Supplementary material – Supplementary figures and tables
for

"Adaptation to infectious disease exposure in indigenous southern African populations" by

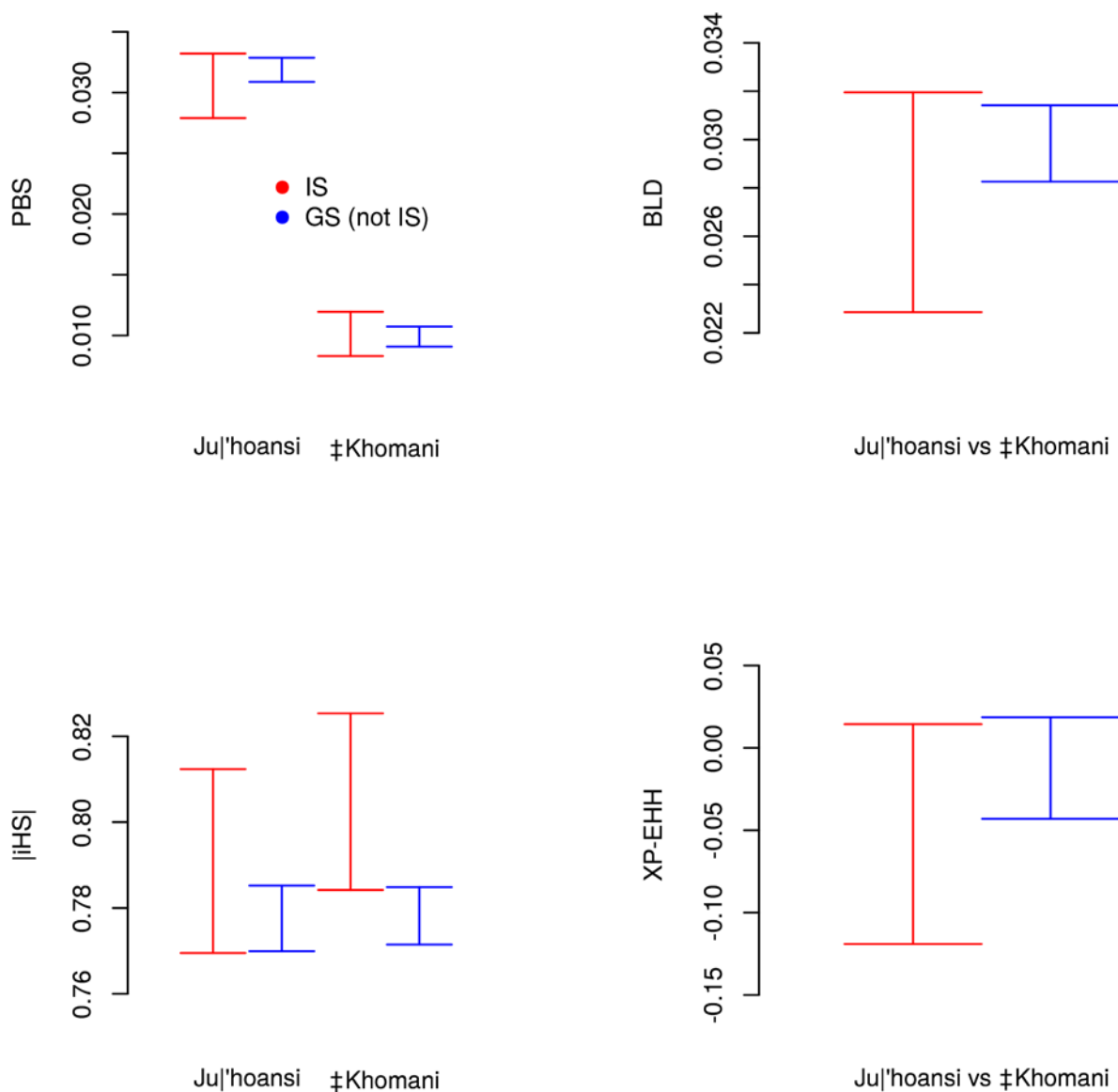Katharine A. Owers, Per Sjödin, Carina M. Schlebusch, Pontus Skoglund, Himla Soodyall, Mattias Jakobsson

Figure S1. Mean plus minus 2 standard deviations for a) PBS b) BLD c) |iHS| and d) XP-EHH based on a weighted block jackknife procedure analysis with 5 Mb windows. Red represents SNPs in immune genes and blue SNPs in other genes.
