HelmholtzZentrum münchen
German Research Center for Environmental Health

Circadian regulation in hypothalamys and hippocampus reveald by transciptome data analysis

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HELMHOLTZ RESEARCH FOR GRAND CHALLENGES

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Experimental Design

Start
10 weeks
of age

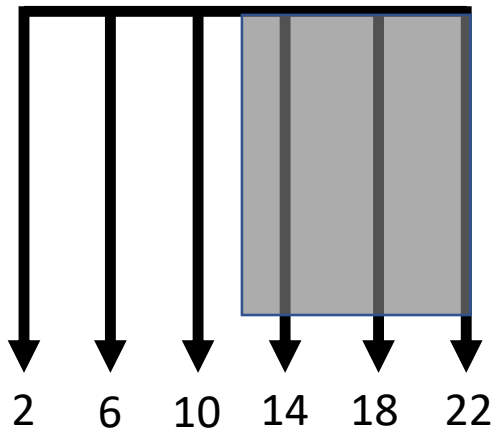
8 weeks of diet

chow

HFD

Tissues collected over 24 hours

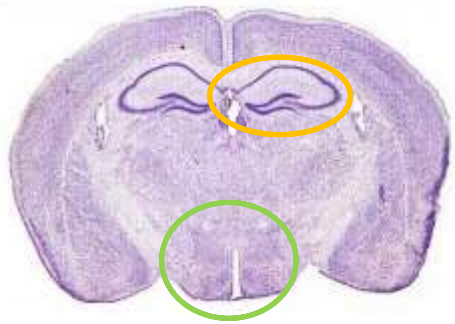
5 replicates per timepoint



Zeitgeber Time (hr)

Rattus norvegicus

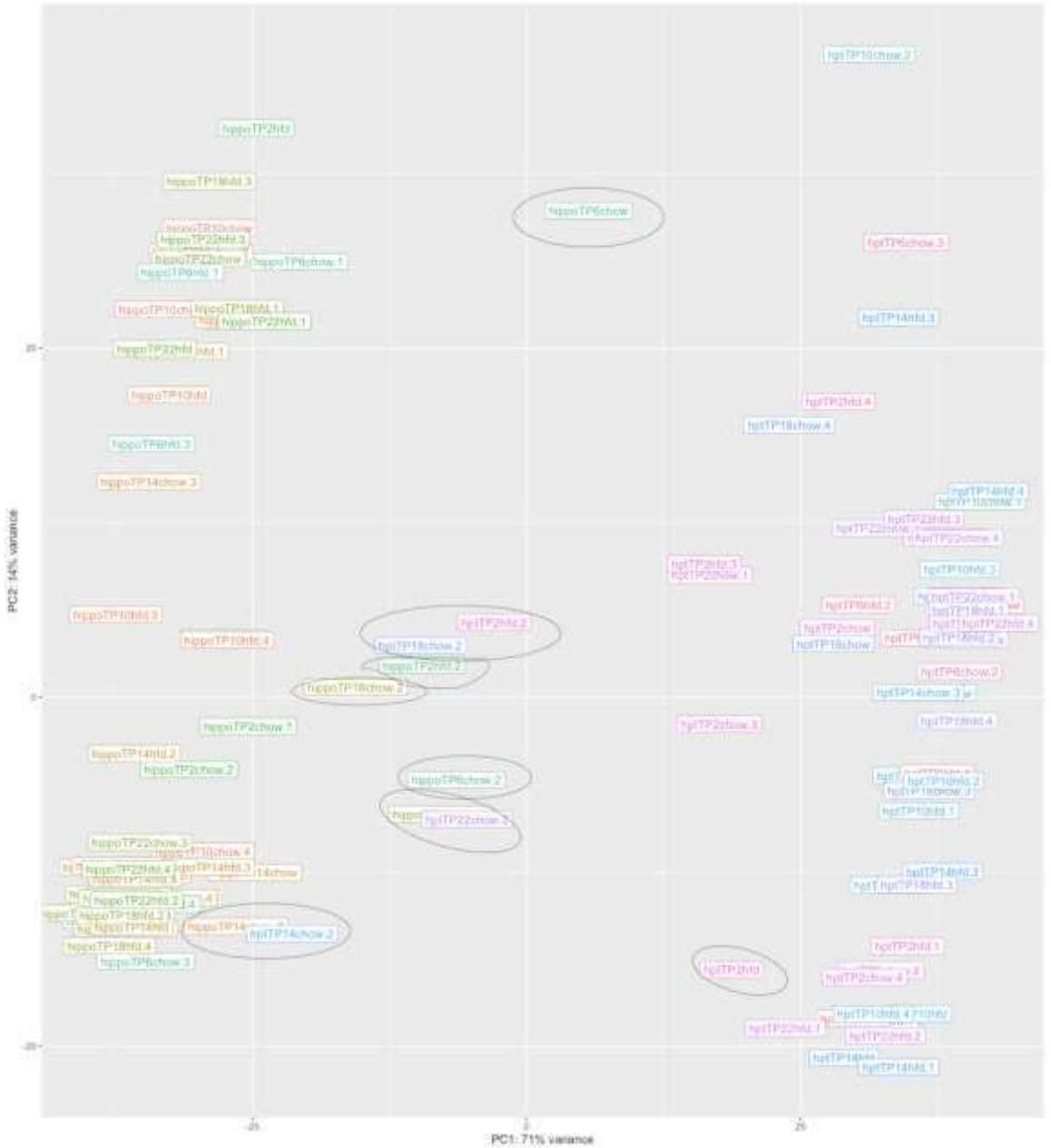
Hippocampus
(Hippo)

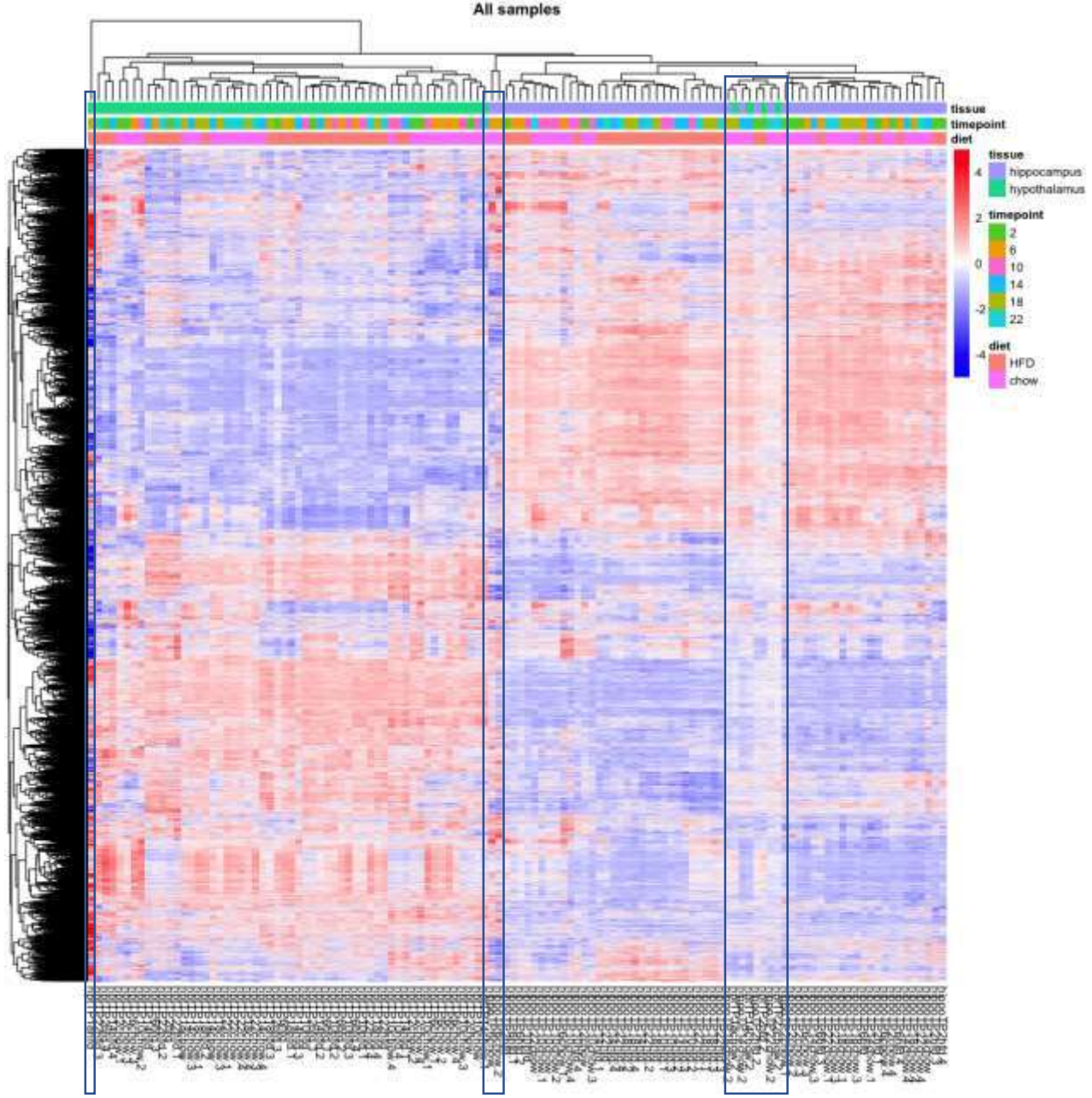


Hypothalamus
(HPT)

