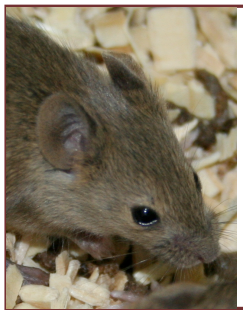

H3K4me3 in wild house mice living under different environmental conditions

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The aim of our study is to investigate whether epigenetic changes play a role in short-term adaptation to environmental conditions. We kept two populations of wild house mice (*Mus musculus domesticus*) in semi-natural enclosures for 9 months (Fig. 1). Group A received standard food whereas group B was fed an fat-enriched diet. In addition, day/night-cycle and mouse density was different between group A and B.

Fig. 1: Two groups of mice were kept in separate enclosures with ample food, water, and nesting material under standard conditions or a fat-enriched diet.

Chromatin IP and high-throughput sequencing

After 8 months, liver DNA of 8 young males from both rooms was pooled and chromatin-immunoprecipitated using an anti-H3K4me3 antibody. Sequencing on an Illumina Genome Analyzer yielded approx. 45 Mio reads per pooled sample, of which 60% were uniquely mapped with `bowtie` onto the mouse reference genome (Fig. 2).

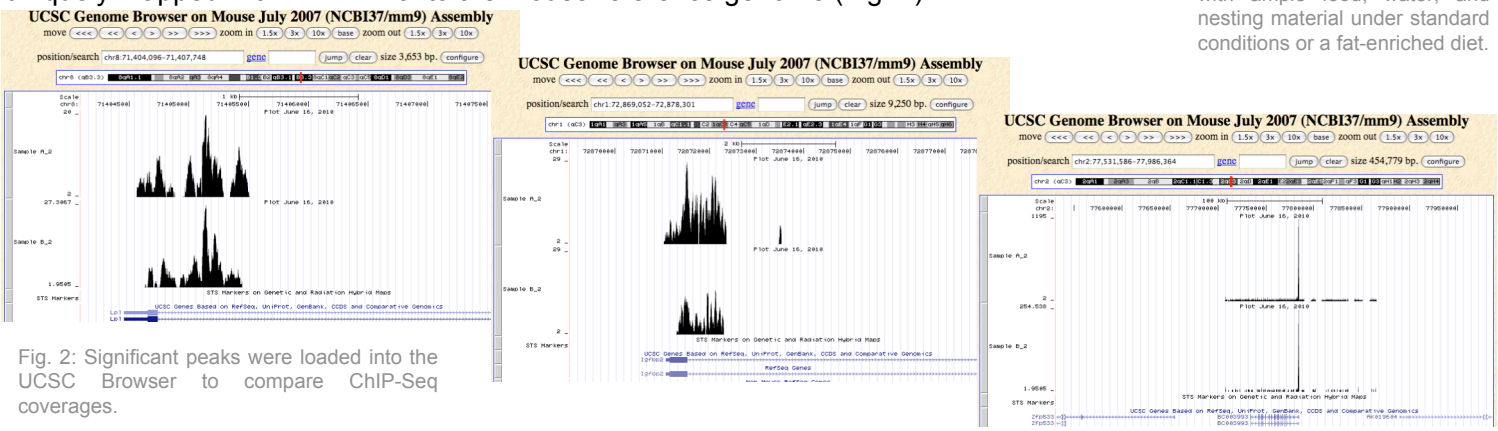


Fig. 2: Significant peaks were loaded into the UCSC Browser to compare ChIP-Seq coverages.

To search for regions with different mark densities, coverages at positions 1000 bp upstream and downstream of known transcription start sites were summed up. Marking at the TSS of gene Cwc22 is increased 5-fold in sample A. Since the background at this locus is also increased, a copy-number variation could be the cause of this high peak.

Correlation between expression and H3K4me3 marking

To compare the chromatin marks to gene expression, mouse liver RNA was quantified on an Agilent Whole Mouse Genome Oligo Microarray. Expression data were analyzed using the `R package LIMMA` (Table). Comparison of expression and H3K4me3 marks was performed using a one-modification model (Fig. 3).

SYMBOL	$\log_2$fc	AveExpr	ChIPseq A/B
Cwc22	2.52	10.07	386255/71926
Cd36	2.09	9.76	0/0
Xdh	1.84	11.33	7062/5609
XM_001475453	1.82	12.75	NA
AK045102	1.70	7.26	1.1
Fndc5	1.67	9.70	0/0
Cux2	1.60	7.23	0/0
Mogat1	1.60	7.16	0/0
XM_618937	1.58	7.21	2409/0
1810053B23Rik	1.47	7.35	2409/0000
Cbr1	1.44	12.33	12592/10522
Bmp7	1.42	7.73	0/0
Apcs	-1.59	11.75	919/1455
Ren1	-1.61	10.23	0/0

Table: Examples of differentially expressed transcripts (265 in total). Aggregate coverages from ChIP-Seq show that some expressed sites were not marked. This could be due to the uniqueness criterion of the mapping.

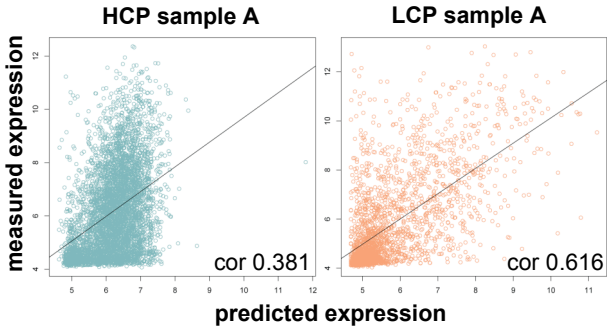
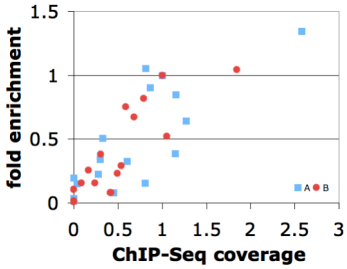


Fig. 3: Correlation between measured and predicted expression levels of promotors with high-CpG content (HCP) and low-CpG content (LCP). Predicted expression was calculated from H3K4me3 marks (Karlic *et al*, 2010).



Quantitative PCR of H3K4me3 ChIP-DNA was performed to check regions that are not easily mappable and to validate the sequencing data (Fig. 4).

Fig. 4: Validation of ChIP-seq results by qPCR at 21 loci. Data from both methods were normalized on the locus Gapdh.

Future Work

Comparison of wild mice and reference mice data

Analysis of epigenetic heritability

References

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