

A Systems Genetic Analysis of High Density Lipoprotein Metabolism and
Network Preservation across Mouse Models
Supplementary figures

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This document collects the supplementary figures (and their captions) for the main article *A Systems Genetic Analysis of High Density Lipoprotein Metabolism and Network Preservation across Mouse Models*.

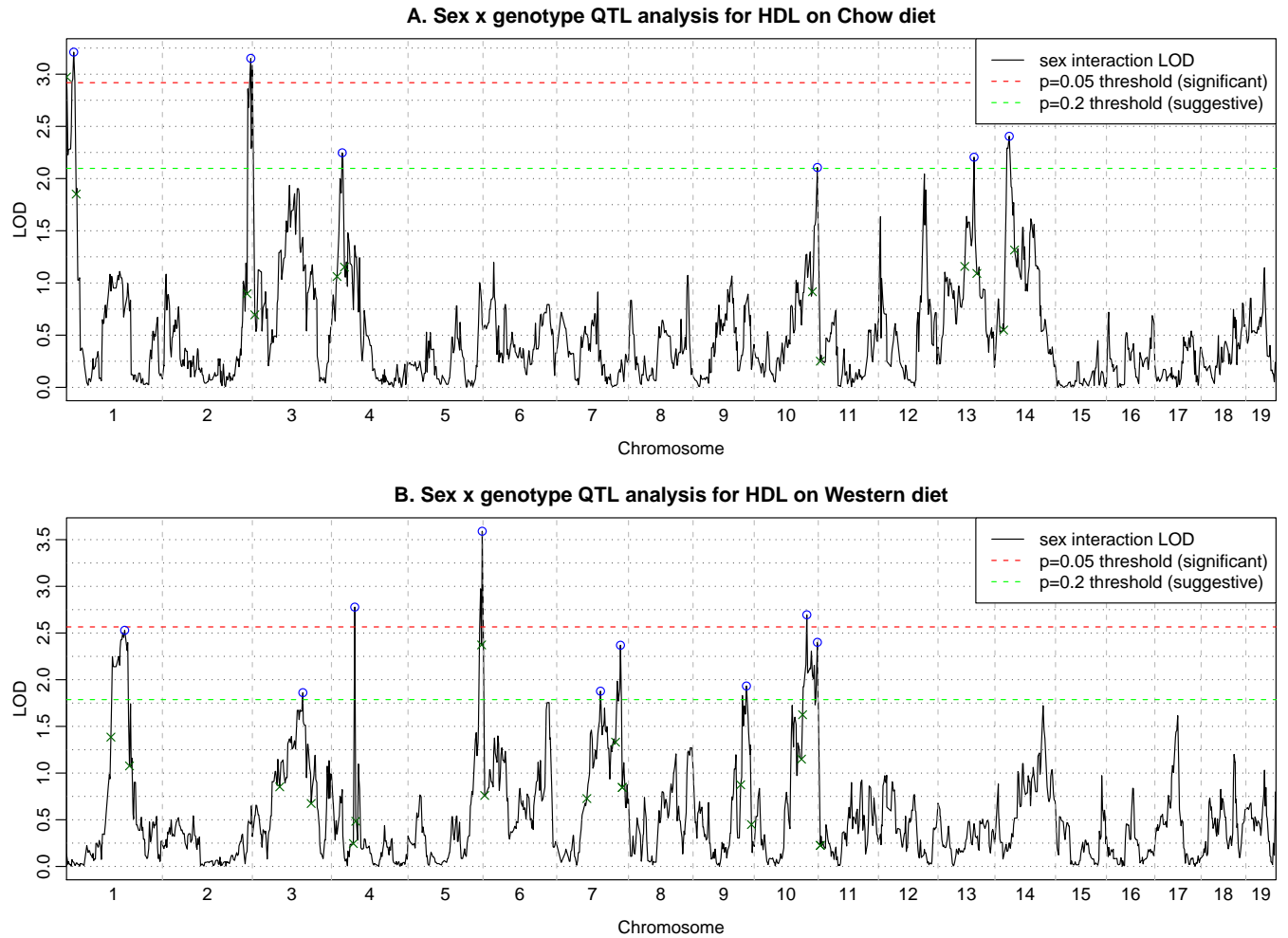


Figure 1. QTL analysis (A) HDL on chow diet and (B) HDL on Western diet, with sex as an additive and interactive trait. Black line shows the LOD scores for the genotyped SNP markers; blue circles identify peaks that reach at least suggestive level of significance (marked by the dotted green line) and green crosses identify the boundaries of peak regions defined as the nearest SNP markers at which the LOD score drops more than 1.5 below the peak LOD. We observe several loci with significant and multiple additional loci with suggestive evidence for a sex-specific allele effect.