global RNA-seq
profiling

PCA plot and sample distance heatmap





Specific genes Hippocampus vs. Hypothalamus

Oxytocin

hippocampus chow					
TP2	TP6	TP10	TP14	TP18	TP22
208	33	8	19	6	21
32	61	42	11	41	6
14	42	2	1631	3657	5778
3	1	7	3	11	9
5	5	59	14	27	5

hypothalamus chow					
TP2	TP6	TP10	TP14	TP18	TP22
11055	6254	7384	13060	12690	9938
5667	2481	2999	4718	7122	3715
5881	8936	11809	2670	4787	5192
4392	3220	2126	10211	7039	16660
13493	5590	6221	4656	10473	6199

hippocampus HFD					
TP2	TP6	TP10	TP14	TP18	TP22
12	3	12	24	12	16
9	9	14	5	3	31
5470	3	2	4	7	9
46	9	2	5	14	4
10	7	19	8	2	4

hypothalamus HFD					
TP2	TP6	TP10	TP14	TP18	TP22
40	4673	8536	3664	272	1029
30083	22142	16037	5680	1058	580
6757	19093	18998	23791	2067	385
4056	1558	4234	15117	7682	23226
23395	2155	5215	6528	4377	5099

AVP

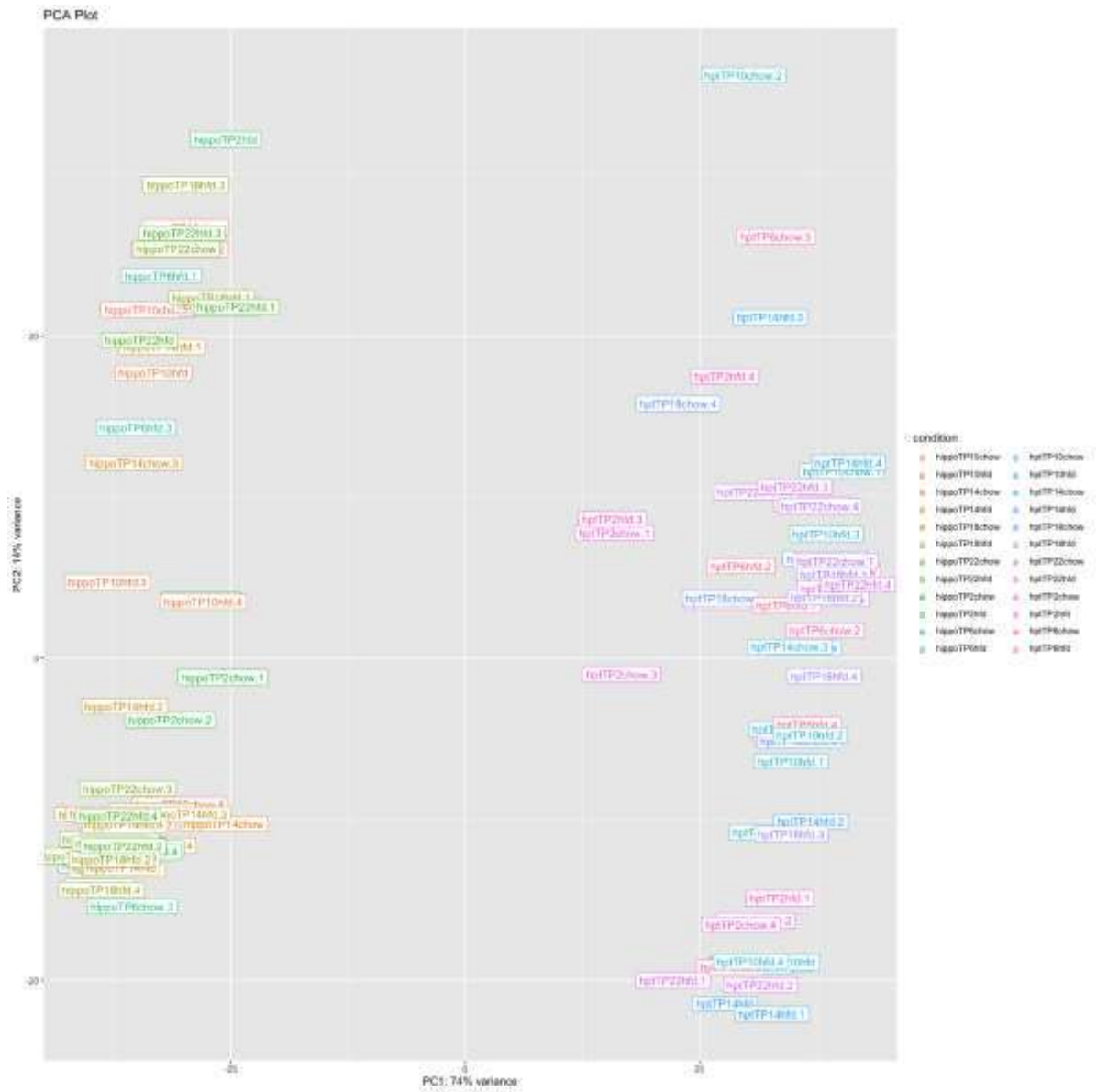
hippocampus chow					
TP2	TP6	TP10	TP14	TP18	TP22
40	130	13	43	22	31
26	163	120	22	76	16
46	209	10	1499	9194	12014
9	11	13	19	18	18
21	16	114	65	72	15

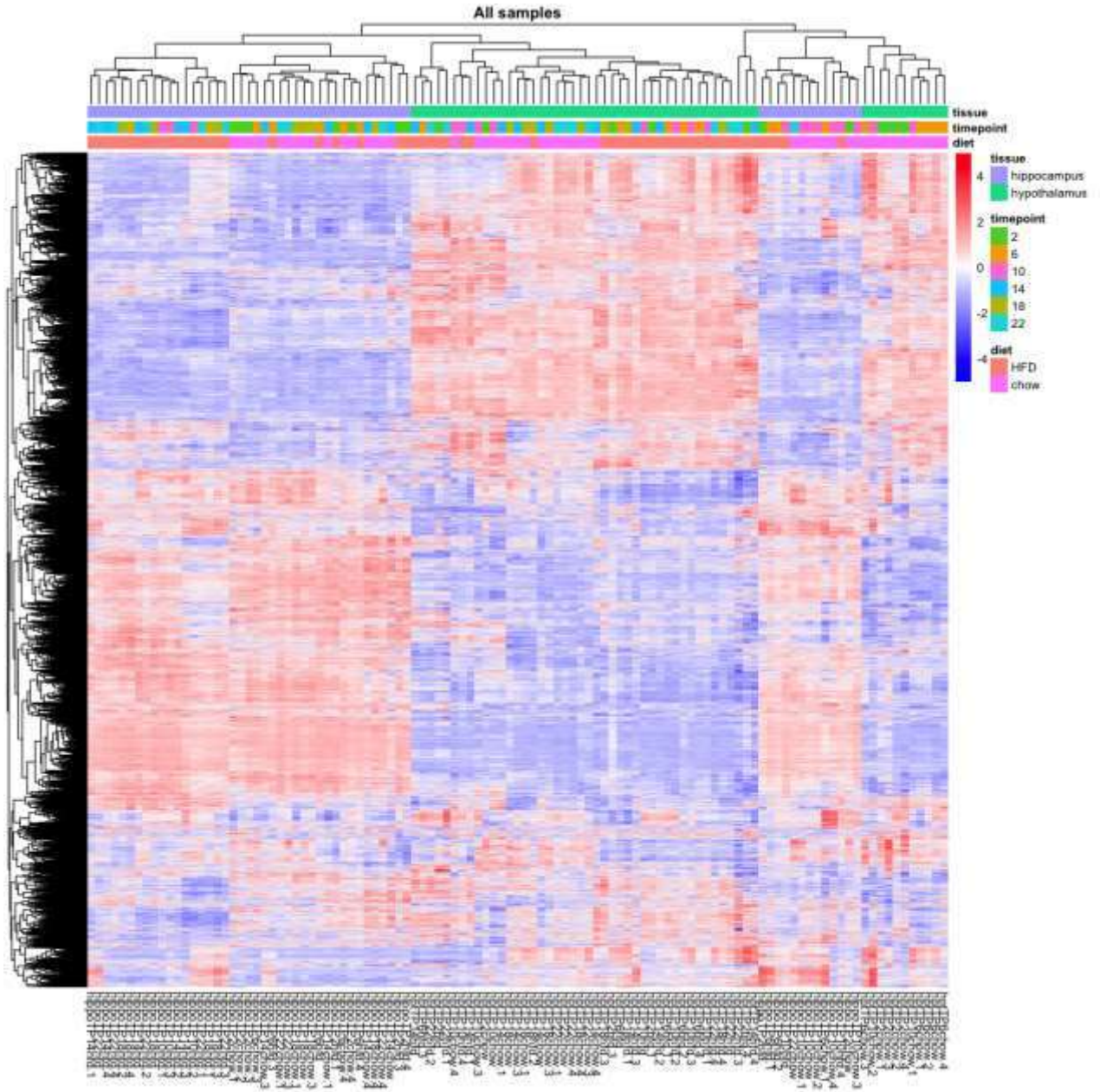
hypothalamus chow					
TP2	TP6	TP10	TP14	TP18	TP22
10765	22616	20437	26212	24536	20894
12960	7541	11946	4766	22361	12440
16457	28188	29622	2576	13080	11136
10283	10380	7186	28928	23082	33731
25179	14246	21110	20993	27262	21033

