



ORIGIN MANUFACTURE
ANSWERS FOR BETTER LIFE

誠信
Integrity

熱情
Passion

創新
Innovation



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Thalassemia

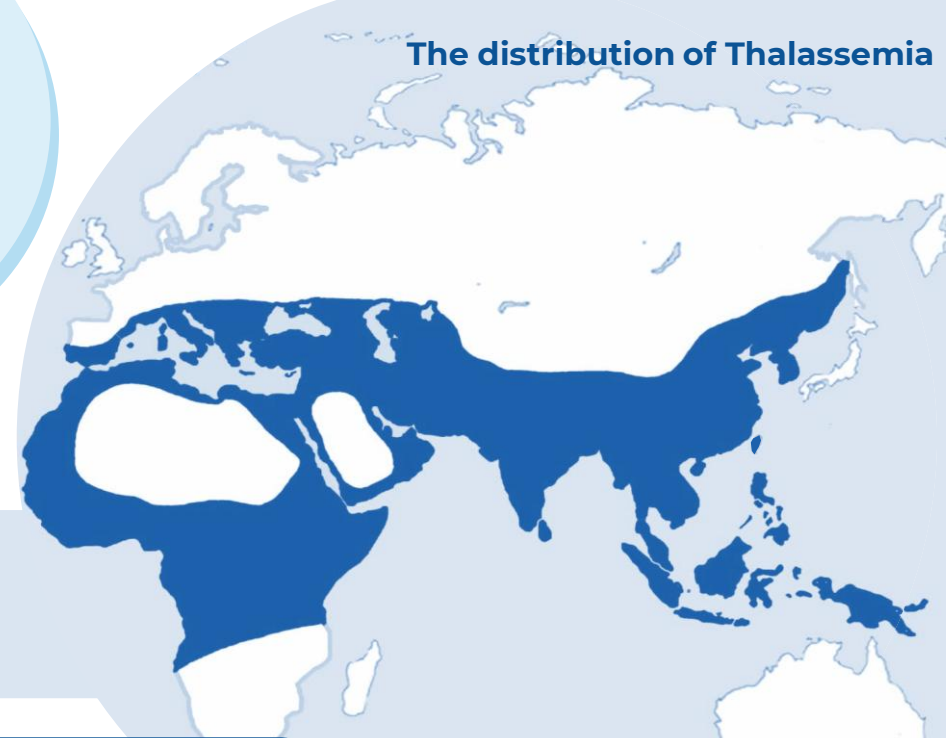
Alpha/Beta Thalassemia detection kit



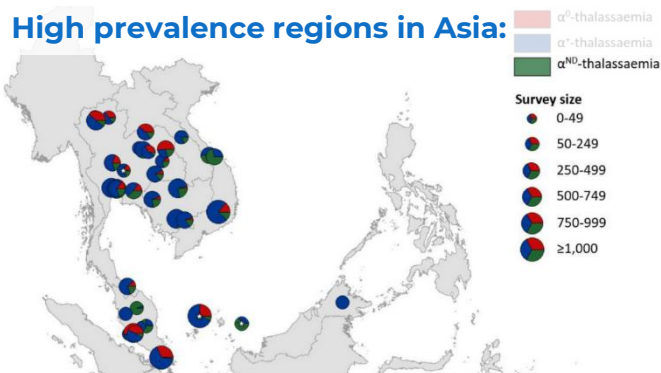
- **Abnormal hemoglobin production**
- **Decreased ability to carry oxygen**
- **Two main types of thalassemia, alpha and beta thalassemia**
- Alpha thalassemia results from mutations in *HBA*
- Beta thalassemia results from mutations in *HBB*
- The widest distribution and the largest population in the world.
- Mainly distributed along the Mediterranean coast, Southeast Asia and Africa
- Alpha and beta thalassemia are the most common, and mutations are regional



The distribution of Thalassemia



High prevalence regions in Asia:



Carrier rate	Alpha	Beta
China	24%	6%
India	18%	8%
Malaysia	4%	12%
Thailand	20%	9%
Vietnam	51%	25%



Symptoms of Thalassemia

- Manifest from 6 months infants.
- Severe alpha can result in stillbirth or death during birth.
- Children with beta do not exhibit symptoms at birth but develop severe anemia in first year.

Associated symptoms include:

1. Headaches
2. Delayed growth and development
3. Pale or jaundiced skin
4. Dark urine
5. Facial bone deformities
6. Increased susceptibility to infections
7. Fatigue



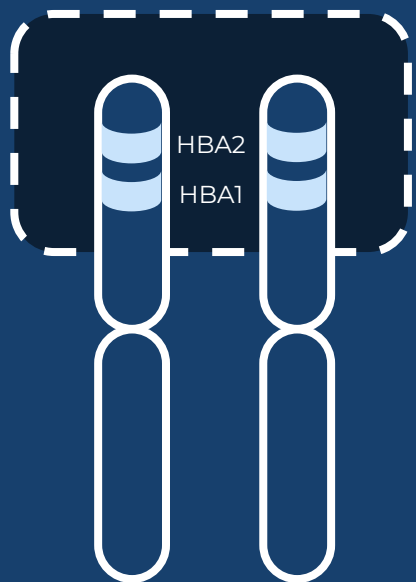
Answers for Better Life
Origin Biotechnology Co., Ltd.