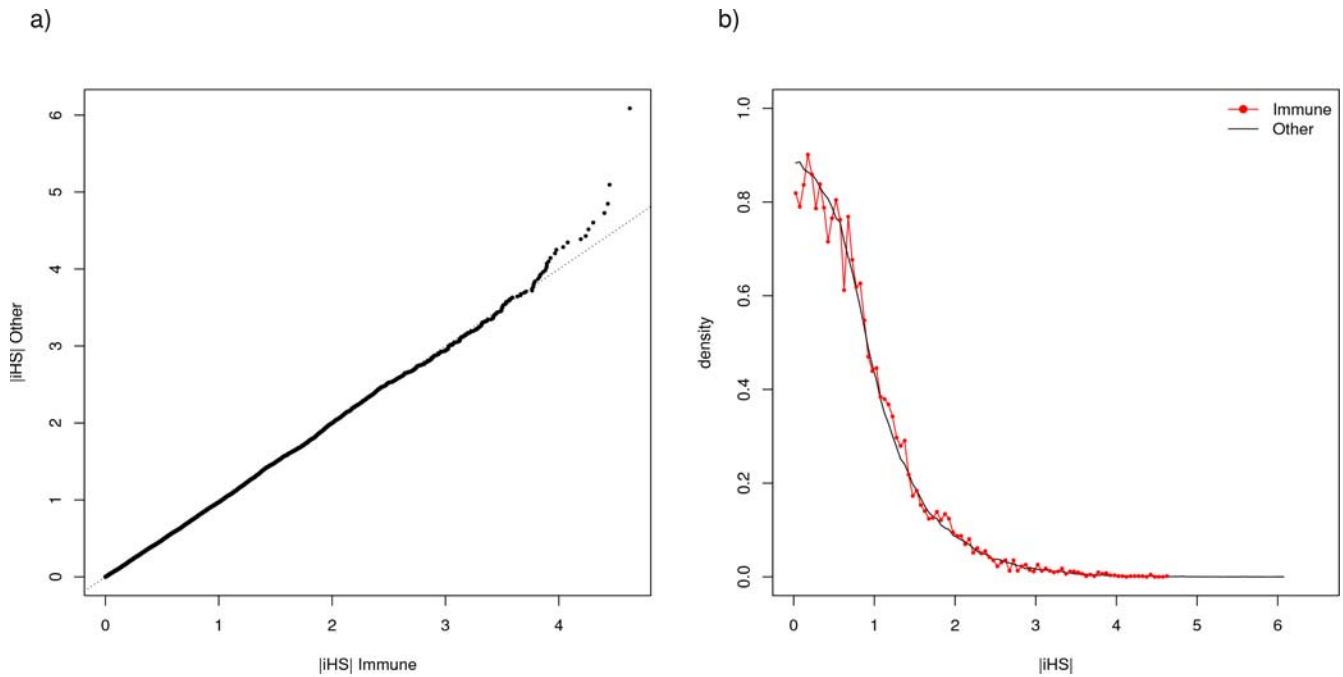
Figure S2. iHS analysis for Herero a) qq-plot SNPs in immune genes (x-axis) vs SNPs in other genes (y-axis); b) distribution of abs(iHS) at SNPs in immune genes (red) and at SNPs in other genes (black). Mean |iHS| = 0.773 among 12383 SNPs in immune genes and mean |iHS| = 0.756 among 387577 SNPs in other genes, p = 0.000115 based on Mann-Whitney U-test.
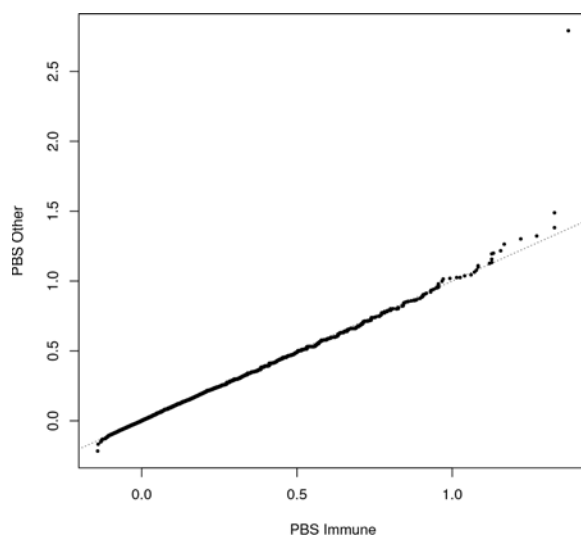
Figure S3. qq-plot of PBS for Herero, SNPs in immune genes (x-axis) vs SNPs in other genes (y-axis). Mean PBS = 0.0761 among 19737 SNPs in immune genes and mean PBS = 0.0760 among 627769 SNPs in other genes, p = 0.195 based on Mann-Whitney U-test.
