Supplementary Figures

Aberrant One-Carbon Metabolism and Ancestral Genetics Underlie Edematous Severe Acute Malnutrition

(Lie et. al.)

Supplementary Figure S1 – Data analysis flowchart

Supplementary Figure S2 – 2D plots of Multidimensional scaling (MDS) components 1-3

Supplementary Figure S3 – Scree plots of Proportion of Variance attributable

Supplementary Figure S4 – LocusZoom plots of top OCM loci

Supplementary Figure S5 – Minor allele frequencies and effect sizes in Jamaica and Malawi

Supplementary Figure S6 – Haploview and linkage disequilibrium (LD) plots for associated SNPs at *GABBR2* in Jamaica and Malawi

Supplementary Figure S7 – Admixture plots for African populations

Supplementary Figure S8 – Violin plots of individual ancestry proportions

Supplementary Figure S9 - Proportion of SNPs at OCM loci with absolute Standardized iHS score > 2

Supplementary Figure S10 – Density plots of Standardized iHS scores by SAM category

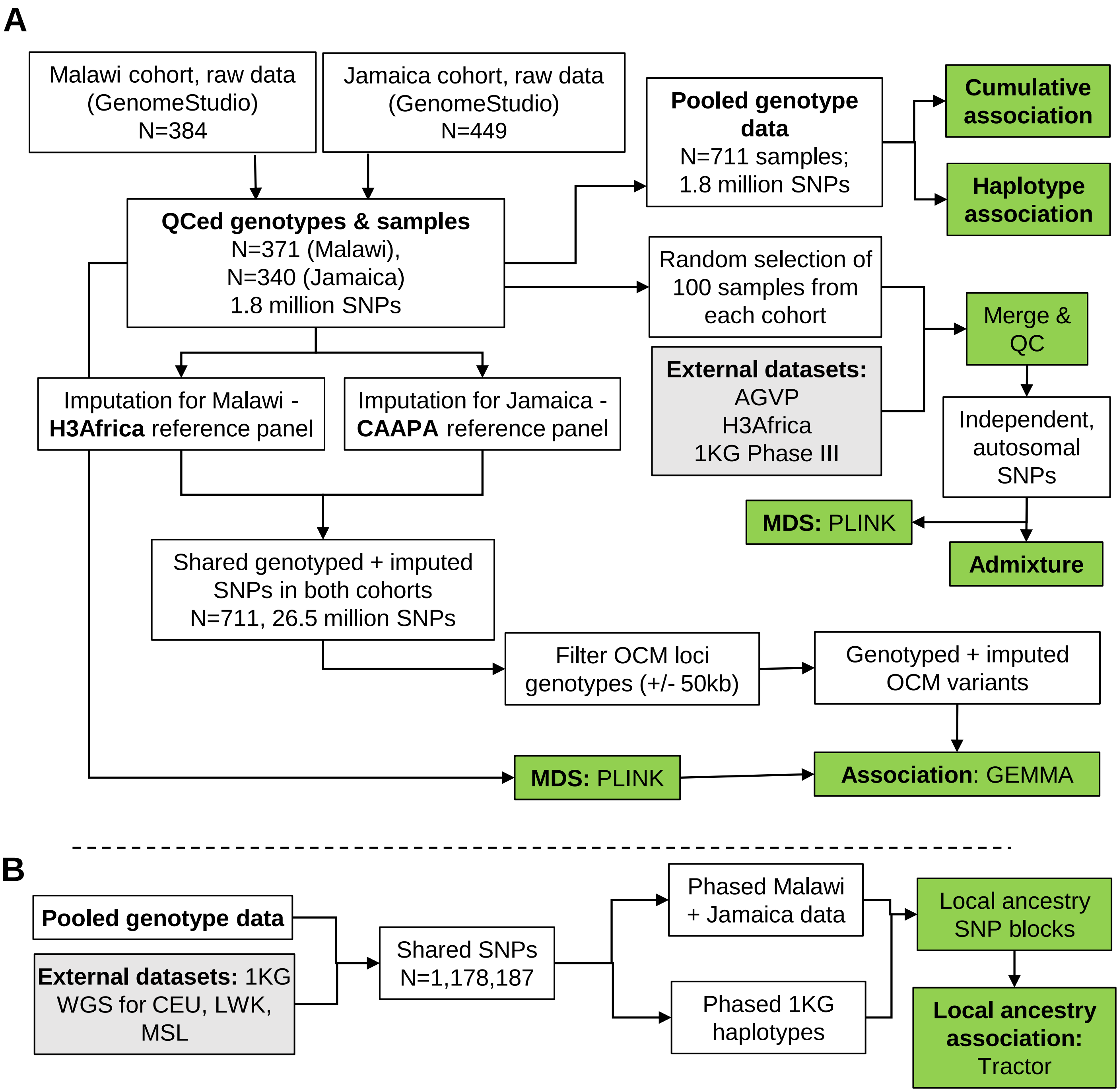

Figure S1 – Flowchart of SAM-OCM analyses. S1A – Data processing and analysis steps for genetic association tests and admixture analysis. **S1B** – Data processing and analysis steps for ancestry-adjusted association analysis. Boxes labelled as “Pooled genotype data” in S1A and S1B refer to the same set of genetic data. 1KG – 1000 Genomes Project populations; MDS – Multidimensional Scaling; QC – Quality control.

