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2 DEFINITIONS / ABBREVIATIONS

IVD: In Vitro Diagnostics.
NGS: Next Generation Sequencing.
IHC: ImmunoHistoChemistry
MSI: Microsatellite Instability
TMB: Tumor Mutational Burden
FDA: Food and Drug Administration
EMA: European Medicines Agency
QC: Quality Control
HRD: Homologous Recombination Deficiency
TMB: Tumor Mutational Burden
MSI: MicroSatellite Instability
FFPE: Formalin Fixed Paraffin Embedded
DNA: Deoxyribonucleic Acid
RNA: Ribonucleic Acid
SNV: Single Nucleotide Variant
CNV: Copy Number Variation
LOH: Loss of Heterozygosity

3 MANUFACTURER INFORMATION



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4 DEVICE NAME

OncoDEEP

5 INFORMATION FOR DEVICE IDENTIFICATION

Each boxes and tubes are labelled with labels conform to the IVD Directive (98/79/EC). The labels display pictograms to provide useful information to the end-user. An example of label is shown in figure 1. The signification of each pictogram is given in figure 2.

Figure 1: OncoDEEP library prep Module 1 Label

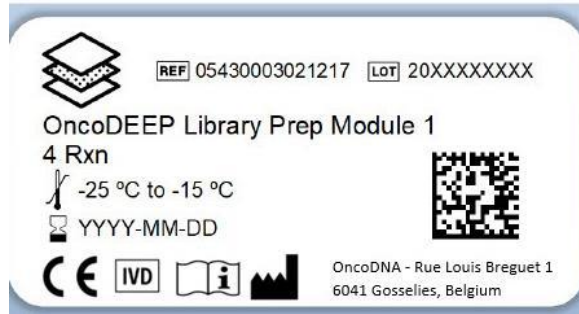










Figure 2: Information displayed on the collection kit and labels

	In vitro diagnostic medical device		Manufacturer
	Catalog Number		Lot Number
	Storage temperature limits		Consult Instructions for use
	Use by (YEAR-MONTH-DAY)		CE Marking conformity

6 DEVICE DESCRIPTION

OncoDEEP Kit is a next-generation sequencing (NGS) assay that enables in-house comprehensive genomic profiling of tumor samples. It supports identification of all relevant DNA variants implicated in various solid tumor types with genes carefully selected based on their biological and therapeutical relevance.

OncoDEEP DNA panel is composed of probes targeting 638 genes for a final content of 1.8 Mb. The OncoDEEP comprehensive gene panel is as shown below (Figure 1).

COMPREHENSIVE GENE PANEL

The OncoDEEP® gene panel contains a total of 638 genes that were carefully selected based on their biological and therapeutical relevance.

