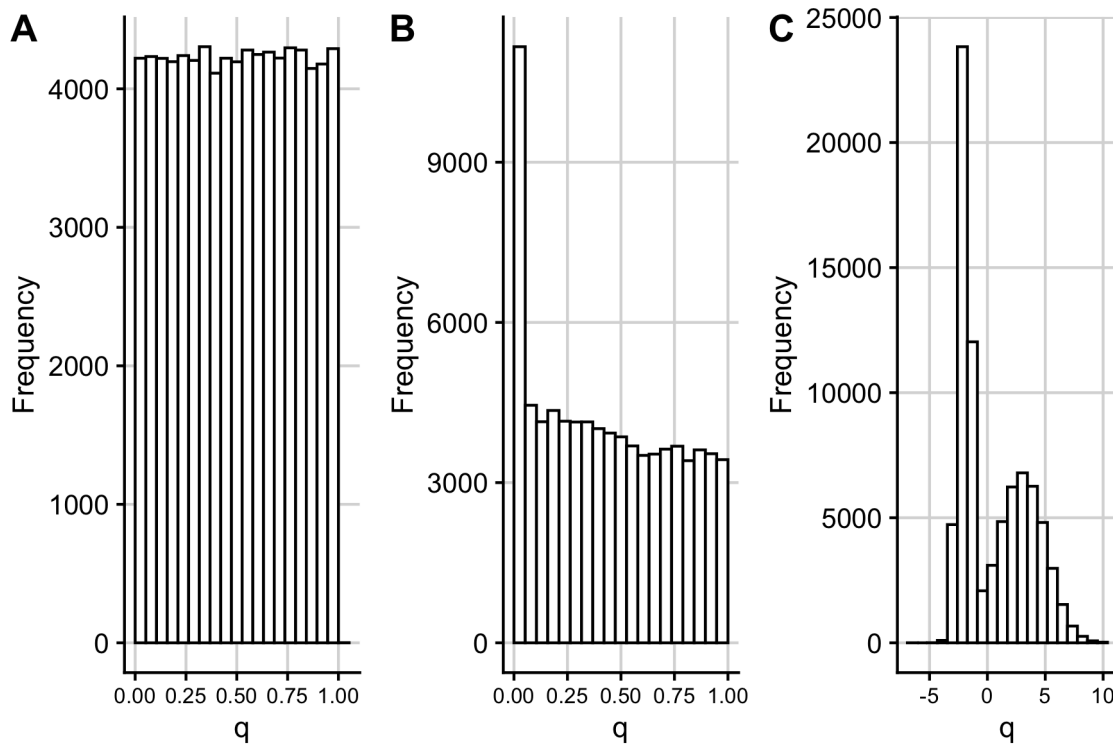


**Figure S1: Illustration of the spline correction procedure.** A spline with 5 knots is fitted to  $\log_{10}(v/p)$  against  $q$  using the ‘bigsplines’ R package (<https://cran.r-project.org/web/packages/bigsplines/index.html>). The distance between each data point and the fitted spline is calculated. If this distance is greater than the value of the ‘dist\_thr’ parameter in the flexible cFDR software (default value is 0.5), then the data point is mapped back to the spline and the corresponding  $v$ -value is recalculated using the fitted spline. In this example, the red line shows the fitted spline and the blue points are mapped back to the spline (using ‘dist\_thr=0.5’).



**Figure S2: Histograms of auxiliary data leveraged in simulation analysis.** (A) Example data leveraged in Figure 1A (simulated from standard uniform distribution). (B) Example data leveraged in Figure 1B (simulated  $p$ -values for related traits). (C) Example data leveraged in Figure 2 (simulated from a mixture normal distribution).

