

Table S1 Methylated cytosines in the skins at TH and TL groups.

Sample	Total mC	mCG	mCHG	mCHH
TH1	10148819	10073793	17150	57876
TH2	6035702	5988462	10764	36476
TH3	9900473	9826949	16703	56821
TL1	2046340	2028205	4091	14044
TL2	3693016	3665646	6131	21239
TL3	8684321	8617217	14983	52121

Table S2 The proportion of methylated cytosines in Tibetans at TH and TL groups.

Samples	mC (%)	mCpG (%)	mCHG (%)	mCHH (%)
TH1	2.69	73.32	0.023	0.020
TH2	1.87	52.14	0.017	0.015
TH3	2.21	59.38	0.019	0.017
TL1	1.40	41.49	0.015	0.012
TL2	2.49	69.90	0.021	0.019
TL3	2.17	59.57	0.019	0.017

Table S3 GO items and pathway related to iron in the results of STRING analysis performed by DMGs

term ID	term description	observed gene count	background gene count	false discovery rate	matching proteins in your network (labels)
GO:0010039	response to iron ion	15	32	6.02E-23	ABAT, ACO1, BCL2, BMP6, CPOX, CYBRD1, DRD2, HFE, HIF1A, MDM2, SLC11A2, SLC40A1, SLC6A3, SNCA, TFAP2A
GO:0055072	iron ion homeostasis	17	83	2.00E-21	ACO1, BMP6, CYBRD1, EGLN1, EPAS1, HFE, HIF1A, IREB2, NEDD8, PICALM, SCARA5, SLC11A2, SLC25A37, SLC40A1, SMAD4, TFRC, TMPRSS6
GO:0006879	cellular iron ion homeostasis	15	66	1.25E-19	ACO1, BMP6, CYBRD1, EGLN1, HFE, HIF1A, IREB2, NEDD8, PICALM, SCARA5, SLC11A2, SLC40A1, SMAD4, TFRC, TMPRSS6
GO:0034755	iron ion transmembrane transport	9	19	2.35E-14	HFE, PICALM, SCARA5, SLC11A2, SLC25A37, SLC39A14, SLC40A1, TFRC, TTYH1
GO:0006826	iron ion transport	10	71	1.22E-11	HFE, IREB2, PICALM, SCARA5, SLC11A2, SLC25A37, SLC39A14, SLC40A1, TFRC, TTYH1
GO:0060586	multicellular organismal iron ion homeostasis	4	9	1.32E-06	BMP6, HFE, SLC11A2, SLC40A1
GO:0071281	cellular response to iron ion	4	10	1.78E-06	BMP6, HFE, SLC40A1, TFAP2A
GO:0033212	iron import into cell	3	11	0.00011	HFE, PICALM, SLC11A2
GO:0010040	response to iron(II) ion	2	4	0.00087	ACO1, SNCA
GO:0098711	iron ion import across plasma membrane	2	6	0.0015	HFE, PICALM
GO:0005381	iron ion transmembrane transporter activity	6	11	2.11E-09	SLC11A2, SLC25A37, SLC39A14, SLC40A1, TFRC, TTYH1

GO:0015093	ferrous iron transmembrane transporter activity	3	4	4.69E-05	SLC11A2,SLC39A14,SLC40A1
GO:0051536	iron-sulfur cluster binding	5	62	0.0001	ABAT,ACO1,FECH,IREB2,SDHB
GO:0030350	iron-responsive element binding	2	2	0.001	ACO1,IREB2
GO:0008198	ferrous iron binding	3	23	0.0014	EGLN1,FECH,SNCA
GO:0051538	3 iron, 4 sulfur cluster binding	2	3	0.0015	ACO1,SDHB
GO:0051539	4 iron, 4 sulfur cluster binding	3	41	0.0047	ACO1,IREB2,SDHB
GO:0005506	iron ion binding	4	147	0.0124	CYP1B1,EGLN1,FECH,SNCA
GO:0051537	2 iron, 2 sulfur cluster binding	2	21	0.0159	FECH,SDHB
HSA-917937	Iron uptake and transport	8	56	5.62E-08	ACO1,CYBRD1,HFE,IREB2,NEDD8,SLC11A2,SLC40A1,TFRC

