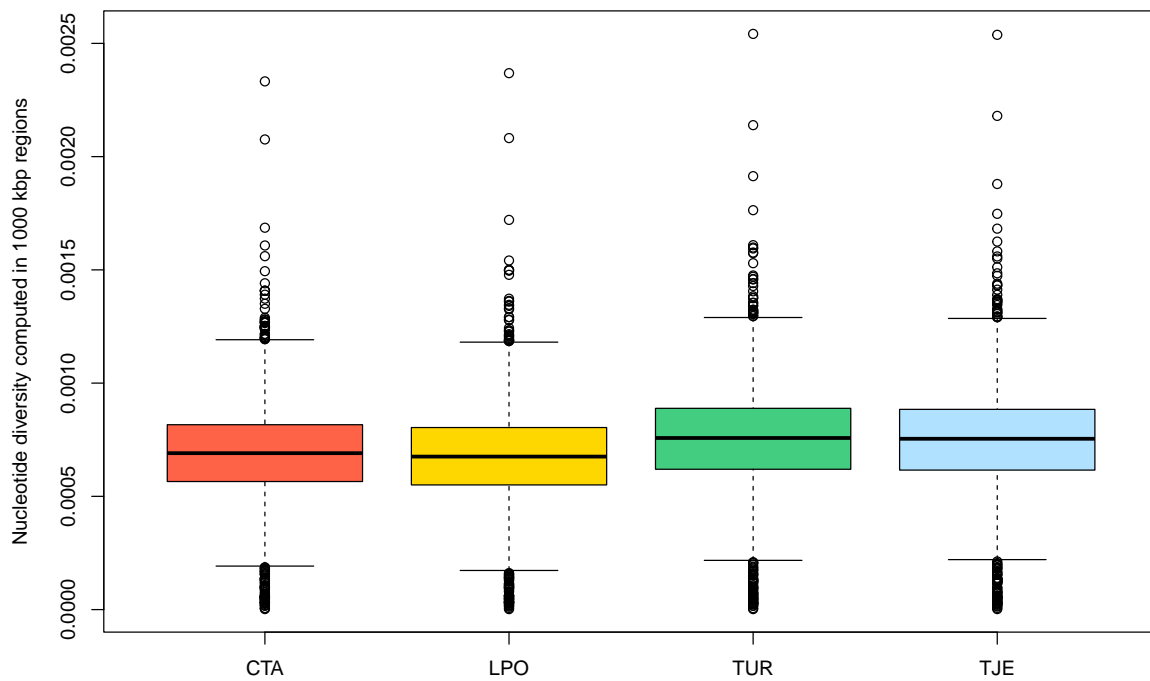


	CTA	LPO	TUR	TJE
total	6430568.5 (17471.1)	6432097.8 (10973.0)	6343818.7 (26602.0)	6332656.6 (5001.0)
CADD_inf_10	6119391.9 (16342.7)	6120943.0 (10338.4)	6038921.3 (24950.9)	6028773.5 (4667.2)
CADD_10_15	233130.1 (934.8)	233117.6 (801.8)	228237.4 (1327.4)	227448.9 (518.9)
CADD_15_20	66076.0 (312.1)	66068.4 (198.1)	64915.6 (411.1)	64838.8 (188.9)
CADD_sup_20	11970.5 (102.5)	11968.8 (107.5)	11744.3 (133.6)	11595.3 (99.1)
CADD_sup_21	6917.5 (83.6)	6887.4 (82.9)	6689.5 (97.1)	6620.8 (79.4)
CADD_sup_22	3114.1 (54.0)	3080.0 (57.3)	2983.8 (51.9)	2977.3 (58.5)
CADD_sup_23	1451.9 (33.2)	1416.4 (44.3)	1371.5 (35.9)	1370.2 (39.7)
CADD_sup_24	887.1 (32.1)	869.0 (31.7)	835.9 (20.0)	837.2 (27.7)
CADD_sup_25	583.8 (25.4)	570.0 (26.9)	558.5 (20.9)	558.1 (20.9)
CADD_sup_26	405.9 (14.5)	393.7 (23.3)	387.5 (21.5)	384.8 (19.9)
CADD_sup_27	303.5 (12.8)	297.3 (16.2)	291.2 (21.0)	286.9 (16.0)
CADD_sup_28	229.6 (11.2)	224.0 (13.0)	223.9 (15.9)	224.7 (14.0)
CADD_sup_29	193.9 (11.7)	186.5 (10.9)	186.7 (11.5)	184.1 (13.4)
CADD_sup_30	151.6 (11.5)	148.7 (10.4)	150.7 (11.1)	147.5 (10.4)

