Table S1. Summary of demographic information for eight cohorts in this study

Cohort	Sample size	Age (mean±sd)	Self-reported sex			Self-reported ethnicity					Phenotype
			Male	Female	NA	Chinese	Malay	Indian	Others	NA	
SEED	1,536	54.1±9.4	644	796	96	603	279	558	0	96	healthy
TTSH	971	40.4±10.7	194	777	0	524	199	248	0	0	healthy
PRISM	100	41.7±13.9	47	53	0	88	7	2	3	0	healthy
Peranakan	79	52.5±16.7	31	48	0	0	0	0	0	79	healthy
Platinum	46	NA	23	23	0	16	15	15	0	0	healthy
HF	1,540	60.3±11.6	1,074	466	0	1,016	357	152	15	0	heart failure
PD	355	61.1±8.5	208	147	0	353	0	0	2	0	Parkinson
Bariatric	226	40.9±10.4	103	119	4	83	76	63	0	4	obesity

Abbreviations: NA, not available; sd, standard deviation; SEED, Singapore Epidemiology of Eye Diseases; TTSH, Tan Tock Seng Hospital; PRISM, SingHealth Duke-NUS Institute of Precision Medicine; HF, heart failure; PD, Parkinson disease.

Related to **Table 1**.

Table S2. Evaluation of final SG10K call set based on array genotyping data of 1,263 samples on chromosome 2

Statistic	Minor allele frequency (MAF) bins			
	0.01-0.05	0.05-0.2	0.2-0.5	All
Number of SNPs on array	1,070	13,208	25,770	40,048
Sensitivity	0.9981	0.9990	0.9973	0.9979
Non-reference sensitivity	0.9991	0.9996	0.9997	0.9997
Precision	0.9976	0.9984	0.9981	0.9982
Overall concordance	0.9995	0.9996	0.9994	0.9995
Heterozygote concordance	0.9973	0.9990	0.9992	0.9992
Non-reference concordance	0.9979	0.9992	0.9993	0.9993

Definitions: Sensitivity, fraction of polymorphic sites in the array data that were also in the sequencing call set with both alleles matched; Non-reference sensitivity, fraction of non-reference genotypes in array data that are also called as non-reference genotypes in sequencing data; Precision, fraction of concordant genotypes across non-reference sites in the sequencing call set; Overall/heterozygote/non-reference concordance, fraction of concordant genotypes across all/heterozygous/non-reference sites in array data.

Related to **Figure 1**.

Table S3. Summary of variants in the final SG10K call set of 4810 samples

	Autosomes		X chromosome	
Variant type	Known+Novel	Novel (%)	Known+Novel	Novel (%)
Bi-allelic SNP	84,725,366	43,353,432 (51%)	3,275,181	1,859,426 (56%)
Tri-allelic SNP	1,112,853	399,558 (36%)	31,853	19,081 (60%)
Quad-allelic SNP	14,669	1,909 (13%)	364	170 (47%)
Insertion	3,059,717	2,112,318 (69%)	124,180	96,892 (78%)
Deletion	5,708,237	3,966,319 (69%)	221,286	170,442 (77%)
Total	94,620,842	49,833,536 (53%)	3,652,864	2,146,011 (59%)

Known variants are those reported in dbSNP150; novel variants are those not in dbSNP150.

Related to **Table 1**.

Table S4. Genetic diversity of SG10K and Asian populations from 1KGP

	Expected heterozygosity (H_e, MAF>0.05)					**Nucleotide diversity** (π)*
Population	SNP	25 kb	50 kb	100 kb	200 kb	
BEB	0.326	0.557	0.648	0.772	0.885	7.52×10^{-4}
STU	0.323	0.553	0.645	0.769	0.882	7.50×10^{-4}
PJL	0.322	0.552	0.644	0.769	0.882	7.54×10^{-4}
ITU	0.322	0.552	0.644	0.768	0.882	7.50×10^{-4}
GIH	0.320	0.549	0.640	0.764	0.878	7.47×10^{-4}
KHV	0.315	0.530	0.617	0.739	0.860	6.84×10^{-4}
CHB	0.313	0.528	0.614	0.736	0.858	6.79×10^{-4}
CHS	0.313	0.527	0.613	0.735	0.858	6.77×10^{-4}
CDX	0.313	0.527	0.613	0.735	0.856	6.78×10^{-4}
JPT	0.311	0.524	0.609	0.731	0.853	6.77×10^{-4}
SG Indian	0.326	0.559	0.652	0.779	0.894	7.31×10^{-4}
SG Malay	0.322	0.546	0.635	0.759	0.878	6.87×10^{-4}
SG Chinese	0.315	0.531	0.618	0.742	0.866	6.59×10^{-4}