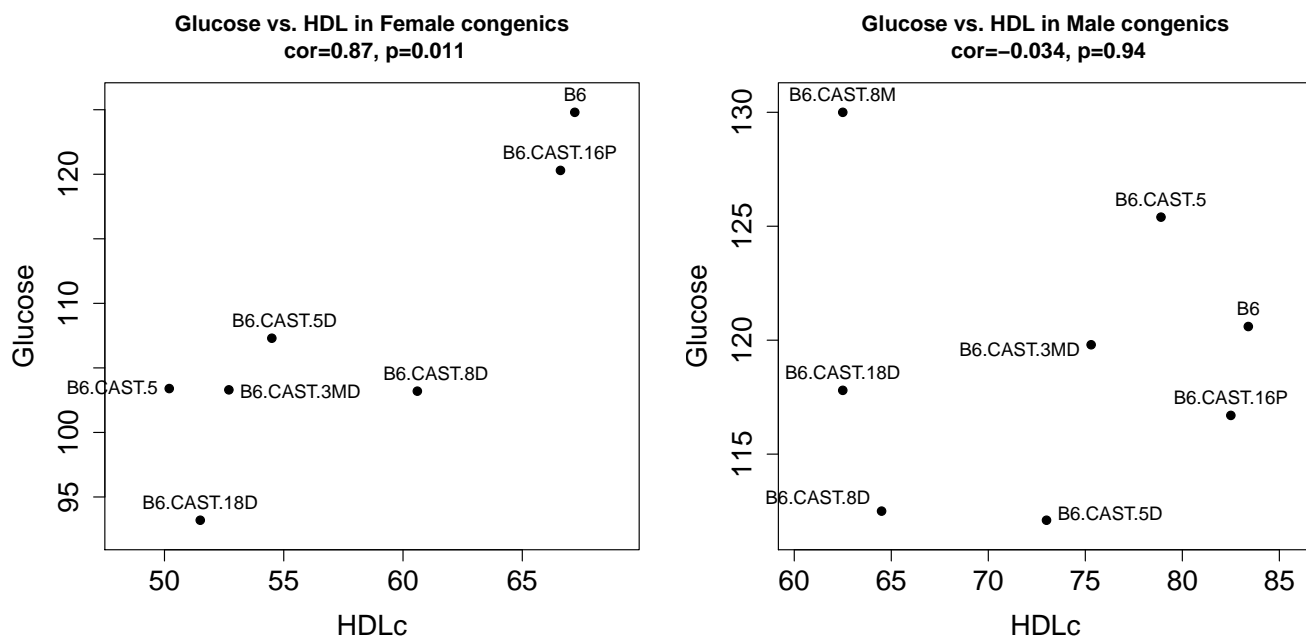


Figure 2. Scatterplots of mean values of plasma glucose (y -axis) vs. mean HDL (x -axis) in female and male congenics. In female congenics there is a strong linear relationships between HDL and glucose, while in the male congenics the relationship is absent.

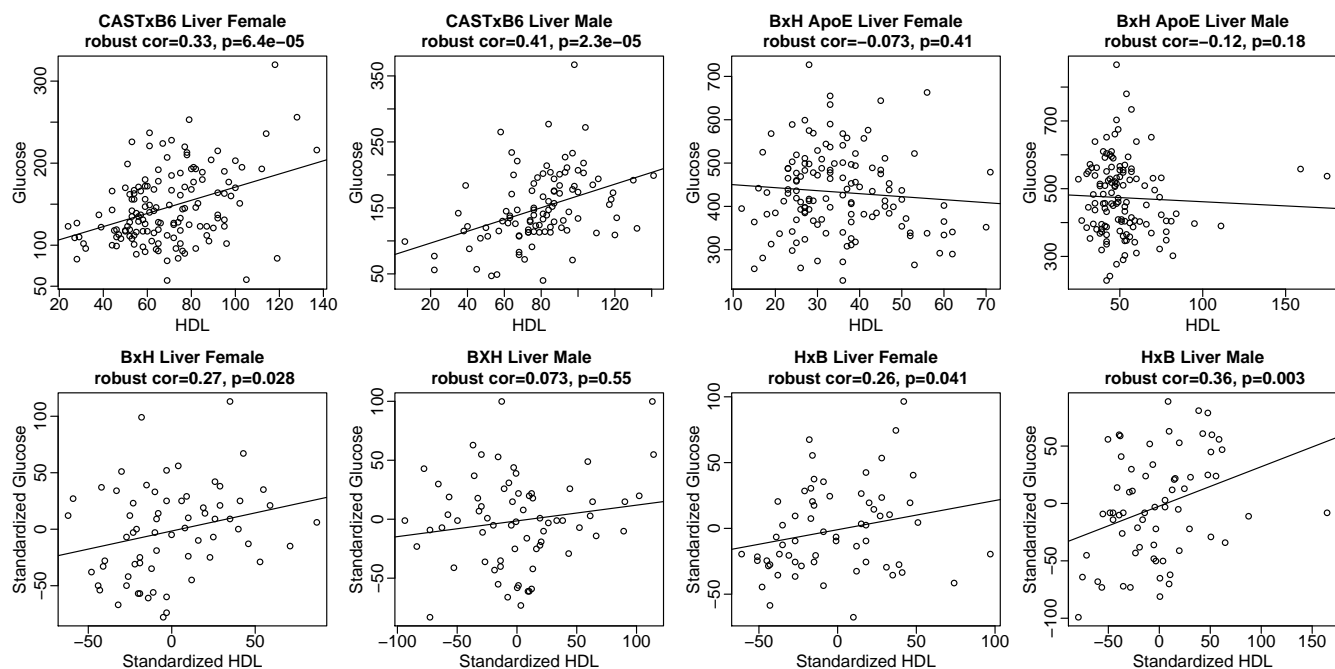


Figure 3. Scatterplots of plasma glucose (y -axis) vs. HDL (x -axis) across the data sets studied in this work. In the BxH wild type crosses the glucose and HDL values were standardized. The relationship between HDL and glucose varies from moderate (for example, in both CASTxB6 female and male data sets) to insignificant (for example, in BxH ApoE data sets).