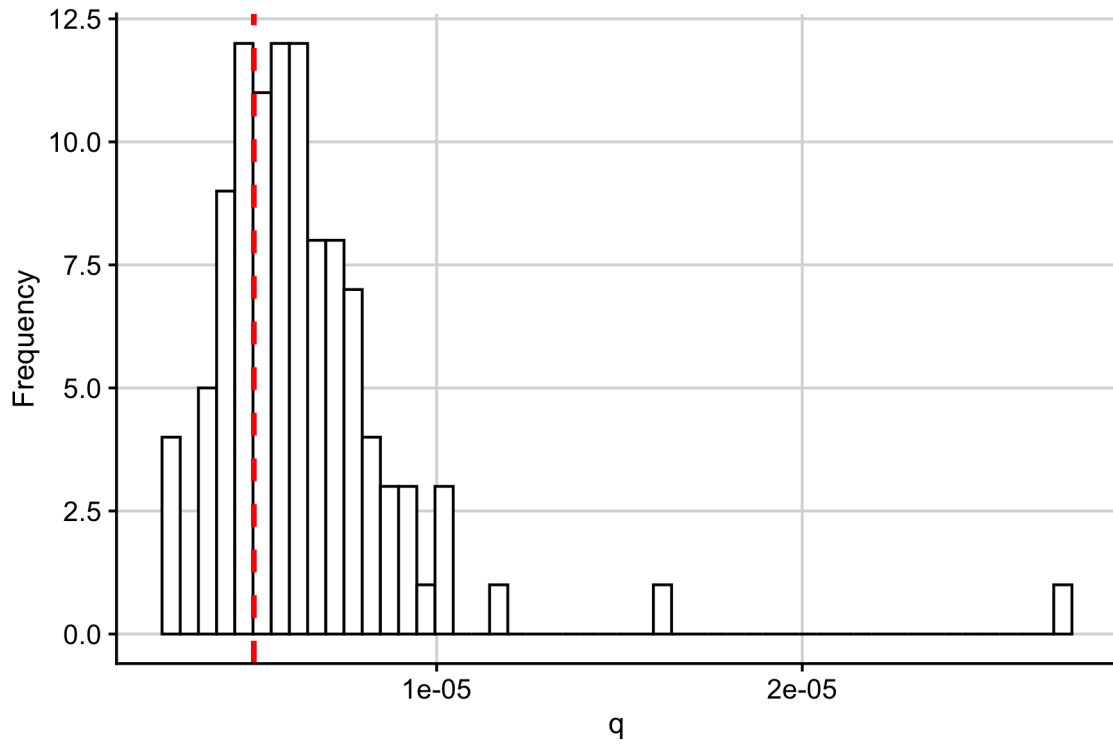


Figure S3: **Choosing an FDR threshold corresponding to genome-wide significance p-value threshold in the simulation analysis.** Histogram of the maximum FDR-adjusted  $p$ -value (using BH method) amongst SNPs with  $p \leq 5 \times 10^{-8}$  in the simulation analysis. Red dashed line at the selected FDR threshold of  $5 \times 10^{-6}$

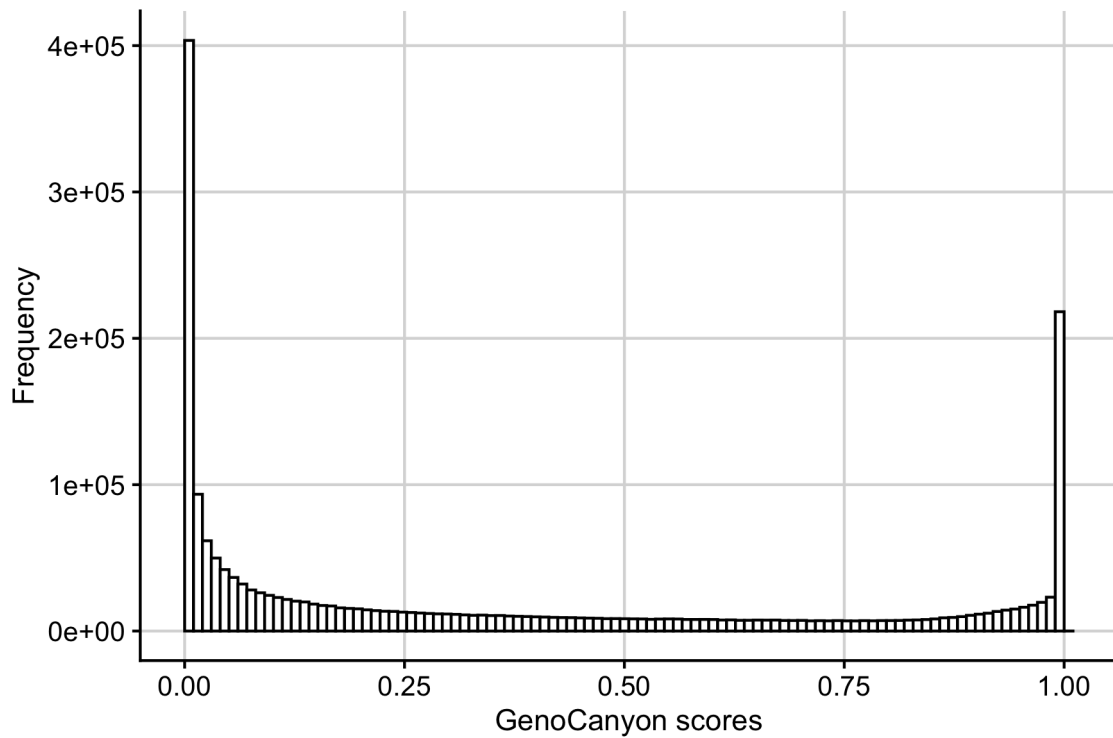


Figure S4: **Histogram of GenoCanyon scores for SNPs in the asthma GWAS data set**

