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CE

AmoyDx® NGS Solutions

Make It Simple

AmoyDx

CONTENTS

Integrated NGS Solution for Clinical Oncology

AmoyDx offers full solutions for NGS testing, from library construction, data analysis to result interpretation. For target sequencing, two different library construction technologies are employed. With HANDLE, fusions are mostly detected based on RNA, while other mutations are detected based on DNA. With ddCAP, all mutations are detected based on DNA, which is applicable for both tissue and liquid biopsy samples. Customized panels are available for both technologies.

HANDLE

One-tube protocol 5 hours turn-around time including 1 hour hands-on time

product:

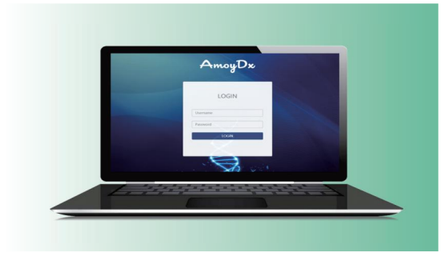
- **Classic (40 genes + MSI)**
- **BRCA Pro**
- **HRR (32 genes)**
- **HRD Focus (BRCA1/2 + GSS)**

ddCAP

DNA based digital capture, specially for liquid biopsy

product:

- **Essential (10 genes)**
- **Comprehensive (128 genes + MSI)**



- ✔ **Pre-installed NGS software**
- ✔ **Automatic analysis pipeline**
- ✔ **Regularly updated database**
- ✔ **Data security**
- ✔ **User-friendly interface**
- ✔ **Local end-to-end solution**

Log In → **Sequencing** → **Data Analysis** → **Result**

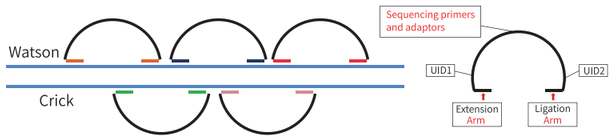
A cup of coffee and you' ll get the final results!

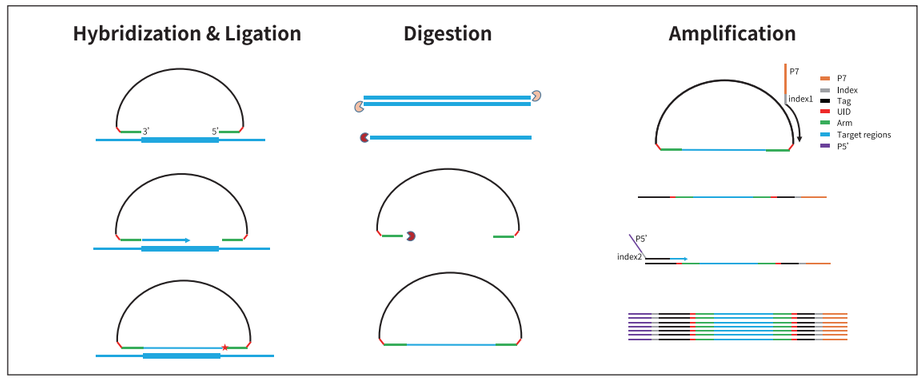
HANDLE Technology:
Halo-shape ANnealing and Defer-Ligation Enrichment

You can handle it with your hands free as much as possible!

HANDLE® is an innovated amplicon-based NGS technology to make the library construction workflow as simple as PCR.The Unique molecular IDentifier (UID) is introduced to both ends of each DNA fragment, and helps trace back to the original template for error correction. The library construction time of HANDLE technology is 5 hours including 1 hour hands-on time. If use RNA sample, a reverse transcription step should be performed before hybridization with probes, and the library construction time is 6 hours including about 1 hour hands-on time.

