

Supplemental Information

Gene-by-Sex Interactions in Mitochondrial

Functions and Cardio-Metabolic Traits

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Table S1. Sex differences in clinical traits. Related to Figure 1

Trait	p-value*	FDR-adjusted p-value†	Average value (males)	Average value (females)	Top significant QTL in males	Top significant QTL in females
Body fat % growth	1.467E-03	2.674E-03	144.013	107.591	chr13:91591879 (6.74e-11)	chr1:5711829 (5.91e-07)
Body fat response	5.312E-02	7.382E-02	16.361	14.409	chr14:11525491 (7.26e-08)	chr7:69214973 (2.01e-07)
Body fat response (normalized to kidney weight)	7.067E-03	1.136E-02	91.348	111.671	chr7:127215079 (1.37e-06)	chr17:43340215 (7.14e-07)
Corpuscular hemoglobin (g/dl)	8.695E-01	8.803E-01	31.871	31.795	chr7:102226175 (3.68e-90)	chr7:102949492 (2.89e-112)
Fat mass % growth	1.088E-02	1.621E-02	287.358	226.789	chr16:93301822 (4.33e-11)	chr10:27777268 (3.09e-06)
Fat mass 0 wks diet	2.032E-01	2.314E-01	3.600	3.305	chr14:14239575 (2.43e-08)	
Fat mass 0 wks diet (normalized to kidney weight)	2.969E-04	6.406E-04	19.784	25.394	chr14:13158638 (5.28e-07)	
Fat mass 8 wks	5.470E-03	9.344E-03	12.273	10.239	chr7:127290257 (4.43e-09)	chr7:66856049 (1.32e-07)
Fat mass 8 wks (normalized to kidney weight)	3.986E-02	5.635E-02	67.837	78.347	chr7:127065727 (3.65e-06)	chr17:66421918 (3.07e-06)
Fat mass response	4.087E-03	7.130E-03	8.673	6.934	chr7:127290257 (2.35e-08)	chr7:66856049 (2.14e-07)
Fat mass response (normalized to kidney weight)	2.442E-01	2.743E-01	48.052	52.953		chr17:66421918 (3.75e-07)
Food intake average	3.195E-05	8.186E-05	3.144	2.829	chr1:178298128 (5.69e-14)	chr1:172751095 (1.31e-09)
Food intake average (normalized to kidney weight)	1.659E-13	1.134E-12	17.265	22.132	chr17:12406998 (5.5e-07)	
Food intake day 1	8.459E-03	1.334E-02	3.230	2.990	chr1:178298128 (3.63e-16)	chr1:172742472 (1.58e-09)
Food intake day 1 (normalized to kidney weight)	3.218E-13	2.030E-12	17.736	23.366	chr1:178465794 (1.41e-06)	
Food intake day 2	2.481E-04	5.498E-04	3.111	2.779	chr1:175768248 (4.39e-07)	chr1:177553977 (7.59e-08)
Food intake day 2 (normalized to kidney weight)	1.536E-10	5.998E-10	17.049	21.737	chr17:11880850 (7.18e-07)	
Food intake day 3	7.242E-05	1.697E-04	3.175	2.845	chr1:175789094 (7.88e-09)	
Food intake day 3 (normalized to kidney weight)	9.882E-11	4.051E-10	17.680	22.383		chr1:90644249 (1.93e-06)
Food intake day 4	5.876E-06	1.721E-05	3.006	2.564	chr9:57610867 (1.77e-06)	
Food intake day 4 (normalized to kidney weight)	8.038E-07	2.441E-06	16.831	20.444		chr5:104948585 (1.29e-06)
Gonadal fat weight	6.739E-02	8.771E-02	1.501	1.325	chr7:74534452 (2.79e-07)	chr17:67199420 (1.39e-07)
Gonadal fat weight (normalized to kidney weight)	8.807E-03	1.363E-02	8.314	10.073	chr7:74534452 (3.43e-07)	
Granulocytes (thousands/ul)	5.099E-05	1.230E-04	1.703	1.382	chr12:49333533 (1.80e-06)	chr11:26100680 (1.79e-06)
Granulocytes (% of white cells)	1.146E-01	1.423E-01	21.722	20.659	chr6:43884850 (1.01e-08)	
HDL	7.534E-13	4.412E-12	166.850	121.555	chr1:168279177 (2.12e-06)	chr1:171208377 (1.90e-06)
Heart weight	8.886E-15	7.287E-14	0.152	0.120	chr17:87783921 (1.96e-06)	
Heart weight (normalized to kidney weight)	3.093E-05	8.182E-05	0.831	0.927		
Hematocrit (%)	8.271E-01	8.478E-01	43.844	43.645	chr7:102226175 (1.38e-24)	chr7:102152386 (3.90e-34)
Hemoglobin (g/dl)	4.899E-01	5.217E-01	13.817	13.693	chr14:52392537 (1.52e-07)	
HOMA-IR	5.519E-12	3.017E-11	64.169	21.507	chr9:104018744 (1.50e-07)	chr15:54129738 (1.60e-06)
Kidney weight	7.062E-27	1.158E-25	0.186	0.131	chr7:107313081 (5.91e-07)	chr10:90146088 (5.04e-07)
LDL	2.246E-04	5.115E-04	43.185	33.166	chr9:67247812 (7.28e-07)	
Lean mass 0 wks HF diet	2.910E-32	7.955E-31	21.686	17.589	chr1:178551913 (4.20e-07)	chr4:101456134 (5.84e-07)
Lean mass 0 wks HF diet (normalized to kidney weight)	5.259E-09	1.797E-08	119.642	136.483	chr17:11880850 (2.35e-09)	
Lean mass 8 wks diet	2.101E-30	4.307E-29	26.210	21.201	chr13:8190622 (1.14e-08)	chr17:48931420 (1.31e-09)
Lean mass 8 wks diet (normalized to kidney weight)	1.903E-09	6.784E-09	144.255	164.151	chr17:10562672 (2.6e-11)	chr18:70827226 (1.54e-06)
Liver phospholipids	1.185E-38	4.860E-37	15.277	10.094		chr4:64250239 (3.60e-06)
Liver total cholesterol	2.000E-08	6.561E-08	3.550	2.747	chr1:178551913 (1.66e-06)	chr5:64528298 (3.52e-07)
Liver triglycerides	1.148E-05	3.245E-05	82.707	50.855	chr9:104875641 (1.56e-06)	
Liver unesterified cholesterol	1.213E-42	9.951E-41	2.394	1.404	chr11:92030285 (2.55e-06)	chr4:53135994 (1.52e-06)
Liver weight	3.832E-07	1.208E-06	1.435	1.138	chr7:117236190 (3.43e-09)	chr17:48914545 (7.24e-07)
Liver weight (normalized to kidney weight)	6.118E-03	1.024E-02	7.834	8.732	chr17:24082554 (1.64e-08)	chr17:32378517 (1.73e-06)
Lung weight	5.852E-02	7.867E-02	0.181	0.172	chr10:125503808 (2.90e-06)	chr19:51166266 (3.78e-06)
Lung weight (normalized to kidney weight)	7.466E-19	8.746E-18	0.994	1.332		
Lymphocyte (% of white cells)	1.521E-01	1.807E-01	71.186	72.331	chr6:43884850 (1.20e-09)	chr7:144676202 (2.95e-06)
Lymphocytes (thousands/ul)	6.982E-03	1.136E-02	5.859	5.060	chr12:82586480 (3.37e-06)	chr17:45252677 (4.67e-07)
Mean corpuscular hemoglobin (pg)	1.378E-01	1.686E-01	14.344	14.505	chr8:87339300 (1.95e-06)	
Mean corpuscular volume (fl)	4.708E-01	5.147E-01	45.461	46.006	chr7:103866951 (1.32e-65)	chr7:104230845 (1.22e-61)
Mean platelet volume (fl)	9.656E-02	1.237E-01	6.229	6.337	chr7:104239041 (1.71e-17)	chr7:104239041 (9.24e-08)
Mesenteric fat weight	4.667E-04	9.333E-04	0.629	0.481	chr14:96517733 (6.59e-07)	chr17:47456894 (6.89e-08)
Mesenteric fat weight (normalized to kidney weight)	4.834E-01	5.216E-01	3.466	3.665		chr7:67542847 (1.78e-07)

