INFORMATION FOR MEDICAL PROFESSIONALS ONLY

OncoStrands™

Comprehensive Panel (Tissue Biopsy)

OncoStrands™ Comprehensive Panel (Tissue) provides an extensive coverage of >520 cancer-relevant genes* in a pan-cancer setting from formalin-fixed, paraffin embedded (FFPE) or cytology tumour material (cell block or smears with an adequate number of tumour cells).

This next generation sequencing (NGS) assay not only targets for different types of mutations including single nucleotide variations (SNVs), copy number variations (CNVs), fusions, and splice variants but also enables accurate analysis of immunotherapy biomarkers including tumour mutation burden (TMB) and microsatellite instability (MSI), and *Homologous recombination deficiency (HRD)-(available soon).*

The assay can detect biomarkers that are frequently mutated in various cancer types. This data, combined with cutting-edge curation and analysis solutions, enables not only the detection of biomarkers but also matching with key and emerging treatment guidelines, FDA-approved targeted therapies, and clinical trials. For many tumour types, the test provides complete coverage of NCCN guidelines.

This enables oncologists to select the most appropriate therapeutic approach, anticipate prognosis of the disease course, and fully personalize the disease management for each patient.

*Full list of genes available upon request

>520 DNA Targets >50 RNA Targets
SNVs, CNVs, fusions (including novel variants), Splice variants, TMB, MSI

Screens All Key and Emerging Sequencing Biomarkers as per NCCN Guidelines

Minimum Tumour Content of 20% Required

High Accuracy at ≥5% Limit of Detection

14 Days Turnaround Time*

Bespoke Consultation with Molecular Pathologists

*Comprehensive report available 14 working days from laboratory sample receipt and subject to sample acceptance criteria

Test Specifications & Validation Characteristics

Based on in-house validation of clinical samples, cell lines and reference standards

Methodology	Next generation sequencing
Aberrations covered	SNVs, indels, CNVs, fusions (including novel variants), splice variants, TMB, MSI
Specimen requirements*	• FFPE tissue block OR minimum 15 unstained sections (each 5µm thick). Minimum tumour content of 20%. • Copy of histology report.

*Please refer to the Molecular Oncology Request Form for full specimen requirements.

Mutation type	Accuracy	Sensitivity	Specificity	Limit of Detection
SNVs/short deletions	100%	100%	100%	≥5%
CNVs*	100%	99.0%	100%	N/A
Fusions	100%	98.0%	100%	5 copies per ng RNA input

*CNVs on NGS platforms is an estimate based on prediction algorithm which considers multiple factors. The assay is validated for gene amplifications of ≥5 and homozygous deletions.

TMB – percentage concordance with samples run on orthogonal tests = 100% (based on TMB-high and TMB-low classifications, with 10 mut/Mb as the threshold value)

MSI – percentage concordance with samples run on orthogonal tests = 100%

LifeStrands
Empowering Lives with Genomics

Assay coverage for genes implicated (Mutations/CNVs/Fusions/MSI/TMB) in multiple cancer types with matched biomarker therapeutic recommendations (FDA, NCCN) as follows:

Cancer Type	Biomarkers, DNA & RNA with Therapeutic/ Diagnostic/Predictive/Prognostic/Clinical Trial eligibility, as per various guidelines[1]	Biomarkers with FDA-Approved Matched Therapy*	NCCN Biomarkers Compendium® Recommended Genes[2]
Pan-Cancer	**Pan Cancer Biomarkers (PCB):** *NTRK1, NTRK2, NTRK3* (fusions) MMR-d/MSI-H TMB-H	• MSI-H, TMB-H: Immunotherapy • *NTRK1/2/3*** fusions: TRK inhibitor therapy	• MSI-H, TMB-H: Immunotherapy • *NTRK1/2/3* fusions: TRK inhibitor therapy
Lung	*AKT1, ALK, BRAF, BRCA2, DDR2, EGFR, ERBB2, FGFR1, FGFR3, HRAS, KRAS, MAP2K1, MET, NRAS, PIK3CA, PTEN, RET, RICTOR, TP53*	*ALK, BRAF, EGFR, KRAS, ROS1, RET, MET,* **PCB**	*ALK, BRAF, EGFR, ERBB2, KRAS, MET, RET, ROS1,* **PCB**
Melanoma	*BRAF, CTNNB1, GNA11, GNAQ, KIT, MAP2K1, NF1, NRAS, PDGFRA, PIK3CA, PTEN, TP53*	*BRAF,* **PCB**	*BRAF, CDKN2A, KIT, NRAS*
Colon	*AKT1, APC, ATM, BRAF, CDH1, CHEK2, EGFR, ERBB2, HRAS, KRAS, MET, MLH1, MSH2, MSH6, MUTYH, NRAS, PIK3CA, PMS2, PTEN, SMAD4, STK11, TP53*	*BRAF, RAS (wild type), MMR genes* **PCB**	*EGFR, KRAS, MMR genes, MUTYH, NRAS, PIK3CA,* **PCB**
Ovarian and Fallopian tube	*AKT1, ARID1A, ATR, BRAF, BRCA1, BRCA2, ERBB2, FOXL2, KRAS, PDGFRA, PTEN, RAD51C, TP53*	*BRCA1, BRCA2,* **PCB** *HRD*	*BRCA1, BRCA2,* **PCB**
Breast	*AKT1, ATM, AR, BRCA1, BRCA2, CDH1, CHEK2, ERBB2, ESR1, FGFR1, FGFR2, MLH1, MSH2, MSH6, NBN, PALB2, PIK3CA, PMS2, PTEN, RAD51C, STK11, TP53*	*BRCA1, BRCA2, ERBB2, PIK3CA,* **PCB**	*BRCA1, BRCA2, ERBB2,* **PCB**
Oesophageal	*ERBB2, MLH1, MSH2, MSH6, NTRK1, NTRK2, NTRK3, PMS2*	*ERBB2,* **PCB**	*ERBB2,* **PCB**
Gastric	*ARID1A, BRAF, ERBB2, KIT, KRAS, MET, MLH1, PDGFRA, TP53*	*ERBB2,* **PCB**	*CDH1, ERBB2,* **PCB**
Bladder	*ATM, ERBB3, FGFR2, FGFR3, MTOR, RB1, TSC1*	*FGFR2, FGFR3,* **PCB**	*FGFR2, FGFR3,* **PCB**
Pancreas	*ARID1A, BRAF, BRCA1, BRCA2, CDK12, CDKN2A, EGFR, EP300, FBXW7, HRAS, KRAS, MLH1, MSH2, NOTCH1, NOTCH2, PALB2, PIK3CA, PTEN, STK11, TP53*	*BRCA1, BRCA2,* **PCB**	*ALK, ATM, BRAF, BRCA1, BRCA2, CDKN2A, ERBB2, FGFR2, KRAS, MMR genes, NRG1, PALB2, RET, ROS1, STK11, TP53,* **PCB**
Prostate	*AR, ATM, ARD1A, BARD1, BRAF, BRCA1, BRCA2, BRIP1, CDKN2A, CDK12, CHEK1, CHEK2, FANCL, PALB2, PTEN, RAD51B, RAD51C, RAD51D, RAD54L, RAF1, TMPRSS2*	*ATM, BARD1, BRCA1, BRCA2, BRIP1, CDK12, CHEK1, CHEK2, FANCL, PALB2, RAD51B, RAD51C, RAD51D, RAD54L,* **PCB**	*AR, ATM, BARD1, BRCA1, BRCA2, BRIP1, CDK12, CHEK1, CHEK2, FANCA, FANCL, HOXB13, MMR genes, PALB2, PPP2R2A, RAD51B, RAD51C, RAD51D, RAD54L, TMPRSS2*
Thyroid	*BRAF, HRAS, KRAS, NRAS, PTEN, RET,*	*RET,* **PCB**	*ALK, BRAF, RET,* **PCB**
Cholangiocarcinoma	*BRAF, FGFR2, IDH1, KRAS*	*FGFR2,* **PCB**	*BRAF, BRCA1, BRCA2, ERBB2, FGFR2, IDH1, RET,* **PCB**
GIST	*APC, ARID1A, ATR, BRAF, EGFR, FGFR1, FGFR2, HRAS, KIT, KRAS, MET, MLH1, MSH2, MSH6, NF1, NRAS, PDGFRA, PMS2, STK11, SMAD4, TP53*	*KIT,* **PCB**	*BRAF, FGFR1, KIT, NF1, NTRK1, NTRK2, NTRK3, PDGFRA,*
Sarcoma	*ALK, APC, BRAF, CDK4, CTNNB1, ETV6, EWSR1, FOX01, GLI1, KJT, MDM2, MYOD1, NAB2, NF1, PAX3, PAX7, PDGFRA, PDGFRB, SDHB, SDHC, SMARCB1, TFE3, WT1*	Various fusions, **PCB**	Various fusions, **PCB**
Thymic carcinoma	*KIT*	-	*KIT*
Head and Neck Squamous cancer	*AR, ARID1A, BRAF, CDK12, CDKN2A, EGFR, EP300, ERBB2, FBXW7, FGFR1, FGFR2, FGFR3, HRAS, KRAS, NOTCH1, NOTCH2, PIK3CA, TP53*	**PCB**	*ERBB2, HRAS, PIK3CA* **PCB**
Brain	*ALK, APC, ATRX, BRAF, CDKN2A, CDKN2B, CTNNB1, EGFR, H3-3A, H3C2, IDH1, IDH2, MET, MYC, NF1, NTRK, PDGFRA, RELA, TERT, TP53*	**PCB**	*APC, ATRX, BRAF, CDKN2A, CDKN2B, CTNNB1, EGFR, H3-3A, H3C2, IDH1, IDH2, MET, MYC, NF1, NTRK, PDGFRA, RELA, TERT, TP53*
Cervical Cancer	**PCB**	**PCB**	**PCB**
Uterine/Endometrial	*AKT1, ARID1A, BARD1, BRAF, CDK12, CDKN2A, FGFR1, FGFR2, FGFR3, NRG1, POLE*	**PCB**	*POLE, TP53,* **PCB** Various fusions for uterine sarcoma