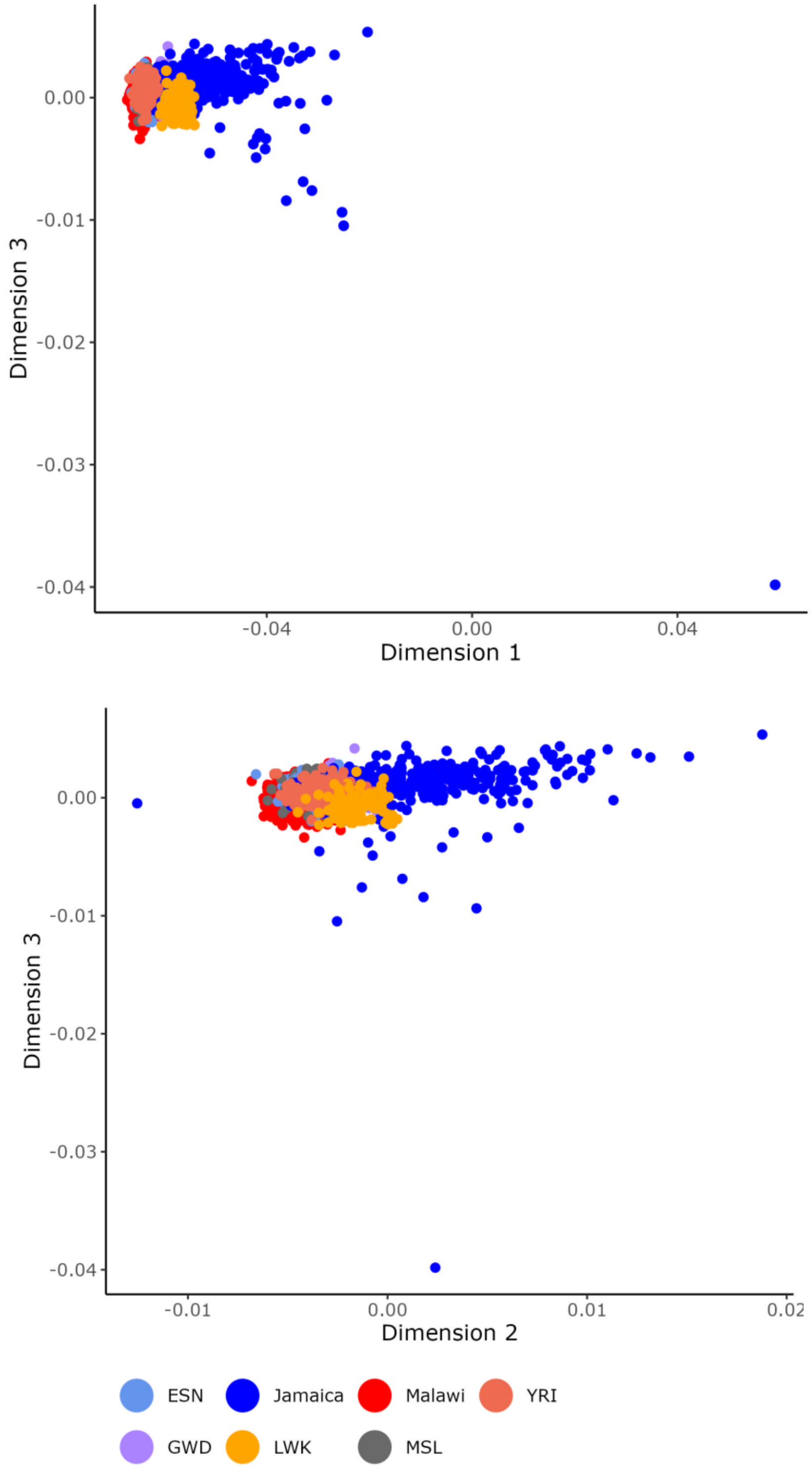

Figure S2 – 2D plots of Multidimensional scaling (MDS) Dimensions 1 to 3. Population abbreviations are per the 1000 Genomes Project: ESN – Esan in Nigeria; GWD – Gambians from Western Division; LWK – Luyha in Webuye, Kenya; MSL - Mende in Sierra Leone; YRI – Yoruba in Ibadan, Nigeria