Children with Thalassemia require lifelong blood transfusions to survive.

- ! Monthly treatment cost is \$10,000 USD.
- ! Stem cell transplant is \$80,000~400,000 USD/ procedure, with a high rate of failure.
- ! \$2.2 million for gene-editing treatments.



Alpha Thalassemia



Chromosome 16

In Southern Asia

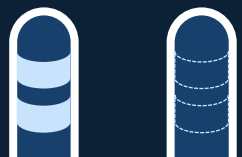
Deletion: 92%
Point mutation: 5%
Both: 1%
Rare type: 2%

Person with 1 mutated allele



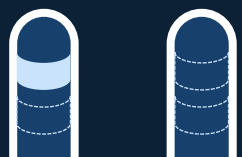
Carrier

Person with 2 mutated alleles



Mild thalassemia

Person with 3 mutated alleles



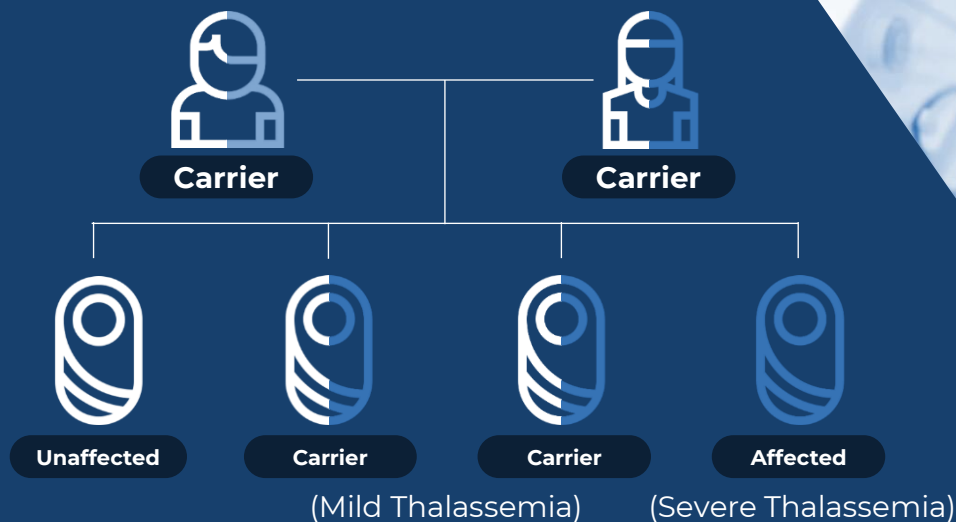
HbH disease

Person with 4 mutated alleles



Hydrops fetalis

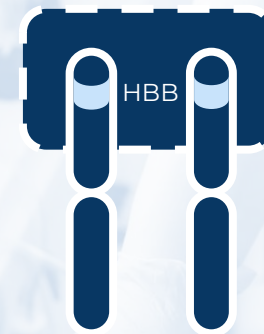
Beta Thalassemia



In Southern Asia

Point mutation: 99%
Deletion: ~0.2%

- 6 point mutations account for >90% of all mutation types



Chromosome 11



Specification

IVD

Alpha+Beta
1 tube PCR

8 deletion subtype

- α3.7
- α4.2
- SEA
- THAI
- FIL* *(MLPA cannot distinguish)
- α20.5
- MEDII/ DutchI
- MEDI

3 non-deletion mutation

- CS, Constant Spring
 - QS, Quong Sze*
 - WS, Westmead*
- *(MLPA doesn't cover)

17- point mutation + HBB deletion

Covering up to 99% of Beta-Thalassemia

1 tube PCR, and 1 CE test

Detecting

11 Alpha del-subtype

17 Beta point mutation & deletion

All in Once

IVD

Alpha+Beta
2 tubes PCR

Mixed the PCR
product for CE test

PCR 1

Alpha



PCR 2

Beta
(Option)



CE 1

Alpha
+ Beta



- We reserved the option for separate or combined diagnosis of Thalassemia.

Origin

Lower than MLPA



MLPA

High cost

3 hours from DNA to result



2 days from DNA to result

One step around 10min



Four steps around 60min

8-del + 2-dup + 3-point Mutations



7-del + 1-dup + 1-point Mutations

- PCR
- CE
- Data analysis



- Denaturation
- Hybridization
- Ligation
- PCR
- CE
- Data analysis

Higher coverage and performance, cheaper



Lower performance, high cost and labor



	Full Coverage	Detect Beta-Thal	Easy-to-Use	Auto-Analysis
Origin				
MLPA				

Origin	MLPA
Lower than MLPA	High cost
3 hours from DNA to result	2 days from DNA to result
One step around 10min	Four steps around 60min
8-del + 2-dup + 3-point Mutations	7-del + 1-dup + 1-point Mutations
• PCR • CE • Data analysis	• Denaturation • Hybridization • Ligation • PCR • CE • Data analysis
Higher coverage and performance, cheaper	Lower performance, high cost and labor