hippocampus HFD					
TP2	TP6	TP10	TP14	TP18	TP22
12	22	35	219	11	20
16	17	44	11	16	78
11092	11	11	13	18	9
108	20	6	24	12	11
24	26	41	19	15	11

hypothalamus HFD					
TP2	TP6	TP10	TP14	TP18	TP22
29	13352	21013	3550	216	2112
54672	51226	32156	8031	5747	1363
13427	43883	51082	66582	8184	578
8353	1240	16118	31067	7014	45099
56579	8465	15846	27724	7101	10225

PCA plot and heatmap





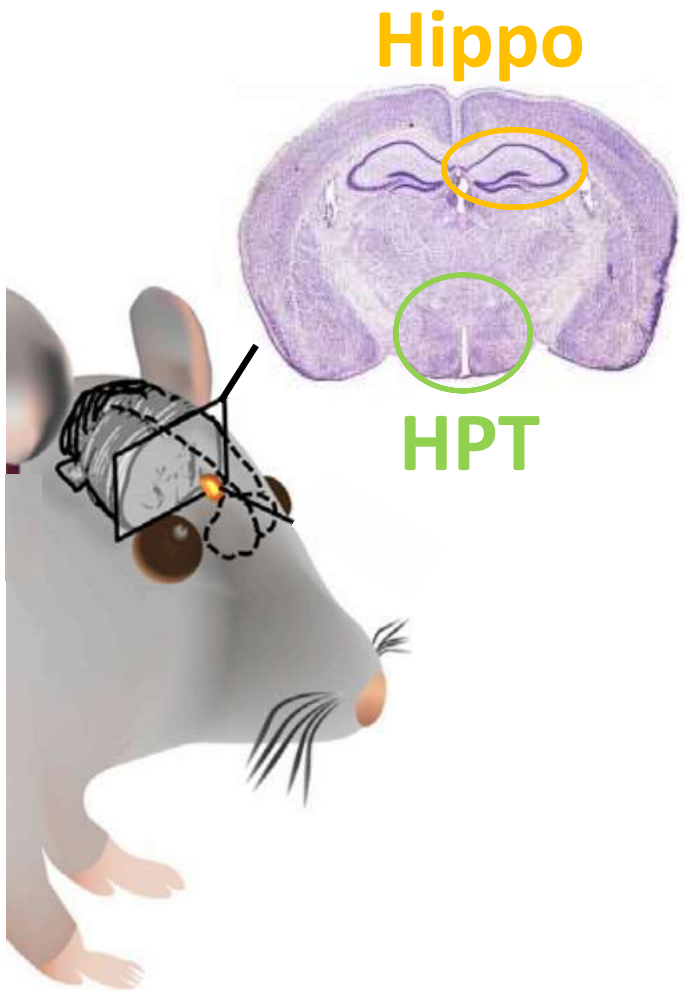
Tissue-specific RNA-Seq heatmaps

chow

HFD

HPT

Hippo



Hippo

Circadian genes

chow

HFD

HPT

Hippo

% of genes

0 5 10

# of circadian genes

1130

39

293

909

193

1348

% of circadian genes

77

3

20

37

8

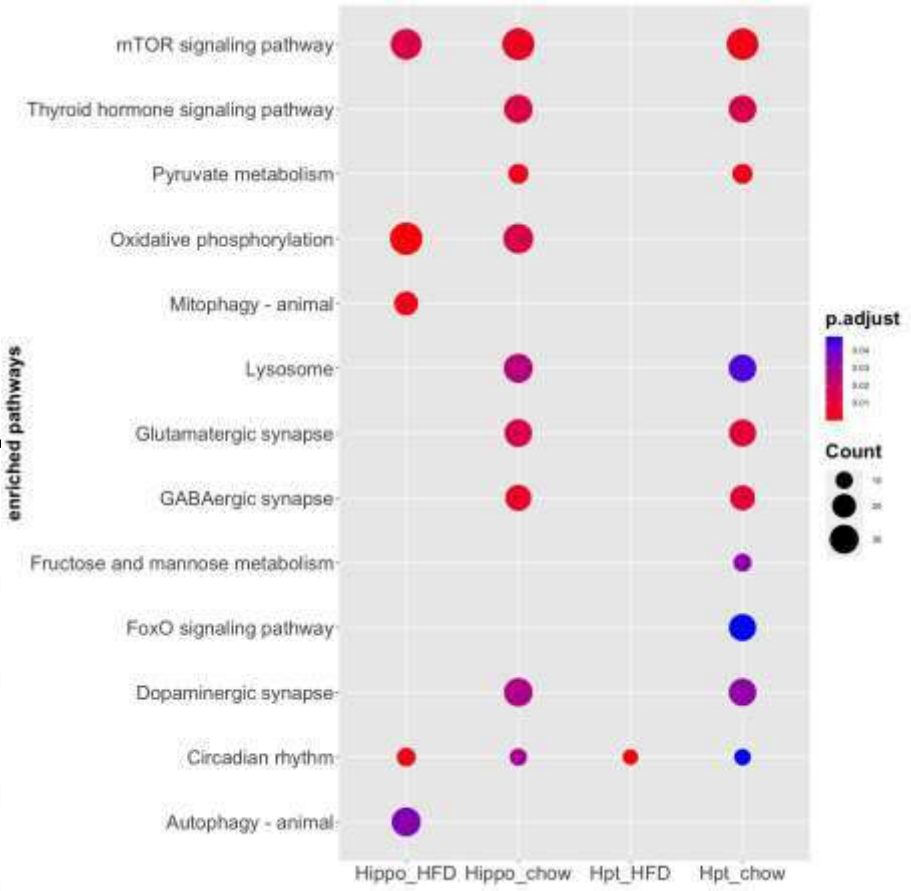
55

amplitude

10.0 7.5 5.0 2.5 0.0

0.0 0.2 0.4 0.6 0.8

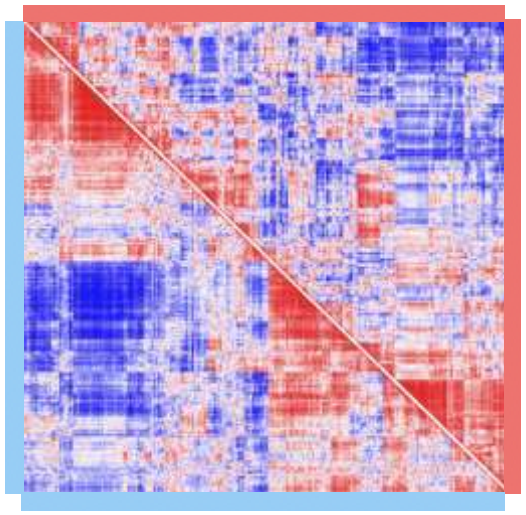
enrichment of selected pathways



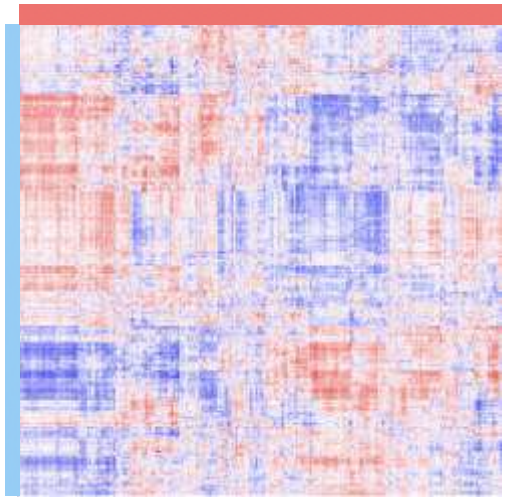
Intra and between diet transcriptome temporal correlation

