AI-BNS-1A

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艾德生物

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NGS Products

AmoyDx® NGS Solutions

Make It Simple

AmoyDx
艾德生物

CONTENTS

Integrated NGS Solution for Clinical Oncology

AmoyDx offers full solutions for NGS (Next Generation Sequencing) 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

Star product:

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

ddCAP

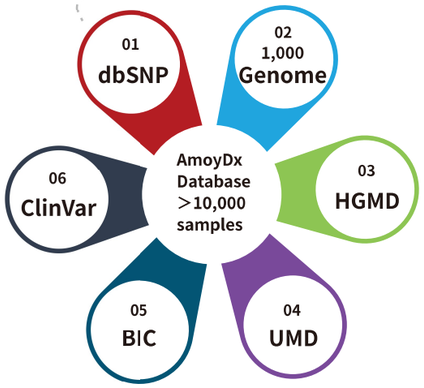
DNA based digital capture, specially for liquid biopsy

Star product:

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

ANDAS: all you need about data analysis is just 7 clicks

User friendly interface



Regular database upgrade

Quick Start Log in → **Sequencing** Monitor / management → **Analyzing** Create / monitor analysis → **Report** View / download result

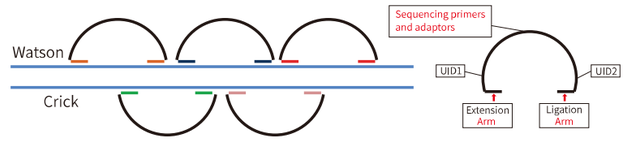
A cup of coffee and you' ll get the final results!

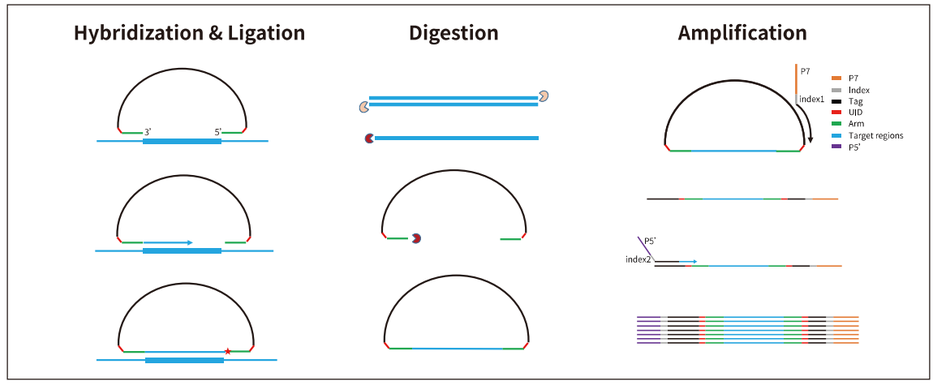
HANDLE Technology:
Halo-shape ANnealing and Defer-Ligation Enrichment

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

HANDLE technology is an improved Molecular Inversion Probe (MIP) technology to capture the target gene region. The Unique molecular IDentifier (UID) is introduced to both ends of each DNA fragment, and helps tracing 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 (sensitivity down to 2%)

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

High effective data yield, lower cost of sequencing

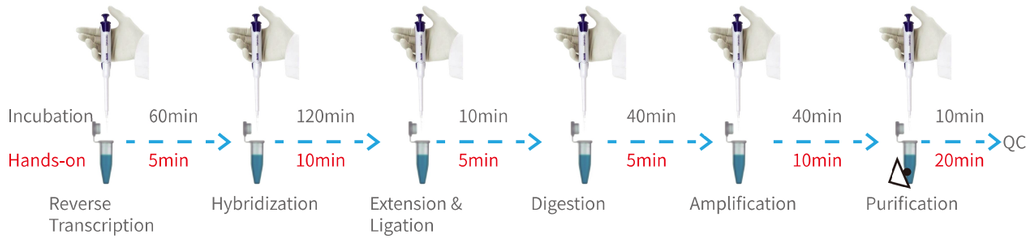
AmoyDx® HANDLE Classic NGS Panel

AmoyDx® HANDLE Classic NGS Panel (Reversible Terminator Sequencing) is a multi-biomarker next generation sequencing (NGS) assay that enables the detection of variants in 40 key solid tumor genes and microsatellite instability (MSI) status using DNA and RNA isolated from formalin-fixed paraffin embedded (FFPE) tumor tissue specimens. The assay allows concurrent analysis of DNA and RNA to simultaneously detect single nucleotide variants (SNVs), insertions and deletions (Indels), fusions, copy number amplifications (CNAs) and MSI in a single workflow.

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 & CNV



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

AmoyDx® BRCA1 and BRCA2 Gene Mutation Detection Kit

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® BRCA1 and BRCA2 Mutation Detection Kit 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 region: All coding regions of BRCA1/2 genes, exon-intron boundaries, some intron and UTR regions.