Trait	p-value*	FDR-adjusted p-value†	Average value (males)	Average value (females)	Top significant QTL in males	Top significant QTL in females
Monocytes (thousands/ul)	1.269E-02	1.858E-02	0.611	0.537	chr18:55974695 (2.71e-08)	
Monocytes (% of white cells)	6.623E-01	6.875E-01	7.077	6.981	chr6:48809036 (6.10e-07)	
Plasma esterified cholesterol	2.455E-10	9.150E-10	164.203	122.213	chr9:67247812 (2.95e-08)	chr1:172429451 (3.02e-06)
Plasma free fatty acids	6.373E-01	6.699E-01	36.574	36.997		
Plasma glucose	3.710E-05	9.218E-05	271.546	224.914	chr7:49397123 (3.88e-08)	chr11:112944793 (3.77e-07)
Plasma glycerol	1.444E-01	1.741E-01	65.385	68.169		
Plasma insulin	3.700E-14	2.758E-13	3797.110	1560.821	chr1:174036719 (3.01e-07)	chr1:172489036 (3.21e-07)
Plasma total cholesterol	4.093E-11	1.865E-10	209.712	153.794	chr9:67247812 (1.36e-08)	chr17:50324480 (2.14e-06)
Plasma triglycerides	4.599E-04	9.333E-04	59.692	41.745	chr7:76638409 (6.08e-09)	chr7:66072499 (1.28e-14)
Plasma unesterified cholesterol	2.958E-11	1.427E-10	45.622	31.582		chr13:109891309 (1.01e-07)
Platelet counts (thousands/ul)	1.558E-03	2.777E-03	300.890	264.543		
Red blood cells (millions/ul)	1.898E-01	2.207E-01	9.646	9.478		
Red cell distribution width (fl)	9.300E-01	9.300E-01	29.595	29.554	chr7:104239041 (3.44e-43)	chr7:104571898 (3.55e-44)
Red cell distribution width (%)	2.554E-02	3.673E-02	17.480	17.084	chr7:102142368 (3.86e-16)	chr7:104230845 (9.22e-21)
Retroperitoneal fat weight	3.959E-16	3.607E-15	0.338	0.197		chr7:68619885 (3.07e-06)
Retroperitoneal fat weight (normalized to kidney weight)	6.765E-04	1.321E-03	1.882	1.508	chr17:3869399 (1.27e-06)	chr7:122597337 (3.42e-06)
Spleen weight	5.490E-02	7.503E-02	0.091	0.100	chr5:105602514 (1.97e-06)	
Spleen weight (normalized to kidney weight)	2.063E-18	2.115E-17	0.498	0.762	chr17:9880957 (3.89e-06)	
Subcutaneous fat weight	9.896E-03	1.503E-02	1.157	0.960		chr7:66856049 (1.26e-06)
Subcutaneous fat weight (normalized to kidney weight)	6.703E-02	8.771E-02	6.417	7.412	chr4:142202686 (5.16e-07)	
Total mass % growth	2.476E-01	2.744E-01	53.986	50.039	chr16:93301822 (1.18e-06)	chr17:43340215 (1.25e-06)
Total mass 0 wks	1.689E-19	2.308E-18	25.706	21.452	chr17:45740224 (3.42e-06)	
Total mass 0 wks (normalized to kidney weight)	7.945E-11	3.429E-10	141.762	166.228	chr17:10070612 (2.5e-09)	
Total mass 8 wks	2.343E-11	1.201E-10	39.450	32.303	chr13:8190622 (4.63e-09)	chr17:45740224 (1.27e-07)
Total mass 8 wks (normalized to kidney weight)	2.978E-05	8.139E-05	217.403	249.126	chr17:10065097 (9.6e-09)	
Total mass growth	3.998E-04	8.407E-04	13.736	10.851	chr9:92273734 (3.68e-07)	chr17:48495769 (3.75e-07)
Total mass growth (normalized to kidney weight)	1.911E-01	2.207E-01	75.625	82.899	chr4:143041959 (8.42e-07)	chr7:66494857 (1.69e-06)
Visceral fat weight	1.196E-03	2.281E-03	2.466	2.003	chr13:8190622 (1.01e-07)	chr17:67197249 (1.38e-07)
Visceral fat weight (normalized to kidney weight)	1.038E-01	1.310E-01	13.647	15.245	chr7:73942680 (1.45e-06)	
White blood cells (thousands/ul)	1.406E-03	2.621E-03	8.168	6.972		chr17:45252677 (3.85e-06)