HPT

Intra diet correlation

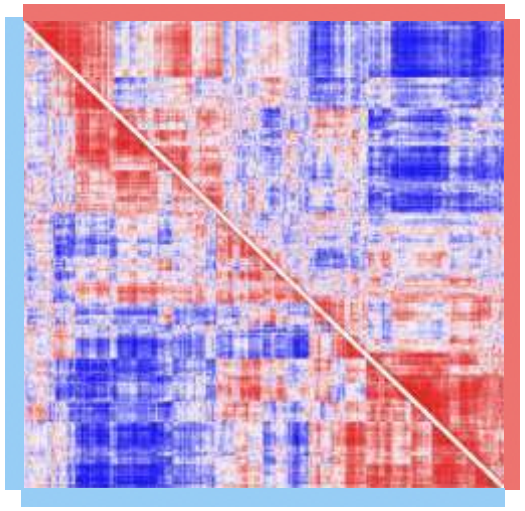


between diet correlation

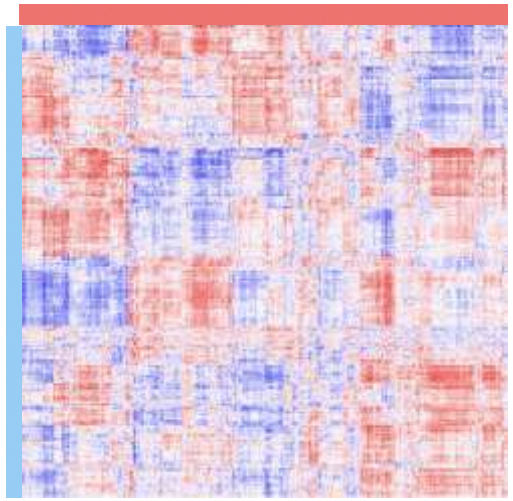


Hippo

Intra diet correlation

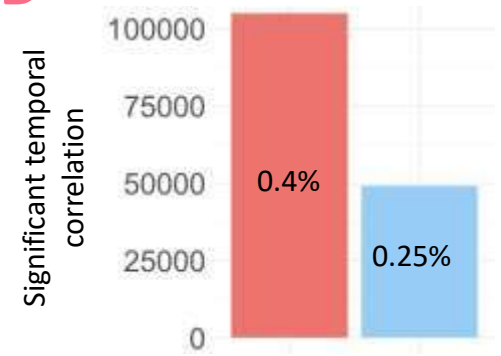


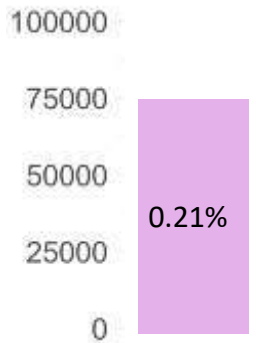
between diet correlation

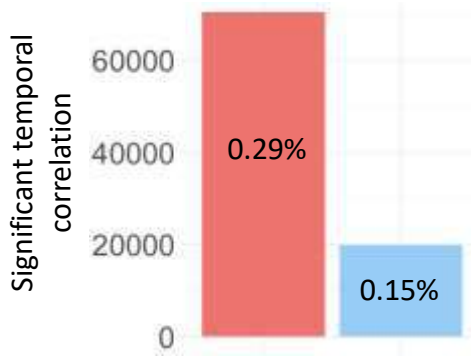


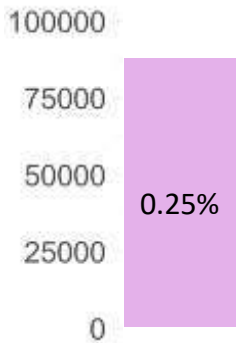
chow

HFD

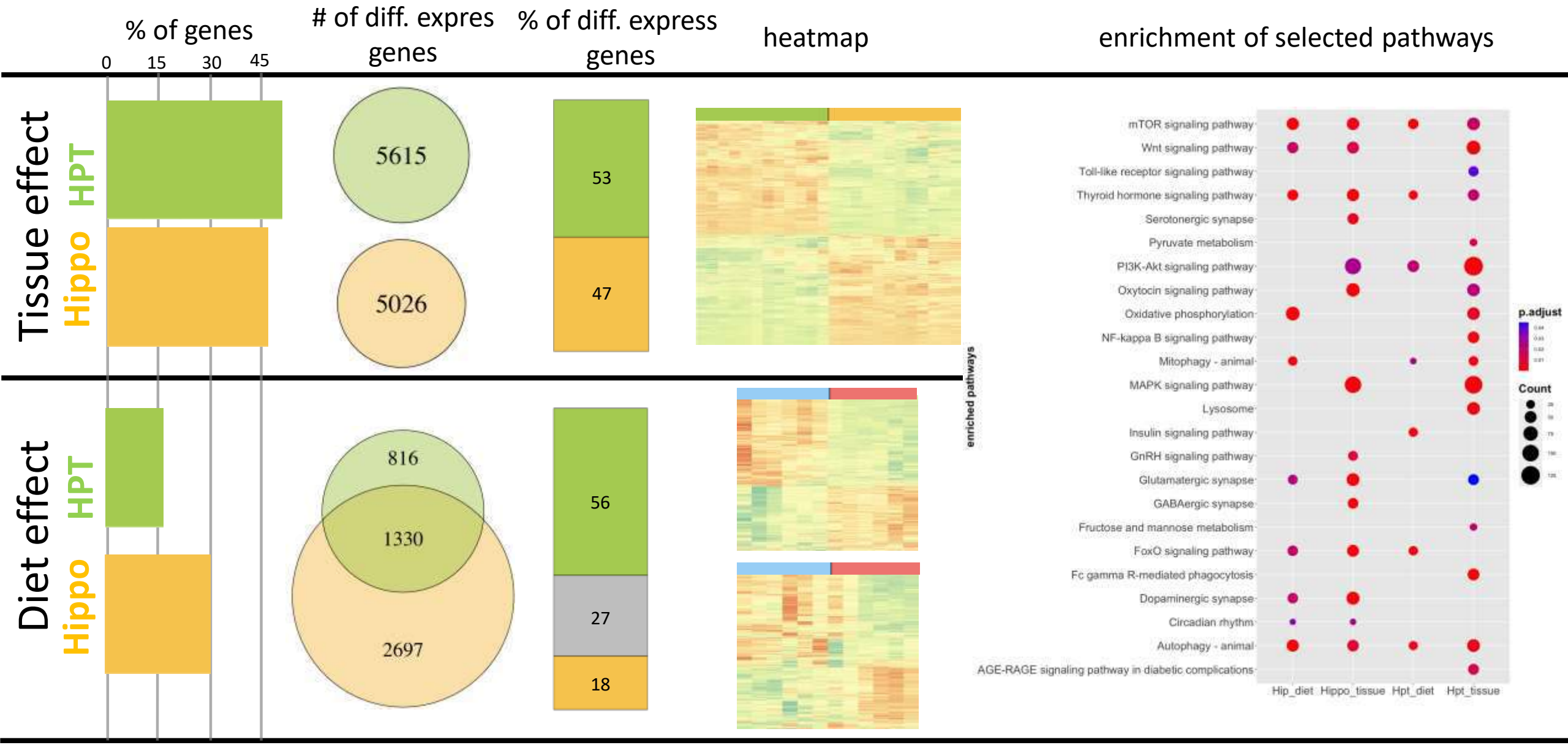








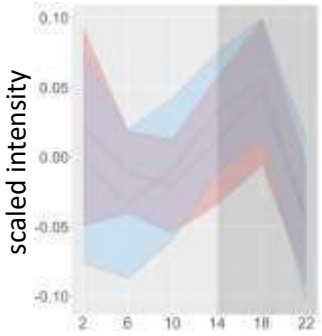
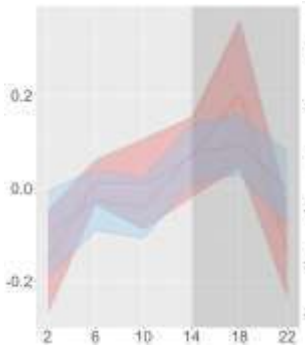
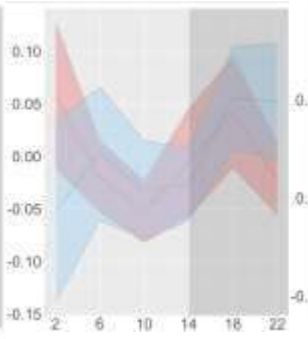
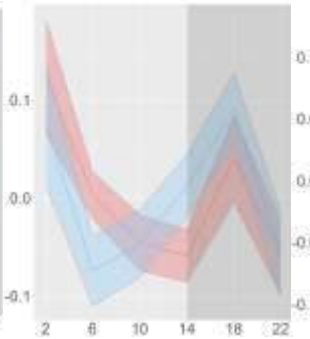
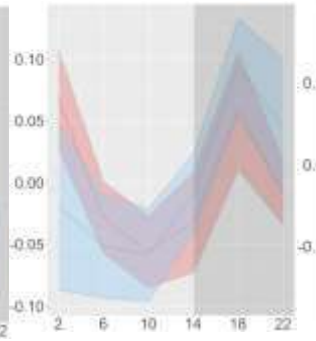
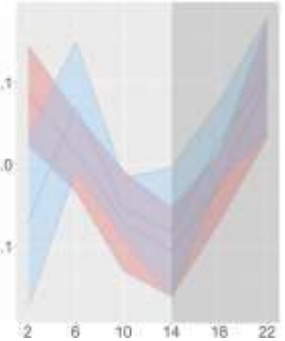
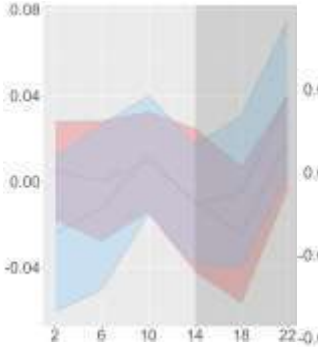
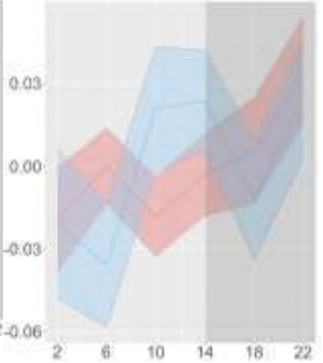
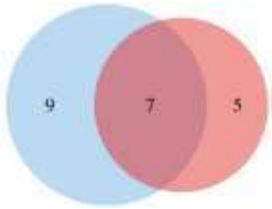
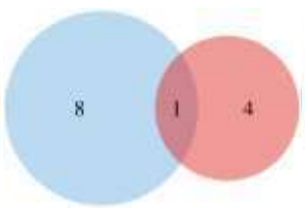
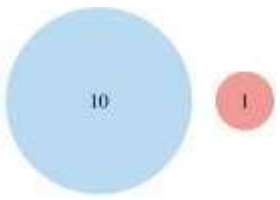
