SUPPLEMENTAL MATERIAL

Tables S1-S4 Legends (please see supplemental Excel files):

Table S1. Selected mRNAs transcripts. mRNA transcripts with greater than 2 fold changes and 10% FDR.

Table S2. Co-expression network of the 4,422 genes showing significant variations in response to either sex, or hypertrophy, or the interaction of sex and hypertrophy. Their membership modules are given in the GO and Panther tabs.

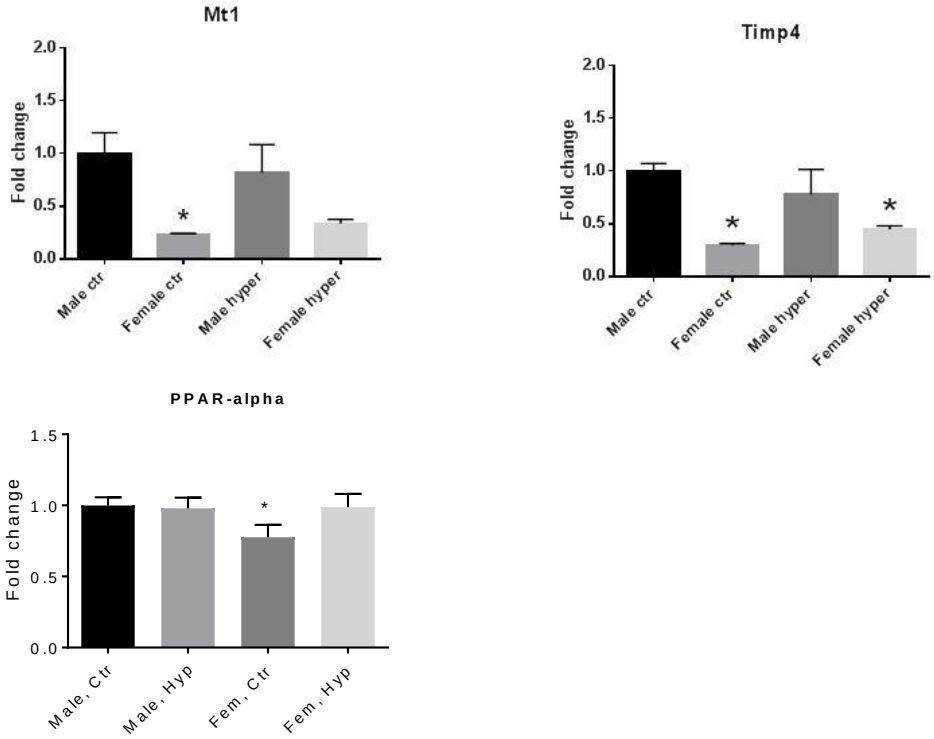
Table S3. Genes that showed significant changes in hypertrophy when sex as a co-factor is controlled, significant sex-dependent variation when hypertrophy as a co-factor is controlled, and significant sex-dependent differential hypertrophy-associated changes. Pathway enrichment analysis results are in tab 2.

Table S4. Data set of microRNAs.

Table S5. Overrepresentation of transcription factor (TF) families in identified genes by interaction model