* using two-sample Student's t-test

† adjusted using Benjamini-Hochberg method

Table S3. Enrichment analysis (DAVID) results for adipose. Related to Figure 2

Category	Term	Count	%	P-Value	Benjamini
UP_KEYWORDS	Transit peptide	264	7.2	3.70E-30	1.80E-27
GOTERM_CC_DIRECT	mitochondrion	652	17.8	1.00E-25	1.10E-22
UP_SEQ_FEATURE	transit peptide:Mitochondrion	238	6.5	1.90E-26	1.30E-22
UP_KEYWORDS	Mitochondrion	443	12.1	8.10E-25	2.00E-22
UP_KEYWORDS	Mitochondrion inner membrane	132	3.6	3.00E-15	4.90E-13
KEGG_PATHWAY	Oxidative phosphorylation	74	2	6.90E-15	2.00E-12
GOTERM_CC_DIRECT	mitochondrial inner membrane	187	5.1	1.20E-14	6.60E-12
UP_KEYWORDS	Electron transport	63	1.7	2.50E-13	3.10E-11
UP_KEYWORDS	Respiratory chain	41	1.1	5.60E-13	5.50E-11
GOTERM_CC_DIRECT	respiratory chain	40	1.1	2.10E-12	7.70E-10
GOTERM_CC_DIRECT	mitochondrial respiratory chain complex I	33	0.9	8.90E-11	2.40E-08
GOTERM_CC_DIRECT	mitochondrial matrix	93	2.5	1.00E-09	1.90E-07
GOTERM_CC_DIRECT	extracellular exosome	853	23.2	9.40E-10	2.00E-07
KEGG_PATHWAY	Alzheimer's disease	83	2.3	1.10E-08	1.60E-06
KEGG_PATHWAY	Parkinson's disease	67	1.8	3.00E-08	2.20E-06
KEGG_PATHWAY	Non-alcoholic fatty liver disease (NAFLD)	79	2.2	2.30E-08	2.20E-06
KEGG_PATHWAY	Citrate cycle (TCA cycle)	25	0.7	3.50E-06	2.10E-04
GOTERM_CC_DIRECT	melanosome	54	1.5	1.50E-06	2.30E-04
KEGG_PATHWAY	Huntington's disease	80	2.2	1.10E-05	5.30E-04
UP_KEYWORDS	Tricarboxylic acid cycle	20	0.5	1.30E-05	1.10E-03
COG_ONTOLOGY	Lipid metabolism	32	0.9	9.20E-05	4.10E-03
KEGG_PATHWAY	Phagosome	64	1.7	1.20E-04	5.20E-03
UP_KEYWORDS	Disulfide bond	536	14.6	9.00E-05	5.60E-03
UP_KEYWORDS	Transport NADH dehydrogenase (ubiquinon	495	13.5	8.70E-05	6.10E-03
GOTERM_MF_DIRECT	activity	20	0.5	3.30E-06	7.60E-03
GOTERM_CC_DIRECT	mitochondrial nucleoid	30	0.8	5.90E-05	7.90E-03
KEGG_PATHWAY	Cardiac muscle contraction	25	0.7	2.30E-04	8.20E-03
UP_KEYWORDS	GTP-binding	118	3.2	1.60E-04	8.70E-03
UP_KEYWORDS	Acetylation	1038	28.3	2.00E-04	9.80E-03
UP_KEYWORDS	Ubiquinone	16	0.4	2.60E-04	1.20E-02
KEGG_PATHWAY	Propanoate metabolism	18	0.5	4.20E-04	1.20E-02
KEGG_PATHWAY	Regulation of actin cytoskeleton	79	2.2	4.10E-04	1.30E-02
GOTERM_CC_DIRECT	myelin sheath	79	2.2	1.80E-04	2.20E-02

Category	Term	Count	%	P-Value	Benjamini
GOTERM_CC_DIRECT	plasma membrane	803	21.9	2.00E-04	2.20E-02
GOTERM_BP_DIRECT	osteoblast differentiation	54	1.5	7.80E-06	2.70E-02
KEGG_PATHWAY	Tuberculosis	70	1.9	1.50E-03	3.80E-02
KEGG_PATHWAY	Fc gamma R-mediated phagocytosis	44	1.2	1.90E-03	4.60E-02
GOTERM_CC_DIRECT	membrane raft	95	2.6	5.00E-04	4.80E-02
GOTERM_BP_DIRECT	tricarboxylic acid cycle	21	0.6	7.40E-06	5.10E-02
KEGG_PATHWAY	Salmonella infection	36	1	2.30E-03	5.20E-02
UP_KEYWORDS	Hydrogen ion transport	21	0.6	1.90E-03	6.50E-02
UP_KEYWORDS	Cell membrane	505	13.8	1.80E-03	6.60E-02
UP_KEYWORDS	Receptor	225	6.1	2.10E-03	6.70E-02
UP_KEYWORDS	Membrane	1435	39.1	1.80E-03	7.10E-02
KEGG_PATHWAY	Osteoclast differentiation	55	1.5	4.00E-03	7.10E-02
KEGG_PATHWAY	B cell receptor signaling pathway	37	1	3.70E-03	7.50E-02
KEGG_PATHWAY	Carbon metabolism	56	1.5	4.00E-03	7.50E-02
UP_KEYWORDS	Glycoprotein	708	19.3	2.60E-03	7.70E-02
UP_KEYWORDS	Glucose metabolism	14	0.4	3.00E-03	8.30E-02
UP_KEYWORDS	4Fe-4S	20	0.5	3.30E-03	8.60E-02
UP_KEYWORDS	Immunity	117	3.2	3.80E-03	9.00E-02
UP_KEYWORDS	Lysosome	85	2.3	3.70E-03	9.20E-02
UP_KEYWORDS	ATP synthesis	9	0.2	4.30E-03	9.60E-02

