

Supplementary Data – Figures

Unravelling genetic susceptibility and causal factors in liver health using MRI quantification of fat, iron, and inflammation in the liver

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Supplementary Figure 1: Overview of study design

Supplementary Figure 2: Bar plots showing the results from the LDSC partitioning analysis of A. cT1, B. PDFF, and C. liver iron.

Supplementary Figure 3: Regional association plots showing association signals for cT1

Supplementary Figure 3A: Regional association plots showing association signals for PDFF

Supplementary Figure 3B: Regional association plots showing association signals for liver iron

Supplementary Figure 3C: Regional association plots of MTAG-identified loci for cT1 (CAD)

Supplementary Figure 3D: Regional association plots of MTAG-identified loci for cT1 (T2D)

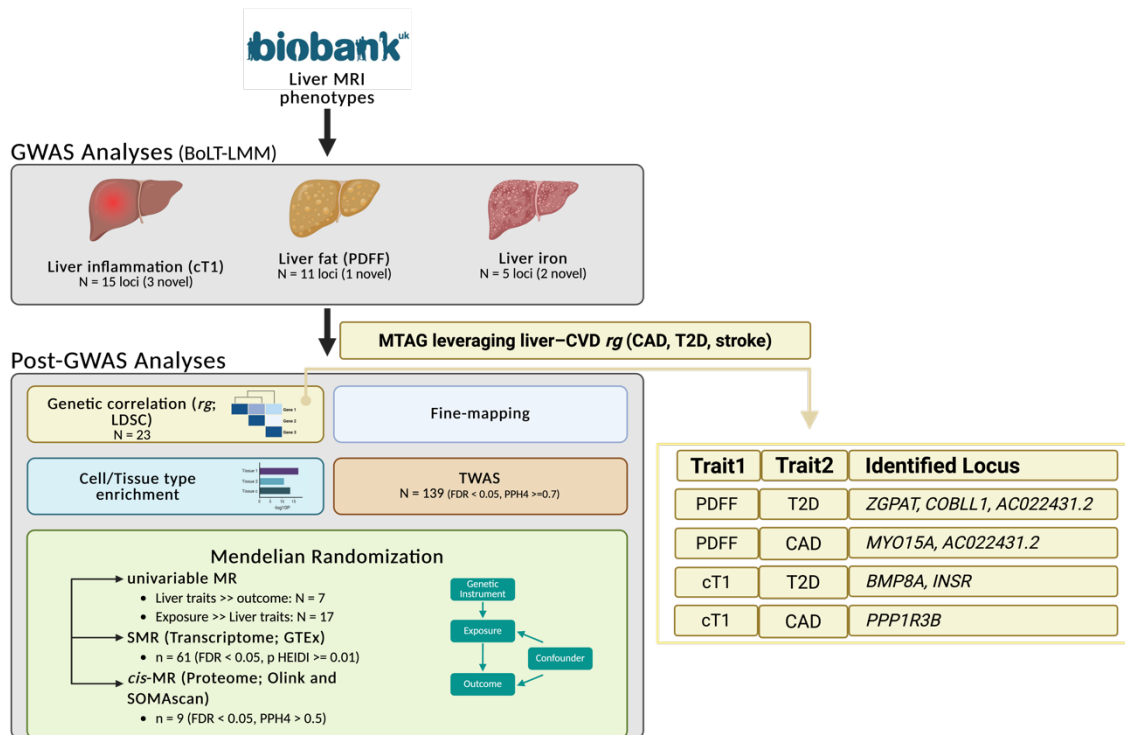
Supplementary Figure 3E: Regional association plots of MTAG-identified loci for PDFF (CAD)

Supplementary Figure 3F: Regional association plots of MTAG-identified loci for PDFF (T2D)

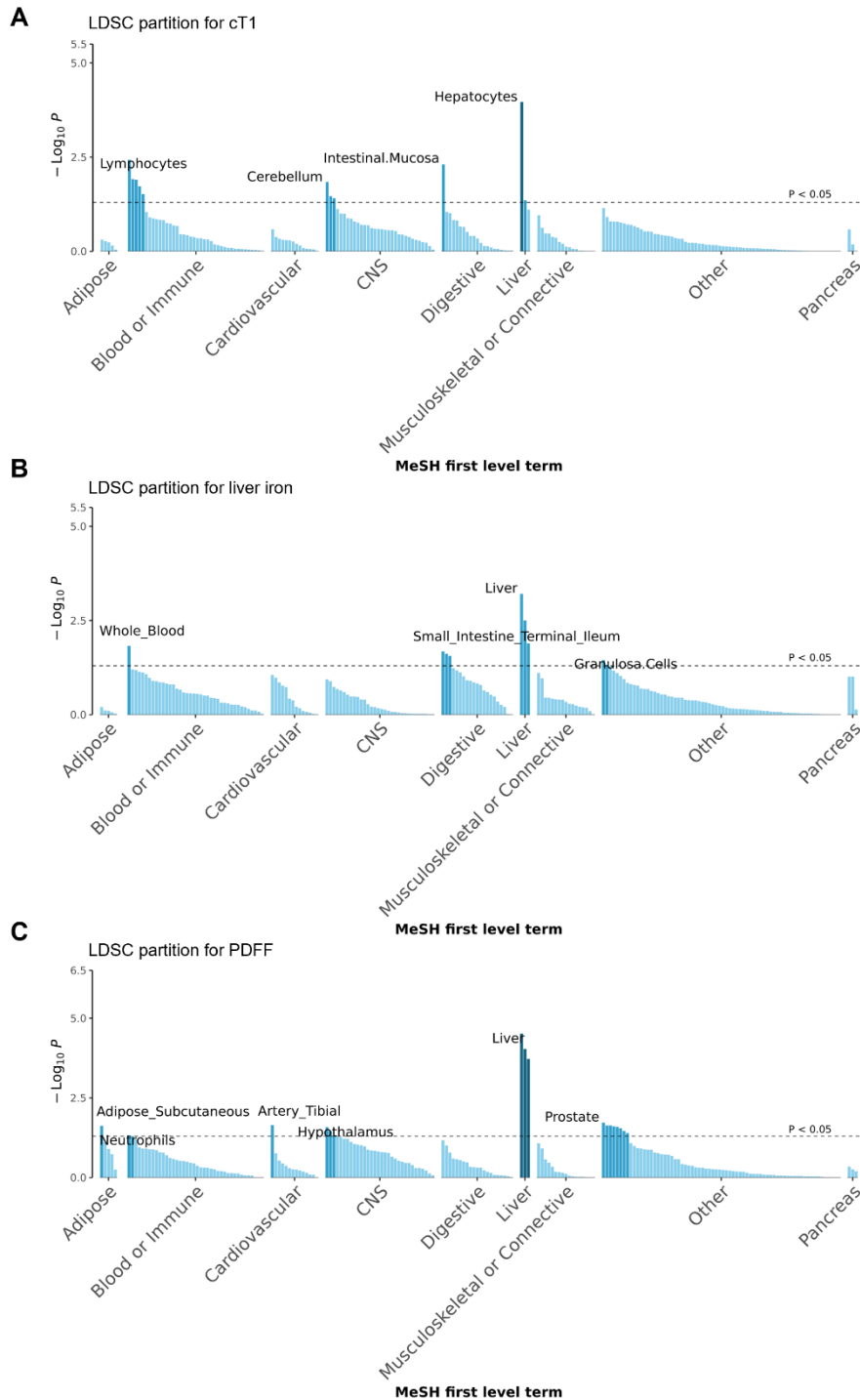
Supplementary Figure 4: LocusCompare plots showing colocalization between liver traits GWAS signals and CAD/T2D associations at selected MTAG loci.

Supplementary Figure 5: Sun plot of association results for sentinel MTAG variants from the lookup in UKB-PPP.

