

Scree plot

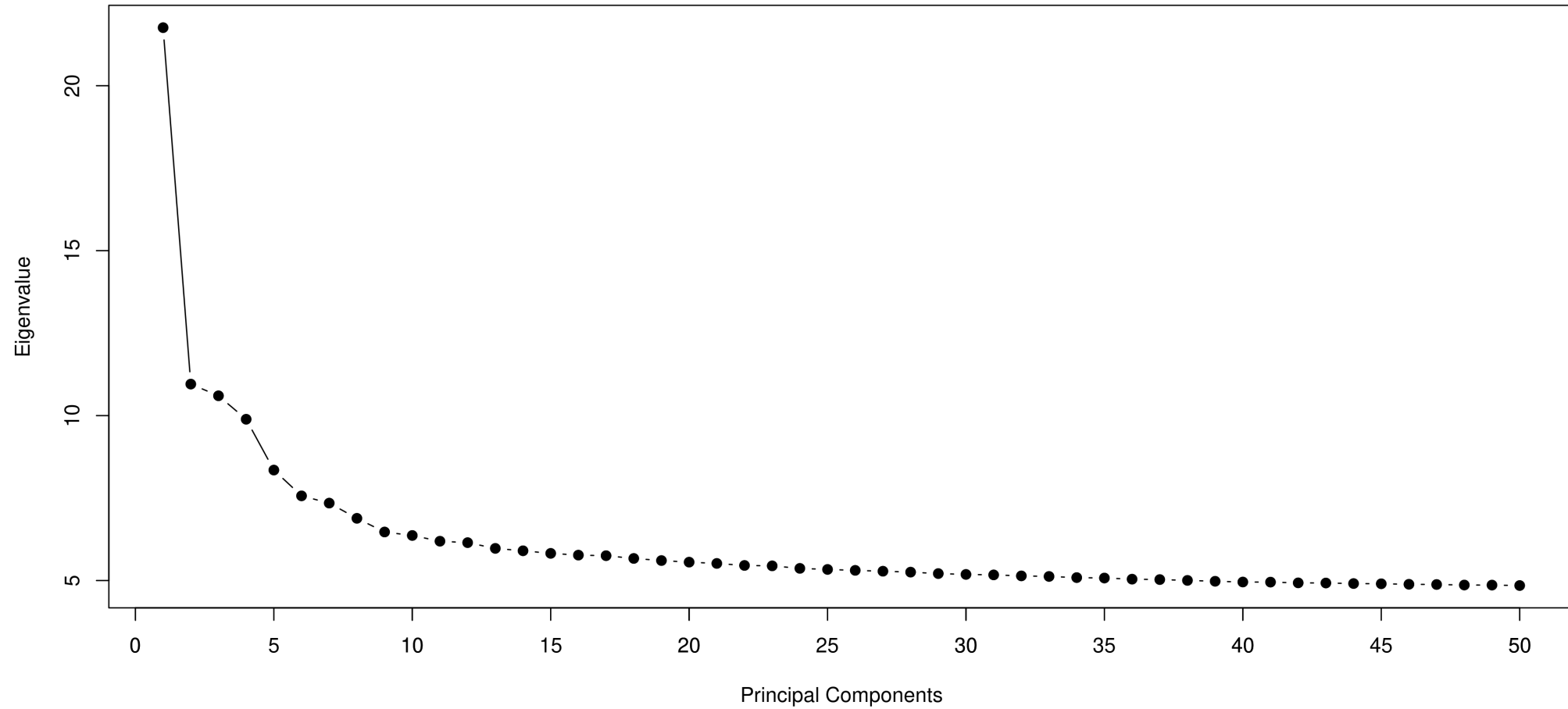
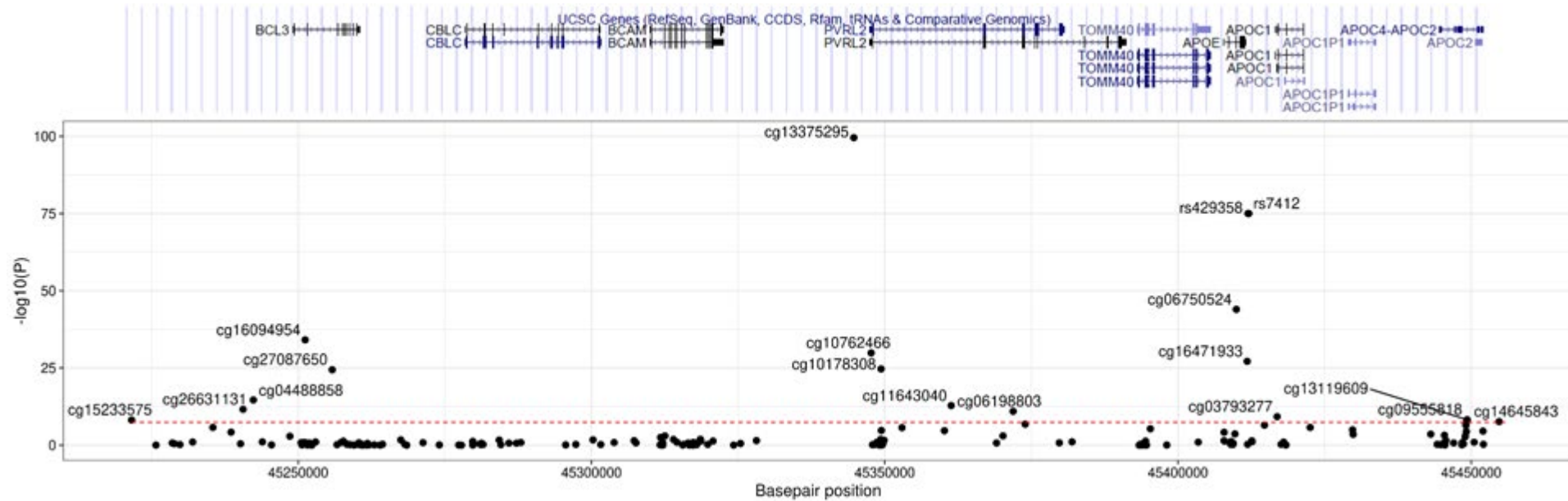
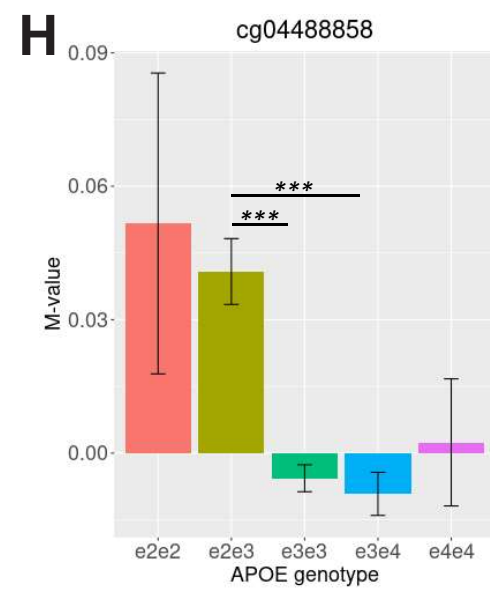