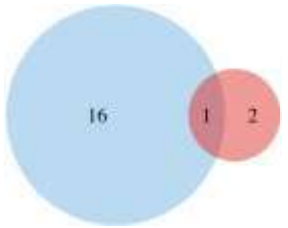
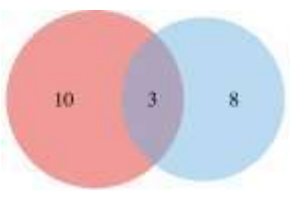
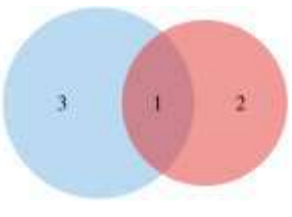
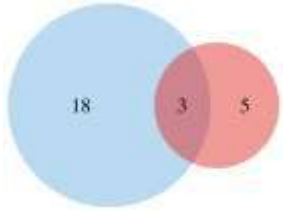
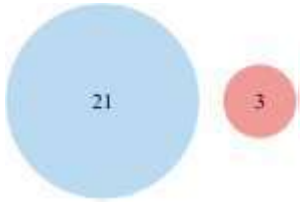
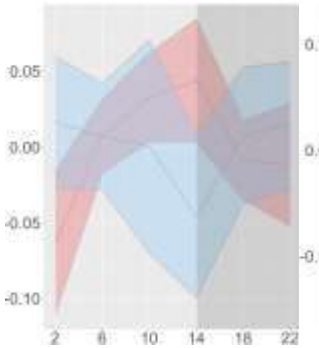
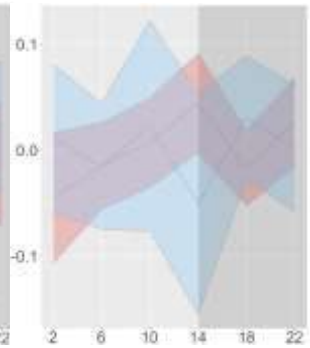
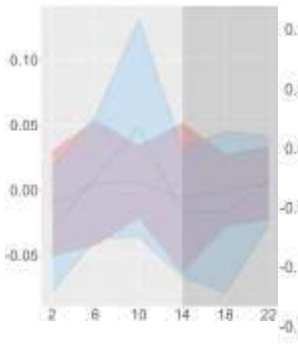
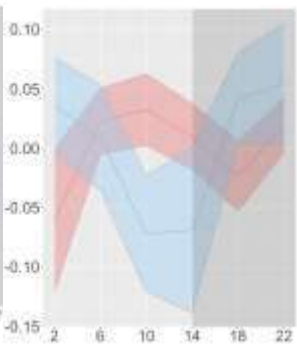
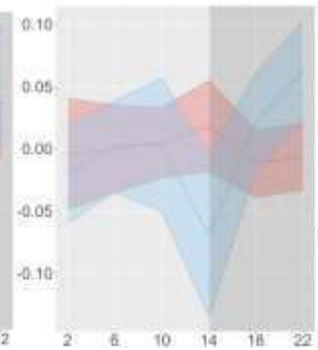
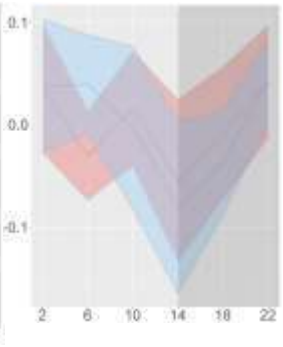
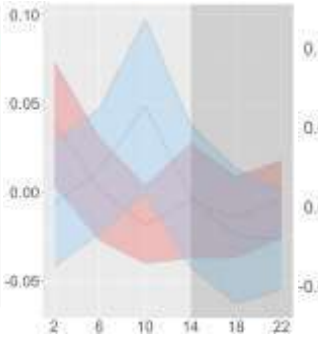
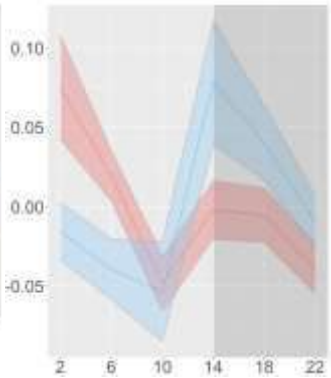
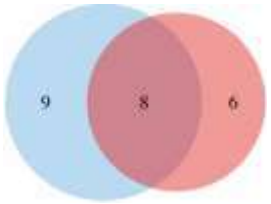
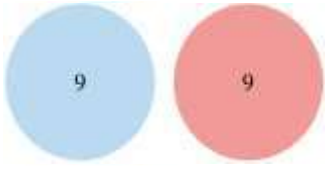
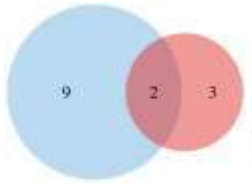
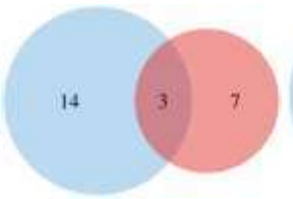
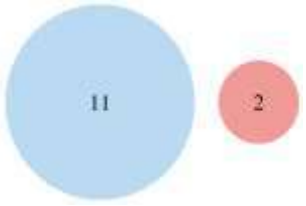
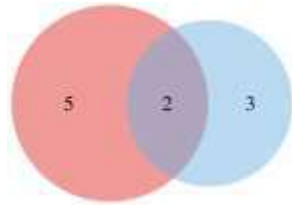
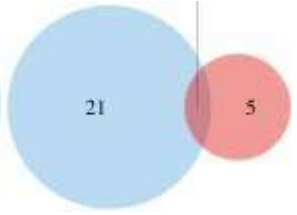
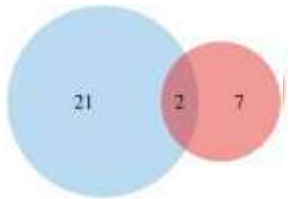
Differential expression - tissue and diet effect