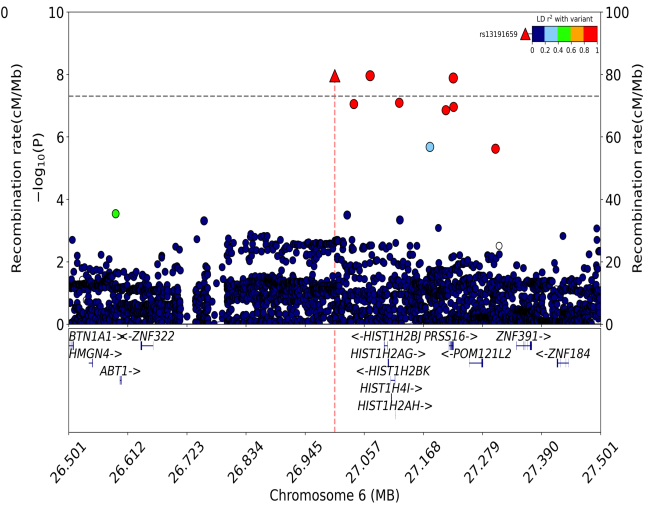
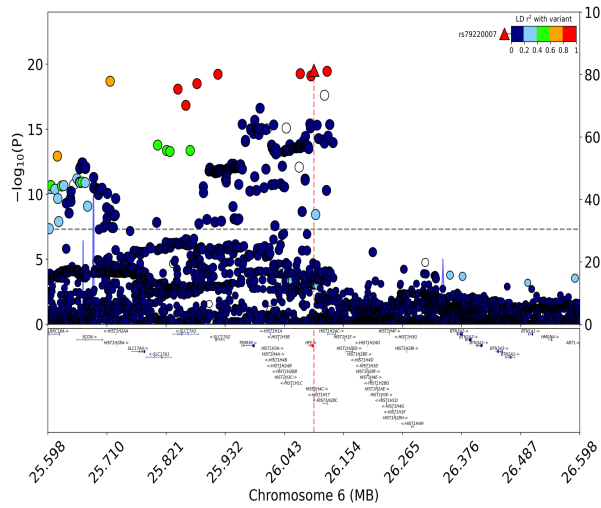
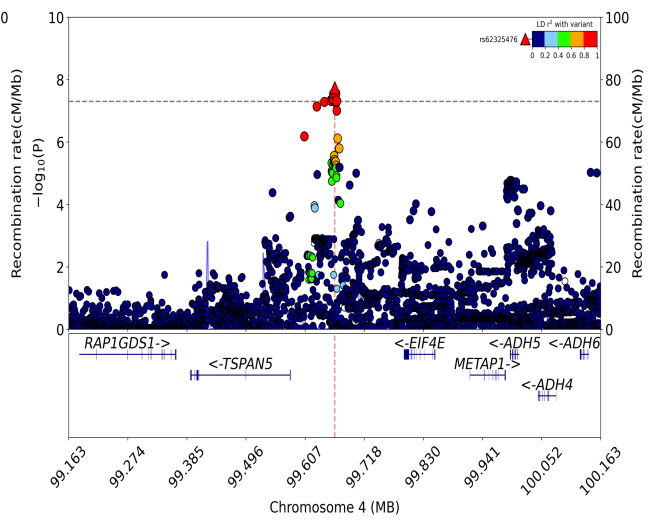
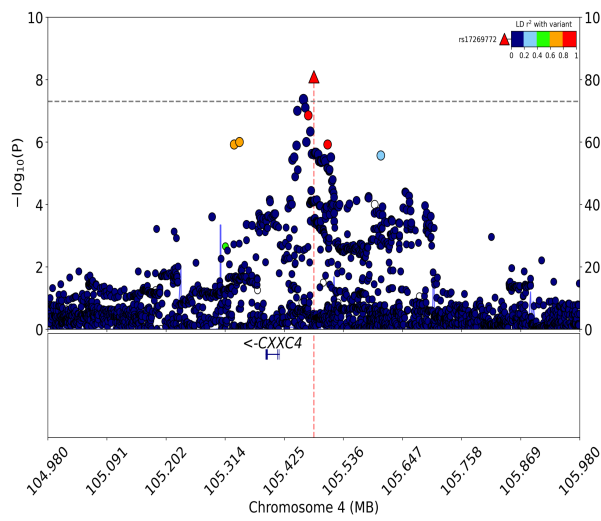
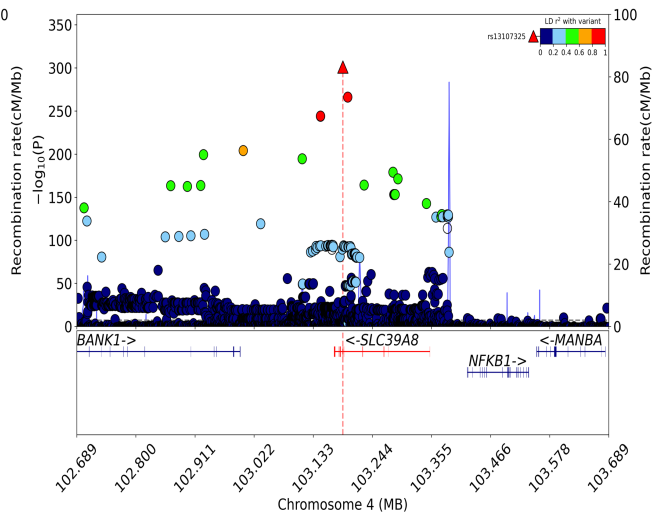
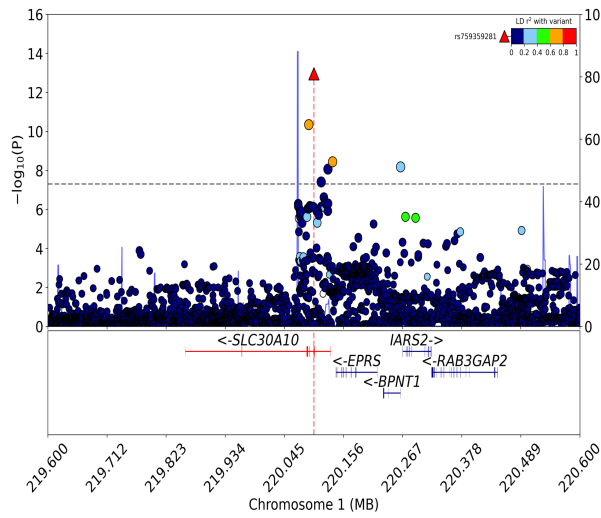
Supplementary Figure 6: Sun plot of association results for sentinel MTAG variants from the lookup in deCODE.