* We note that nucleotide diversity π should be identical to the SNP-based heterozygosity H_e if they were computed from the same set of SNPs. In this table, we computed π on all sites without the polymorphic restriction. The values of π might not be directly comparable between 1KGP and SG10K populations because of their difference in sequencing depths (7.4× for 1KGP vs. 13.7× for SG10K). In contrast, we calculated H_e based on SNPs with MAF>0.05, for which shallow sequencing would also have high genotype calling quality, such that the values of H_e are less sensitive to sequencing depths.

Abbreviations for 1KGP populations: BEB, Bengali; GIH, Gujarati; ITU, Telugu; PJL, Punjabi; STU, Sri Lankan Tamil; CDX, Chinese Dai; CHB, Han Chinese in Beijing; CHS, Southern Han Chinese; JPT, Japanese; KHV, Kinh.

Related to **Figure 3**.

Table S5. Reported GWAS associations within candidate loci for natural selection identified by PBS

Physical positions	GWAS mapped genes	GWAS traits or Diseases						
		Cardiovascular	Metabolism	Neuro-psychiatry	Immunity/Inflammation	Cancers	Physical/ Physiological measures	Lifestyle/Medication response
chr1: 172680465-172880359	*AIMP1P2; FASLG; LOC105371618; PADI3; SLC25A38P1; TNFSF18*				Allergy; Psoriasis; Vitiligo; Celiac disease; IBD (Crohn's/UC); Sclerosing cholangitis; Mosquito bite reaction/itch intensity		Hair shape	
chr2: 25945982-26206255	*DTNB; KIF3C; LOC105374332; NDUFB4P4*	Atrial fibrillation			Cough		Mean corpuscular hemoglobin concentration	Response to angiotensin-converting enzyme inhibitor
chr2: 97477374-98332858	*FAM178B*			Schizophrenia; Bipolar disorder				Response to lithium ion
chr2: 108727043-109625736	*CCDC138; EDAR; GCC2; KCNF1; LIMS1; LOC101929733; PDIA6; RANBP2; SMIM12P1; SULT1C2P1; SULT1C4*		Blood protein	Self-reported education	Androgenetic alopecia; Gut microbiome; TNF receptor superfamily member *EDAR*		Mean platelet volume; Hirsutism; Facial hair thickness; Synophrys; Hair/Lip/Chin/Ear morphology	
chr2: 216258169-216322388	*FN1; LOC102724849; LOC105373868*	CAD; Angina pectoris; Ischemic cardiomyopathy; Myocardial infarction; Percutaneous transluminal coronary angioplasty; Coronary artery bypass; Pulse pressure	LDLC; Fibronectin (fragment ¾)				Endometriosis	
chr3: 49523947-50514612	*ACTBP13; APEH; BSN; CACNA2D2; CAMKV; CDHR4; CYB561D2; DAG1; GNAI2; GNAT1; IP6K1; LOC102724438; MON1A; MST1; MST1R; RASSF1; RBM5; RBM6; RN7SL217P; RNF123; SEMA3F; SEMA3F-AS1; TRAIP; UBA7*	DBP; Resting heart rate	T1D; HDLC; Blood protein; Thioredoxin domain-containing protein 12; BMI	Schizophrenia; Self-reported education; Intelligence; Intraocular pressure	Autoimmune disease; Autoimmune thyroid disease; Immunodeficiency; SLE; Psoriasis; Celiac disease; IBD (Crohn's/UC); Sclerosing cholangitis; MIP-1b/HGFL measurements; Childhood ear infection		Age at menarche; Reticulocyte count; Grip strength	
chr4: 99762388-100322106	*ADH1B; ADH1C; ADH5; EIF4E; IDUA; LOC100507053; NDUFS5P4; RNU7-149P; SLC26A1; SLC2A9*		HDLC; Serum/blood metabolites; Blood protein; Uric acid/Urate; BMI	Alzheimer's disease	Gout	Oral cavity cancer; Oropharynx cancer; Pharynx cancer; Esophageal carcinoma; Upper aerodigestive tract neoplasm	Age at menopause; Mean corpuscular hemoglobin concentration	Alcohol dependence/consumption

