQ: Enabling discoveries in biopharma

By offering reliable, ultra-sensitive detection of genomic alterations along the RAS-RAF and PI3K pathways, RAS-RAF-SEQ can accelerate clinical development of novel therapeutic strategies across multiple cancer types.

RAS-RAF-SEQ is CLIA-validated and joins the portfolio of ultra-sensitive Plasma-Safe-SeqS tests available through Sysmex Inostics' CLIA lab services in Baltimore, Maryland.

Sample requirements and processing time

Sample specification

2x10mL tubes of whole blood

Pre-analytical sample handling

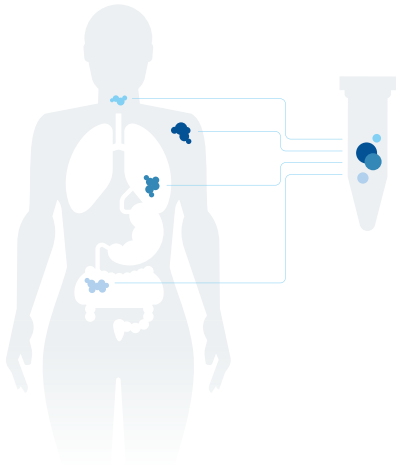
Sysmex Inostics' validated shipping kits and temperature loggers ensure sample stability

Result turnaround time

7 – 10 business days

PLASMA-SAFE-SEQS TECHNOLOGY

Ultra-sensitive across clinically relevant genomic regions



Sysmex Inostics' Plasma-Safe-SeqS technology offers highly sensitive mutation detection across the most clinically relevant gene targets. Plasma-Safe-SeqS is designed specifically for the measurement of ctDNA and panels are developed for particular clinical intended uses where highly sensitive detection may provide unique insights and improve outcomes.

Plasma-Safe-SeqS demonstrates equivalent performance to OncoBEAM digital PCR and is 10 times more sensitive than other liquid biopsy NGS Methods. This level of sensitivity allows clinical trial sponsors to accelerate trial enrollment and evaluate biomarker hypotheses with greater power.

Have a question about RAS-RAF-SEQ?

Please visit www.sysmex-inostics.com/contact-us.

REFERENCES

1 Aigrain, L., Gu, Y., & Quail, M. A. (2016). Quantitation of next generation sequencing library preparation protocol efficiencies using droplet digital PCR assays - a systematic comparison of DNA library preparation kits for Illumina sequencing. BMC Genomics, 17(1), 458.

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