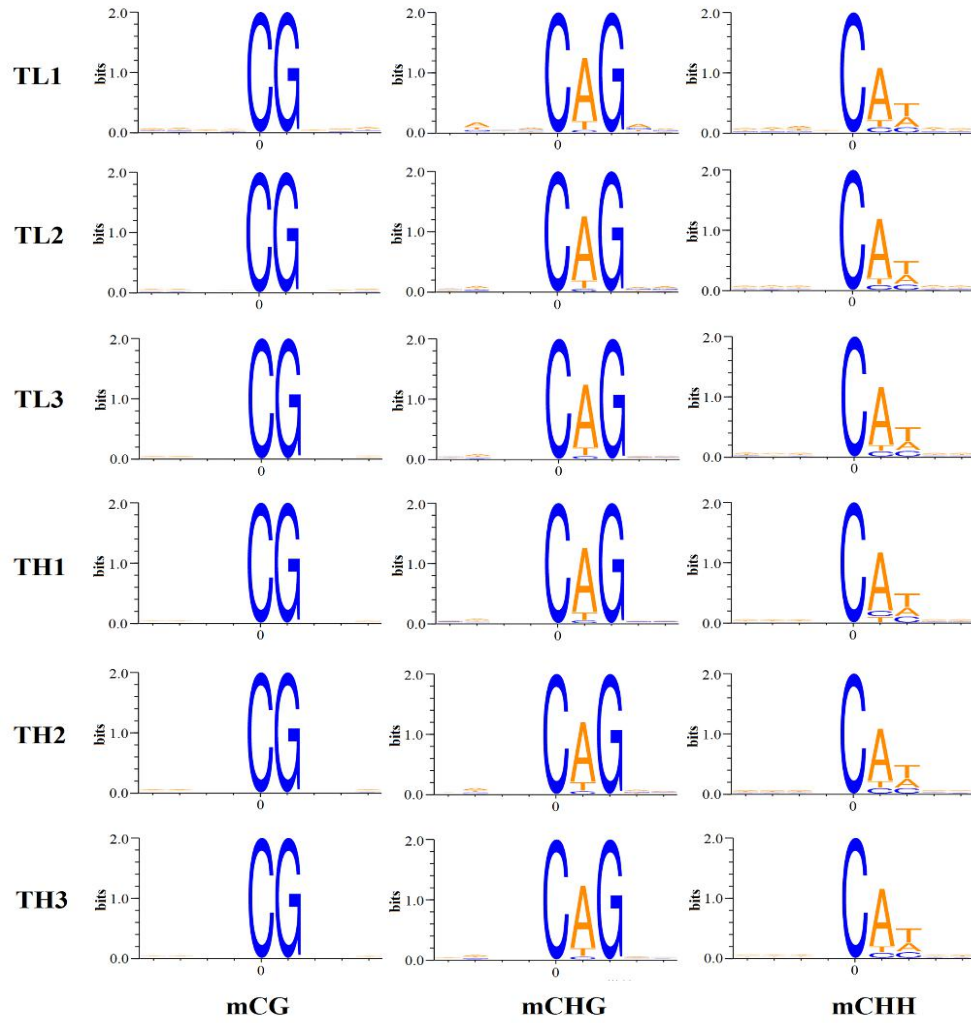


Fig. S1. Sequence feature analysis of 9bp sequences near three methylation types CG, CHG and CHH. Sequence preference around the methylated C sites in CG, CHG, and CHH contexts. TL1, TL2 and TL3 are normal SF groups. TH1, TH2, and TH3 are high SF groups.

