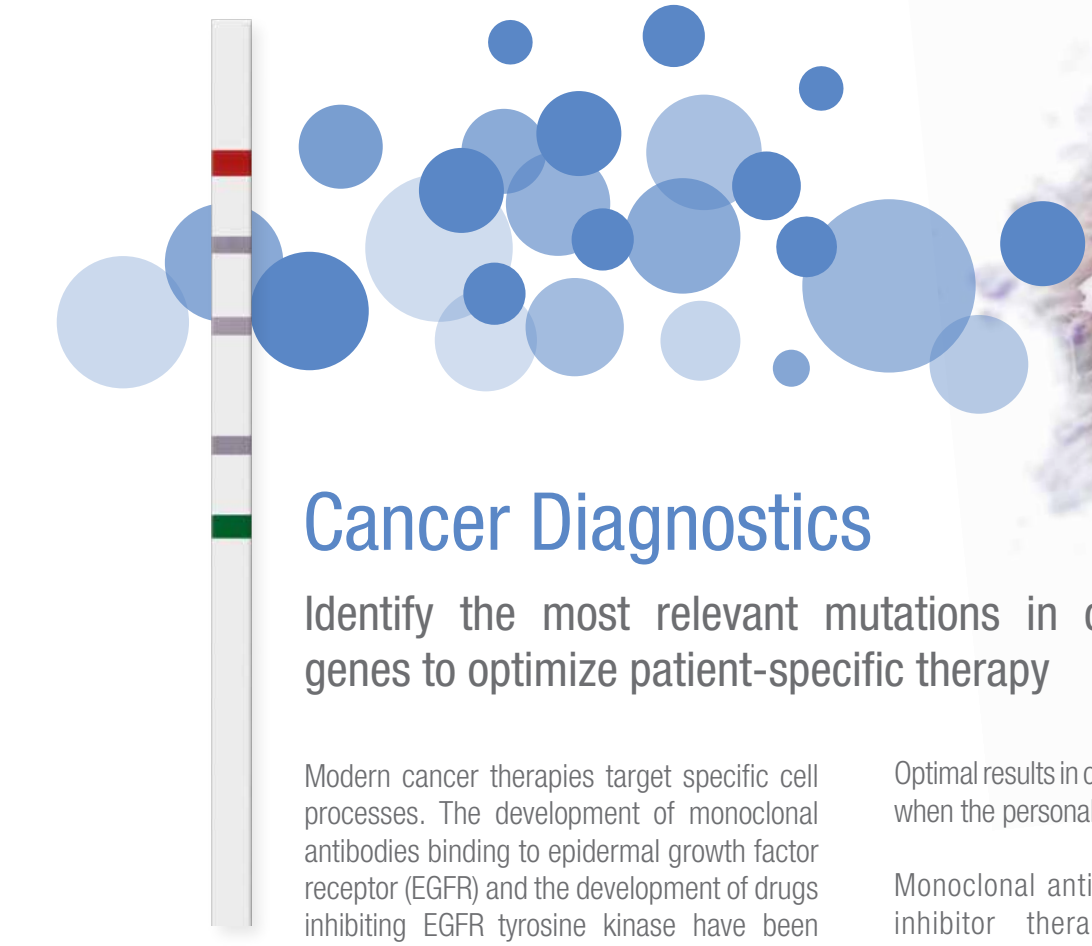
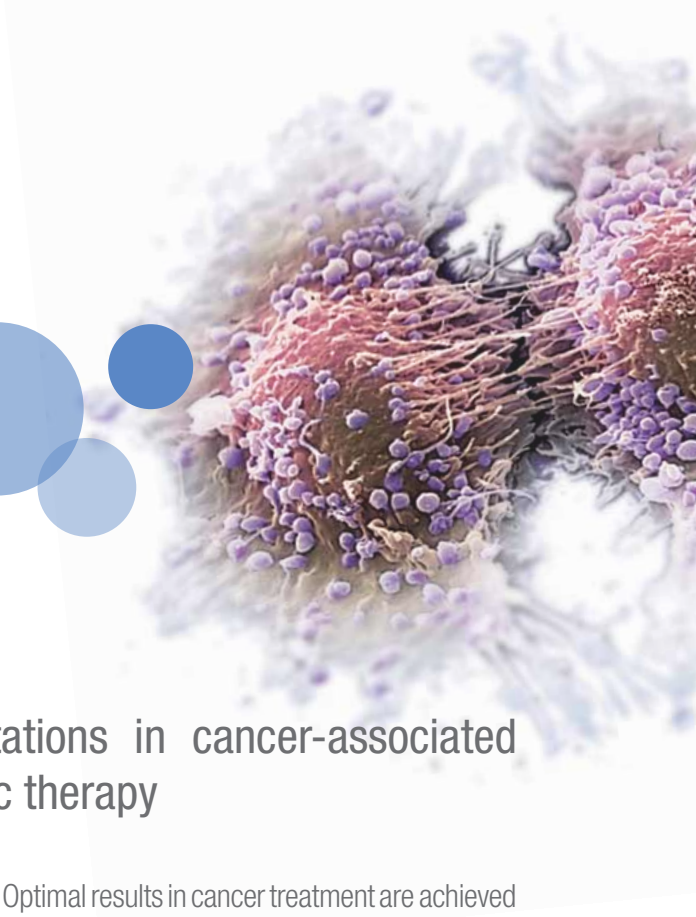
VIENNA LAB
ESTABLISHED INNOVATIONS IN DIAGNOSTICS