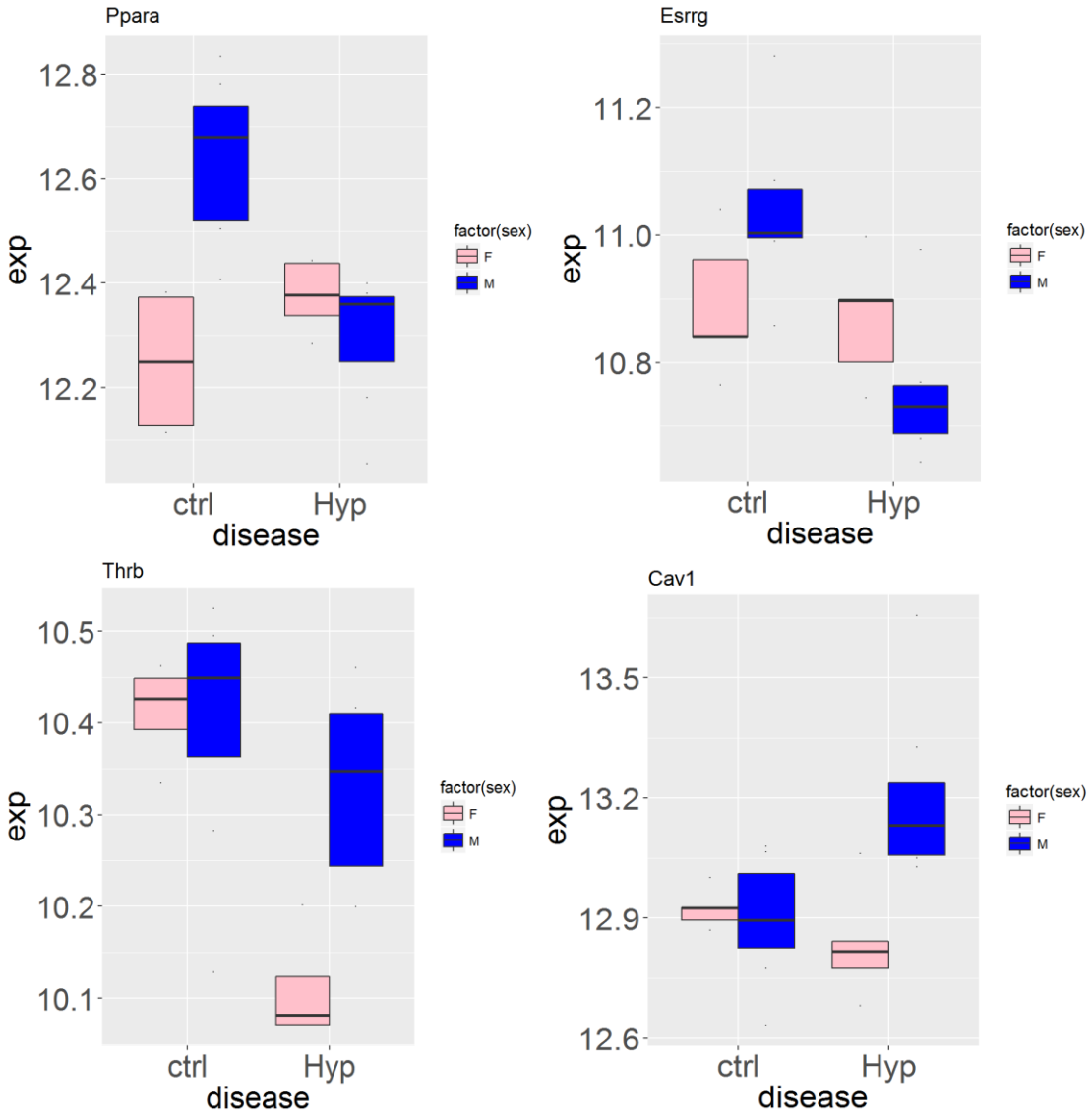
TF Families	Over representation	Z-Score	Gene list for TF family	Full name
V$ZF02	1.7	28.52	Zbtb7a Zbtb7b Zfp148 Zfp202 Zfp219 Zfp281,Zkscan3	zinc finger and BTB domain containing
V$EGRF	1.67	28.03	Egr1 Egr2 Egr3 Egr4, Wt1	early growth response
V$ZF5F	1.96	26.13	Zbtb14	zinc finger and BTB domain containing 14
V$E2FF	1.6	25.97	E2f1 E2f2 E2f3 E2f4 E2f5 E2f6 E2f7 E2f8	E2F transcriptional factor
V$SP1F	1.65	24.15	Sp1 Sp2 Sp3 Sp4 Sp5 Sp6 Sp7 Sp8	trans-acting transcription factor
V$KLFS	1.45	23.15	Klf1 Klf12 Klf13 Klf15 Klf17 Klf2 Klf3 Klf4 Klf6 Klf7 Klf8 Klf9 Klf10 Klf11 Klf16 Klf5	Kruppel-like factor 1 (erythroid)
V$BEDF	1.86	22.62	Zbed4	zinc finger, BED type containing 4provided
V$CTCF	1.68	20.33	Ctcf Ctcfl	
V$PLAG	1.63	19.93	Plag1 Plagl1 Plagl2	
V$MAZF	1.71	19.71	Maz Patz1	
V$GCF2	2.08	19.69	Lrrfip1	
V$NDPK	1.74	18.69	Nme1 Nme2	