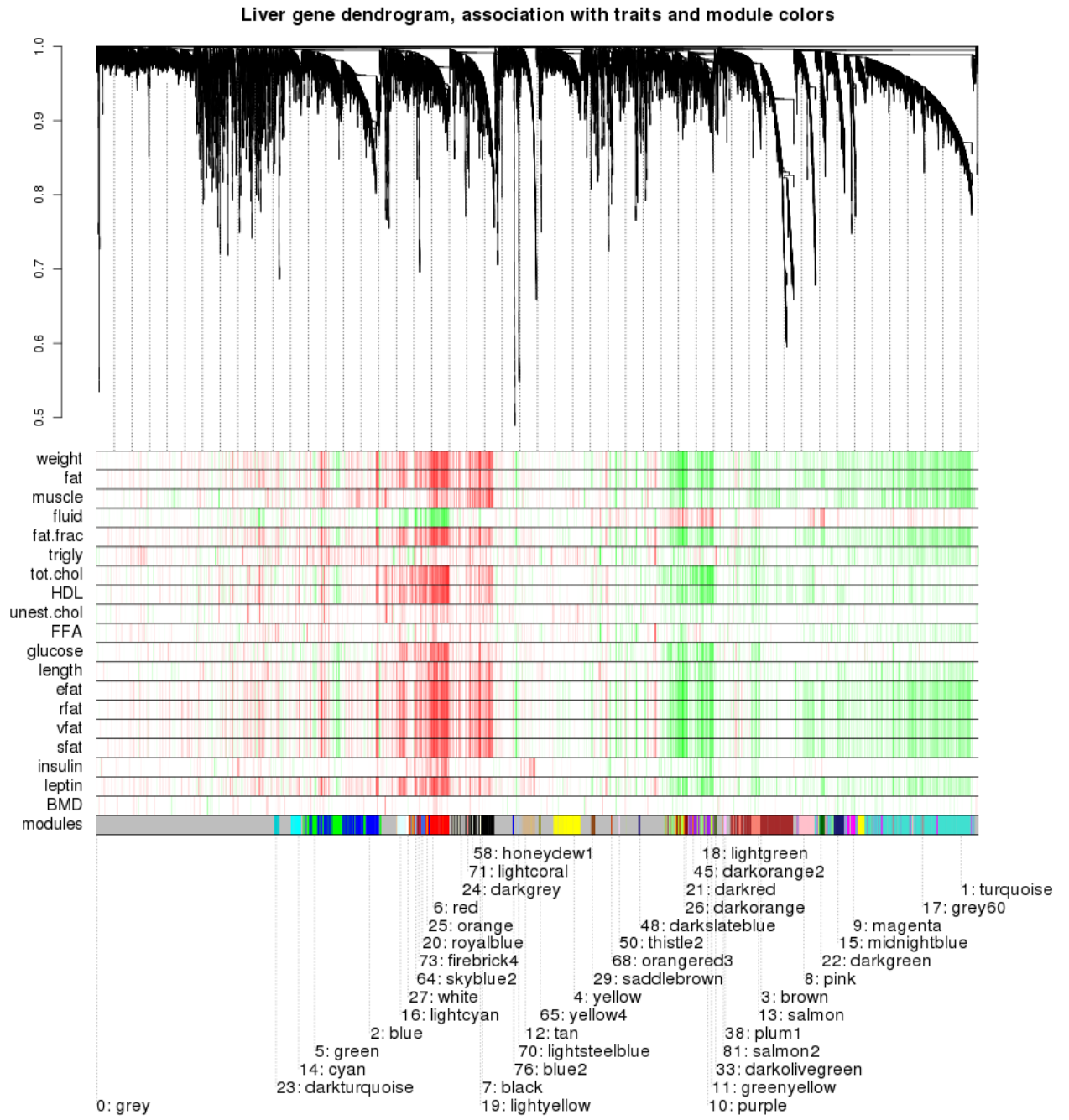


Figure 4. Upper panel shows the probe clustering tree (dendrogram) in the CASTxB6 female liver data. Branches of the dendrogram correspond to modules, shown in the “modules” color row below the dendrogram. Modules are also identified by their numeric and text labels in below the “module” color row. Other color rows below the dendrogram indicate gene significance for (i.e., association with) measured traits. Green color indicates negative correlation and red color indicates positive correlation. The figure suggests that the data contain robust co-expression patterns and that some of the modules group together genes associated with particular traits.