Table S4. Enrichment analysis (DAVID) results for liver, Related to Fig 2

Category	Term	Count	%	P-Value	Benjamini
UP_TISSUE	Liver	1090	33.1	1.60E-13	4.50E-11
GOTERM_CC_DIRECT	extracellular exosome	785	23.8	3.30E-12	3.40E-09
GOTERM_CC_DIRECT	endoplasmic reticulum	399	12.1	6.80E-09	3.50E-06
UP_TISSUE	Kidney	646	19.6	1.70E-07	2.50E-05
UP_KEYWORDS	Endoplasmic reticulum	307	9.3	7.60E-08	3.70E-05
UP_TISSUE	Bone marrow	491	14.9	3.20E-06	3.10E-04
UP_KEYWORDS	Microsome	49	1.5	5.40E-06	1.30E-03
UP_TISSUE	Amnion	122	3.7	9.70E-05	6.90E-03
UP_KEYWORDS	Acetylation	943	28.6	6.20E-05	7.50E-03
UP_TISSUE	Pancreas	187	5.7	1.60E-04	9.30E-03
UP_KEYWORDS	Monooxygenase	38	1.2	6.00E-05	9.70E-03
UP_TISSUE	Placenta	226	6.9	2.20E-04	1.00E-02
GOTERM_CC_DIRECT	endoplasmic reticulum membrane	210	6.4	6.10E-05	2.10E-02
UP_KEYWORDS	Lysosome	83	2.5	2.30E-04	2.30E-02
KEGG_PATHWAY	Metabolic pathways	378	11.5	1.60E-04	2.30E-02
GOTERM_CC_DIRECT	cytosol	515	15.6	1.10E-04	2.90E-02
KEGG_PATHWAY	Retinol metabolism	31	0.9	1.00E-04	3.00E-02
UP_KEYWORDS	Oxidoreductase	175	5.3	5.00E-04	3.40E-02
UP_KEYWORDS	Lipid metabolism	125	3.8	4.30E-04	3.40E-02
GOTERM_CC_DIRECT	organelle membrane	36	1.1	2.00E-04	4.00E-02
UP_KEYWORDS	Complement pathway	16	0.5	1.20E-03	7.00E-02
UP_KEYWORDS	Steroid metabolism	31	0.9	1.40E-03	7.40E-02
UP_KEYWORDS	Alternative initiation	29	0.9	1.60E-03	7.60E-02

Supplemental Figures

Figure S1. Examples of sexually dimorphic correlations in phenotypes from highlighted sections of Figure 1A. Body fat response after 8 weeks high-fat diet versus lean mass before starting high-fat diet in A) females and B) males. Subcutaneous fat mass versus hemoglobin levels in C) females and D) males. Correlations were calculated using biweight midcorrelation (bicor) as implemented in the WGCNA R package. Shaded areas represent 95% confidence intervals from a linear model of the two traits shown.

Figure S2. Related to Figure 4. Lyplal1 mRNA in different strains of hfHMDP and relation to pathways in adipose. A) Pathway enrichment analysis of the genes correlating the most positively (red) and negatively (blue) with Lyplal1 expression in female adipose tissue. The gene ontologies were uncovered using ToppGene suite. B) Lyplal1 expression in adipose tissue of female and male mice in the HMDP. mRNA expression of Lyplal1 is highlighted for C57BL6J mice.

Figure S3. Related to Figure 5 and Figure 6. Gonadectomy impacts global liver gene expression and adipose tissue Ucp1. A) Variable contribution for each gene to PC1 and PC2 in gonadectomized liver samples from Fig 5B. B) Ucp1 mRNA expression in adipose tissue of intact and gonadectomized C57BL6J mice of both sexes related to Fig. 6D. Results are presented as mean \pm SEM. * $P < 0.05$ and ** $P < 0.01$ between gonadectomized group (GDX) and sham operated controls. P values were calculated using a students t-test (two-way).

Figure S4. Related to Figure 5. Expression levels and sex differences in eQTL genes in adipose tissue and liver. All panels show information for eQTL genes divided into groups based on overlap between tissue and sex. The groups are color coded as in color legend in Figure 5. Notches represent 95% confidence interval. A) and B) show distribution of expression level of genes in the different groups, while C) and D) show female to male fold change. Within tissue differences between groups are not significant.

Figure S5. Related to Figure 6. UCP-1 phenotype correlations in males and females. Each point represents the correlation coefficient of UCP1 to a phenotype in males (y axis) and female (x axis) hfHMDP. Correlations that are significant (corrected $p < 0.05$, permuted based) in both sexes are marked by red square, associations that are significant in one sex only are marked in blue triangles (males) and orange dots (females). Grey stars mark correlations that do not reach significance thresholds.

Figure S6. Related to Figure 6. Correlation between expression of UCP1 and beige related genes in hfHMDP. UCP1 expression in adipose tissue was correlated to four other genes implicated in adipocyte browning - Cidea, Ppargc1a, Hobx8 and Ebf2. Pink dots represent correlation in female hfHMDP while blue triangles represent correlations in male hfHMDP. Red and blue lines represent the fitted linear model for female and male data.

Figure S7. Related to Figure 7. Sex differences in mitochondrial respiration after a high-fat, high-sucrose diet. Mice were fed a high-fat, high sucrose diet (HF/HS) for 8 weeks. Mitochondria were isolated from gonadal adipose of strains (A) A/J and (B) C57BL/6J, respectively and oxidative functions tested using a Seahorse XF24 Analyzer. Different mitochondrial states were measured as described in Materials and Methods. Oxygen consumption rate (OCR) was normalized per μg mitochondrial protein ($\text{pmol/min}/\mu\text{g}$ protein). $N = 3-4$ mice per group.

