SUPPLEMENTARY MATERIALS

Supplementary Information 1 – FADS haplotype analysis

We are able to replicate results from Mathieson (2015), which indicate there are two LD blocks in the FADS region (Supplementary fig. 1). "Block 1" (chr11:61547000-61625000) overlaps with *FADS1* entirely and with half of *FADS2*, while "block 2" (chr11:61627000-61673000) overlaps with the other half of *FADS2* and with *FADS3* entirely. These are mostly evident in when looking at Europeans (CEU+TSI panels), but Block 1 is also present when looking at East Asians (CHB+JPT). These patterns of LD are much weaker in Africans than in Eurasians, however.

The haplotype network plots reveal interesting relationship patterns between the different haplotypes (fig. 3). Even though the Altai Neanderthal and Denisova belong to sister populations, their closest respective haplotype clusters in the region are present-day human haplotypes. In block 1, these are different present-day haplotypes: the one closest to Altai Neanderthal is largely present in Africans, while the one closest to Denisova is largely present in Americans. In block 2, the closes haplotype to both archaic humans is a South Asian haplotype. These patterns do not appear to be consistent with a simple model of introgression, however. While the haplotype structure plots show distinct haplotypes coexisting in Eurasia (fig. 2), none of the present-day human haplotypes are particularly close to the archaic human haplotypes, relative to their distance to other present-day human haplotypes (fig. 3), as observed for other, more clear, cases of adaptive introgression (Huerta-Sánchez et al. 2014, Racimo et al. 2015).

We note that the haplotype networks we obtain are also quite distinct from those obtained in Mathieson (2015), in which the haplotypes from the two archaic genomes lie in between two present-day human haplotype clusters. It is unclear to us why this may be, but we are able to recover a more similar pattern to the one in the blog post when restricting our analysis to the 20kb region around rs174546 (as Mathieson does). We note, however, that the region Mathieson used does not cover the whole physical extent of LD block 1. When using this narrower region, we observe two distinct present-day haplotype clusters, with each of the archaic genomes clustering with one of the clusters (Supplementary fig. 3). However, in this case, the archaic genomes do not lie in the branch that connects the clusters. One possible reason for the discrepancy is the inclusion of Eskimo and Papuan sequences in the Mathieson (2015) blog post, which we did not include in this study. This network is more suggestive of the time-varying positive selection model described in Mathieson (2015), which would include at least three positive selection events and an archaic introgression event in Eurasia, but could also suggest ancestral structure or long-term balancing selection in the region.

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Supplementary Information 2 - Inference of targets of selection

The present-day sequences were computationally phased using large panels by the 1000 Genomes consortium (Genomes Project, et al. 2015) and likely have quite reliable phasing. However, the low coverage ancient DNA data are more difficult to phase. In particular, the use of present-day reference panels may bias haplotype inferences to look more similar to the ones observed in present-day data, thereby introducing a potential source of bias. We instead used a likelihood model to compare present-day phased haplotypes to unphased two-locus genotypes from the ancient data. A summary of the data used in these analyses is given in Suppl. tables 1 and 2.

We implemented a likelihood model expressing the sampling probabilities of the ancient DNA two-locus genotype frequencies as functions of the present-day haplotype frequencies and a parameter modeling change in allele frequency. We compared three models:

Model 1: Selection acts to change the allele frequencies in rs174546 and the change of allele frequency in rs174594 is a secondary effect driven by linkage with rs174546.

Model 2: Selection acts to change the allele frequencies in rs174594 and the change of allele frequency in rs174546 is a secondary effect driven by linkage with rs174594.

Model 3: Selection acts on the haplotype that carries the derived allele for both rs174546 and rs174594 (DD).

The statistical model we use then first calculates the expected haplotype frequencies in the Bronze age data given the present-day haplotype frequencies and a certain change in allele frequency q. Let f_{AA}, f_{DA}, f_{AD}, and f_{DD} denote, respectively, the frequencies of ancestral/ancestral, derived/ancestral, ancestral/ derived, and derived/derived genotypes in the present-day data for SNPs rs174546/rs174594. Then for Model 1, given an increase in the derived allele frequency in rs174546 of q, the expected allele frequencies in the Bronze age data are

$$
\begin{gathered}
f_{AA}(q) = -q\, f_{AA}/(f_{AA} + f_{AD}) + f_{AA},\\
f_{AD}(q) = -q\, f_{AD}/(f_{AA} + f_{AD}) + f_{AD},\\
f_{DA}(q) = q\, f_{DA}/(f_{DA} + f_{DD}) + f_{DA},\\
f_{DD}(q) = q\, f_{DD}/(f_{DA} + f_{DD}) + f_{DD}.
\end{gathered}
$$

for $f_{AA} + f_{AD}\_ - 1 \leq q \leq f_{AA} + f_{AD}$. The Bronze Age two-locus genotype probabilities can then be calculated using standard calculations, for example the frequency of genotype (AD, AD) is 2 $f_{AA}(q)\, f_{DD}(q) + 2\, f_{DA}(q)\, f_{AD}(q)$.

The two-locus genotype probabilities can be calculated equivalently for model 2. For model 3 the haplotype probabilities are calculated as

$$
\begin{gathered}
f_{AA}(q) = q\, f_{AA}/(1 - f_{DD}) + f_{AA},\\
f_{DA}(q) = q\, f_{AD}/(1 - f_{DD}) + f_{AD},\\
f_{AD}(q) = q\, f_{DA}/(1 - f_{DD}) + f_{DA},\\
f_{DD}(q) = -q + f_{DD}.
\end{gathered}
$$

for $f_{DD} - 1 \leq q \leq f_{DD}$. The two-locus genotype probabilities are then computed from the expected haplotype probabilities using the same method as for Models 1 and 2. For each model we form a likelihood function by assuming multinomial sampling of genotypes. Notice that this approach ignores sampling variance among the present-day haplotype frequencies. We assume that the sample sizes are sufficiently large that this variance can be ignored. The likelihood values of the three different values are given below:

SI2 Table 1

Model	**Maximum log likelihood value**	**Maximum likelihood estimate of *q***
Model 1	-211.13	0.17
Model 2	-199.54	0.23
Model 3	-200.00	0.22

Notice that there is most support for Model 2 and 3. With a difference in log likelihood of 10, standard model selection criteria such as the Akaike Information Criterion would select models 2 and 3. But with a difference in log likelihood between Model 2 and 3, there is not sufficient evidence in the data to rule out Model 3 in favor of Model 2.

We also repeated the analysis using SNPs rs174594 and rs174455 to determine which of these SNPs selection most likely has acted on. In this case, the hypotheses investigated are:

Model 1: Selection acts to change the allele frequencies in rs174455 and the change of allele frequency in rs174594 is a secondary effect driven by linkage with rs174455.

Model 2: Selection acts to change the allele frequencies in rs174594 and the change of allele frequency in rs174455 is a secondary effect driven by linkage with rs174594.