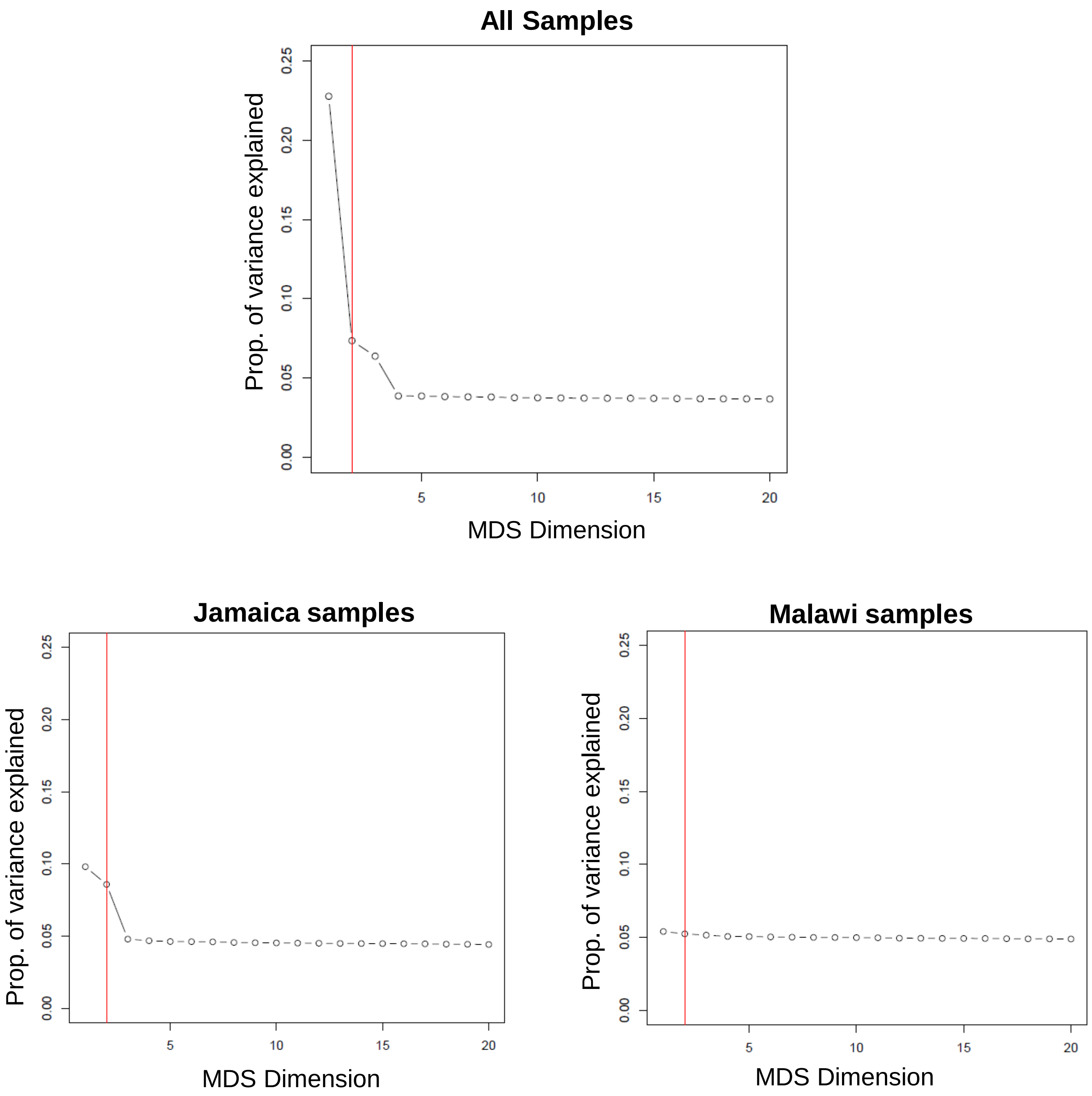

Figure S3 – Multidimensional Scaling (MDS) variance scree plots - MDS eigenvalues are calculated based on first 20 MDS dimensions and scree plots were generated for three cohorts – All samples, Jamaica samples alone and Malawi samples alone.

