THE PATHCARE NEWS

Solid Tumour NGS panel (Oncomine Focus)

We are pleased to announce the launch our Next Generation Sequencing panel for Solid tumours (Oncomine Focus assay).

This has been done in an attempt to improve and streamline our molecular pathology testing offering. As opposed to testing for single gene anomalies separately, next generation sequencing (NGS) technology allows for testing of multiple genes at one time. This increases **cost efficiency** and **reduces the amount of tissue required**, since only three scrolls of tissue are utilized, and all genes of interest are included in a single test.

The Oncomine Focus assay is designed to detect single nucleotide variants (SNVs), small insertions / deletions, copy number variants (CNVs) and gene fusions in DNA and RNA derived from FFPE tissue. **52 genes** are analysed, including BRAF, EGFR, KRAS, NRAS, ALK, MET and ROS1 (see overleaf for full gene list).

A number of studies[1-6] have demonstrated the excellent sensitivity of NGS methods relative to single-gene targeted assays, particularly for single-nucleotide substitution mutations. NGS typically requires less input DNA and can accommodate smaller samples with lower concentrations of malignant cells. A reduced need for repeat biopsy is an additional benefit of this approach.

In addition to a standard Meditech report, requesting clinicians will receive a summarised **Oncomine Knowledgebase Reporter (OKR) report,** with additional information regarding relevant therapies and clinical trials based on the patient's genotype. A full (extended) report including ALL the clinical trial information will be available to clinicians, on request.

How to request:

- Phone or email the PathCare histopathology laboratory that reported the initial biopsy, to request a Solid Tumour NGS Panel test (Mnemonic W5821).
- Please ask the laboratory to add you, as the requesting clinician, as a copy doctor.

Batching: The samples will be batched and run once a week, starting on a Monday morning. Scrolls from the tissue block must be received in the molecular laboratory by the Sunday evening for inclusion in the batch for the week. Results will be available by the following Monday.

Result availability: Within 10 working days.

Cost: **The price of the Oncomine Focus assay depends on your patient's medical aid –** please contact PathCare for individualised pricing information.

Please see overleaf for full gene list and pricing comparisons

Although analysis for point mutations, insertions and deletions is done using DNA, analysis of gene fusions (e.g. ALK, ROS1) is done by using RNA. RNA is unfortunately more sensitive to fragmentation/ degradation than DNA. Factors that affect RNA integrity include effective fixation by formaldehyde, size of the specimen, temperature at which the specimen is processed as well as storage time [7]. It must therefore be noted that specimens older than one year may not contain enough RNA of adequate quality for accurate analysis of gene fusions. This must be taken into account in specimens where gene fusions are of interest (e.g. lung adenocarcinoma).

If you require any additional information, please email molecularoncology@pathcare.co.za, or contact the following:

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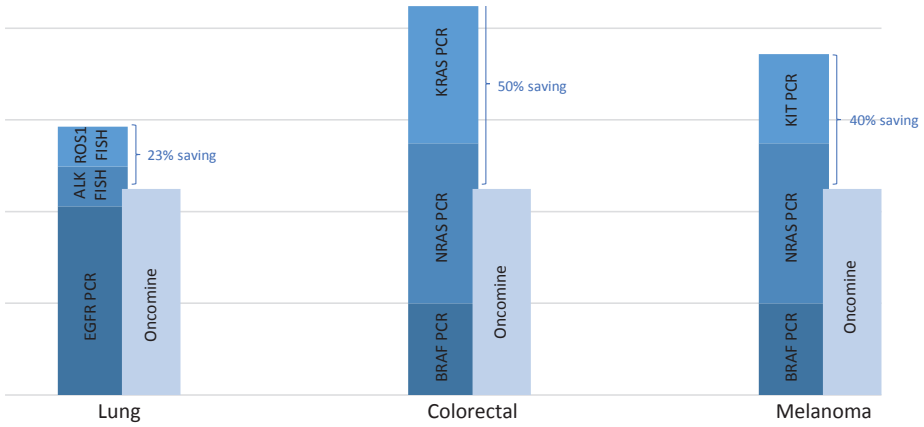
Cost of Oncomine Focus vs Single test requests:



These are only examples of 3 tumour types. There are also **many current and future applications** with regards to other cancer types. International studies have shown that if two or three genes are examined, a panel-based approach is less expensive than single gene testing[8].

Solid Tumour NGS panel gene list:

DNA Panel				RNA Panel	
Hotspot analysis - 35 genes		Copy Number Variant (CNV) analysis – 19 genes		Fusion driver analysis – 23 genes	
AKT1	IDH1	ALK	FGFR3	ABL1	FGFR2
ALK	IDH2	AR	FGFR4	AKT3	FGFR3
AR	JAK1	BRAF	KIT	ALK	MET
BRAF	JAK2	CCND1	KRAS	AXL	NTRK1
CDK4	JAK3	CDK4	MET	BRAF	NTRK2
CTNNB1	KIT	CDK6	MYC	ERG	NTRK3
DDR2	KRAS	EGFR	MYCN	ETV1	PDGFRA
EGFR	MAP2K1	ERBB2	PDGFRA	ETV4	PPARG
ERBB2	MAP2K2	FGFR1	PIK3CA	ETV5	RAF1
ERBB3	MET	FGFR2		EGFR	RET
ERBB4	MTOR			ERBB2	ROS1
ESR1	NRAS			FGFR1	
FGFR2	PDGFRA				
FGFR3	PIK3CA				
GNA11	RAF1				
GNAQ	RET				
HRAS	ROS1				
	SMO				

Hotspots only · CNVs only · Fusions only · Hotspot & CNVs
Hotspot & CNVs & Fusions · Hotspot & Fusions · CNV & Fusions

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3. Han JY, Kim SH, Lee YS, et al: Comparison of targeted next- generation sequencing with conventional sequencing for predicting the responsiveness to epidermal growth factor receptor-tyrosine kinase inhibitor (EGFR-TKI) therapy in never-smokers with lung adenocarcinoma. Lung Cancer 2014, 85:161e167
4. Tuononen K, Maki-Nevala S, Sarhadi VK, et al: Comparison of targeted next-generation sequencing (NGS) and real-time PCR in the detection of EGFR, KRAS, and BRAF mutations on formalin-fixed, paraffin- embedded tumor material of non-small cell lung carcinoma superiority of NGS. Genes Chromosomes Cancer 2013, 52:503e511
5. Scarpa A, Sikora K, Fassan M, et al: Molecular typing of lung adenocarcinoma on cytological samples using a multigene next generation sequencing panel. PLoS One 2013, 8:e80478
6. Endris V, Penzel R, Warth A, et al: Molecular diagnostic profiling of lung cancer specimens with a semiconductor-based massive parallel sequencing approach: feasibility, costs, and performance compared with conventional sequencing. J Mol Diagn 2013, 15:765e775
7. S. von Ahlfen et al. Determinants of RNA Quality from FFPE Samples. PLoS ONE 2(12): e1261.
8. Hamblin A, Wordsworth S, Fermont JM, et al: Clinical applicability and cost of a 46-gene panel for genomic analysis of solid tumours: Retrospective validation and prospective audit in the UK National Health Service. PLoS Med 2017, 14(2):e1002230