Target genes over time

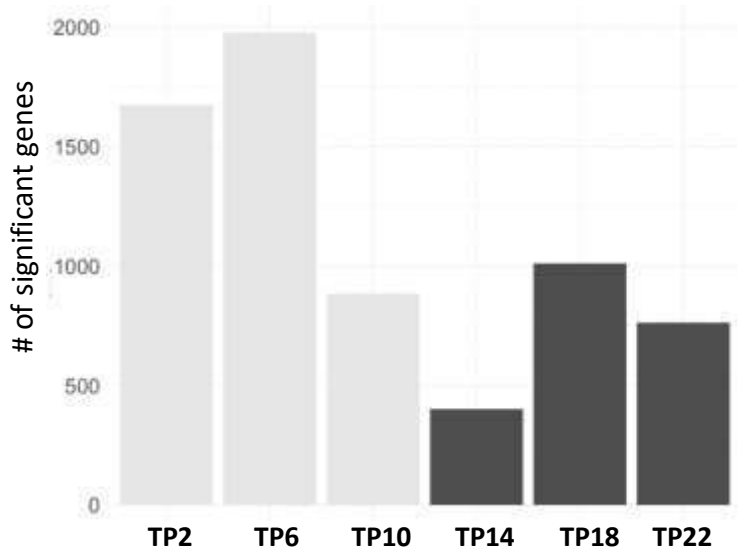
chow

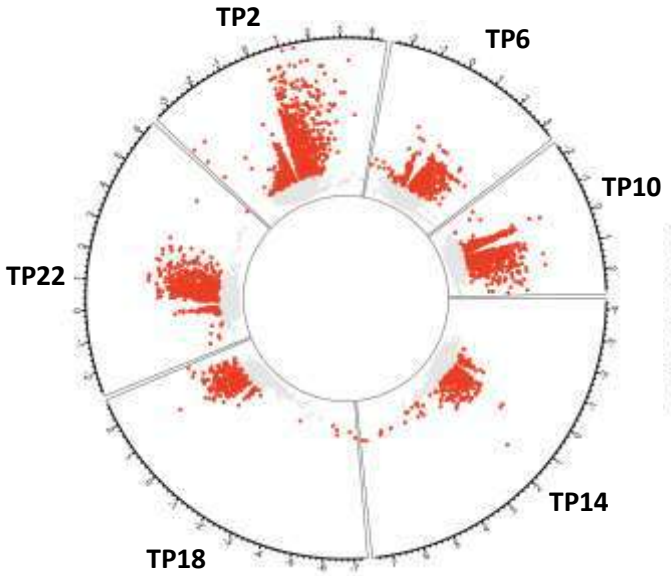
HFD

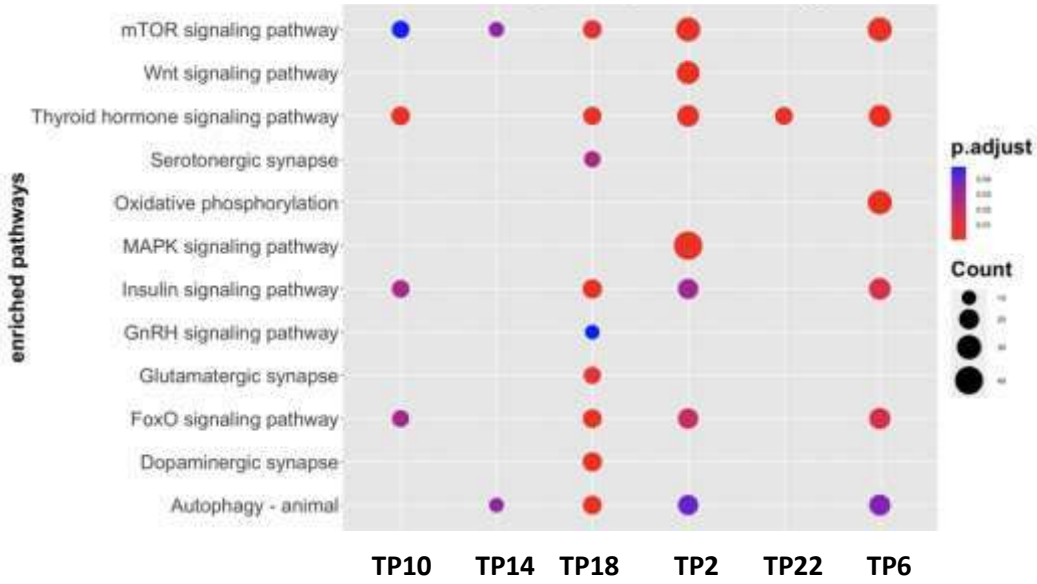
	clock (n=65)	obesity (n=49)	diabetes (n=51)	synaptic plastisty (n=71)	insultin pathway (n=60)	cytokinese recptor (n=26)	fatty acid metab. (n=64)	glucose metab. (n=69)
HPT scaled intensity								
# of circadian genes								
Hippo scaled intensity								
# of circadian genes								