Results are presented as mean \pm SEM. * $P < 0.05$ and ** $P < 0.01$ between the sexes. P values were calculated using a students t-test (two-way).

Figure S1. Examples of sexually dimorphic correlations in phenotypes from highlighted sections of Figure 1A. Body fat response after 8 weeks high-fat diet versus lean mass before starting high-fat diet in A) females and B) males. Subcutaneous fat mass versus hemoglobin levels in C) females and D) males. Correlations were calculated using biweight midcorrelation (bicor) as implemented in the WGCNA R package. Shaded areas represent 95% confidence intervals from a linear model of the two traits shown.

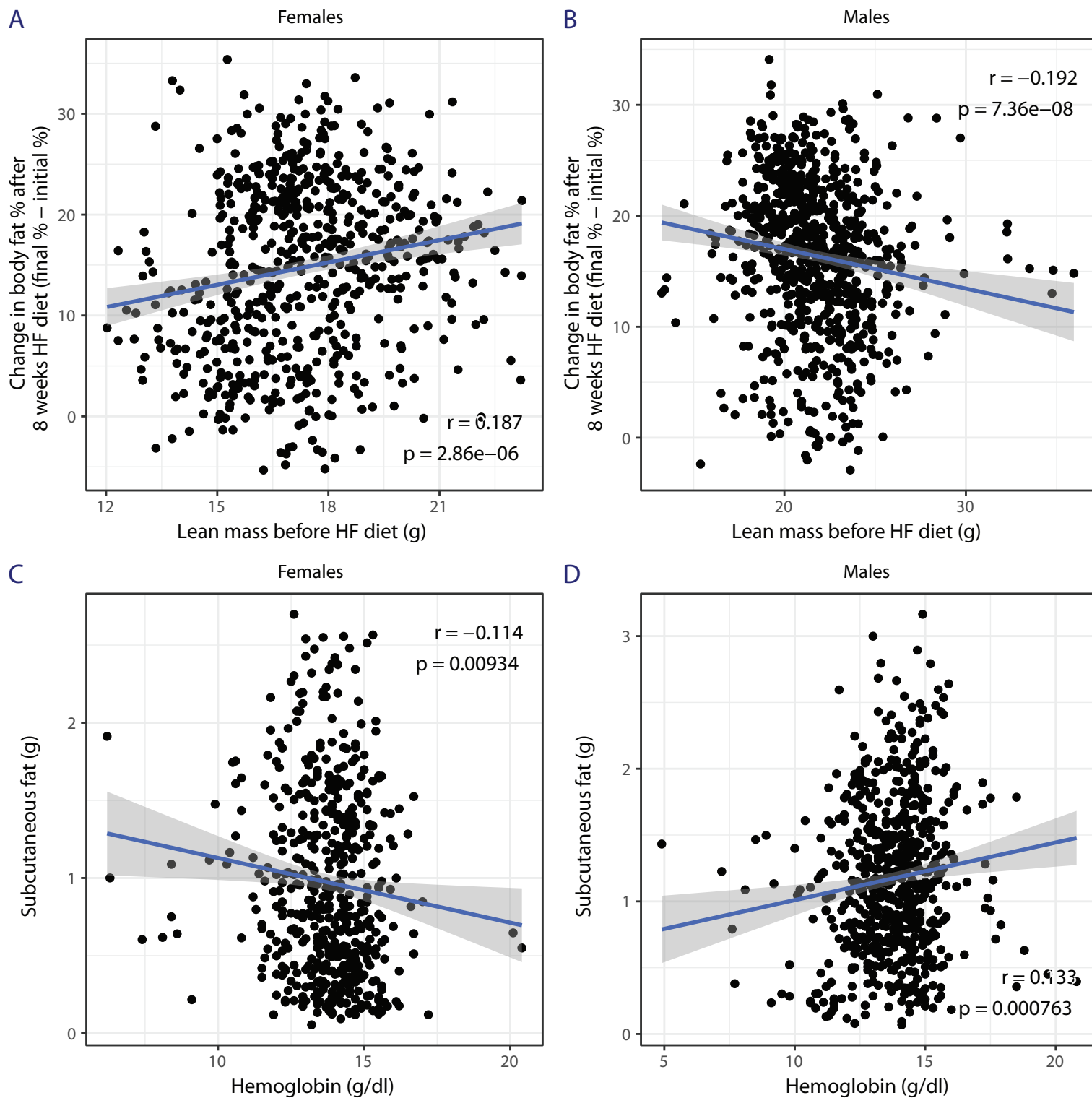


Figure S2. related to Figure 4. *Lyplal1* mRNA in different strains of HMDP and relation to pathways in adipose. A) Pathway enrichment analysis of the genes correlating the most positively (red) and negatively (blue) with *Lyplal1* expression in female adipose tissue. The gene ontologies were uncovered using ToppGene suite. B) *Lyplal1* expression in adipose tissue of female and male mice in the Hybrid Mouse Diversity Panel (HMDP). mRNA expression of *Lyplal1* is highlighted for C57BL/6J mice.