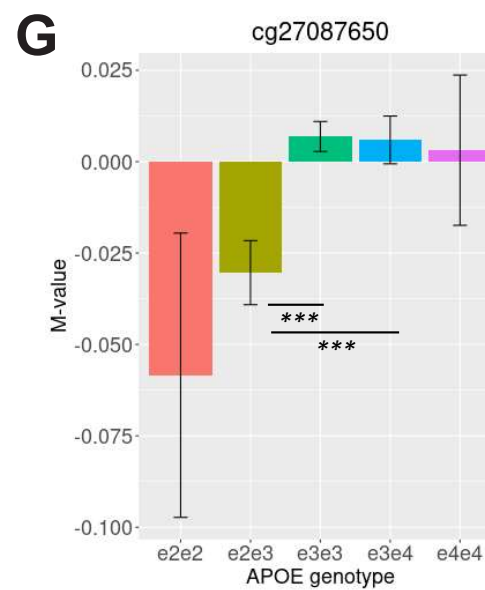
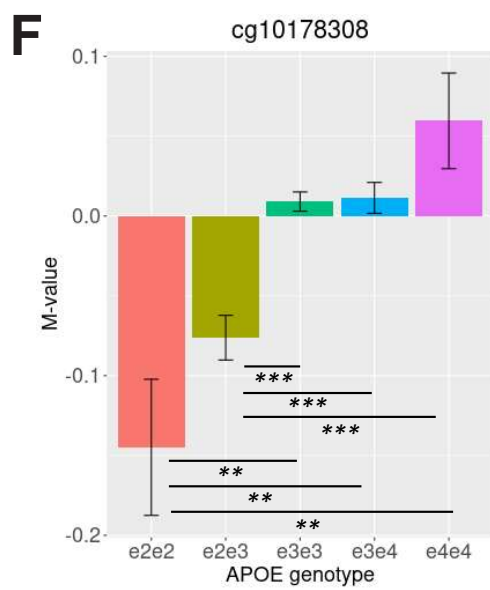
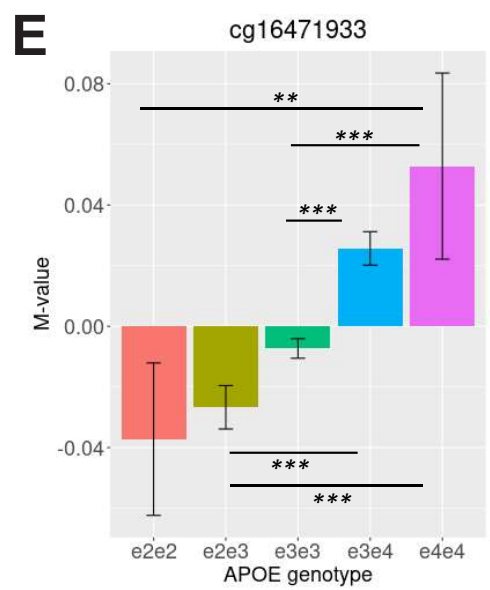
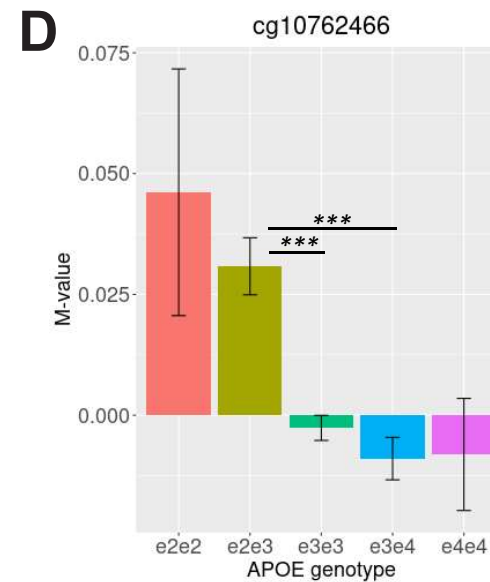