Diet effect per time point

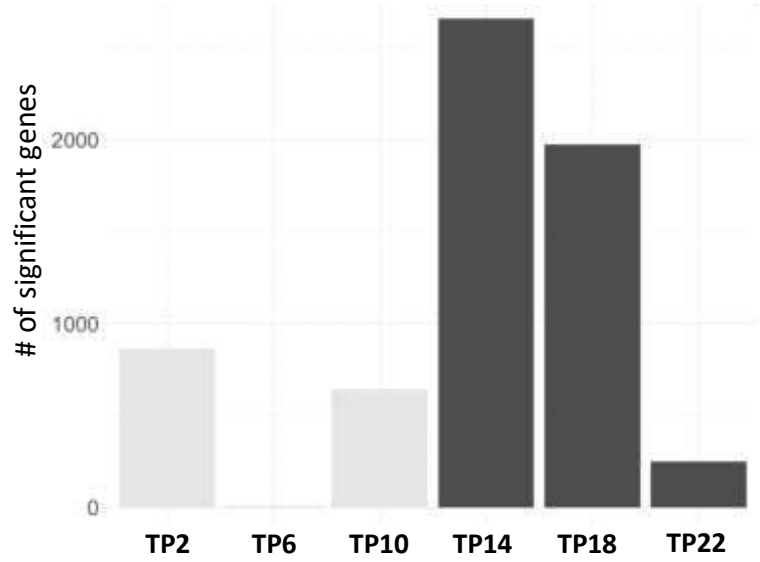
HPT

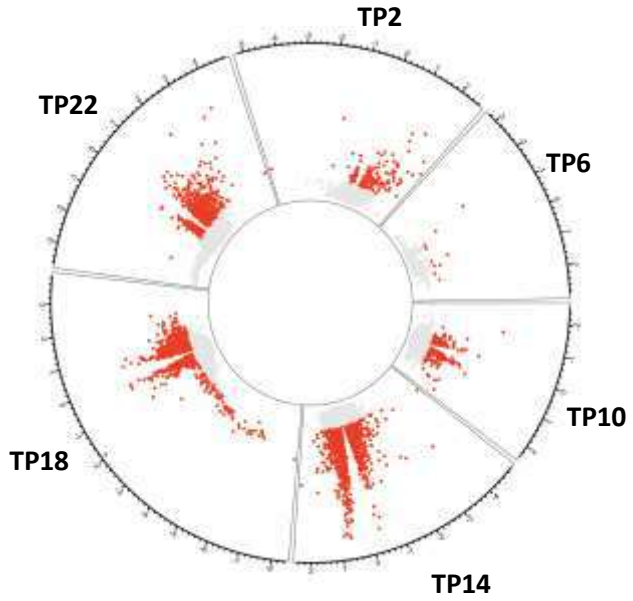


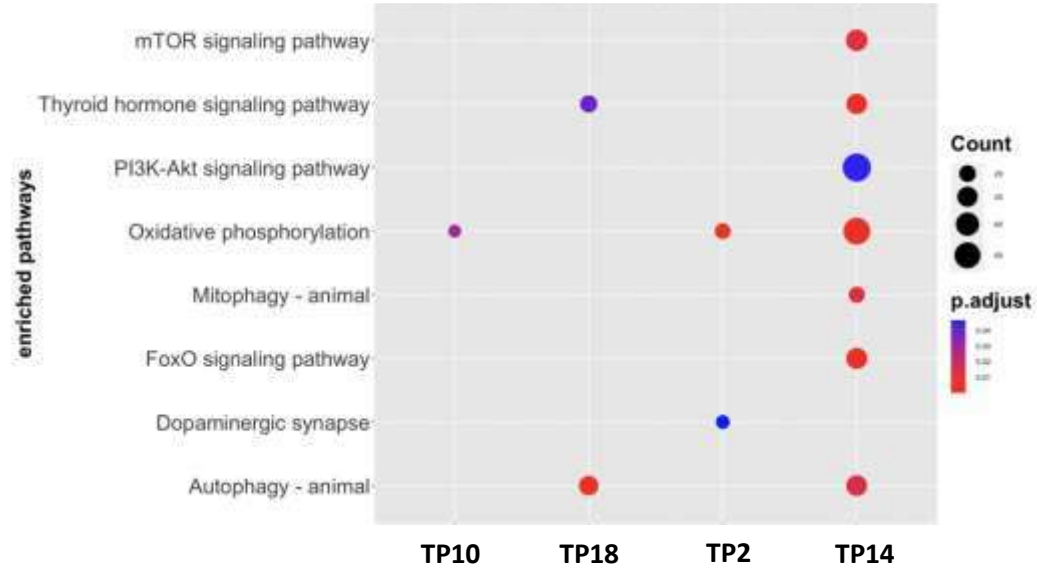




Hippo

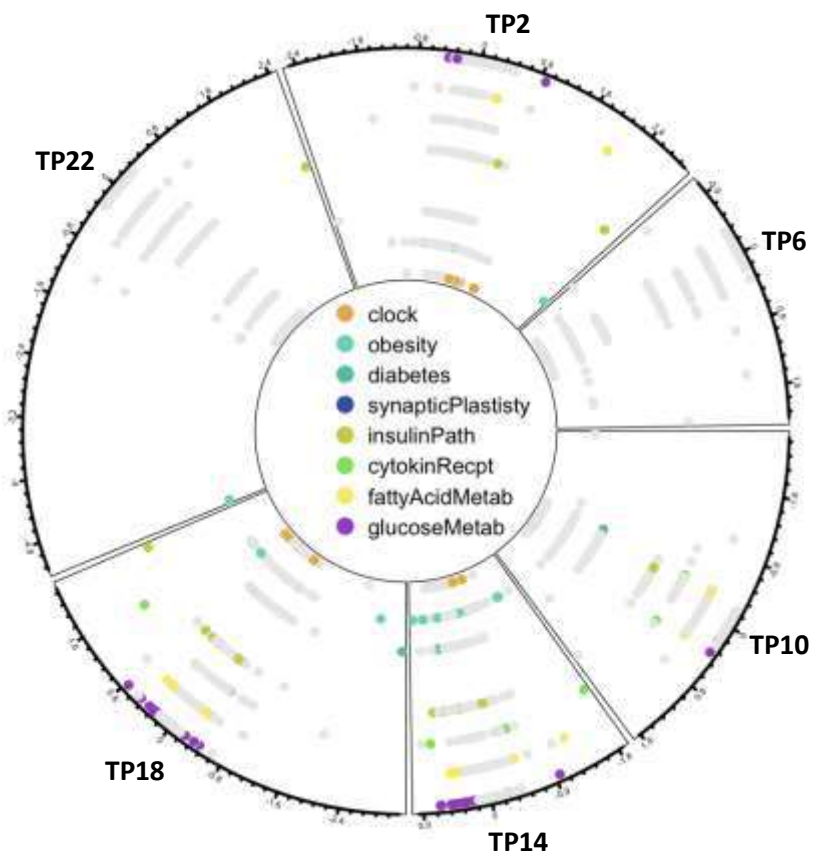




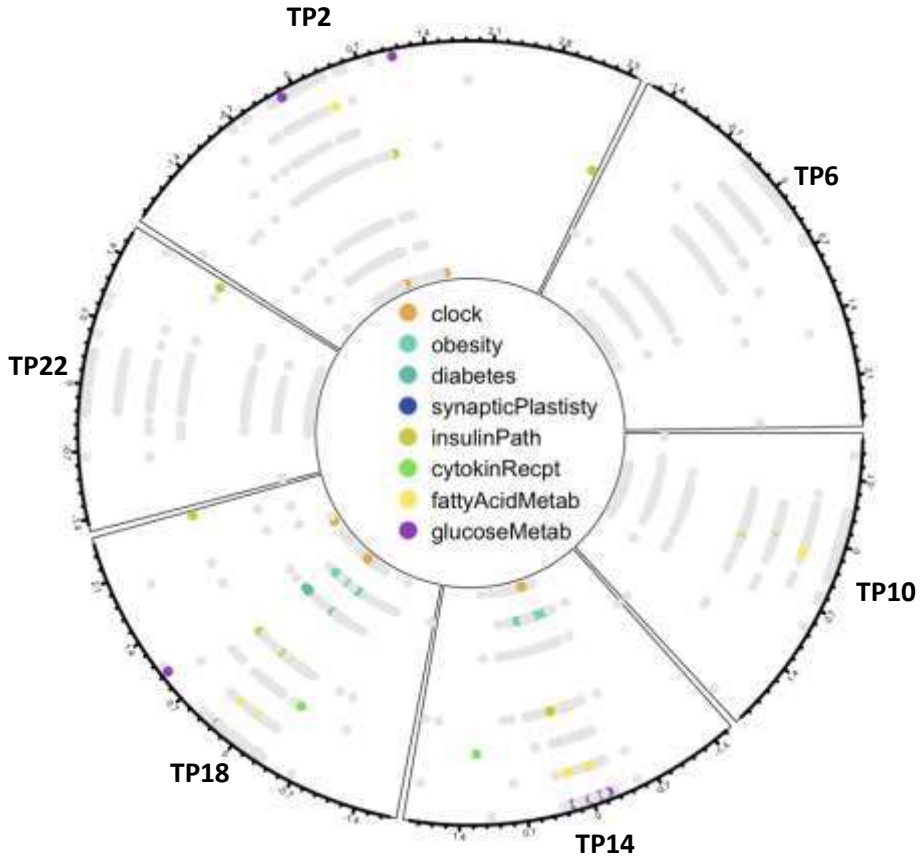


Diet effect per time point of target genes

Hippo



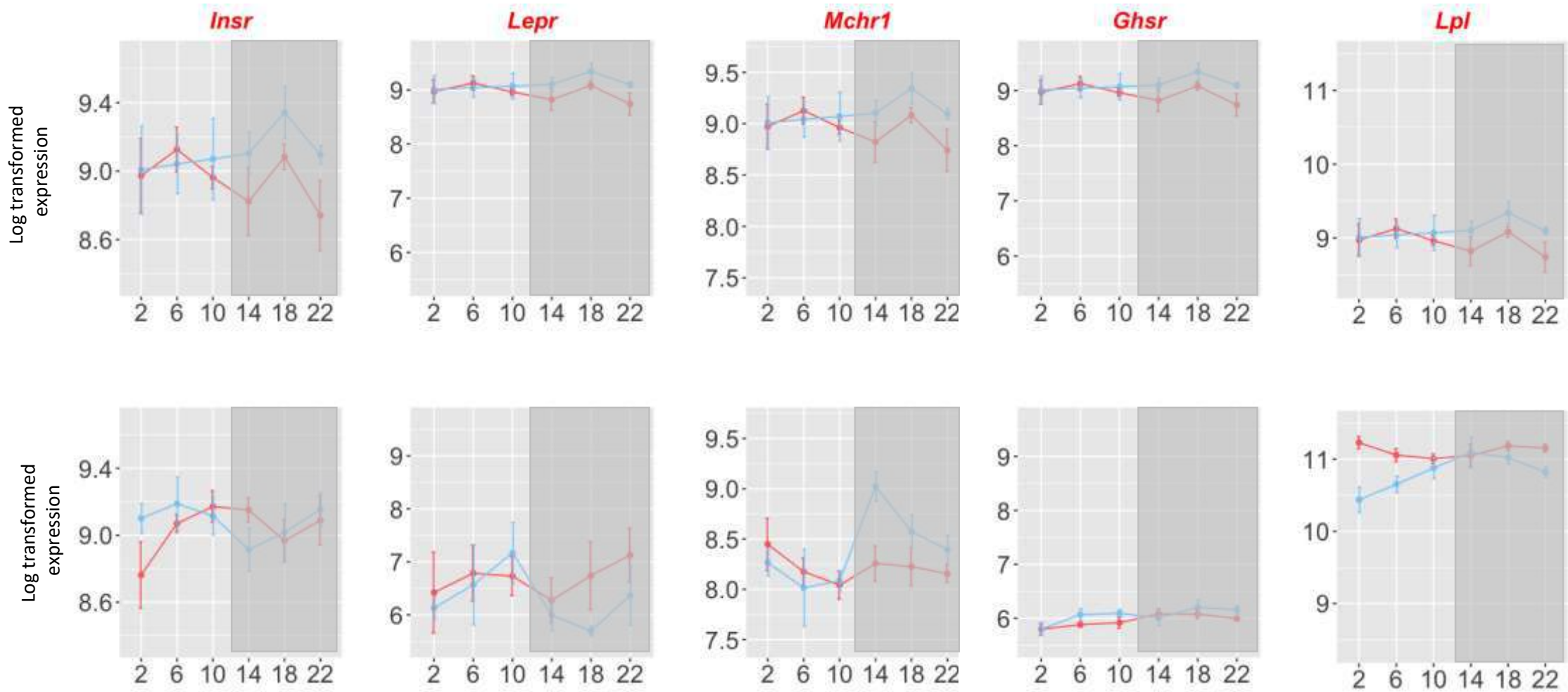
HPT



Target genes enrichment - Hypothalamus

HPT

Hippo



Gene association with periphery data

chow

HFD

barplot

positive assoc.

negative assoc.