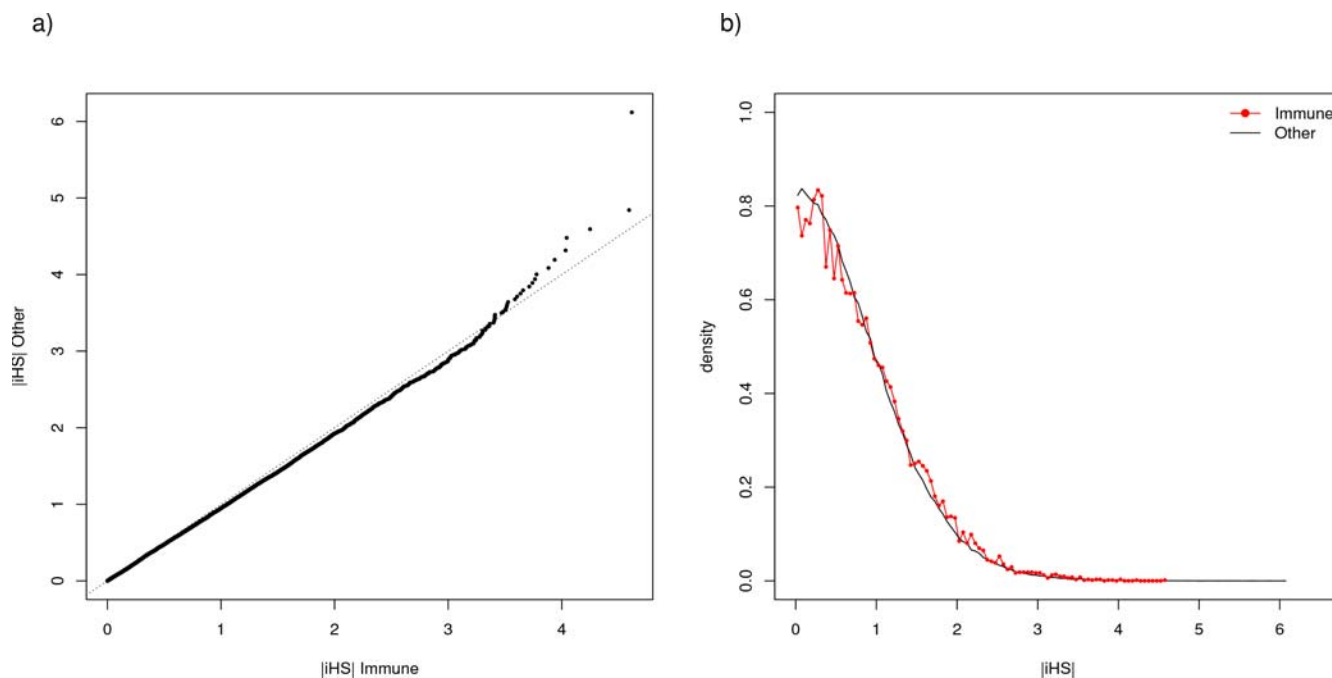
a)

b)

Figure S4. iHS analysis for Karretjie a) qq-plot SNPs in immune genes (x-axis) vs SNPs in other genes (y-axis); b) distribution of abs(iHS) at SNPs in immune genes (red) and at SNPs in other genes (black). Mean |iHS| = 0.821 among 12950 SNPs in immune genes and mean |iHS| = 0.783 among 414027 SNPs in other genes, p = 0.000115 based on Mann-Whitney U-test.