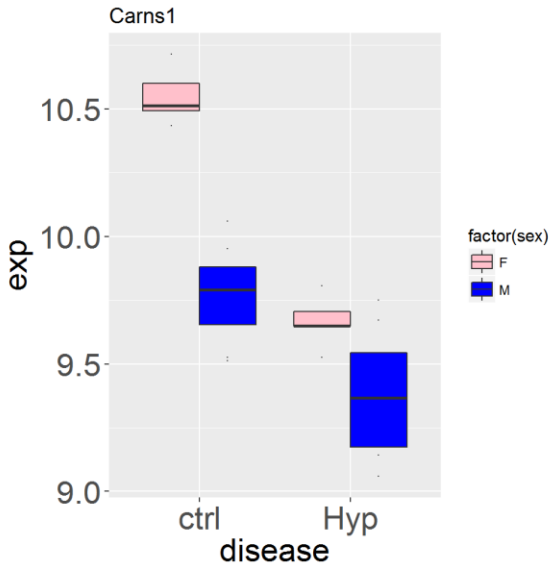
Figure S1. qPCR measurement



Confirmation of transcripts showing a sex difference. Quantitative polymerace chain reaction (PCR) analysis confirming the RNA-seq data for metallothionein (Mt) and Metalloproteinase inhibitor 4 (TIMP4). mRNA transcripts were quantified using SYBR green (n=3-7 per group). 18s RNA was used for normalizations. Data are mean +/_ standard error measurement (SEM) normalized to the male control. *p<0.05 vs. male control.

Figure S2. Sex differences in expression changes of genes identified by network analysis in figure 7.