*Matched therapy details are part of report contents for each patient

**Specific NTRK1, NTRK3 mutations with acquired resistance to TRK inhibitors are FDA listed contraindication for TRK inhibitors

1 NCCN, ASCO, ESMO, CIVIC, Jackson's Laboratory, OncoKB, My Cancer Genome, current as of July 2022.

2 NCCN Biomarkers Compendium® viewed July 2022, <https://www.nccn.org/compendia-templates/compendia/biomarkers-compendium>

OncoStrands™ Comprehensive Panel

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LifeStrands
Empowering Lives with Genomics

Report Summary

A pathological variant in KRAS gene is detected, which may have prognostic significance in patients with pancreatic cancer. This variant may also have implications for participation in clinical trial. A variant in TP53 gene is detected and may have implications for participation in clinical trial, but there are no reportable therapeutic options. A variant is detected in CCND3 and is currently is not associated with any reportable therapeutic or clinical trial options.

The sample does not harbour any mutation that is currently matched to FDA approved therapy in pancreatic cancer.

IA	IB	IIC	IID	TMB	MSI	Trials
0	1	1	1	Low 1.6 muts/Mb	Stable 2.6% Unstable Sites	4

The Report Summary section highlights the important findings at a glance, including the detected Tier 1-3 variants, TMB and MSI scores, and the number of associated clinical trials

Clinical Implications

TIER	VARIANT DETECTED (GENE/SYNTAX)	CLINICAL IMPACT		SELECT CLINICAL TRIALS
IB	KRAS p.G12R	May benefit from:	Selumetinib or Binimetinib	2
		In Tumor Type:	Langerhans cell histiocytosis or Langerhans cell histiocytosis - category	
		May benefit from:	Cobimetinib or Trametinib	
		In Tumor Type:	Langerhans cell histiocytosis, Erdheim-Chester disease, or Langerhans cell histiocytosis - category	
		May benefit from:	Cabozantinib	
		In Tumor Type:	Medullary thyroid carcinoma	