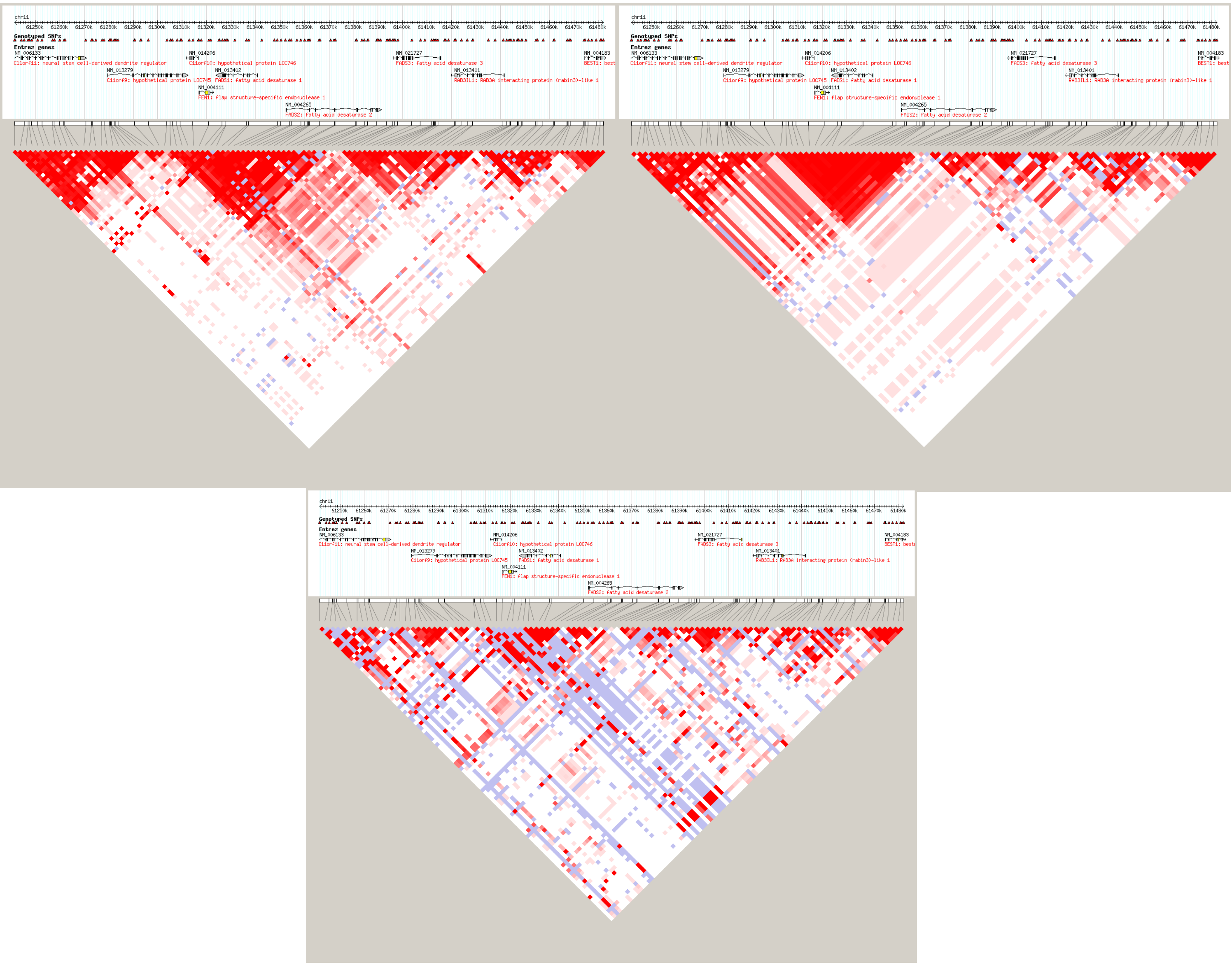
Model 3: Selection acts on the haplotype that carries the derived allele for both rs174455 and rs174594 (DD).

The likelihood values of the three different values are given below:

SI2 Table 2

Model	**Maximum log likelihood value**	**Maximum likelihood estimate of *q***
Model 1	-233.86	0.18
Model 2	-221.30	0.24
Model 3	-228.04	0.21

In this case, there is strong support for Model 2, i.e. the most likely scenario is selection acting on rs174594 with changes in rs174455 being induced by linkage disequilibrium.

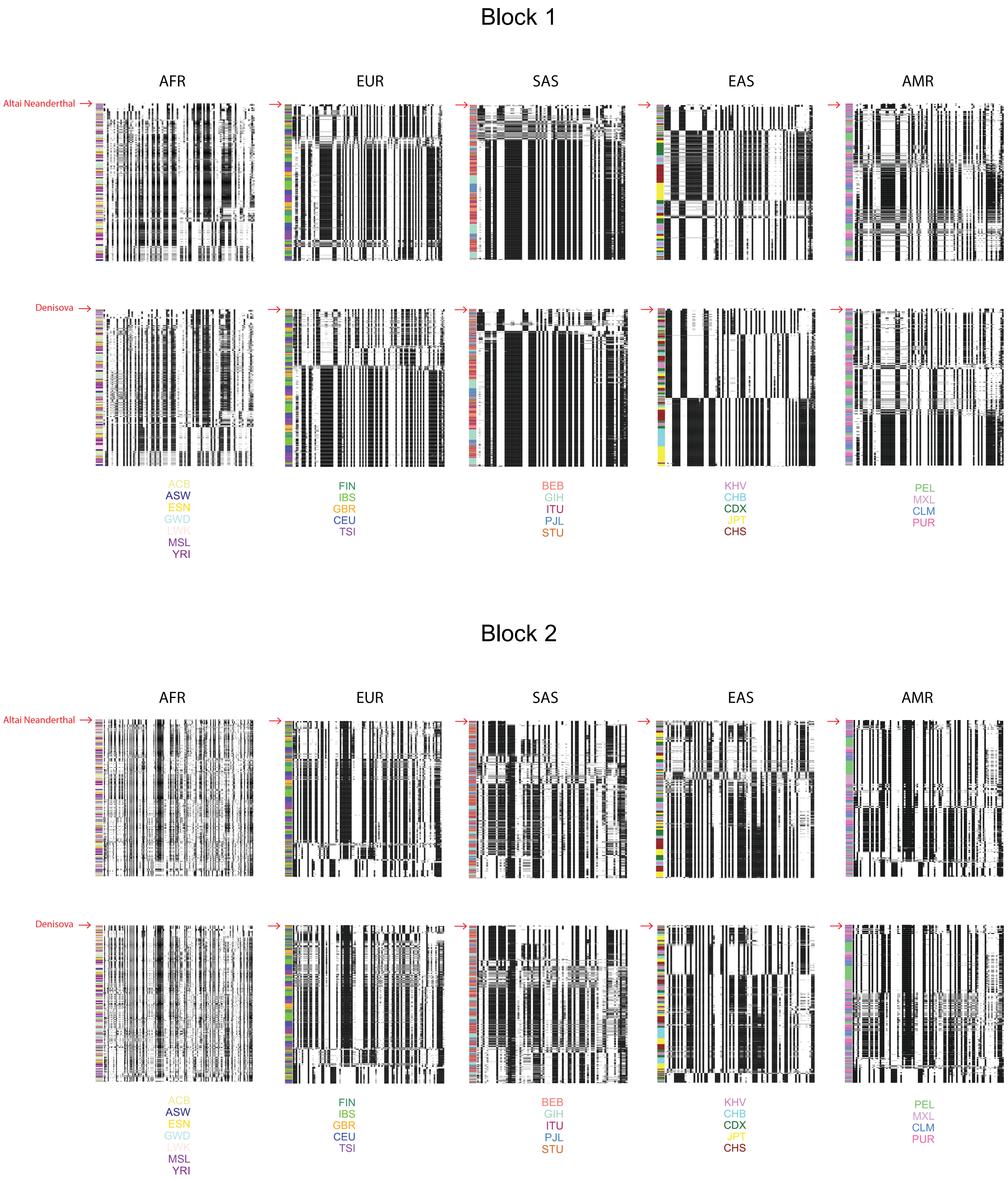


CEU+TSI

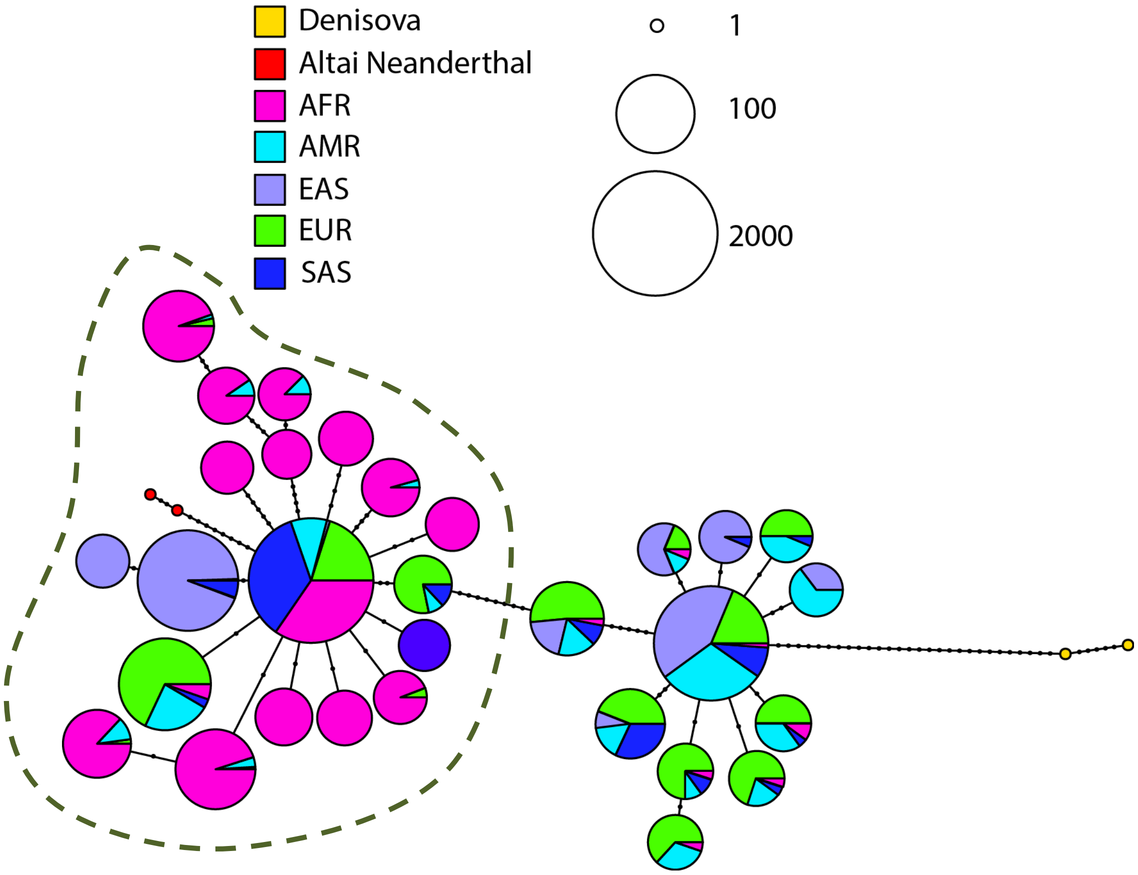
CHB+JPT

YRI

Supplementary fig. 1. Linkage disequilibrium plots for the FADS region for CEU+TSI (top left), CHB+JPT (top right) and YRI (bottom). Each colored cell corresponds to a SNP pair. For SNP pairs with LOD scores smaller than 2, values of D’ = 1 are denoted in blue, while values of D’ < 1 are denoted in white. For SNP pairs with LOD scores larger than 2, values of D’ are represented in a pink-to-red color scheme, with stronger shades of red corresponding to higher values of D’. Note that the SNP positions in the top scale of each LD plot are in hg18 coordinates.



