

Integrated network analysis reveals distinct regulatory roles of transcription factors and microRNAs

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SUPPLEMENTARY FIGURE LEGENDS

Supplementary Figure 1 Synergistic effect of TF and miRNA regulation on the protein interactions of their targets. Average pairwise distance of protein products of gene targets regulated by multiple TFs **(A)** or miRNAs **(B)** in the protein-protein interaction network. Difference in the average pairwise distances between the first and last bins is calculated by the t-test.

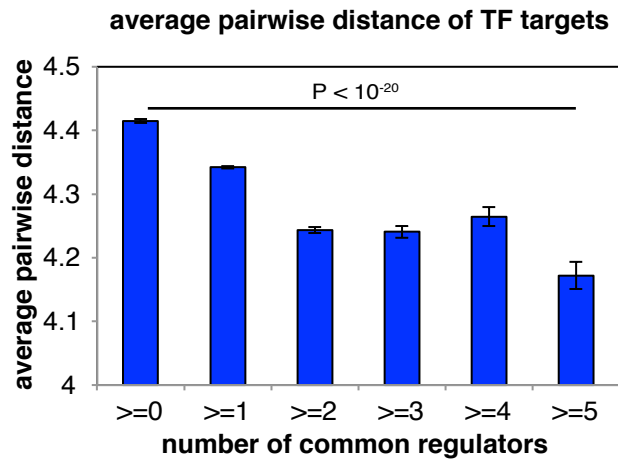
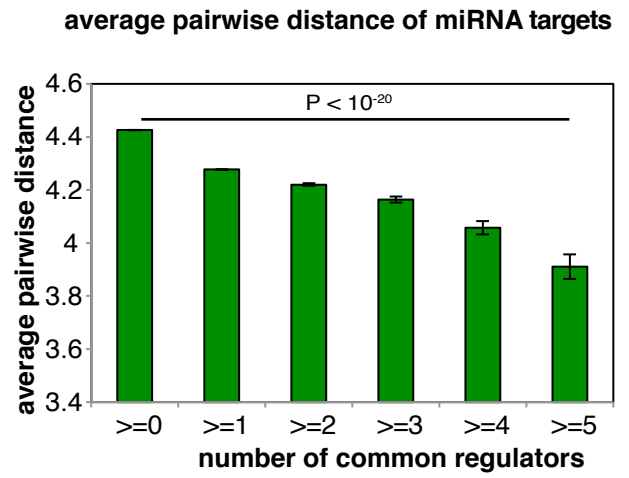
Supplementary Figure 2 Analysis of the synergistic effects of miRNAs on target genes using experimentally verified miRNA targets. **(A)** LOD values for enrichment of mRNA co-expression between gene pairs jointly regulated by multiple miRNAs. **(B)** LOD values for enrichment of protein co-expression between gene pairs jointly regulated by multiple miRNAs. **(C)** LOD values for enrichment of protein-protein interactions between gene pairs jointly regulated by miRNAs **(D)** LOD values for the likelihood of gene pairs jointly regulated by multiple miRNAs to be associated with the same disease. * $P < 0.05$. P -values are calculated by the Z -test. Difference between the first and last bins of each panel is calculated by the chi-squared test.

Supplementary Figure 3 Co-regulation of gene targets by inter-regulating TFs and miRNAs. **(A)** Percentage of miRNAs that share targets with TFs that regulate them. **(B)** Percentage of TFs that share targets with miRNAs that regulate them. Error bars indicate \pm SE.

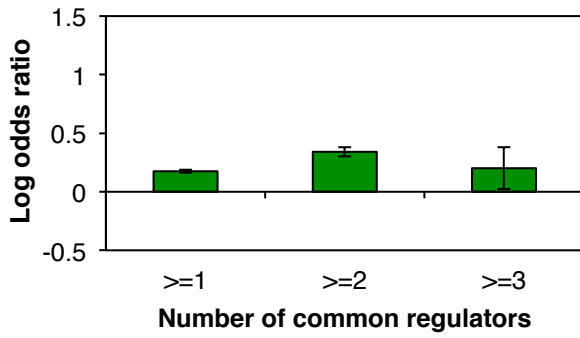
Supplementary Figure 4 Inter-regulation of TFs and miRNAs. Distribution of the fraction of co-expressed targets of **(A)** TF pairs regulated by the same miRNA, **(B)** TF pairs regulated by the same TF, and **(C)** miRNA pairs regulated by the same TF.