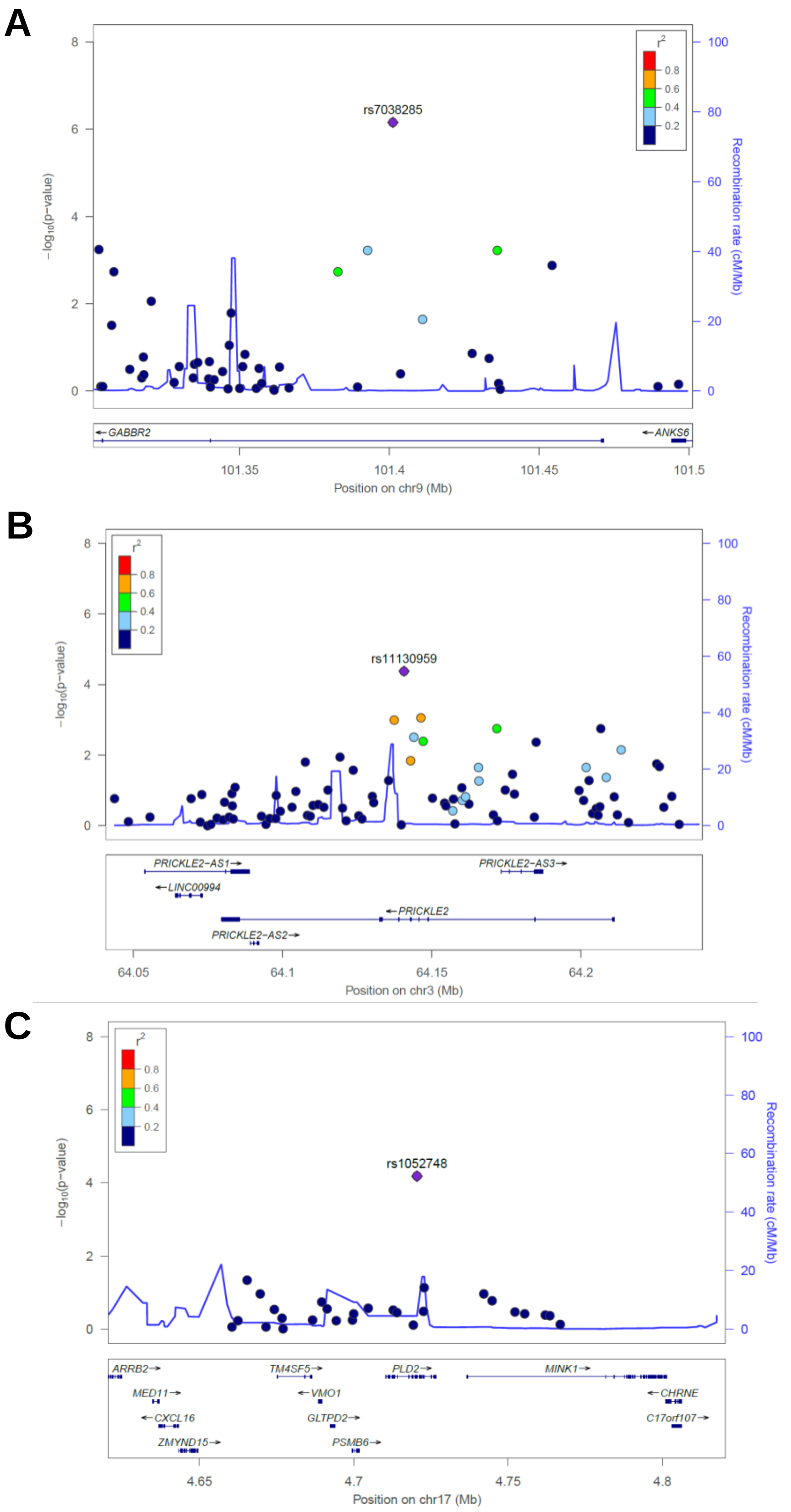

Figure S4 – LocusZoom plots of top OCM loci associated with ESAM. S1A – *GABBR2* on chromosome 9; S1B- *PRICKLE2* on chromosome 13; S1C- *PLD2* on chromosome 17. Recombination rates and LD (r^2) are given relative to 1000 AFR populations