Sample type: Peripheral whole blood or FFPE tissue.

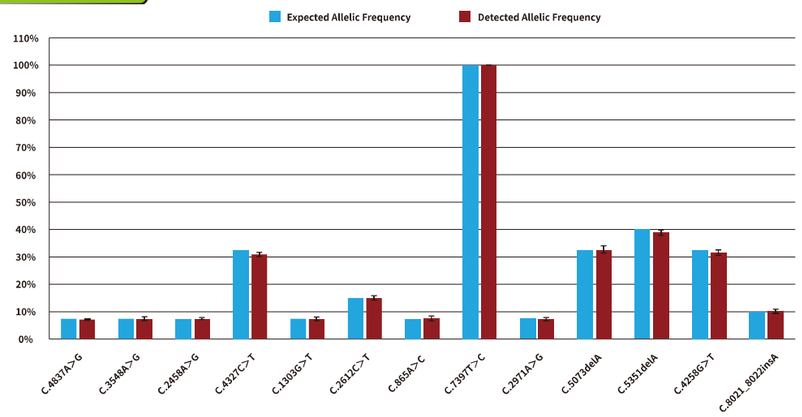
DNA amount: Peripheral whole blood: minimum 30ng, optimal 50ng.
FFPE tissue: minimum 30ng, optimal 100ng.

Alteration detected: SNV, InDel, LR.

Sensitivity: 2%

Validation Results

SNV & InDel (Commercial Standard Reference):



AmoyDx® HANDLE HRR NGS Panel

The Homologous Recombination Repair (HRR) pathway plays a vital role in double strand break, which is the 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 of SNVs/InDels in whole coding region and exon-intron boundaries of 27 HRR genes and hotspots in 5 driver genes, with a sensitivity of 5%, and it's able to detect CNV for BRCA1/2 genes (germline).

AR	*CDH1*	*HDAC2*	*PPP2A2R*
ATM	*CDK12*	*HOXB13*	*PTEN*
ATR	*CHEK1*	*KRAS**	*RAD51B*
BARD1	*CHEK2*	*MRE11A*	*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 home made reference samples were used to validate the performance of this kit comprehensively. The accuracy and specificity was 100% at a sensitivity of 5%. The allele frequency was highly consistent as expected by commercial standard reference.

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

The Homologous Recombination Repair (HRR) pathway plays an important role in double strand break, which is the major cause of cancer development. It has been demonstrated that loss of function of HRR genes (Homologous Recombination Deficiency (HRD) will cause a higher risk of developing cancer, and patients with HRD showed higher response to PARPi and platinum-containing therapies. HRD Score testing and BRCA1/2 mutations testing have been approved for patient selection for PARPi therapy.

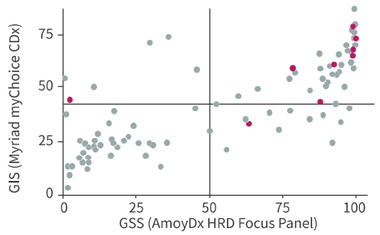
AmoyDx® HRD Focus Panel is a next generation sequencing-based in vitro diagnostic test designed to determine a patient' s HRD (Homologous Recombination Deficiency) status. It detects SNVs and Indels in whole coding regions and exon-intron boundaries of the BRCA1 and BRCA2 genes and determines a genomic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

Specifications

Sensitivity	5% for SNVs/InDels
Input DNA	Minimum 50 ng (optimal 100 ng)
TAT for library prep	5 hours (1 hour for hands-on time)
TAT from sample to report	3 days
Recommended sequencer	NextSeq 500, NovaSeq 6000
Sequencing type	PE150
Throughput	10 samples for NextSeq 500 Mid-Output V2 chemistry
	30 samples for NextSeq 500 High-Output V2 chemistry

Validation Results

In terms of the HRD genomic instability measure between AmoyDx HRD Focus Panel and Myriad myChoice CDx (N=98), the analytical results show a high concordance between AmoyDx HRD Focus Genomic Scar Score (GSS) and Myriad myChoice CDx Genomic Instability Score (GIS), with a PPA, NPA and OPA at 88.0%, 75.0%, 81.6%, respectively.