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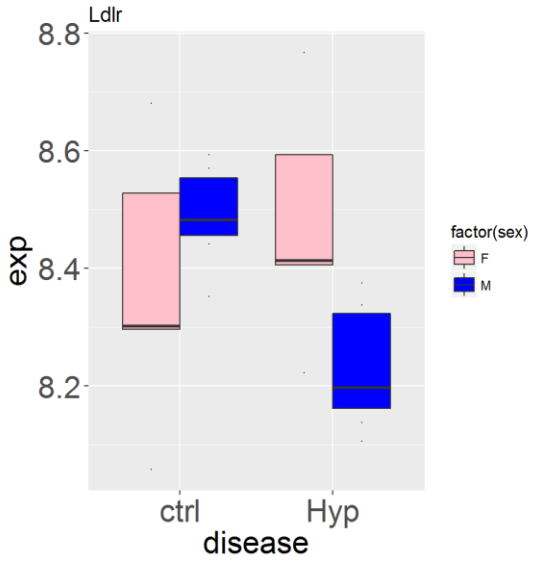
9.5
9.0
exp
ctrl
Hyp
disease
factor(sex)
F
M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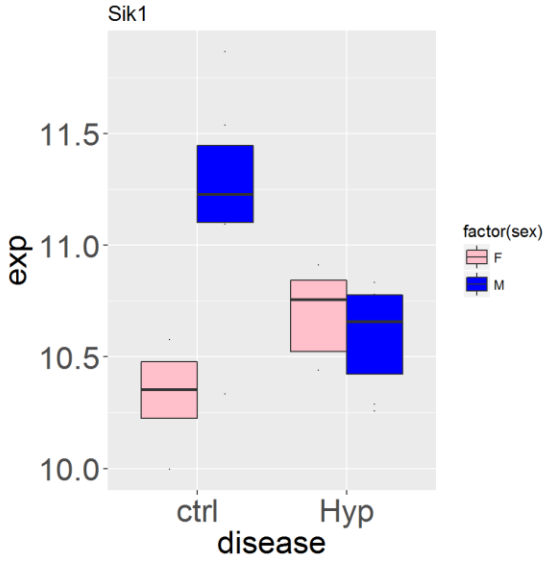
8.6
8.4
8.2
exp
ctrl
Hyp
disease
factor(sex)
F
M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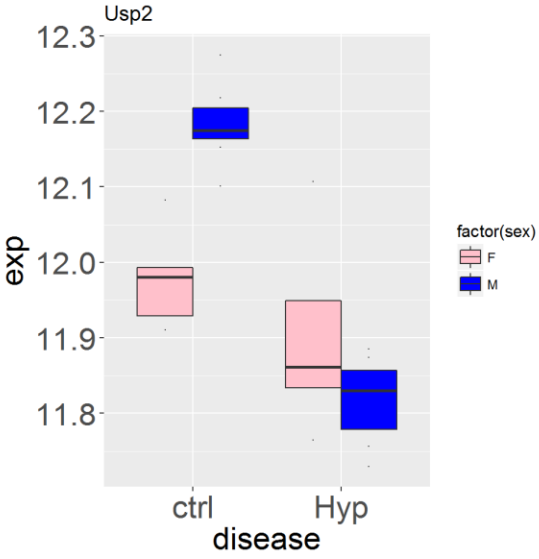
ctrl
Hyp
disease
factor(sex)
F
M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12.1