Supplementary Figure 5 Inter-regulation of TFs and miRNAs. Distribution of the fraction of interacting targets of **(A)** TF pairs regulated by the same miRNA, **(B)** TF pairs regulated by the same TF, and **(C)** miRNA pairs regulated by the same TF.

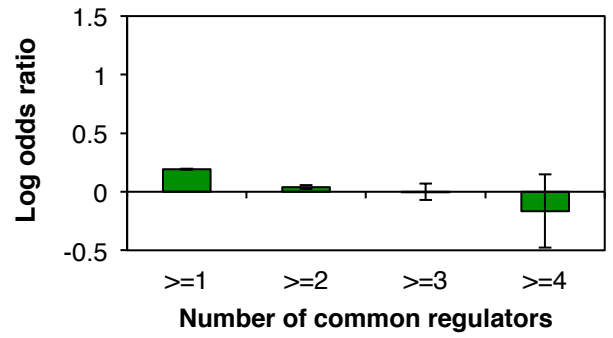
Supplementary Figure 6 Inter-regulation of TFs and miRNAs. Distribution of the similarity scores of **(A)** TF pairs regulated by the same miRNA, **(B)** TF pairs regulated by the same TF, and **(C)** miRNA pairs regulated by the same TF.

A**B**

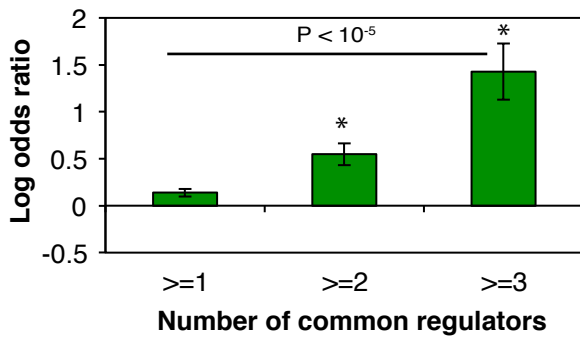
A Enrichment of mRNA co-expression



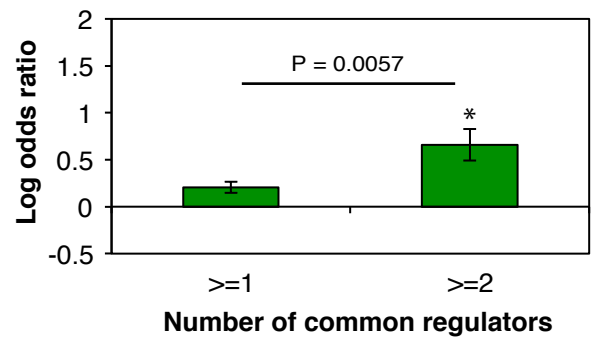
B Enrichment of protein co-expression

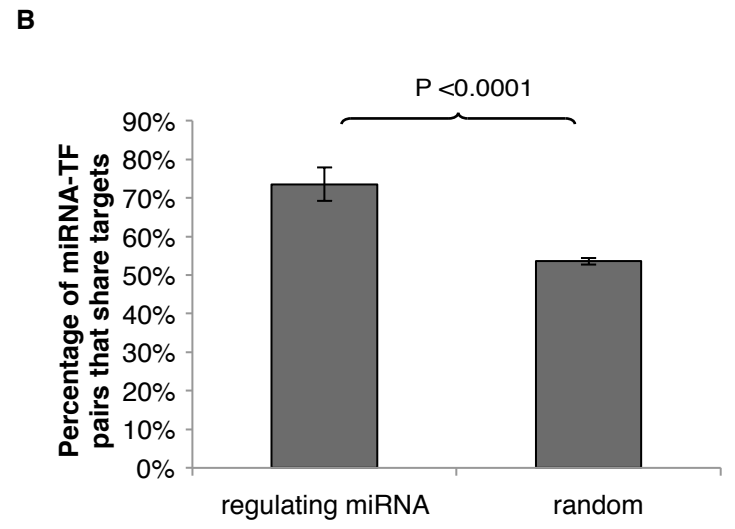
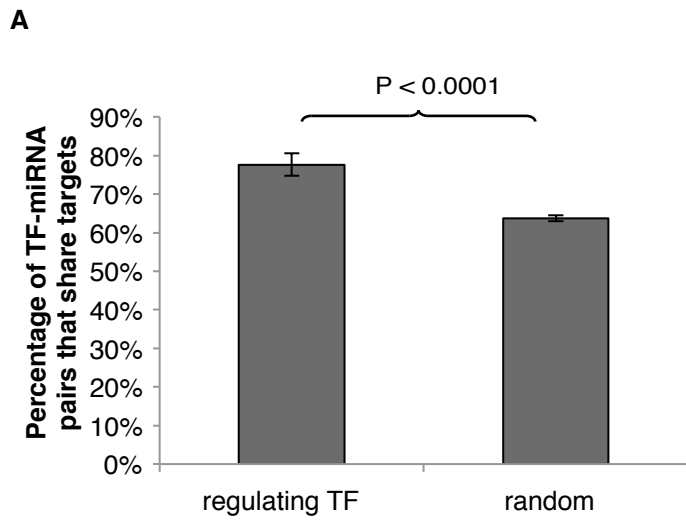


