LENA Q51

Leukemia Fusion Genes DX test

Make Molecular Detection for Blood Disorders Easier, Faster and More Comprehensive

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FDA DISCLAIMER

LENA Q51 ® is offered to professionals only as a “RUO”, For research Only and not for Diagnostics purposes.

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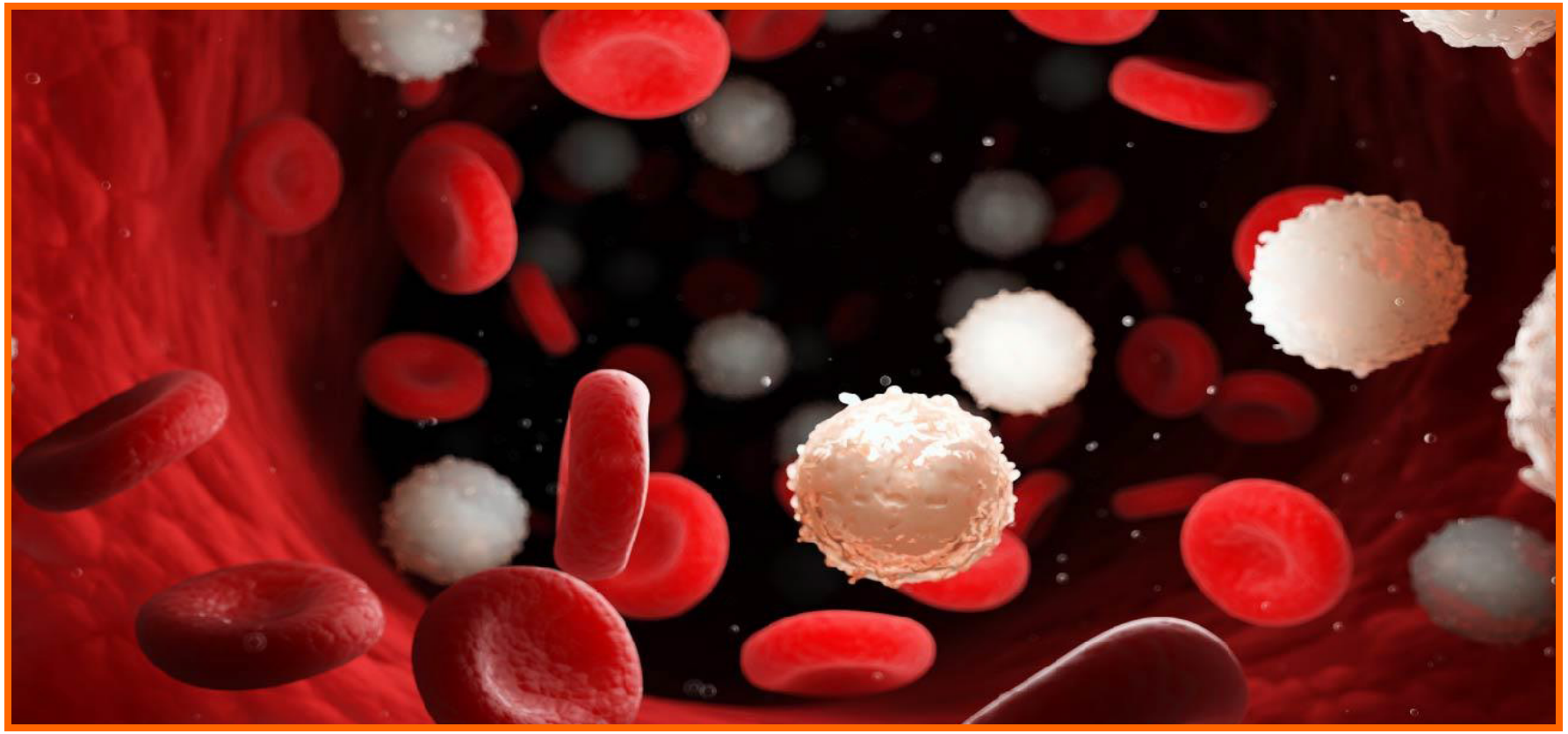
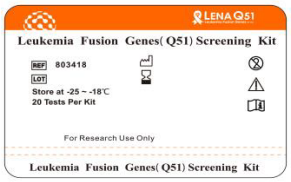
Leukemia

Leukemia is an umbrella term for several different cancers of the blood and the blood-forming tissues of the body. All start with problems in the creation of blood cells



Alercell Provides Comprehensive Solutions for Blood Molecular Detection



Nucleic Acid Extraction System, Lab-Aid 824s
Total RNA Blood Kit (Lab-Aid)

Nucleic Acid Extraction System, Lab-Aid 896
Total RNA Blood Kit (Lab-Aid 896)

Sample Extraction

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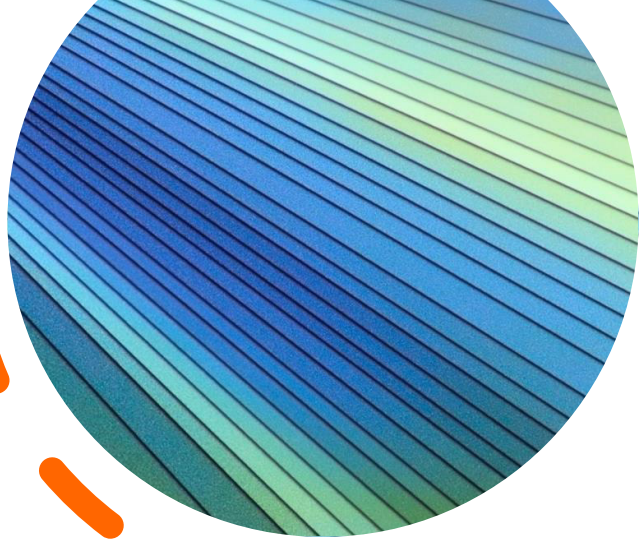
LENA Q51 Fusion Genes Screening Kit
Leukemia Fusion Genes Quantification Kit

Fluorescent PCR Assay

Why 52 Genes?



- There are currently more than 200 fusion genes. LENA Q51 actually detects 52 fusion genes. The selection of these 52 fusion genes is to consider an optimal cost performance.

- The 52 fusion genes we selected had a total of more than 200 breakpoints by the time of product development.

- The selection of these 52 fusion genes is based on the fact that the total mutation frequency of these 52 genes exceeds 85%, and the mutation frequency of the remaining more than 100 fusion genes does not exceed 15%.

