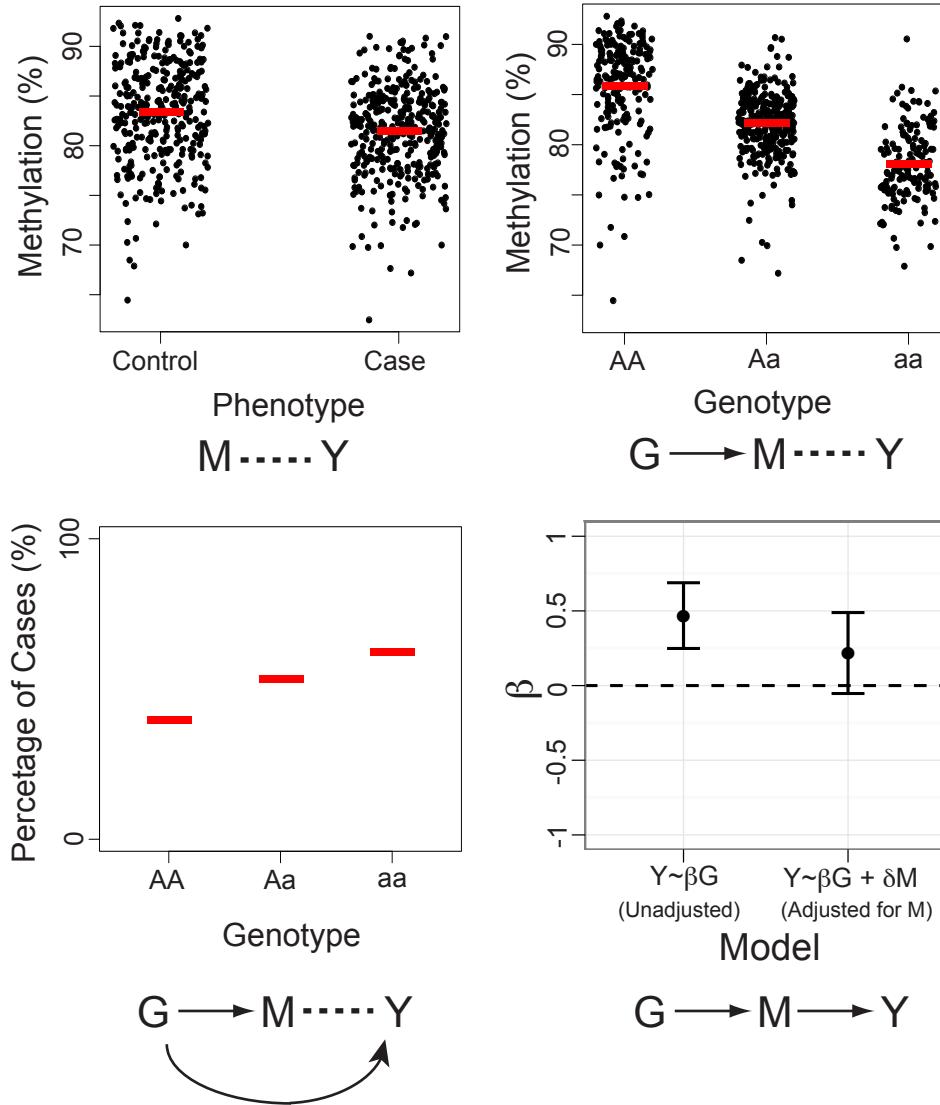