Supplementary fig. 2. Haplotype structure plots of the two LD blocks in the *FADS* region, ordered by decreasing similarity to either the Altai Neanderthal or the Denisova genomes, for each 1000 Genomes continental panel. The SNPs within each plot were filtered for a minor allele frequency > 5%. Black squared represent derived alleles, while white squared represent ancestral alleles.



Supplementary fig. 3. Haplotype network plots of the 20kb region around rs174546 (Mathieson 2015), using the phase 3 1000 Genomes data, built using pegas (Paradis et al. 2010). The colors denote the continental populations to which each haplotype belongs. The size of the pie charts is proportional to log2(n) where n is the number of individuals carrying the haplotype. The black dots on each connecting line denote the number of differences separating each haplotype from its neighbors. The dotted line denotes the haplotype cluster in which the derived allele from rs174546 (from Mathieson's blog post) is located.

Supplementary table 1. LD between selected SNPs by 1000 Genomes Population

Variant Color Key
Lead SNP in Mathieson (2015) / Ameur (2012)
HDS from this study
Selected SNP in Inuit (Fumagalli 2015)
Lead SNP in Mathias et al (2012)
Indel from Kothapalli et al (2016)

A.

R^2 for rs373263659	Population							
Pairwise Variant	CEU	FIN	GBR	TSI	IBS	BEB	ITU	YRI
rs174546	0.271	0.373	0.229	0.082	0.161	0.767	0.661	0.049
rs174594	0.197	0.324	0.172	0.087	0.121	0.681	0.243	0.001
rs97384	0.215	0.328	0.154	0.065	0.105	0.522	0.188	0.049
rs174455	0.117	0.190	0.031	0.041	0.060	0.005	0.018	0.002
rs174465	0.100	0.142	0.042	0.036	0.089	0.000	0.016	0.1314
rs174570	0.075	0.170	0.118	0.009	0.041	0.353	0.215	0.024
rs174537	0.259	0.373	0.229	0.088	0.161	0.739	0.473	0.024

B.

R^2 for rs174537	Population							
Pairwise Variant	CEU	FIN	GBR	TSI	IBS	BEB	ITU	YRI
rs174546	0.978	1.000	1.000	0.975	1.000	0.897	0.646	1.000
rs174594	0.837	0.904	0.872	0.686	0.773	0.681	0.228	0.000
rs97384	0.762	0.864	0.830	0.648	0.706	0.522	0.210	0.001
rs174455	0.291	0.365	0.392	0.412	0.303	0.017	0.043	0.000
rs174465	0.245	0.205	0.347	0.272	0.275	0.006	0.032	0.052
rs174570	0.337	0.389	0.368	0.306	0.317	0.464	0.290	1.000
rs373263659	0.259	0.373	0.229	0.088	0.161	0.739	0.473	0.024

C.

R^2 for rs174570	Population							
Pairwise Variant	CEU	FIN	GBR	TSI	IBS	BEB	ITU	YRI
rs174546	0.345	0.389	0.368	0.313	0.317	0.544	0.449	1.000
rs174594	0.309	0.352	0.320	0.221	0.245	0.366	0.156	0.000
rs97384	0.297	0.339	0.320	0.221	0.235	0.288	0.145	0.000
rs174455	0.077	0.223	0.174	0.150	0.085	0.005	0.000	0.000
rs174465	0.038	0.037	0.084	0.032	0.021	0.003	0.003	0.052
rs174537	0.337	0.389	0.368	0.306	0.317	0.464	0.290	1.000
rs373263659	0.075	0.170	0.118	0.009	0.041	0.353	0.215	0.024

D.

R^2 for rs174546	Population							
Pairwise Variant	CEU	FIN	GBR	TSI	IBS	BEB	ITU	YRI
rs174594	0.857	0.904	0.872	0.668	0.773	0.709	0.406	0.000
rs97384	0.782	0.864	0.830	0.631	0.706	0.546	0.329	0.001
rs174455	0.277	0.365	0.392	0.397	0.303	0.007	0.008	0.000
rs174465	0.230	0.205	0.347	0.258	0.275	0.001	0.006	0.052
rs174537	0.978	1.000	1.000	0.975	1.000	0.897	0.646	1.000
rs373263659	0.271	0.373	0.229	0.082	0.161	0.767	0.661	0.049
rs174570	0.345	0.389	0.368	0.313	0.317	0.544	0.449	1.000

E.

R^2 for rs174594	Population							
Pairwise Variant	CEU	FIN	GBR	TSI	IBS	BEB	ITU	YRI
rs174546	0.857	0.904	0.872	0.668	0.773	0.709	0.406	0.000
rs97384	0.917	0.921	0.912	0.915	0.920	0.747	0.759	0.127
rs174455	0.373	0.438	0.484	0.508	0.420	0.015	0.015	0.545
rs174465	0.258	0.234	0.362	0.327	0.342	0.006	0.006	0.055
rs174537	0.837	0.904	0.872	0.686	0.773	0.681	0.228	0.000
rs373263659	0.197	0.324	0.172	0.087	0.121	0.681	0.243	0.001
rs174570	0.309	0.352	0.320	0.221	0.245	0.366	0.156	0.000

F.

R^2 for rs174455	Population							
Pairwise Variant	CEU	FIN	GBR	TSI	IBS	BEB	ITU	YRI
rs174546	0.277	0.365	0.392	0.397	0.303	0.007	0.008	0.000
rs174594	0.373	0.438	0.484	0.508	0.420	0.015	0.015	0.545
rs97384	0.405	0.435	0.484	0.508	0.446	0.001	0.022	0.261
rs174465	0.776	0.617	0.758	0.762	0.725	0.887	0.871	0.131
rs174537	0.291	0.365	0.392	0.412	0.303	0.017	0.043	0.000
rs373263659	0.117	0.190	0.031	0.041	0.060	0.005	0.018	0.002
rs174570	0.077	0.223	0.174	0.150	0.085	0.005	0.000	0.000

Supplementary table 2. Allelic heterogeneity results from CAVIAR analysis.

