Allele specific gene expression in F1 mice from a reciprocal cross

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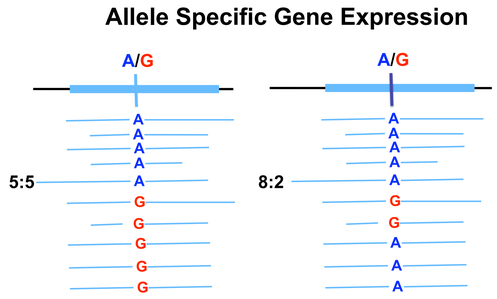
Introduction

Allele specific gene expression (ASE) occurs when one of the two alleles is preferentially transcribed in a heterozygous locus. Allele specificity may be influenced by local genetic variation or by parent-of-origin imprinting effects.

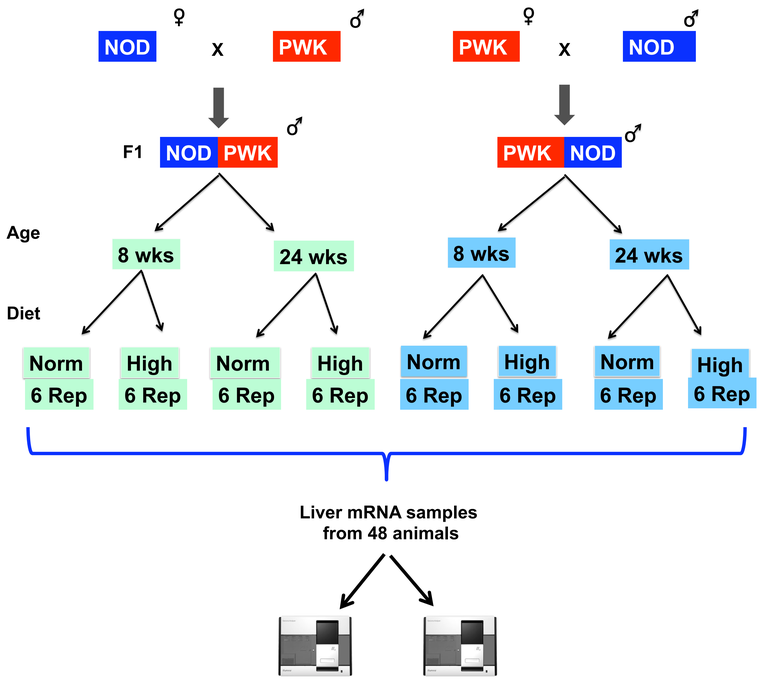
We crossed the divergent inbred mouse strains NOD/LtJ and PWK/PhJ in both directions to obtain reciprocal F1 progeny. We obtained RNA-Seq data on liver RNA samples using Illumina high-throughput sequencing using an experimental design with biological and technical replication.

The same experimental design was repeated twice with two diets. In one experiment, mice received a standard chow diet or vitamin D rich diet and in the second experiment, the mice received control and methionine deprivation diets. Thus we are able to examine the influence of diet, age, parent-of-origin and genotype on ASE.

Our results demonstrate that ASE is prevalent across the genome and the primary driver of ASE is local genotype. A few specific instances of parent-of-origin effect were observed and they were all well known imprinted loci.