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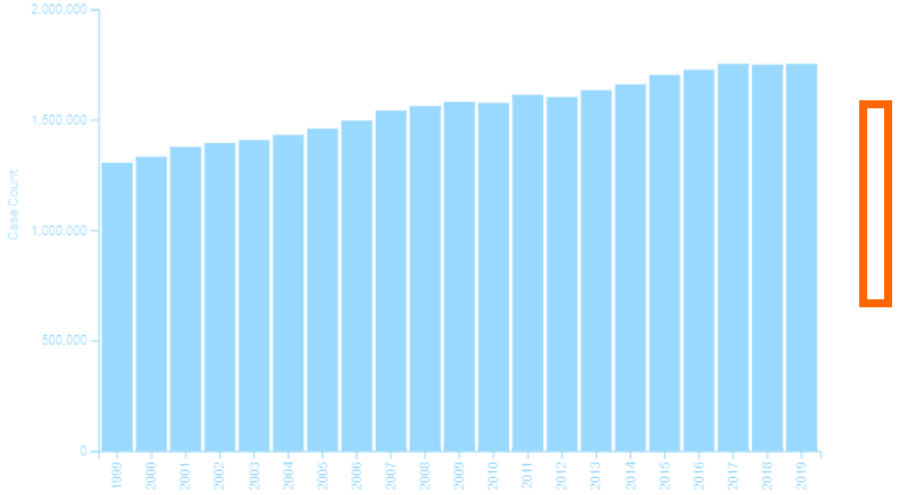
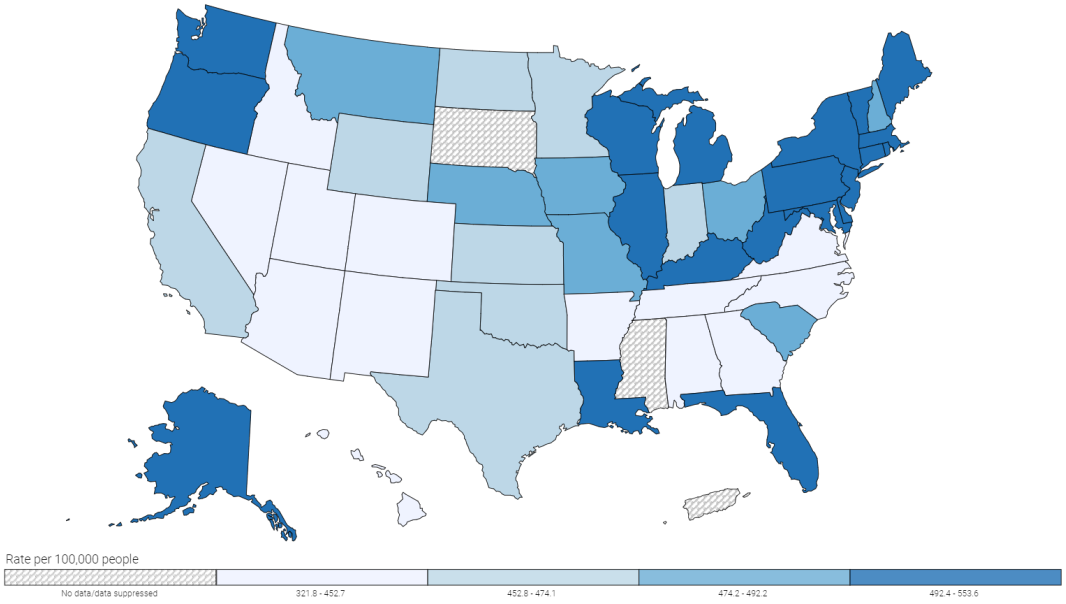
I Leukemia Molecular Detection Products

Harm of Leukemia to Human Health Keeps Increasing

- Leukemia, commonly known as **blood cancer**, is a malignant disease of the blood system
- The incidence rate ranks the first among cancers in children under 15 years old, accounting for about **1/3** of all childhood tumors
- The number of leukemia incidence is increasing year by year, The American Cancer Society's estimates for acute lymphocytic leukemia (ALL) in the United States for 2022 (including both children and adults) are: About 6,660 new cases of ALL (3,740 in males and 2,920 in females)

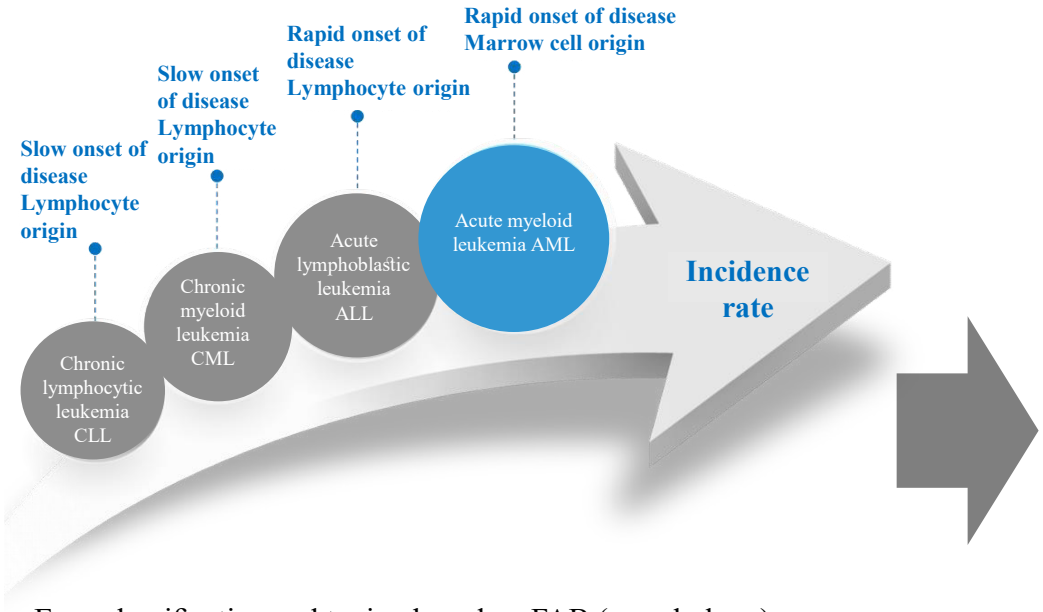
Cancer Trend: 1999-2019.





Source - U.S. Cancer Statistics Working Group. U.S. Cancer Statistics Data Visualizations Tool, based on 2021 submission data (1999- 2019): U.S. Department of Health and Human Services, Centers for Disease Control and Prevention and National Cancer Institute; https://www.cdc.gov/cancer/dataviz, released in November 2022.

More Accurate Classification with Fusion Genes for Precise Diagnosis and Treatment of Leukemia



Easy classification and typing based on FAB (morphology)

Table 1. WHO classification of myeloid neoplasms and acute leukemia

Acute myeloid leukemia (AML) and related neoplasms
AML with recurrent genetic abnormalities
AML with t(8;21)(q22;q22.1);*RUNX1-RUNX1T1*
AML with inv(16)(p13.1q22) or t(16;16)(p13.1;q22);*CBFB-MYH11*
APL with *PML-RARA*
AML with t(9;11)(p21.3;q23.3);*MLLT3-KMT2A*
AML with t(6;9)(p23;q34.1);*DEK-NUP214*
AML with inv(3)(q21.3q26.2) or t(3;3)(q21.3;q26.2); *GATA2, MECOM*
AML (megakaryoblastic) with t(1;22)(p13.3;q13.3);*RBM15-MKL1*
Provisional entity: AML with BCR-ABL1
AML with mutated *NPM1*
AML with biallelic mutations of *CEBPA*
Provisional entity: AML with mutated RUNX1
AML with myelodysplasia-related changes
Therapy-related myeloid neoplasms

WHO uses **fusion gene** as criteria for leukemia subtype classification since 2016