12.0
11.9
11.8
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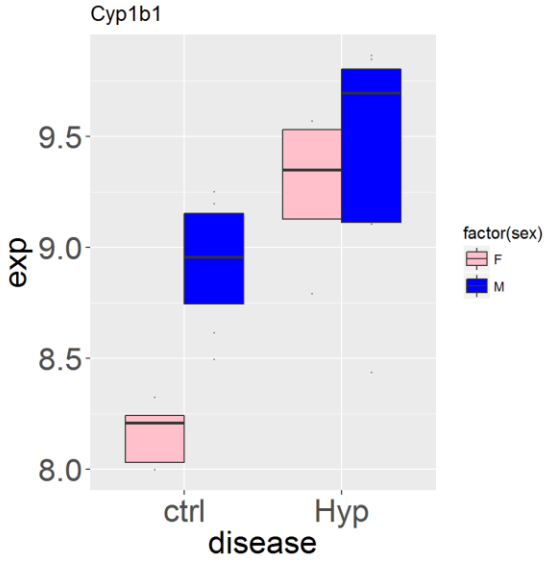
ctrl
Hyp
disease
factor(sex)
F
M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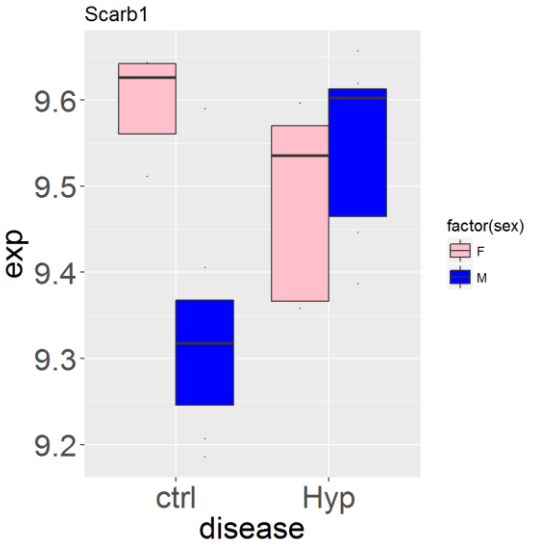
ctrl
Hyp
disease
factor(sex)
F
M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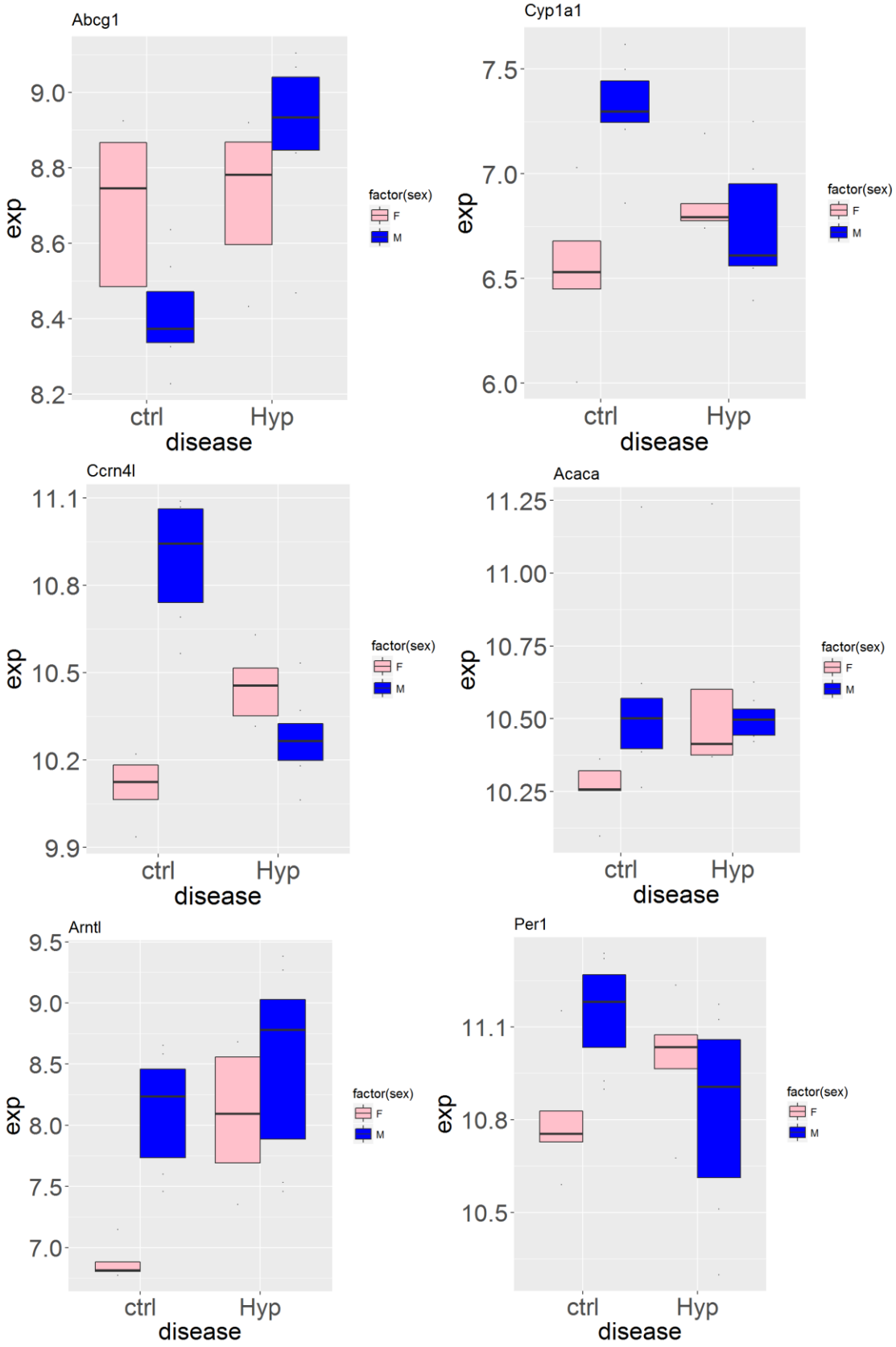
ctrl
Hyp
disease
factor(sex)
F