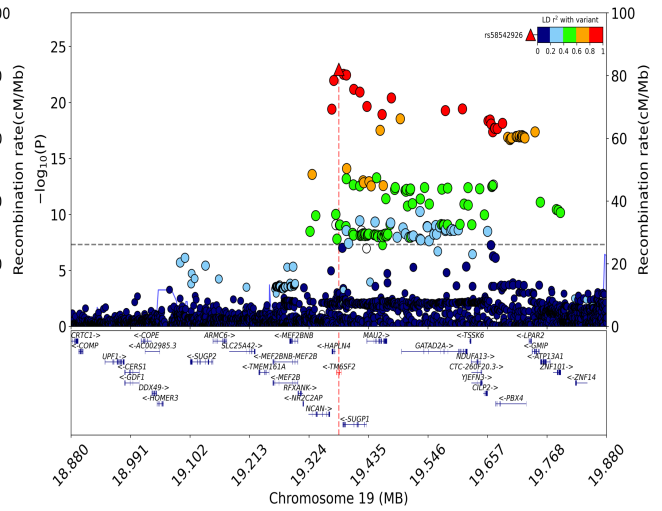
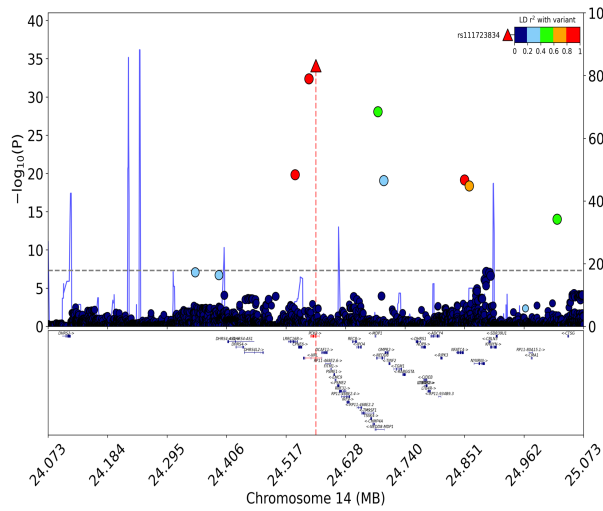
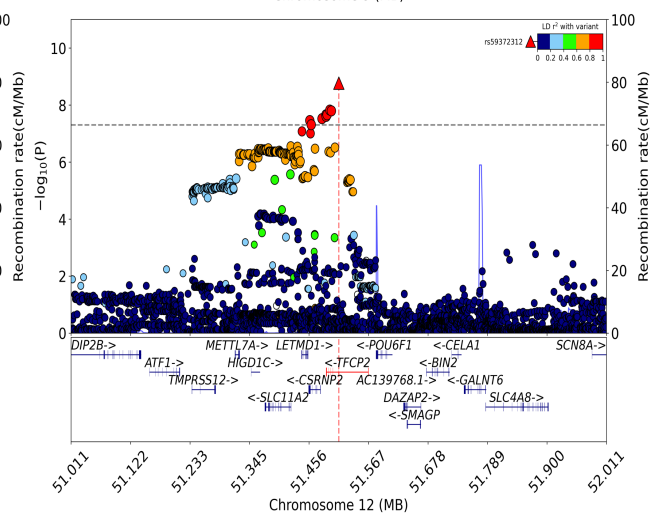
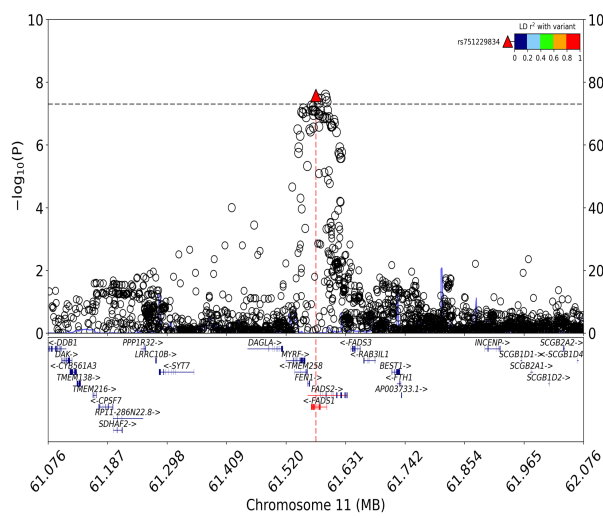
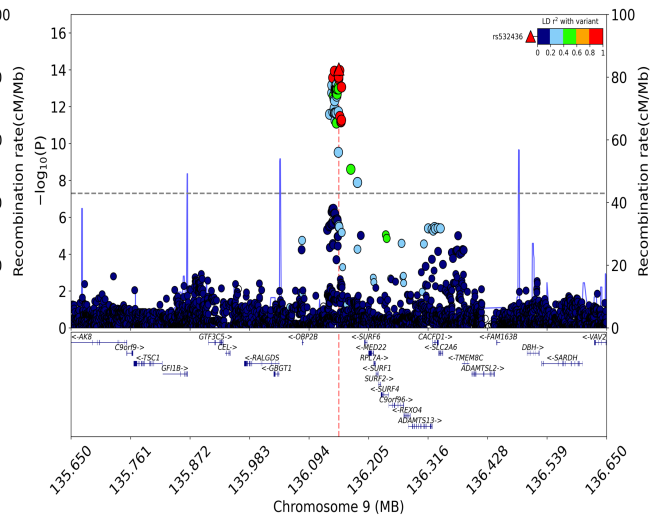
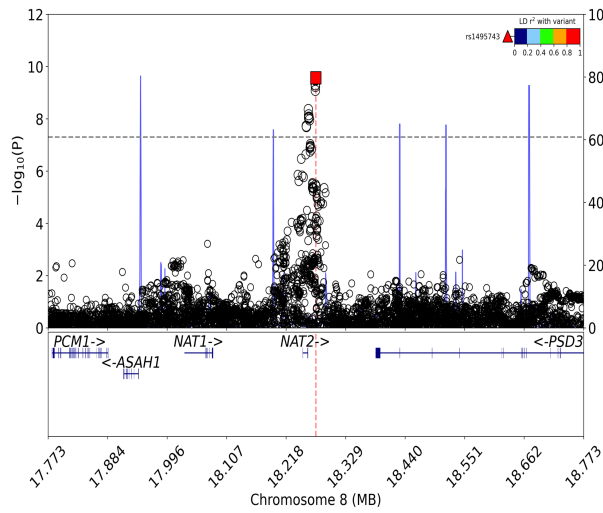


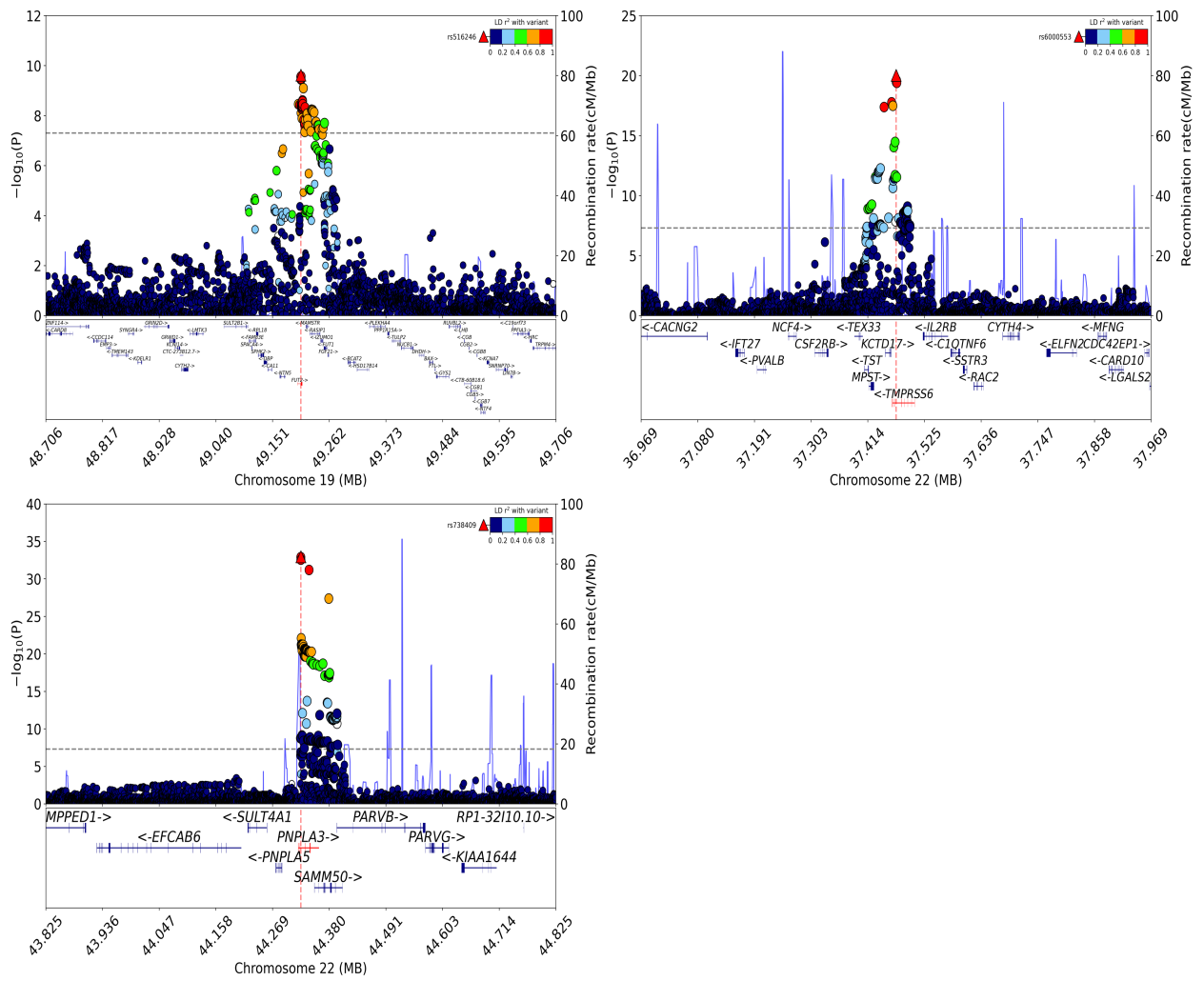
Supplementary Figure 1: Overview of study design. N, sample size; GWAS, genome-wide association study; MTAG, multi-trait analysis of GWAS; CAD, coronary artery disease; T2D, type 2 diabetes; LDSC, linkage disequilibrium score regression; TWAS, transcriptome-wide association study; SMR-HEIDI, summary-data-based Mendelian randomization–heterogeneity in dependent instruments; GTEx, Genotype-Tissue Expression project. Created in Biorender.com.