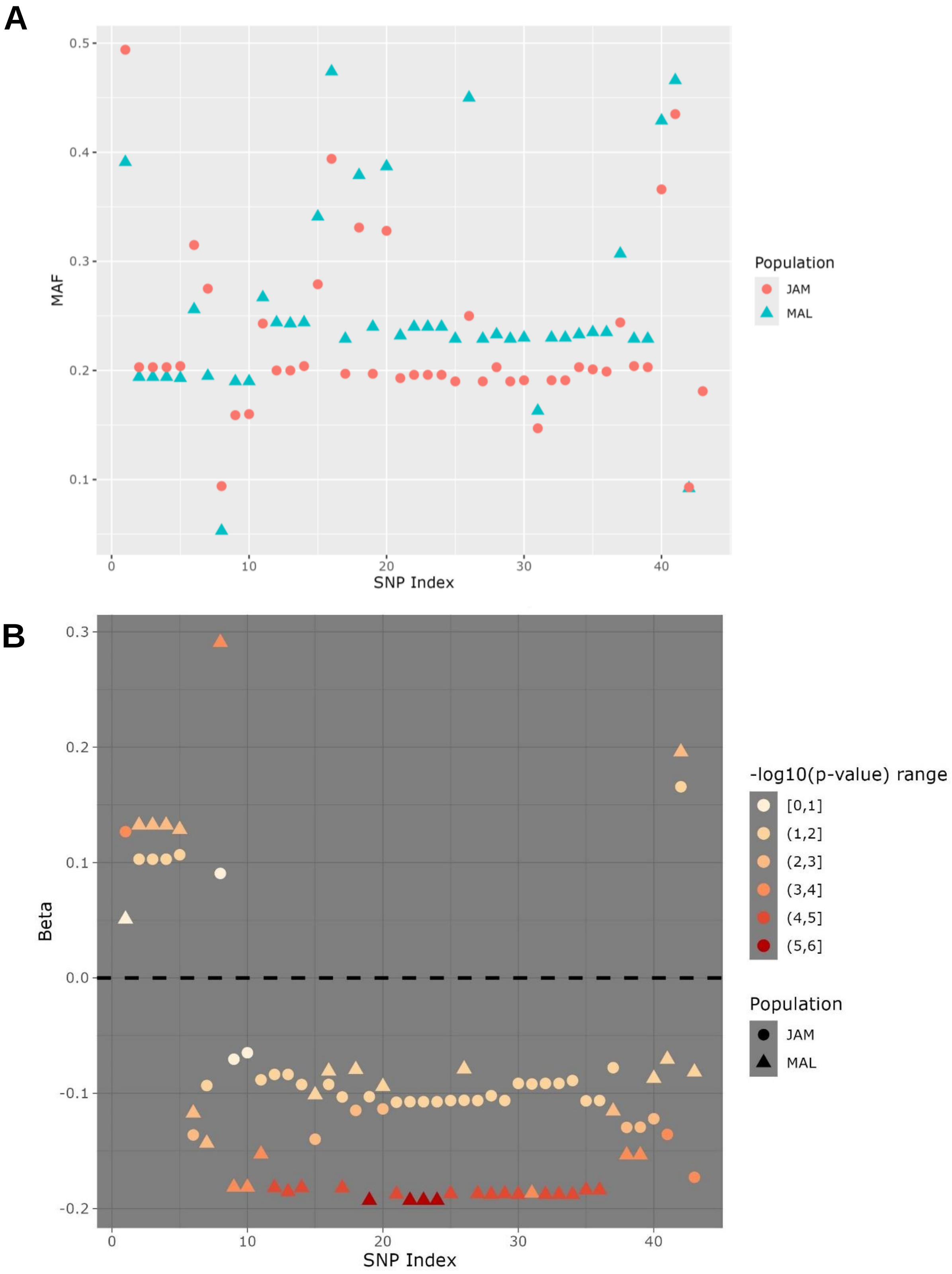

Figure S5 – Minor allele frequencies (MAF; **S5A**) and effect sizes (Beta; **S5B**) in Jamaica and Malawi for ESAM associated OCM SNPs indexed in Supplementary Tables S3 & S4.

A

REF	G C A A G
ALT	A A G G A

GABBR2

	MAF_Jam	MAF_Mal	P_Jam	P_Mal
A A G G A	0.141	0.163	0.049	7.575E-04
A C A A A	0.085	0.104	0.072	0.551
G C A A A	0.150	0.141	0.774	0.304
G C A A G	0.562	0.509	8.307E-04	0.116

B

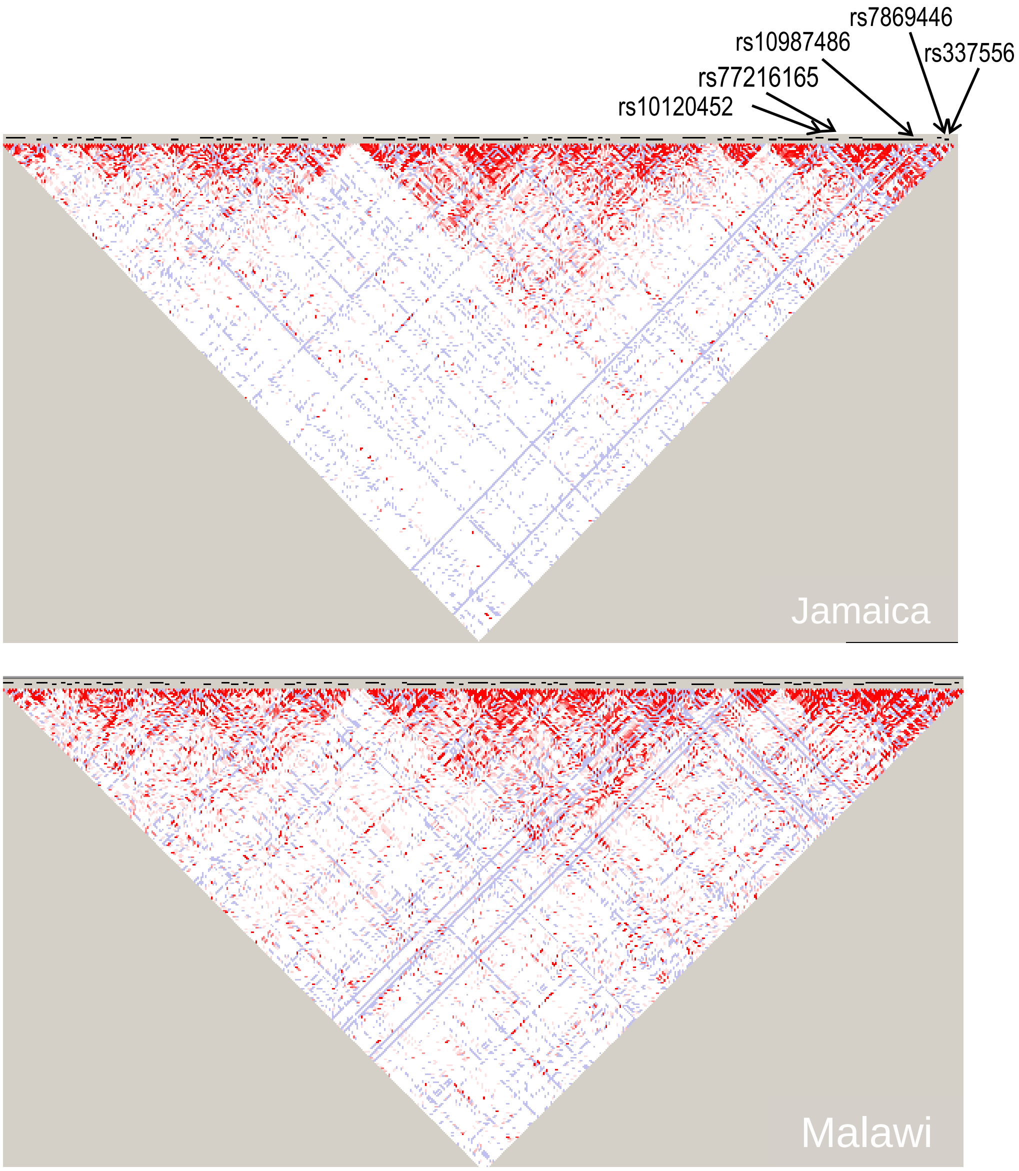

Figure S6 – Haplotype association (A) and linkage disequilibrium (LD) (B) for SNPs surpassing locus threshold at *GABBR2* in Jamaica and Malawi. Haplotype SNPs [rs10120452; rs77216165; rs10987486; rs7869446; rs337556] are as ordered from 5-prime to 3-prime. MAF – minor allele frequency. In the LD plot, SNPs are plotted on horizontal and color at intersection of two SNPs represents pairwise LD (D'), where red = D' >0.9; blue D' 0.6-0.89; white D' <0.6.