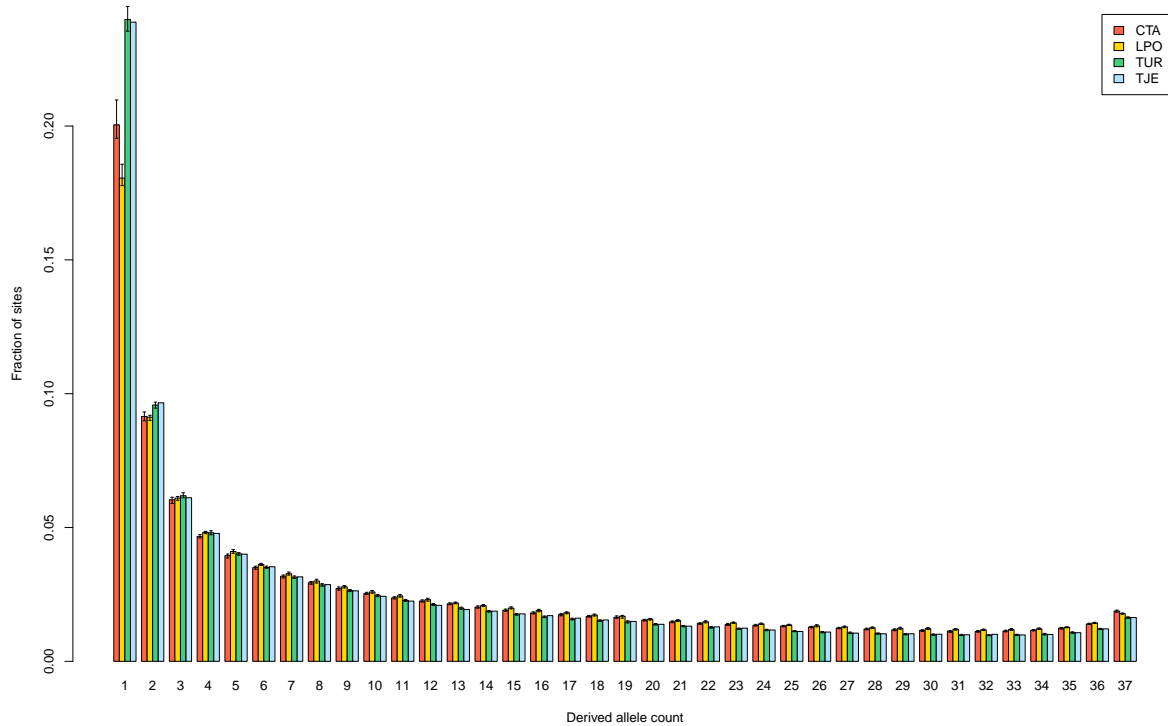
Supplementary Table 1: **Mean (standard deviation) per-individual number of derived variants for each population studied.** Variants were stratified in several CADD classes reflecting the severity of the deleterious effect: neutral (below 10), moderate (10 to 15), large (15 to 20) and extreme (from above 20 to above 30). Populations: Turkmen (TUR) and Tadjik (TJE) from Central Asia, Tampuan (CTA) and Pacoh (LPO) from Southeast Asia.

	CTA	LPO	TUR	TJE
total	1524955.3 (17575.7)	1528420.0 (10094.7)	1440261.7 (27244.0)	1429694.8 (4770.7)
CADD_inf_10	1456649.0 (16557.3)	1459981.0 (9565.8)	1377118.1 (25575.8)	1367409.7 (4524.7)
CADD_10_15	51040.8 (794.6)	51152.8 (488.7)	47081.8 (1270.2)	46443.6 (267.8)
CADD_15_20	14744.0 (229.4)	14755.5 (110.7)	13735.8 (364.9)	13581.1 (105.8)
CADD_sup_20	2521.5 (55.9)	2530.9 (43.2)	2326.0 (79.6)	2260.4 (38.4)
CADD_sup_21	1404.6 (42.2)	1404.5 (28.1)	1262.3 (52.1)	1228.4 (24.9)
CADD_sup_22	568.0 (24.6)	563.5 (15.3)	496.3 (25.3)	487.6 (14.9)
CADD_sup_23	226.0 (11.5)	216.0 (13.1)	186.2 (17.2)	177.4 (11.3)
CADD_sup_24	128.4 (10.0)	123.5 (10.3)	101.5 (11.2)	98.1 (9.8)
CADD_sup_25	82.7 (8.4)	79.5 (7.5)	68.0 (7.7)	65.8 (7.4)
CADD_sup_26	57.4 (6.8)	54.1 (6.7)	47.0 (5.6)	45.5 (6.7)
CADD_sup_27	42.5 (6.0)	40.4 (4.3)	33.7 (4.6)	32.7 (4.4)
CADD_sup_28	32.0 (4.4)	30.0 (4.0)	26.9 (3.9)	27.4 (3.9)
CADD_sup_29	28.7 (4.3)	26.1 (4.0)	24.1 (3.1)	23.9 (4.4)
CADD_sup_30	21.7 (4.4)	20.8 (3.4)	19.7 (3.0)	19.8 (3.6)

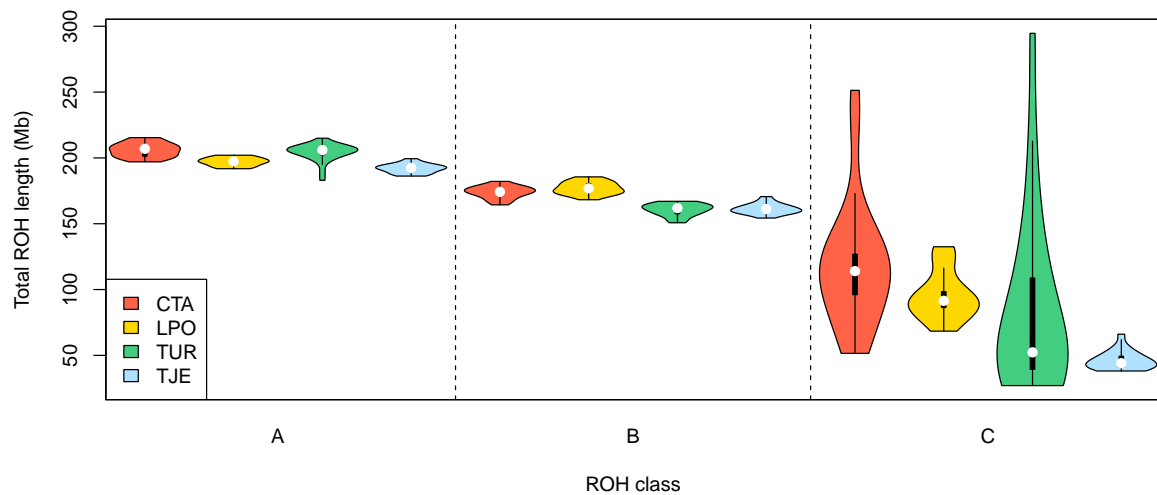
Supplementary Table 2: **Mean (standard deviation) per-individual number of derived homozygotes for each population studied.** Variants were stratified in several CADD classes reflecting the severity of the deleterious effect: neutral (below 10), moderate (10 to 15), large (15 to 20) and extreme (from above 20 to above 30). Populations: Turkmen (TUR) and Tadjik (TJE) from Central Asia, Tampuan (CTA) and Pacoh (LPO) from Southeast Asia.