ABL1	BABAM1	CD79B	CXCR4	EPHB1	FGF10	GEN1	HNRNPK	KIF5B	MPL	P2RY8	PPM1D	RICTOR	SMARCB1	TGFBR1
ABL2	BAP1	CDC42	CYLD	EPHB4	FGF12	GID4	HOXB13	KIT	MRE11A	PAK1	PPP2R1A	RIT1	SMARCD1	TGFBR2
ACVR1	BARO1	CDC73	CYP17A1	ERBB2	FGF14	GLI1	HRAS	KLF4	MSH2	PAK3	PPP2R2A	RNF43	SMARCE1	TIPARP
ACVR1B	BBC3	CDH1	CYP19A1	ERBB3	FGF19	GNA11	HSD3B1	KLF5	MSH3	PAK7	PPP4R2	ROS1	SMC1A	TMEM127
ADARB2	BCL10	CDH4	CYP2C19	ERBB4	FGF2	GNA13	HSP90AA1	KLHL6	MSH6	PALB2	PPP6C	RPS6KA4	SMC3	TMPRSS2
AGO1	BCL2	CDK12	CYP2D6	ERCC1	FGF23	GNAQ	ICOSLG	KMT2A	MSI1	PARK2	PRDM1	RPS6KB1	SMO	TNFAIP3
AGO2	BCL2L1	CDK4	CYSLTR2	ERCC2	FGF3	GNAS	ID3	KMT2B	MSI2	PARP1	PRDM14	RPS6KB2	SMYD3	TNFRSF14
AJUBA	BCL2L11	CDK6	DAXX	ERCC3	FGF4	GNB1	IDH1	KMT2C	MSI1	PARP2	PREX2	RPTOR	SNCAIP	TOP1
AKT1	BCL2L2	CDK7	DCUN1D1	ERCC4	FGF5	GPR124	IDH2	KMT2D	MST1R	PARP3	PRKAR1A	RRAGC	SNTG2	TOP2A
AKT2	BCL6	CDK8	DDR1	ERCC5	FGF6	GPS2	IFNGR1	KMT5A	MTAP	PAX3	PRKCI	RRAS	SOCS1	TP53
AKT3	BCOR	CDKN1A	DDR2	ERF	FGF7	GREM1	IGF1	KNSTRN	MTOR	PAX5	PRKDI	RRAS2	SOS1	TP53BP1
ALB	BCORL1	CDKN1B	DDX41	ERG	FGF8	GRIN2A	IGF1R	KRAS	MUTYH	PAX7	PRKDC	RSP02	SOX10	TP63
ALK	BCR	CDKN2A	DHX15	ERRF1	FGF9	GRM3	IGF2	LAMP1	MYB	PAX8	PRSS8	RTEL1	SOX17	TPMT
ALOX12B	BIRC3	CDKN2B	DICER1	ESR1	FGFR1	GSK3B	IKBKE	LATS1	MYC	PBRM1	PTCH1	RUNX1	SOX2	TRAF2
AMER1	BLM	CDKN2C	DIS3	ETAA1	FGFR2	H3F3A	IKZF1	LATS2	MYCL	PD-1	PTEN	RUNX1T1	SOX9	TRAF7
ANKRD11	BMPRI1A	CEBPA	DNAJB1	ETS1	FGFR3	H3F3B	IL10	LMO1	MYCN	PD-L1	PTP4A1	RXRA	SPEN	TRIP13
ANKRD26	BRAF	CENPA	DNMT1	ETV1	FGFR4	H3F3C	IL7R	LRP1B	MYD88	PD-L2	PTPN11	RYBP	SPOP	TSC1
APC	BRCA1	CHD2	DNMT3A	ETV4	PH	H3F3D	INHBA	LTK	MYO1D	PDGFRA	PTPR	SCG5	SPRED1	TSC2
APLNLR	BRCA2	CHD4	DNMT3B	ETV5	FLCN	HGF	INHBA	LYN	NAB2	PDGFRB	PTPRN2	SDC4	SPRNT	TSHR
AR	BRD4	CHEK1	DOT1L	ETV6	FLI1	HIST1H1C	INPP4A	LZTR1	NADK	PDK1	PTPRS	SDHA	SPTA1	TYRO3
ARAF	BRIP1	CHEK2	DPYD	EWSR1	FLT1	HIST1H2BD	INPP4B	MAD2L2	NBN	PDPK1	PTPRT	SDHAF2	SRC	U2AF1
ARFRP1	BTG1	CIC	DROSHA	EZH1	FLT3	HIST1H3A	INPL1	MALG2	NCOA3	PGBD5	QKI	SDHB	SRSF2	UGT1A1
ARHGAP35	BTG2	CMTR2	DUSP4	EZH2	FLT4	HIST1H3B	INSR	MALT1	NCOR1	PGR	RAB35	SDHC	STAG1	UPF1
ARID1A	BTK	CNTN4	EZF3	EZR	FOXA1	HIST1H3C	IRF2	MAP2K1	NEGR1	PHF6	RAC1	SDHD	STAG2	USP8
ARID1B	CALR	CREBBP	EED	FAM175A	FOXF1	HIST1H3D	IRF4	MAP2K2	NF1	PHOX2B	RAC2	SERPINB3	STAT3	VEGFA
ARID2	CARD11	CRKL	EGFL7	FAM46C	FOXL2	HIST1H3E	IRS1	MAP2K4	NF2	PIGA	RAD21	SERPINB4	STAT4	VHL
ARID5B	CARM1	CRLF2	EGFR	FAM58A	FOXO1	HIST1H3F	IRS2	MAP3K13	NFE2L2	PIK3C2B	RAD50	SESN1	STAT5A	VTCN1
ASXL1	CASP8	CSDE1	EIF1AX	FANCA	FOXP1	HIST1H3G	JAK1	MAP3K14	NFKBIA	PIK3C2G	RAD51	SESN2	STAT5B	WHSC1
ASXL2	CBF8	CSF1R	EIF4A2	FANCC	FRS2	HIST1H3H	JAK2	MAP3K14	NKX2-1	PIK3C3	RAD51B	SESN3	STK11	WHSC1L1
ATM	CBL	CSF3R	EIF4E	FANCD2	FUBP1	HIST1H3I	JAK3	MAP3K4	NKX3-1	PIK3CA	RAD51C	SETBP1	STK19	WISP3
ATR	CNBB3	CSNK1A1	ELF3	FANCE	FYN	HIST1H3J	JUN	MAPK1	NOTCH1	PIK3CB	RAD51D	SETD2	STK40	WT1
ATRX	CNND1	CTCF	EML4	FANCF	GAB1	HIST2H3A	KAT6A	MAPK3	NOTCH2	PIK3CD	RAD52	SETDB1	SUFU	WWTR1
ATXN7	CNND2	CTLA4	EMSY	FANCG	GAB2	HIST2H3C	KBTBD4	MAPK3	NOTCH3	PIK3CG	RAD54L	SFBF1	SUZ12	XIAP
AURKA	CNND3	CTNNA1	EP300	FANCI	GABRA6	HIST2H3D	KDM5A	MAPKAP1	NOTCH4	PIK3R1	RAF1	SGK1	SYK	XPO1
AURKB	CCNE1	CTNNB1	EPAS1	FANCL	GATA1	HIST3H3	KDM5C	MAX	NPM1	PIK3R2	RANBP2	SH2B3	TAF1	XRCC2
AXIN1	CD276	CTR9	EPCAM	FAS	GATA2	HLA-A	KDM6A	MCL1	NRAS	PIK3R3	RARA	SH2D1A	TAP1	YAP1
AXIN2	CD70	CUL3	EPHA3	FAT1	GATA3	HLA-B	KDR	MDC1	NRG1	PIM1	RASA1	SHO2	TAP2	YES1
AXL	CD74	CUL4A	EPHA5	FBXW7	GATA4	HLA-C	KEAP1	MDM2	NSD1	PLCG2	RB1	SHQ1	TBX3	ZBTB2
B2M	CD79A	CUX1	EPHA7	FGF1	GATA6	HLA-D	KEL	MDM4	NSD1	PLCG2	RB1	SHQ1	TBX3	ZBTB2
								MED12	NTSC2	PLK2	RBM10	SLC34A2	TCEB1	ZBTB7A
								MEF2B	NTHL1	PMAIP1	RECQL	SLFN11	TCF3	ZFH3
								MEN1	NTRK1	PMS1	RECQL4	SLIT2	TCF7L2	ZNF217
								MET	NTRK2	PMS2	REL	SLX4	TEK	ZNF703
								MGA	NTRK3	PNRC1	REST	SMAD2	TERT	ZNF93
								MITF	NUF2	POLD1	RET	SMAD3	TET1	ZRSR2
								MLH1	NUP93	POLE	RFWD2	SMAD4	TET2	
								MLL1	NUTM1	POT1	RHEB	SMARCA2	TFF3	
								MLL3	OPCML	PPARG	RHOA	SMARCA4	TFR3	