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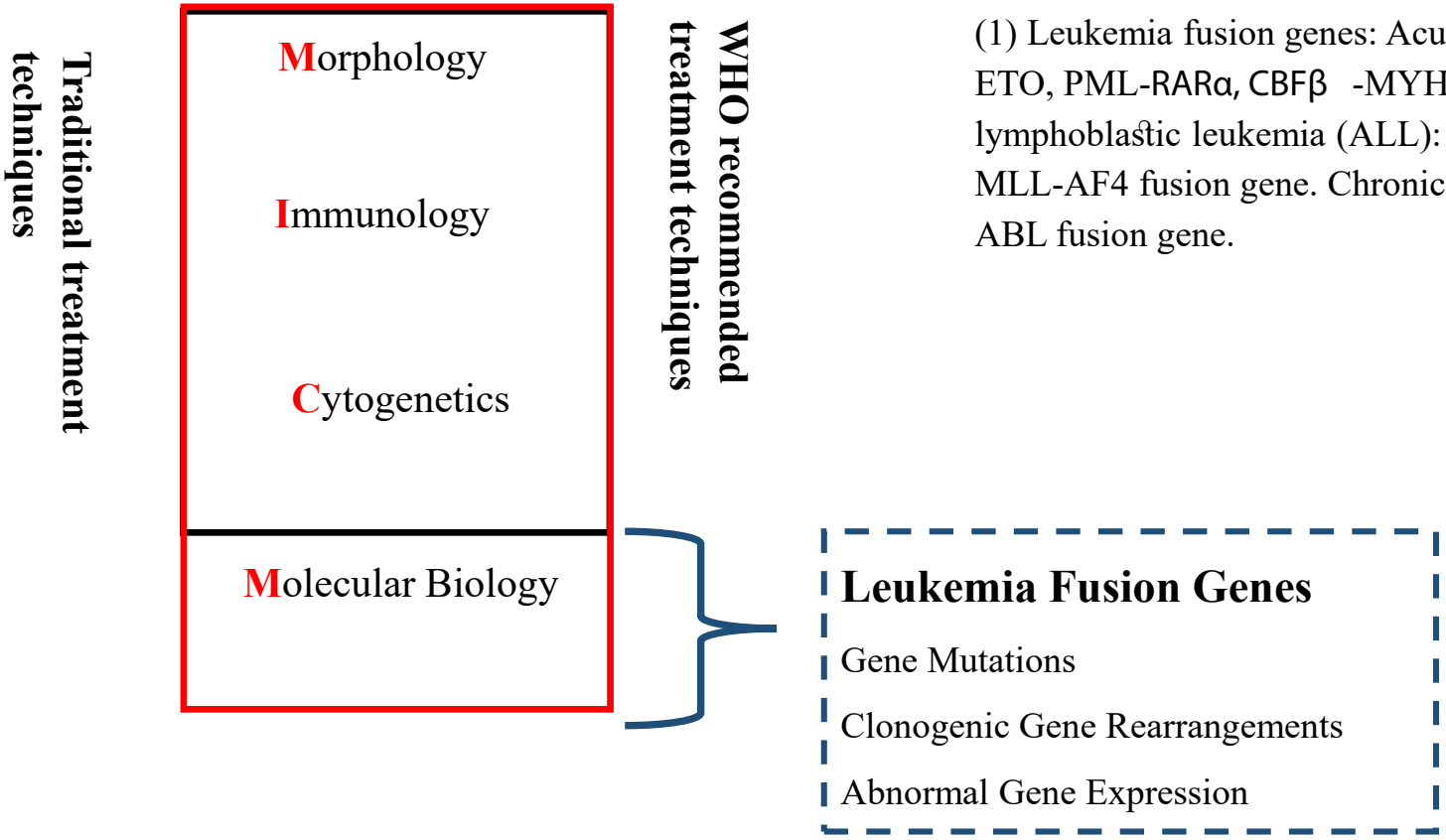
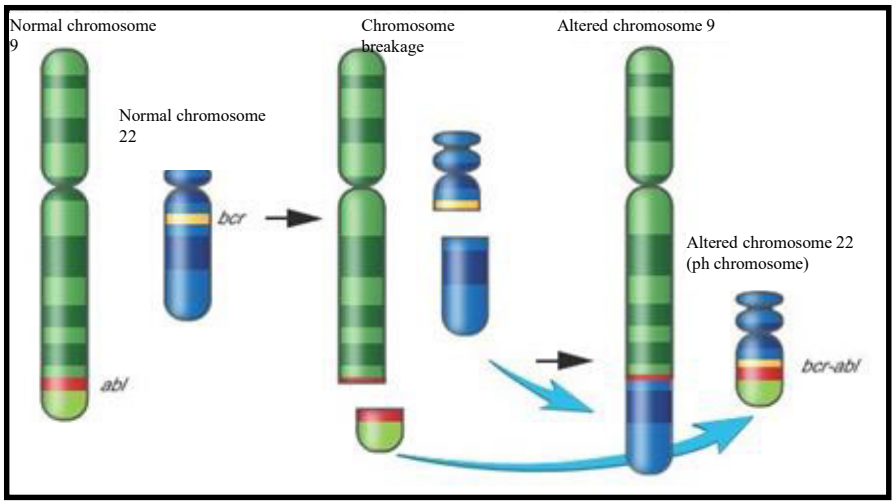
Adopting next-generation sequencing (NGS) technology for identification of gene fusion in patients with acute leukemia can be a good alternative to conventional tests



(1) Leukemia fusion genes: Acute myeloid leukemia (AML): AML-ETO, PML-RARα, CBFβ -MYH11, MLL-AF9 fusion genes. Acute lymphoblastic leukemia (ALL): TEL-AML, E2A-PBX1, BCR-ABL, MLL-AF4 fusion gene. Chronic myeloid leukemia (CML): BCR-ABL fusion gene.

Fusion Genes are the Most Common Biomarkers in Leukemia



Fusion Genes

- Fusion genes are one of the most common biomarkers in leukemia and are caused by chromosome breakages and recombination.
- More than 200 types of fusion genes have been identified, and about 50% of leukemia patients have fusion genes.
- Different disease subtypes have different fusion genes profiles.

Fusion Genes Detection Helps Building Precision Leukemia Treatment

Drug Prediction

• BCR-ABL1: It indicates that patients could benefit from targeted drug gleevec

• PML-RARα: It indicates that retinoic acid and arsenic trioxide treatment are effective for patients

Disease prognosis

•AML1-ETO: It is common in AML-M2 patients, and a good prognostic factor

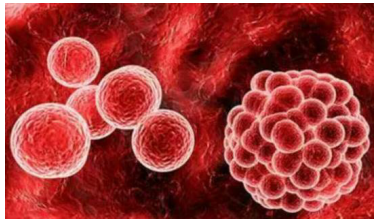
•MLL-AF4: Poor prognosis, and patients need to be given high-risk treatment solutions

Help building leukemia precise treatment, improve the survival rate of patients

Treatment process monitoring

•Monitor the effect of treatment by measuring the fusion genes content to indicate the change of tumor cells during the treatment

MRD detection



•When the treatment reaches the early stage of complete remission, MRD is tested regularly and the treatment method, schedule and treatment time are adjusted according to the level of MRD.

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Fusion Genes Detection Helps Building Precision Leukemia Treatment and is a less expensive path

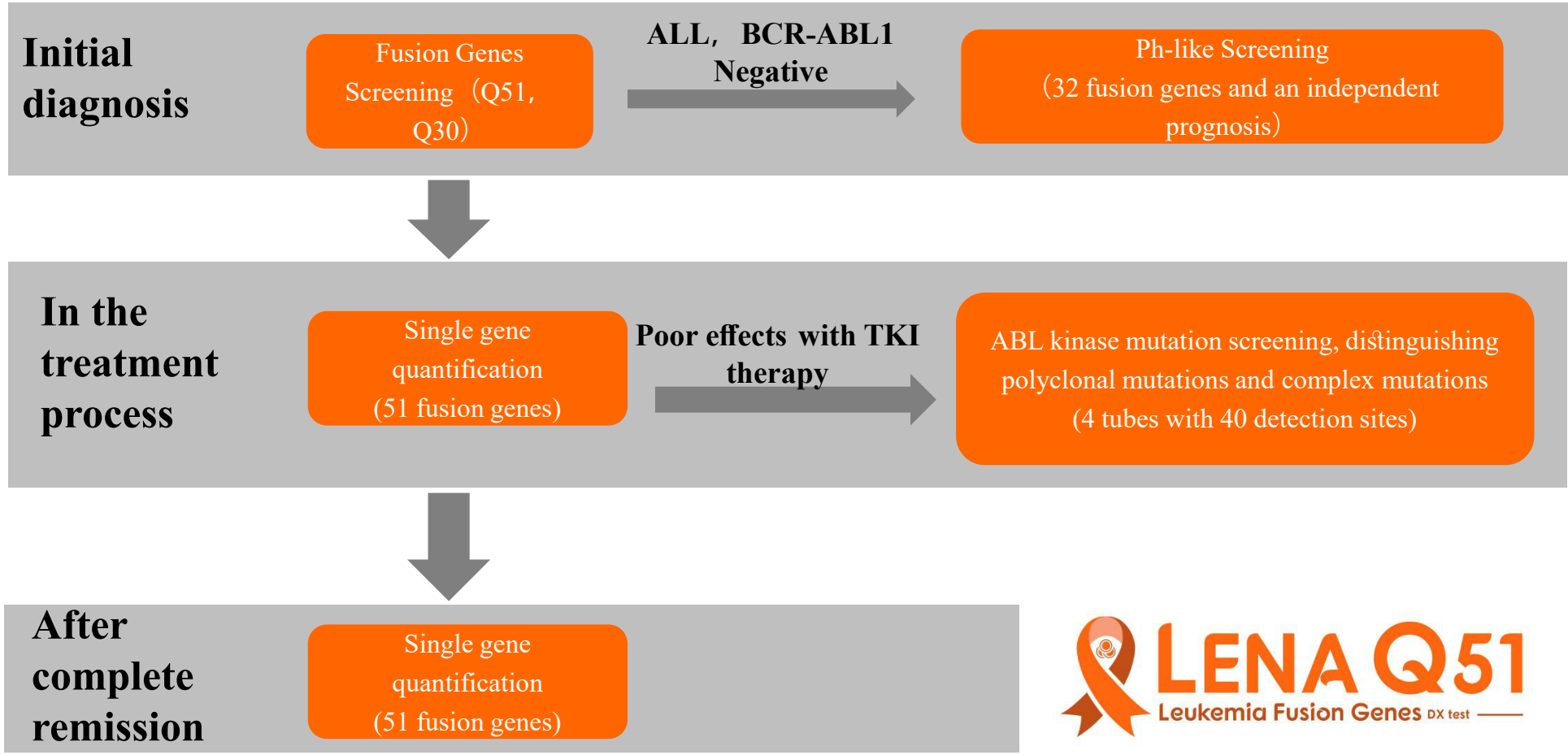
- The average cost of treatment for leukemia patients is $300,000 to $900,000
- Fusion genes screening charges is less than $10,000
- Quantitative detection charges is even lower four times a year, with an average 10-year survival, total quantitative testing costs les than $30,000