Gene	Tissue	Pr(no causal)	Pr(1 causal)	Pr(2 causal)	Pr(3 causal)	Pr(4 causal)	Pr(5 causal)	Pr(6 casual)
FADS1	Artery_Tibial	2.33E-03	1.84E-01	6.51E-01	1.53E-01	9.26E-03	1.97E-04	2.54E-06
FADS1	Brain_Cerebellar_Hemisphere	1.06E-04	8.25E-01	1.70E-01	4.35E-03	5.62E-05	4.91E-07	3.26E-09
FADS1	Brain_Cerebellum	4.86E-11	7.88E-01	2.05E-01	7.15E-03	1.15E-04	1.20E-06	9.21E-09
FADS1	Brain_Hippocampus	4.81E-02	9.10E-01	4.12E-02	6.76E-04	7.02E-06	5.38E-08	3.28E-10
FADS1	Brain_Putamen_basal_ganglia	1.53E-02	9.22E-01	6.11E-02	1.13E-03	1.24E-05	9.85E-08	6.12E-10
FADS1	Esophagus_Mucosa	2.12E-06	8.76E-01	1.21E-01	3.13E-03	4.17E-05	3.76E-07	2.57E-09
FADS1	Heart_Left_Ventricle	2.41E-02	9.21E-01	5.40E-02	1.02E-03	1.10E-05	8.45E-08	5.02E-10
FADS1	Muscle_Skeletal	4.29E-05	8.66E-01	1.31E-01	3.39E-03	4.61E-05	4.29E-07	3.04E-09
FADS1	Nerve_Tibial	3.34E-07	8.77E-01	1.20E-01	3.24E-03	4.68E-05	4.64E-07	3.50E-09
FADS1	Pancreas	5.23E-17	6.91E-01	2.97E-01	1.24E-02	2.71E-04	4.21E-06	5.01E-08
FADS1	Stomach	1.64E-05	9.20E-01	7.80E-02	1.83E-03	2.50E-05	2.40E-07	1.77E-09
FADS1	Testis	2.18E-02	9.27E-01	5.04E-02	9.04E-04	9.58E-06	7.29E-08	4.34E-10
FADS1	Thyroid	1.29E-02	9.05E-01	8.03E-02	2.22E-03	3.05E-05	2.81E-07	1.96E-09
FADS2	Adipose_Subcutaneous	6.67E-03	8.29E-01	1.53E-01	1.12E-02	4.29E-04	9.35E-06	1.31E-07
FADS2	Adipose_Visceral_Omentum	2.72E-02	7.20E-01	2.33E-01	1.93E-02	5.05E-04	7.37E-06	7.71E-08
FADS2	Artery_Aorta	1.02E-05	7.89E-01	2.05E-01	5.94E-03	8.14E-05	7.34E-07	4.97E-09
FADS2	Artery_Tibial	1.50E-03	8.67E-01	1.28E-01	3.02E-03	3.62E-05	2.94E-07	1.81E-09
FADS2	Breast_Mammary_Tissue	2.45E-04	5.22E-01	4.33E-01	4.35E-02	1.27E-03	1.96E-05	2.03E-07
FADS2	Cells_Transformed_fibroblasts	1.18E-27	2.31E-01	7.25E-01	4.36E-02	9.15E-04	1.20E-05	1.13E-07
FADS2	Colon_Sigmoid	1.11E-04	6.84E-01	3.03E-01	1.24E-02	2.02E-04	2.01E-06	1.43E-08
FADS2	Colon_Transverse	1.62E-15	6.36E-01	3.49E-01	1.40E-02	2.46E-04	2.85E-06	2.45E-08
FADS2	Esophagus_Gastroesophageal_Junction	1.14E-05	9.52E-01	4.68E-02	8.50E-04	9.83E-06	8.41E-08	5.69E-10
FADS2	Esophagus_Mucosa	1.52E-04	5.25E-01	4.47E-01	2.74E-02	5.95E-04	7.68E-06	7.06E-08
FADS2	Esophagus_Muscularis	3.24E-19	5.68E-01	4.08E-01	2.32E-02	4.85E-04	6.49E-06	6.41E-08
FADS2	Heart_Atrial_Appendage	1.85E-04	8.91E-01	1.07E-01	2.50E-03	3.09E-05	2.63E-07	1.71E-09
FADS2	Heart_Left_Ventricle	1.12E-09	2.21E-01	7.39E-01	3.98E-02	7.46E-04	8.16E-06	6.30E-08
FADS2	Lung	1.99E-03	8.86E-01	1.09E-01	2.68E-03	3.34E-05	2.82E-07	1.81E-09
FADS2	Muscle_Skeletal	6.71E-05	7.31E-01	2.60E-01	8.56E-03	1.23E-04	1.13E-06	7.60E-09
FADS2	Nerve_Tibial	4.22E-10	8.24E-01	1.70E-01	5.39E-03	8.43E-05	8.81E-07	6.90E-09

FADS2	Pancreas	2.10E-02	8.57E-01	1.16E-01	6.38E-03	2.16E-04	4.66E-06	6.80E-08
FADS2	Small_Intestine_Terminal_Ileum	1.00E-15	9.25E-01	7.33E-02	2.06E-03	3.73E-05	4.84E-07	4.79E-09
FADS2	Spleen	2.58E-17	8.16E-01	1.78E-01	5.11E-03	8.45E-05	9.86E-07	8.86E-09
FADS2	Stomach	5.21E-03	5.80E-01	3.67E-01	4.57E-02	2.17E-03	4.84E-05	6.23E-07
FADS2	Testis	4.94E-02	7.37E-01	2.00E-01	1.41E-02	3.55E-04	4.78E-06	4.30E-08
FADS2	Thyroid	2.29E-15	4.11E-01	5.65E-01	2.40E-02	4.29E-04	4.89E-06	4.09E-08
FADS2	Whole_Blood	2.94E-102	7.51E-09	1.79E-01	7.43E-01	7.39E-02	3.79E-03	8.43E-05
FADS3	Brain_Cerebellar_Hemisphere	1.72E-02	8.50E-01	1.30E-01	3.36E-03	4.31E-05	3.67E-07	2.35E-09
FADS3	Brain_Cerebellum	8.00E-03	9.43E-01	4.85E-02	9.17E-04	1.08E-05	9.33E-08	6.31E-10
FADS3	Esophagus_Gastroesophageal_Junction	1.53E-01	7.11E-01	1.31E-01	4.18E-03	6.61E-05	6.84E-07	5.25E-09
FADS3	Liver	2.07E-02	8.88E-01	8.86E-02	2.54E-03	3.59E-05	3.35E-07	2.34E-09
FADS3	Nerve_Tibial	1.23E-02	3.18E-01	5.08E-01	1.50E-01	1.15E-02	3.90E-04	7.41E-06

Supplementary table 2A. Complete GTEx eQTL results for 4 HDSs and rs174546**,** ordered by p-value.

Gene Symbol	SNP ID	P-Value	Effect Size	Tissue
FADS2	rs174546	4.00E-29	-0.77	Whole Blood
FADS2	rs174594	2.90E-21	-0.63	Whole Blood
FADS2	rs97384	9.30E-20	-0.62	Whole Blood
FADS1	rs174546	1.40E-15	0.73	Pancreas
FADS2	rs174546	5.80E-13	-0.26	Cells - Transformed fibroblasts
FADS1	rs174546	2.30E-12	0.72	Brain - Cerebellum
FADS2	rs174546	8.80E-12	-0.42	Thyroid
FADS2	rs174465	3.80E-11	-0.46	Whole Blood
FADS2	rs174546	3.90E-11	-0.5	Esophagus - Muscularis
FADS2	rs174455	6.20E-11	-0.45	Whole Blood
FADS2	rs174594	9.40E-11	-0.46	Esophagus - Muscularis
FADS2	rs174546	1.00E-10	-0.37	Colon - Transverse
FADS1	rs174594	1.10E-10	0.6	Pancreas
FADS2	rs97384	3.10E-10	-0.46	Esophagus - Muscularis
FADS1	rs174546	4.60E-10	0.41	Esophagus - Mucosa
FADS2	rs174594	5.50E-10	-0.21	Cells - Transformed fibroblasts
FADS1	rs97384	5.90E-10	0.6	Pancreas
FADS2	rs174546	1.20E-09	-1	Spleen
FADS1	rs174546	1.20E-09	0.37	Nerve - Tibial
FADS2	rs174546	9.20E-09	-0.38	Heart - Left Ventricle
FADS2	rs97384	1.00E-08	-0.2	Cells - Transformed fibroblasts
FADS1	rs97384	1.10E-08	0.58	Brain - Cerebellum
FADS1	rs174594	1.20E-08	0.58	Brain - Cerebellum
FADS2	rs174455	1.50E-08	-0.42	Esophagus - Muscularis
FADS2	rs174546	1.60E-08	-0.27	Muscle - Skeletal
FADS2	rs174594	1.90E-08	-0.37	Heart - Left Ventricle
FADS2	rs97384	2.50E-08	-0.32	Colon - Transverse
FADS1	rs174594	2.70E-08	0.58	Brain - Cerebellar Hemisphere
FADS1	rs97384	3.10E-08	0.2	Muscle - Skeletal
FADS2	rs174546	4.00E-08	-0.37	Nerve - Tibial
FADS2	rs174594	5.40E-08	-0.32	Thyroid
FADS1	rs174594	5.70E-08	0.19	Muscle - Skeletal