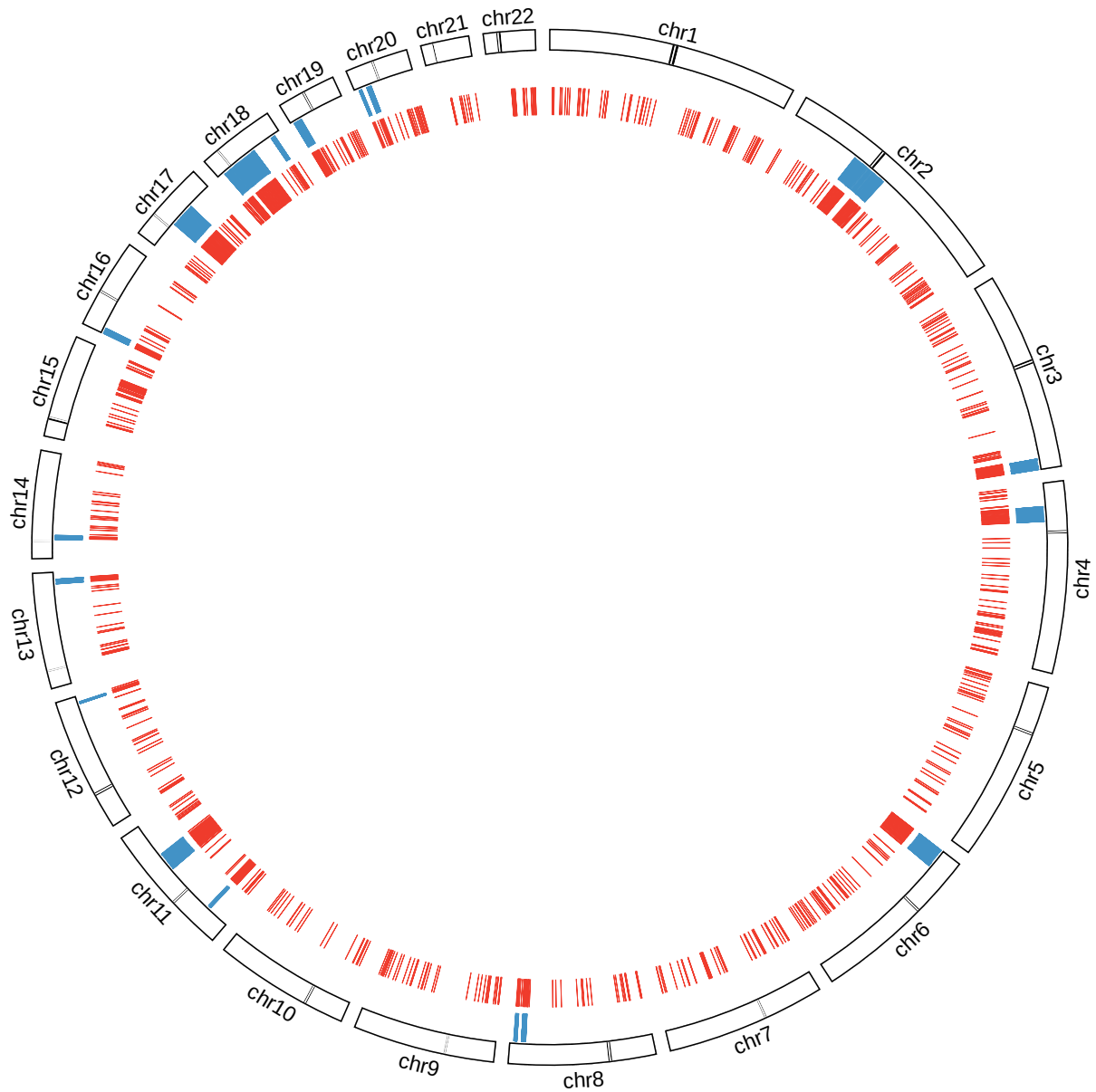
Supplementary Figure 1: **Genetic diversity of the four populations studied.** The nucleotide diversity was computed in 1000 kb regions for the four populations studied: Turkmen (TUR) and Tadjik (TJE) from Central Asia, Tampuan (CTA) and Pacoh (LPO) from Southeast Asia.



