ORIGIN MANUAL

ANSWERS FOR BETTER LIFE

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Thalassemia

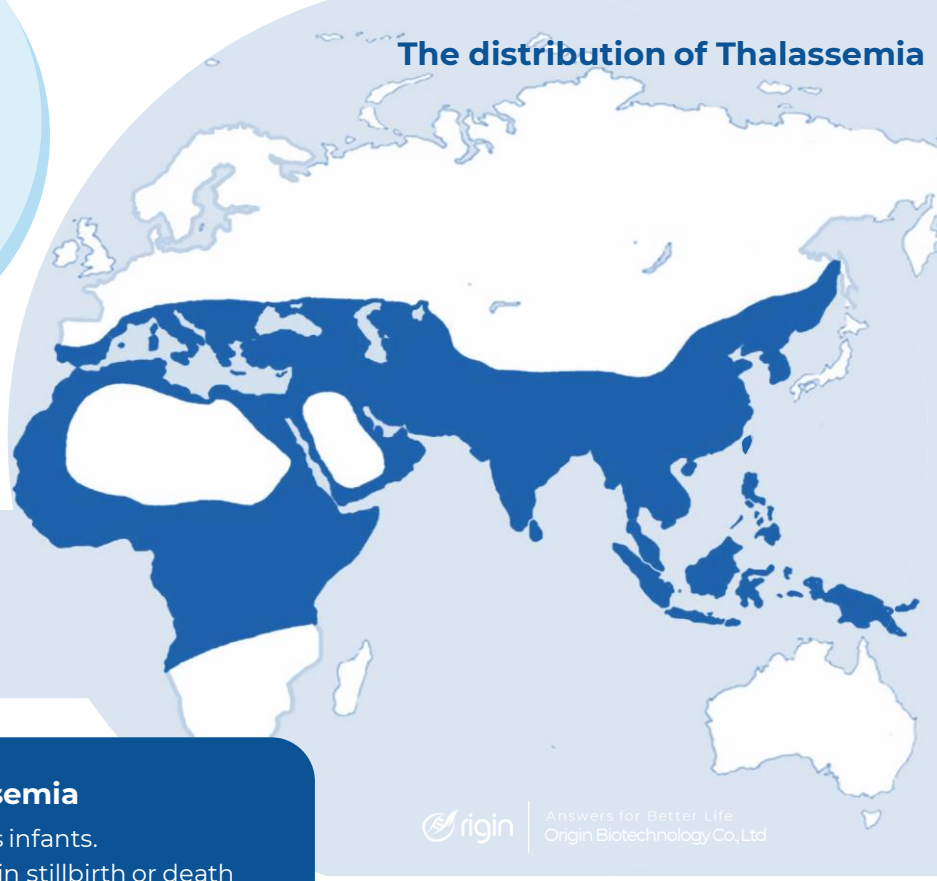
Alpha/Beta Thalassemia detection kit

- **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



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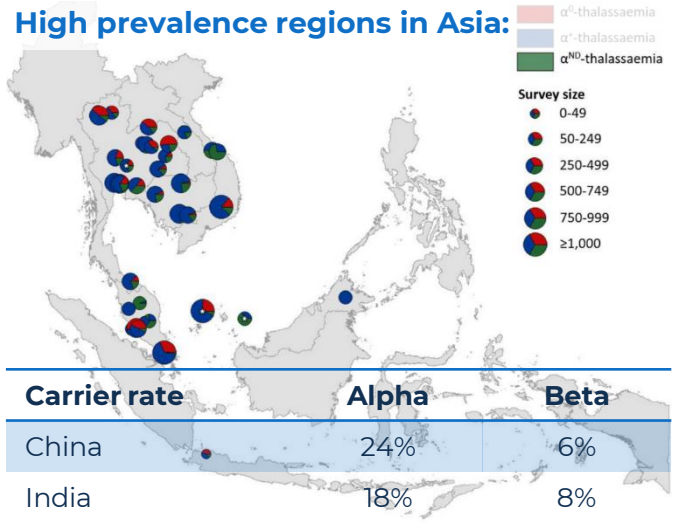
High prevalence regions in Asia:



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.

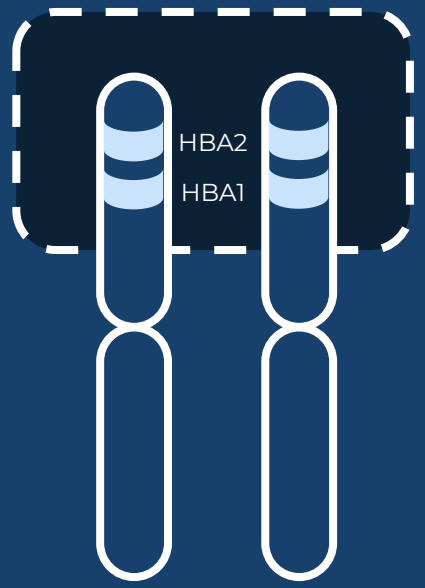
Associated symptoms include:

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

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

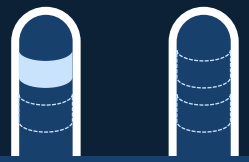
Person with 1 mutated allele

Carrier

Person with 2 mutated alleles

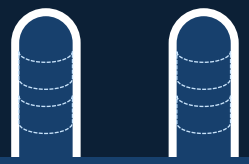
Mild thalassemia

Person with 3 mutated alleles



HbH disease

Person with 4 mutated alleles

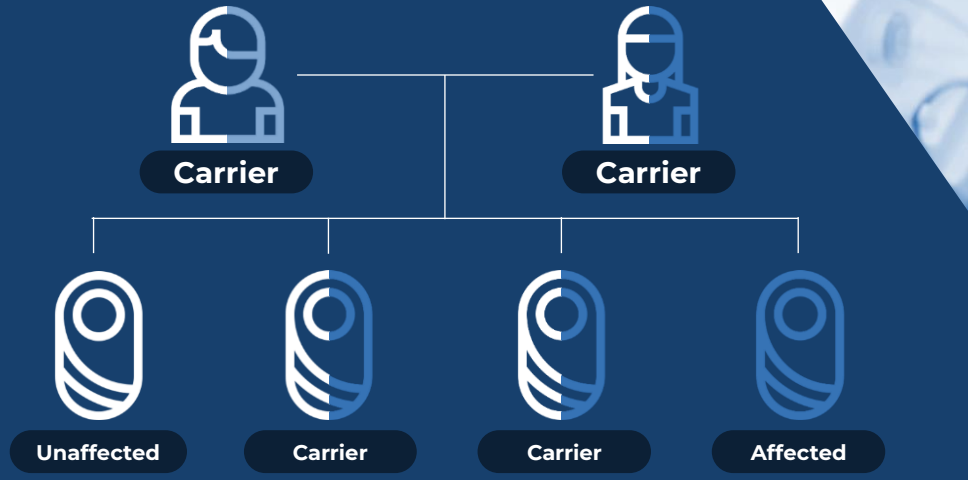


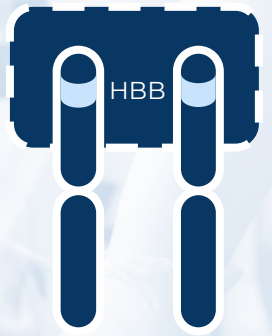
Hydrops fetalis

In Southern Asia

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

Beta Thalassemia





Chromosome 11

In Southern Asia

Point mutation: 99%
Deletion: ~0.2%

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

Specification

IVD
Alpha+Beta
1 tube PCR

8 deletion subtype

-α3.7
-α4.2
--SEA
--THAI
--FIL* *(MLPA cannot distinguish)
-α20.5
--MEDII/ Dutch1
--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

Separate Alpha- and Beta- as two kits

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		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

	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
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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
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	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.**
aa/aa	181
ααα4.2/aa	8
ααα3.7/aa	2
aaa4.2/-a3.7	1
--SEA/aa	227
--SEA/--SEA	9
-α3.7/aa	77
-α3.7/-α3.7	3
-α4.2/aa	30
--THAI/aa	9
--FIL/aa	37
--FIL/--SEA	2
--FIL/-α3.7	2
--SEA/-α3.7	4
-a4.2/-α3.7	1
--SEA/-α4.2	2
--SEA/ααα3.7	3
--THAI/ααα3.7	1
Hb-WS	7
Hb-QS	12
Hb-CS	5
Total	**623**

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-Thal validation: 667 / 667

Clinical samples	
Genotype	**No.**
NORMAL	288
β:cd 26	11
β:IVSⅡ-nt 654	18
β: -28	6
β:-29(A>G)	3
β:IVS-I-1(G>T)	2
β:cd 71/72	2
β:cd 41/42	23
β:cd 27/28+C	2
β:IVS-I-5	2
β:cd 43	2
β:cd 17	11
β:cd 41/42 major	2
β:-28 + cd 27/28 major	1
β:cd 27-28+IVSⅡ-nt 654	2
β:cd 26 major	1
β:IVSⅡ-nt 654 major	2
β:cd 17 + cd 41/42 major	1
β:-28 + cd 41/42 major	1
β:-28 + IntM	1
β:Taiwan deletion type	1
β:Chinese deletion type	1
β:Southeast Asian deletion type	1
Total	385

Beta Thalassemia specifications is open for customization.

100%
Consistency

Origin VS **Sanger Sequencing**

Beta Validation: 385 / 385

NGS-based competitor

Devyser Thalassemia 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.

Dvysr®

COMPARISON

	Origin	MRC-Holland	Devyser
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 Thalassemia 3. Used to Newborn, Prenatal, and Carrier screening, and diagnose	1. Higher cost, complex procedures, and longer turnaround times 2. Basic SPEC in Alpha thalassemia 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

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