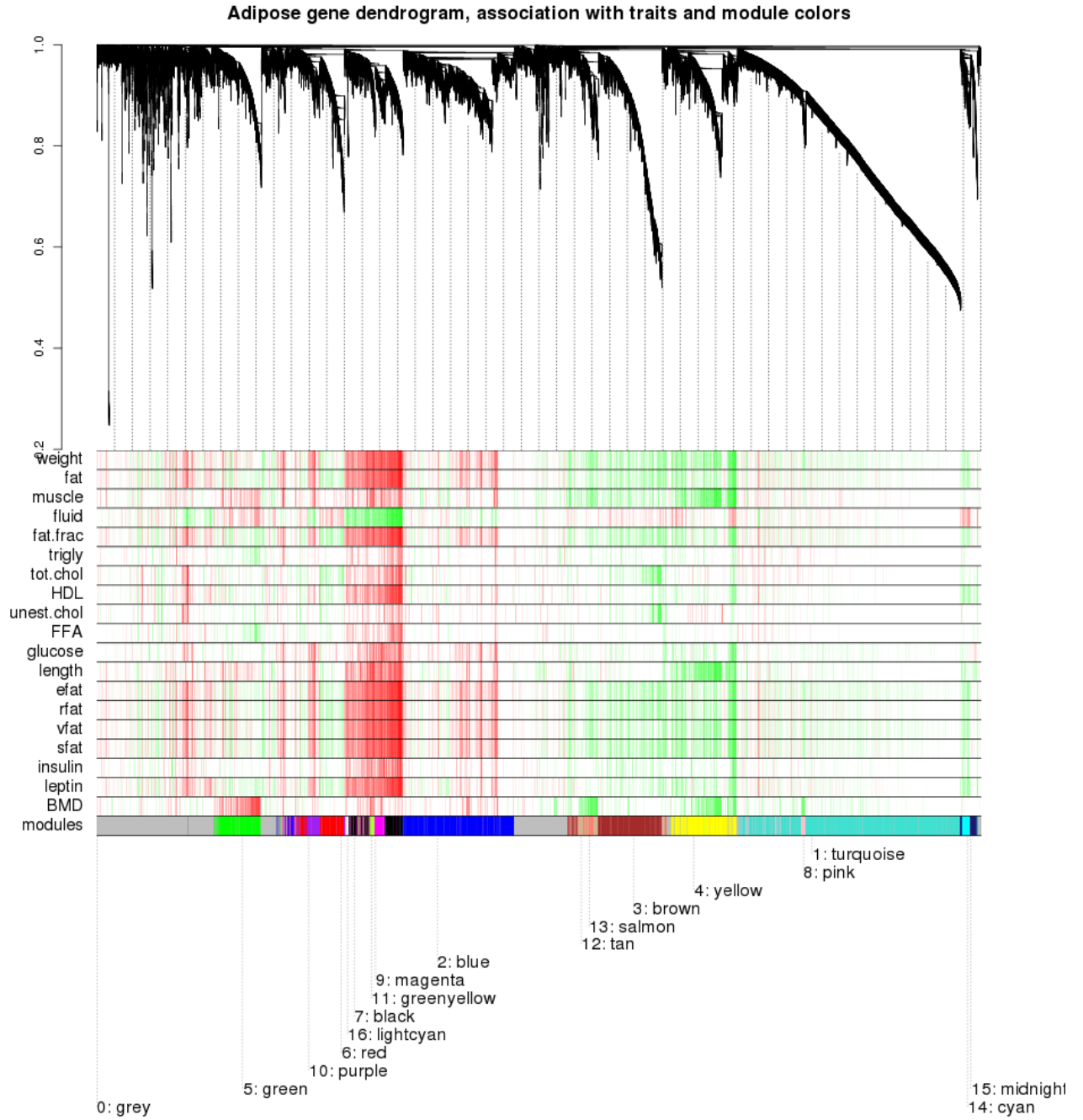


Figure 5. Upper panel shows the probe clustering tree (dendrogram) in the CASTxB6 female adipose data. Branches of the dendrogram correspond to modules, shown in the “modules” color row below the dendrogram. Modules are also identified by their numeric and text labels in below the “module” color row. Other color rows below the dendrogram indicate gene significance for (i.e., association with) measured traits. Green color indicates negative correlation and red color indicates positive correlation. The figure suggests that the data contain robust co-expression patterns and that some of the modules group together genes associated with particular traits.

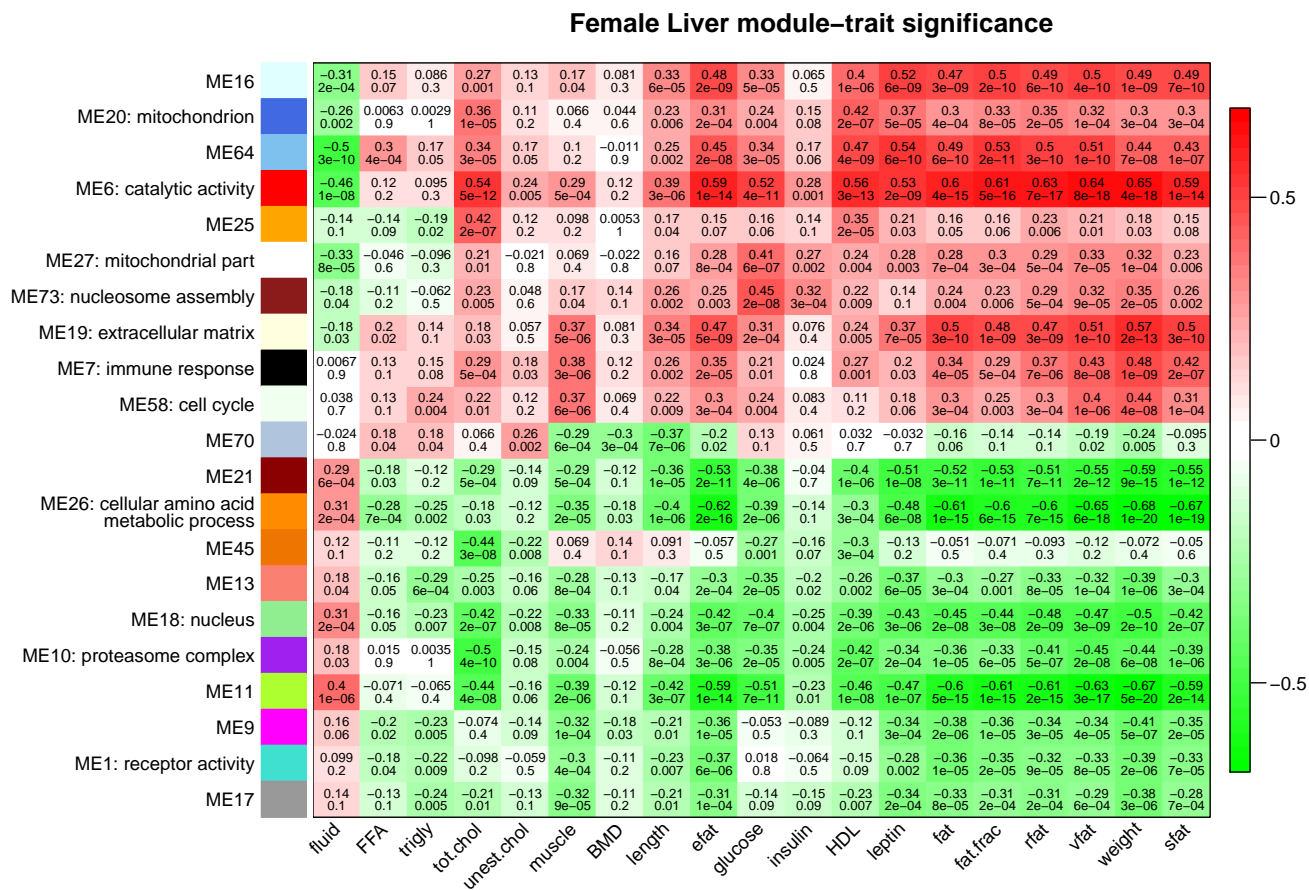


Figure 6. Module-trait associations for selected modules in CASTxB6 female liver data. We show modules whose module eigengene significance is at least 0.35 for at least one trait. Entries in the table show the module eigengene significances (that is, robust correlations of the module eigengene and the trait) and the corresponding p-values. Cells in the table are colored according to the color legend, i.e., cells with positive correlations are colored red and cells with negative correlations are colored green.