% of genes

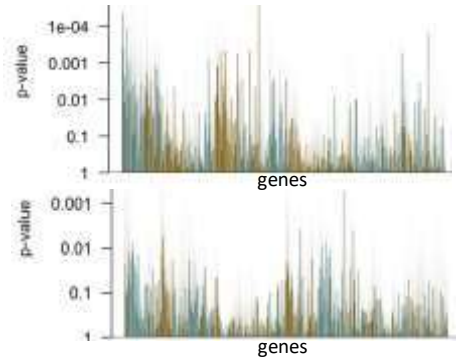
# of assoc. genes

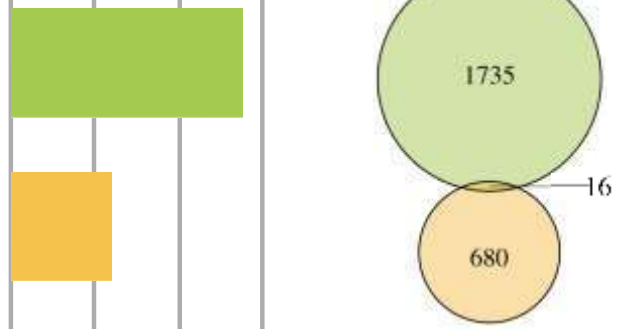
% of assoc. genes

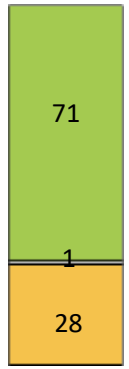
enrichment of selected pathways

glucose

Hippo HPT

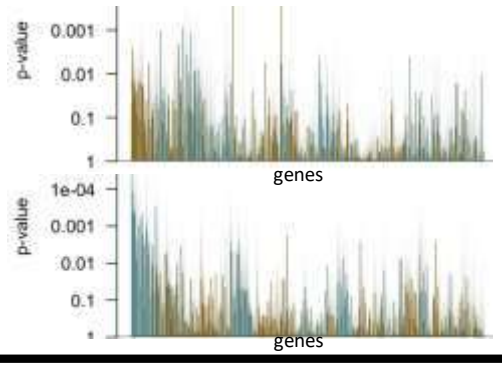


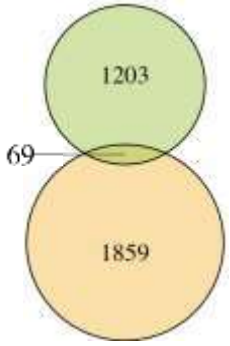


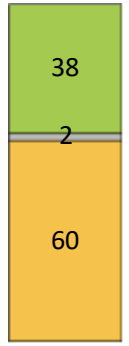


insulin

Hippo HPT

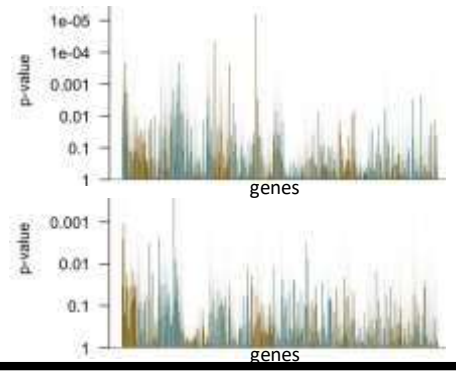


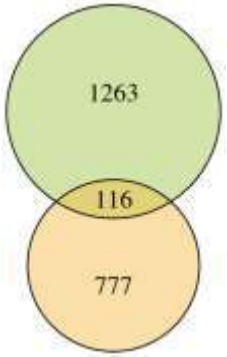


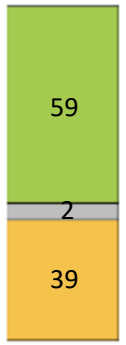


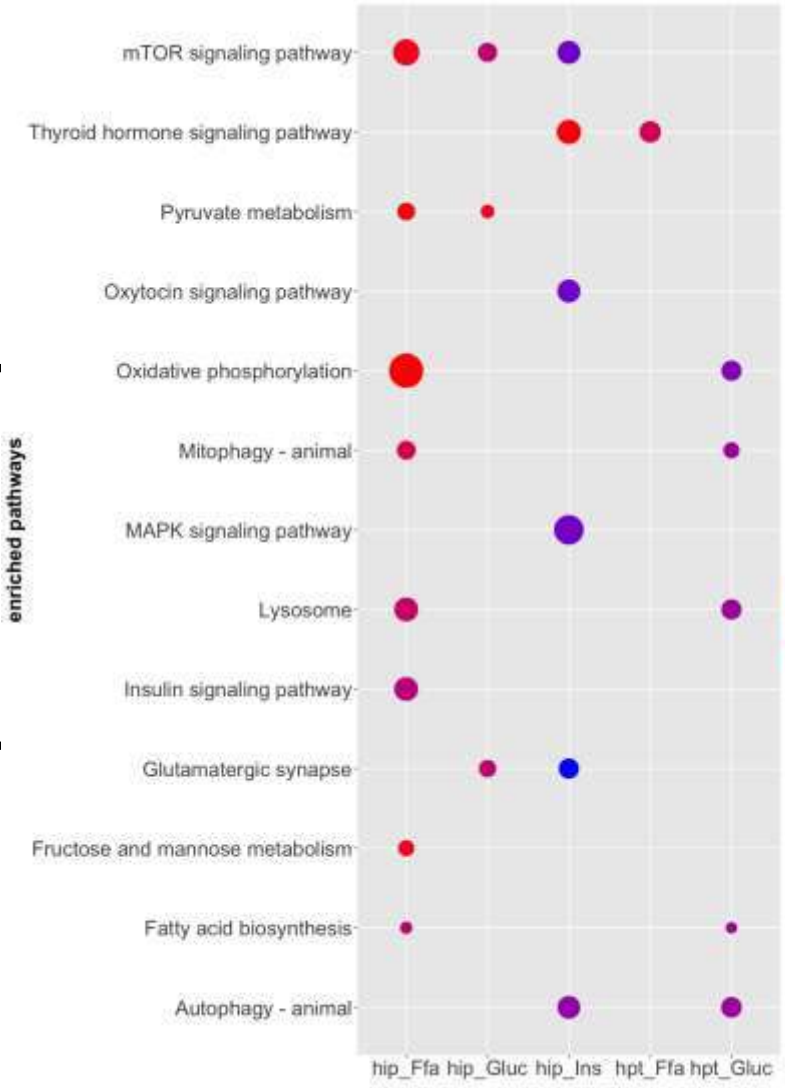
Free fatty acids

Hippo HPT









Summary

- Data preprocessing and filtering
- Identification of circadian genes
- Differential expression analysis – tissue and diet effect
- Identification differential diet effect at each time point
- Testing association of expression and peripherical data

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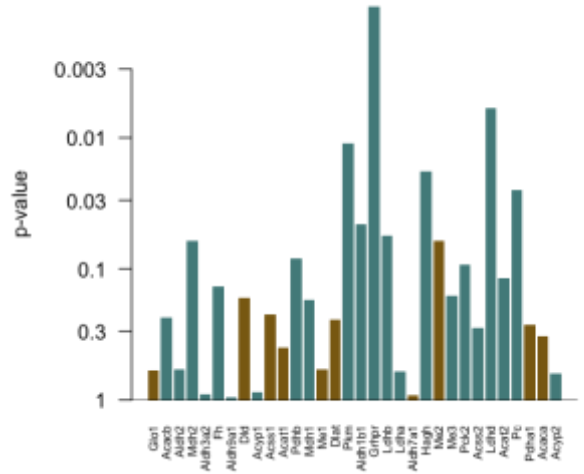
HELMHOLTZ RESEARCH FOR GRAND CHALLENGES

Pathway association with peripheral data

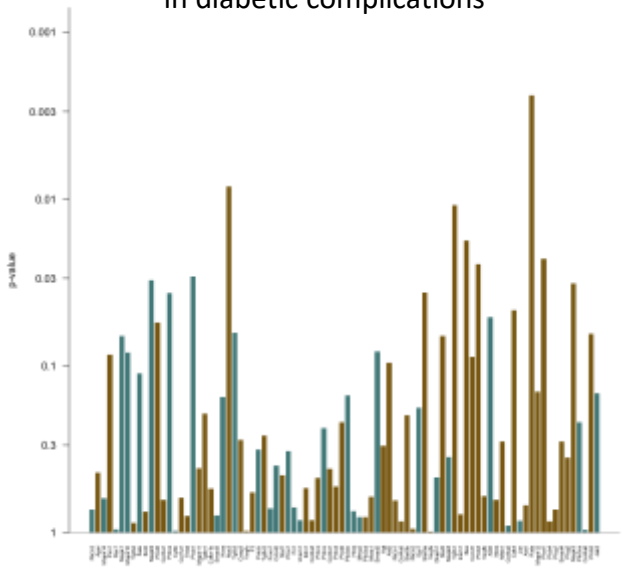
HPT

Hippo

Glucose ~ Pyruvate_metab



Glucose ~ AGE-RAGE signaling pathway in diabetic complications



Insulin ~ Insulin signaling pathway