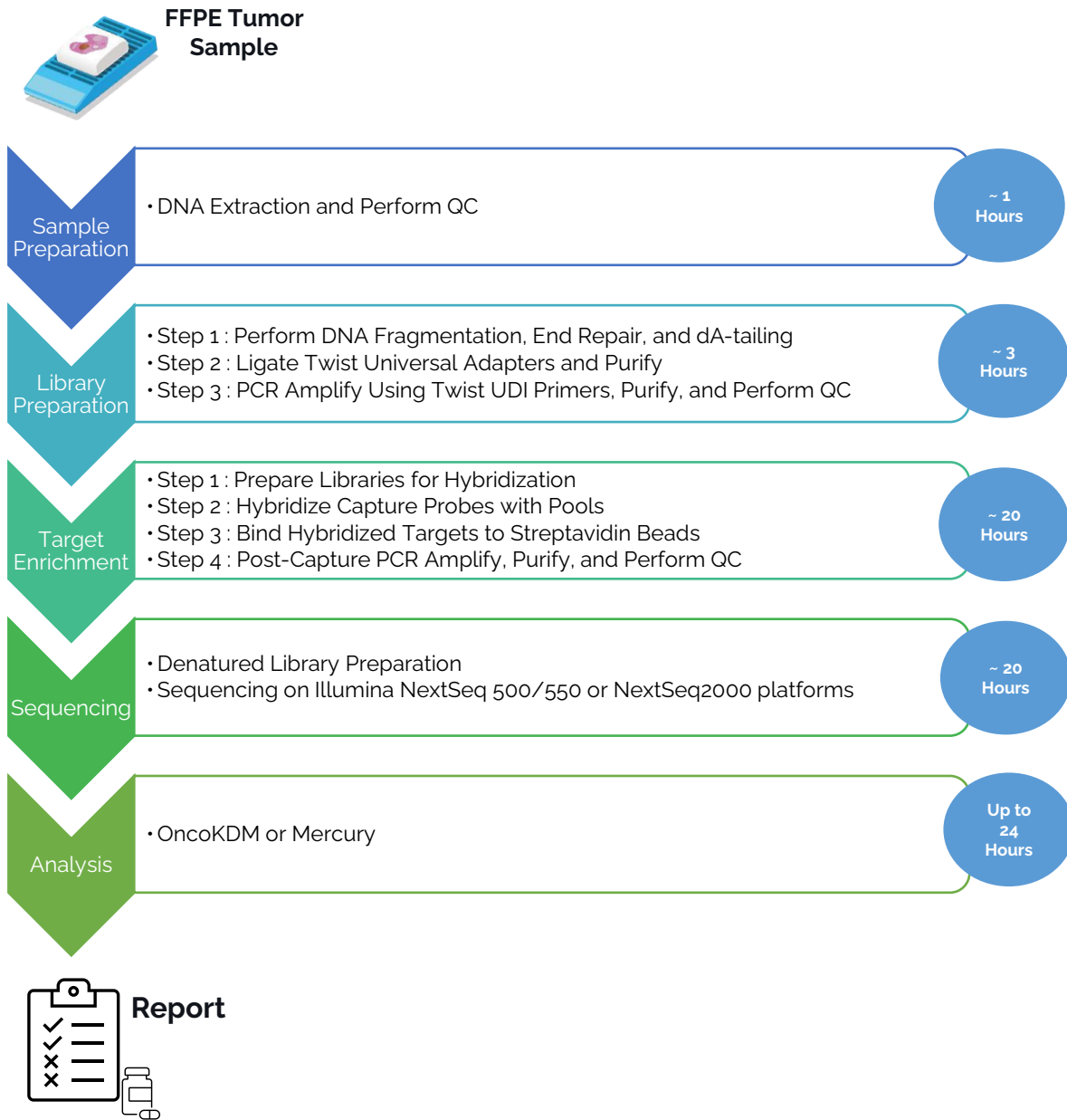
Figure 1: List of genes covered by the OncoDEEP panel

