

Supplementary Table S1. Sampling distribution of 14 cities in Hunan Province

City	Total population*	Thalassemia carrier rate, %	Samples
Changsha	6,192,142	5	2,098
Zhuzhou	5,036,241	8	1,212
Xiangtan	6,720,139	5	2,121
Hengyang	5,223,156	8	918
Shaoyang	8,015,293	8	1,272
Yueyang	7,859,248	3	3,302
Changde	4,131,011	3	3,572
Zhangjiajie	4,324,888	4	2,492
Yiyang	5,478,790	4	2,649
Chenzhou	4,658,278	11	904
Yongzhou	3,026,515	12	810
Huaihua	6,045,994	8	1,288
Loudi	2,904,968	5	2,083
Xiangxi	1,687,625	8	1,225
Total	71,304,288		25,946

Note. *Population data are from the sixth census in China.

Supplementary Table S2. HGVS names of all mutations

α-thalassemia mutation		β-thalassemia mutation	
Common name	HGVS name	Common name	HGVS name
$-\alpha^{3.7}/$	$-\alpha^{3.7}/$	IVS-II-654 (C>T)	HBB:c.316-197C>T
$--_{SEA}/$	$--_{SEA}/$	Codons 41/42 (-TTCT)	HBB:c.126_129delCTTT
$-\alpha^{4.2}/$	$-\alpha^{4.2}/$	Codon 17 (A>T)	HBB:c.52A>T
$\alpha^{WS}\alpha/$	HBA2:c.369C>G	Codons 71/72 (+A)	HBB:c.216_217insA
$\alpha^{CS}\alpha/$	HBA2:c.427T>C	-28 (A>G)	HBB:c.-78A>G
$\alpha^{OS}\alpha/$	HBA2:c.377T>C	Hb E	HBB:c.79G>A
Alpha2 Codon 30 del GAG	HBA2:c.91_93delGAG	5'UTR+43 to +40 (-AAAC)	HBB:c.-11_8delAAAC
Codon 108 (ACC>AAC)	HBA2:c.326C>A	Codons 27/28 (+C)	HBB:c.84_85insC
Codon 61 (AAG>TAG)	HBA2:c.184A>T	-50 (G>A)	HBB:c.-100G>A
Hb Phnom Penh	HBA1:c.354_355insATC	Codon 43 (G>T)	HBB:c.130G>T
CAP +29 (G>C)	HBA1:c.-9G>C	-29 (A>G)	HBB:c.-79A>G
Hb Agrinio	HBA2:c.89T>C	SEA-HPFH	SEA-HPFH
Hb Cervantes	HBA2:c.356C>T	-31 (A>C)	HBB:c.-81A>C
Hb Iberia	HBA2:c.313T>C	Codons 14/15 (+G)	HBB:c.45_46insG
IVS-I-117 (G>A)	HBA2:c.96-1G>A	CAP +8 (C>T)	HBB:c.-43C>T
$\alpha 2$ Codon 31 (AGG>AAG)	HBA2:c.95G>A	ChineseGgamma	ChineseGgamma
$--_{THAI}/$	$--_{THAI}/$	IVS-II-848 (C>T)	HBB:c.316-3C>T
		-56 (G>C)	HBB:c.-106G>C
		-72 (T>A)	HBB:c.-122T>A
		beta nt-77 (G>C)	HBB:c.-127G>C
		Codon 20/21 (-TGGA)	HBB:c.62_65delTGGA
		Hb Knossos	HBB:c.82G>T
		Poly A (A>G)	HBB:c.*111A>G

Supplementary Table S3. Distribution of abnormal hemoglobin mutations

Mutation type	Number	Ratio, %	Mutation type	Number	Ratio, %
Hb Zambia	1	0.79	Hb J-Bangkok	7	5.51
Hb Agrinio	1	0.79	Hb Knossos	1	0.79
Hb Athens-GA	1	0.79	Hb Manitoba II	1	0.79
Hb Broomhill	4	3.15	Hb Mantes-La-Jolie	1	0.79
Hb Cervantes	1	0.79	Hb Nevers	1	0.79
Hb Fuchu-I	1	0.79	Hb New York	29	22.83
Hb Fulwood	1	0.79	Hb Owari	10	7.87
Hb G-Coushatta	6	4.72	Hb Penang	2	1.57
Hb G-Honolulu	3	2.36	Hb Phnom Penh	3	2.36
Hb Gorwihl	1	0.79	Hb Port Phillip	1	0.79
Hb Groene Hart	3	2.36	Hb Pretoria(α 2)	1	0.79
Hb G-taipei	3	2.36	Hb Q-Thailand	3	2.36
Hb G-Waimanalo	1	0.79	Hb Shenyang	1	0.79
Hb Hachioji	3	2.36	Hb Shizuoka	1	0.79
Hb Hamilton	1	0.79	Hb Tokoname	1	0.79
Hb Handsworth	1	0.79	Hb Ty Gard	1	0.79
Hb Haringey	1	0.79	Hb Yaounde	1	0.79
Hb Hekinan II	17	13.39	Hb Zengcheng	7	5.51
Hb I	2	1.57	Hb Zurich-Albisrieden	1	0.79
Hb Iberia	1	0.79	Hb Zurich-Langstrasse	1	0.79

Supplementary Table S4. Analysis of hematological phenotypes by factorial ANOVA

Hematological phenotype	Df	Sum Sq	Mean Sq	F value	Pr (>F)
RBC	1.00	0.25	0.25	0.94	0.34
HB	1.00	0.03	0.03	0.11	0.74
MCV	1.00	0.04	0.04	0.16	0.69
MCH	1.00	0.64	0.64	2.46	0.12
Hb_A	1.00	0.02	0.02	0.08	0.78
Hb_A2	1.00	0.18	0.18	0.71	0.40
HBF	1.00	0.15	0.15	0.56	0.46
Residuals	60.00	15.69	0.26	NA	NA