	All in One	α only	β only
Target	One-tube Identify : α 8 del-subtype + HS40 deletion, 2 duplication, 3 non-deletion β 17 point mutations, deletion	One-tube Identify : α 8 del-subtype + HS40 deletion, 2 duplication, 3 non-deletion	One-tube Identify : β 17 point mutations Determine 0, 1, ≥2 copy
Procedure	1.PCR (2.5hr) 2.CE (45min) 3.Data analysis		
Time	3 Hours		
Characters	Distinguishing between α-, β-thalassemia patients, carriers, and normal individuals	Distinguishing between α-thalassemia patients, carriers, and normal individuals	Distinguishing between β-thalassemia patients, carriers, and normal individuals

Clinical Validation α

Clinical samples	
Genotype	No.
αα/αα	536
ααα4.2/αα	10
ααα4.2/-α3.7	1
ααα3.7/αα	5
HKαα/αα	2
-α4.2/αα	30
-α4.2/-α3.7	1
16p13.3 deletion/-α4.2	1
-α3.7/αα	118
-α3.7/-α3.7	10
-α3.7/αCSα	4
-α3.7/αWSα	2
--SEA/αα	528
--SEA/--SEA	30
--SEA/--FIL	2
--SEA/αα3.7	3
--SEA/-α3.7	12
--SEA/-α4.2	2
--SEA/αQSα	7
--SEA/αCSα	1
--SEA/HKαα	3
--THAI/αα	25
--THAI/-α3.7	1
--FIL/αα	63
--FIL/--SEA	4
--FIL/-α3.7	2
αWSα/αα	7
αQSα/αα	22
αCSα/αα	10
Total	1442

Coriell DNA	
Genotype	No.
aa/aa	15
aaa3.7/aa	4
Trisomy 16	2
--SEA/aa	3
-a3.7/aa	16
--FIL/aa	1
-a3.7/-a3.7	2
--FIL/--SEA	1
Total	44

100%
Consistency

Origin **VS** MLPA P140 + Gap PCR

α validation: **1486 / 1486**

Clinical samples	
Genotype	No.
NORMAL	483
β → cd 26	12
β → IVS II -nt 654	24
β → -28	9
β → -29(A>G)	3
β → IVS-I-1(G>T)	2
β → cd 71/72	3
β → cd 41/42	34
β → cd 27/28+C	2
β → IVS-I-5	2
β → cd 43	2
β → cd 17	12
β → IntM	1
β → cd 41/42 major	3
β → -28 + cd 27/28 major	1
β → cd 27-28+IVS II -nt 654	2
β → cd 26 major	1
β → IVS II -nt 654 major	2
β → cd 17 + cd 41/42 major	1
β → -28 + cd 41/42 major	1
β → -28 + IntM	1
β → HBB deletion	4
β → -28+HBB deletion	1
Total	606

Over 2,000 clinical samples were verified, including

- 1,061 positive samples,
- 1,034 negative samples.

Beta Thalassemia specifications is open for customization.

Coriell DNA	
Genotype	No.
β → cd 71/72 + IVS II -nt 654	1
β → cd 26	1
β → IVS-I-1(G>A)	1
Total	3

100%
Consistency

Origin **VS** Sanger Sequencing

Beta Validation: **609 / 609**

NGS-based competitor

Devyser Thalassaemia for NGS

- **Single-tube NGS assay** for simultaneous comprehensive analysis of the HBA and the HBB gene clusters.
- Full gene sequencing of **HBA1, HBA2 and HBB genes** enables detection of all SNVs.
- Robust CNV detection with two combined strategies for CNV detection:
 - Direct detection of 17 CNVs
 - Coverage based detection of CNVs in both the HBA and the HBB gene clusters
- Built in rapid sample mix-up control through sex chromosome markers.



COMPARISON

	Origin	MRC-Holland	Devysr
Platform	QF-PCR (PCR-CE)	MLPA (PCR-CE)	NGS
Sample Type	Whole blood, Amniotic Fluid, Villus		Whole blood only
SPEC	Alpha CNV + point mutation Beta del + point mutation Gender Marker	Alpha CNV +CS only (point mutation)	Alpha CNVs + SNVs Beta CNVs + SNVs Gender Marker
Duration	3 hour (PCR+CE)	2 days (MLPA+CE)	at least 2 days (Library + Sequencing)
Cost & Labor	\$	\$\$	\$\$\$\$\$
Equipment	ABI Genetic Analyzers		Illumina iSeq, MiSeq and MiniSeq
Notes	1. Short turnaround time for comprehensive test and cheap 2. Comprehensive SPEC for Alpha and Beta Thalassaemia 3. Used to Newborn, Prenatal, and Carrier screening, and diagnose	1. Higher cost, complex procedures, and longer turnaround times 2. Basic SPEC in Alpha thalassaemia only	1. Expensive cost and time 2. Need to wait for sufficient samples for NGS 3. Only used to diagnose

10X ONLY

COST FOR SINGEL GENE DISORDER

LIMITED SAMPLE TYPE FOR PATIENT DIAGNOSTIC ONLY