In addition, specific sequences have been added to cover key regions associated with phenotypes of interest like tumor mutational burden (TMB), microsatellite instability (MSI), loss of heterozygosity (LOH) in tumor suppressor genes (TSGs), introns tilling for genes ALK/ROS1/RET and MET-ex14, sub-telomeric single-nucleotide polymorphisms (SNPs) for homologous recombination deficiency (HRD) calculation and promotor of TERT.

Translational and clinical research require rapid approaches that are compatible with small input amounts of nucleic acids derived from challenging research samples such as formalin-fixed, paraffin embedded (FFPE) tissues. OncoDEEP Kit has been validated with FFPE samples and has shown to achieve highly confident results with high sensitivity and specificity, thanks to Twist hybrid-capture chemistry using enzymatic fragmentation and unique dual indexes (UDIs), Illumina sequencing by synthesis (SBS) sequencing technology, and our sophisticated bioinformatics.

With our complete portfolio of secure online platforms, sequencing data can quickly and easily be analysed, matching them with the latest therapies in oncology, and help build personalized reports. Sample to report workflow can be achieved in 3-4 days with OncoDEEP DNA Kit as illustrated in Figure 2.

Figure 2: OncoDEEP DNA Kit Sample-to-Result workflow



OncoDEEP Sample-to-Result workflow. The complete NGS workflow takes you from sample preparation to NGS sequencing and data analysis. Sample to results can be achieved in 3-4 days.