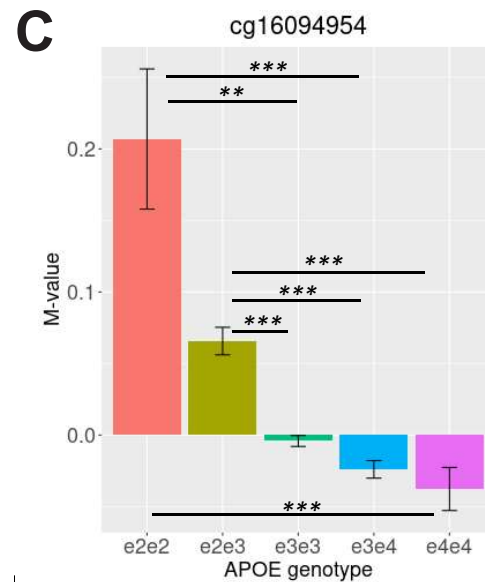
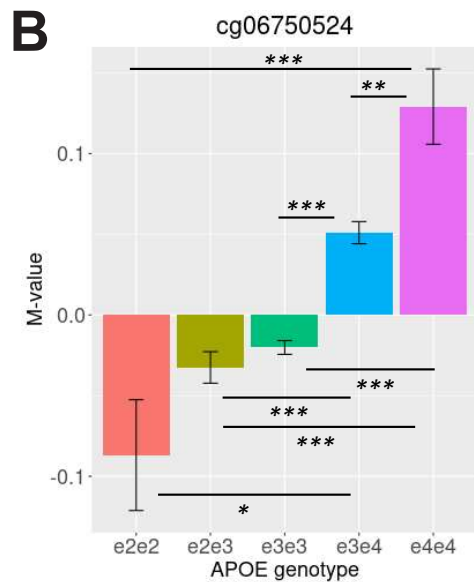
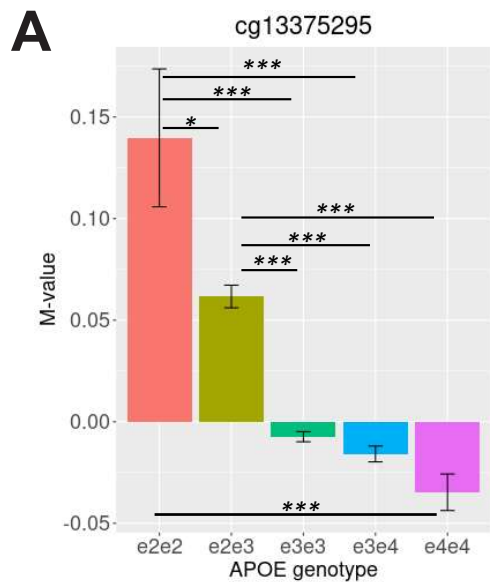
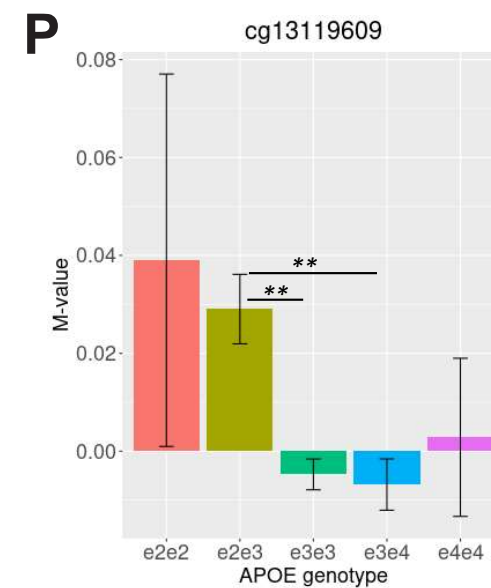