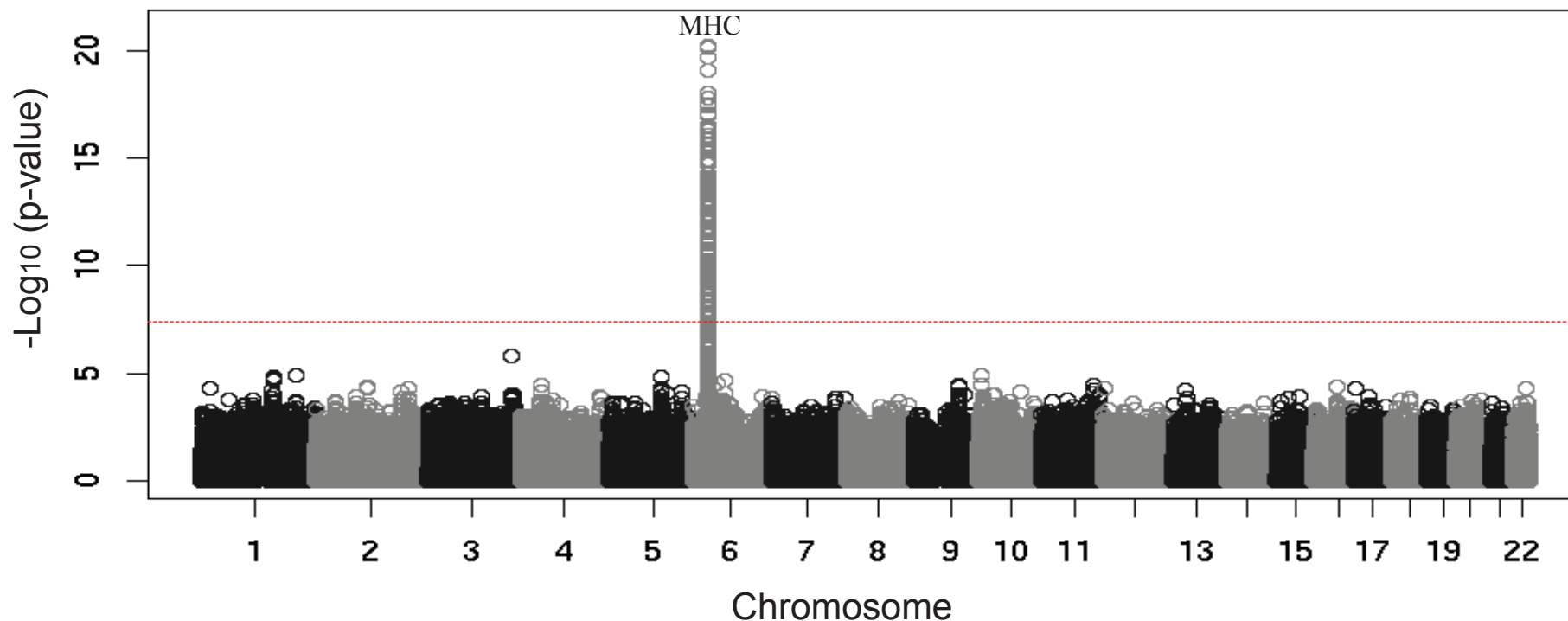