chr5: 132009154-132128510	*KIF3A; SEPT8; SOWAHA*				Atopic eczema; Atopic march; Mosquito bite reaction (itch intensity/size)			
chr6: 126608815-127080700	*CENPW; LOC105377989; LOC105377992; LOC105377993; MIR588; PRELID1P1; RNU6-200P; YAP1P3*	CAD	T1D; T2D; Hip circumference; BMI; Height (infant)	Intelligence; Intraocular pressure/volume	Androgenetic alopecia; Sclerosing cholangitis		Age at menarche; Hematocrit; Bone density; Synophrys	Food addiction; Eating behaviour
chr10: 107053687-107568998	*LOC101927549; LOC107984266; RNU6-463P*					Melanoma	Airway imaging	
chr12: 111994852-113018479	*ACAD10; ALDH2; ATXN2; BRAP; HECTD4; MAPKAPK5-AS1; MIR1302-1; NAA25; PTPN11; RPL6; SLC2A9; TMEM116; TRAFD1*	CHD; Myocardial infarction; Tetralogy of fallot; Ischemic stroke; Small artery occlusion; Cystatin C measurement; Mean arterial pressure; DBP; SBP	T1D; T2D; Metabolic syndrome; Cholesterol; Triglyceride; Blood urea nitrogen; Uric acid/Urate; Renal system; Blood protein; Serum AAT/ALT/GGT; Thyroid peroxidase antibody; BMI	AMD; Atrophic macular degeneration; Wet macular degeneration	Immune system disease; SLE; Psoriasis; Celiac disease; IBD; PBC; CKD; Basophil/Eosinophil/Granulocyte/Leukocyte/Monocyte/Neutrophil/Reticulocyte/Myeloid white cell count; Eosinophil/Neutrophil percentage of granulocytes; Eosinophil percentage of leukocytes; CRP; Tonsillectomy risk	Esophageal carcinoma; Upper aerodigestive tract neoplasm	Cleft palate; Cleft lip; Fibrinogen; Hemoglobin; Mean corpuscular hemoglobin/volume; Hematocrit; Platelet count/component distribution	Alcohol dependence/consumption; Smoking; Coffee consumption
chr15: 28179676-28260309	*OCA2*					Cutaneous squamous cell carcinoma	Eye color; Suntan	
chr16: 30449906-31155458	*AXIN1; BCKDK; BCL7C; CTF1; CTF2P; FBXL19; ITGAL; KAT8; MIR4519; PRR14; PRSS53; SEPHS2; SETD1A; STX1B; STX4; VKORC1; ZNF646; ZNF689; ZNF785*	DBP	WHR; BMI	Parkinson's disease; Alzheimer's disease; Lewy body dementia; Neuroticism	Ankylosing spondylitis; SLE; Psoriasis; IBD (Crohn's/UC); Sclerosing cholangitis; Erythrocyte/Myeloid white cell/Eosinophil/Leukocyte/Lymphocyte/Monocyte count; Neutrophil/Lymphocyte percentage of leukocytes		Mean corpuscular hemoglobin/volume /concentration; Hair shape	Smoking; Response to anticoagulant
chrX: 71841429-72970288	*PABPC1L2A; PABPC1L2B*						Eye morphology	

Abbreviations: AAT, alpha-1-antitrypsin; ALT, alanine aminotransferase; AMD, age-related macular degeneration; BMI, body mass index; CAD, coronary artery disease; CHD, coronary heart disease; CKD, chronic kidney disease; CRP, C-reactive protein; DBP, diastolic blood pressure; GGT, gamma-glutamyl transferase; HDLC, high-density lipoprotein cholesterol; HGFL, hepatocyte growth factor-like protein; IBD, inflammatory bowel disease; LDLC, low-density lipoprotein cholesterol; MIP-1b, macrophage inflammatory protein 1b; PBC, primary biliary cirrhosis; SBP, systolic blood pressure; SLE, systemic lupus erythematosus; UC, ulcerative colitis; WHR, waist to hip circumference ratio.