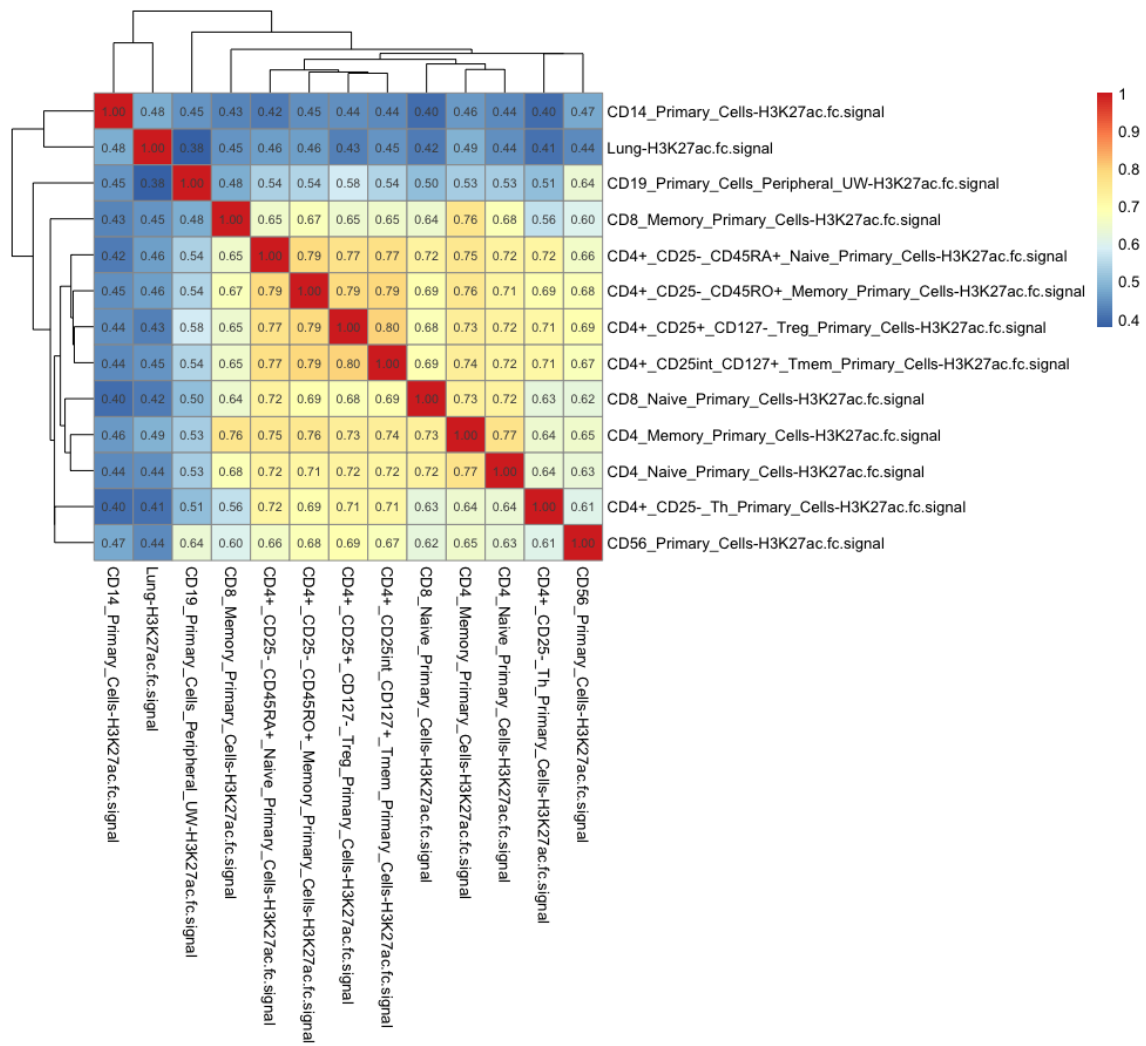


Figure S5: Heatmap of the correlations between H3K27ac fold change values amongst asthma relevant cell types