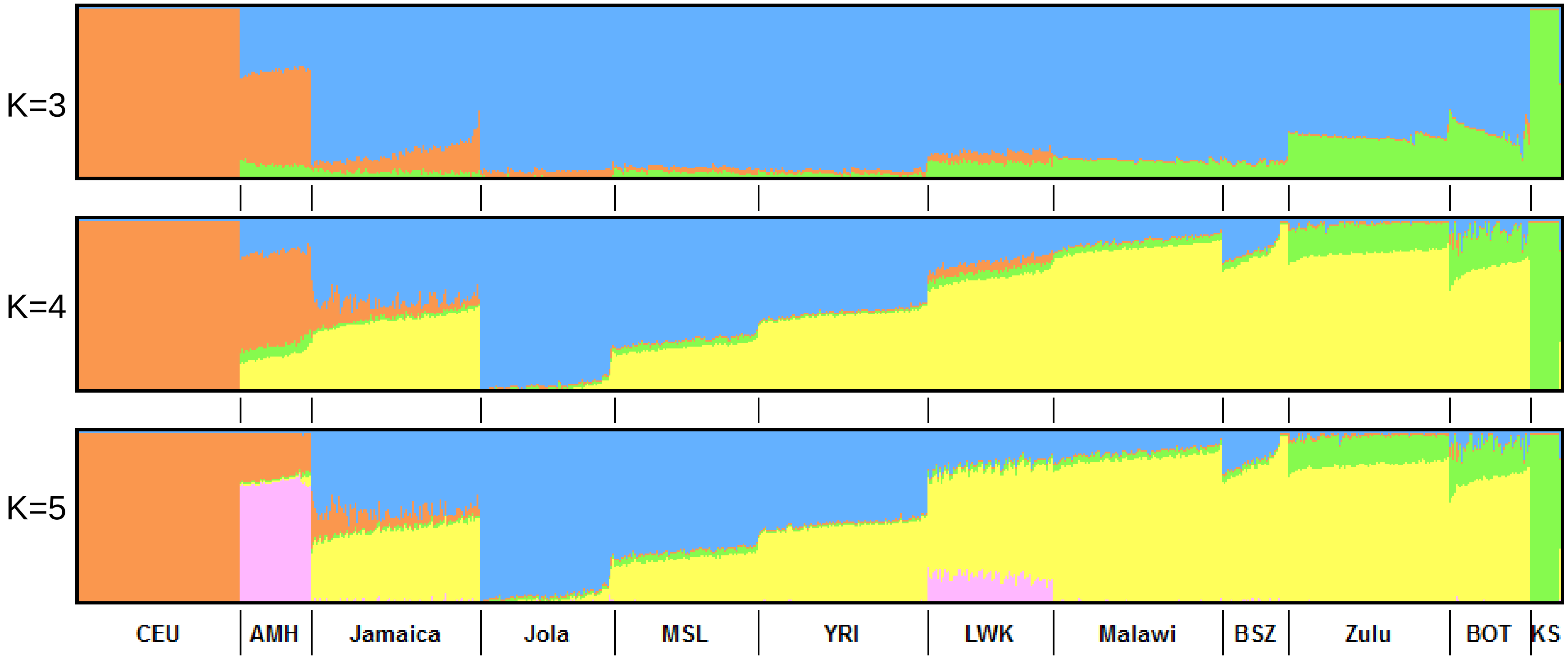

Figure S7 – Admixture plots for Jamaica and Malawi alongside potential ancestral source populations. Country codes are as given in Figure 4b. The CV error is minimized at K=5.