Cancer Diagnostics

Identify the most relevant mutations in cancer-associated genes to optimize patient-specific therapy

Modern cancer therapies target specific cell processes. The development of monoclonal antibodies binding to epidermal growth factor receptor (EGFR) and the development of drugs inhibiting EGFR tyrosine kinase have been major steps towards personalized cancer treatment.

Targeted therapy generally causes less damage to healthy cells compared to conventional chemotherapy.

Optimal results in cancer treatment are achieved when the personalized approach is chosen.

Monoclonal antibody and tyrosine kinase inhibitor therapies work exceptionally well in many, but not in all cases. Treatment response is highly dependent on the genetic profile of the tumor.

Thus, genetic tests identifying relevant mutations in oncogenes and tumor suppressor genes facilitate an efficient patient-specific therapy.

ViennaLab StripAssays® and RealFast™ Assay

- Simple protocol for complex diagnostic questions
- Manual or automated processing
- No expensive lab equipment
- Ready-to-use reagents
- CE/IVD-labeled complete kits

KRAS & NRAS

KRAS and NRAS are members of the RAS oncoprotein family that act as mitogen-activated protein kinase (MAPK) signaling pathway GTPases downstream of the epidermal growth factor receptor (EGFR).

Activating *RAS* mutations predict a lack of response to anti-EGFR monoclonal antibody therapies (cetuximab or panitumumab) in colorectal cancer (CRC) patients. KRAS and NRAS mutations are mutually exclusive.

In the Panitumumab Randomized Trial in Combination with Chemotherapy for Metastatic Colorectal Cancer to Determine Efficacy (PRIME) study, NRAS mutations were detected in a fraction of approximately 7% KRAS wild-type CRC tumors.

Published data suggest that NRAS mutations, in addition to KRAS mutations, predict a lack of response to anti-EGFR therapy in metastatic CRC patients.

BRAF

Mutations in the BRAF gene have been reported to contribute to the progression of thyroid cancer and melanoma.

BRAF encodes a serine/threonine kinase, which is a key factor in the MAPK pathway that transduces signals from the RAS oncogenes.

BRAF mutations have been identified in thyroid cancer, melanoma and in some other types of cancer. Certain mutations significantly increase kinase activity and by doing so they can continuously activate transcription-mediated proliferation, which supports neoplastic growth.

Mutations covered by the KRAS, NRAS & BRAF StripAssays®

StripAssay®	Position	Mutations	KRAS REF 5-590	KRAS XL REF 5-680	NRAS XL REF 5-620	BRAF REF 5-570	BRAF REF 600/601 REF 5-560	KRAS-BRAF REF 5-580
KRAS (29 mutations)	Codon 12	G12A, G12R, G12D, G12C, G12I, G12L, G12S, G12V	x	x				x
	Codon 13	G13D, G13C	x	x				x
		G13A, G13R, G13D, G13C, G13S, G13V		x				
	Codon 59	A59E, A59G, A59T		x				
	Codon 60	G60V		x				
	Codon 61	Q61R, Q61H [+)], Q61L, Q61K		x				
	Codon 117	K117N [#)], K117E		x				
	Codon 146	A146P, A146T, A146V		x				
NRAS (22 mutations)	Codon 12	G12A, G12R, G12D, G12C, G12S, G12V			x			
	Codon 13	G13R, G13D, G13C, G13V			x			
	Codon 59	A59D, A59T			x			
	Codon 60	G60R, G60E			x			
	Codon 61	Q61R, Q61E, Q61H [*)], Q61L, Q61K, Q61P			x			
	Codon 146	A146T			x			
BRAF (9 mutations)	Codon 600	V600E [x)]				x	x	x
		V600A, V600D, V600E [~)], V600G, V600K, V600M, V600R					x	
	Codon 601	K601E					x	

KRAS: [+)] p.Q61H (c. 183A>C) and p.Q61H (c. 183A>T); [#)] p.K117N (c. 351A>C) and p.K117N (c. 351A>T)

NRAS: [*)] p.Q61H (c. 183A>C) and p.Q61H (c. 183A>T); BRAF: [x)] p.V600E (c. 1799T>A) ; [~)] p.V600E (c. 1799_1800delTGinsAA)

EGFR

Non-small cell lung cancer (NSCLC) comprises approximately 85% of all lung cancers. Somatic mutations in the epidermal growth factor receptor tyrosine kinase (EGFR-TK) domain influence the treatment with EGFR-TK inhibitors.

First-line TK inhibitors, such as erlotinib and gefitinib, are effective anti-cancer drugs in NSCLC patients carrying activating EGFR mutations.