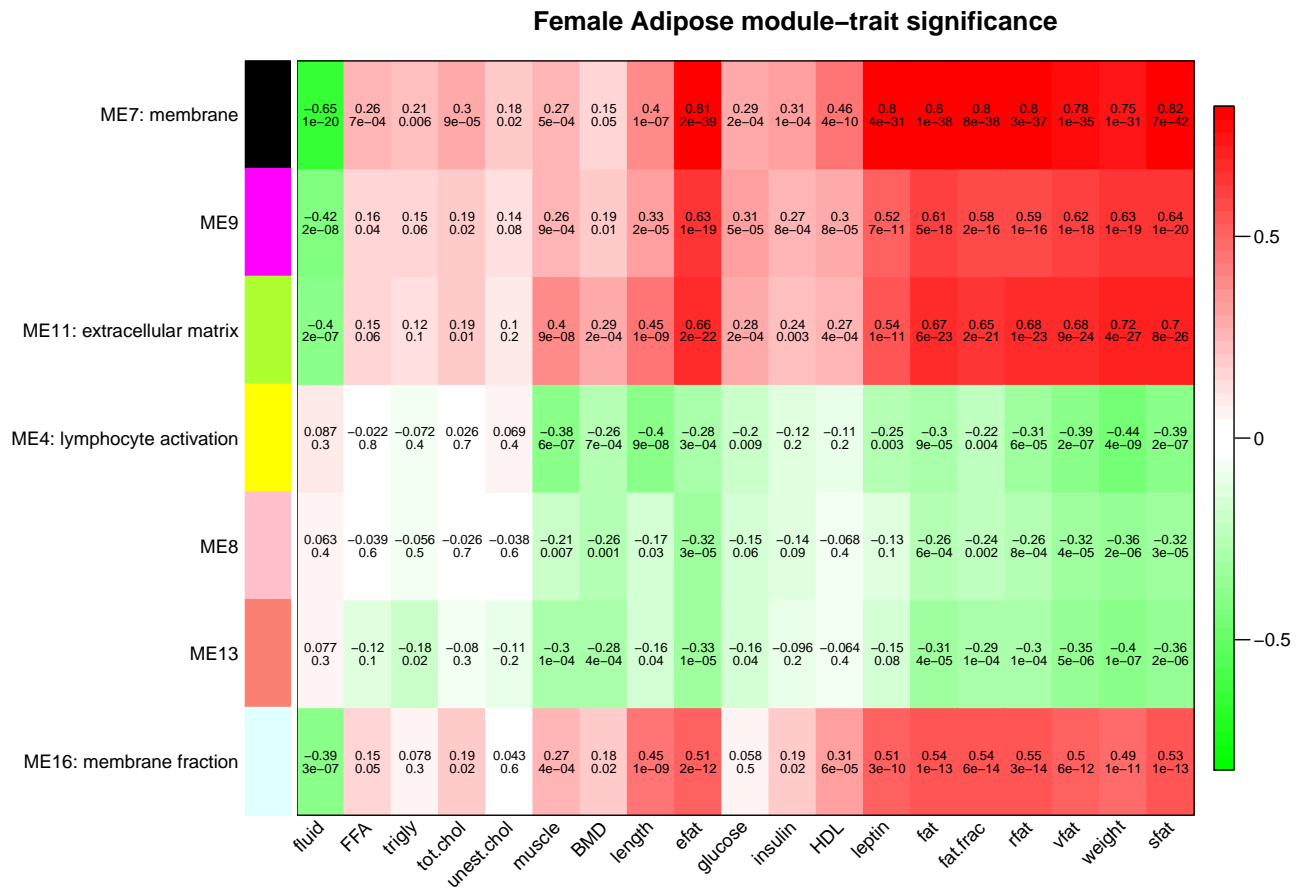


Figure 7. Module-trait associations for selected modules in CASTxB6 female adipose data. We show modules whose module eigengene significance is at least 0.35 for at least one trait. Entries in the table show the module eigengene significances (that is, robust correlations of the module eigengene and the trait) and the corresponding p-values. Cells in the table are colored according to the color legend, i.e., cells with positive correlations are colored red and cells with negative correlations are colored green.