FADS2	rs174594	6.30E-08	-0.3	Colon - Transverse
FADS1	rs174546	7.60E-08	0.21	Muscle - Skeletal
FADS1	rs97384	1.00E-07	0.57	Brain - Cerebellar Hemisphere
FADS2	rs97384	1.60E-07	-0.31	Thyroid
FADS2	rs97384	1.80E-07	-0.35	Heart - Left Ventricle
FADS2	rs174594	3.30E-07	-0.33	Nerve - Tibial
FADS1	rs174546	3.40E-07	0.57	Brain - Cerebellar Hemisphere
FADS1	rs174594	4.00E-07	0.32	Esophagus - Mucosa
FADS2	rs174546	4.40E-07	-0.36	Artery - Aorta
FADS2	rs174546	4.50E-07	-0.25	Artery - Tibial
FADS2	rs174465	4.70E-07	-0.38	Esophagus - Muscularis
TMEM258	rs174546	5.20E-07	-0.2	Skin - Sun Exposed (Lower leg)
FADS1	rs174594	6.60E-07	0.29	Nerve - Tibial
FADS2	rs97384	7.30E-07	-0.33	Nerve - Tibial
FADS2	rs97384	9.40E-07	-0.5	Colon - Sigmoid
FADS2	rs174594	0.000001	-0.32	Artery - Aorta
FADS1	rs174546	0.0000013	0.33	Stomach
FADS1	rs174465	0.0000013	0.46	Pancreas
TMEM258	rs174546	0.0000017	-0.17	Artery - Tibial
FADS2	rs174594	0.000002	-0.79	Spleen
TMEM258	rs174546	0.0000042	-0.17	Cells - Transformed fibroblasts
FADS2	rs174465	0.0000045	-0.28	Thyroid
FADS1	rs97384	0.0000058	0.21	Artery - Tibial
FADS2	rs174546	0.0000063	-0.25	Lung
FADS1	rs174465	0.0000063	0.28	Nerve - Tibial
FADS2	rs174546	0.000007	-0.33	Heart - Atrial Appendage
FADS2	rs97384	0.000007	-0.3	Artery - Aorta
FADS2	rs174455	0.000007	-0.27	Thyroid
FADS2	rs174594	0.0000076	-0.2	Muscle - Skeletal
TMEM258	rs174594	0.000008	-0.15	Artery - Tibial
TMEM258	rs97384	0.0000084	-0.17	Skin - Sun Exposed (Lower leg)
TMEM258	rs174594	0.0000089	-0.15	Whole Blood
FADS1	rs97384	0.00001	0.3	Esophagus - Mucosa
FADS1	rs174546	0.000013	0.24	Thyroid
FADS1	rs174455	0.000013	0.16	Muscle - Skeletal
FADS1	rs97384	0.000021	0.26	Nerve - Tibial

Supplementary table 2B. Complete list of GTEx tissue types.

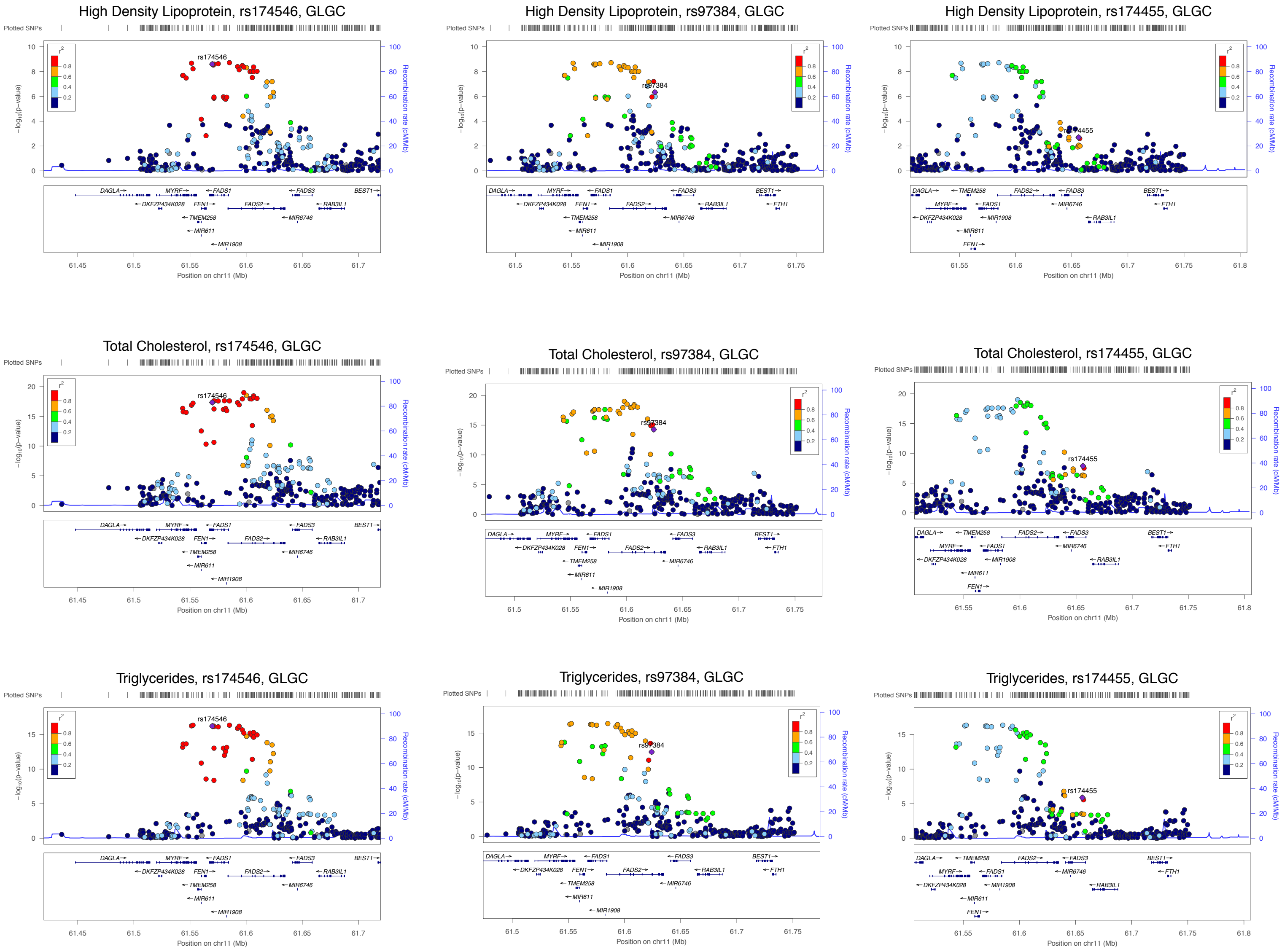
Tissue	Number of Samples
Muscle - Skeletal	361
Whole Blood	338
Skin - Sun Exposed (Lower leg)	302
Adipose - Subcutaneous	298
Artery - Tibial	285
Thyroid	278
Lung	278
Nerve - Tibial	256
Esophagus - Mucosa	241
Cells - Transformed fibroblasts	272
Skin - Not Sun Exposed (Suprapubic)	196
Esophagus - Muscularis	218
Adipose - Visceral (Omentum)	185
Artery - Aorta	197
Heart - Left Ventricle	190
Breast - Mammary Tissue	183
Colon - Transverse	169
Heart - Atrial Appendage	159
Stomach	170
Testis	157
Pancreas	149
Esophagus - Gastroesophageal Junction	127
Colon - Sigmoid	124
Adrenal Gland	126
Artery - Coronary	118
Brain - Cerebellum	103
Liver	97
Cells - EBV-transformed lymphocytes	114
Brain - Caudate (basal ganglia)	100
Brain - Cortex	96
Brain - Nucleus accumbens (basal ganglia)	93
Brain - Frontal Cortex (BA9)	92

Prostate	87
Brain - Cerebellar Hemisphere	89
Spleen	89
Pituitary	87
Brain - Putamen (basal ganglia)	82
Ovary	85
Brain - Hypothalamus	81
Vagina	79
Brain - Hippocampus	81
Small Intestine - Terminal Ileum	77
Brain - Anterior cingulate cortex (BA24)	72
Uterus	70
Brain - Amygdala	62
Brain - Spinal cord (cervical c-1)	59
Brain - Substantia nigra	56
Minor Salivary Gland	51
Kidney - Cortex	26
Bladder	11
Cervix - Ectocervix	6
Fallopian Tube	6
Cervix - Endocervix	5

Supplementary table 3. Functional Characterization of HDSs

SNP	Ref.	Anc.	CADD Score (Raw)	GERP Score	SEGWAY	WashU Epigenomics Browser
rs174546	C	T	1.259214	4.54	GS (Gene Body, Start)	In intron of FADS1
rs174594	C	C	0.123898	0.546	TF1 (transcription factor activity)	In intron of FADS2
rs97384	T	T	0.128068	2.21	GM0 (Gene Body, Middle)	In intron of FADS2
rs174455	G	G	-0.128837	3.6	GM1 (Gene Body, Middle)	In enhancer / flanking active TSS region of FADS3 (TSS for adipose, muscle, osteoblast and ventricle tissues)
rs174465	C	C	1.908472	3.01	GS (Gene Body, Start)	In Promoter region of FADS3

Supplementary fig. 4. Additional LocusZoom plots of GLGC data for High Density Lipoproteins, Total Cholesterol, and Triglycerides.