Probe design:





TAT: 5 hours including 1 hour hands-on time

Better coverage and higher specificity

Take advantages of both PCR and capture to achieve better coverage and higher specificity

Accurate and sensitive

High accuracy and sensitivity by the use of UID (detects mutations down to 1% VAF)

One-tube protocol

All probes in one tube, easy to use and fast to get the results (TAT: 5 hours including 1 hour hands-on time)

Comprehensive mutation detection capability

Can detect DNA and RNA at the same time;
All mutations (SNV/InDel/CNV/Fusion/MSI) can be detected simultaneously

Save your data and cost

Lower cost of sequencing

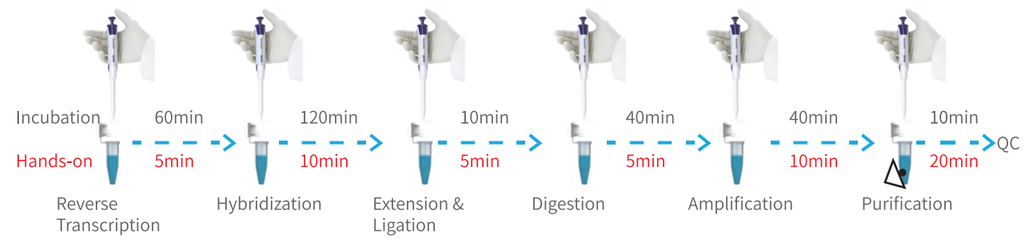
AmoyDx® HANDLE Classic NGS Panel

AmoyDx® HANDLE Classic NGS Panel is a next-generation sequencing (NGS) based in vitro diagnostic assay intended for qualitative detection of single nucleotide variants (SNVs), insertions and deletions (InDels), gene fusions, copy number amplifications (CNAs) and microsatellite instability (MSI) in 40 key solid tumor genes, using DNA and RNA isolated from formalin-fixed paraffin embedded (FFPE) tumor tissue specimens. The assay is intended to provide tumor mutation profiling to be used by qualified health care professionals in accordance with professional guidelines in oncology for patients with solid malignant neoplasms.

This kit is designed for clinical target therapy and focuses on biomarkers that are relevant to currently approved and under developed target therapies of solid tumor. The target region was proposed by several key opinion leaders of oncology globally. The kit was recommended by ESMO (2019) as one of the NGS kit to be used for NTRK-fusion detection.

AKT1	△	FGFR1	△ #	MAP2K1	△	PDGFRA	△
ALK	△ #	FGFR2	△ #	MET	△ # &	PIK3CA	△
BRAF	△	FGFR3	△ #	MYC	&	POLE	△
CDK4	&	FGFR4	△	NFE2L2	△	PTEN	△
CTNNB1	△	HRAS	△	NKX2-1	&	RB1	△
DDR2	△	IDH1	△	NRAS	△	RET	△ #
DPYD	△	IDH2	△	NRG1	#	ROS1	△ #
EGFR	△	KEAP1	△	NTRK1	△ #	STK11	△
ERBB2	△ &	KIT	△	NTRK2	△ #	TP53	△
ESR1	△	KRAS	△	NTRK3	△ #	UGT1A1	△

△ SNV/InDel # Fusion & CNA



One-tube protocol, TAT for library preparation: 6 hours including 1 hour hands-on time

AmoyDx® BRCA Pro Panel

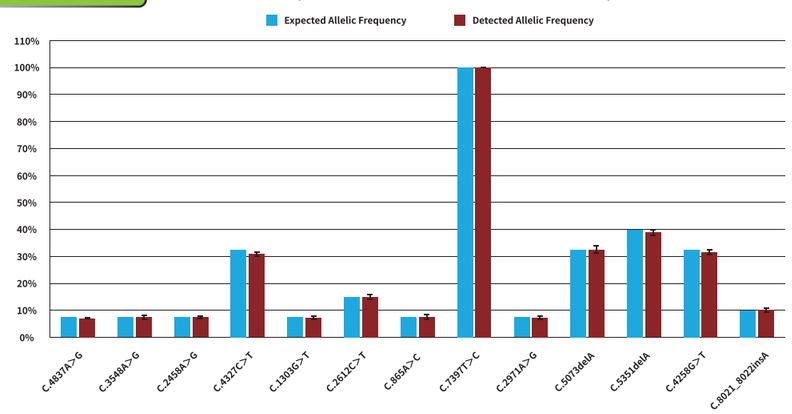
BRCA1 gene and BRCA2 gene play an important role in the Homologous Recombination Repair (HRR) pathway. Pathogenic BRCA1/2 mutations will cause a much higher risk of developing breast cancer, ovarian cancer, pancreatic and prostate cancer. Patients with BRCA-mutant cancer may benefit from poly ADP ribose polymerase inhibitors (PARPi) and platinum-containing therapy. Several PARPi have been approved for the treatment of patients with BRCA1/2 mutations.