Precise medication

Timely adjustment of the treatment schedule

Relapse warning

Provides a Complete Set of Solutions for Leukemia Fusion Genes Detection



Leukemia Fusion Genes Detection Products

A complete set of screening and quantification products

- Leukemia Fusion Genes (Q30) Screening Kit
- Leukemia Fusion Genes (Q51) Screening Kit
  (Screen the mutations of 30 fusion genes)
- BCR-ABL1 Genotyping Kit
  (Determine the type: p190, p210 and p230)
- PML-RARα Genotyping Kit
  (Determine the type: L, S and V)

- BCR-ABL1 p190 Detection Kit
- BCR-ABL1 p210 Detection Kit
- PML-RARα L Kit
- PML-RARα S Kit
- PML-RARα V Kit
- AML1-ETO Detection Kit
- CBFβ-MYH11 Kit
- Wt1 Detection Kit

Clinical Significance

Drug Prediction → **Disease Prognosis Assessment** → **Treatment Process Monitoring** → **MRD Detection**

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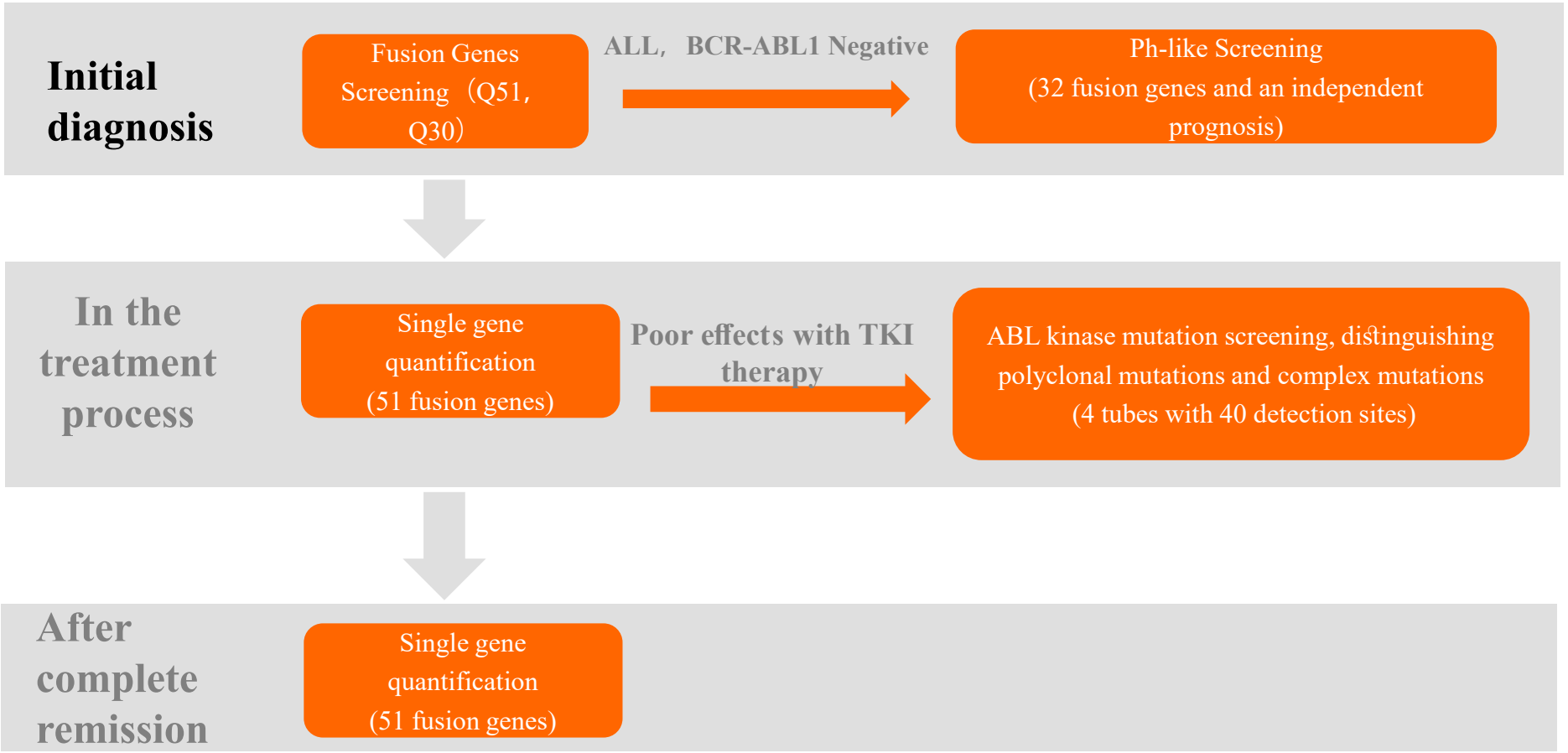
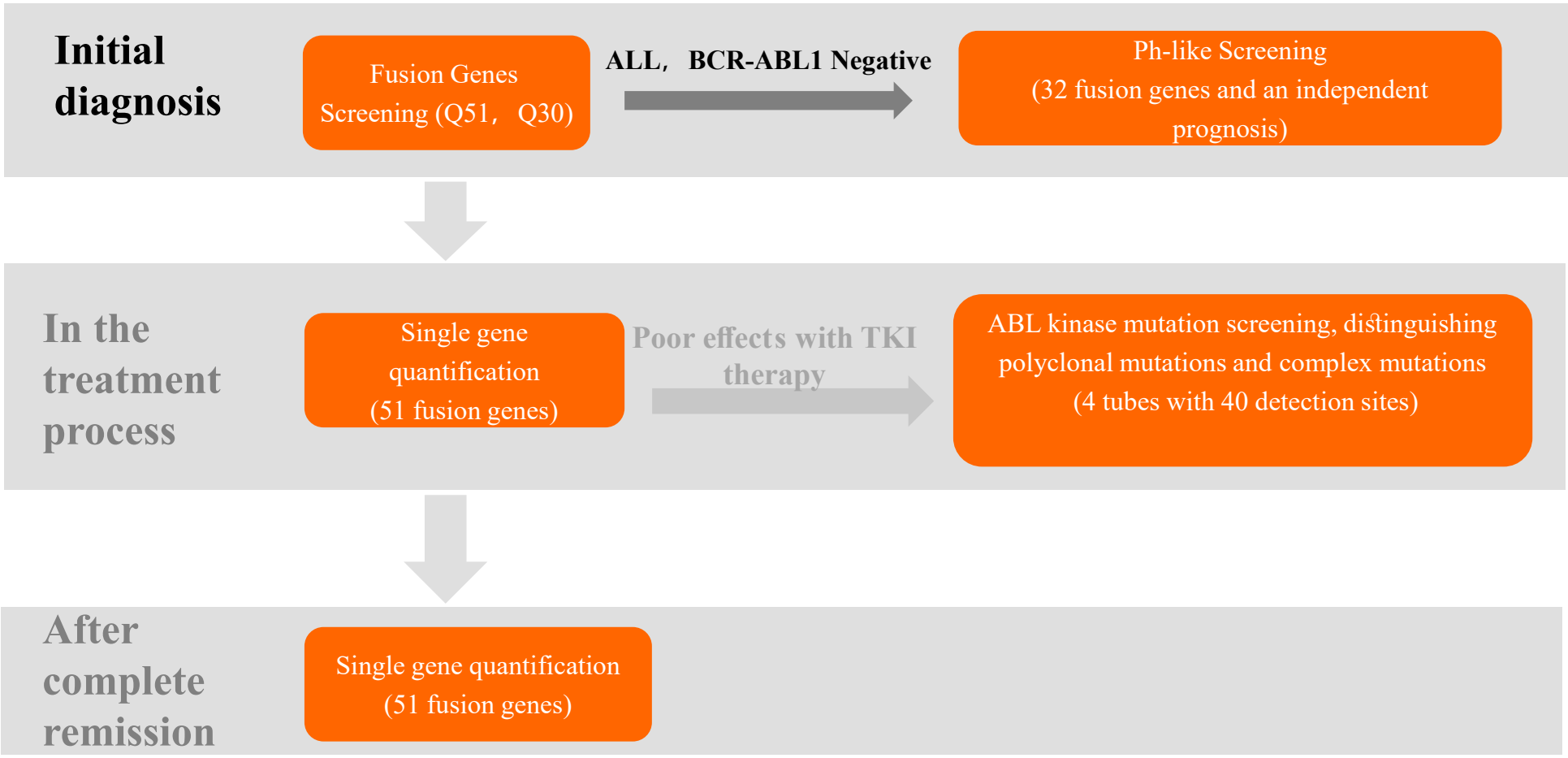
Provides a Complete Set of Solutions for Leukemia Fusion Genes Detection