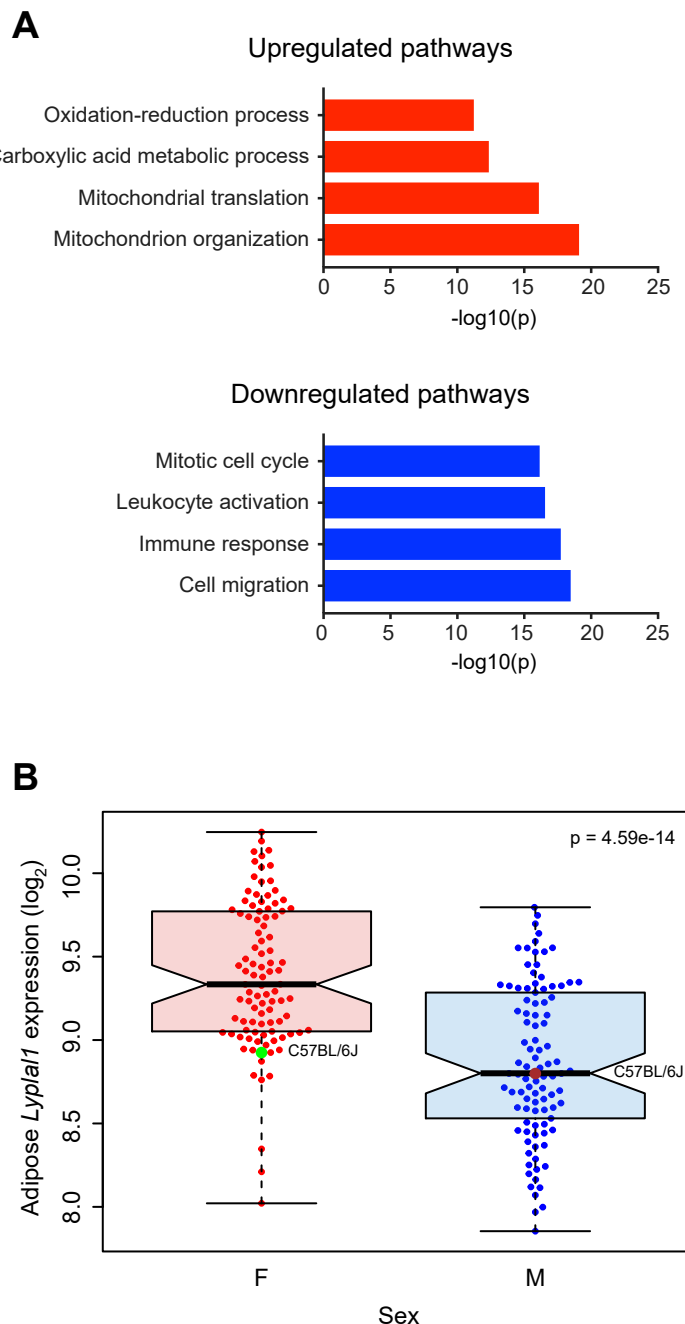


Figure S3. Related to Figure 5 and Figure 6. Gonadectomy impacts on global liver gene expression and adipose tissue Ucp1.A) Variable contribution for each gene to PC1 and PC2 in gonadectomized liver samples from Fig 5B. B) Ucp1 mRNA expression in adipose tissue of intact and gonadectomized C57BL76J mice of both sexes related to Fig. 6D. Results are presented as mean \pm SEM. *P<0.05 and **P<0.01 between gonadectomized group (GDX) and sham operated controls. P values were calculated using a students t-test (two-way).

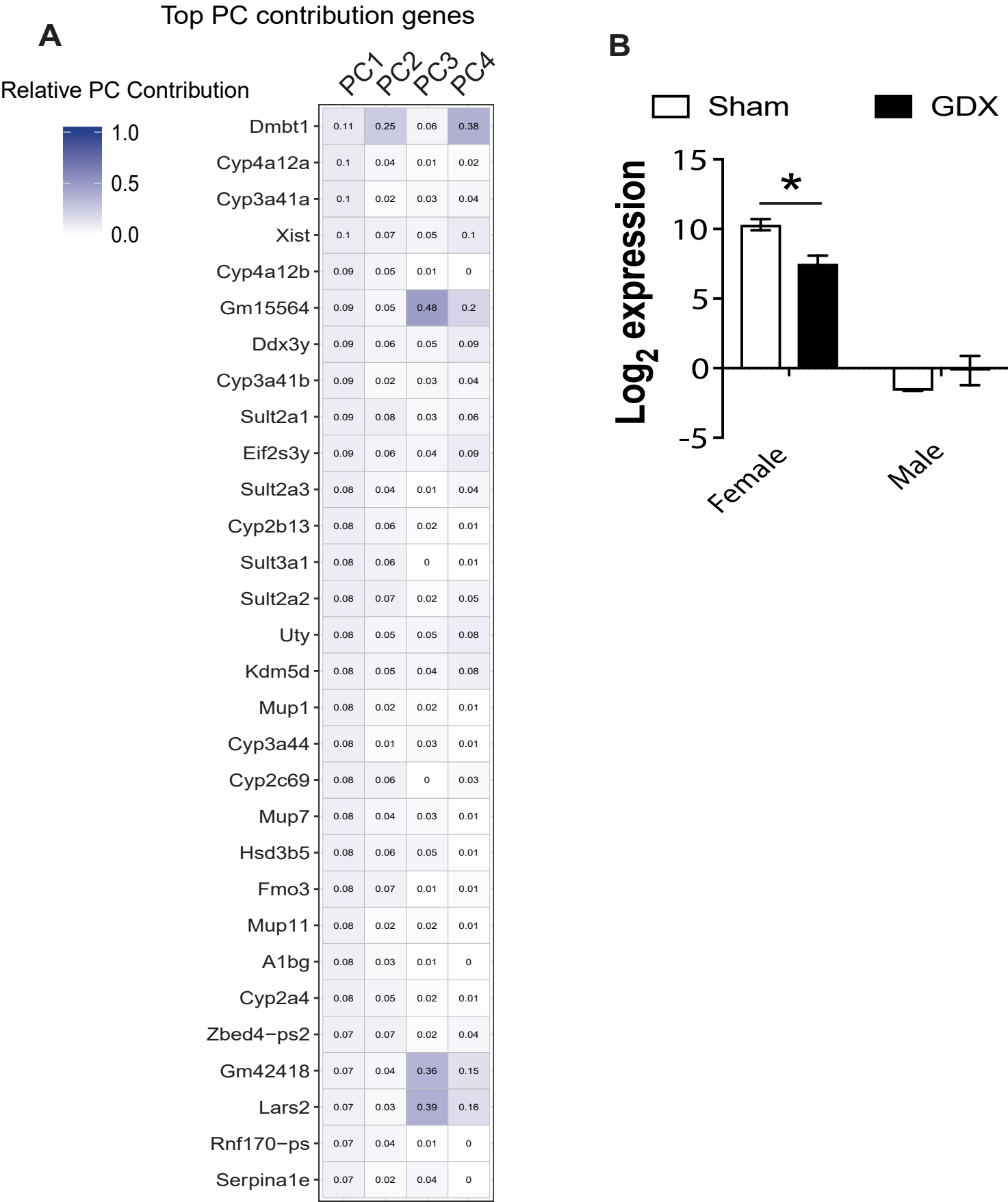


Figure S4. Related to Figure 5. Expression levels and sex differences in eQTL genes in adipose tissue and liver. All panels show information for eQTL genes divided into groups based on overlap between tissue and sex. The groups are color coded as in color legend in Figure 5. Notches represent 95% confidence interval. A) and B) show distribution of expression level of genes in the different groups, while C) and D) show female to male fold change. Within tissue differences between groups are not significant.