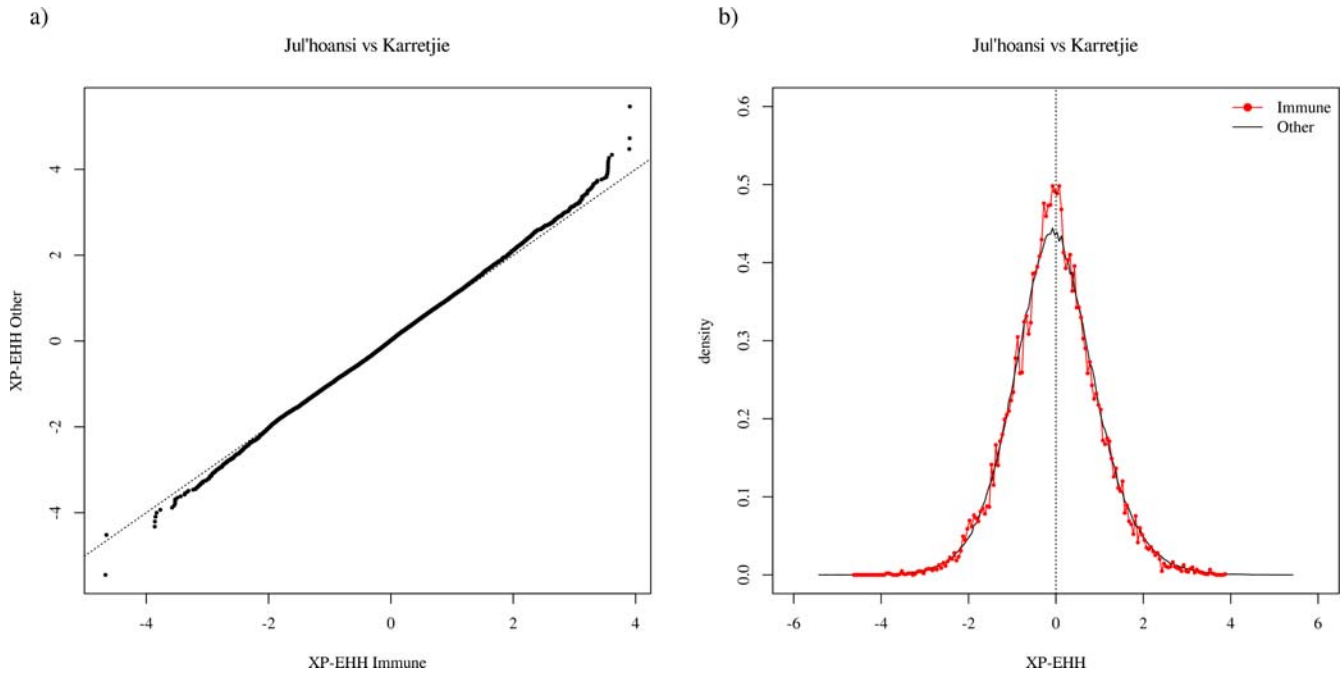
Figure S5. XP-EHH analysis for Ju/'hoansi vs Karretjie a) qq-plot SNPs in immune genes (x-axis) vs SNPs in other genes (y-axis); b) distribution at SNPs in immune genes (red) and at SNPs in other genes (black). Mean XP-EHH = -0.0371 among 20676 SNPs in immune genes and mean XP-EHH = -0.0194 among 648051 SNPs in other genes, p = 0.00938 based on the Student's t-test.
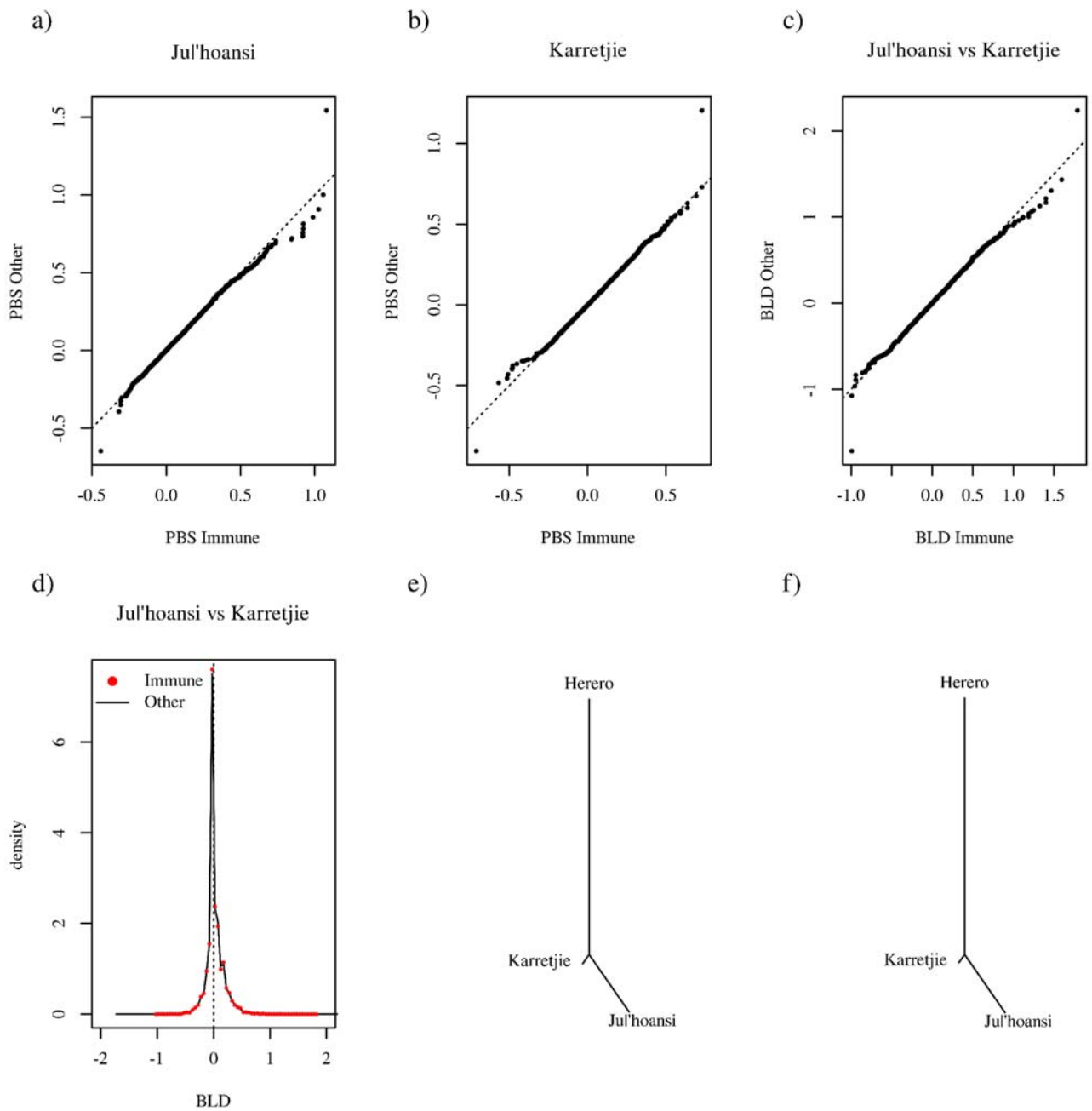
Figure S6. PBS and BLD analysis for Ju|'hoansi versus Karrejie (p-values based on Mann-Whitney U-test) a) qq plot of PBS-values for SNPs in immune genes (n=19210, x-axis) and SNPs in all genes (n=611265, y-axis) in Ju|'hoansi, (mean PBS= 0.0327 among SNPs in immune genes and mean PBS = 0.0331 among SNPs in other genes, p = 0.235) b) qq plot of PBS-values for SNPs in immune genes (x-axis) and SNPs in all genes (y-axis) in ‡Khomani (mean PBS= 0.00523 among SNPs in immune genes and mean PBS = 0.00464 among SNPs in other genes, p = 0.0443) c) qq-plot for BLD-values of SNPs in immune genes (x-axis) and SNPs in all genes (y-axis) in Ju|'hoansi vs ‡Khomani (mean BLD = 0.0275 among SNPs in immune genes and mean BLD = 0.0285 among SNPs in other genes, p = 0.0815) d) distribution of BLD at SNPs in immune genes (red) and at SNPs in all genes (black) e) tree representation of PBS values for SNPs in immune genes f) tree representation of PBS values for SNPs in other genes.