C Enrichment of protein-protein interactions

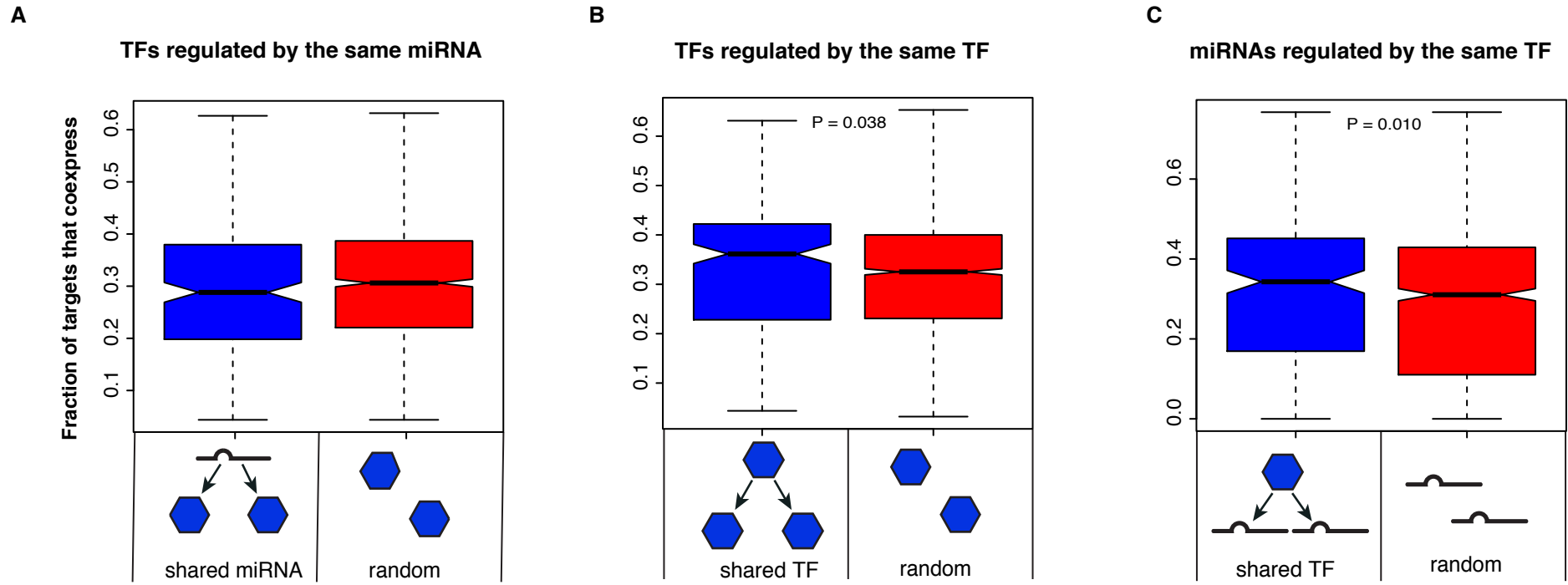


D Enrichment of target gene pairs causing the same disease

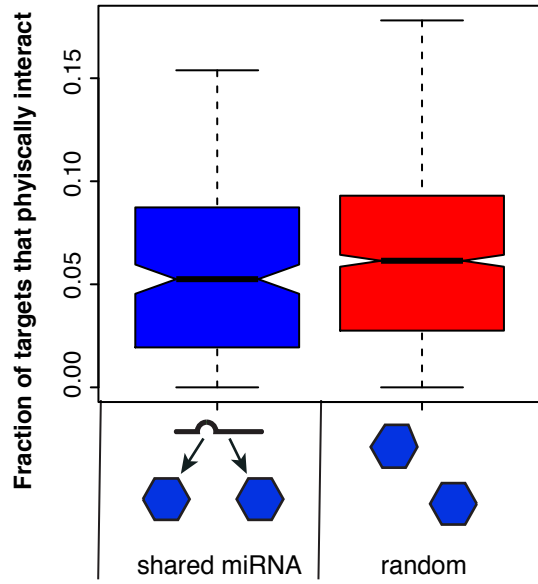
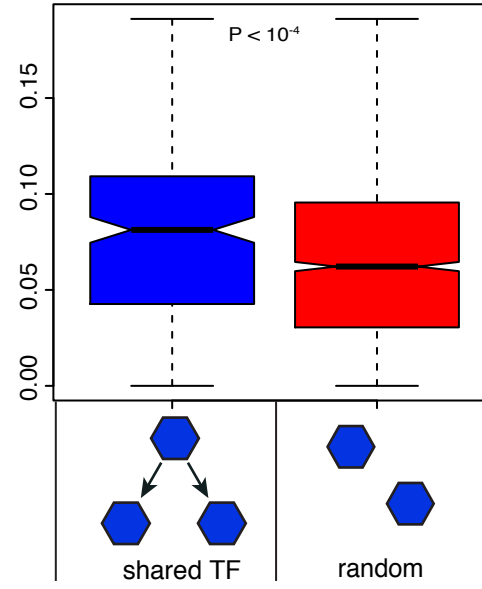
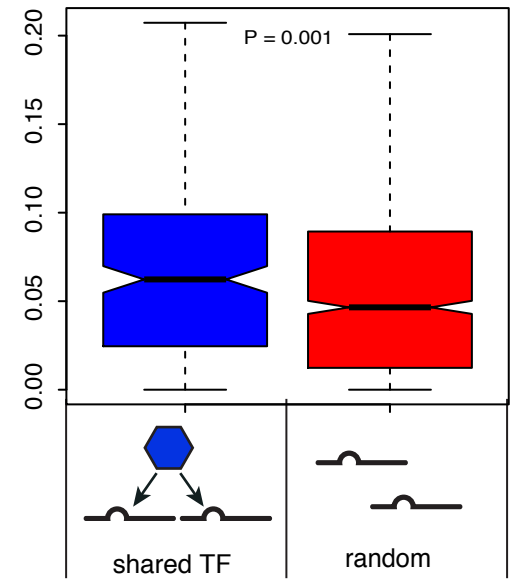