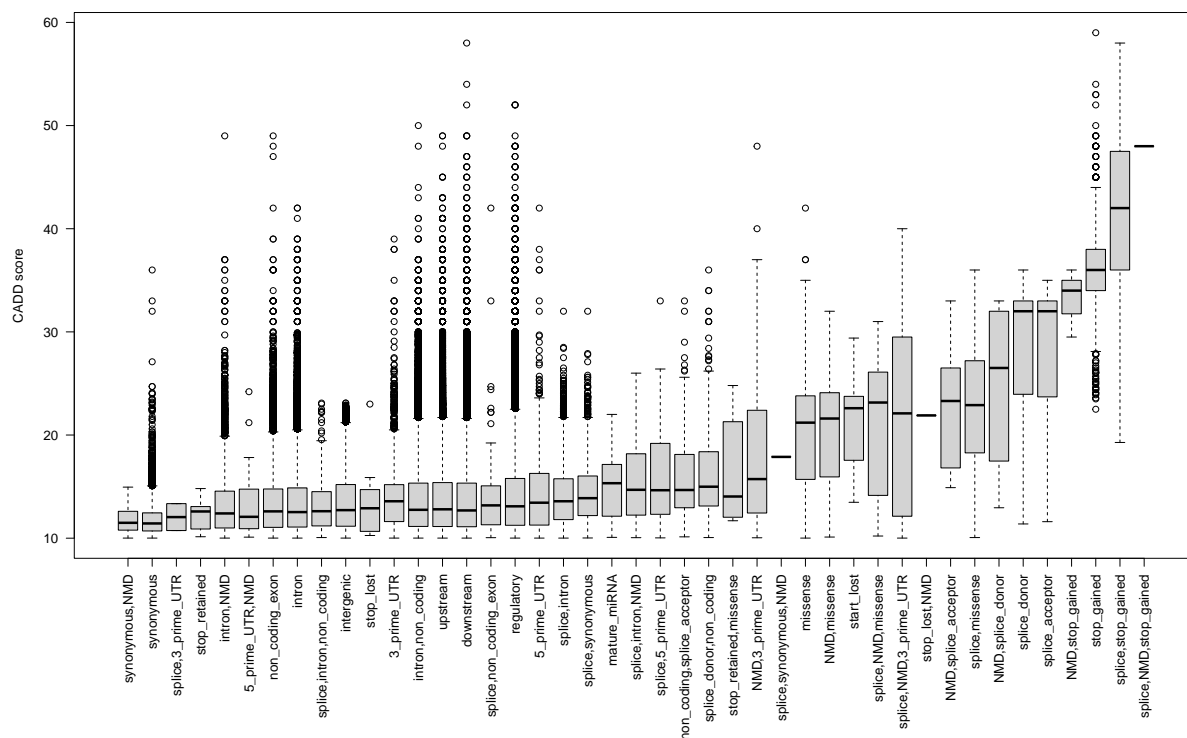
Supplementary Figure 2: **Derived allele frequency spectra of the four populations studied:** Turkmen (TUR) and Tadjik (TJE) from Central Asia, Tampuan (CTA) and Pacoh (LPO) from Southeast Asia.



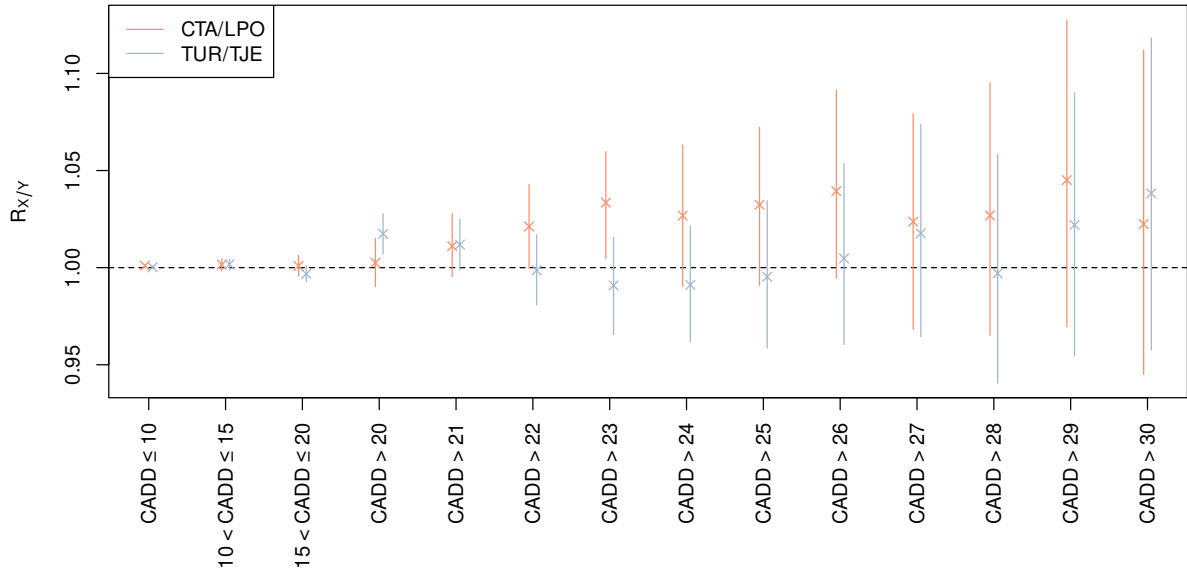
Supplementary Figure 3: **Distribution of ROHs.** Total length of ROHs in each individual genome, grouped by population, for class A, class B and class C ROHs. Populations: Turkmen (TUR) and Tadjik (TJE) from Central Asia, Tampuan (CTA) and Pacoh (LPO) from Southeast Asia.