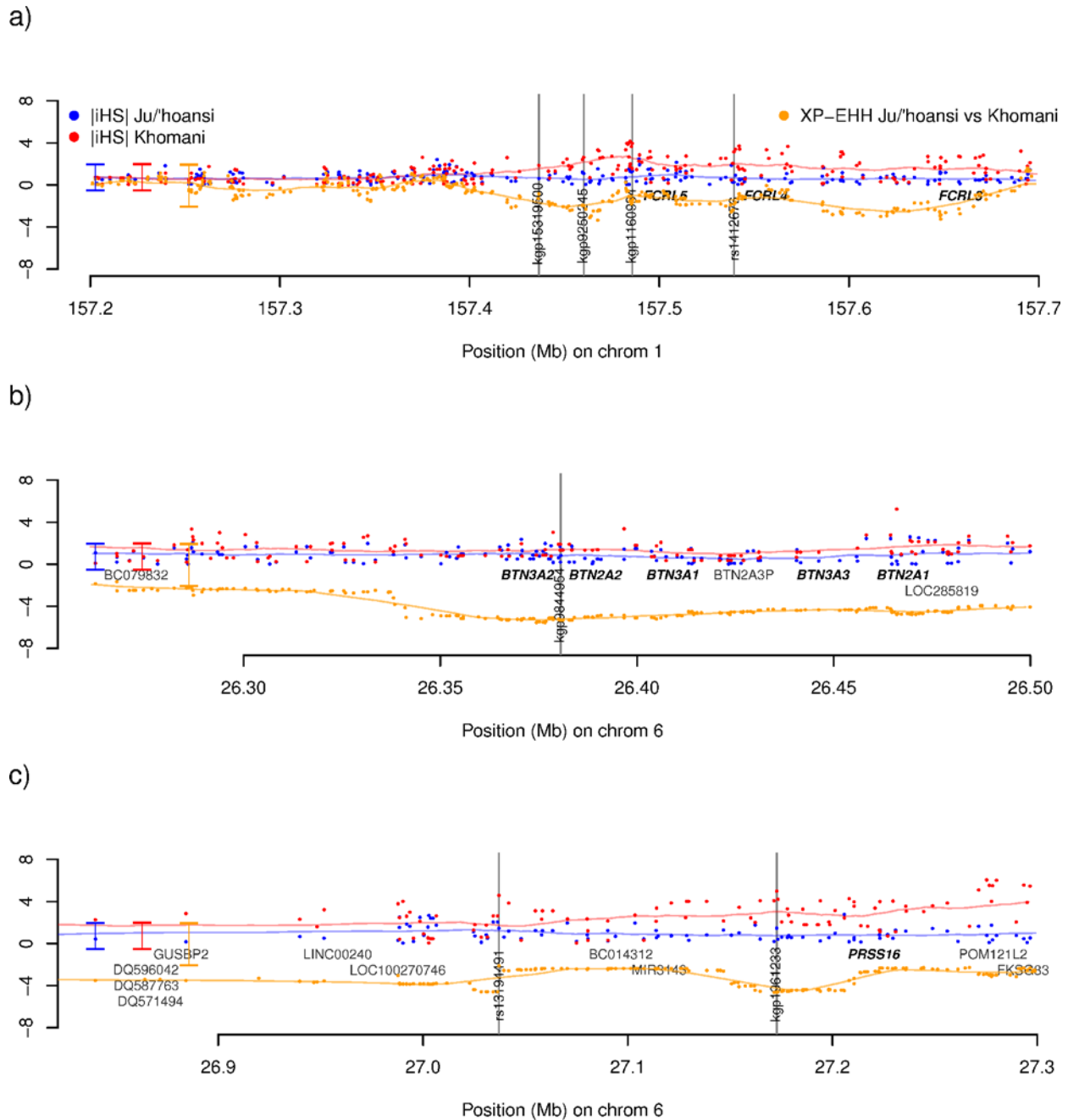
Figure S7. |iHS| values for ‡Khomani (red) and Ju|'hoansi (blue) as well as XP-EHH (orange) for these two populations are shown for each SNP (dots) and averaged over 30 SNPs (lines). The genome wide means ± 2 s.d. are indicated in the left hand of the graph. Immune genes are shown in italic and bold font. The immune genes are a) FCRL3, FCRL4 and FCRL 5 (FCRL3 is however more than 100 kb away from any of the candidate SNPs), b) the BTN family (BT2A3P is a pseudogene), c) PRSS16. There were also a large number of tRNAs and Histones in b) and c) and these have not been included.
