

Table S1. Comparison of thalassemia mutations detected by gap-PCR & NGS with routine genotyping tests (the gap-PCR & RDB method) in 152 individuals with thalassemia mutations.

Case ID	α _Gap-PCR	β _SNP(NGS)	New variants (NGS)	Routine genotyping test	HbA2
Case1	$\alpha\alpha/\alpha\alpha$	IVS-II-654 (C>T)	N	IVS-II-654 (C>T)	5.3
Case2	$\alpha\alpha/--SEA$	N	N	$\alpha\alpha/--SEA$	2.4
Case3	$\alpha\alpha/--SEA$	N	N	$\alpha\alpha/--SEA$	2.3
Case4	$\alpha\alpha/\alpha\alpha$	Codons 41/42 (-TTCT)	N	Codons 41/42 (-TTCT)	5.6
Case5	$\alpha\alpha/\alpha\alpha$	-28 (A>G)	HBA1:c.412A>G(Thr>Ala)	-28 (A>G)	5.2
Case6	$\alpha\alpha/-\alpha3.7$	N	N	$\alpha\alpha/-\alpha3.7$	2.4
Case7	$\alpha\alpha/-\alpha4.2$	N	N	$\alpha\alpha/-\alpha4.2$	2.3
Case8	$\alpha\alpha/-\alpha3.7$	Codons 41/42 (-TTCT)	N	$\alpha\alpha/-\alpha3.7$ and Codons 41/42 (-TTCT)	5.8
Case9	$\alpha\alpha/--SEA$	N	N	$\alpha\alpha/--SEA$	2.1
Case10	$\alpha\alpha/\alpha\alpha$	-28 (A>G)	N	-28 (A>G)	5.2
Case11	$\alpha\alpha/--SEA$	N	N	$\alpha\alpha/--SEA$	2.2
Case12	$\alpha\alpha/\alpha\alpha$	Hb E	N	Hb E	3.5
Case13	$\alpha\alpha/\alpha\alpha$	Codons 41/42 (-TTCT)	N	Codons 41/42 (-TTCT)	5.4
Case14	$\alpha\alpha/--SEA$	N	N	$\alpha\alpha/--SEA$	2.3
Case15	$\alpha\alpha/\alpha\alpha$	IVS-II-654 (C>T)	N	IVS-II-654 (C>T)	4.9
Case16	$\alpha\alpha/\alpha\alpha$	Codon 17 (A>T)	N	Codon 17 (A>T)	6.1
Case17	$\alpha\alpha/--SEA$	N	N	$\alpha\alpha/--SEA$	2.4
Case18	$\alpha\alpha/--SEA$	N	N	$\alpha\alpha/--SEA$	2.3
Case19	$\alpha\alpha/\alpha\alpha$	-28 (A>G)	N	-28 (A>G)	5.4
Case20	$\alpha\alpha/\alpha\alpha$	Codons 41/42 (-TTCT)	N	Codons 41/42 (-TTCT)	5.4
Case21	$\alpha\alpha/--SEA$	N	N	$\alpha\alpha/--SEA$	2.1
Case22	$\alpha\alpha/--SEA$	N	N	$\alpha\alpha/--SEA$	1.8