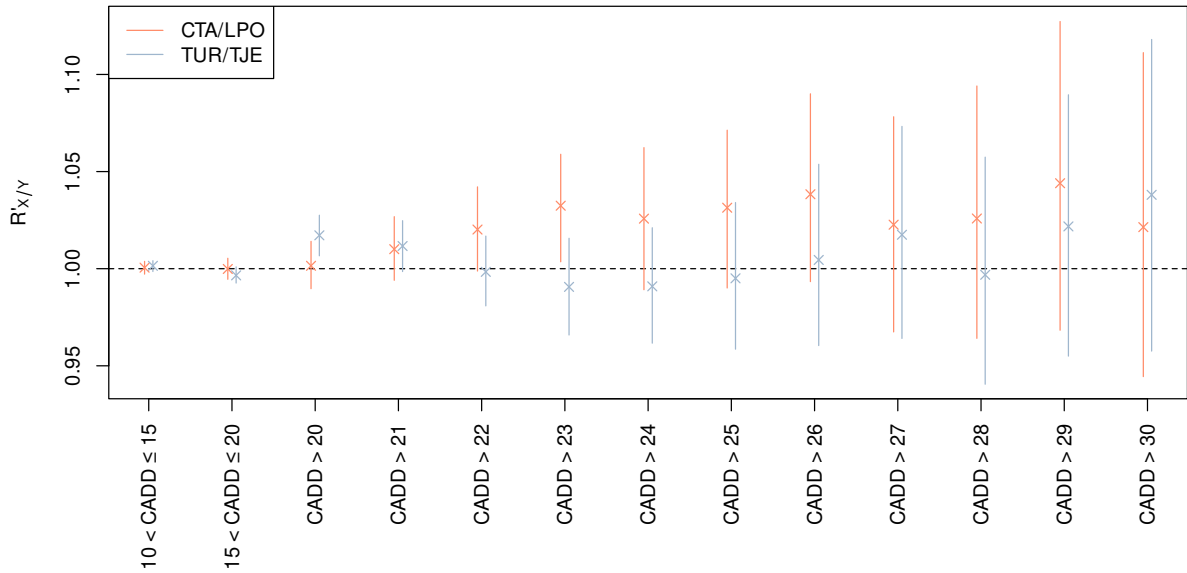
Supplementary Figure 4: **FSuite and GARLIC comparison.** Comparison of the distribution of autozygous segments inferred by FSuite and long ROH segments inferred by GARLIC for a Tampuan individual, born from first cousins. Circos plot (Krzywinski M, Schein J, Birol I, Connors J, Gascoyne R, Horsman D, Jones SJ, Marra MA. 2009. Circos: An information aesthetic for comparative genomics. *Genome Research* 19:1639–1645).



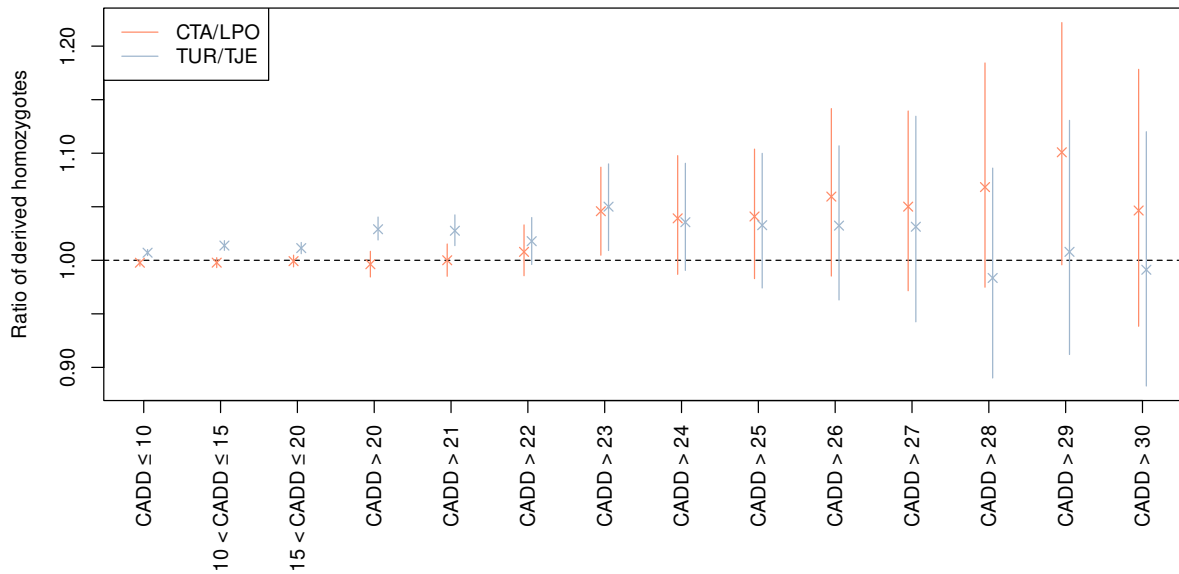
Supplementary Figure 5: **CADD score versus ENSEMBL category**. The box plot represents the median and 25th and 75th percentiles of CADD scores for each consequence predictor annotation. Only CADD values higher than 10 were considered.