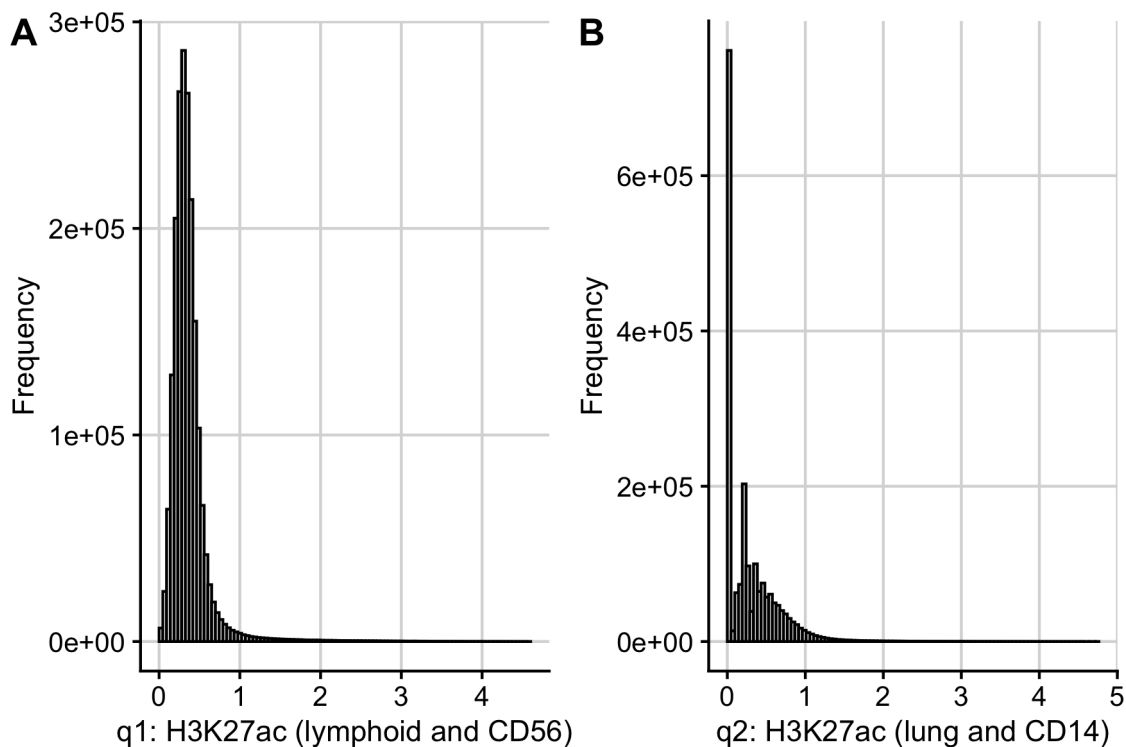


Figure S6: **Histograms of auxiliary data used in H3K27ac application.** (A) q1 is the average of (log transformed) H3K27ac fold change values in lymphoid and CD56 cell types (B) q2 is the average of (log transformed) H3K27ac fold change values in lung tissue and CD14+ cells.