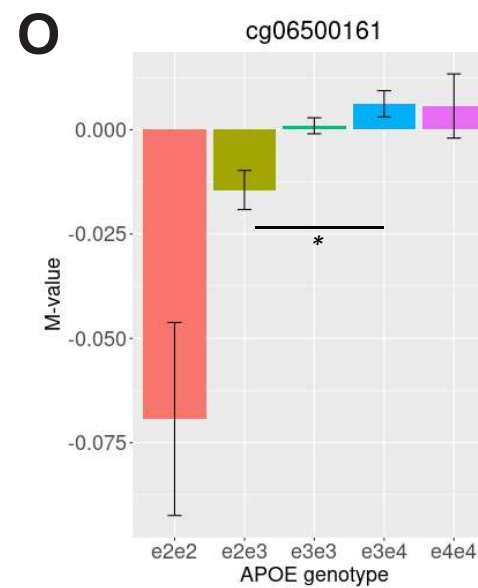
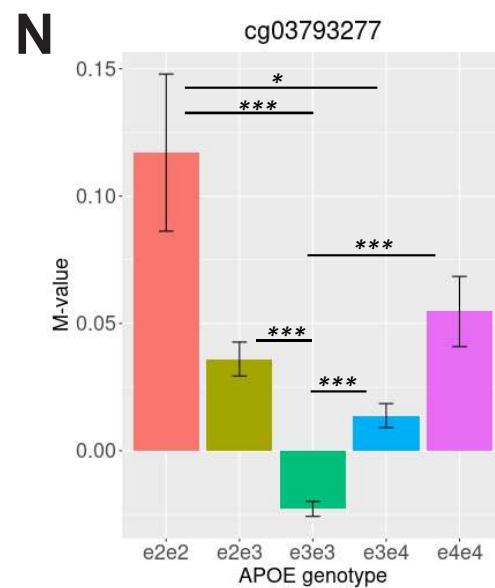
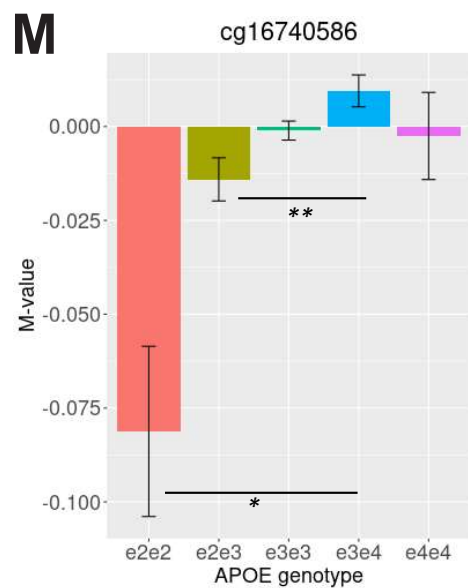
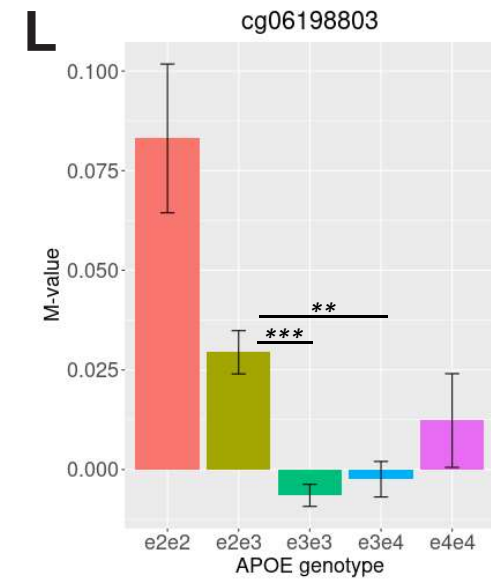