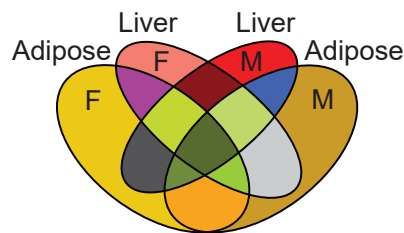
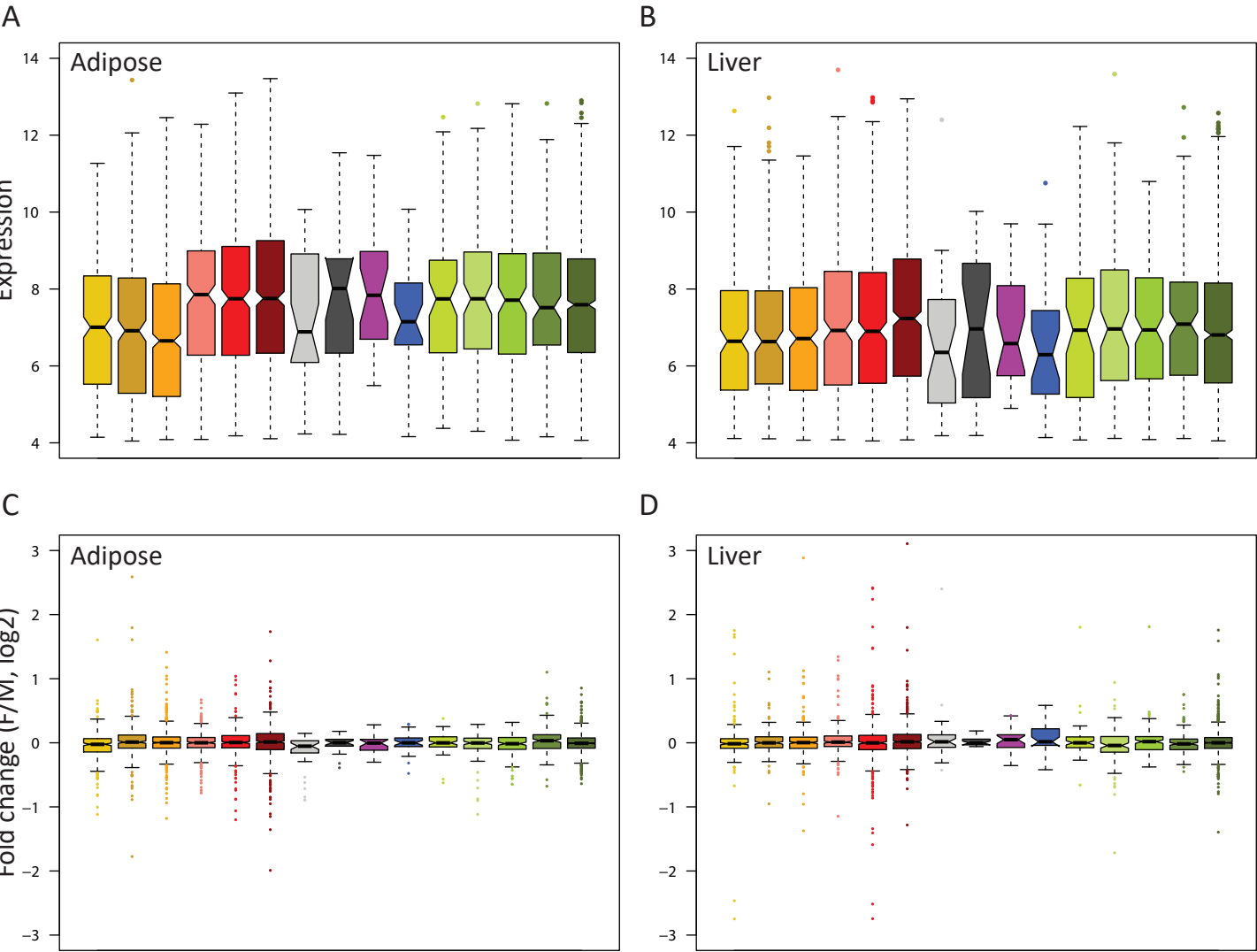


Figure S5. Related to Figure 6. UCP-1 phenotype correlations in males and females. Each point represents the correlation coefficient of UCP1 to a phenotype in males (y axis) and female (x axis) hfHMDP. Correlations that are significant (corrected $p < 0.05$, permuted based) in both sexes are marked by red square, associations that are significant in one sex only are marked in blue triangles (males) and orange dots (females). Grey stars mark correlations that do not reach significance thresholds.