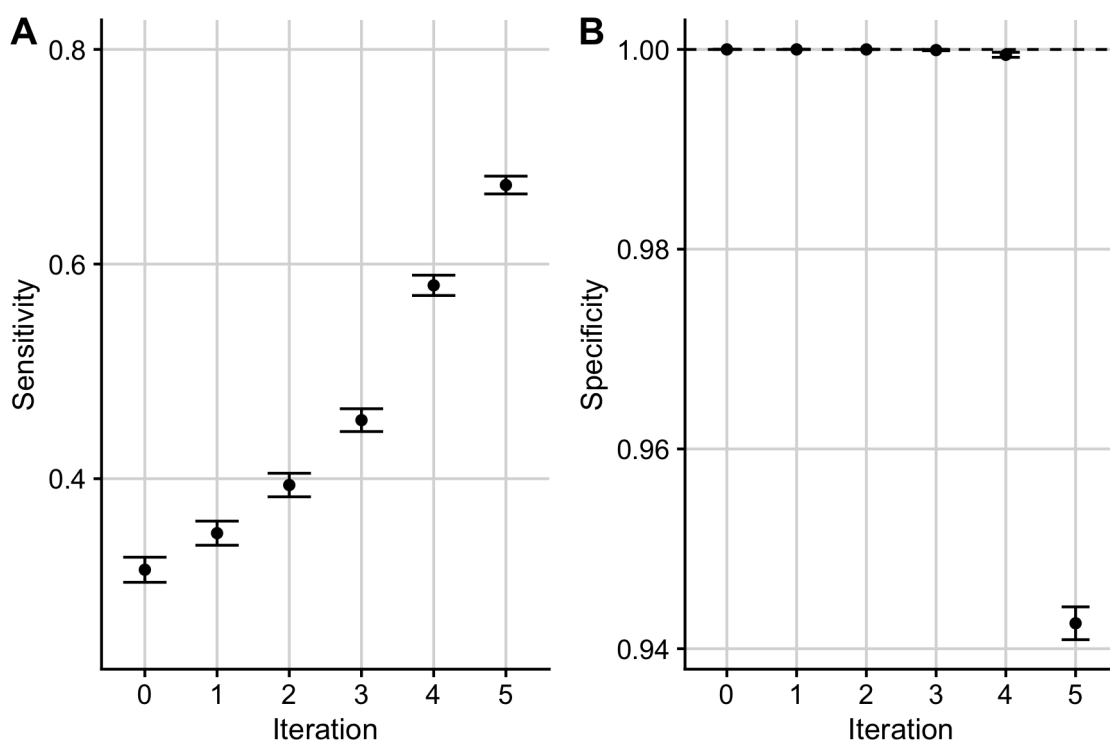


Figure S7: **Simulation results for using flexible cFDR to iteratively leverage exactly the same auxiliary data.** Mean  $\pm$  standard error for the sensitivity (A) and specificity (B) of FDR-adjusted  $v$ -values (using the BH method) from flexible cFDR when iterating over the same dependent auxiliary data ("simulation E"). Iteration 0 corresponds to the original FDR-adjusted  $p$ -values. Sensitivity is calculated as the proportion of SNPs with  $r^2 \geq 0.8$  with a causal variant, that were detected with an FDR less than  $5 \times 10^{-6}$ . Specificity is calculated as the proportion of SNPs with  $r^2 \leq 0.01$  with all the causal variants, that were not detected with an FDR less than  $5 \times 10^{-6}$ . A dashed line is shown where specificity =  $1 - 5 \times 10^{-6}$ . Results were averaged across 1,000 simulations.

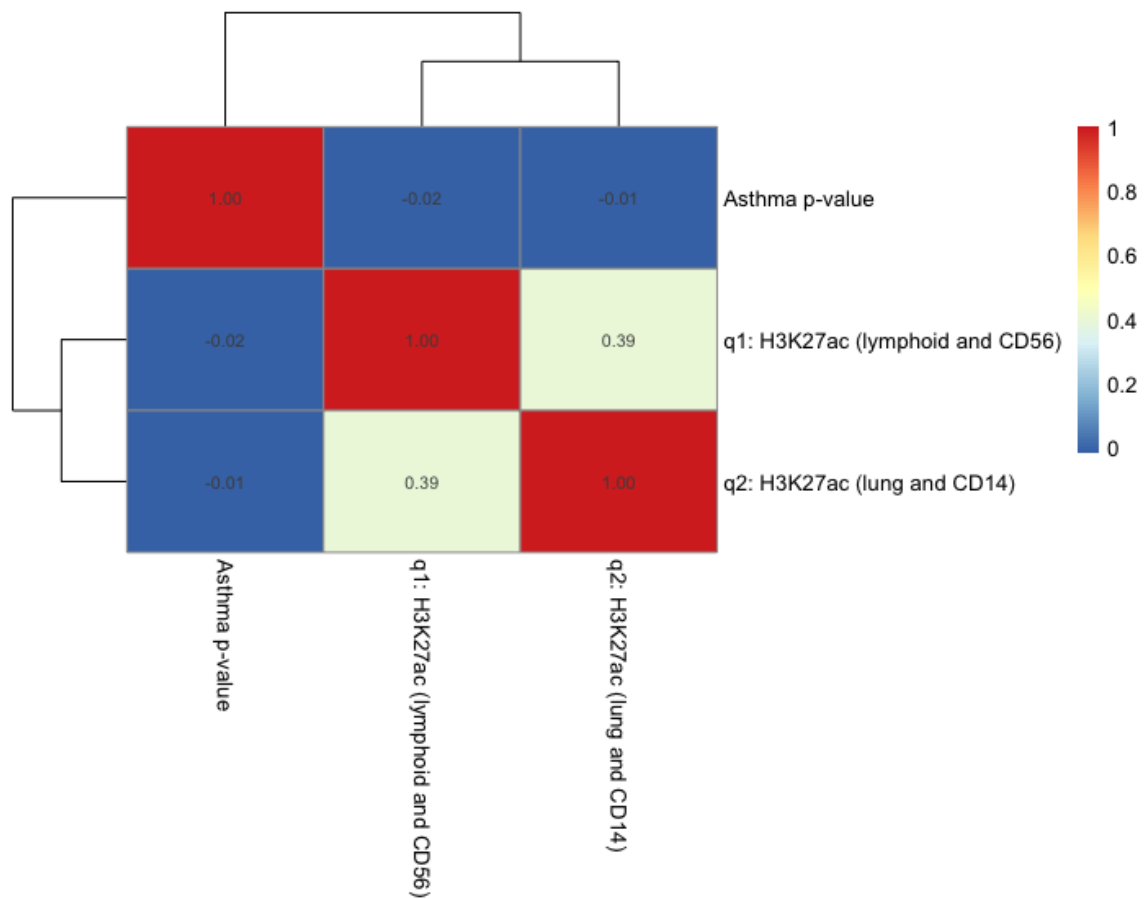


Figure S8: **Heatmap of correlations between asthma GWAS  $p$ -values and the summarised H3K27ac fold change values leveraged by flexible cFDR.** q1 is the average of (log transformed) H3K27ac fold change values in lymphoid and CD56 cell types. q2 is the average of (log transformed) H3K27ac fold change values in lung tissue and CD14+ cells.