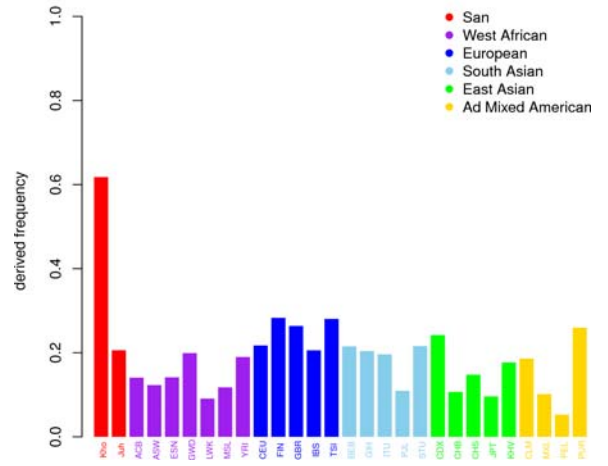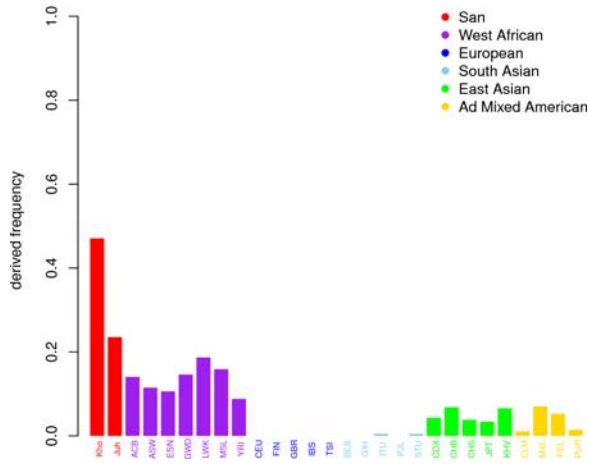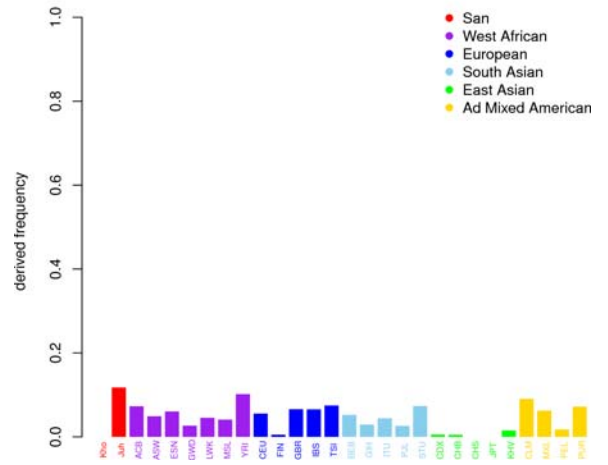
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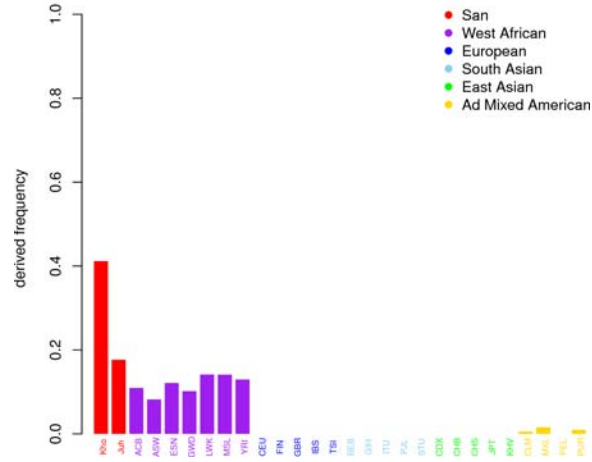
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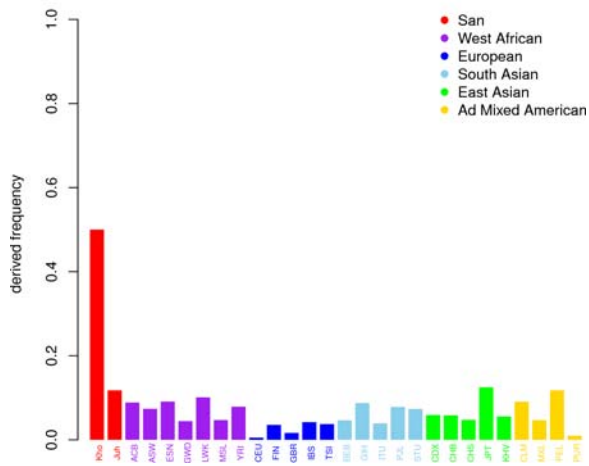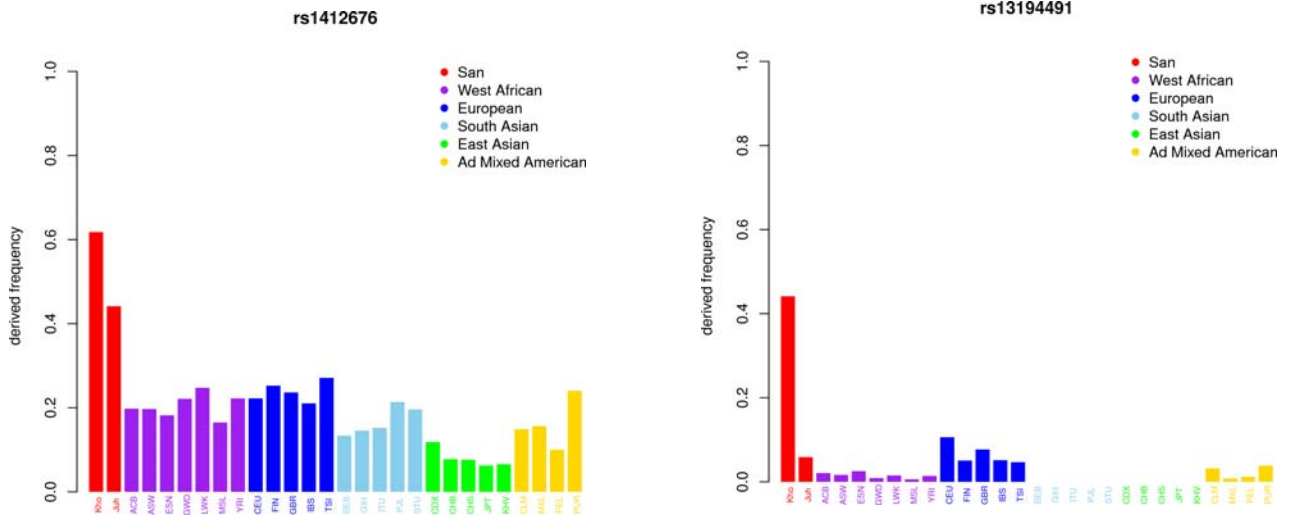

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Figure S8. Worldwide (derived) frequencies of the candidate SNPs in table 3 in the main text in populations from the 1000 genomes panel.

Table S1. The genomic blocks that appear to be driving the difference between immune SNPs and SNPs in other genes for the different statistics. The regions are ordered (within each statistic) according to how much they increase the p-value.

	Number of immune genes	Number of other genes	Immune genes
Juhoansi |iHS|			
chr6:30Mb-35MB	32	156	*includes MHC region*
Khomani |iHS|			
chr6:30Mb-35Mb	32	156	*includes MHC region*
chr3:85Mb90Mb	1	9	CADM2
chr3:145Mb-150Mb	4	21	AK309441,HPS3,WWTR1-AS1,WWTR1
chr4:50Mb-55Mb	5	11	CHIC2,LNX1,FIP1L1,PDGFRA,GSX2