Case23	$\alpha\alpha/\alpha\alpha$	Codons 41/42 (-TTCT)	N	Codons 41/42 (-TTCT)	5.7
Case24	$\alpha\alpha/--SEA$	N	N	$\alpha\alpha/--SEA$	2.1
Case25	$\alpha\alpha/-\alpha3.7$	N	N	Hb Constant Spring (Hb CS)	1.7
Case26	$\alpha\alpha/--SEA$	N	N	$\alpha\alpha/--SEA$	2.2
Case27	$\alpha\alpha/\alpha\alpha$	Codon 17 (A>T)	N	Codon 17 (A>T)	5.5
Case28	$\alpha\alpha/--SEA$	N	N	$\alpha\alpha/--SEA$	2.1
Case29	$\alpha\alpha/--SEA$	N	N	$\alpha\alpha/--SEA$	2.3
Case30	$\alpha\alpha/--SEA$	Codons 41/42 (-TTCT)	N	$\alpha\alpha/--SEA$ and Codons 41/42 (-TTCT)	
Case31	$\alpha\alpha/--SEA$	N	N	$\alpha\alpha/--SEA$	2.4
Case32	$\alpha\alpha/--SEA$	N	N	$\alpha\alpha/--SEA$	2
Case33	$-\alpha4.2/--SEA$	N	N	$-\alpha4.2/--SEA$	1.3
Case34	$\alpha\alpha/\alpha\alpha$	IVS-II-654 (C>T)	N	IVS-II-654 (C>T)	5.1
Case35	$\alpha\alpha/-\alpha4.2$	N	N	$\alpha\alpha/-\alpha4.2$	2.4
Case36	$\alpha\alpha/--SEA$	N	N	$\alpha\alpha/--SEA$	2.4
Case37	$\alpha\alpha/--SEA$	N	N	$\alpha\alpha/--SEA$	2.1
Case38	$\alpha\alpha/--SEA$	N	N	$\alpha\alpha/--SEA$	2.3
Case39	$\alpha\alpha/--SEA$	N	N	$\alpha\alpha/--SEA$	2.4
Case40	$\alpha\alpha/--SEA$	N	N	$\alpha\alpha/--SEA$	2.2
Case41	$\alpha\alpha/--SEA$	N	N	$\alpha\alpha/--SEA$	2.2
Case42	$\alpha\alpha/\alpha\alpha$	Codon 43 (G>T)	N	Codon 43 (G>T)	4.9
Case43	$\alpha\alpha/--SEA$	N	N	$\alpha\alpha/--SEA$	2.1
Case44	$\alpha\alpha/-\alpha3.7$	N	N	$\alpha\alpha/-\alpha3.7$	2.3
Case45	$\alpha\alpha/\alpha\alpha$	Codons 41/42 (-TTCT)	N	41-42/N	5.7
Case46	$\alpha\alpha/\alpha\alpha$	-28 (A>G)	N	-28 (A>G)	5.4
Case47	$\alpha\alpha/--SEA$	N	N	$\alpha\alpha/--SEA$	2.1
Case48	$\alpha\alpha/\alpha\alpha$	Codon 17 (A>T)	N	Codon 17 (A>T)	5.5

Case49	$\alpha\alpha/--SEA$	N	N	$\alpha\alpha/--SEA$	2.4
Case50	$\alpha\alpha/-\alpha3.7$	N	N	$\alpha\alpha/-\alpha3.7$	2.3
Case51	$\alpha\alpha/\alpha\alpha$	Codons 41/42 (-TTCT)	N	Codons 41/42 (-TTCT)	5.5
Case52	$\alpha\alpha/\alpha\alpha$	Codons 71/72 (+A)	N	Hb Westmead and Codons 71/72 (+A)	5.6
Case53	$\alpha\alpha/\alpha\alpha$	Codons 41/42 (-TTCT)	N	Codons 41/42 (-TTCT)	5.5
Case54	$\alpha\alpha/--SEA$	N	N	$\alpha\alpha/--SEA$	2.2
Case55	$\alpha\alpha/--SEA$	N	N	$\alpha\alpha/--SEA$	2.2
Case56	$-\alpha3.7/--SEA$	N	N	$-\alpha3.7/--SEA$	1.1
Case57	$\alpha\alpha/--SEA$	N	N	$\alpha\alpha/--SEA$	2.1
Case58	$\alpha\alpha/-\alpha3.7$	N	N	$\alpha\alpha/-\alpha3.7$	2.4
Case59	$\alpha\alpha/\alpha\alpha$	Codon 17 (A>T)	N	Codon 17 (A>T)	5.8
Case60	$\alpha\alpha/\alpha\alpha$	Hb E	N	Hb E	3.6
Case61	$\alpha\alpha/\alpha\alpha$	-28 (A>G)	N	-28 (A>G)	6
Case62	$\alpha\alpha/--SEA$	N	N	$\alpha\alpha/--SEA$	2.1
Case63	$\alpha\alpha/\alpha\alpha$	Hb E	N	Hb E	3.8
Case64	$\alpha\alpha/--SEA$	N	N	$\alpha\alpha/--SEA$	2.3
Case65	$\alpha\alpha/\alpha\alpha$	Codons 71/72 (+A)	N	Codons 71/72 (+A)	5.9
Case66	$\alpha\alpha/--SEA$	N	N	$\alpha\alpha/--SEA$	2.2
Case67	$\alpha\alpha/\alpha\alpha$	Codons 41/42 (-TTCT)	N	Codons 41/42 (-TTCT)	5.7
Case68	$\alpha\alpha/--SEA$	N	N	$\alpha\alpha/--SEA$	2.4
Case69	$\alpha\alpha/\alpha\alpha$	N	Hb Hekinan II	Hb Westmead	1.8
Case70	$\alpha\alpha/--SEA$	N	N	$\alpha\alpha/--SEA$	2.2
Case71	$\alpha\alpha/--SEA$	N	N	$\alpha\alpha/--SEA$	2.2
Case72	$\alpha\alpha/--SEA$	N	N	$\alpha\alpha/--SEA$	2.4
Case73	$\alpha\alpha/--SEA$	N	N	$\alpha\alpha/--SEA$	2.4
Case74	$\alpha\alpha/--SEA$	N	N	$\alpha\alpha/--SEA$	2.4