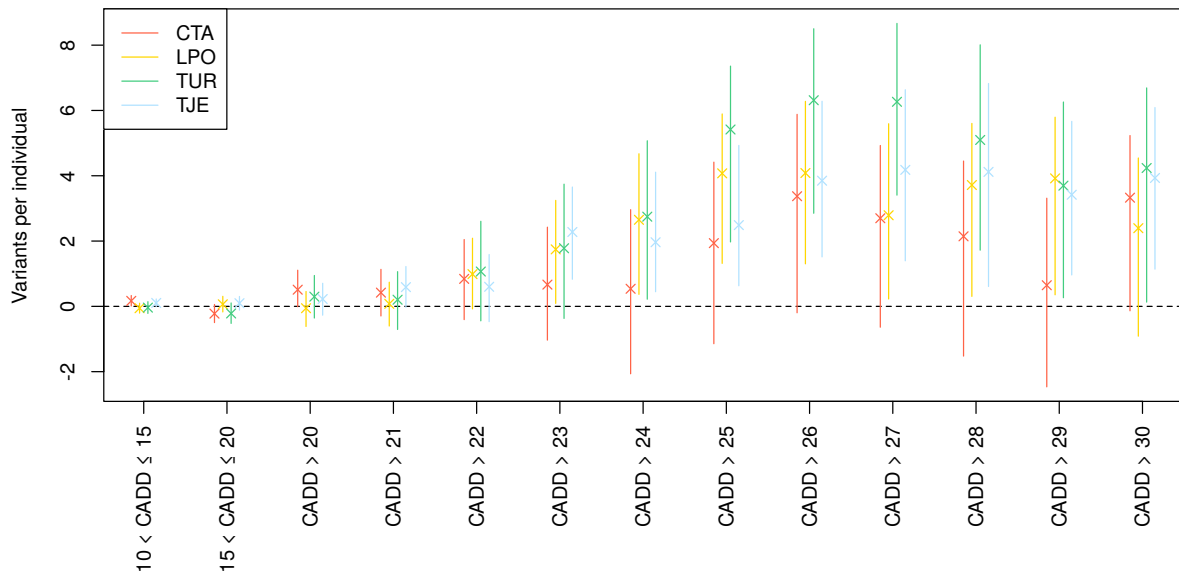
Supplementary Figure 6: $R_{X/Y}$ ratios for variants stratified in several CADD classes reflecting the severity of the deleterious effect: neutral (below 10), moderate (10 to 15), large (15 to 20), and extreme (from above 20 to above 30 to assess the sensitivity of the statistics to this threshold). Error bars represent the 95% confidence intervals obtained from 1,000 block-bootstrap resampling. Populations: Turkmen (TUR) and Tadjik (TJE) from Central Asia, Tampuan (CTA) and Pacoh (LPO) from Southeast Asia.



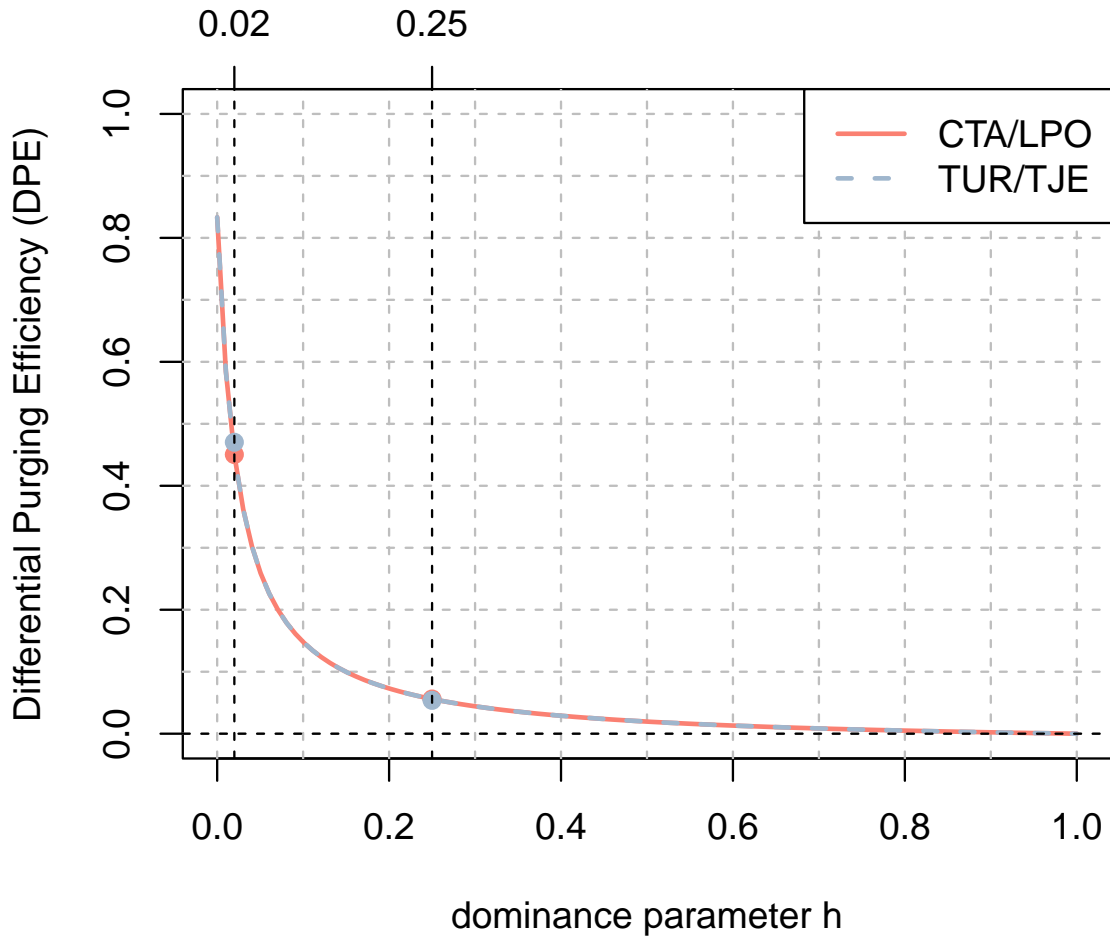
Supplementary Figure 7: $R'_{X/Y}$ ratios for variants stratified in several CADD classes reflecting the severity of the deleterious effect: neutral (below 10), moderate (10 to 15), large (15 to 20), and extreme (from above 20 to above 30 to assess the sensitivity of the statistics to this threshold). Error bars represent the 95% confidence intervals obtained from 1,000 block-bootstrap resampling. Populations: Turkmen (TUR) and Tadjik (TJE) from Central Asia, Tampuan (CTA) and Pacoh (LPO) from Southeast Asia.