This section provides recommendations for therapeutic agents matched with variants detected according to FDA and other professional guidelines

Clinical Interpretations

KRAS p.G12R c.34G>C Tier IB NM_033360.2 VAF: 12.4% Depth: 647

GENE

KRAS, KRAS proto-oncogene, GTPase, is a member of the small GTPase superfamily and a key regulator of the MAPK, PI3K/AKT/mTOR pathways (PMID: 23622131) that plays a role in regulation of cell proliferation (PMID: 31988705). KRAS mutations are identified in a wide range of cancers (PMID: 28666118), including colorectal cancer (PMID: 31952666, PMID: 32241284), non-small cell lung cancer (PMID: 32062493, PMID: 32244355), and pancreatic cancer (PMID: 32005945).

VARIANT

KRAS G12R is a hotspot mutation that lies within a GTP-binding region of the Kras protein (UniProt.org). G12R results in decreased Kras GTPase activity and increased activation of downstream signaling in cell culture (PMID: 23455880, PMID: 26037647).

THERAPEUTICS

In a preclinical study, AT7519 treatment induced tumor regression and apoptosis in a patient-derived xenograft (PDX) model of pancreatic ductal adenocarcinoma harboring KRAS G12R (PMID: 33879459).In a preclinical study, the combination treatment of

An in-depth account of genes and variants detected is provided in the Clinical Interpretations section

Clinical Trials

Clinical Trials associated with this patient's genomic profile and tumor type as displayed below.

TITLE	TRIAL IDENTIFIER	PHASE	VARIANT
Efficacy of Olaparib in advanced cancers occurring in patients with germline mutations or somatic tumor mutations in homologous recombination genes.	2018-002966-37 https://www.clinicaltrialsregister.eu/ctr-search/search?query=2018-002966-37	II	TP53 p.G245S c.733G>A
Study of Safety, Pharmacokinetics, and Antitumor Activity of BGB-3245 in Participants With Advanced or Refractory Tumors	NCT04249843 https://clinicaltrials.gov/show/NCT04249843	I	KRAS p.G12R c.34G>C
Safety Study of SAR442720 in Combination With Pembrolizumab in Patients With Advanced Malignancies	NCT04418661 https://clinicaltrials.gov/show/NCT04418661	I	KRAS p.G12R c.34G>C

Current ongoing clinical trials as per FDA, EMA, NCCN, ESMO etc. within the region is provided in the Clinical Trials section of the report

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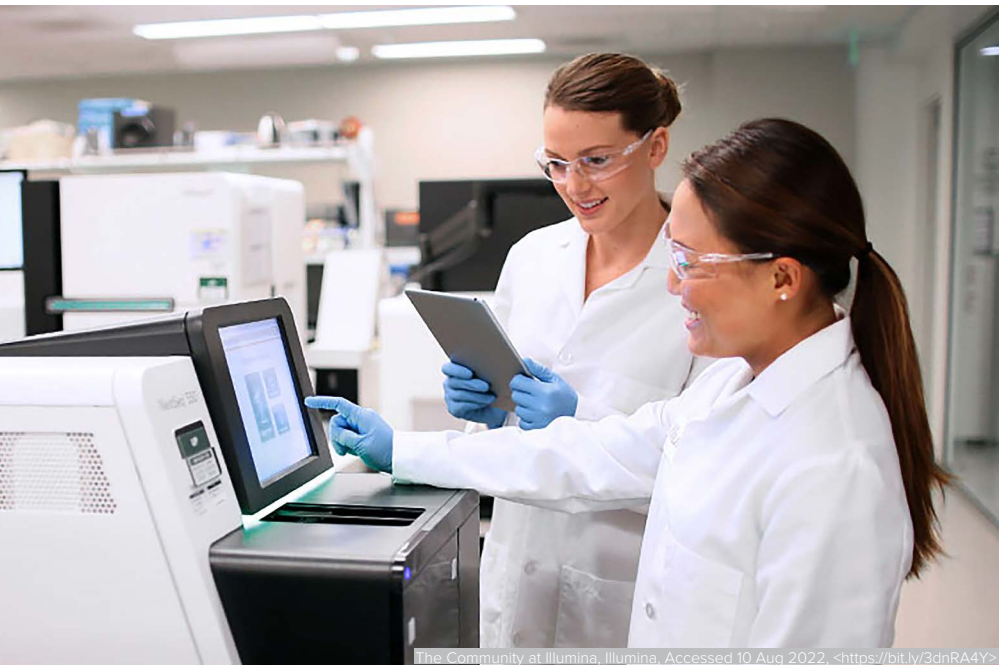
Services Include