Case75	$\alpha\alpha/--SEA$	N	N	$\alpha\alpha/--SEA$	2.4
Case76	$\alpha\alpha/\alpha\alpha$	IVS-II-654 (C>T)	N	IVS-II-654 (C>T)	5
Case77	$\alpha\alpha/\alpha\alpha$	Codons 41/42 (-TTCT)	N	Codons 41/42 (-TTCT)	6.4
Case78	$\alpha\alpha/--SEA$	N	N	$\alpha\alpha/--SEA$	2.3
Case79	$\alpha\alpha/\alpha\alpha$	Codons 41/42 (-TTCT)	N	Codons 41/42 (-TTCT)	5.4
Case80	$\alpha\alpha/--SEA$	N	N	$\alpha\alpha/--SEA$	1.7
Case81	$\alpha\alpha/\alpha\alpha$	IVS-II-654 (C>T)	N	IVS-II-654 (C>T)	5.2
Case82	$\alpha\alpha/\alpha\alpha$	Codon 43 (G>T)	N	Codon 43 (G>T)	5.5
Case83	$\alpha\alpha/\alpha\alpha$	Codon 17 (A>T)	N	Codon 17 (A>T)	5.7
Case84	$\alpha\alpha/--SEA$	N	N	$\alpha\alpha/--SEA$	2.2
Case85	$\alpha\alpha/\alpha\alpha$	IVS-II-654 (C>T)	Hb New York	IVS-II-654 (C>T)	4.6
Case86	$\alpha\alpha/--SEA$	N	N	$\alpha\alpha/--SEA$	1.1
Case87	$\alpha\alpha/--SEA$	N	N	$\alpha\alpha/--SEA$	2
Case88	$\alpha\alpha/--SEA$	N	N	$\alpha\alpha/--SEA$	2.2
Case89	$\alpha\alpha/--SEA$	N	N	$\alpha\alpha/--SEA$	2.4
Case90	$\alpha\alpha/--SEA$	N	N	$\alpha\alpha/--SEA$	2.2
Case91	$\alpha\alpha/--SEA$	N	N	$\alpha\alpha/--SEA$	2.4
Case92	$\alpha\alpha/\alpha\alpha$	Codons 41/42 (-TTCT)	N	Codons 41/42 (-TTCT)	4.8
Case93	$\alpha\alpha/\alpha\alpha$	Codons 41/42 (-TTCT)	N	Codons 41/42 (-TTCT)	5.5
Case94	$\alpha\alpha/\alpha\alpha$	Codons 41/42 (-TTCT)	HBB:c.*+5G>A	Codons 41/42 (-TTCT)	5.6
Case95	$\alpha\alpha/-\alpha 3.7$	N	N	$\alpha\alpha/-\alpha 3.7$	2.4
Case96	$\alpha\alpha/\alpha\alpha$	Codons 41/42 (-TTCT)	N	Codons 41/42 (-TTCT)	5.7
Case97	$\alpha\alpha/\alpha\alpha$	IVS-II-654 (C>T)	N	IVS-II-654 (C>T)	4.8
Case98	$\alpha\alpha/--SEA$	N	N	$\alpha\alpha/--SEA$	2.2
Case99	$\alpha\alpha/--SEA$	N	N	$\alpha\alpha/--SEA$	2.1
Case100	$\alpha\alpha/\alpha\alpha$	IVS-II-654 (C>T)	HBA2:c.46G>A(Gly>Ser)	IVS-II-654 (C>T)	5.5