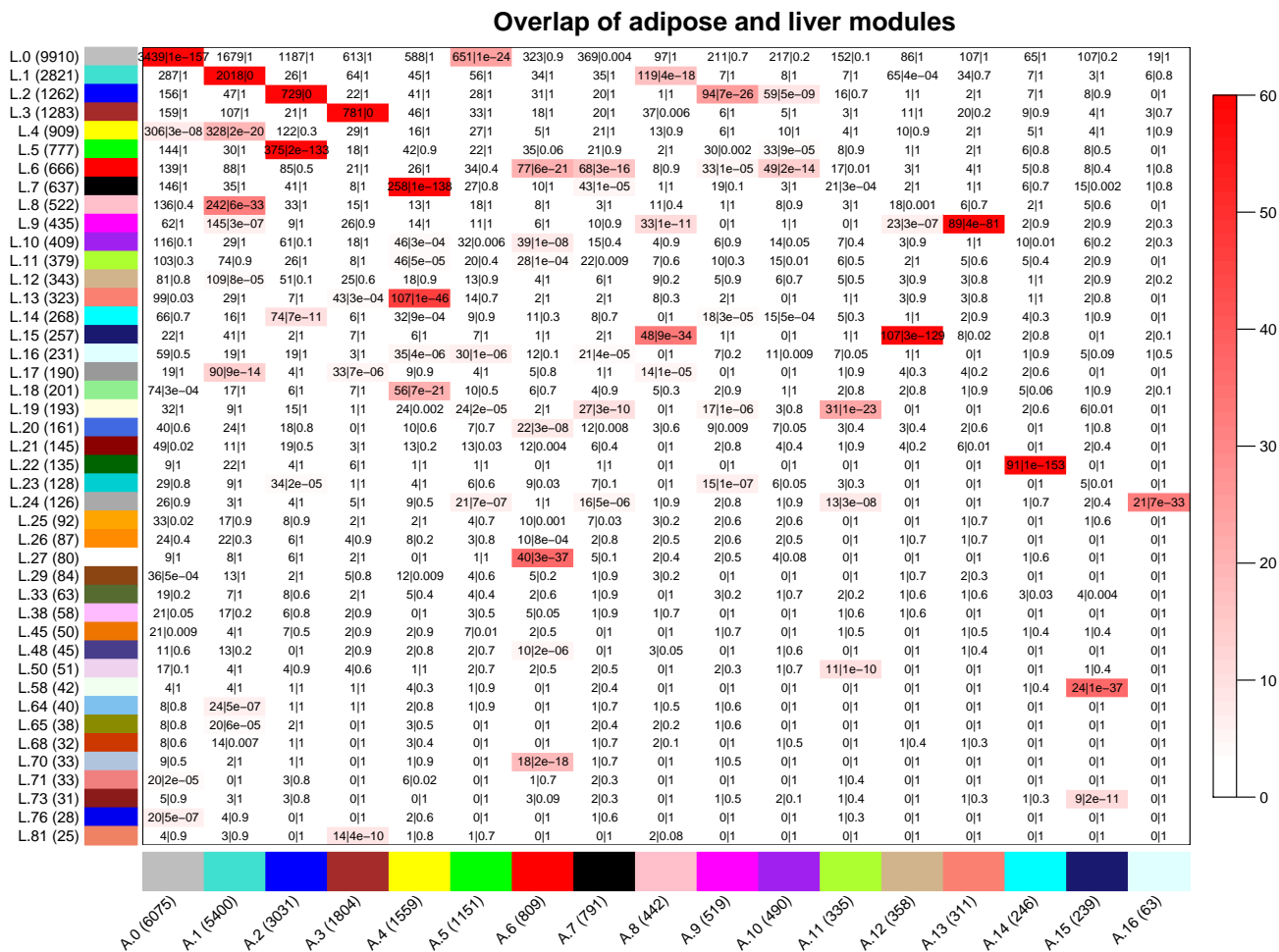


Figure 8. Overlap of liver and adipose modules in the CASTxB6 female data. Each row corresponds to a liver module (labeled by number and color), and each column corresponds to an adipose module. Numbers in the table give the number of probes in the overlap of the corresponding modules and the Fisher exact test p-values. Table cells are colored so that very significant p-values are colored with string red color; scale on the left denotes $-\log_{10} p$.

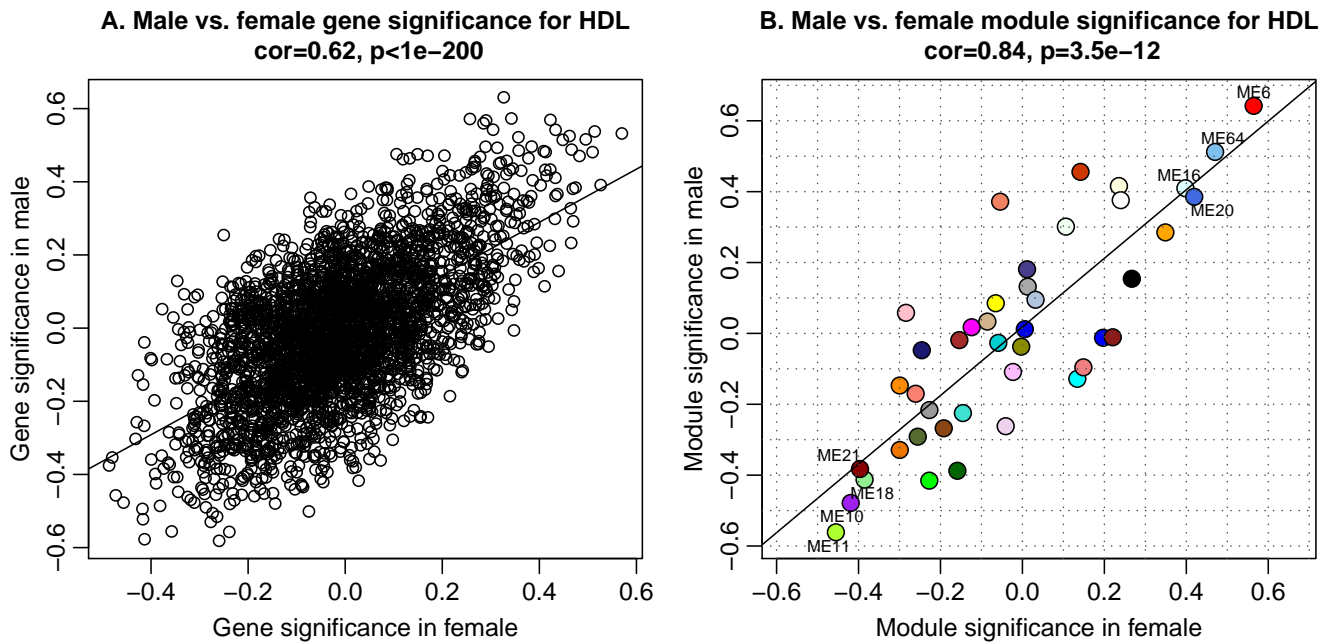


Figure 9. Preservation of (A) gene significance and (B) module eigengene significance for HDL between the CASTxB6 female (x -axis) and male (y -axis) data. In panel A every point represents a probe. In panel B every point represents a module (more precisely, its eigengene). HDL-associated modules are indicated by their numeric labels. Clearly, module eigengene significance is highly preserved: eigengenes strongly positively (negatively) associated with HDL in the female data are also highly positively (negatively) associated in the male data.