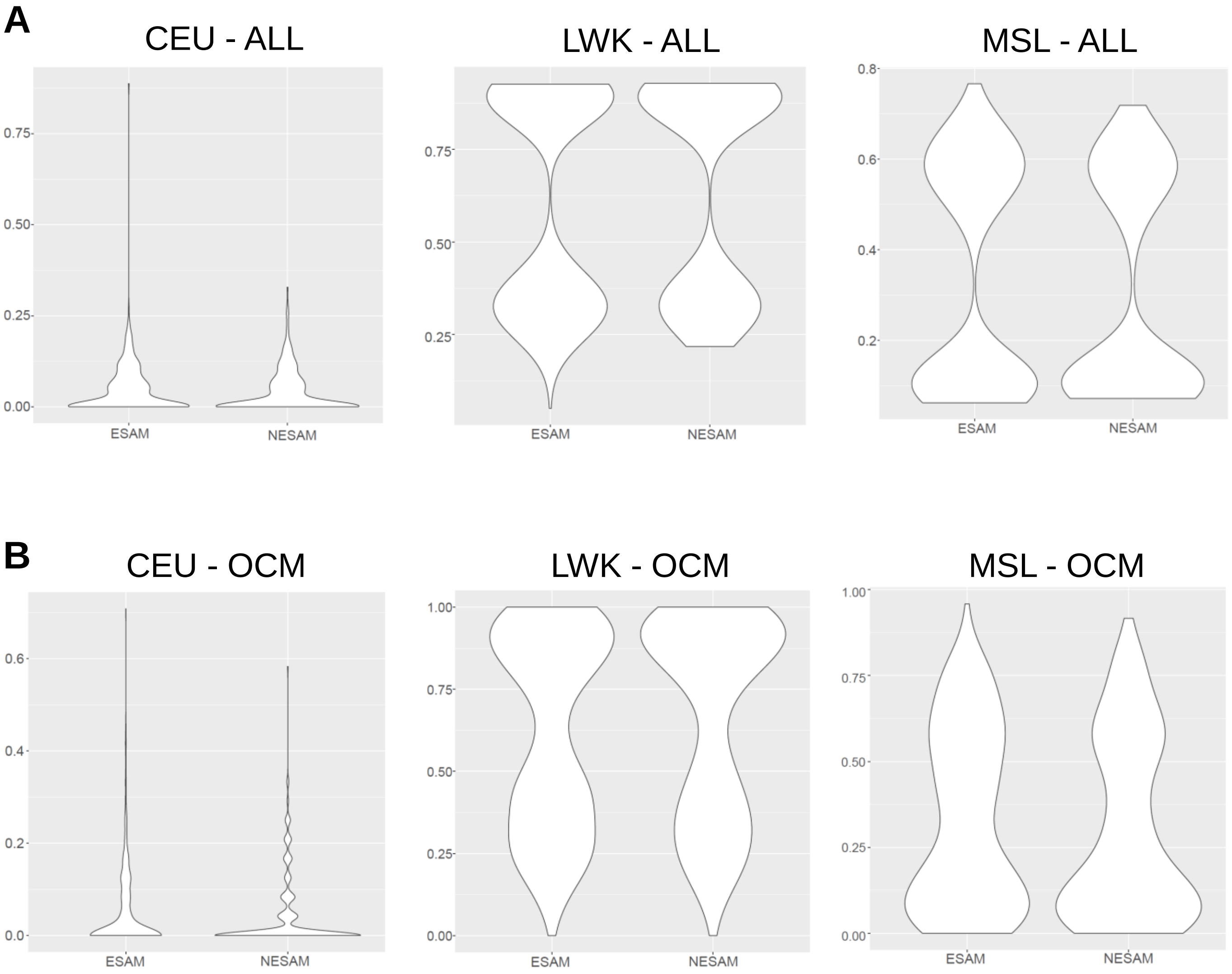

Figure S8 – Violin plots of individual ancestry proportions in ESAM and NESAM across all SNPs (**A**) and at OCM SNPs (**B**). CEU = CEPH from Utah; LWK = Luyha from Weyube, Kenya, MLS = Mende from Sierra Leone.