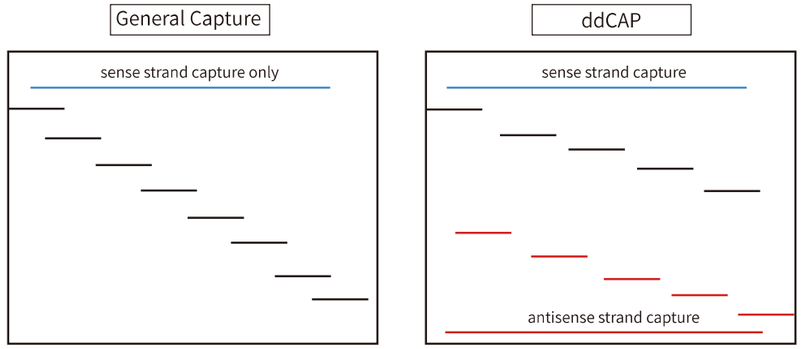
AmoyDx HRD Focus Panel vs. Myriad myChoice CDx

PPA (%)	NPA (%)	OPA (%)
88.0	75.0	81.6

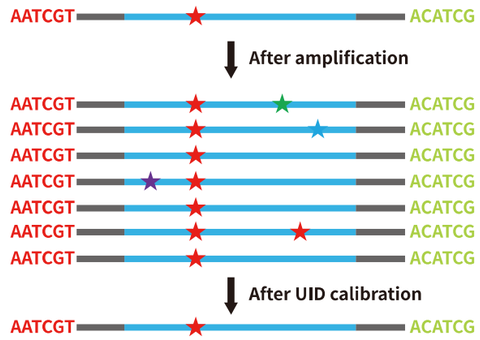
Resource: Wilko Weichert, et al. An evaluation of the performance of molecular assays to identify homologous recombination deficiency-positive tumors in ovarian cancer. (E-poster presented at the 22nd European Congress on Gynaecological Oncology (ESGO), 2021.)

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 based on ddCAP technology for multiplex and targeted deep sequencing of variants in 10 driver genes. The assay allows detection of SNVs, InDels and Fusions in fresh-frozen and FFPE tissue and plasma samples with a sensitivity of down to 0.2%. MET CNV can be detected for fresh-frozen and FFPE tissue samples.

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

Validation Results

AmoyDx Essential panel shows a high sensitivity for liquid biopsy testing, all the variants at 0.3% allele frequency can be correctly detected across 20 replicates with 10ng cfDNA input.

Gene	Alteration Type	Variants	Expected MAF	Detection Rate
EGFR	SNV	exon18:c.2170G>A:p.G724S	0.30%	100% (20/20)
EGFR	SNV	exon19:c.2231T>C:p.I744T	0.30%	100% (20/20)
EGFR	SNV	exon20:c.2324G>A:p.C775Y	0.30%	100% (20/20)
EGFR	SNV	exon20:c.2369C>T:p.T790M	0.30%	100% (20/20)
EGFR	SNV	exon20:c.2374C>G:p.L792V	0.30%	100% (20/20)
EGFR	SNV	exon20:c.2375T>A:p.L792H	0.30%	100% (20/20)
EGFR	SNV	exon20:c.2386G>A:p.G796S	0.30%	100% (20/20)
KRAS	SNV	exon2:c.35G>C:p.G12A	0.30%	100% (20/20)
NRAS	SNV	exon3:c.175G>A:p.A59T	0.30%	100% (20/20)
NRAS	SNV	exon3:c.181C>A:p.Q61K	0.30%	100% (20/20)
PIK3CA	SNV	exon10:c.1633G>A:p.E545K	0.30%	100% (20/20)
EGFR	InDel	exon19:c.2235_2249del15:p.E746_A750del	0.30%	100% (20/20)
EGFR	InDel	exon19:c.2236_2250del15:p.E746_A750del	0.30%	100% (20/20)
EGFR	InDel	exon19:c.2253_2276del24:p.S752_I759del	0.30%	100% (20/20)
EGFR	InDel	exon20:c.2290_2291ins12:p.A763_Y764insFQEA	0.30%	100% (20/20)
EGFR	InDel	exon20:c.2308_2309ins9:p.V769_D770insASV	0.30%	100% (20/20)
EGFR	InDel	exon20:c.2311_2312ins9:p.D770_N771insSVD	0.30%	100% (20/20)
MET	Exon 14 skipping	exon14:c.3028G>A:p.D1010N	0.30%	100% (20/20)
MET	Exon 14 skipping	exon14_intron14:c.3028_3028+16del17:p.?	0.30%	95% (19/20)
MET	Exon 14 skipping	intron13:c.2888-41_2888-2del40:p.?	0.30%	100% (20/20)

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.

NGS Testing

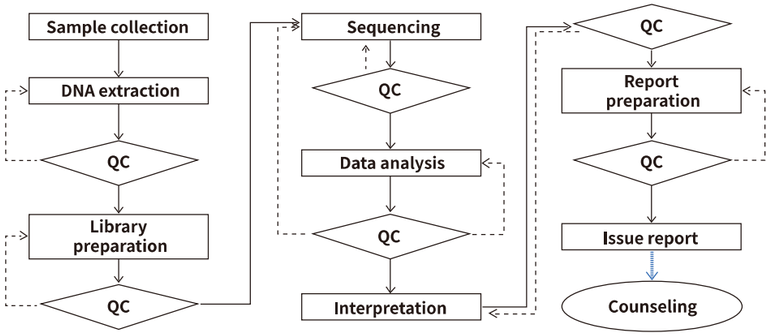
01 For patients
Assistance for therapy

02 For Pharma companies
Select new bio-markers for new drugs

03 For clinical experts
Assistance for research and new discoveries

Testing Process and Quality Control System

Standard work flow for all testing procedures including a double check for each step. The turn-around time is 10 working days upon sample arrival.