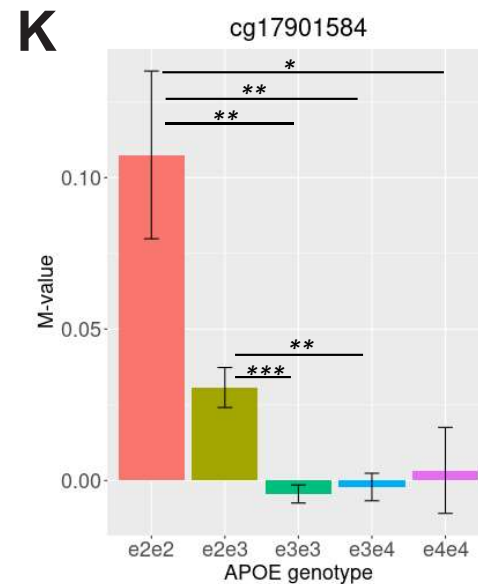
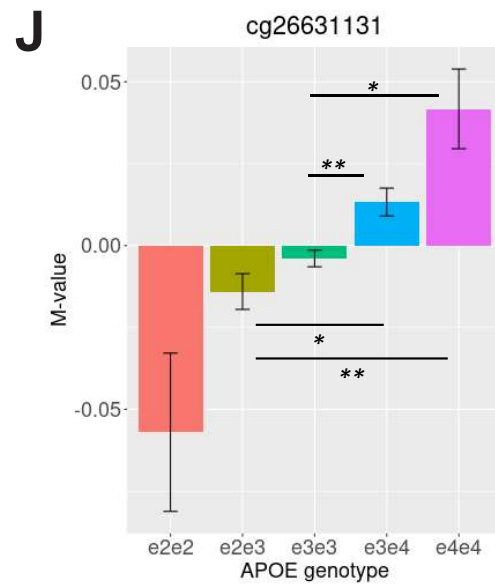
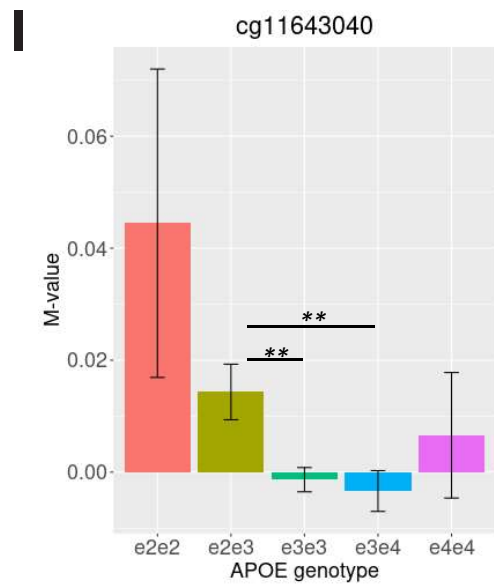


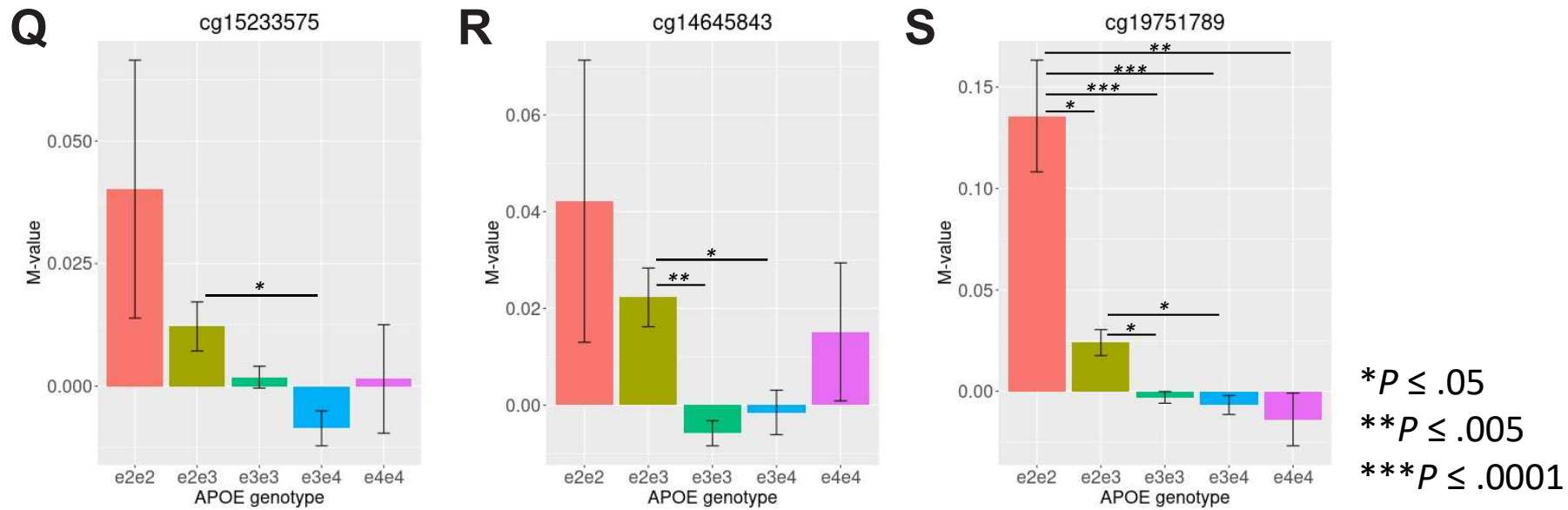
Fig. S1. Scree plot showing the eigenvalues of the first 50 genetic principal components for the Generation Scotland: Scottish Family Health Study.