Case101	$\alpha\alpha/--SEA$	N	N	$\alpha\alpha/--SEA$	2.2
Case102	$\alpha\alpha/--SEA$	N	N	$\alpha\alpha/--SEA$	2.4
Case103	$\alpha\alpha/--SEA$	N	N	$\alpha\alpha/--SEA$	2.1
Case104	$\alpha\alpha/\alpha\alpha$	IVS-II-654 (C>T)	N	IVS-II-654 (C>T)	4.8
Case105	$\alpha\alpha/\alpha\alpha$	Codons 41/42 (-TTCT)	HBB:c.-180G>C	Codons 41/42 (-TTCT)	4.9
Case106	$\alpha\alpha/--SEA$	N	N	$\alpha\alpha/--SEA$	2.3
Case107	$\alpha\alpha/--SEA$	N	N	$\alpha\alpha/--SEA$	2.3
Case108	$\alpha\alpha/-\alpha 4.2$	N	Hb G-Honolulu	$\alpha\alpha/-\alpha 4.2$	1.7
Case109	$\alpha\alpha/\alpha\alpha$	Codons 41/42 (-TTCT)	N	Codons 41/42 (-TTCT)	5.2
Case110	$\alpha\alpha/\alpha\alpha$	IVS-II-654 (C>T)	N	IVS-II-654 (C>T)	5
Case111	$\alpha\alpha/\alpha\alpha$	Codons 41/42 (-TTCT)	N	Codons 41/42 (-TTCT)	5.6
Case112	$\alpha\alpha/\alpha\alpha$	N	N	Hb Quong Sze	1.8
Case113	$\alpha\alpha/--SEA$	N	N	$\alpha\alpha/--SEA$	2.3
Case114	$\alpha\alpha/\alpha\alpha$	-28 (A>G)	N	-28 (A>G)	5.7
Case115	$\alpha\alpha/--SEA$	N	N	$\alpha\alpha/--SEA$	2.3
Case116	$\alpha\alpha/-\alpha 3.7$	N	N	$\alpha\alpha/-\alpha 3.7$	2.4
Case117	$\alpha\alpha/\alpha\alpha$	Codons 41/42 (-TTCT)	N	Codons 41/42 (-TTCT)	5.9
Case118	$\alpha\alpha/--SEA$	N	N	$\alpha\alpha/--SEA$	2.1
Case119	$\alpha\alpha/\alpha\alpha$	Codons 41/42 (-TTCT)	N	Codons 41/42 (-TTCT)	6.4
Case120	$\alpha\alpha/-\alpha 3.7$	Hb E	N	$\alpha\alpha/-\alpha 3.7$ and Hb E	3.7
Case121	$\alpha\alpha/--SEA$	N	N	$\alpha\alpha/--SEA$	2.4
Case122	$\alpha\alpha/--SEA$	N	N	$\alpha\alpha/--SEA$	2.4
Case123	$\alpha\alpha/\alpha\alpha$	Codon 17 (A>T)	N	Codon 17 (A>T)	5.2
Case124	$-\alpha 3.7/--SEA$	N	N	$-\alpha 3.7/--SEA$	1.2
Case125	$\alpha\alpha/\alpha\alpha$	Codons 41/42 (-TTCT)	N	Codons 41/42 (-TTCT)	5.4
Case126	$\alpha\alpha/--SEA$	N	N	$\alpha\alpha/--SEA$	2.2