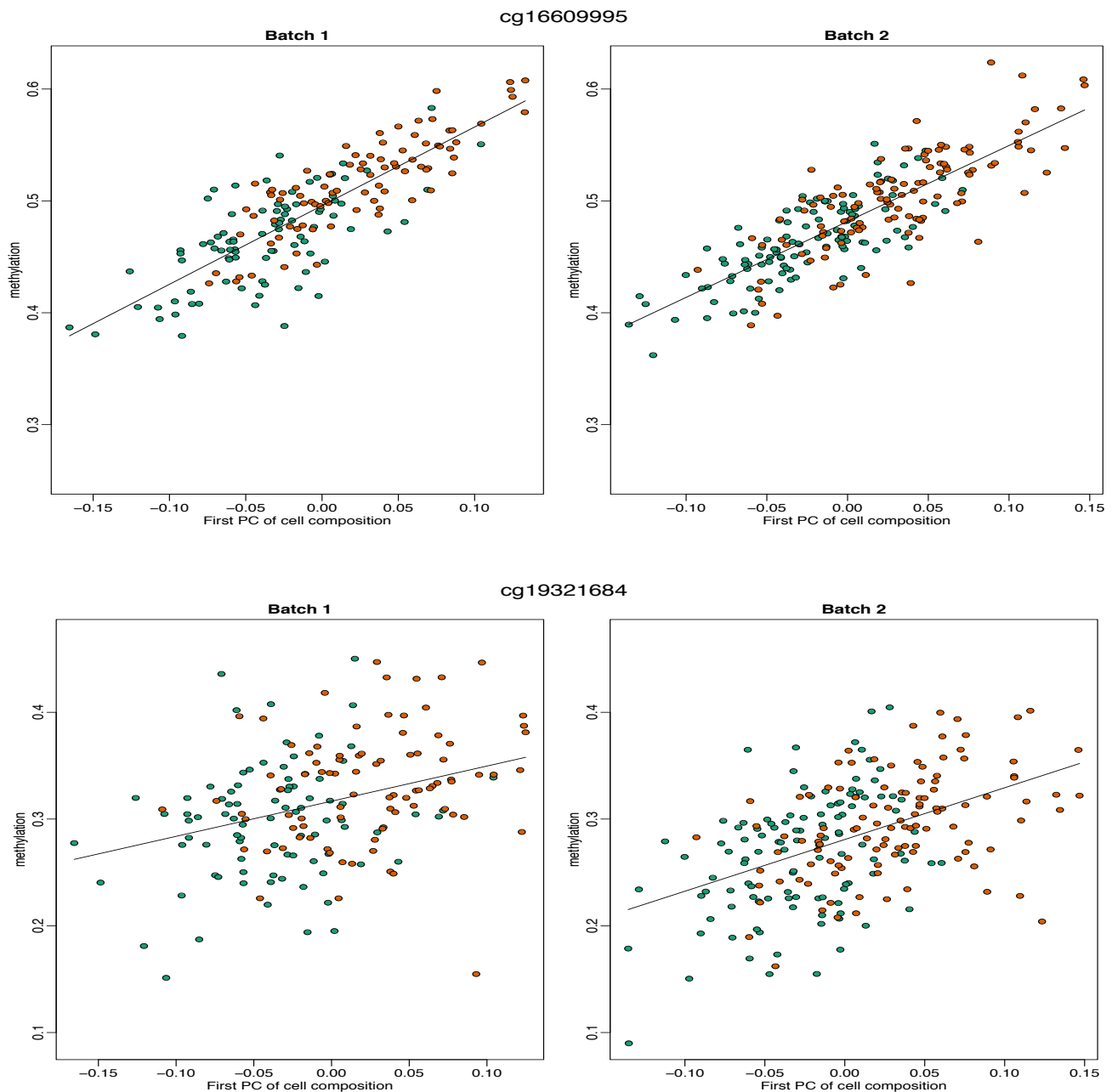
cg00462104, rs3996993



Supplementary Figure 1 Genotype-dependent candidate DMPs that mediate genetic risk outside the MHC region. The association plots are organized and displayed as in Fig. 4a

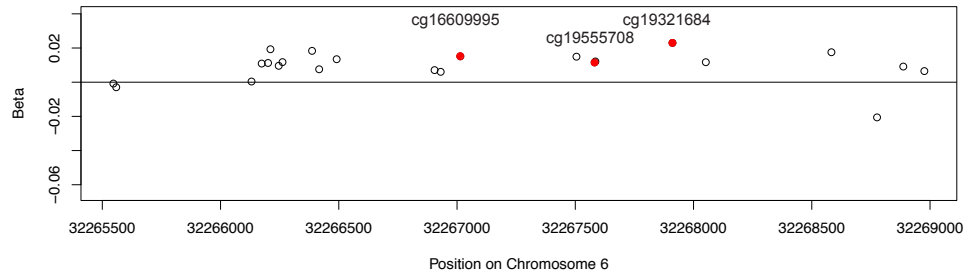


Supplementary Figure 2 Manhattan plot of the $-\log_{10}(p\text{-values})$ versus genomic position for RA-associated SNPs without considering for DNA methylation. The p-value was calculated by fitting phenotype (case vs. control) to a standard allelic dosage model at each SNP ($n = 1,196,263$) using the 354 ACPA positive RA cases and 337 controls selected for the Illumina 450K methylation assay. The red dotted line represents the threshold used for statistical significance (Bonferroni-adjusted $p = 0.05$). Genomic position is ordered from chromosomes 1 to 22 (left to right).