AmoyDx® BRCA Pro Panel is based on **HANDLE** technology and intended to detect BRCA1/2 variants in peripheral blood-derived DNA or FFPE tumor tissue DNA. This kit can work on all the Illumina sequencing platforms and is CE-IVD approved.

Target Regions	All coding regions of BRCA1/2 genes, exon-intron boundaries, some intron and UTR regions
Alterations Detected	SNV & Indel (somatic/germline), LR (germline)
Sample Type	DNA from FFPE tissue, whole blood
DNA Input	Optimal 50ng (minimum 30ng)
Limit of Detection (LoD)	2% VAF for non-polymer regions, 5% VAF for polymer and STR regions
Data Output per Sample	0.06 Gb for germline variants 0.3 Gb for somatic variants
Sequencer	Illumina MiSeqDx, NextSeq 500, NextSeq 550Dx
TAT for Library Preparation	5 h (hands-on time <1 h)
TAT from Sample to Report	3 days

Validation Results

SNV & InDel (Commercial Standard Reference):



AmoyDx® HANDLE HRR NGS Panel

The Homologous Recombination Repair (HRR) pathway plays an important role in the repair of double-strand breaks, and a deficient HRR pathway could be a major cause of cancer development. It has been demonstrated that loss of function of HRR genes (e.g. BRCA1, BRCA2, PALB2) and Homologous Recombination Deficiency (HRD) will cause a higher risk of developing cancer, and patients with HRR gene mutations showed higher response to PARPi and platinum-containing therapies.

AmoyDx® HANDLE HRR NGS Panel is based on **HANDLE** technology and was developed for multiplex and targeted deep sequencing for the detection of SNVs/InDels in the whole coding region and exon-intron boundaries of 27 HRR genes and hotspots in 5 diver genes, with a LOD of 5% VAF, and it' s able to detect germline large rearrangement for BRCA1/2 genes.

AR	*CDH1*	*HDAC2*	*PPP2A2R*
ATM	*CDK12*	*HOXB13*	*PTEN*
ATR	*CHEK1*	*KRAS**	*RAD51B*
BARD1	*CHEK2*	*MRE11*	*RAD51C*
*BRAF**	*ERBB2**	*NBN*	*RAD51D*
BRCA1	*ESR1*	*NRAS**	*RAD54L*
BRCA2	*FANCA*	*PALB2*	*STK11*
BRIP1	*FANCL*	*PIK3CA**	*TP53*

*For hotspot mutation detection.

Validation Results

Commercial standard reference samples, cell lines and in-house reference samples were both 100% with a LOD of 5% VAF. The allele frequencies detected were highly consistent with the expected values of the commercial reference standards.

Gene	Mutation	Expected AF%	Detected AF%
ATM	*NM_000051.3:exon23:c.3380C>T:p.A1127V*	4.50%	5.25%
ATR	*NM_001184.3:exon43:c.7343C>T:p.T2448I*	5.49%	5.31%
BRCA1	*NM_007294.3:exon13:c.4327C>T:p.R1443**	4.66%	4.76%
BRCA2	*NM_000059.3:exon11:c.2886T>C:p.(H962=)*	5.30%	7.39%
BRIP1	*NM_032043.2:exon6:c.550G>T:p.D184Y*	5.42%	4.89%
CDH1	*NM_004360.3:intron14:c.2295+2T>C:p.?*	4.79%	5.12%
TP53	*NM_000546.5:exon10:c.1079G>A:p.G360E*	4.96%	6.23%
ATM	*NM_000051.3:intron34:c.5178-4_5178-3insT:p.?*	4.76%	4.51%
ATR	*NM_001184.3:intron33:c.5739-14_5739-6delinsT:p.?*	4.52%	7.81%
BRCA2	*NM_000059.3:exon23:c.9097delA:p.T3033Lfs*29*	4.83%	6.75%
CDH1	*NM_004360.3:exon7:c.944_945insA:p.N315Kfs*6*	4.63%	5.17%
MRE11	*NM_005591.3:exon13:c.1441delA:p.T481Hfs*43*	5.14%	5.34%
PPP2R2A	*NM_002717.3:exon2:c.43delT:p.S15Lfs*3*	5.11%	6.02%
PTEN	*NM_000314.4:3'UTR:c.*10delT:p.?*	4.91%	4.00%
RAD54L	*NM_001142548.1:exon19:c.2050_2052delTGT:p.C684del*	5.06%	5.19%

AmoyDx® HRD Focus Panel

AmoyDx® HRD Focus Panel is a next generation sequencing-based in vitro diagnostic test designed to determine a patient' s HRD (Homologous Recombination Deficiency) status. It detects SNVs and InDels in whole coding regions and exon-intron boundaries of the BRCA1 and BRCA2 genes and determines a genomic scar score (GSS) using DNA from neutral formalin-fixed paraffin-embedded (FFPE) tissue samples.