7 LEGAL

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8 PRECAUTIONS OF USE

- Warnings, precautions and/or measures to be taken in the event of malfunction of the device or its degradation as suggested by changes in its appearance that may affect performance: not applicable.
- Warnings, precautions and/or measures to be taken in regard to the exposure to reasonably foreseeable external influences or environmental conditions, such as magnetic fields, external electrical and electromagnetic effects, electrostatic discharge, radiation associated with diagnostic or therapeutic procedures, pressure, humidity, or temperature: the reagents of the kit must be stored at appropriate temperature and protected from light/humidity as stated in chapter 14 storage conditions.
- Warnings, precautions and/or measures to be taken in regard to the risks of interference posed by the reasonably foreseeable presence of the device during specific diagnostic investigations, evaluations, therapeutic treatment or other procedures (e.g. electromagnetic interference emitted by the device affecting other equipment): not applicable.
- Precautions related to materials incorporated into the device that are carcinogenic, mutagenic or toxic, or that have endocrine disrupting properties or that could result in sensitization or allergic reaction of the patient or user: not applicable.
- OncoDEEP is a device is intended for single use.
- Any warnings and/or precautions related to potentially infectious material that is included in the device: not applicable.
- Wear appropriate protective equipment (lab coat, gloves, and protective glasses or goggles) at all times when performing this protocol.
- For best results, read this document before performing the protocol, and follow the instructions provided. OncoDNA cannot guarantee the performance of the OncoDEEP Library Preparation Kit using Enzymatic/Mechanical Fragmentation and the Twist Universal Adapter System if modifications are made to the protocol.
- This library preparation method may yield more material than needed for target enrichment. Excess product can be stored at - 20°C for later use.
- Test the compatibility of your thermal cycler and PCR tubes by incubating at 95°C for up to 5 minutes to ensure the PCR tubes do not crack under heat and pressure. Adjust the tightness of the thermal cycler lid and/or use a spacer specific to the thermal cycler model.
- To minimize contamination, two sample handling areas should be designated: Pre- and Post- PCR.

9 INTENDED USE

The intended purpose statement for the device described in this technical file is:

The OncoDEEP Kit is an integrated solution that combines a pan-cancer NGS assay for the in-house comprehensive biomarker testing of solid tumor tissues. The solution contains a panel of 638 genes carefully selected for their clinical relevance in advanced solid tumor types. The OncoDEEP Kit screens for cancer gene mutations in the DNA and RNA (SNVs, Indels, CNV, fusion genes and unusual splicing events) as well as measures complex genomic signatures such as homologous recombination deficiency (HRD), tumor mutational burden (TMB) and microsatellite instability (MSI) from FFPE tumor tissue specimens.

The OncoDEEP Kit contains all the necessary reagents to prepare the NGS libraries and comes together with an integrated bioinformatics pipeline for data analysis and interpretation.

10 INTENDED USER

The OncoDEEP kit is intended to be used by laboratory professionals with a background in molecular biology and Next Generation Sequencing (lab technicians, biologists).

Patients have no contact with the device.

11 ENVIRONMENT

The device must be used in a laboratory environment with appropriate measures to prevent any contamination of the sample or its byproduct during the analysis process.

12 CONTRA-INDICATIONS

OncoDEEP kit is only meant to be used for every solid tumor in adults or for glioblastoma in children.

13 DESCRIPTION OF THE REAGENTS

Please refer to the specific protocols for DNA and RNA analysis in annex of this document for detailed information about the reagents to be used by the end-user at each step of the protocol.

14 LIST OF MATERIAL TO BE SUPPLIED BY USERS

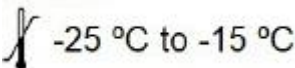
Please refer to the specific protocols for DNA and RNA analysis in annex of this document for detailed information about the list of material to be supplied by the end-user.

15 INFORMATION ABOUT DEVICES TO BE USED IN COMBINATION

Compatible Sequencers Name
Illumina NextSeq series

16 STORAGE CONDITIONS

Depending on the reagent type, storage conditions may vary. Please check the information

displayed by the following symbol  on each box to know the appropriate storage conditions. The ideal storage conditions are mentioned next to the symbol by giving the range of acceptable temperature for long term storage.

Appropriate storage conditions must be executed upon reception to prevent performance degradation.

17 IN-USE STABILITY

Reagent stability is ensured until the date mentioned on the specific label affixed to the reagent container. The appropriate date to take into account is the “use by date” displayed next to the hourglass.

18 STERILISATION

Not applicable.

19 ONCODEEP PROTOCOL FOR DNA ANALYSIS

Please check the following annex: OD002-B-04- OncoDEEP DNA protocol

20 ONCODEEP PROTOCOL FOR RNA ANALYSIS

Please check the following annex: OD003-B-04- OncoDEEP RNA protocol