Juhoansi vs Khomani XP-EHH			
chr2:25Mb-30Mb	2	77	POMC,ALK
chr4:100Mb-105Mb	2	33	PPP3CA,BANK1
Juhoansi PBS			
chr2:100Mb-105Mb	6	22	IL1RL2,IL18R1,IL1RL1,IL1R2,IL1R1,IL18RAP
chr4:100Mb-105Mb	2	33	PPP3CA,BANK1
Khomani PBS			
chr19:5Mb-10Mb	10	112	CD70,C3,FCER2,CCL25,TNFSF14,CD209,INSR,CD320,CLEC4M,FUT3
chr2:100Mb-105Mb	6	22	IL1RL2,IL18R1,IL1RL1,IL1R2,IL1R1,IL18RAP
Juhoansi vs Khomani BLD			
chr2:100Mb-105Mb	6	22	IL1RL2,IL18R1,IL1RL1,IL1R2,IL1R1,IL18RAP
chr4:100Mb-105Mb	2	33	PPP3CA,BANK1

Table S2. Precipitation and temperature differences between Askham (the town closest to the location of the sampled ‡Khomani individuals) and Tsumkwe (the town closest to the location of the sampled Ju'hoansi individuals). Based on www.worldweatheronline.com/askham-weather-averages/northern-cape/za.aspx and www.worldweatheronline.com/tsumkwe-weather-averages/otjozondjupa/na.aspx.

	Askham	Tsumkwe
Precipitation (mm)	12.61	39.2
Average rain fall (days)	0.1178	0.1589
Average Low Temperature (°C)	10.21	15.14
Average High Temperature (°C)	27.81	31.49