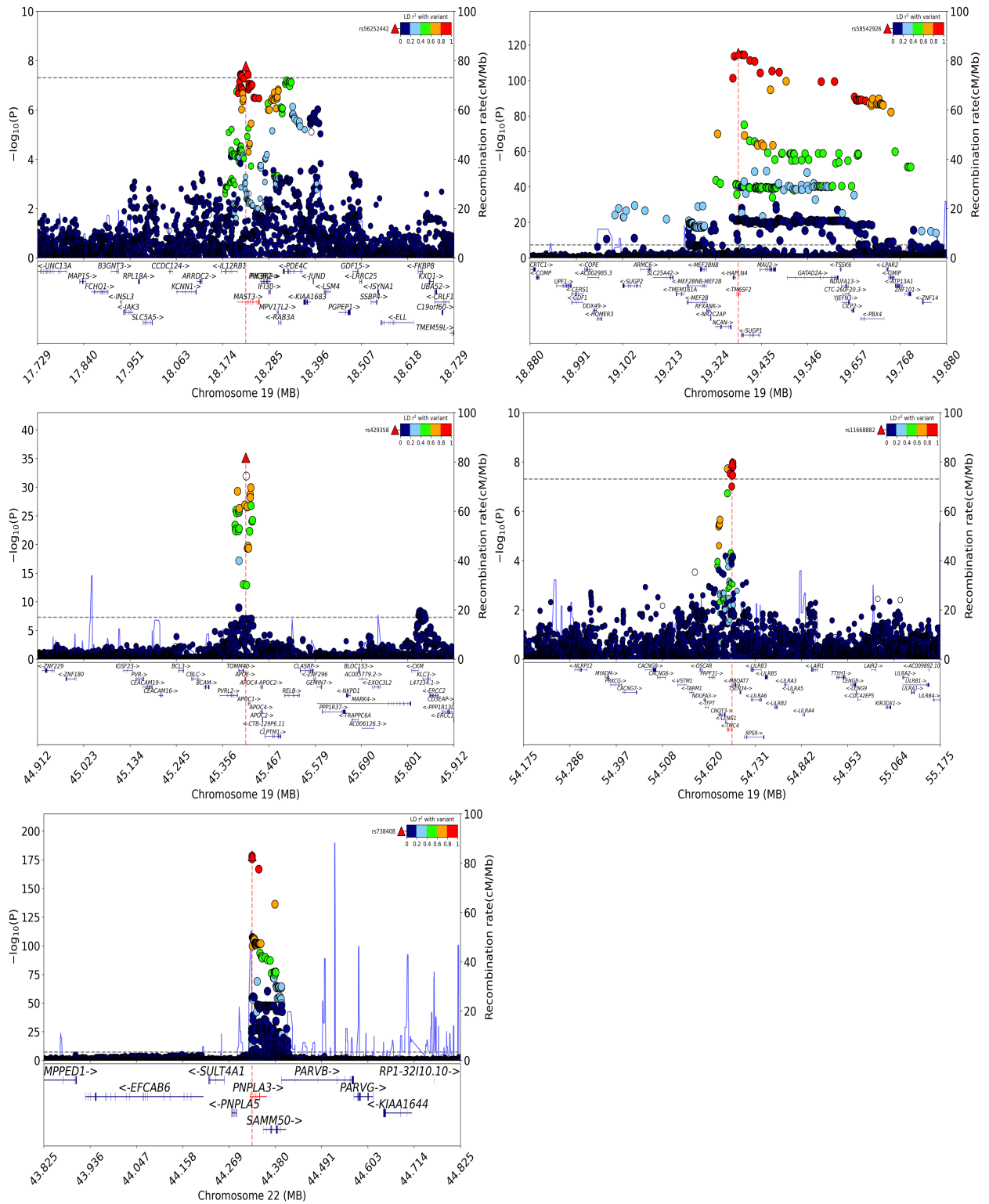
Supplementary Figure 2: Bar plots showing the results from the LDSC partitioning analysis of A. cT1, B. PDFF, and C. liver iron. The x-axis shows the MeSH first level term of the functional category. The horizontal line shows a nominal significance level. The top tissue that is at least nominally significant was labelled within each category. Non-significant tissues were coloured light blue, nominal significant tissues were coloured blue, and FDR-significant tissues were coloured dark blue.