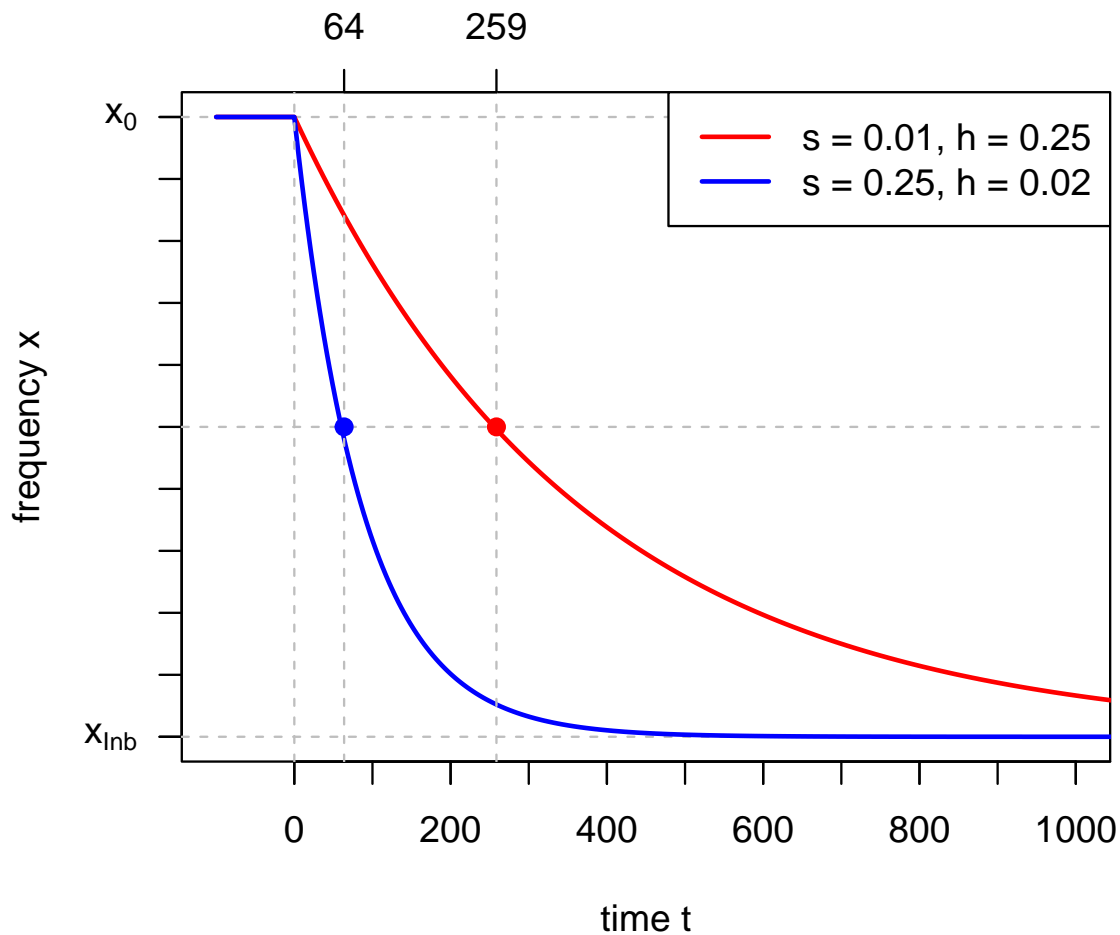
Supplementary Figure 8: **Between-population ratios of the mean per-individual number of homozygous sites** for variants stratified in several CADD classes reflecting the severity of the deleterious effect: neutral (below 10), moderate (10 to 15), large (15 to 20), and extreme (from above 20 to above 30 to assess the sensitivity of the statistics to this threshold). Error bars represent the 95% confidence intervals obtained from 1,000 block-bootstrap resampling. Populations: Turkmen (TUR) and Tadjik (TJE) from Central Asia, Tampuan (CTA) and Pacoh (LPO) from Southeast Asia.