High Density Lipoprotein, rs174546, GLGC

High Density Lipoprotein, rs97384, GLGC

High Density Lipoprotein, rs174455, GLGC

Total Cholesterol, rs174546, GLGC

Total Cholesterol, rs97384, GLGC

Total Cholesterol, rs174455, GLGC

Triglycerides, rs174546, GLGC

Triglycerides, rs97384, GLGC

Triglycerides, rs174455, GLGC

Supplementary table 5A. Extended Results – Top 100 Associations from AdditionPRO Metabolomics Phenotypes. 3 SNPs, 231 Different Phenotypes, 3 time points (30min, 120min, fasting) tested.

SNP ID	P-Value	Effect Size	Phenotype Code
rs174546	2.71E-13	-0.924	fasting LA/FA
rs174546	2.98E-13	-0.9114	30min LA/FA
rs174594	9.16E-13	-0.9418	fasting LA/FA
rs174546	2.7E-12	0.02137	120min UnSat
rs174546	4.44E-12	-0.8802	120min LA/FA
rs174594	4.72E-12	-0.902	30min LA/FA
rs174594	2.43E-11	-0.8874	120min LA/FA
rs174594	8.77E-10	0.01948	120min UnSat
rs174546	9.7E-10	0.01726	fasting UnSat
rs174546	9.85E-10	0.01749	30min UnSat
rs174594	0.000000114	0.01574	30min UnSat
rs174594	0.000000129	0.01543	fasting UnSat
rs174455	0.00000416	-0.6264	fasting LA/FA
rs174594	0.00000456	-0.1031	30min LA
rs174594	0.0000161	-0.09642	fasting LA
rs174594	0.0000199	-0.09301	120min LA
rs174546	0.0000246	-0.09309	30min LA
rs174546	0.000028	-0.08965	120min LA
rs174546	0.0000282	0.2872	30min SFA/FA
rs174455	0.0000332	-0.5705	120min LA/FA
rs174594	0.0000372	0.2918	30min SFA/FA
rs174455	0.0000419	-0.5543	30min LA/FA
rs174546	0.000053	-0.08883	fasting LA
rs174594	0.0000974	0.276	fasting SFA/FA
rs174546	0.0001172	0.2642	fasting SFA/FA
rs174455	0.0001232	0.01292	120min UnSat
rs174594	0.0001967	0.2667	120min SFA/FA
rs174546	0.0002593	0.2518	120min SFA/FA
rs174594	0.0004326	1.257	120min XL-HDL-PL_%
rs174594	0.0006381	1.054	fasting XL-HDL-PL_%
rs174594	0.0006383	-1.031	120min XL-HDL-CE_%
rs174594	0.0007008	-1.019	120min XL-HDL-C_%

rs174455	0.0008194	0.01039	30min UnSat
rs174546	0.001074	0.9723	fasting XL-HDL-PL_%
rs174546	0.001087	1.122	120min XL-HDL-PL_%
rs174594	0.001586	-0.8159	fasting XL-HDL-C_%
rs174546	0.001679	0.04112	fasting HDL-C
rs174594	0.001965	-0.8049	fasting XL-HDL-CE_%
rs174546	0.00215	5.81E-08	fasting L-HDL-P
rs174546	0.0022	0.03724	fasting L-HDL-L
rs174546	0.002234	0.01496	fasting L-HDL-CE
rs174546	0.002282	0.01975	fasting L-HDL-C
rs174546	0.002387	0.004811	fasting L-HDL-FC
rs174546	0.002398	0.01648	fasting L-HDL-PL
rs174546	0.002443	-0.8787	120min XL-HDL-CE_%
rs174546	0.00266	0.03962	120min HDL-C
rs174546	0.002844	-0.8629	120min XL-HDL-C_%
rs174455	0.003284	-0.07057	30min LA
rs174594	0.00331	-0.2309	30min L-HDL-PL_%
rs174546	0.003578	0.04165	fasting TotPG
rs174546	0.003689	0.03428	fasting HDL2-C
rs174546	0.003751	-0.7215	fasting XL-HDL-C_%
rs174546	0.003925	-0.2557	120min XL-HDL-TG_%
rs174455	0.004141	0.008717	fasting UnSat
rs174455	0.004533	-0.06631	120min LA
rs174594	0.004613	0.928	30min XL-HDL-PL_%
rs174546	0.004664	0.02327	fasting ApoA1
rs174546	0.004685	-0.7087	fasting XL-HDL-CE_%
rs174546	0.004752	-0.2471	30min XL-HDL-TG_%
rs174546	0.004882	0.02601	fasting HDL-D
rs174546	0.005003	0.03347	120min HDL2-C
rs174546	0.00526	0.005929	fasting HDL3-C
rs174546	0.005349	-0.2492	fasting XL-HDL-TG_%
rs174546	0.005391	0.001039	fasting L-HDL-TG
rs174594	0.005415	0.3881	30min L-HDL-C_%
rs174546	0.005434	0.01399	120min L-HDL-CE
rs174546	0.005483	-0.2086	30min L-HDL-PL_%
rs174546	0.005488	0.3695	30min L-HDL-C_%
rs174546	0.005504	0.0185	120min L-HDL-C
rs174546	0.005522	0.008083	fasting M-HDL-PL
rs174546	0.005691	0.002096	fasting M-HDL-FC
rs174546	0.005772	0.004516	120min L-HDL-FC
rs174546	0.005782	0.03761	fasting PC
rs174546	0.005913	0.03439	120min L-HDL-L
rs174546	0.006021	5.34E-08	120min L-HDL-P

rs174546	0.006098	0.01521	120min L-HDL-PL
rs174594	0.006237	-0.2466	30min XL-HDL-TG_%
rs174455	0.006545	-0.8344	120min XL-HDL-C_%
rs174594	0.006903	0.2839	30min L-HDL-CE_%
rs174455	0.007151	0.9929	120min XL-HDL-PL_%
rs174546	0.00749	-0.1436	120min VLDL-D
rs174546	0.007627	0.2678	30min L-HDL-CE_%
rs174546	0.008026	0.0118	fasting XL-HDL-PL
rs174546	0.008188	0.03861	fasting TotCho
rs174455	0.008203	-0.814	120min XL-HDL-CE_%
rs174546	0.00843	-0.351	120min MUFA/FA
rs174455	0.008509	-0.0627	fasting LA
rs174455	0.009005	0.8415	fasting XL-HDL-PL_%
rs174546	0.009173	0.01674	fasting M-HDL-L
rs174546	0.009422	3.85E-08	fasting M-HDL-P
rs174546	0.00944	0.09985	30min L-HDL-FC_%
rs174546	0.009514	0.003933	120min S-HDL-C
rs174546	0.009583	0.02636	120min HDL-D
rs174594	0.009893	-0.236	120min XL-HDL-TG_%
rs174546	0.01005	-0.02059	120min M-VLDL-TG
rs174594	0.01028	-0.2361	fasting XL-HDL-TG_%
rs174546	0.01055	0.05052	fasting M-HDL-FC_%
rs174546	0.01062	0.01155	120min XL-HDL-PL
rs174546	0.0107	0.02108	120min ApoA1
rs174546	0.01079	0.007016	120min M-HDL-PL

Supplementary table 5B. Phenotype Full Descriptions and Phenotype Codes

Phenotype Full Description	Phenotype Code
Concentration of chylomicrons and extremely large VLDL particles	XXL-VLDL-P
Total lipids in chylomicrons and extremely large VLDL	XXL-VLDL-L
Phospholipids in chylomicrons and extremely large VLDL	XXL-VLDL-PL
Total cholesterol in chylomicrons and extremely large VLDL	XXL-VLDL-C
Cholesterol esters in chylomicrons and extremely large VLDL	XXL-VLDL-CE
Free cholesterol in chylomicrons and extremely large VLDL	XXL-VLDL-FC
Triglycerides in chylomicrons and extremely large VLDL	XXL-VLDL-TG
Concentration of very large VLDL particles	XL-VLDL-P
Total lipids in very large VLDL	XL-VLDL-L
Phospholipids in very large VLDL	XL-VLDL-PL
Total cholesterol in very large VLDL	XL-VLDL-C
Cholesterol esters in very large VLDL	XL-VLDL-CE
Free cholesterol in very large VLDL	XL-VLDL-FC
Triglycerides in very large VLDL	XL-VLDL-TG
Concentration of large VLDL particles	L-VLDL-P
Total lipids in large VLDL	L-VLDL-L
Phospholipids in large VLDL	L-VLDL-PL
Total cholesterol in large VLDL	L-VLDL-C
Cholesterol esters in large VLDL	L-VLDL-CE
Free cholesterol in large VLDL	L-VLDL-FC
Triglycerides in large VLDL	L-VLDL-TG
Concentration of medium VLDL particles	M-VLDL-P
Total lipids in medium VLDL	M-VLDL-L
Phospholipids in medium VLDL	M-VLDL-PL
Total cholesterol in medium VLDL	M-VLDL-C
Cholesterol esters in medium VLDL	M-VLDL-CE
Free cholesterol in medium VLDL	M-VLDL-FC
Triglycerides in medium VLDL	M-VLDL-TG
Concentration of small VLDL particles	S-VLDL-P
Total lipids in small VLDL	S-VLDL-L
Phospholipids in small VLDL	S-VLDL-PL
Total cholesterol in small VLDL	S-VLDL-C
Cholesterol esters in small VLDL	S-VLDL-CE
Free cholesterol in small VLDL	S-VLDL-FC