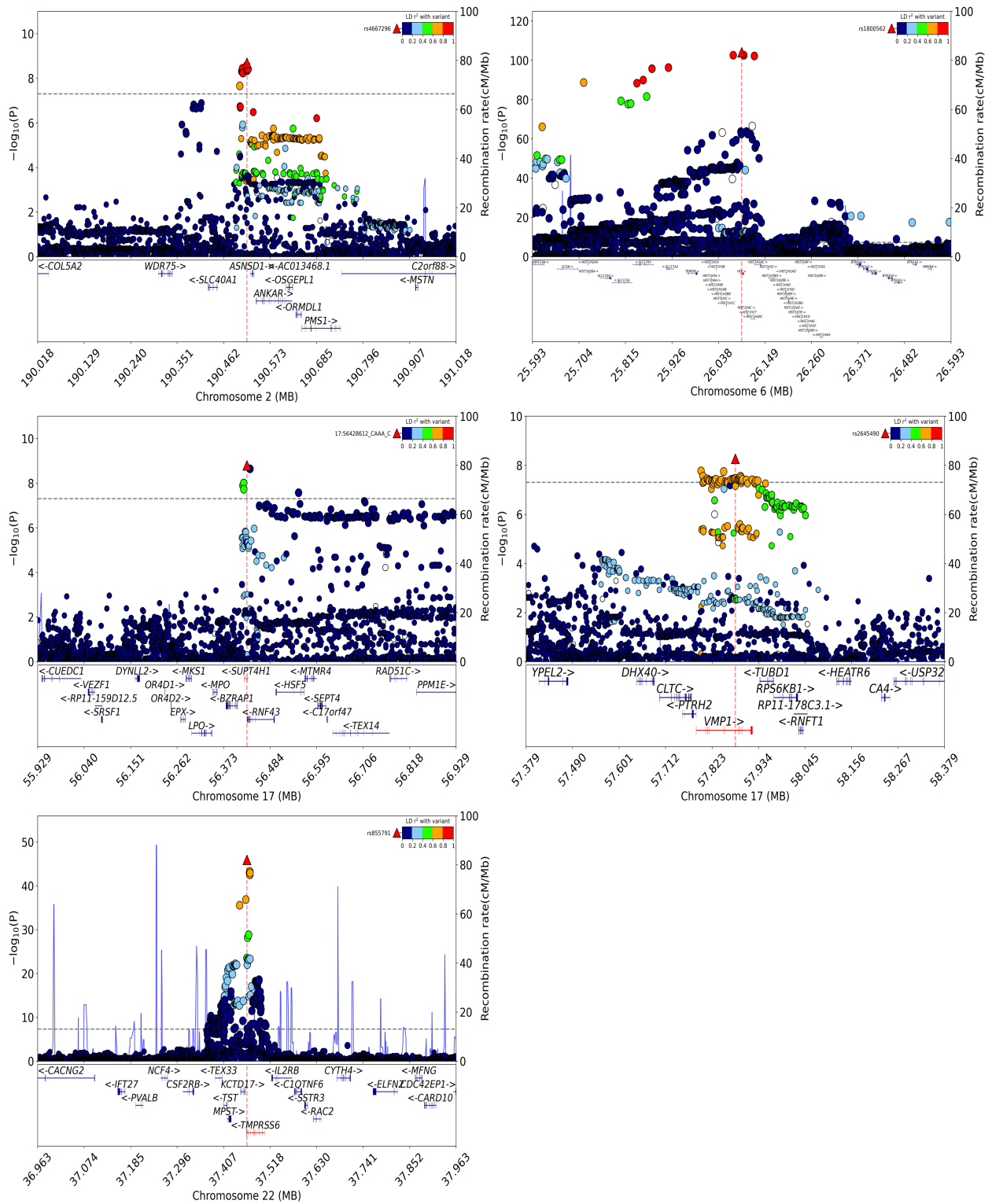




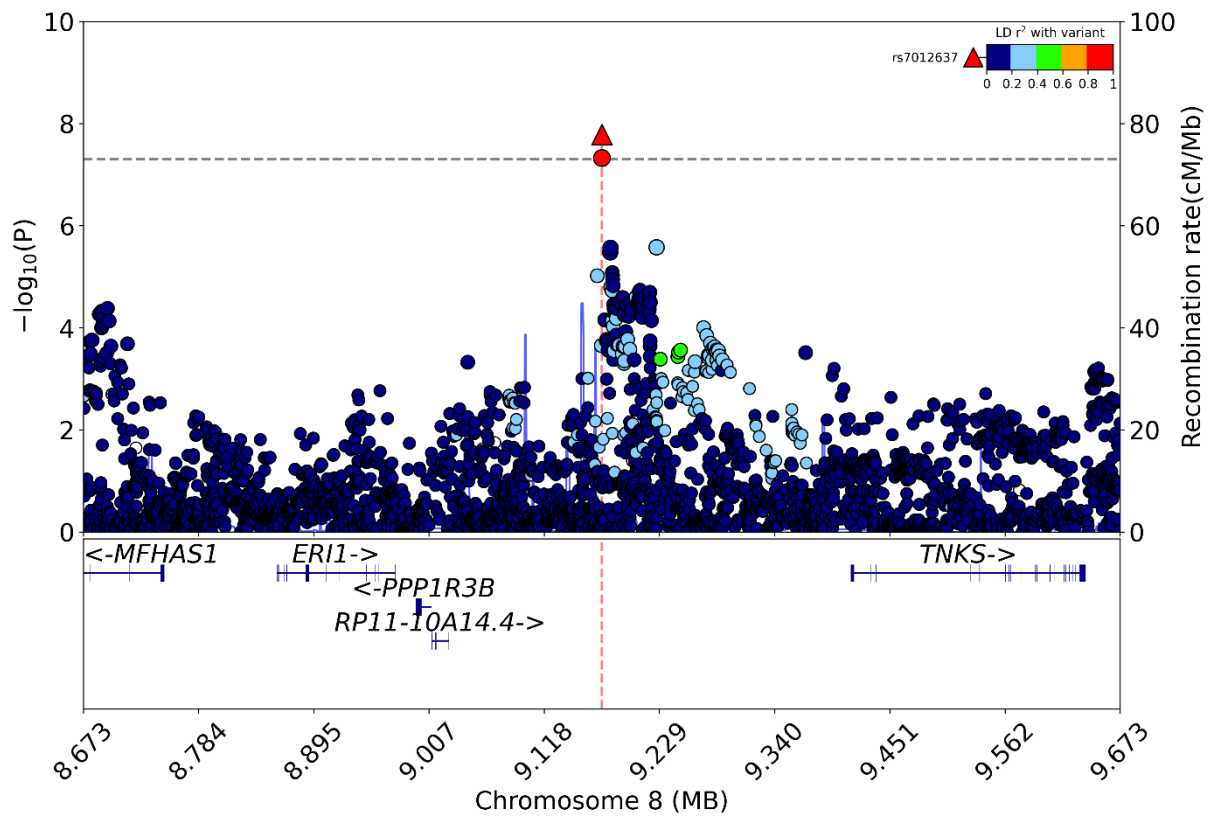
Supplementary Figure 3: Regional association plots showing association signals for cT1 across all loci identified in the univariate GWAS of cT1 study. Each plot displays the $-\log_{10}(P)$ values of variants in the region, with the lead SNP indicated by the red diamond. Linkage disequilibrium (LD) is represented by color scale relative to the lead SNP.