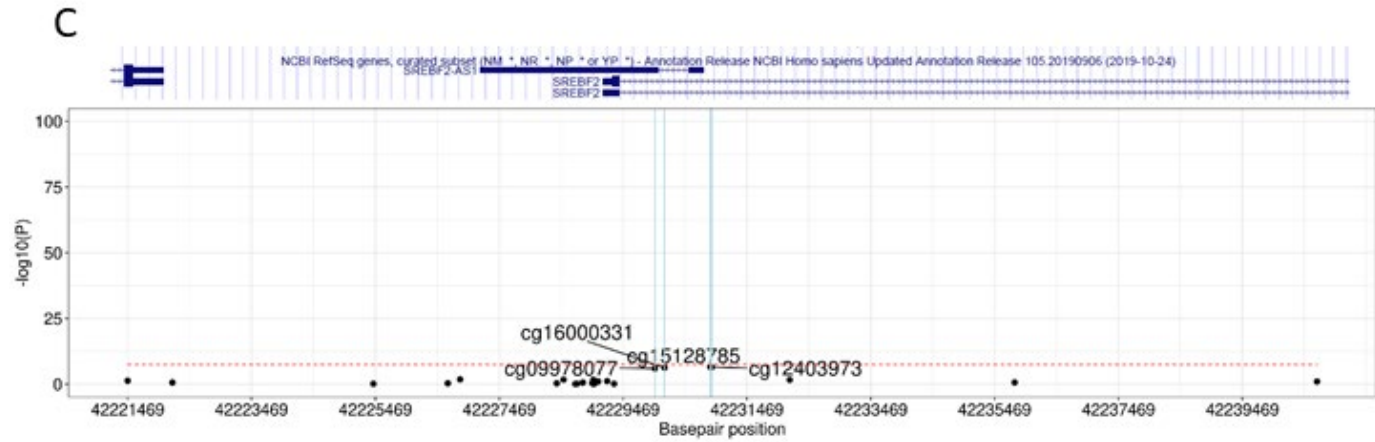
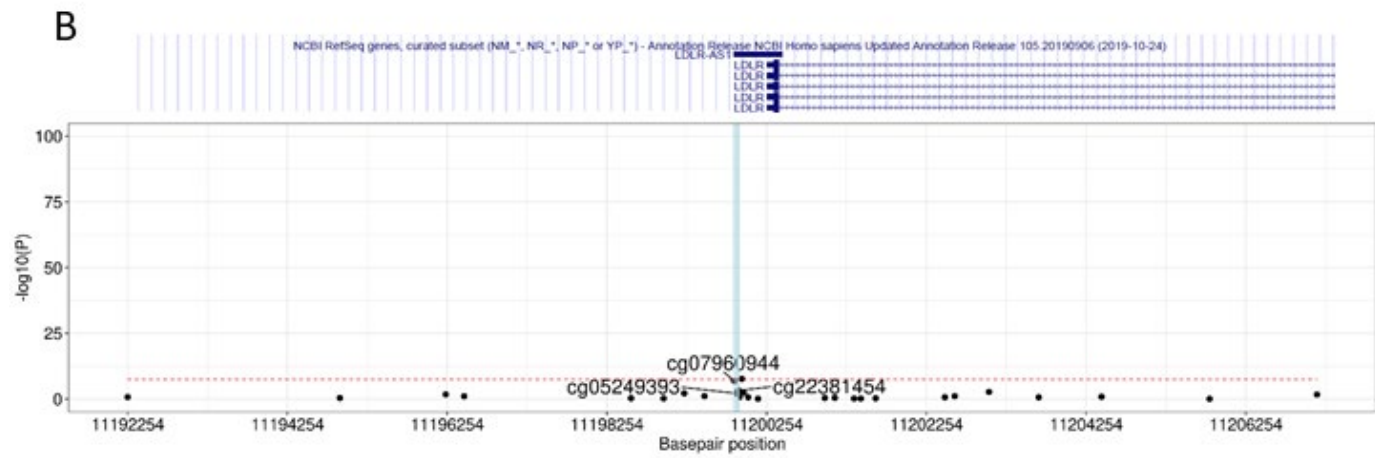
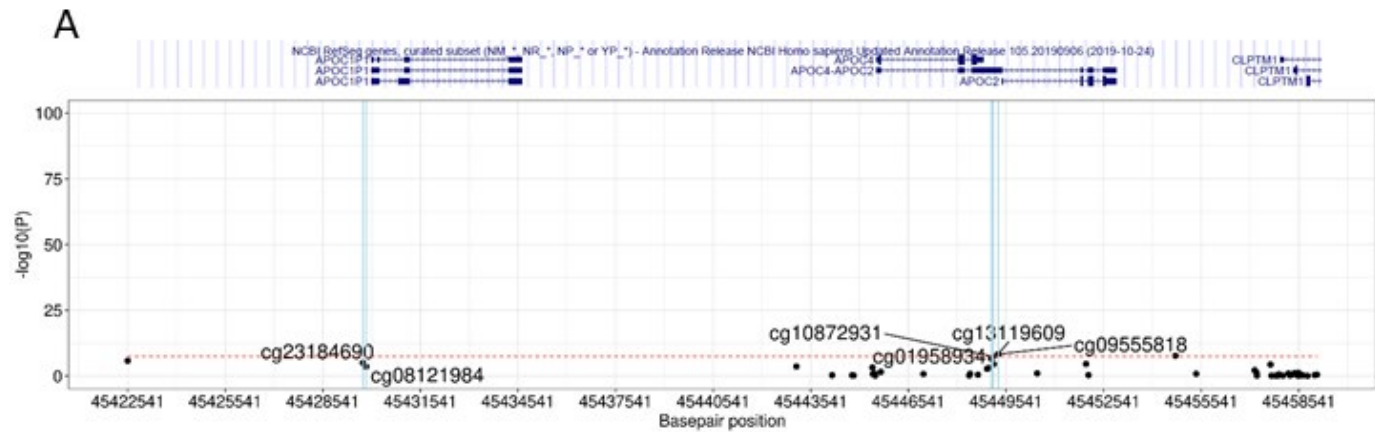
**Fig. S2.** The genomic region encompassing *APOE*, which contains 16 of the *APOE*  $\epsilon 4$  vs.  $\epsilon 2$ -associated DMPs identified by meta-analysis (chr19: 45,221,584 – 45,454,752; GRCh37/hg19). The upper panel, downloaded from the UCSC Genome Browser (GRCh37/hg19) indicates the location of genes (NCBI RefSeq gene track). The lower panel indicates CpG sites in the region. The position of the CpG on the y-axis is determined by the  $-\log_{10}$  of its meta-analysis *P*-value and its position on the x-axis is determined by its genomic location. The dashed red line indicates the threshold for significance ( $p \leq 3.6 \times 10^{-8}$ ) and CpGs attaining significance are labelled with their identifier. The two *APOE* SNPs, rs429358 and rs7412, which define the *APOE*  $\epsilon 2/\epsilon 3/\epsilon 4$  haplotype are also indicated.







**Fig. S3.** Bar charts showing the mean methylation levels (M-values) in the discovery sample for the 20 meta-DMPs split by *APOE* genotype ( $\epsilon 2/\epsilon 2$ ,  $\epsilon 2/\epsilon 3$ ,  $\epsilon 3/\epsilon 3$ ,  $\epsilon 3/\epsilon 4$ , and  $\epsilon 4/\epsilon 4$ ). Error bars indicated standard errors