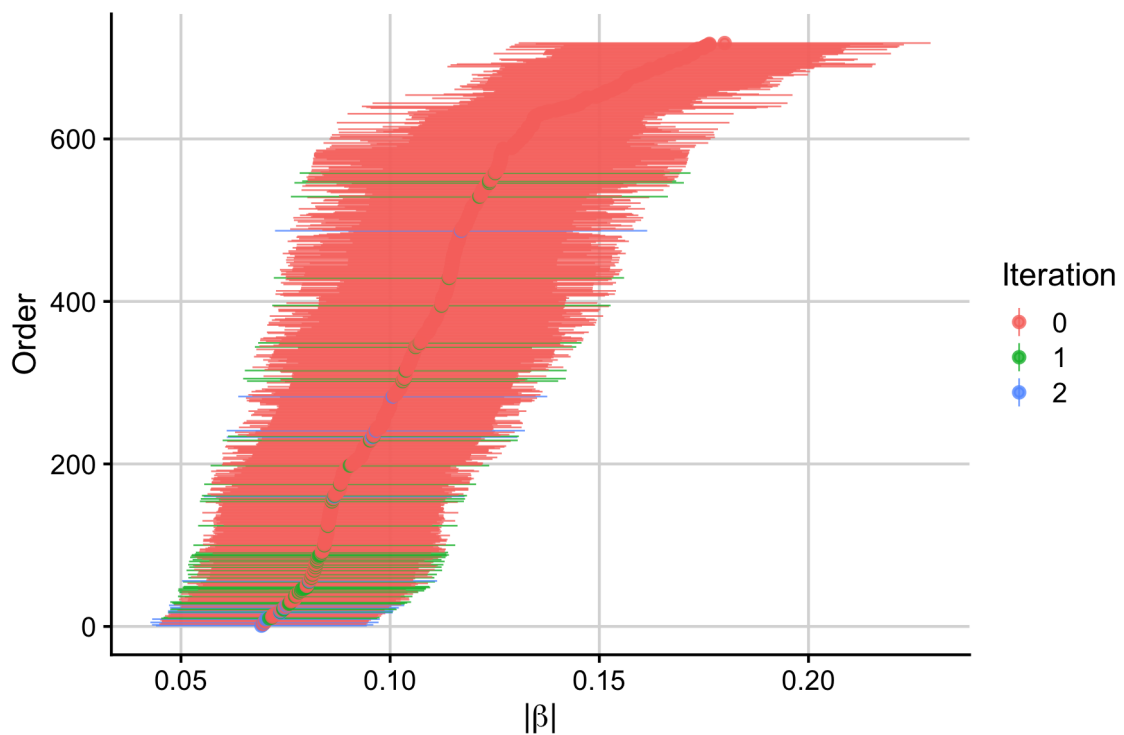


Figure S9: **Effect sizes of significant SNPs.** Absolute estimated effect sizes ( $|\beta|$ ; log OR)  $\pm 1.96 \times SE$  of SNPs significantly associated ( $FDR \leq 0.000148249$ ) with asthma in the original discovery GWAS data set ("Iteration 0") and those newly significant after iteration 1 and 2 of cFDR.