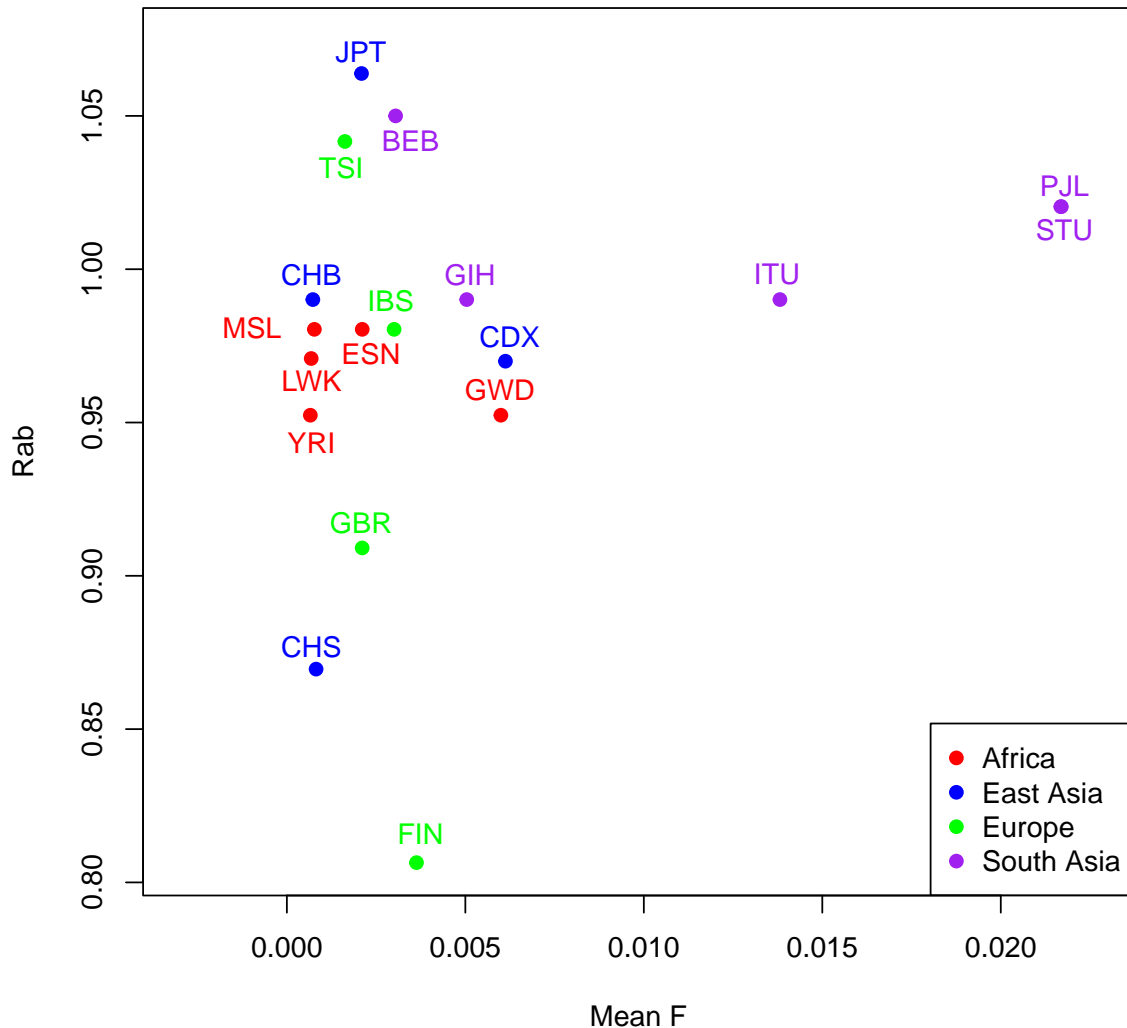
Supplementary Figure 9: **Mean number of recessive lethal variants based on the suppression of highly homozygous deleterious variants** (from CADD above 20 to CADD above 30 to assess the sensitivity of the statistics to this threshold). Populations: Turkmen (TUR) and Tadjik (TJE) from Central Asia, Tampuan (CTA) and Pacoh (LPO) from Southeast Asia.



Supplementary Figure 10: **Differential Purging Efficiency (DPE) for a deleterious variant between a population with high inbreeding and a population with low inbreeding, as a function of the dominance parameter h , for two pairs of populations: CTA ($F = 0.024$) / LPO ($F = 0.004$) in South-East-Asia and TUR ($F = 0.020$) / TJE ($F = 0.001$) in Central-Asia.** DPE measures the relative reduction in the expected frequency of the deleterious variant at mutation/selection equilibrium between the two populations. The dotted vertical lines indicate dominance values commonly reported for weakly selected variants ($h = 0.25$) and major effect variants ($h = 0.02$).



Supplementary Figure 11: **Expected change in the frequency x of a deleterious variant as a function of time t , measured in generations, in a population with an inbreeding coefficient $F = 0.024$, for weakly selected co-dominant variants ($s = 0.01, h = 0.25$) and major effect recessive variants ($s = 0.25, h = 0.02$).** The frequency curve approximately follows a negative exponential function from the initial frequency x_0 at time $t = 0$ to the mutation-selection equilibrium frequency x_{Inb} . The dotted vertical lines indicate the time needed to reach $(x_0 + x_{Inb})/2$.



Supplementary Figure 12: **Mutational load (R_{ab}) from Narasimham et al. (2016) (CEU as denominator) versus mean population inbreeding coefficient (F) from Gazal et al. (2015) for the 1,000 Genomes Project populations.** People of African ancestry in the SW USA (ASW); African Caribbean in Barbados (ACB); Bengali in Bangladesh (BEB); British from England and Scotland (GBR); Chinese Dai in Xishuangbanna, China (CDX); Esan in Nigeria (ESN); Finnish in Finland (FIN); Gambian in Western Division – Mandinka (GWD); Gujarati Indians in Houston, Texas, USA (GIH); Han Chinese in Beijing (CHB); Han Chinese South, China (CHS); Iberian populations in Spain (IBS); Indian Telugu in the U.K. (ITU); Japanese in Tokyo, Japan (JPT); Luhya in Webuye, Kenya (LWK); Mende in Sierra Leone (MSL); Punjabi in Lahore, Pakistan (PJL); Sri Lankan Tamil in the UK (STU); Toscani in Italy (TSI); Utah residents of northern and western European ancestry (CEU); Yoruba in Ibadan (YRI), Nigeria.