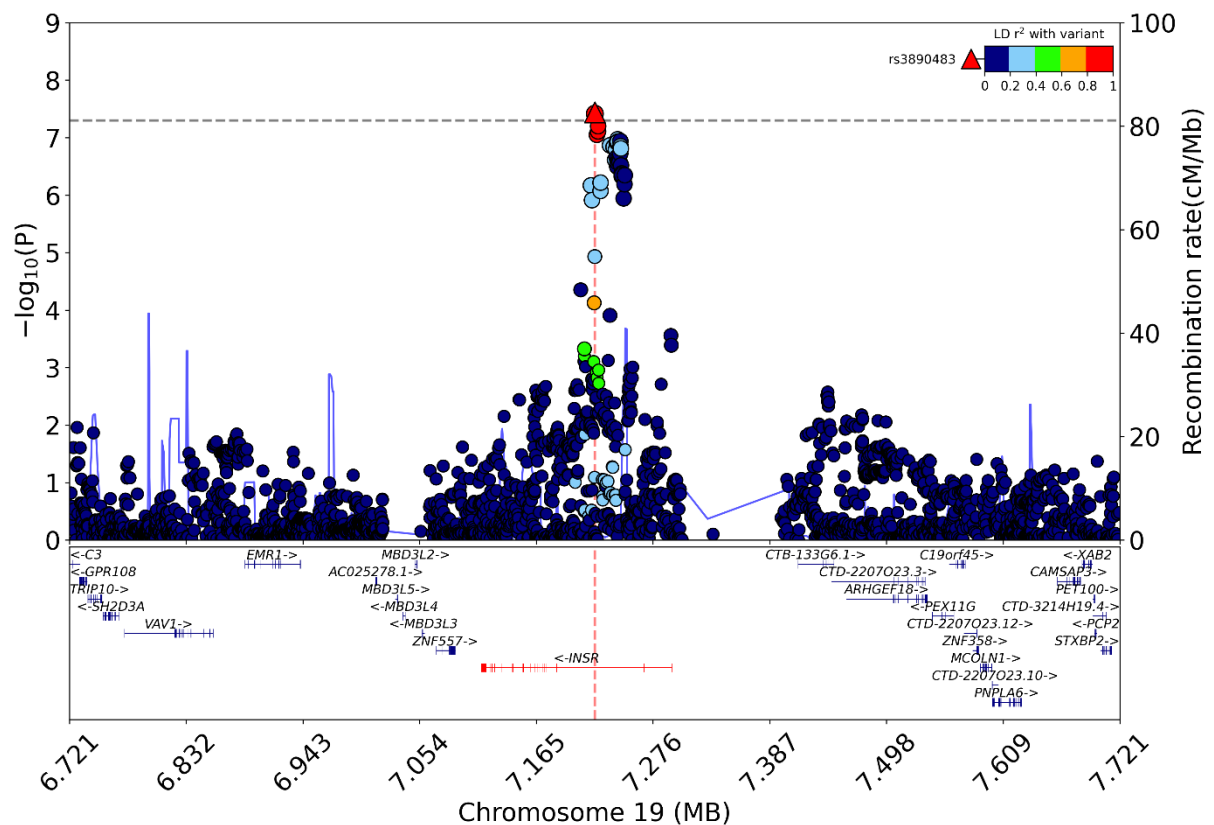
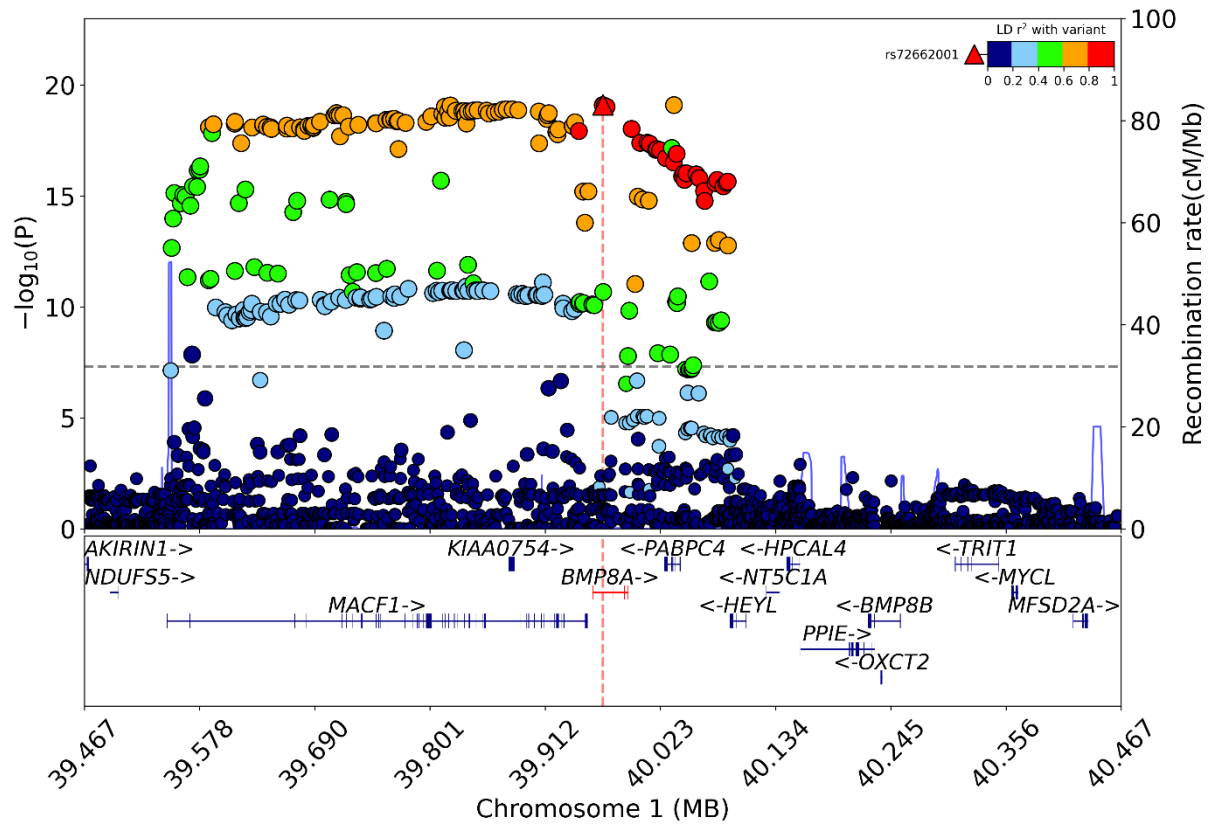
Supplementary Figure 3A: Regional association plots showing association signals for PDFF across all loci identified in the univariate GWAS of PDFF study. Each plot displays the $-\log_{10}(P)$ values of variants in the region, with the lead SNP indicated by the red diamond. Linkage disequilibrium (LD) is represented by color scale relative to the lead SNP.



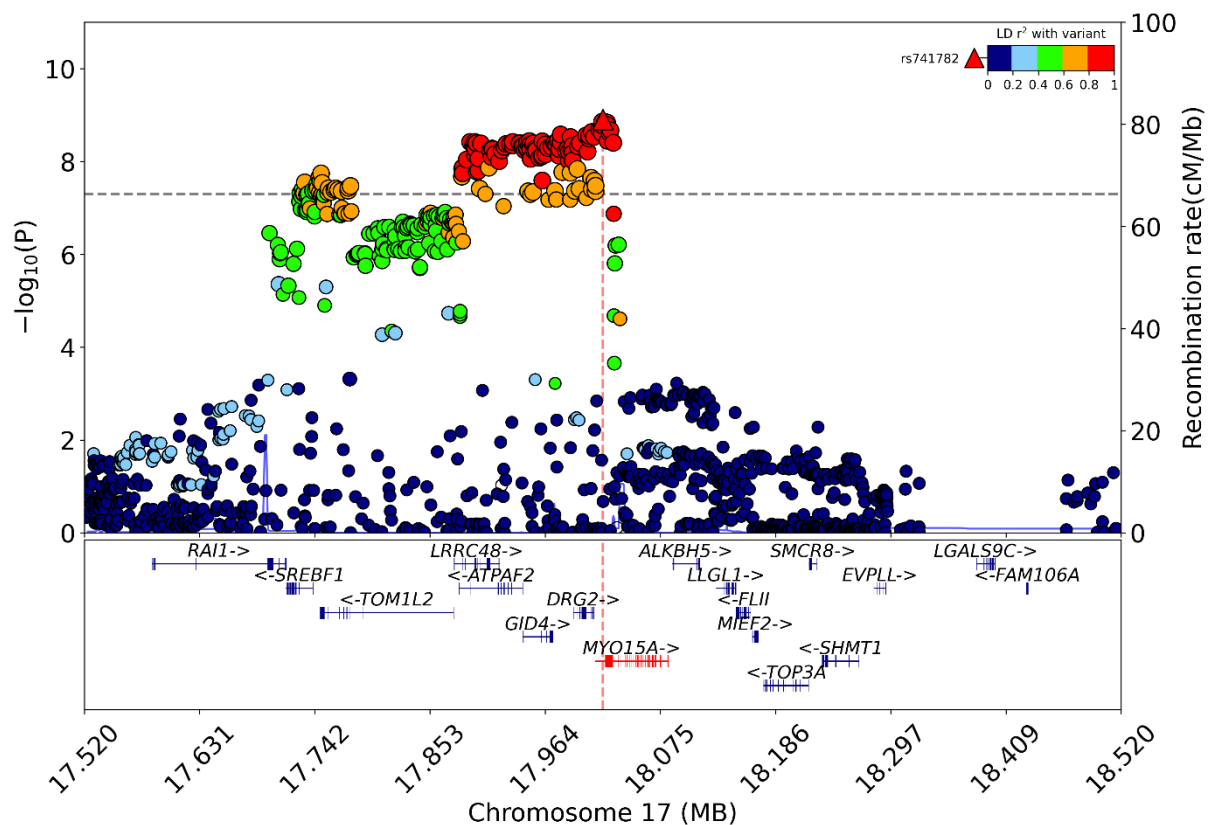
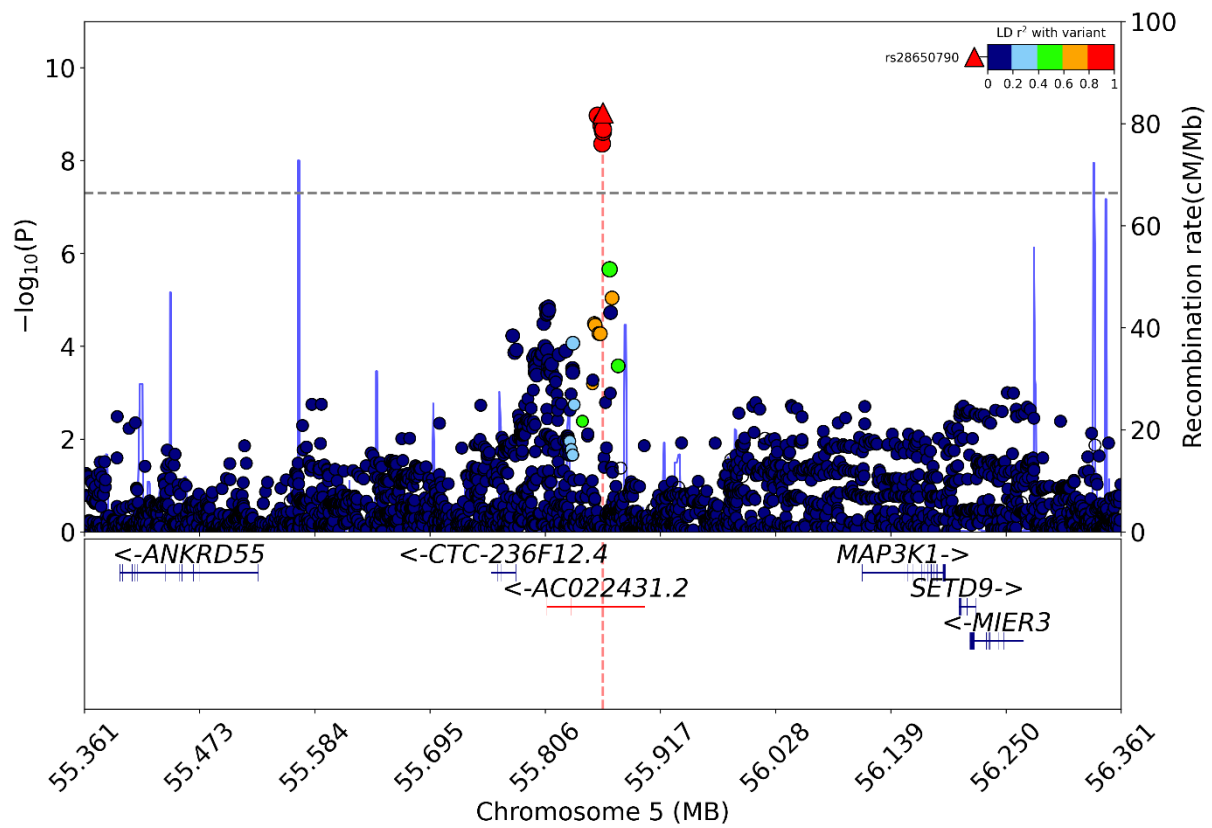
Supplementary Figure 3B: Regional association plots showing association signals for liver iron across all loci identified in the univariate GWAS of liver iron study. Each plot displays the $-\log_{10}(P)$ values of variants in the region, with the lead SNP indicated by the red diamond. Linkage disequilibrium (LD) is represented by color scale relative to the lead SNP.