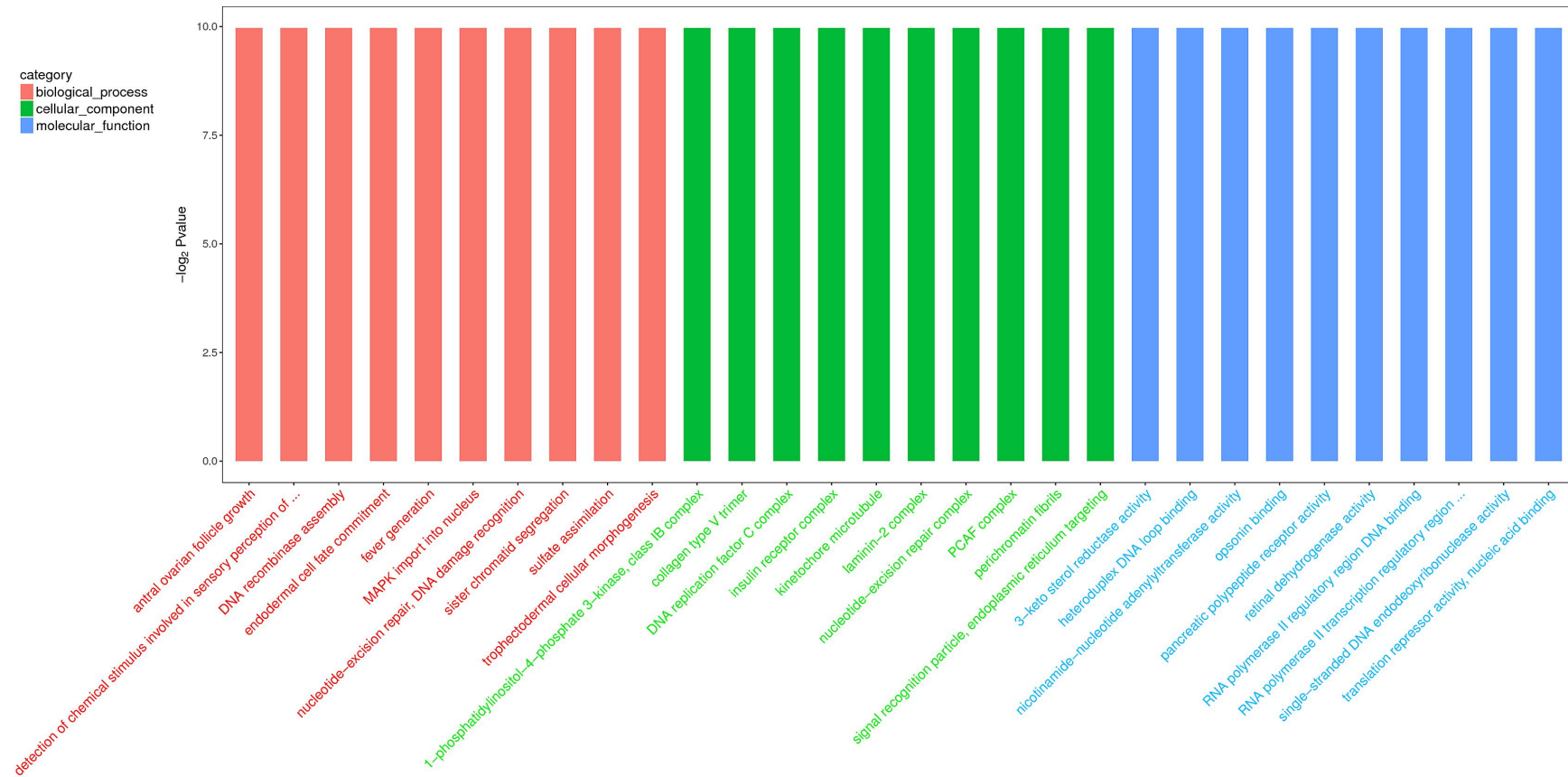


Fig.S2 Gene Ontology analysis of differentially methylated genes. A total of 10 significantly enriched terms of biological processes, cell components and molecular functions are shown, respectively. The P-value was set to 0.05, and terms of the same category were sorted by P-value.

