Supplemental figures for

**Genetic architecture modulates diet induced mRNA and miRNA expression profile in Diversity Outbred mouse**

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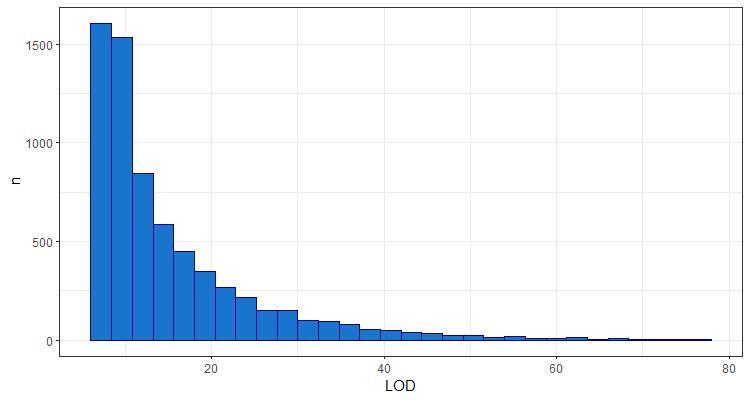
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**Supplemental Figure 1**: Distribution of LOD scores significant at p < 0.05 in the genome scan with diet as an additive covariate, as determined by the null distribution of max LODs from 1,000 permuted genome scans.

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**Supplemental Figure 2:** **Magnitude of correlation is greater in non-mapping miRNA-mRNA pairs than in those with mRNA with eQTL.** Expression data was used to generate correlations between pairs of miRNA (n = 246) and mRNA (n = 24,004). The results were filtered for BH-corrected significance (α ≤ 0.05) and Spearman’s rho was plotted against the eQTL status of the mRNA from the additive genome scan. Wilcoxon rank sum test found a significant difference between the absolute correlations of *cis* and *trans*-mapping eQTL (p < 2.22 x 10-16) with the median of *trans*-eQTL being 0.234, whereas *cis* was 0.233. A less significant trend was observed that non-mapping mRNA had lower miRNA correlations than mapping mRNA (p < 1.1 x 10-5). The median value for no eQTL was 0.232.

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**Supplemental Figure 3: eQTL and mirQTL have similar effect size in Diversity Outbred mice fed different diets** (**A**, **B**) Wilcoxon rank sum tests reveal a significant difference in the phenotypic variance explained between *cis* *and* *trans*-eQTL of mice fed a HFCA diet or a HP diet. The median phenotypic variance explained by *cis*-eQTL in the HFCA is 0.349 whereas it is 0.244 in *trans*. Similarly, in the HP, the variance explained by *cis*-eQTL is 0.356 and 0.282 in *trans*. (**C, D**) Wilcoxon rank sum tests reveal a significant difference in the phenotypic variance explained between *cis* and *trans*-mirQTL and a similar but insignificant (p ≥ 0.05) difference in the phenotypic variance explained between the *cis* and *trans*-mirQTL of mice fed a HP diet. The median phenotypic variance explained by *cis*-mirQTL in the HFCA is 0.465 whereas it is 0.251 in *trans*. Similarly, in the HP, the variance explained by *cis*-mirQTL is 0.525 and 0.302 in *trans*.

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**Supplemental Figure 4:** **Alleles from Wild Derived strains contribute to eQTL and mir-eQTL.** (**A**) Boxplot representation of center-scaled BLUP coefficients from all significant eQTL in the HFCA-fed mice. Kruskal-Wallis rank sum test indicates significant differences (p < 2.2 x 10-16) among founder effects. Dunn's post-hoc test confirms significantly (BH-adjusted p < 1.0 x 10-4) larger effects from the CAST/EiJ and PWK/PhJ strains relative to all other strains. (B) Boxplot representation of center-scaled BLUP coefficients from all significant mirQTL in the HFCA-fed mice. Kruskal-Wallis rank sum test indicates no significant differences (p = 0.34) among founder effects. **C**) Boxplot of center-scaled BLUP coefficients from all significant eQTL in the HP-fed mice. Kruskal-Wallis rank sum test indicates significant differences (p < 2.2 x 10-16) among founder effects. Dunn's post-hoc test confirms significantly (p < 1.0 x 10-4, BH-adjusted) larger effects from the CAST/EiJ and PWK/PhJ strains relative to all other strains. (**D**) Boxplot of center-scaled BLUP coefficients from all significant mirQTL in the HP-fed mice. Kruskal-Wallis rank sum test does not indicate significant differences (p < 0.064) among founder effects.

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**Supplemental Figure 5: Magnitude of correlation of miRNA-mRNA pairs with eQTL status differs by diet.** Expression data was used to generate correlations between pairs of miRNA (n = 246) and mRNA (n = 24,004). The results were filtered for FDR-corrected significance (α ≤ 0.05) and Spearman’s rho was plotted against the eQTL status of the mRNA from the HFCA model **(A)** and the HP model **(B)**. Wilcoxon rank sum test reveals a significant difference between the absolute correlations of *cis* and *trans*-mapping eQTL in the HFCA and HP model (HFCA, p < 2.2 x 10-16; HP, p < 0.0005).

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**Supplemental Figure 6: Overlap between results of additive and interactive models revealed large architectural differences in *trans*-eQTLs compared to *cis*-eQTLs.**  Differences in the genetic architecture of eQTL and mirQTL in the additive and interactive QTL analyses. Global architecture of significant eQTL (**A**) and mirQTL (**B**) from the interactive scan. We observed larger overlaps between additive and interactive scans in *cis*-regulated QTL (**C** and **D**) and sparser overlaps between *trans*-regulated QTL (**E** and **F**).