Related to **Figure 4**.

Table S6. Imputation error rate in 56 worldwide populations using three reference panels

Region	Population	Imputation reference panel		
		1KGP	SG10K	Combined
Africa	Bantu (Kenya)	**0.0427**	0.2196	0.0784
Africa	Bantu (S. Africa)	**0.0584**	0.2394	0.0976
Africa	Biaka Pygmy	**0.1190**	0.2671	0.1602
Africa	Mandenka	**0.0410**	0.2253	0.0801
Africa	Mbuti Pygmy	**0.1393**	0.2776	0.1813
Africa	San	**0.1981**	0.2902	0.2290
Africa	Yoruba	**0.0263**	0.2276	0.0664
America	Colombian	**0.0183**	0.0323	0.0198
America	Karitiana	**0.0172**	0.0304	0.0185
America	Maya	**0.0198**	0.0380	0.0220
America	Pima	**0.0183**	0.0347	0.0205
America	Surui	**0.0165**	0.0309	0.0181
Central/South Asia	Balochi	**0.0275**	0.0361	0.0278
Central/South Asia	Brahui	0.0276	0.0367	**0.0271**
Central/South Asia	Burusho	0.0299	0.0311	**0.0273**
Central/South Asia	Hazara	0.0282	0.0296	**0.0262**
Central/South Asia	Kalash	0.0262	0.0297	**0.0250**
Central/South Asia	Makrani	**0.0288**	0.0458	0.0299
Central/South Asia	Pathan	0.0274	0.0311	**0.0253**
Central/South Asia	SG Indian	0.0287	0.0259	**0.0225**
Central/South Asia	Sindhi	0.0274	0.0365	**0.0255**
Central/South Asia	Uygur	0.0290	0.0300	**0.0258**
East Asia	Cambodian	0.0299	**0.0204**	0.0211
East Asia	Dai	0.0224	0.0175	**0.0154**
East Asia	Daur	0.0288	0.0251	**0.0241**
East Asia	Han	0.0266	0.0166	**0.0162**
East Asia	Han (N. China)	0.0256	0.0206	**0.0196**
East Asia	Hezhen	0.0283	0.0259	**0.0244**
East Asia	Japanese	0.0246	0.0255	**0.0210**
East Asia	Lahu	0.0283	0.0222	**0.0216**
East Asia	Miao	0.0261	0.0193	**0.0182**
East Asia	Mongola	0.0276	0.0248	**0.0230**
East Asia	Naxi	0.0302	0.0235	**0.0223**
East Asia	Oroqen	0.0276	0.0264	**0.0234**
East Asia	SG Chinese	0.0267	**0.0134**	**0.0134**
East Asia	SG Malay	0.0316	**0.0157**	0.0161
East Asia	She	0.0262	**0.0131**	0.0135
East Asia	Tu	0.0298	0.0246	**0.0235**
East Asia	Tujia	0.0274	**0.0193**	**0.0193**
East Asia	Xibo	0.0275	0.0239	**0.0220**
East Asia	Yakut	0.0291	0.0290	**0.0260**
East Asia	Yi	0.0270	0.0221	**0.0210**
Europe	Adygei	**0.0284**	0.0382	0.0293
Europe	Basque	**0.0159**	0.0391	0.0175
Europe	French	**0.0200**	0.0386	0.0216
Europe	Italian	**0.0237**	0.0407	0.0250
Europe	Orcadian	**0.0152**	0.0369	0.0165
Europe	Russian	**0.0193**	0.0359	0.0205
Europe	Sardinian	**0.0249**	0.0428	0.0268
Europe	Tuscan	**0.0234**	0.0396	0.0248
Middle East	Bedouin	**0.0354**	0.0608	0.0413
Middle East	Druze	**0.0316**	0.0458	0.0336
Middle East	Mozabite	**0.0310**	0.0874	0.0434
Middle East	Palestinian	**0.0353**	0.0602	0.0403
Oceania	Melanesian	0.0454	**0.0379**	0.0380
Oceania	Papuan	0.0484	**0.0392**	0.0401

The best performed reference panel for imputing each population is in bold.

Related to **Figure 5**.