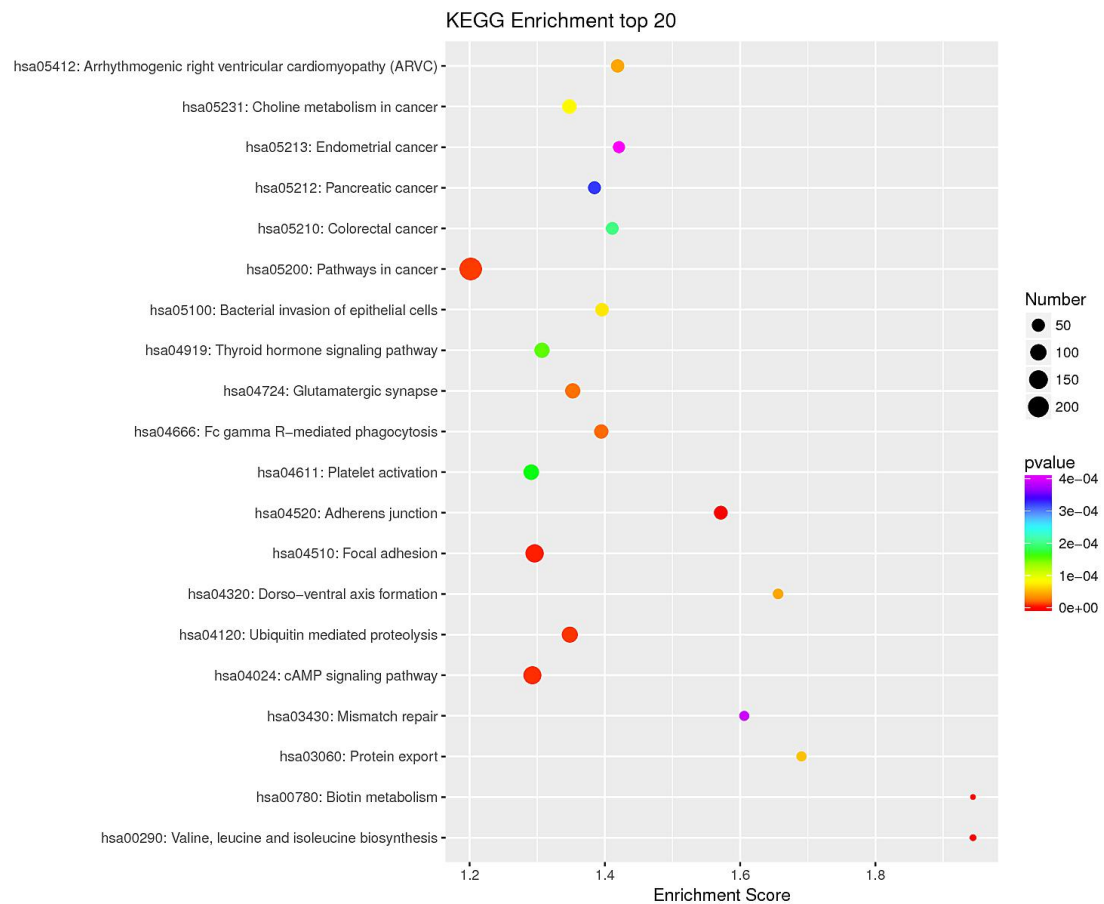


Fig.S3 Kyoto Encyclopedia of Genes and Genomes pathway analysis of differentially methylated genes. Kyoto Encyclopedia of Genes and Genomes pathways were divided into the following subcategories, containing metabolism, environmental information processing and organismal systems, and the P-value was set to 0.05.

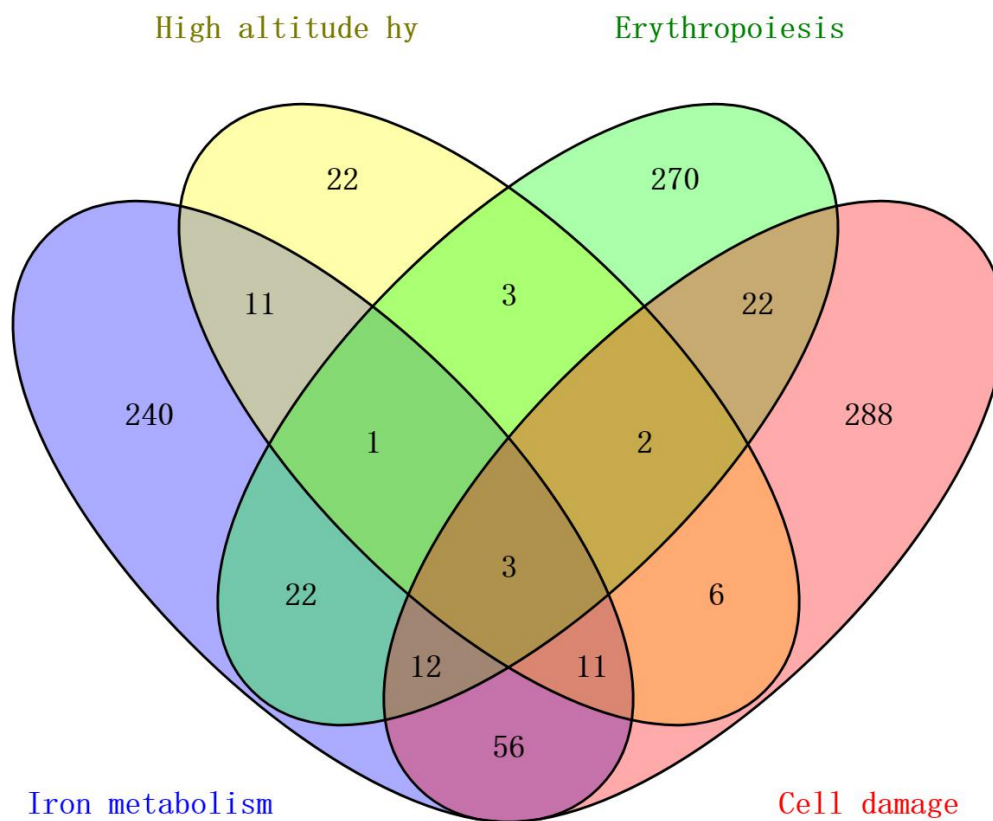


Fig.S4 Wayne diagram of iron metabolism related genes, erythropoiesis related genes, high altitude hypoxia related genes and cell damage related genes.