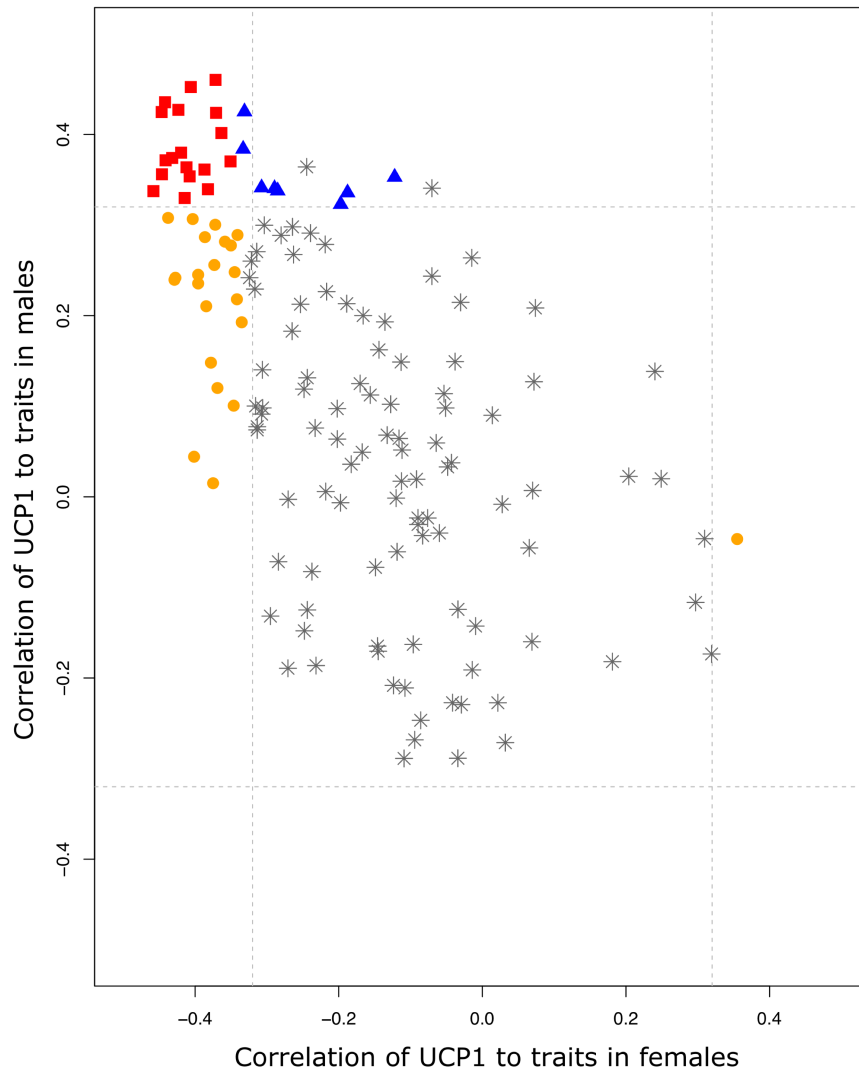


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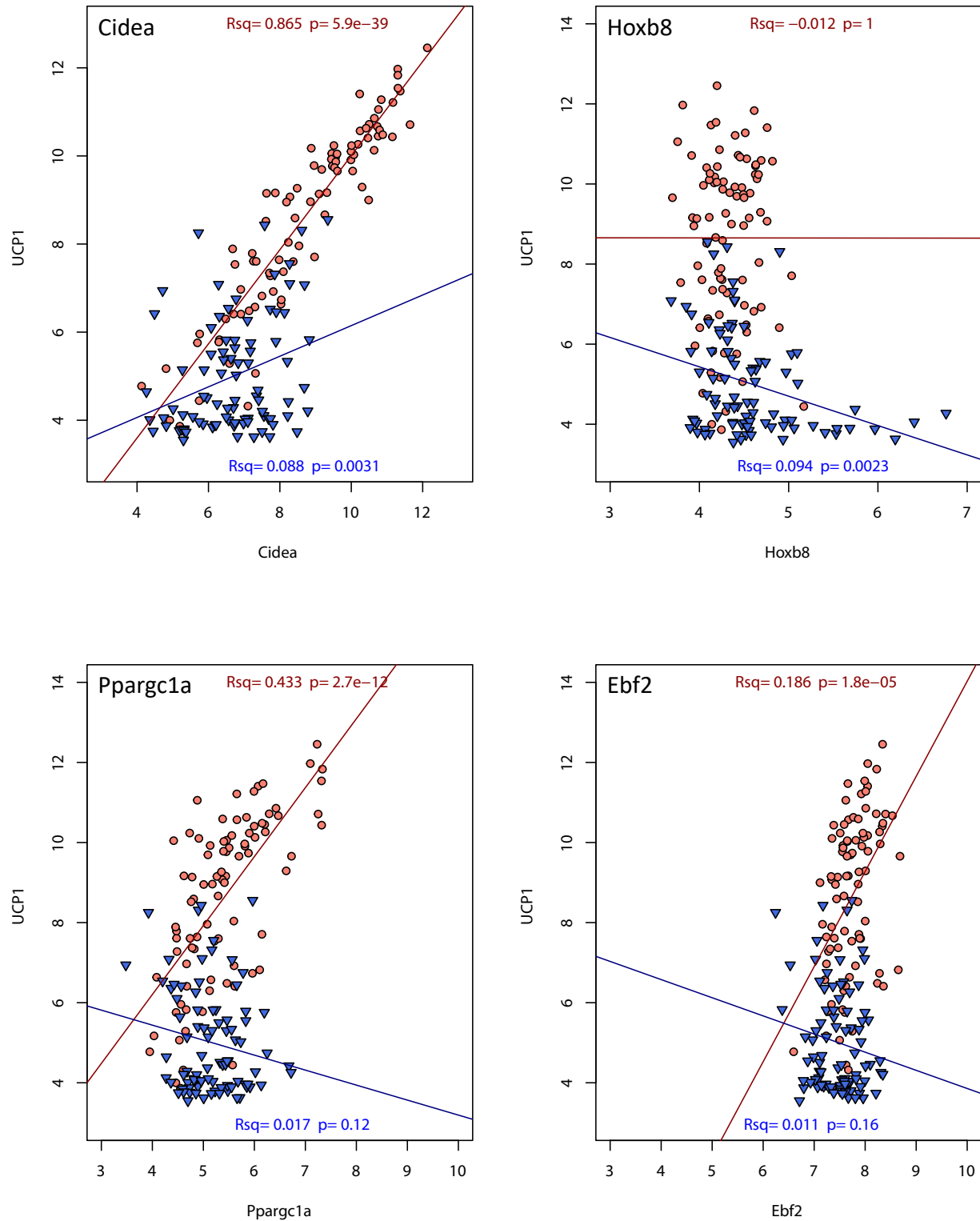


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