Case127	$\alpha\alpha$ - α 3.7	N	N	$\alpha\alpha$ - α 3.7	2.1
Case128	$\alpha\alpha/\alpha\alpha$	N	N	$\alpha\alpha$ CS/ $\alpha\alpha$	2.1
Case129	$\alpha\alpha/\alpha\alpha$	Codons 71/72 (+A)	N	Codons 71/72 (+A)	5.3
Case130	$\alpha\alpha$ - α 4.2	N	N	$\alpha\alpha$ - α 4.2	2.4
Case131	$\alpha\alpha$ --SEA	N	N	$\alpha\alpha$ --SEA	2.4
Case132	$\alpha\alpha/\alpha\alpha$	Codons 41/42 (-TTCT)	N	Codons 41/42 (-TTCT)	5.9
Case133	$\alpha\alpha/\alpha\alpha$	Codons 41/42 (-TTCT)	N	41-42/N	5.5
Case134	$\alpha\alpha$ --SEA	N	N	$\alpha\alpha$ --SEA	2.4
Case135	$\alpha\alpha/\alpha\alpha$	IVS-II-654 (C>T)	N	IVS-II-654 (C>T)	5.1
Case136	$\alpha\alpha/\alpha\alpha$	IVS-II-654 (C>T)	N	IVS-II-654 (C>T)	4.7
Case137	$\alpha\alpha$ --SEA	N	N	$\alpha\alpha$ --SEA	2.2
Case138	$\alpha\alpha$ --SEA	N	N	$\alpha\alpha$ --SEA	2.3
Case139	$\alpha\alpha$ --SEA	N	N	$\alpha\alpha$ --SEA	2.4
Case140	$\alpha\alpha$ --SEA	N	N	$\alpha\alpha$ --SEA	2.3
Case141	$\alpha\alpha$ - α 3.7	N	N	$\alpha\alpha$ - α 3.7	2.4
Case142	$\alpha\alpha$ --SEA	N	N	$\alpha\alpha$ --SEA	2.4
Case143	$\alpha\alpha/\alpha\alpha$	-28 (A>G)	N	(-28/N)	5.9
Case144	$\alpha\alpha$ - α 4.2	N	N	$\alpha\alpha$ - α 4.2	2.3
Case145	$\alpha\alpha$ - α 4.2	IVS-II-654 (C>T)	N	$\alpha\alpha$ - α 4.2 and IVS-II-654 (C>T)	5.2
Case146	$\alpha\alpha/\alpha\alpha$	Codons 41/42 (-TTCT)	N	Codons 41/42 (-TTCT)	5.3
Case147	$\alpha\alpha/\alpha\alpha$	IVS-II-654 (C>T)	N	IVS-II-654 (C>T)	5.1
Case148	$\alpha\alpha$ - α 3.7	Codons 41/42 (-TTCT)	N	$\alpha\alpha$ - α 3.7 and Codons 41/42 (-TTCT)	5.9
Case149	$\alpha\alpha/\alpha\alpha$	Codons 41/42 (-TTCT)	N	Codons 41/42 (-TTCT)	5.5
Case150	$\alpha\alpha/\alpha\alpha$	Codons 41/42 (-TTCT)	N	Codons 41/42 (-TTCT)	5.5
Case151	$\alpha\alpha$ --SEA	N	N	$\alpha\alpha$ --SEA	2.3
Case152	$\alpha\alpha/\alpha\alpha$	Codon 17 (A>T)	N	Codon 17 (A>T)	6.3