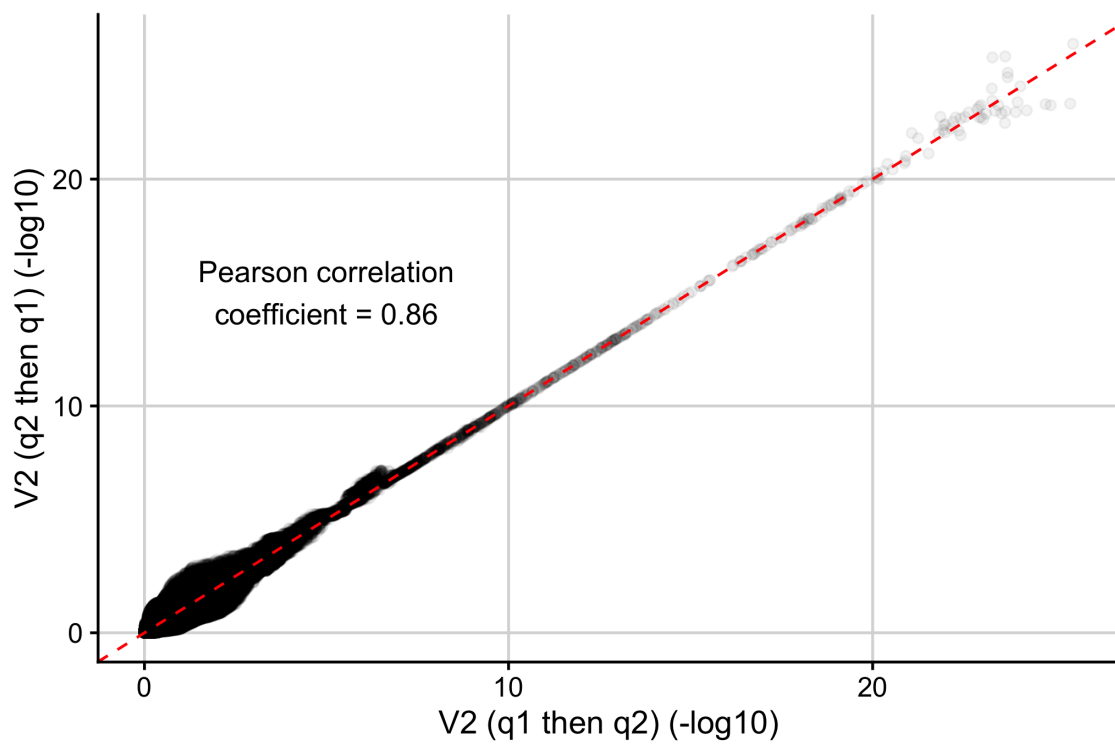


Figure S10: **Switching the order of iteration.**  $(-\log_{10})$  V2 values after 2 iterations of flexible cFDR leveraging H3K27ac data when iterating over q2 and then q1 against  $(-\log_{10})$  V2 values when iterating over q1 then q2.

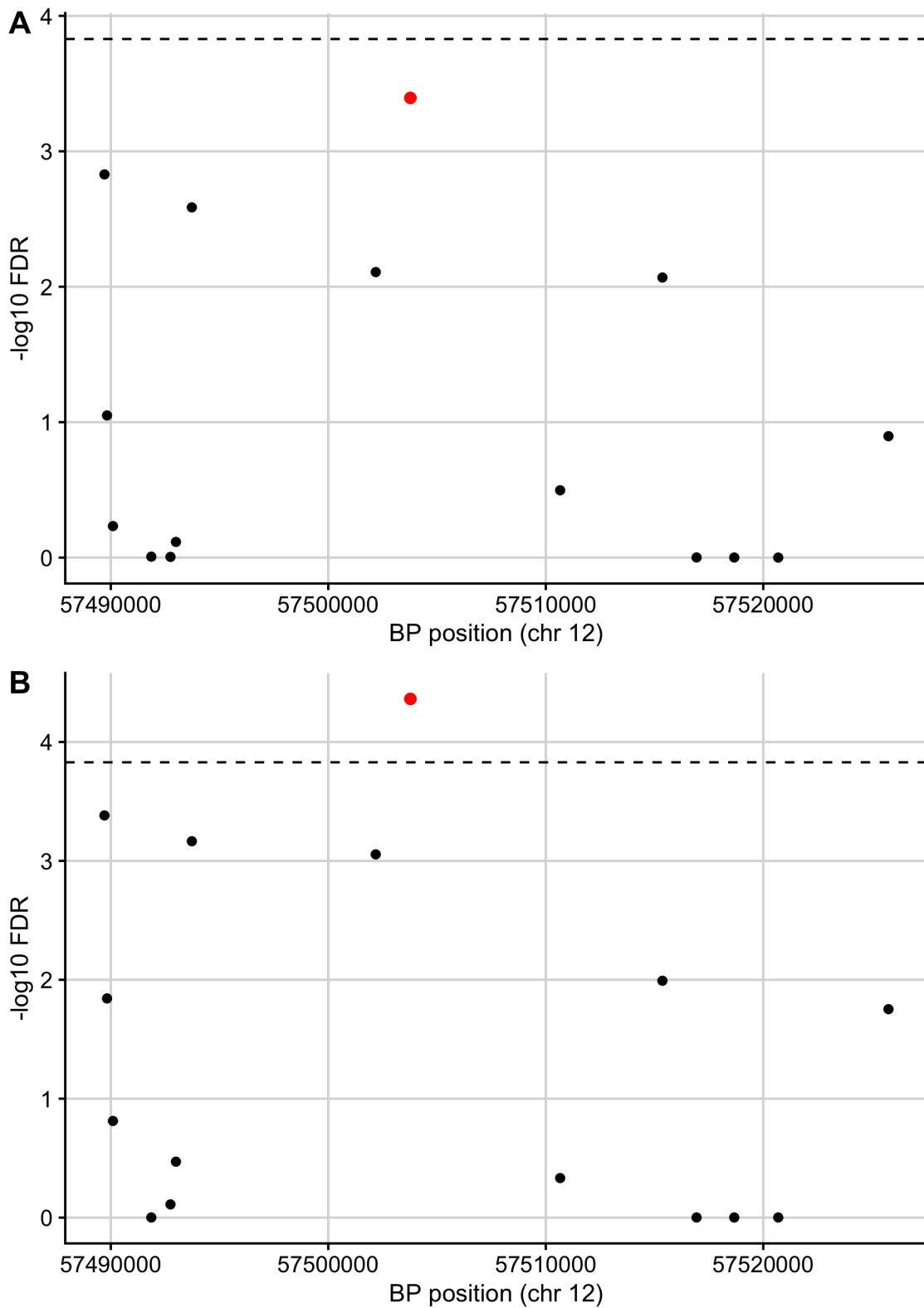


Figure S11: **FDR Manhattan plots for genomic region containing the *STAT6* gene.** Manhattan plots of FDR adjusted  $p$ -values (using BH method) before (A) and after (B) applying flexible cFDR for the region containing the *STAT6* gene (chr12:57489187-57525922). Black dashed line at FDR significant threshold. Red SNP is rs167769 (index SNP).