Precise Typing on More Fusion Genes to Help Clinical Precision Diagnosis and Treatment

	LENA Q51 Leukemia Fusion Genes DX test	Competitive product (56)	Clinical significance
PDGFRA Series	• FIP1L1-PDGFRA • ETV6-PDGFRA	Indistinguishable	• Seen in about 23% of CELs with a good response to Gleevec • Present in AML, tyrosine kinase inhibitors have some effect
BCR-ABL Series	• BCR-ABL1 p210 • BCR-ABL1 p230	Indistinguishable	• Seen in about 95% of CML with a good response to Gleevec • Rare type, CML or CNL
AML1 series	• AML1-MDS1/EV11 • AML1-MTG16	Indistinguishable	• 1% AML is a poor prognostic factor • Though sensitive to chemotherapy, it has strong toxicity of chemotherapy
MLL series	• MLL-AF4 • MLL-AF9 • MLL-ENL • MLL-AF10 • MLL-SEPT6 • MLL-ELL • MLL-AF17 • MLL-AF1q • MLL-AF1P • MLL-AF6 • MLL-AFX1	Indistinguishable	• ALL, poor prognosis, requires intensive therapy • AML, poor prognosis, suggests poorer prognosis • ALL, mostly neonatal congenital leukemia, poor prognosis • AML-M5-type, poor prognosis • AML, poor prognosis, slightly better with bone marrow transplantation • Adult AML, very poor prognosis, bone marrow transplantation recommended • AML • AML • ALL, AML and MDS, prognosis related to gender and typing • AML, very poor prognosis, almost no remission, short survival • AML, ALL and CLL in infants and children, poor prognosis

Biotech Provides a Complete Set of Solutions for Leukemia Fusion Genes Detection



Philadelphia chromosome (Ph) -like acute lymphoblastic leukemia (ALL), is a high risk subset with a gene expression profile that shares significant overlap with that of Ph -positive (Ph $^{+}$) ALL

Acute lymphoblastic leukemia (ALL), a malignant clone originating from lymphoid precursor cells, accounts for more than 70% of childhood leukemias.

Currently, treatment schedules based on different subtypes of ALL have achieved good results, but some patients are still poorly treated and prone to relapse. Among them, the newly discovered subtype **Ph-like ALL** is included, accounting for about 10% to 30% of all in adults and 15% of all in children.

Diagnosis and Treatment Norms for Adult Acute Lymphoblastic Leukemia (2018 Edition)

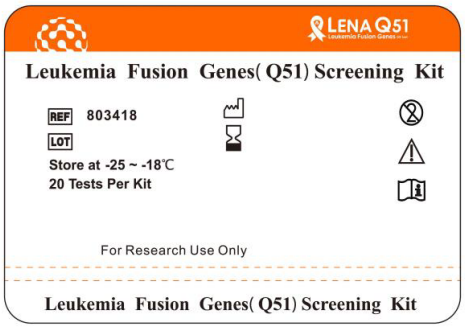
Tentative typing: BCR-ABL1 -like ALL

The definition of this type of AL is still difficult. In 2009, two research groups identified a new high-risk subtype of Ph-negative ALL and proposed the concept of Ph-like ALL, which has a similar genetic profile to BCR-ABL 1-positive ALL with IKZF1 or other lymphoid transcriptional regulator deficiency and a similar clinical prognosis, and is therefore called Ph-like ALL (Ph like ALL or BCR/ABL1-like ALL).

WHO lymphoblastic leukemia/lymphoma typing 2016 edition
ALL
B lymphoblastic leukemia/lymphoma
ALL, PTCL-U
ALL with recurrent genetic abnormalities
ALL with t (9; 22) (q34.1; q11.2); BCR-ABL1
ALL with t (v; 11q23.3) ; KMT2A
ALL with t (12; 21) (p13.2; q22.1) : ETV6-RUNX1
ALL with hyperdiploid karyotype
ALL with hypodiploid karyotype
ALL with t (5; 14) (q31.1; q32.3); IL3-IGH
ALL with t (1; 19) (q23; p13.3); TCF3-PBX1
Tentative typing : BCR-ABL1-like ALL[a]
Tentative typing: B-ALL[a] with internal amplification of chromosome 21
T-lymphoblastic leukemia/lymphoma
Tentative typing: early pre-t-cell lymphoblastic leukemia [a]
Tentative typing: natural killer (NK) cell-lymphocytic leukemia [a]
Note: l) [a] is a newly added typing. 2) ALL = B lymphoblastic leukemia.