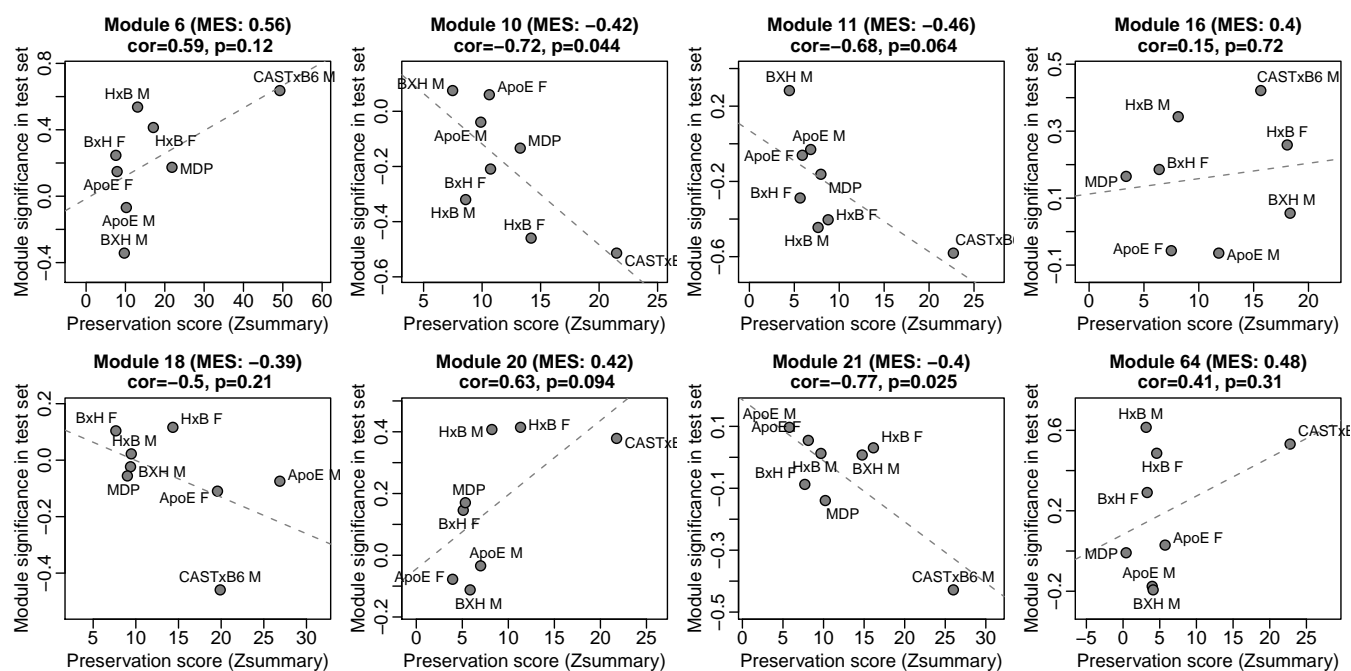


Figure 10. Significance for HDL tends to be better preserved for strongly preserved modules. Each panel presents a scatterplot of module significance for HDL (y-axis) vs. summary preservation measure Zsummary (x-axis) across all data sets. Each plot corresponds to a single module indicated in the title together with its significance for HDL in the reference female CASTxB6 data. Within each plot, each point corresponds to a test data set indicated by a short label next to each point. A linear model regression line is shown within each plot, and the corresponding correlation and p-value is shown in each title. For all modules, the module significance on average increases (in absolute value) as the summary preservation statistic increases.