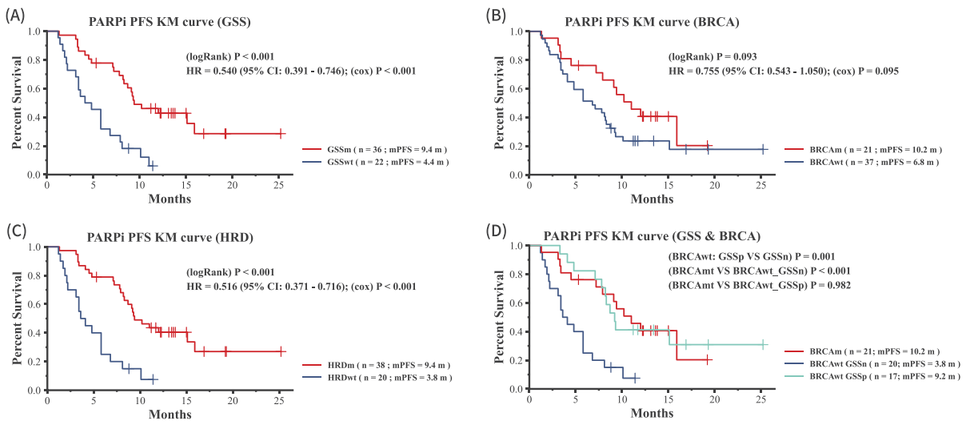
Specifications

DNA Input	Optimal 100ng (minimum 50ng)
Limit of Detection (LoD)	5% MAF for SNVs/Indels; minimum 30% tumor content
Data output per sample	4 Gb
Sequencing type	PE150
Sequencer	Illumina NextSeq 550Dx
TAT for library prep	5h (hands-on time <1h)
TAT from sample to report	3 days

High Concordance with Myriad myChoice

- 100% positive percent agreement
- 80% negative percent agreement
- 87.8% overall percent agreement

Longer PFS with PARPi Treatment for GSS-positive Group [1]

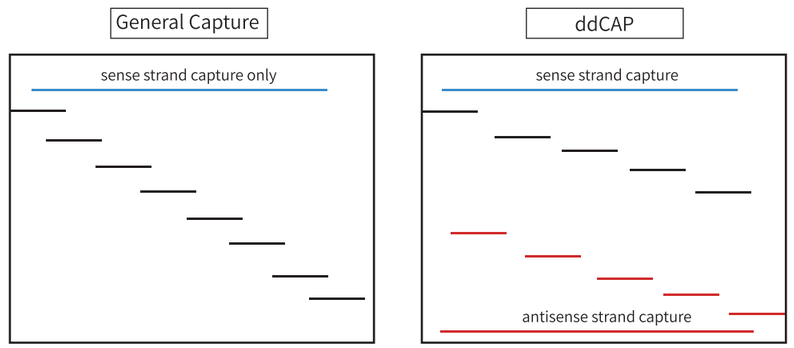


The study has shown remarkable results highlighting the promising values of GSS in identifying patients who may respond favorably to PARPi treatment.

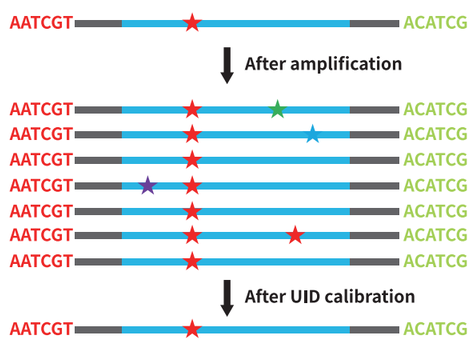
[1] Yuan W, Ni J, Wen H, et al. Genomic Scar Score: A robust model predicting homologous recombination deficiency based on genomic instability. BJOG. 2022;129 Suppl 2:14-22. doi:10.1111/1471-0528.17324.

ddCAP Technology: Digital and Dual Directional Probes Based Capture

Dual directional probes: Designed for double strands to get better coverage, especially for degraded samples.