Experimental Design

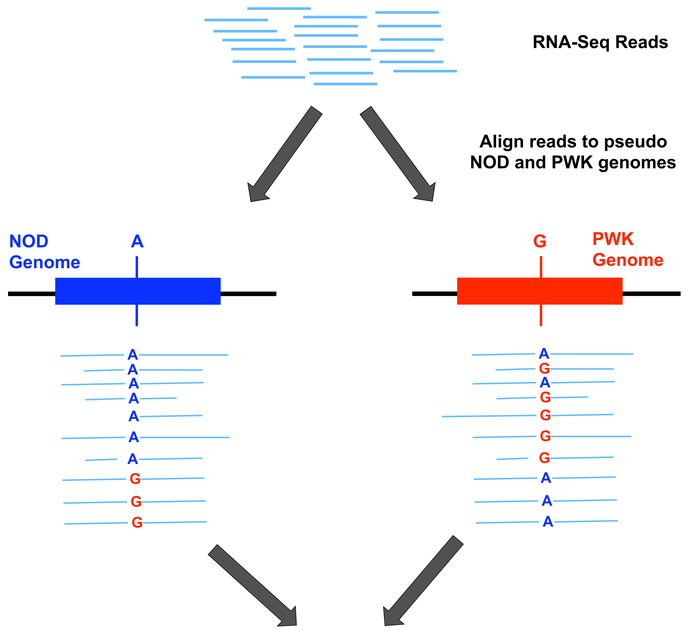


Liver mRNA samples from 48 animals

Illumina GA Iix: Single end reads of length 68bp

Vitamin D Diet: Chow vs Vitamin D rich diet
Methionine Diet: Methionine deficient and sufficient diet

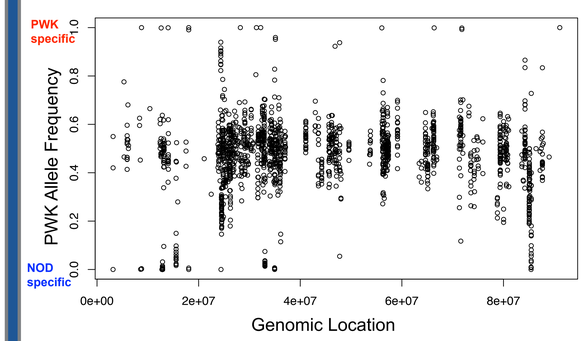
Quantifying Allele Specific Expression Using RNA-Seq

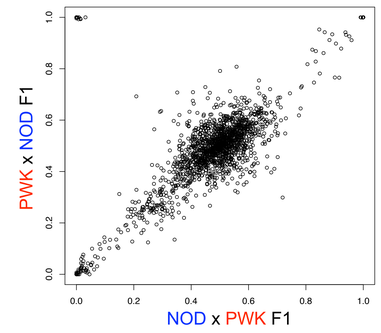


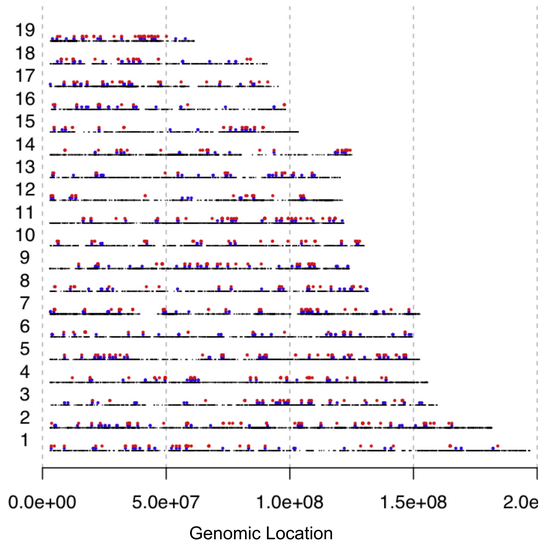
Count average number of NOD and PWK alleles, at known Sanger SNP locations

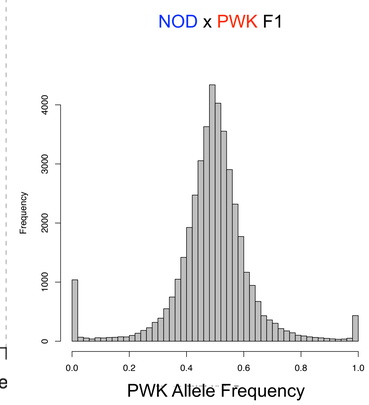
$$\text{PWK Allele Frequency} = \frac{\text{Number of reads with PWK alleles}}{\text{Total number of matched reads}}$$

Allele Specific Gene Expression Is Prevalent









Conclusions

- Allele specific expression is prevalent across the genome.
- The majority of the allele specific expression is influenced by the local genotype
- Only a few instances of parent of origin effect on allele specific expression were found.
  - Snrprn, Commd1, Dtnb, Meg3, Igf2r, and Impact

Current/Future Work

- Allele specific expression in methionine diet
- Effect of diet and age on allele specific expression
- Statistical method that utilizes the experimental design to find significant allele specific expression

Acknowledgements

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