Table S2. Genotypes and constituent ratio of α -thalassemia carriers

HBA mutation	cases	constituent ratio (%)
-- ^{SEA} α / $\alpha\alpha$	92	44.4
- $\alpha^{3.7}$ / $\alpha\alpha$	53	25.6
α^{WS} α / $\alpha\alpha$	20	9.7
- $\alpha^{4.2}$ / $\alpha\alpha$	15	7.2
α^{CS} α / $\alpha\alpha$	7	3.4
α^{QS} α / $\alpha\alpha$	4	1.9
Hb Hekinan II/ $\alpha\alpha$	2	1.0
-- ^{SEA} / $\alpha^{3.7}$	2	1.0
α HBA2: c.46G>A/ $\alpha\alpha$	1	0.5
Hb Owari/ $\alpha\alpha$	1	0.5
Alpha2 Codon 30 del GAG/ $\alpha\alpha$	1	0.5
-- ^{SEA} / $\alpha^{4.2}$	1	0.5
- $\alpha^{3.7}$ / $\alpha^{4.2}$	1	0.5
Hb G-Honolulu/Hb G-Honolulu	1	0.5
HBA2: c.190G>A/ $\alpha\alpha$	1	0.5
α^{WS} α /Hb Hekinan II	1	0.5
- $\alpha^{4.2}$ / $\alpha^{Hb\ G-Honolulu}$ $\alpha^{Hb\ G-Honolulu}$	1	0.5
- $\alpha^{4.2}$ /Hb Owari	1	0.5
- $\alpha^{3.7}$ / α^{WS} α^{WS}	1	0.5
- $\alpha^{3.7}$ / α^{CS} α^{CS}	1	0.5
Total	207	100

Table S3. Genotypes and constituent ratio of β -thalassemia carriers

HBB mutation	cases	constituent ratio (%)
Codons 41/42 (-TTCT)/ β^A	24	34.3
IVS-II-654 (C>T)/ β^A	11	15.7
Codon 17 (A>T)/ β^A	8	11.4
-28 (A>G)/ β^A	6	8.6
-50 (G>A)/ β^A	5	7.1
Hb E/ β^A	3	4.3
HBB: c.*+129T>A/ β^A	3	4.3
Codons 71/72 (+A)/ β^A	2	2.9
Codon 43 (G>T)/ β^A	2	2.9
HBB: c.-64G>C/ β^A	2	2.9
HBB: c.-180 G>C/Codons 41/42 (-TTCT)	1	1.4
HBB: c.*+5G>A/Codons 41/42 (-TTCT)	1	1.4
Hb New York/IVS-II-654 (C>T)	1	1.4
HBB: c.-113A>G/ β^A	1	1.4
Total	70	100

Table S4. Genotypes and constituent ratio of 8 carriers of composite α - and β -thalassemia mutations

HBA mutation	HBB mutation	cases	constituent ratio (%)
$-\alpha^{3.7}/\alpha\alpha$	Codons 41/42 (-TTCT)/ β^A	2	25.0
$--^{SEA}/\alpha\alpha$	Codons 41/42 (-TTCT)/ β^A	1	12.5
$-\alpha^{3.7}/\alpha\alpha$	Hb E/ β^A	1	12.5
$-\alpha^{4.2}/\alpha\alpha$	IVS-II-654 (C>T)/ β^A	1	12.5
$\alpha^{WS}/\alpha\alpha$	Codons 71/72 (+A)/ β^A	1	12.5
HBA2: c.46G>A/ $\alpha\alpha$	IVS-II-654 (C>T)/ β^A	1	12.5
HBA1: c.412A>G/ $\alpha\alpha$	-28 (A>G)/ β^A	1	12.5
Total	-	8	100

Table S5. Sensitivity and specificity of MM for thalassemia carriers screened by NGS