M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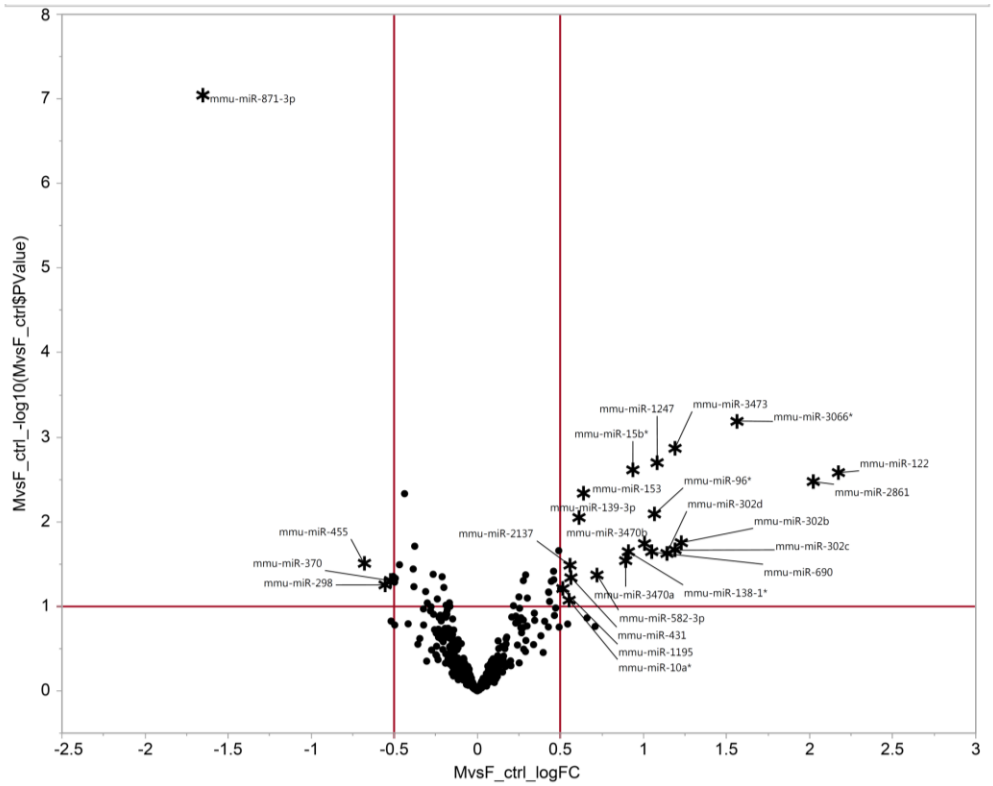
8.4
8.2
exp
ctrl
Hyp
disease
factor(sex)
F
M
Cyp1a1
7.5
7.0
6.5
6.0
exp
ctrl
Hyp
disease
factor(sex)
F
M
Ccrn4l
11.1
10.8
10.5
10.2
9.9
exp
ctrl
Hyp
disease
factor(sex)
F
M
Acaca
11.25
11.00
10.75
10.50
10.25
exp
ctrl
Hyp
disease
factor(sex)
F
M
Arntl
9.5
9.0
8.5
8.0
7.5
7.0
exp
ctrl
Hyp
disease
factor(sex)
F
M
Per1
11.1
10.8
10.5
exp
ctrl
Hyp
disease
factor(sex)
F
M