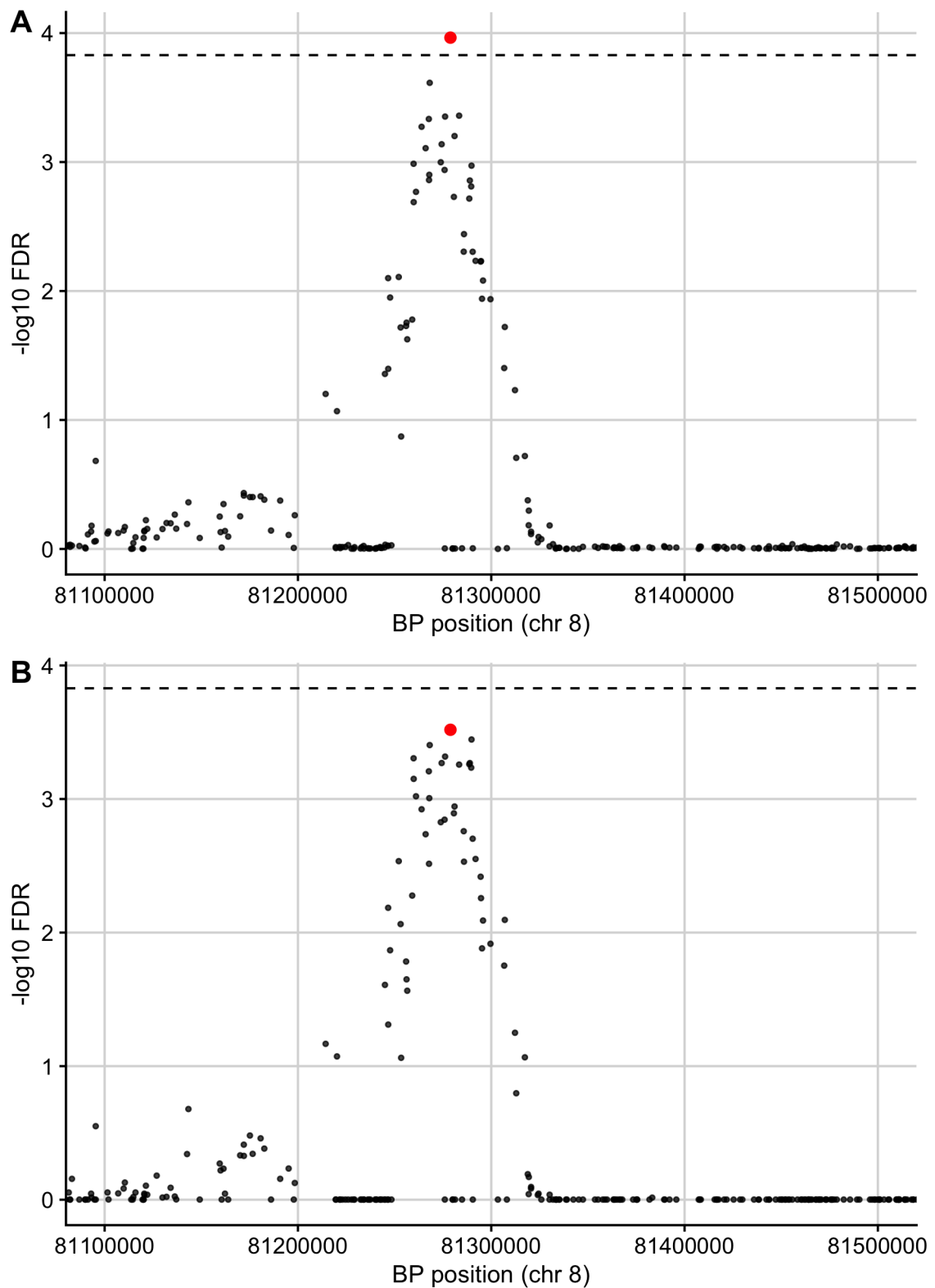


Figure S12: FDR Manhattan plots for region containing the index SNP rs12543811 that is no longer FDR significant after applying flexible cFDR. Manhattan plots of FDR adjusted  $p$ -values before (A) and after (B) applying flexible cFDR for the region (chr8:81100000-81500000) containing index SNP rs12543811 (chr6:81278885) that is no longer FDR significant when applying flexible cFDR.