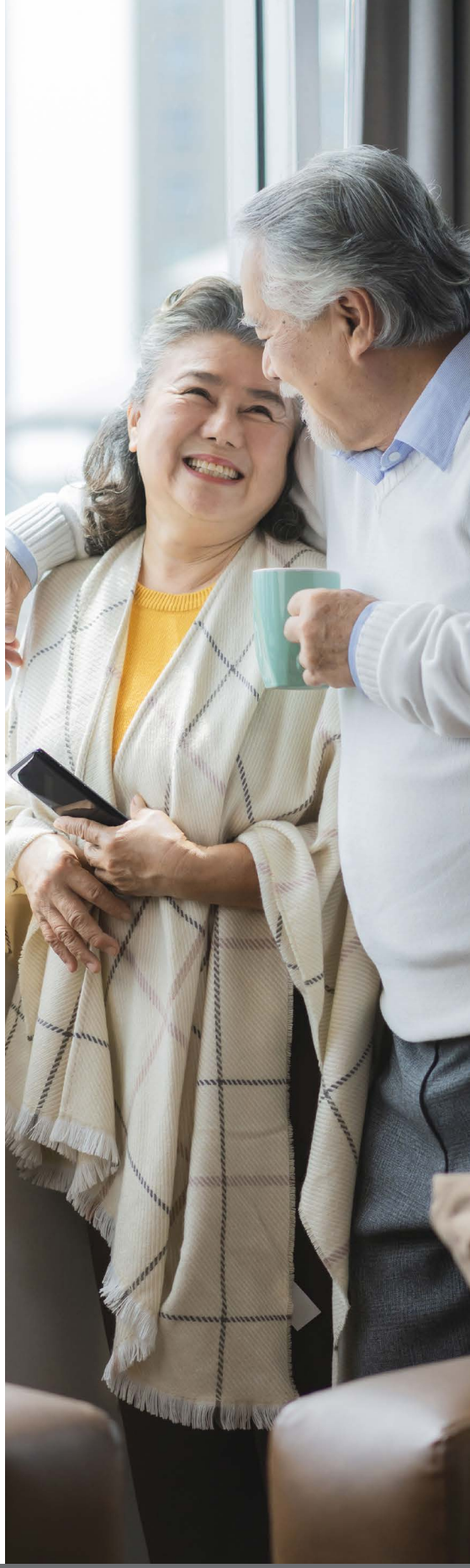
- Quality control for tissue adequacy performed by staff pathologist
- Tests run in house by qualified scientific and clinical staff under an accredited environment
- Complimentary consultation on various aspects of testing (e.g., appropriate test options based on tumour type, tissue availability, etc) provided by qualified staff molecular pathologist

Additional Available Services

- IHC- MMR, PDL-1, *ALK*, *ROS1*
- HRD scoring (available soon — only with this panel)
- Range of Oncostrands™ (oncosomatic) and hereditary panels.



The Community at Illumina, Illumina, Accessed 10 Aug 2022, <https://bit.ly/3dnRA4Y>



About Us

At LifeStrands Genomics laboratories we believe that everyone should have access to better healthcare through the advancement of clinical genomics. Within our accredited laboratories, our dedicated team of medical professionals and scientists work together to deliver high-quality and reliable genomic solutions to clinicians, patients and researchers.

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