Figure S3. Volcano plots of miRNA with sex and hypertrophy

A



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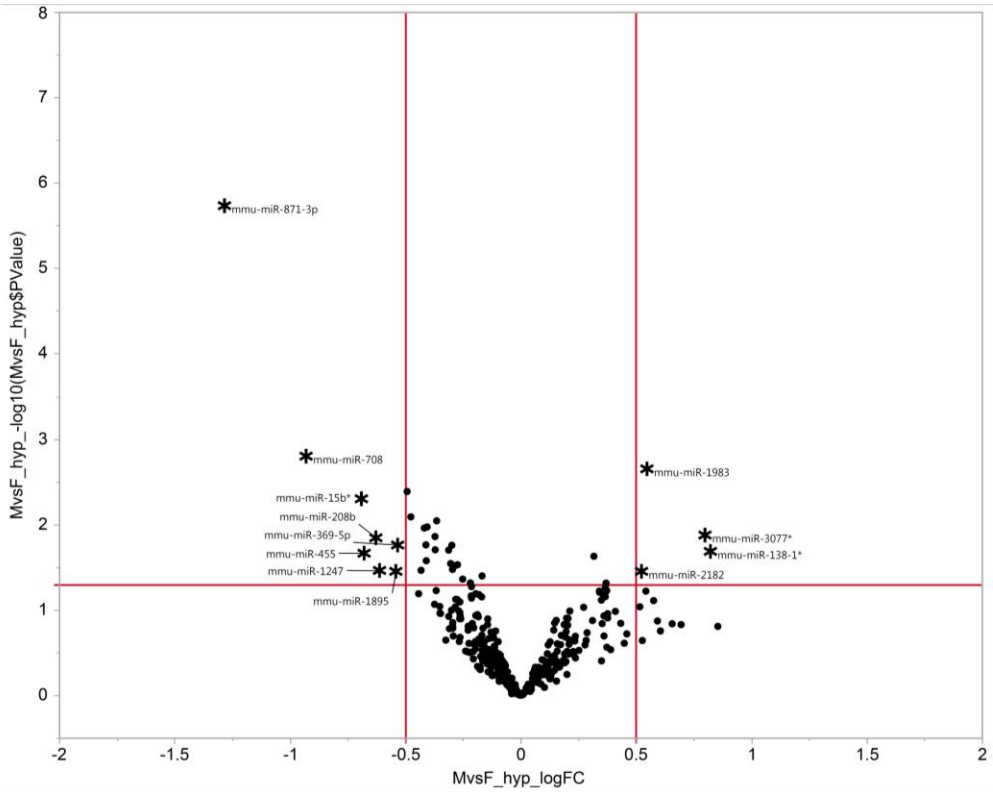