4 tubes of Pre-packed Dry Powder Screening Reagent for Selected Ph-like Patients

	Fusion genes	Medication instruction
A tube	**ABL1**-ETV6, NUP214, RCSD1, RANBP2, SNX2, ZMIZ1, FOXP1 **CSF1R**-SSBP2 **IL2RB**-MYH9	Dasatinib JAK2 inhibitors JAK1 and/or JACK3 inhibitors
B tube	**JAK2**-ATF7IP, BCR, EBF1, ETV6, SSBP2, STRN3, TPR **CRLF2**-P2RY8 **TSLP**-IQGAP2	JAK2 inhibitors JAK2 inhibitors JAK2 inhibitors
C tube	**JAK2**-BCR, PAX5, PPFIBP1, TERF2 **NTRK3**-ETV6 **TYK2**-MYB	JAK2inhibitors Crizotinib JAK2 inhibitors
D tube	**ABL2**-PAG1, RCSD1, ZC3HAV1 **PDGFRB**-EBF1, SSBP2, TNIP1, ZEB2. ATF7IP **IKZF1** (IK6)Independent prognosis	Dasatinib Dasatinib



- **Four- tube**, four - color multi- detection system
- **Pre- pakced dry powder form**, no solution dispensing required, shipping at room temperature
- Detects **32** fusion genes (42 fusion forms) and **one independent prognostic** factor

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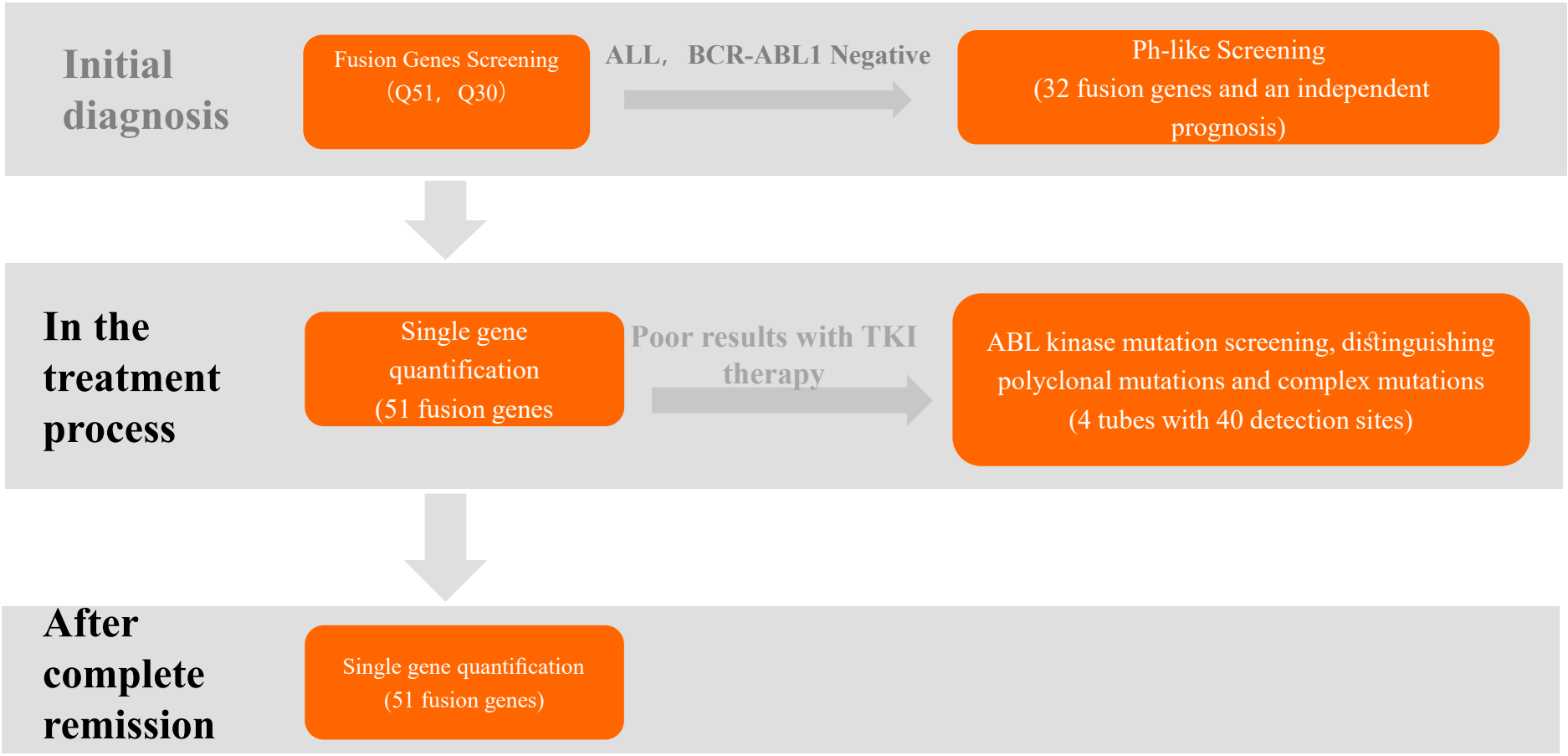
Provides a Complete Set of Solutions for Leukemia Fusion Genes Detection



Quantitative Detection Using an Innovative Single-Tube Dual System, Saving 50% of Manual Operations

Single-tube dual system PK traditional independent system

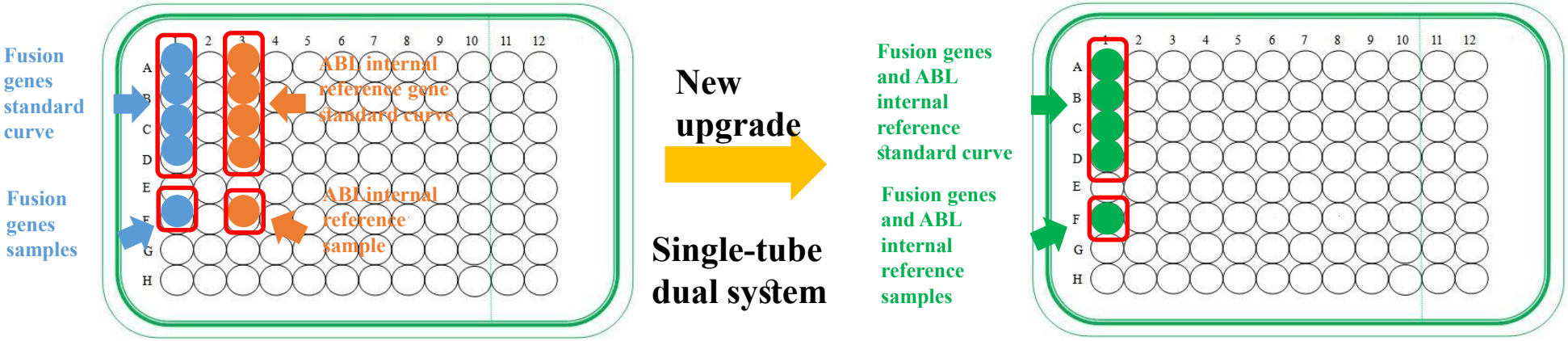
Single-tube dual system

Two-in-one target fusion gene and internal reference gene, fast and convenient

VS

Traditional independent system

The target fusion genes and the internal reference genes are separately spiked. The samples should be added separately, which is tedious and time-consuming.



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A Comprehensive and Diverse Range of Quantitative Products to Meet Different Customer Needs

Operation method: One-step method
Advantages: detected by adding samples only, easy operation, less contamination, high sensitivity

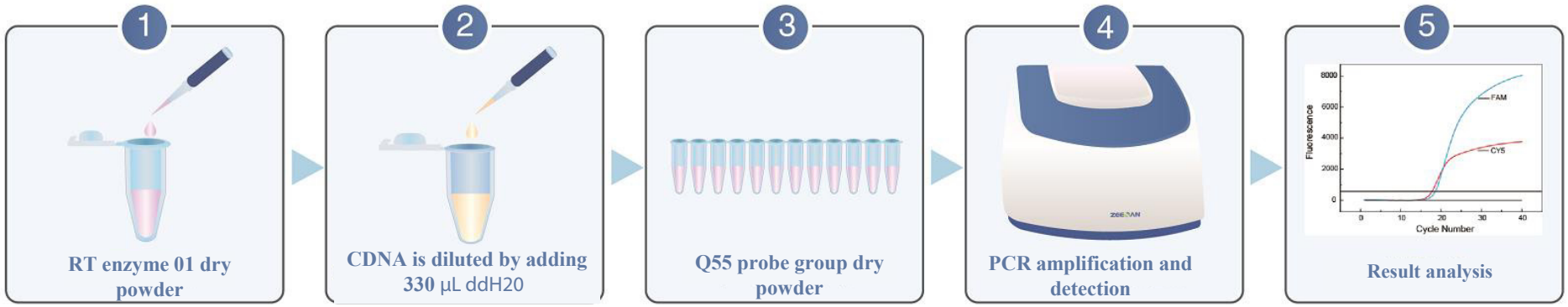
Operation method: Two-step method
Advantages: CDNA samples can be saved and other RNA assays can be performed when detection is carried out