Triglycerides in small VLDL	S-VLDL-TG
Concentration of very small VLDL particles	XS-VLDL-P
Total lipids in very small VLDL	XS-VLDL-L
Phospholipids in very small VLDL	XS-VLDL-PL
Total cholesterol in very small VLDL	XS-VLDL-C
Cholesterol esters in very small VLDL	XS-VLDL-CE
Free cholesterol in very small VLDL	XS-VLDL-FC
Triglycerides in very small VLDL	XS-VLDL-TG
Concentration of IDL particles	IDL-P
Total lipids in IDL	IDL-L
Phospholipids in IDL	IDL-PL
Total cholesterol in IDL	IDL-C
Cholesterol esters in IDL	IDL-CE
Free cholesterol in IDL	IDL-FC
Triglycerides in IDL	IDL-TG
Concentration of large LDL particles	L-LDL-P
Total lipids in large LDL	L-LDL-L
Phospholipids in large LDL	L-LDL-PL
Total cholesterol in large LDL	L-LDL-C
Cholesterol esters in large LDL	L-LDL-CE
Free cholesterol in large LDL	L-LDL-FC
Triglycerides in large LDL	L-LDL-TG
Concentration of medium LDL particles	M-LDL-P
Total lipids in medium LDL	M-LDL-L
Phospholipids in medium LDL	M-LDL-PL
Total cholesterol in medium LDL	M-LDL-C
Cholesterol esters in medium LDL	M-LDL-CE
Free cholesterol in medium LDL	M-LDL-FC
Triglycerides in medium LDL	M-LDL-TG
Concentration of small LDL particles	S-LDL-P
Total lipids in small LDL	S-LDL-L
Phospholipids in small LDL	S-LDL-PL
Total cholesterol in small LDL	S-LDL-C
Cholesterol esters in small LDL	S-LDL-CE
Free cholesterol in small LDL	S-LDL-FC
Triglycerides in small LDL	S-LDL-TG
Concentration of very large HDL particles	XL-HDL-P
Total lipids in very large HDL	XL-HDL-L
Phospholipids in very large HDL	XL-HDL-PL
Total cholesterol in very large HDL	XL-HDL-C
Cholesterol esters in very large HDL	XL-HDL-CE
Free cholesterol in very large HDL	XL-HDL-FC
Triglycerides in very large HDL	XL-HDL-TG

Concentration of large HDL particles	L-HDL-P
Total lipids in large HDL	L-HDL-L
Phospholipids in large HDL	L-HDL-PL
Total cholesterol in large HDL	L-HDL-C
Cholesterol esters in large HDL	L-HDL-CE
Free cholesterol in large HDL	L-HDL-FC
Triglycerides in large HDL	L-HDL-TG
Concentration of medium HDL particles	M-HDL-P
Total lipids in medium HDL	M-HDL-L
Phospholipids in medium HDL	M-HDL-PL
Total cholesterol in medium HDL	M-HDL-C
Cholesterol esters in medium HDL	M-HDL-CE
Free cholesterol in medium HDL	M-HDL-FC
Triglycerides in medium HDL	M-HDL-TG
Concentration of small HDL particles	S-HDL-P
Total lipids in small HDL	S-HDL-L
Phospholipids in small HDL	S-HDL-PL
Total cholesterol in small HDL	S-HDL-C
Cholesterol esters in small HDL	S-HDL-CE
Free cholesterol in small HDL	S-HDL-FC
Triglycerides in small HDL	S-HDL-TG
Phospholipids to total lipds ratio in chylomicrons and extremely large VLDL	XXL-VLDL-PL_%
Total cholesterol to total lipids ratio in chylomicrons and extremely large VLDL	XXL-VLDL-C_%
Cholesterol esters to total lipids ratio in chylomicrons and extremely large VLDL	XXL-VLDL-CE_%
Free cholesterol to total lipids ratio in chylomicrons and extremely large VLDL	XXL-VLDL-FC_%
Triglycerides to total lipids ratio in chylomicrons and extremely large VLDL	XXL-VLDL-TG_%
Phospholipids to total lipds ratio in very large VLDL	XL-VLDL-PL_%
Total cholesterol to total lipids ratio in very large VLDL	XL-VLDL-C_%
Cholesterol esters to total lipids ratio in very large VLDL	XL-VLDL-CE_%
Free cholesterol to total lipids ratio in very large VLDL	XL-VLDL-FC_%
Triglycerides to total lipids ratio in very large VLDL	XL-VLDL-TG_%
Phospholipids to total lipds ratio in large VLDL	L-VLDL-PL_%
Total cholesterol to total lipids ratio in large VLDL	L-VLDL-C_%
Cholesterol esters to total lipids ratio in large VLDL	L-VLDL-CE_%
Free cholesterol to total lipids ratio in large VLDL	L-VLDL-FC_%
Triglycerides to total lipids ratio in large VLDL	L-VLDL-TG_%
Phospholipids to total lipds ratio in medium VLDL	M-VLDL-PL_%
Total cholesterol to total lipids ratio in medium VLDL	M-VLDL-C_%

Cholesterol esters to total lipids ratio in medium VLDL	M-VLDL-CE_%
Free cholesterol to total lipids ratio in medium VLDL	M-VLDL-FC_%
Triglycerides to total lipids ratio in medium VLDL	M-VLDL-TG_%
Phospholipids to total lipds ratio in small VLDL	S-VLDL-PL_%
Total cholesterol to total lipids ratio in small VLDL	S-VLDL-C_%
Cholesterol esters to total lipids ratio in small VLDL	S-VLDL-CE_%
Free cholesterol to total lipids ratio in small VLDL	S-VLDL-FC_%
Triglycerides to total lipids ratio in small VLDL	S-VLDL-TG_%
Phospholipids to total lipds ratio in very small VLDL	XS-VLDL-PL_%
Total cholesterol to total lipids ratio in very small VLDL	XS-VLDL-C_%
Cholesterol esters to total lipids ratio in very small VLDL	XS-VLDL-CE_%
Free cholesterol to total lipids ratio in very small VLDL	XS-VLDL-FC_%
Triglycerides to total lipids ratio in very small VLDL	XS-VLDL-TG_%
Phospholipids to total lipds ratio in IDL	IDL-PL_%
Total cholesterol to total lipids ratio in IDL	IDL-C_%
Cholesterol esters to total lipids ratio in IDL	IDL-CE_%
Free cholesterol to total lipids ratio in IDL	IDL-FC_%
Triglycerides to total lipids ratio in IDL	IDL-TG_%
Phospholipids to total lipds ratio in large LDL	L-LDL-PL_%
Total cholesterol to total lipids ratio in large LDL	L-LDL-C_%
Cholesterol esters to total lipids ratio in large LDL	L-LDL-CE_%
Free cholesterol to total lipids ratio in large LDL	L-LDL-FC_%
Triglycerides to total lipids ratio in large LDL	L-LDL-TG_%
Phospholipids to total lipds ratio in medium LDL	M-LDL-PL_%
Total cholesterol to total lipids ratio in medium LDL	M-LDL-C_%
Cholesterol esters to total lipids ratio in medium LDL	M-LDL-CE_%
Free cholesterol to total lipids ratio in medium LDL	M-LDL-FC_%
Triglycerides to total lipids ratio in medium LDL	M-LDL-TG_%
Phospholipids to total lipds ratio in small LDL	S-LDL-PL_%
Total cholesterol to total lipids ratio in small LDL	S-LDL-C_%
Cholesterol esters to total lipids ratio in small LDL	S-LDL-CE_%
Free cholesterol to total lipids ratio in small LDL	S-LDL-FC_%
Triglycerides to total lipids ratio in small LDL	S-LDL-TG_%
Phospholipids to total lipds ratio in very large HDL	XL-HDL-PL_%
Total cholesterol to total lipids ratio in very large HDL	XL-HDL-C_%
Cholesterol esters to total lipids ratio in very large HDL	XL-HDL-CE_%
Free cholesterol to total lipids ratio in very large HDL	XL-HDL-FC_%
Triglycerides to total lipids ratio in very large HDL	XL-HDL-TG_%
Phospholipids to total lipds ratio in large HDL	L-HDL-PL_%
Total cholesterol to total lipids ratio in large HDL	L-HDL-C_%
Cholesterol esters to total lipids ratio in large HDL	L-HDL-CE_%
Free cholesterol to total lipids ratio in large HDL	L-HDL-FC_%
Triglycerides to total lipids ratio in large HDL	L-HDL-TG_%