International general laboratory operating standards (ISO15189, CAP, GLP) are strictly followed for operation management and quality control.

Regular maintenance and calibration

Systematic QA files and QC records

People | **Instrument** | **Reagents** | **Files** | **Laboratory**

Regular training and assessment

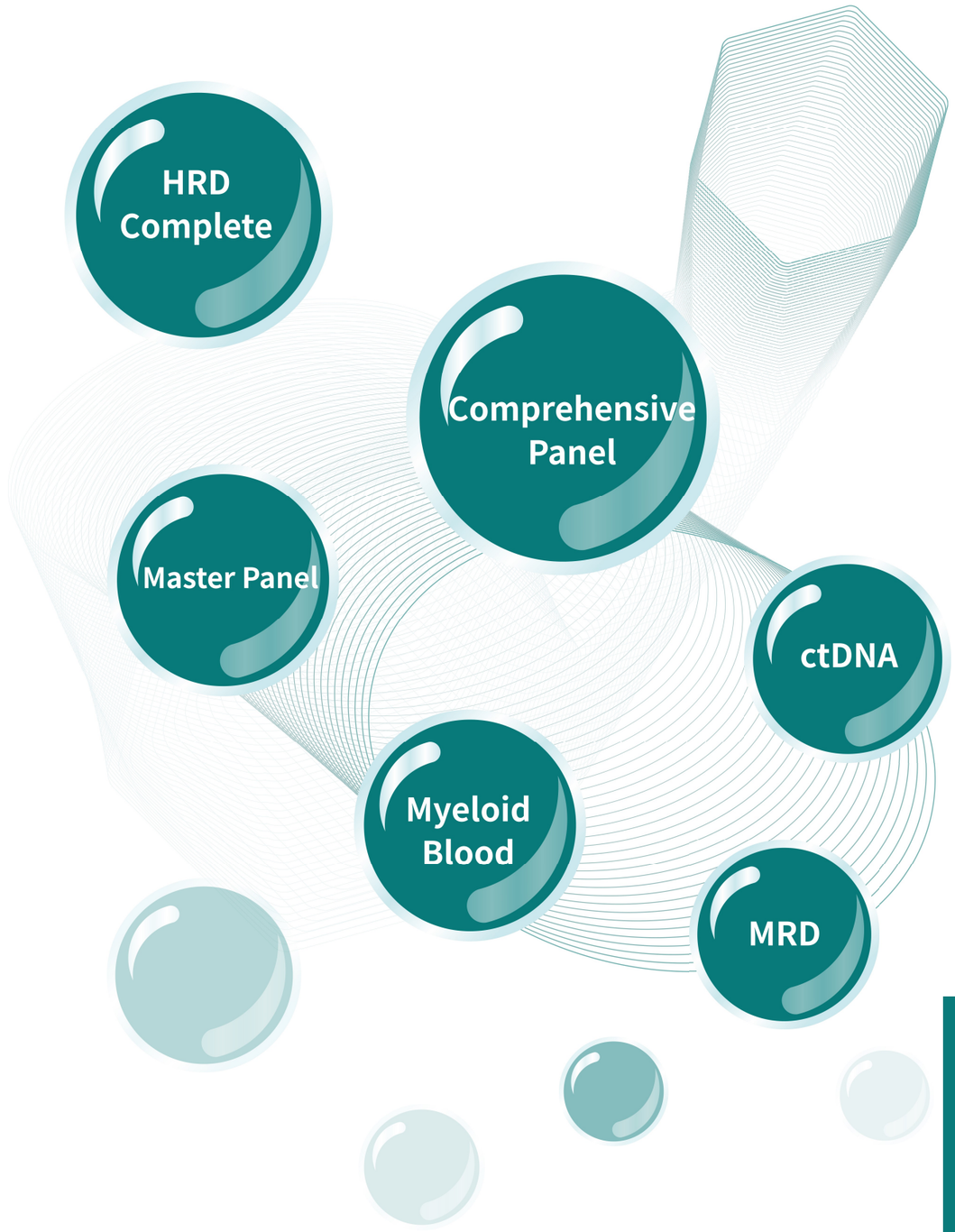
First in first out; QC before use; QC during test

Regular audit; Reasonable layout; Strict clean and maitenance system

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.

New Products under Development (RUO ONLY)



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

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