Two methods are available, with flexible options to meet different clinical needs

Number	Karyotype	Fusion gene	Number	Karyotype	Fusion gene
1	t(9;11)(p22;q23)	MLL-AF9	31	t(1;11)(q23;p15)	NUP98-PMX1
2	t(15;17)(q24;q21)	PML-RARα	32	t(2;11)(q31;p15)	NUP98-HOXD13
3	t(8;21)(q22; q22)	AML1-ETO	33	t(7;11)(p15;p15)	NUP98-HOXA9
4	t(4;11)(q21;q23)	MLL-AF4	34	t(7;11)(p15;p15)	NUP98-HOXA13
5	t(12;21)(p13;q22)	TEL-AML1	35	t(11;12)(p15;q13)	NUP98-HOXC11
6	t(1;19)(q23;p13)	E2A-PBX1	36	t(7;11)(p15;p15)	NUP98-HOXA11
7	t(11;19)(q23;p13.3)	MLL-ENL	37	der(17) (q21)	STAT5b-RARα
8	t(9;22)(q34;q11)	BCR-ABL1	38	t(11;17)(q13;q21)	NUMA- RARα
9	de1(1)(p32)	SIL-TAL1	39	t(4;17)(q12;q21)	FIPIL1-RARα
10	t(10;11)(p12;q23)	MLL-AF10	40	der(17)(q21;q24)	PRKAR1A- RARα
11	inv(16)(p13;q22)	CBFβ-MYH11	41	t(10;11)(p13;q21)	CALM-AF10
12	t(3;21)(q26;q22)	AML1-MDS1/EV11	42	t(9;12)(p24;p13)	TEL-JAK2
13	de1(4)(q12)	FIP1L1-PDGFRA	43	t(x;11)(q13; q23)	MLL-AFX1
14	de1(9)(q34)	SET-CAN	44	t(4;12)(q12;p13)	ETV6-PDGFRA
15	t(17;19)(q22;p13)	E2A-HLF	45	(11q23)	dupMLL
16	t(6;9)(p23;q34)	DEK-CAN	46	t(10;14)(q24;q11)	Hox11
17	t(X;11)(q24;q23)	MLL-SEPT6	47	t(5;14)(q35;q32)	HOX11L2
18	t(16;21)(p11;q22)	TLS-ERG	48	t(3;3)(q21;q26)	EVI-1
19	t(5;12)(q33;p13)	TEL-PDGFRB	49	t(9;22)(q34;q11)	BCR-ABL1 p190
20	t(11;19)(q23;p13.1)	MLL-ELL	50	t(9;22)(q34;q11)	BCR-ABL1 p210
21	t(11;17)(q23;q12-21)	MLL-AF17	51	t(15;17)(q24;q21)	PML-RARα S-type
22	t(5;17)(q35;q21)	NPM-RARα	52	t(15;17)(q24;q21)	PML-RARα V-type
23	t(3;5)(q25;q34)	NPM-MLF1	53	t(15;17)(q24;q21)	PML-RARα L-type
24	t(11;17)(q23;q21)	PLZF-RARα	54	t(2;5)(p23;q35)	NPM1-ALK
25	t(1;11)(q21;q23)	MLL-AF1q			
26	t(1;11)(p32;q23)	MLL-AF1P			
27	t(9;12)(q34;p13)	TEL-ABL1			
28	t(16;21)(q24;q22)	AML1-MTG16			
29	t(3;21)(q26;q22)	AML1-EAP			
30	t(6;11)(q27;q23)	MLL-AF6			

The most comprehensive fusion genes quantitative detection reagent

Easy to Operate and Complete PCR Detection in 2 Hours



15 mins

5 mins

Screening: 2h20mins
Quantification: 1h45mins
Ph-like: 1h40mins
Kinase mutation: 2.5h

Blood total RNA extraction kit and Lab-Aid 824S Nucleic Acid Extraction System, can realize the automatic blood total RNA extraction easily and quickly, subverting all the existing manual extraction methods

Open Platform for Mainstream Fluorescent PCR Instruments

ABI 7500

Bio-Rad
CFX96

Stratagene
Mx3000/300
5P

Hongshi SLAN-
96P/S

Applicable for instruments with FAM, HEX/JOE, ROX and Cy5 detection channels

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II

Fully Automated Blood RNA Extraction System

Equipped with Own Brand Lab-Aid 824S Automatic Extraction System

- Complete **24** blood RNA extracts in **37** minutes
- **No need for pre- treatment**, high quality RNA can be obtained in one step of sample addition
- **One reagent strip for one sample**, flexible for 1 - 24 samples extraction, effectively avoiding reagent waste
- The maximum volume of sample is **2 ml** to ensure the total RNA extraction
- Perfectly extract the whole blood samples, leukocyte samples and heparin anticoagulated bone marrow blood samples

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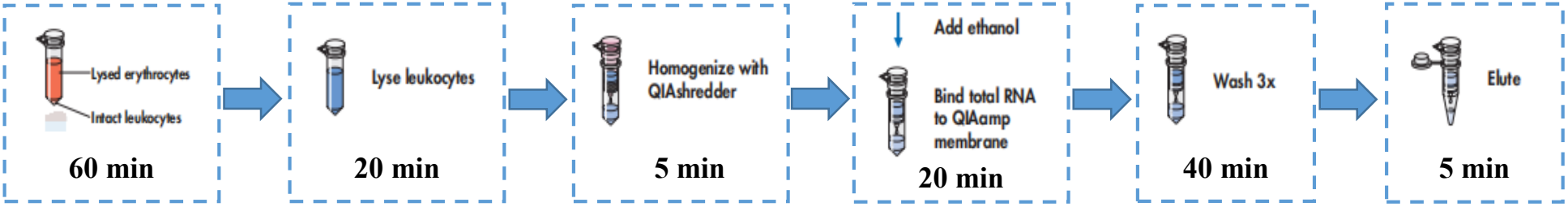
ALERCELL

Manual Operation Time Reduced by 90% and Total Time Reduced by 65%



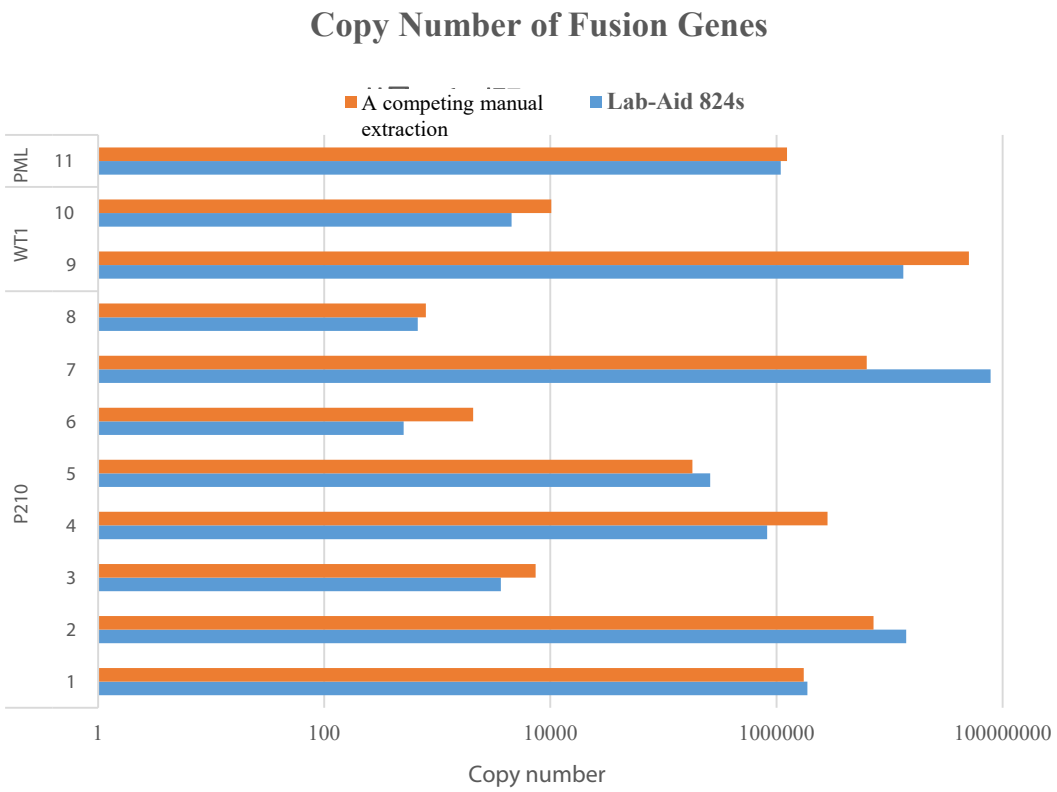
Total extraction time of an imported manual extraction reagent: **150 mins**