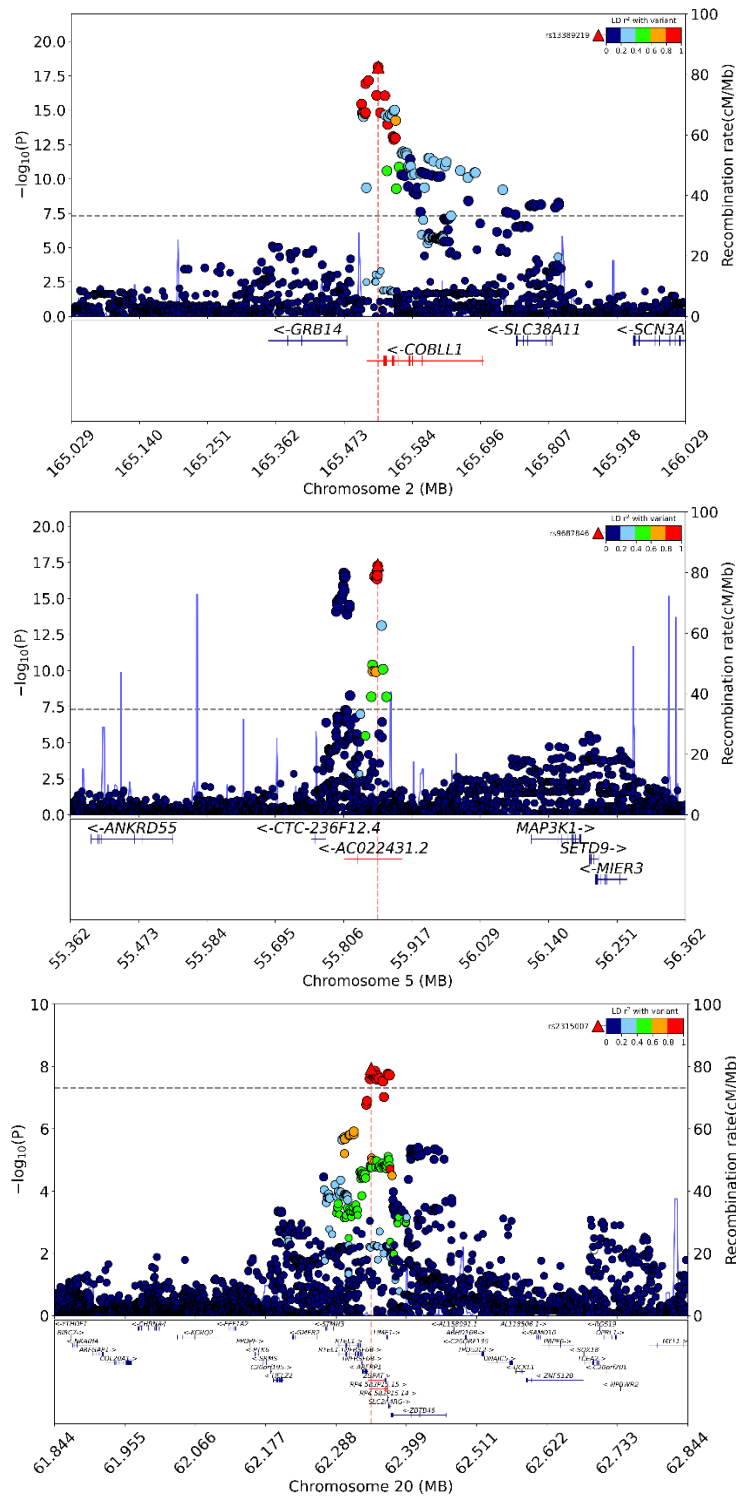
Supplementary Figure 3C: Regional association plots showing association signals for cT1 across all loci identified in the MTAG analysis (cT1 combined with CAD). Each plot displays the $-\log_{10}(P)$ values of variants in the region, with the lead SNP indicated by the red diamond. Linkage disequilibrium (LD) is represented by color scale relative to the lead SNP.