Conversely, patients carrying the resistance mutation T790M do not benefit from first-line EGFR-TK inhibitor therapy.

Identification of EGFR mutations allows the decision whether an EGFR-TK inhibitor is suitable for use in NSCLC therapy.

EGFR T790M

Designed to identify the resistance mutation T790M in the EGFR gene in plasma-derived, circulating cell-free DNA from NSCLC patients, this assay allows the selection of patients eligible for an alternative EGFR-TK inhibitor therapy with osimertinib (Tagrisso®).

FCGR

Fc gamma receptor (FCGR) genotyping helps to identify high and low responders in antibody-based immunotherapy.

In colorectal cancer 56% of patients with FCGRIIIA F158F genotype responded to treatment with cetuximab plus bevacizumab, compared to 25% with heterozygous F158V and 8% with homozygous V/V genotype.

Breast cancer patients with the genotype FCGRIIA H131H and/or FCGRIIIA V158V responded favourably to trastuzumab therapy.

PGX-5FU

The majority of the 3 to 5% of patients not adequately metabolizing 5-fluorouracil (5-FU) carry a specific mutation in their DPYD gene.

While heterozygous patients should be given lower 5-FU doses, homozygous patients should receive alternative chemotherapeutic treatment.

Mutations covered by the EGFR XL StripAssay® and the EGFR T790M RealFast™ Assay

StripAssay®	Exon	Mutations
EGFR XL (30 mutations)	Exon 18	G719A
		G719C
		G719S
	Exon 19	K745_E749del
		E746_A750del
		E746_A750delinsIP
		E746_A750del
		E746_T751delinsIP
		E746_T751del
		E746_T751delinsA
		E746_T751delinsV
		E746_T751delinsVA
		E746_S752delinsI
		E746_S752delinsA
		E746_S752delinsV
		E746_S752delinsD
		E746_P753delinsVS
		L747_E749del
		L747_A750delinsP*
		L747_A750delinsP*)
		L747_T751delinsP
		L747_T751delinsS
		L747_T751del
		L747_S752del
		L747_S752delinsQ
		L747_P753delinsQ
		L747_P753delinsS
	Exon 20	T790M
	Exon 21	L858R
		L861Q
* p.L747_A750delinsP (c. 2238_2248delinsGC)		
*) p.L747_A750delinsP (c. 2239_2248delinsC)		
RealFast™ Assay	**Exon**	**Mutation**
EGFR T790M NEW!	Exon 20	T790M

Mutations covered by the FCGR & PGX-5FU StripAssays®

StripAssay®	Gene	SNP	FCGR REF 5-670	PGX-5FU REF 4-720
FCGR	FCGRIIA	H131R	x	
	FCGRIIIA	F158V	x	
PGX-5FU	DPYD	IVS14+1 G>A		x

ESTABLISHED INNOVATIONS IN DIAGNOSTICS

ViennaLab StripAssays® and RealFast™ Assay identify the most relevant mutations to support therapy decisions for colorectal cancer, thyroid cancer, lung cancer, melanoma as well as breast cancer.

Disease	Oncogene	Therapy
Colorectal cancer	KRAS/NRAS	Anti-EGFR mAbs (e.g. cetuximab, panitumumab)
Melanoma	BRAF	Small molecule inhibitors (e.g. vemurafenib, dabrafenib, trametinib)
Thyroid cancer	BRAF	Small molecule inhibitors (e.g. vemurafenib) under evaluation
Lung cancer	EGFR	Thyrosine kinase inhibitors (e.g. afatinib, erlotinib, gefitinib, osimertinib)

Disease	Gene	Therapy
Colorectal cancer Breast cancer	FCGRIIA FCGRIIIA	Under evaluation
Various types of cancers	DPYD	Personalized 5-FU therapy: Heterozygotes: lower doses of 5-FU Homozygotes: alternative drugs

The three steps of the StripAssays®

Step	Requirement
1. Amplification: Multiplex PCR. Simultaneous biotin-labeling	Thermocycler
2. Hybridization: Directly on the StripAssay® teststrips	Incubator
3. Identification: Labeled products detected by streptavidin-alkaline phosphatase	Naked eye or scanner & software

REF:

PGX-5FU StripAssay®:	4-720 (20 tests/kit)	EGFR XL StripAssay®:	5-630 (20 tests/kit)
BRAF 600/601 StripAssay®:	5-560 (20 tests/kit)	FCGR StripAssay®:	5-670 (20 tests/kit)
BRAF StripAssay®:	5-570 (20 tests/kit)	KRAS XL StripAssay®:	5-680 (20 tests/kit)
KRAS-BRAF StripAssay®:	5-580 (20 tests/kit)	EGFR T790M RealFast™ Assay:	8-110 (100 rxn)
KRAS StripAssay®:	5-590 (20 tests/kit)	EGFR T790M RealFast™ Assay:	8-113 (32 rxn)
NRAS XL StripAssay®:	5-620 (20 tests/kit)		

ViennaLab offers StripAssays® and RealFast™ Assays for a wide range of diagnostic applications. Visit www.viennalab.com

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