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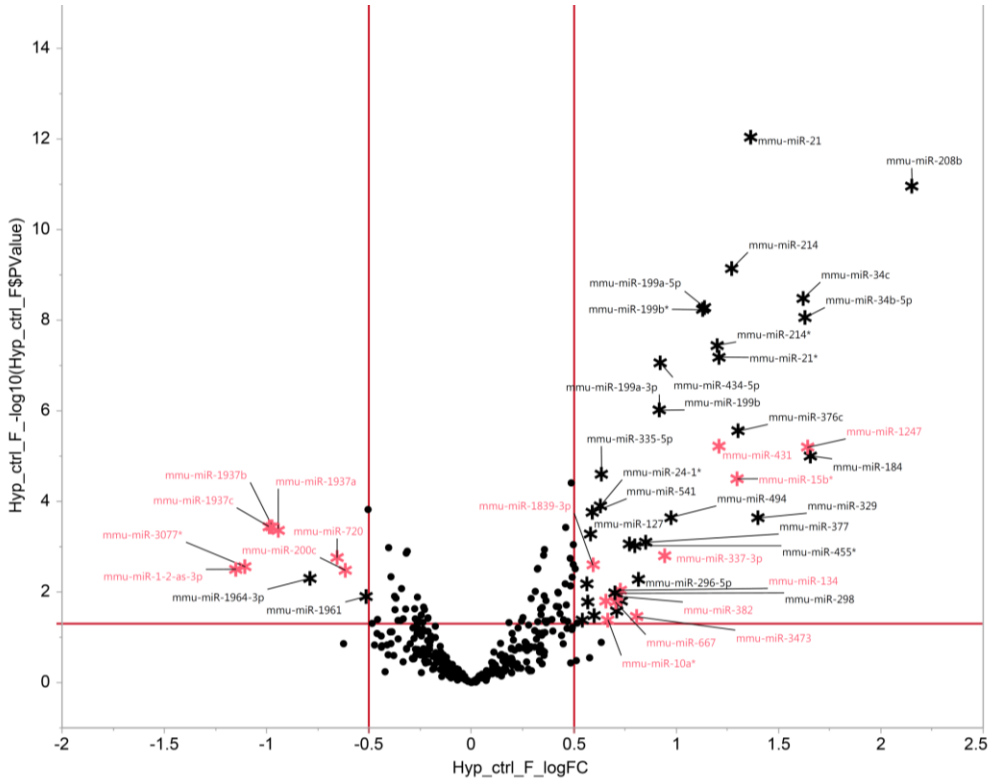
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Hyp_ctrl_F_logFC
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mmu-miR-208b
mmu-miR-214
mmu-miR-34c
mmu-miR-34b-5p
mmu-miR-199a-5p
mmu-miR-199b*
mmu-miR-214*
mmu-miR-21*
mmu-miR-199a-3p
mmu-miR-434-5p
mmu-miR-199b
mmu-miR-376c
mmu-miR-1247
mmu-miR-335-5p
mmu-miR-431
mmu-miR-184
mmu-miR-1937b
mmu-miR-1937a
mmu-miR-24-1*
mmu-miR-15b*
mmu-miR-1937c
mmu-miR-541
mmu-miR-1839-3p
mmu-miR-494
mmu-miR-329
mmu-miR-127
mmu-miR-377
mmu-miR-3077*
mmu-miR-720
mmu-miR-200c
mmu-miR-337-3p
mmu-miR-455*
mmu-miR-1-2-as-3p
mmu-miR-296-5p
mmu-miR-134
mmu-miR-1964-3p
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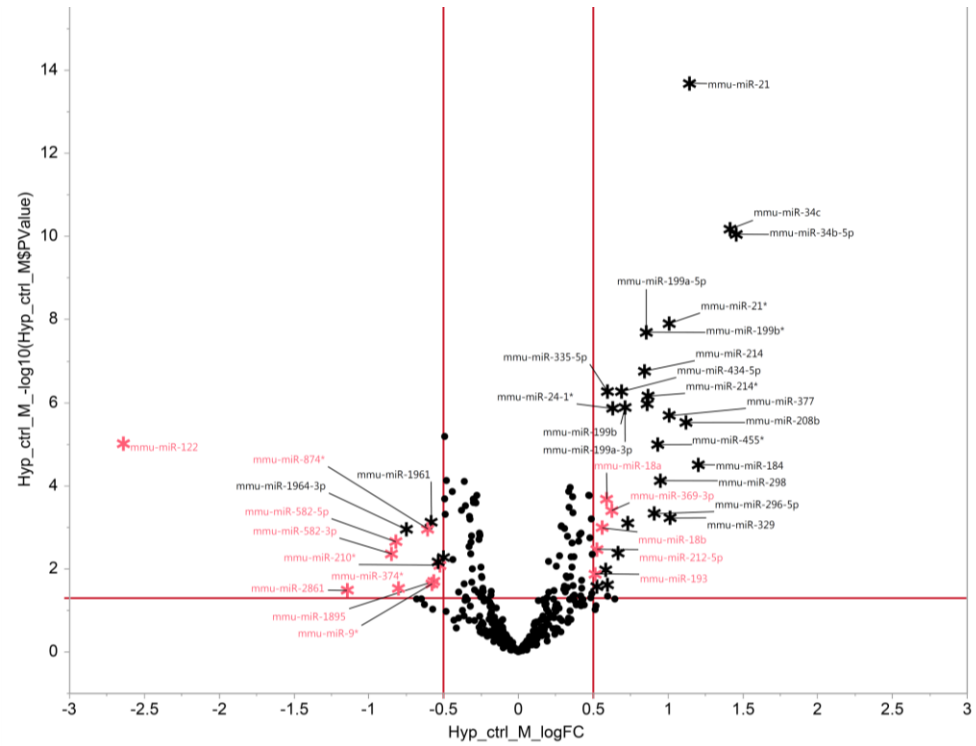
mmu-miR-10a*

D


Hyp_ctrl_M_-log10(Hyp_ctrl_M$PValue)
Hyp_ctrl_M_logFC
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mmu-miR-34c
mmu-miR-34b-5p
mmu-miR-199a-5p
mmu-miR-21*
mmu-miR-199b*
mmu-miR-335-5p
mmu-miR-214
mmu-miR-434-5p
mmu-miR-214*
mmu-miR-24-1*
mmu-miR-377
mmu-miR-208b
mmu-miR-199b
mmu-miR-455*
mmu-miR-199a-3p
mmu-miR-122
mmu-miR-18a
mmu-miR-184
mmu-miR-874*
mmu-miR-298
mmu-miR-1961
mmu-miR-369-3p
mmu-miR-1964-3p
mmu-miR-296-5p
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mmu-miR-212-5p
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