Phospholipids to total lipds ratio in medium HDL	M-HDL-PL_%
Total cholesterol to total lipids ratio in medium HDL	M-HDL-C_%
Cholesterol esters to total lipids ratio in medium HDL	M-HDL-CE_%
Free cholesterol to total lipids ratio in medium HDL	M-HDL-FC_%
Triglycerides to total lipids ratio in medium HDL	M-HDL-TG_%
Phospholipids to total lipds ratio in small HDL	S-HDL-PL_%
Total cholesterol to total lipids ratio in small HDL	S-HDL-C_%
Cholesterol esters to total lipids ratio in small HDL	S-HDL-CE_%
Free cholesterol to total lipids ratio in small HDL	S-HDL-FC_%
Triglycerides to total lipids ratio in small HDL	S-HDL-TG_%
Mean diameter for VLDL particles	VLDL-D
Mean diameter for LDL particles	LDL-D
Mean diameter for HDL particles	HDL-D
Serum total cholesterol	Serum-C
Total cholesterol in VLDL	VLDL-C
Remnant cholesterol (non-HDL, non-LDL -cholesterol)	Remnant-C
Total cholesterol in LDL	LDL-C
Total cholesterol in HDL	HDL-C
Total cholesterol in HDL2	HDL2-C
Total cholesterol in HDL3	HDL3-C
Esterified cholesterol	EstC
Free cholesterol	FreeC
Serum total triglycerides	Serum-TG
Triglycerides in VLDL	VLDL-TG
Triglycerides in LDL	LDL-TG
Triglycerides in HDL	HDL-TG
Diacylglycerol	DAG
Ratio of diacylglycerol to triglycerides	DAG/TG
Total phosphoglycerides	TotPG
Ratio of triglycerides to phosphoglycerides	TG/PG
Phosphatidylcholine and other cholines	PC
Sphingomyelins	SM
Total cholines	TotCho
Apolipoprotein A-I	ApoA1
Apolipoprotein B	ApoB
Ratio of apolipoprotein B to apolipoprotein A-I	ApoB/ApoA1
Total fatty acids	TotFA
Estimated description of fatty acid chain length, not actual carbon number	FALen
Estimated degree of unsaturation	UnSat
22:6, docosahexaenoic acid	DHA
18:2, linoleic acid	LA
Conjugated linoleic acid	CLA
Omega-3 fatty acids	FAw3

Omega-6 fatty acids	FAw6
Polyunsaturated fatty acids	PUFA
Monounsaturated fatty acids; 16:1, 18:1	MUFA
Saturated fatty acids	SFA
Ratio of 22:6 docosahexaenoic acid to total fatty acids	DHA/FA
Ratio of 18:2 linoleic acid to total fatty acids	LA/FA
Ratio of conjugated linoleic acid to total fatty acids	CLA/FA
Ratio of omega-3 fatty acids to total fatty acids	FAw3/FA
Ratio of omega-6 fatty acids to total fatty acids	FAw6/FA
Ratio of polyunsaturated fatty acids to total fatty acids	PUFA/FA
Ratio of monounsaturated fatty acids to total fatty acids	MUFA/FA
Ratio of saturated fatty acids to total fatty acids	SFA/FA
Glucose	Glc
Lactate	Lac
Pyruvate	Pyr
Citrate	Cit
Alanine	Ala
Glutamine	Gln
Histidine	His
Isoleucine	Ile
Leucine	Leu
Valine	Val
Phenylalanine	Phe
Tyrosine	Tyr
Acetate	Ace
Acetoacetate	AcAce
3-hydroxybutyrate	bOHBut
Creatinine	Crea
Albumin	Alb

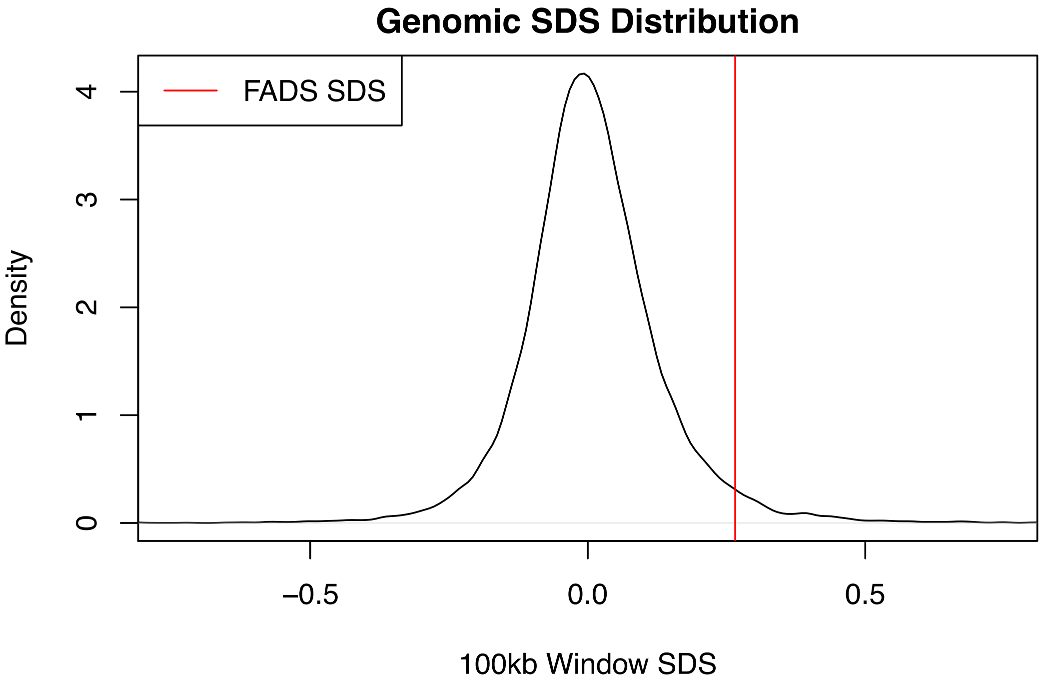
Supplementary Table 6. Association of rs174594 (derived allele) with cardiovascular biomarkers in the Nurses' and Health Professionals Follow-Up Study

Trait	Beta	SE	P value
Plasma arachidonic acid (c20:4 n-6)	1.18	0.06	<0.0001
Plasma EPA (c20:5 n-3)	0.096	0.014	<0.0001
Plasma total cholesterol (mg/dL)	3.495	1.28	0.006
Plasma LDL cholesterol (mg/dL)	3.03	1.16	0.009
Plasma HDL cholesterol (mg/dL)	0.60	0.48	0.21
Plasma triglycerides (mg/dL)	-2.86	2.76	0.30
Plasma CRP (mg/dL)	-0.003	0.02	0.87

Supplementary Table 7. Sample IDs of Bronze Age data from Allentoft et al (2015).

54 Bronze Age European Samples					
Sample ID	Country	Sample ID	Country	Sample ID	Country
RISE486	Italy	RISE568	CzechRep	RISE154	Poland
RISE487	Italy	RISE569	CzechRep	RISE577	CzechRep
RISE489	Italy	RISE566	CzechRep	RISE586	CzechRep
RISE349	Hungary	RISE567	CzechRep	RISE71	Denmark
RISE479	Hungary	RISE446	Germany	RISE21	Denmark
RISE480	Hungary	RISE434	Germany	RISE61	Denmark
RISE483	Hungary	RISE435	Germany	RISE42	Denmark
RISE484	Hungary	RISE436	Germany	RISE47	Denmark
RISE247	Hungary	RISE471	Germany	RISE276	Denmark
RISE254	Hungary	RISE431	Poland	RISE175	Sweden
RISE371	Hungary	RISE1	Poland	RISE179	Sweden
RISE373	Hungary	RISE94	Sweden	RISE207	Sweden
RISE374	Hungary	RISE174	Sweden	RISE210	Sweden
RISE559	Germany	RISE00	Estonia	RISE97	Sweden
RISE560	Germany	RISE109	Poland	RISE98	Sweden
RISE562	Germany	RISE139	Poland	RISE598	Lithuania
RISE563	Germany	RISE145	Poland	RISE595	Montenegro
RISE564	Germany	RISE150	Poland	RISE596	Montenegro

Supplementary Figure 5. Singleton Density Score (SDS) Distribution. A 100kb window including the *FADS* genes has an average FADS score of 0.266, which is greater than 97% of other 100kb windows tiled across the genome, providing evidence that *FADS* genes have been under recent selection. SDS scores (available from http://pritchardlab.stanford.edu/software.html) were calculated using UK10K Project data.



Supplementary Figure 6. No clear evidence of balancing selection found utilizing the composite likelihood ratio test method described by DeGiorgio et al (2014) on CEU data. FADS score denoted in red.