MM	Sensitivity (%95 CI)	Specificity (%95 CI)	PPV (%95 CI)	NPV (%95 CI)	True positive	False positive	True negative	False negative
α -thalassemia	73.49% (67.06%- 79.26%)	89.12% (87.53%- 90.57%)	46.47% (42.55%- 50.44%)	96.32% (95.44%- 97.03%)	158	182	1491	57
α α /--SEA	97.85% (92.45%- 99.74%)	86.13 % (84.44%- 87.69%)	26.76% (24.49%- 29.16%)	99.87 % (99.49%- 99.97%)	91	249	1546	2
α α /- α 3.7	55.17% (41.54%- 68.26%)	82.20 % (80.31%- 83.97%)	9.41% (7.46%- 11.80%)	98.20 % (97.62%- 98.65%)	32	308	1422	26
α α /- α 4.2	83.33% (58.58%- 96.42%)	82.62% (80.83%- 84.31%)	4.41% (3.54%- 5.48%)	99.81 % (99.46%- 99.93%)	15	325	1545	3
β -thalassemia	85.90% (76.17%- 92.74%)	84.92 % (83.18%- 86.54%)	19.71% (17.56%- 22.04%)	99.29 % (98.78%- 99.59%)	67	273	1537	11
Codons 41/42 (-TTCT)	96.55% (82.24%- 99.91%)	83.22% (81.44%- 84.89%)	8.24% (7.36%- 9.21%)	99.94 % (99.56%- 99.99%)	28	312	1547	1

IVS-II-654 (C>T)	100.00%	82.60 %	4.12%	100.00 %	14	326	1548	0
	(76.84%- 100.00%)	(80.81%- 84.29%)	(3.75%- 4.53%)					
-28 (A>G)	100.00%	82.30 %	2.06%	100.00 %	7	333	1548	0
	(59.04%- 100.00%)	(80.50%- 84.00%)	(1.87%- 2.26%)					
Codon 17 (A>T)	100.00%	82.34 %	2.35%	100.00 %	8	332	1548	0
	(63.06%- 100.00%)	(80.54%- 84.04%)	(2.14%- 2.59%)					

Table S6. Sensitivity and specificity of HbA2 for thalassemia carriers screened by NGS

HbA2	Sensitivity (%95 CI)	Specificity (%95 CI)	PPV (%95 CI)	NPV (%95 CI)	True positive	False positive	True negative	False negative
α -thalassemia	65.12% (57.49%- 72.21%)	77.04 % (72.63% -81.05%)	54.63% (49.42%- 59.75%)	83.87 % (80.81%-86.53%)	112	93	312	60
α α /--SEA	86.81% (78.10% -93.00%)	74.07 % (69.94%- 77.92%)	38.54% (34.59%- 42.64%)	96.77 % (94.64%-98.08%)	79	126	360	12
α α /- α 3.7	39.47% (24.04%-56.61%)	64.75 % (60.55%- 68.79%)	7.32% (4.98%-10.63%)	93.82 % (92.10%-95.18%)	15	190	349	23
α α /- α 4.2	37.50% (15.20%-64.57%)	64.53 % (60.41%- 68.49%)	2.93% (1.56%-5.42%)	97.31 % (96.10%-98.15%)	6	199	362	10
β -thalassemia	95.65% (87.82%- 99.09%)	99.61% (98.59%-99.95%)	97.06% (89.21%-99.25%)	99.41 % (98.24%-99.80%)	66	2	506	3
Codons 41/42 (-TTCT)	96.55% (82.24%-99.91%)	92.7 % (90.19%-94.73%)	41.18% (34.01%-48.74%)	99.80% (98.67%- 99.97%)	28	40	508	1

IVS-II-654 (C>T)	100.00%	90.41 %	20.59%	100.00 %	14	54	509	0
	(76.84%- 100.00%)	(87.67%-92.71%)	(16.75%-25.04%)					
-28 (A>G)	100.00%	89.3 %	10.29%	100.00 %	7	61	509	0
	(59.04%- 100.00%)	(86.47%-91.71%)	(8.30%-12.70%)					
Codon 17 (A>T)	100.00%	89.46 %	11.76%	100.00 %	8	60	509	0
	(63.06%- 100.00%)	(86.64%-91.86%)	(9.50%-14.48%)					