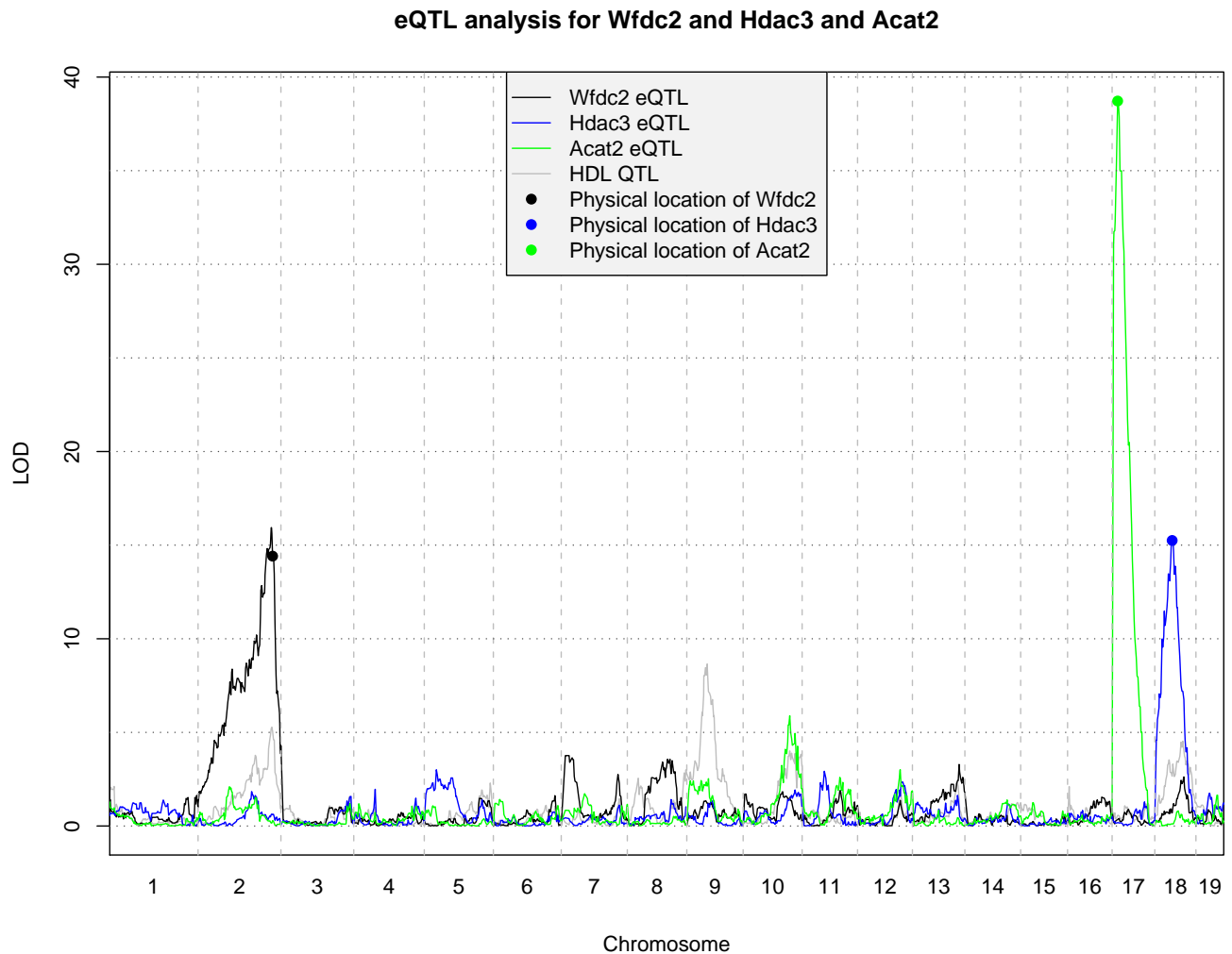


Figure 11. eQTL analysis of top 3 genes (*Wfdc2*, *Hdac3*, *Acat2*) that are consistently related to HDL and pass a causality test in the CASTxB6 data. The black, blue, and green lines show the LOD scores of *Wfdc2*, *Hdac3*, *Acat2*, respectively, at each of the nearly 1400 genotyped markers. All 3 genes have a strong cis-eQTL peak (their physical location is indicated by the filled circle on their respective LOD curves). For *Wfdc2* the cis-eQTL peak coincides with a QTL peak for HDL (grey line); for *Hdac3* the cis-eQTL peak is on the same chromosome (18) but some 30MB away from the HDL QTL peak. *Acat2* is located on chromosome 17 where HDL does not have peak, but the gene has a moderately strong trans-eQTL peak near the HDL QTL peak on chromosome 10.

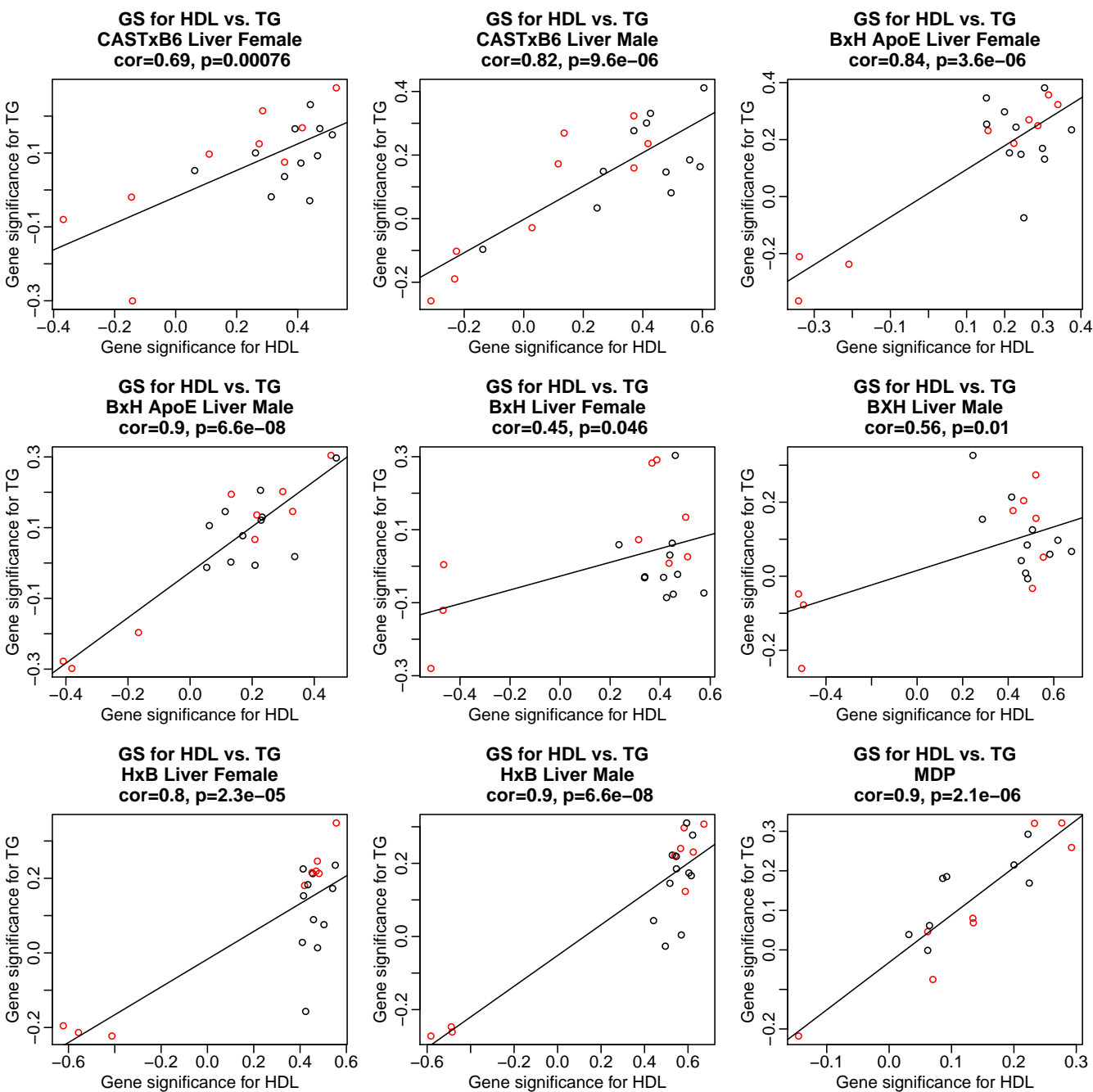


Figure 12. Gene significance for triglycerides (TG) (*y*-axis) vs. gene significance for HDL (*x*-axis) for the top 20 genes consistently associated with HDL in liver. Each scatterplot displays the relationship in one of the data sets (indicated in the title of each plot). In the scatterplots, each point corresponds to one gene. Red color identifies genes whose consistent association with TG passes the FDR threshold of 0.01. A linear model fit line is displayed in each plot, and the corresponding correlations and p-values are indicated in the title of each plot. We conclude that the gene significances for HDL and TG of the 20 top genes show significant positive correlations but the associations with TG tend to be weaker.