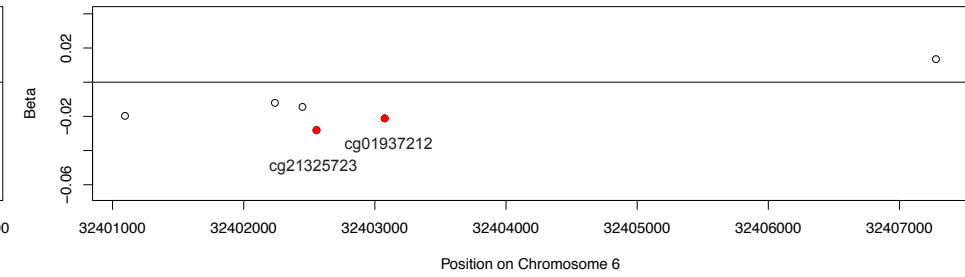


Supplementary Figure 3 Adjustment for batch effects and cell type composition. The first principal component (PC) of cell type composition (x-axis) was calculated within each batch using a balanced number of cases and controls. A linear regression model was used to fit methylation values to this PC. The residuals represent estimates adjusted for batch and cell type composition. Batch 1 contains samples run in 2011; Batch 2 contains samples run in 2012.

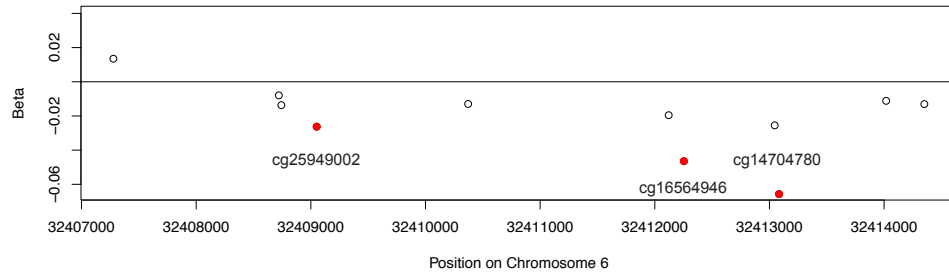
Region 1



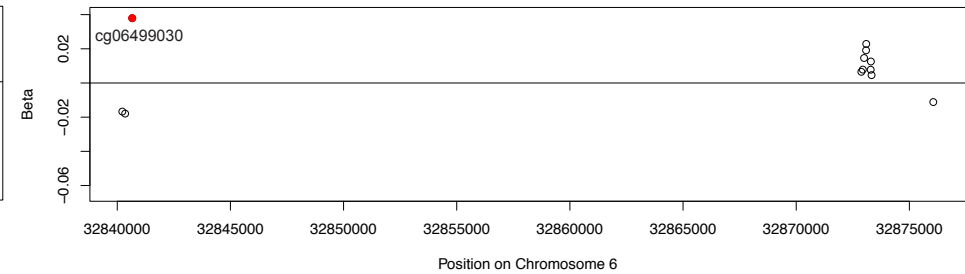
Region 2



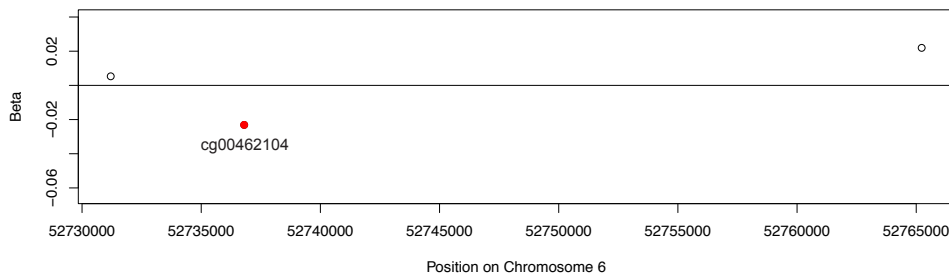
Region 3



Region 4



Region 5



Supplementary Figure 4 Top 10 DMPs represent signals across 5 genomic regions. The top 10 DMPs are indicated in red.