of the mean. Pairwise differences were assessed using Tukey's test of Honestly Significant Differences and significant differences are indicated by asterisks (\* $P \leq .05$ , \*\* $P \leq .005$ , \*\*\* $P \leq .0001$ ).



**Fig. S4.** The genomic regions containing the six identified DMRs. **A.** indicates the three DMRs within the *APOE* locus (i. cg01958934 and cg10872931; ii. cg01958934 and cg10872931; iii. cg23184690 and cg08121984); **B.** shows the *LDLR* DMR; and **C.** shows the two *SREBF2* DMRs (i. cg15128785 and cg1240397; ii. cg09978077 and cg16000331). Each plot shows an extended region spanning from 10 kb downstream of the most 5' DMR CpG to 10 kb upstream of the most 3' DMR CpG. In each plot, the upper panel, downloaded from the UCSC Genome Browser (GRCh37/hg19) indicates the location of genes (NCBI RefSeq gene track). The lower panel indicates CpG sites in the region. The position of the CpG on the y-axis is determined by the  $-\log_{10}$  of its meta-analysis  $P$ -value and its position on the x-axis is determined by its genomic location. The dashed red line indicates the threshold for significance ( $p \leq 3.6 \times 10^{-8}$ ) in the EWAS. The vertical blue lines indicate the locations of CpGs that are involved in a DMR and these CpGs are labelled with their probe ID.