Digital capture: Unique identifier (UID) sequence for tracing back to the original template for digital testing of mutations and error correction.



Advantages:

Better coverage for target region

Dual directional probe design makes it work better for degraded samples

Accurate and sensitive

High accuracy and sensitivity by the use of UID (sensitivity down to 0.2%)

DNA based comprehensive detection

Various mutation types can be detected: SNV, InDel, CNV, translocation (Fusion)

Ideal target sequencing solution for liquid biopsy

Perfect compatible with ctDNA, detection of various mutations with high sensitivity

AmoyDx® Essential NGS Panel

AmoyDx® Essential NGS Panel is a next-generation sequencing (NGS) based in vitro diagnostic assay intended for qualitative detection of single nucleotide variants (SNVs), insertions and deletions (InDels), gene fusions, and copy number variations (CNVs) in 10 oncogenic driver genes, using DNA isolated from formalin-fixed paraffin embedded (FFPE) tumor tissue specimens, or circulating cell-free DNA (cfDNA) isolated from plasma derived from anti-coagulated peripheral whole blood specimens. The detection of CNVs is available for tissue-derived DNA only. The assay is intended to provide tumor mutation profiling to be used by qualified health care professionals in accordance with professional guidelines in oncology for patients with non-small cell lung cancer (NSCLC) and colorectal cancer (CRC).

A precise NGS panel, focus on 10 essential genes for clinical targeted therapy.

Genes included in this Panel				
EGFR	*ALK*	*ROS1*	*KRAS*	*NRAS*
BRAF	*HER2*	*MET*	*RET*	*PIK3CA*

Suitable for lung cancer and colorectal cancer

Features

- ✔ Sample Type - Tissue, liquid biopsy
- ✔ High Ability - Detect SNV/InDel/Fusion/CNV
- ✔ Limit of Detection (LoD) - FFPE DNA: 1% MAF, cfDNA: 0.3% MAF
- ✔ High Reliability - 100% EQA pass rate; 1000+ clinical validation

Specifications

Parameter	Specifications
Certification	CE-IVD
Technology	ddCAP
Alterations Detected	SNV, InDel, Fusion, CNV*
Sample Type	FFPE tumor tissue, liquid biopsy
DNA Input	FFPE DNA: 100ng cfDNA: optimal 30 ng (minimum 10 ng)
Limit of Detection (LoD)	FFPE DNA: 1% MAF cfDNA: 0.3% MAF
Data Output per Sample	1 Gb
Average Sequencing Depth	⩾ 10,000 ×
Sequencing Type	PE150
Sequencer	Illumina NextSeq 500, Nextseq 550Dx
TAT for Library Preparation	2 d (hands-on time 4h)
TAT from Sample to Report	5 days

* CNV detection is available for tissue only.

AmoyDx® Comprehensive Panel

The AmoyDx® Comprehensive Panel is a next-generation sequencing (NGS) based assay intended for the qualitative detection of single nucleotide variants (SNVs), insertions and deletions (InDels), gene fusions, and copy number variations (CNVs) in 110 genes, single nucleotide polymorphisms (SNPs) in 19 genes, and tumor MSI status. The assay allows the detection of SNVs, InDels, fusions, CNVs, SNPs and MSI using DNA isolated from formalin-fixed paraffin-embedded (FFPE) tissue specimens, and the detection of SNVs, InDels, fusions and SNPs using circulating cell-free DNA (cfDNA) isolated from plasma derived from anti-coagulated peripheral whole blood specimens.

✔ Genetic Risk Management
- 5 Lynch syndrome related genes (EPCAM, MLH1, MSH2, MSH6, PMS2)
- BRCA1/2, APC, VHL

✔ Targeted Therapy
- Genotyping genes and prognostic related genes
- Drug-related genes for therapy indications

✔ Immunotherapy
- MSI (> 50 sites)
- Positive genes: POLE, POLD1...
- Negative genes: STK11, JAK1/2...