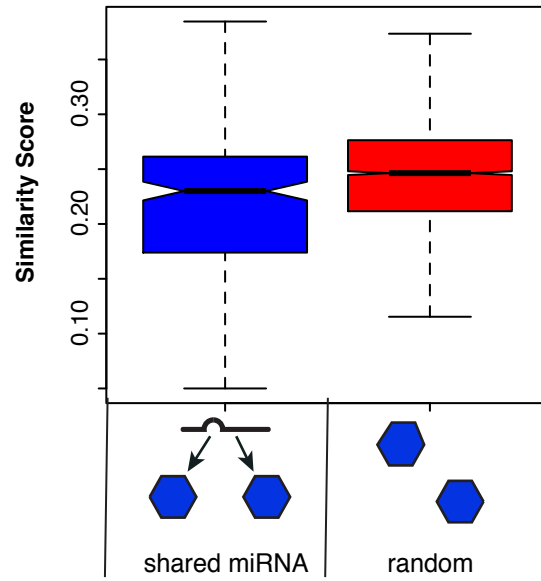
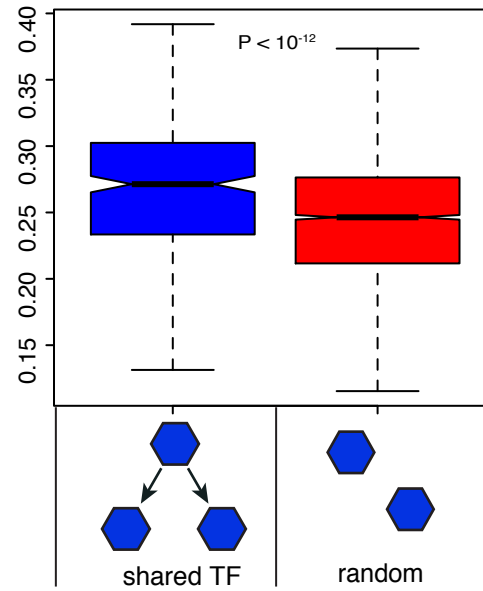


Supplementary Figure 3



Supplementary Figure 4

A**TFs regulated by the same miRNA****B****TFs regulated by the same TF****C****miRNAs regulated by the same TF**

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