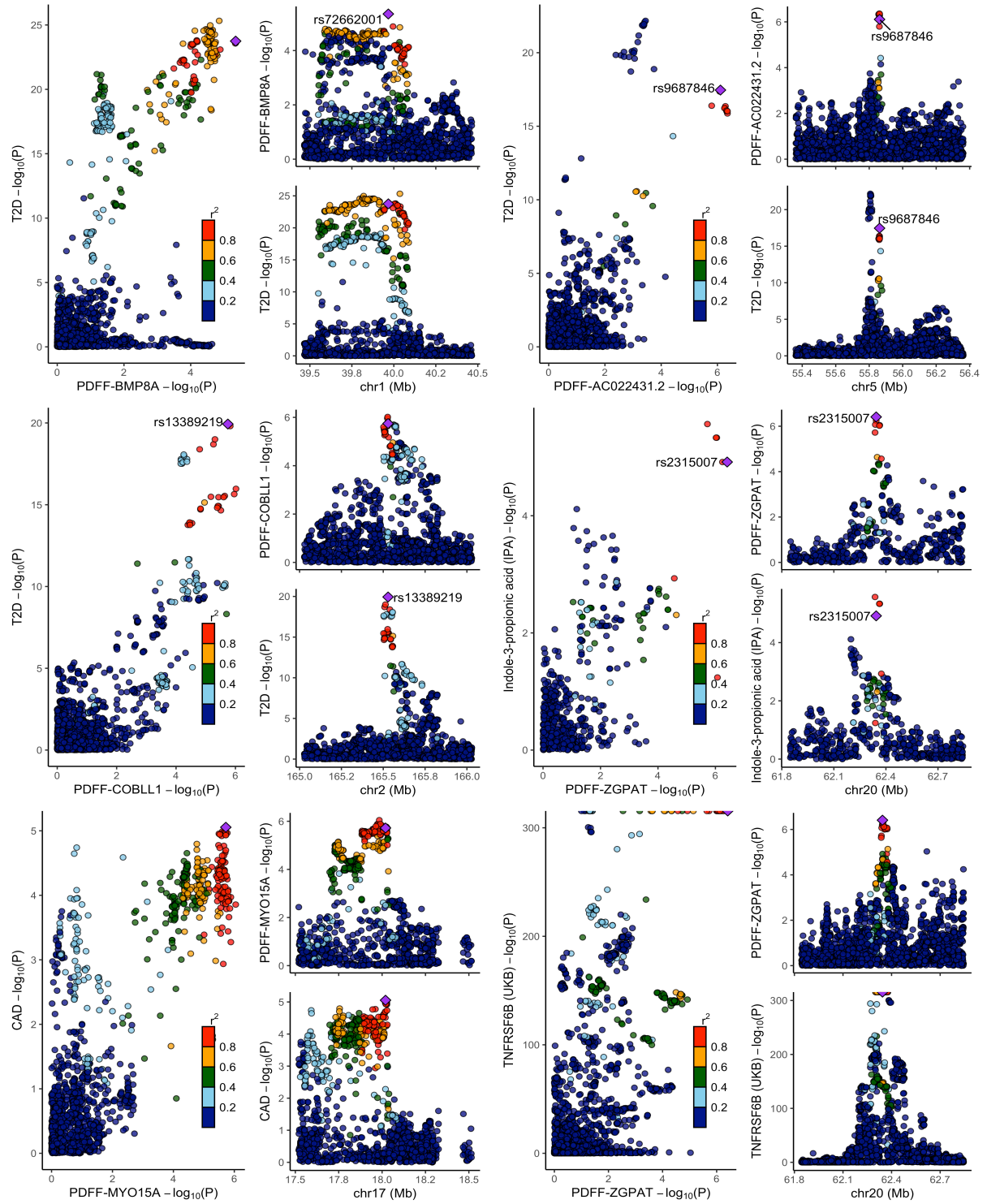
Supplementary Figure 3D: Regional association plots showing association signals for cT1 across all loci identified in the MTAG analysis (cT1 combined with T2D). Each plot displays the $-\log_{10}(P)$ values of variants in the region, with the lead SNP indicated by the red diamond. Linkage disequilibrium (LD) is represented by color scale relative to the lead SNP.

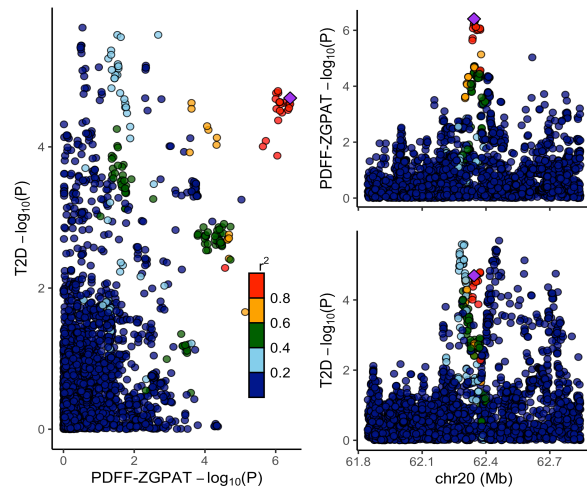


Supplementary Figure 3E: Regional association plots showing association signals for PDDF across all loci identified in the MTAG analysis (PDDF combined with CAD). Each plot displays the $-\log_{10}(P)$ values of variants in the region, with the lead SNP indicated by the red diamond. Linkage disequilibrium (LD) is represented by color scale relative to the lead SNP.

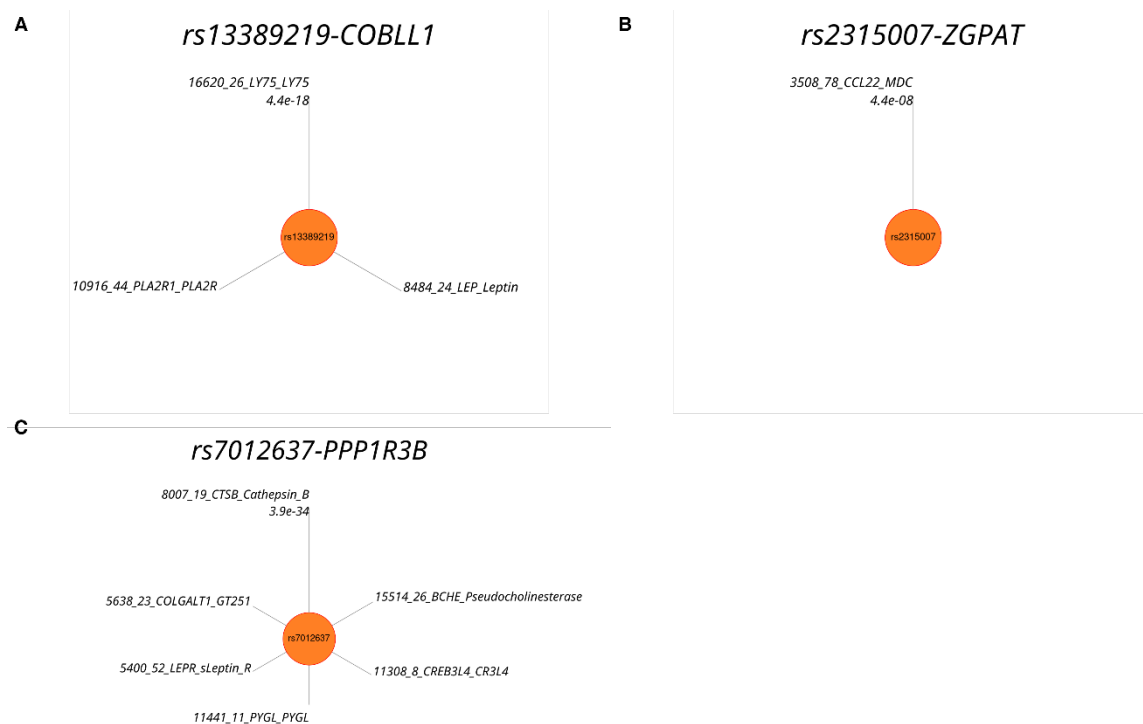


Supplementary Figure 3F: Regional association plots showing association signals for PDFF across all loci identified in the MTAG analysis (PDFF combined with T2D). Each plot displays the $-\log_{10}(P)$ values of variants in the region, with the lead SNP indicated by the red diamond. Linkage disequilibrium (LD) is represented by color scale relative to the lead SNP.





Supplementary Figure 4: LocusCompare plots showing colocalization between liver traits GWAS signals and CAD/T2D associations at selected MTAG loci. Each point represents a variant present in both datasets, plotted by $-\log_{10}(P)$ values from the liver trait univariate GWAS (x-axis) and univariate CAD/T2D GWAS (y-axis). Variants in strong linkage disequilibrium (LD) with the lead SNP are highlighted. Colocalization patterns suggest shared genetic signals between PDFF with (A) T2D at BMP8A (B) T2D at AC022431.2 (C) T2D at COBLL1 (D) IPA3 at ZGPAT (E) CAD at MYO15A (F) TNFRSF6B levels at ZGPAT and (G) T2D at ZGPAT.



Supplementary Figure 6: Sun plot of association results for sentinel MTAG variants from the lookup in deCODE genetics. Protein quantitative trait locus (pQTL) lookup results (cis and trans) are plotted for a single SNP with $p < 5 \times 10^{-8}$ ($-\log_{10}$ p-value). The length of each line corresponds to the significance of the association, with the most significant result positioned at the top (“noon”) and subsequent results arranged clockwise. The p-value of the most significant association is shown to provide a sense of scale. Plots were created using PheWAS-View.