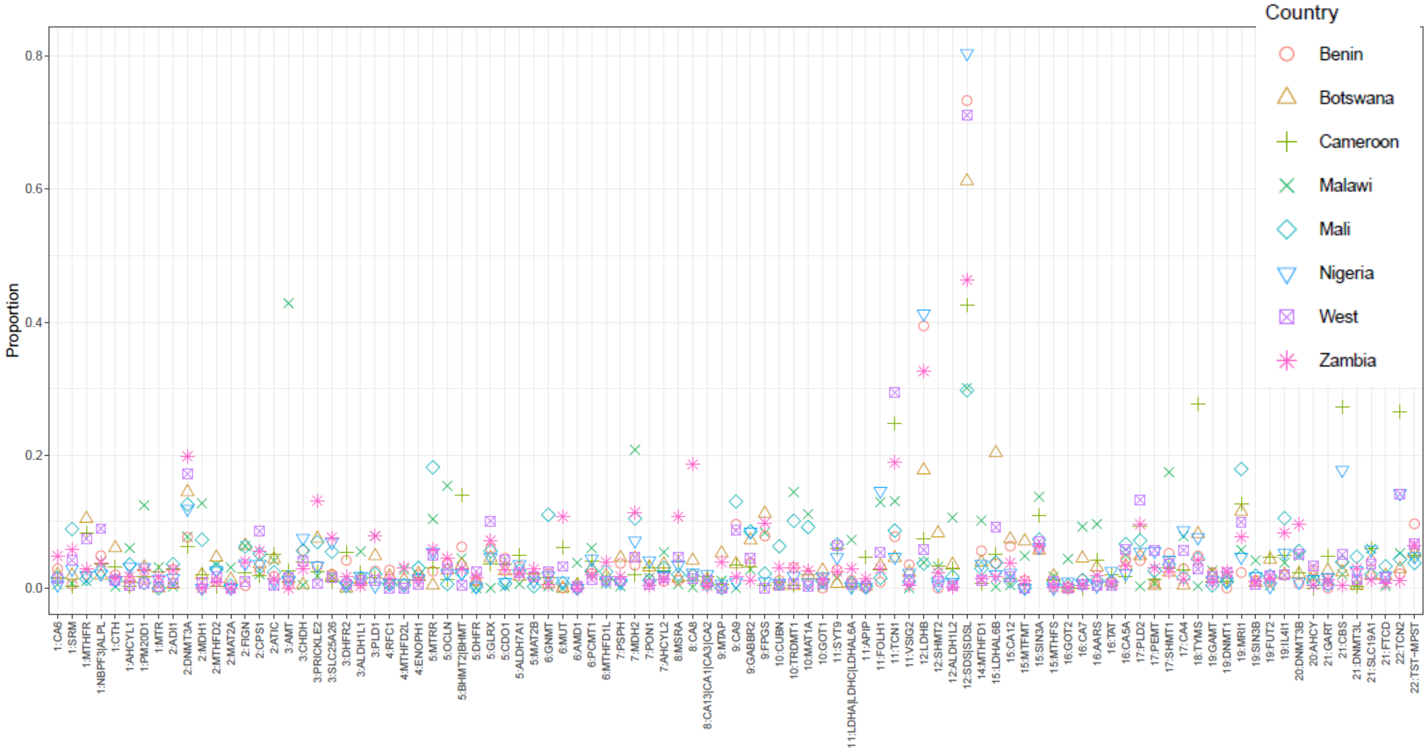

Figure S9 – Proportion of SNPs at OCM loci with absolute standardized iHS scores > 2 in H3Africa populations and among Malawi WGS cohort.

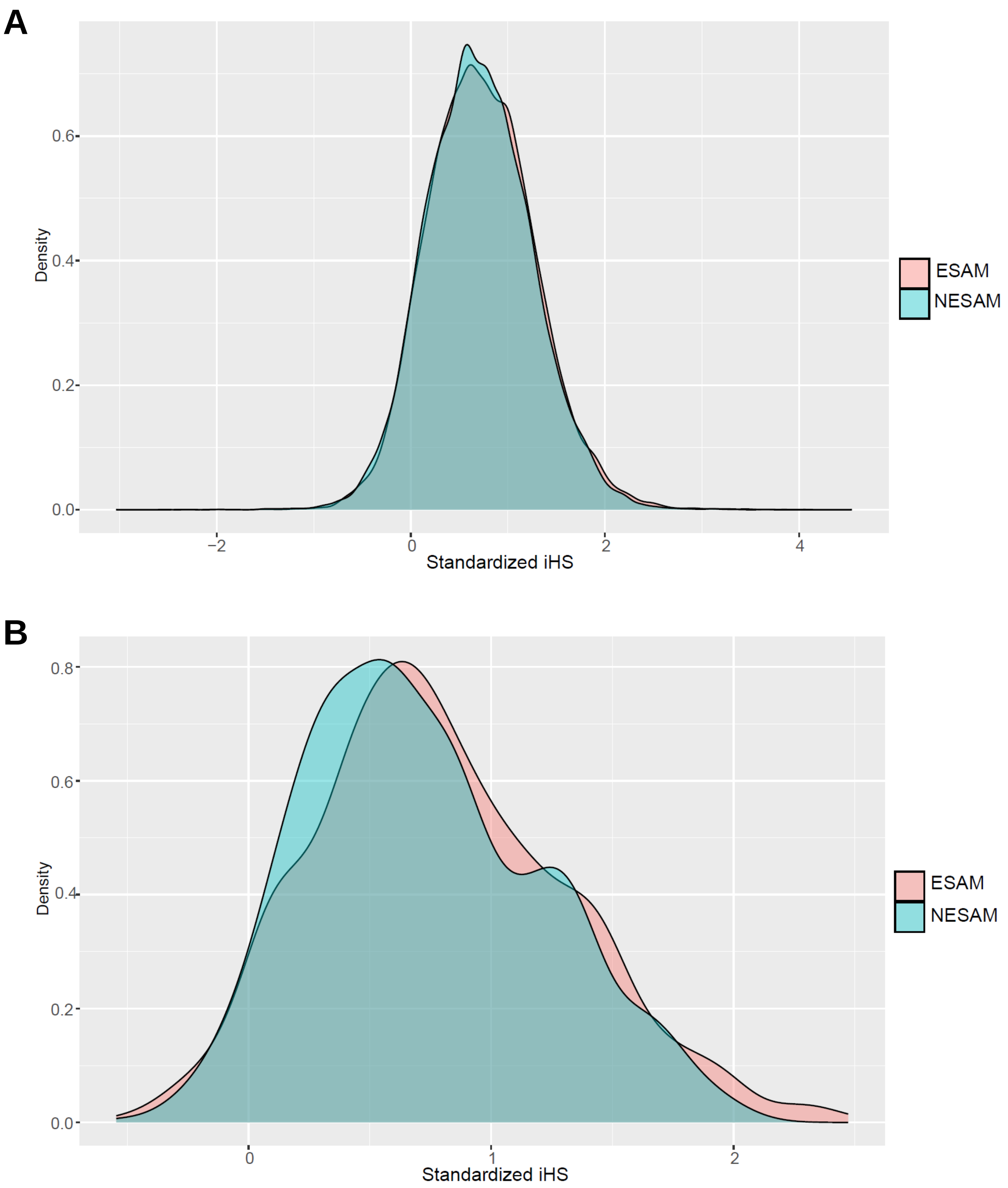

Figure S10 – Density plots of Standardized iHS scores by SAM category for all SNPs genomewide (**A**) and across OCM loci (**B**).