Take 24 samples as an example

Total extraction time for Lab-Aid 824s: **52 minutes**

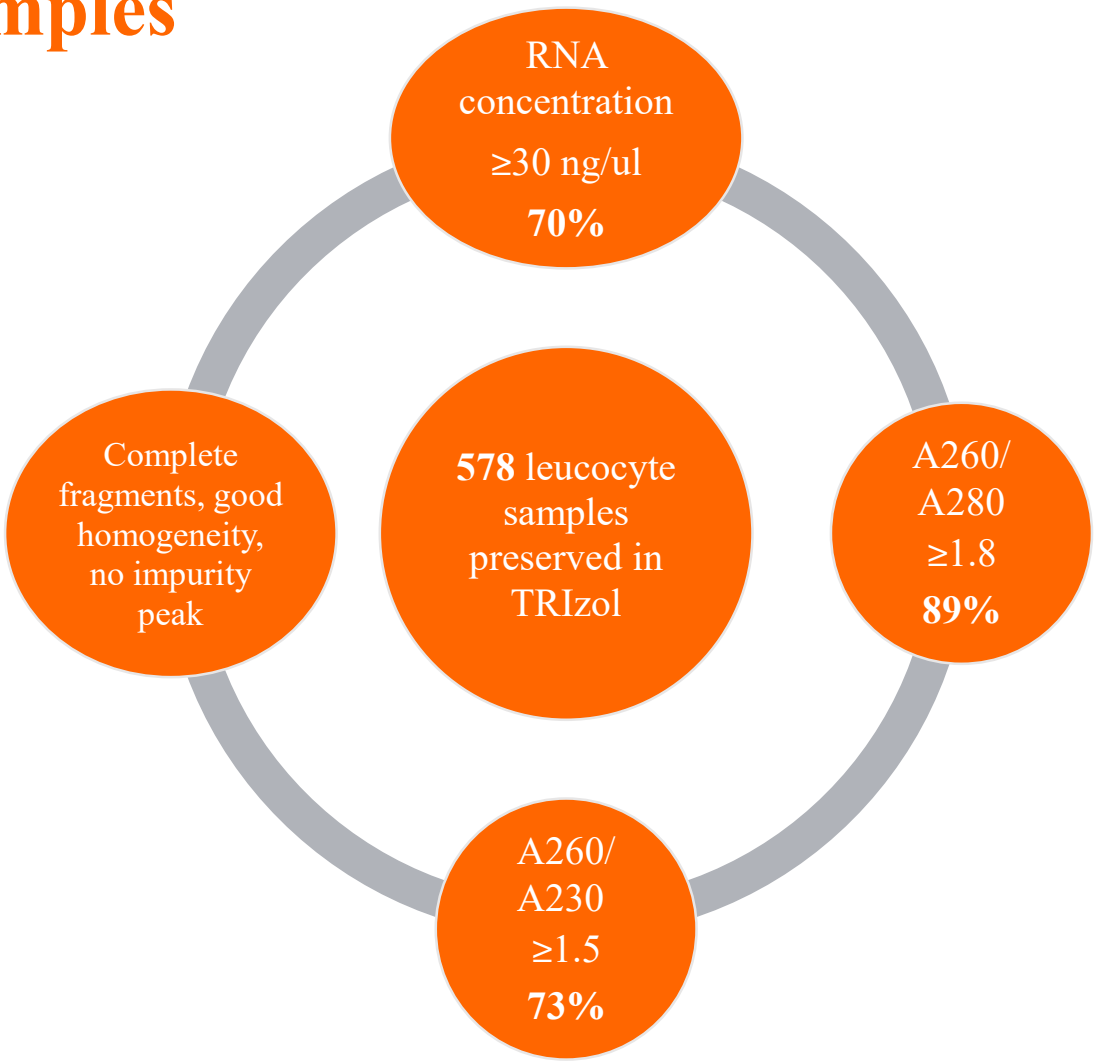
Manual operation：**15 minutes**

High Extraction Efficiency of the Whole Blood Samples, Perfectly Suited for Subsequent Quantitative Assays

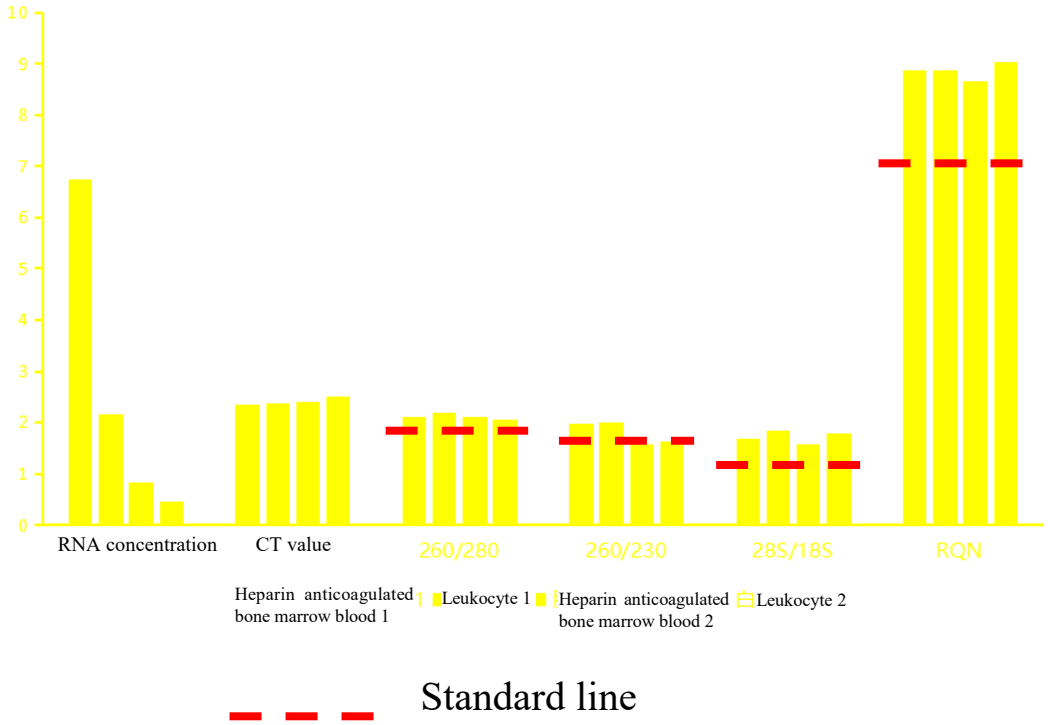


The copy number of quantitative RNA is comparable between the **200 μL** blood sample extracted by Lab-Aid 824s and the **1 mL** blood sample extracted by a competing manual operation , with high extraction efficiency.

High Quality Extraction of Long-term Preserved Leukocyte Samples



High Quality Extraction of Heparin-anticoagulated Bone Marrow Blood Samples



- Lab-Aid 824s extracts 500 μL of highly concentrated heparin-anticoagulated bone marrow blood, the RNA concentration, purity and integrity of which can meet the requirements;
- It can remove inhibitors in the blood without affecting subsequent amplification.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Alercell®
ONCOLOGY

LENA Q51

Leukemia Fusion Genes DX test

ALERCELL

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