✔ Chemotherapy
- Molecular diagnosis to reduce drug toxicity

Specifications

Technology	dual directional Capture (ddCap)
Target Regions	128 genes and MSI
Alterations Detected	SNVs, InDels, fusions, CNVs, SNPs, MSI [2]
Sample Type	FFPE tumor tissue, liquid biopsy
DNA Input	FFPE DNA: optimal 100 ng (minimum 50 ng) Plasma cfDNA: optimal 30 ng (minimum 10 ng)
Limit of Detection	FFPE DNA: 5% allele frequency, minimum 20% tumor content Plasma cfDNA: 0.5% allele frequency
Data Output per Sample	FFPE DNA: 1.5 Gb/sample Plasma cfDNA: 8 Gb/sample
Sequencer	Illumina NextSeq 500, NovaSeq 6000
Recommended Samples per Run	NextSeq 500 Mid Output flow cell: 26 FFPE DNA samples or 5 cfDNA samples NextSeq 500 High Output flow cell: 80 FFPE DNA samples or 15 cfDNA samples NovaSeq SP flow cell: up to 96[3] FFPE DNA samples or 31 cfDNA samples NovaSeq 6000 S1 flow cell: up to 96 FFPE DNA samples or 62 cfDNA samples
TAT for Library Preparation	2 days (hands-on time 4 hours)
TAT[4] from Sample to Report	5 days

2. The detection of CNVs and MSI is available for tumor tissue sample only.
3. Maximum number combinations of index available
4. Turn-around time (TAT) may vary depending on the number of samples multiplexed and server load.

Introduction of NGS Testing Service

AmoyDx Medical Institute was established in 2013 and has been approved by the National Health and Family Planning Commission for Medical Institutions. The two central laboratories established in Xiamen and Shanghai are both College of American Pathologists (CAP) accredited.

AmoyDx Medical Institute has a significant experience providing laboratory service. There have been over 500 hospitals and institutions cooperating with AmoyDx for genetic testing in China. The test volume is ~30,000 samples every year, with over 3,000 tests performed on NGS platforms. The NGS platform is based on Illumina series of sequencers, including iSeq, MiSeq, MiniSeq, NextSeq 500 and NovaSeq 6000. Different throughput of sequencers makes it much more flexible and makes daily testing easier.

External Quality Assessment (EQA)

Different EQA tests have been continuously passed, including CAP, EMQN (European Molecular Genetics Quality Network), NCCL (National Center For Clinical Laboratories), CNAS (China National Accreditation Service for Conformity Assessment), PQCC (Pathology Quality Control Center) etc. The NGS platform has passed the somatic testing EQA for three consecutive years with full score, including testing for liquid biopsy samples.

Abbreviations

1	ANDAS	AmoyDx NGS Data Analysis System
2	BC	Breast Cancer
3	BER	Base Excision Repair
4	BIC	Breast Cancer Information Core
5	CAP	College of American Pathologists
6	CE	Conformite Europeenne
8	CNV	Copy Number Variation
9	CR	Colorectal Cancer
10	ddCAP	Digital and Dual directional probe-based Capture
11	DRG	DNA Repair Gene
12	GA	Gastric Cancer
13	HANDLE	Halo-shape ANnealing and Defer-Ligation Enrichment
14	HGMD	Human Gene Mutation Database
15	HRD	Homologous Recombination Deficiency
16	HRR	Homologous Recombination Repair
17	InDel	Insertion and Deletion
18	IVD	In Vitro Diagnosis
19	KOL	Key Opinion Leader
20	LC	Lung Cancer
21	LCP	Lung Cancer Panel
22	LOH	Loss of Heterozygosity
23	MMR	Miss Match Repair
24	MLPA	Multiplex Ligation-dependent Probe Amplification
25	MSI	Microsatellite Instability
26	NGS	Next Generation Sequencing
27	NMPA	National Medical Products Administration
28	OC	Ovarian Cancer
29	R&D	Research and Development
30	RUO	Research Use Only
31	SNP	Single Nucleotide Polymorphism
32	SNV	Single Nucleotide Variation
33	TAT	Turn-around Time
34	TC	Thyroid Cancer
35	TMB	Tumor Mutational Burden
36	UID	Unique molecular IDentifier
37	UMD	Universal Mutation Database
38	VUS	Variants of Uncertain Significance
39	WES	Whole Exon Sequencing