Nuclear receptor variation in mice

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Abstract

Nuclear receptors (NRs) are a large family of ligand-activated transcription factors, that bind directly to DNA to regulate the expression of target genes. They regulate critical functions in cell control, inflammation, fibrosis and tumor formation and are involved in metabolism, development and reproduction. Nuclear receptors act on the metabolism and signalling of cells by changing the expression of target genes. Thus, they are associated with numerous pathologies such as cancer, cardiovascular disease, inflammation, and reproductive abnormalities. This paper will investigate the knockout phenotypes and genetic variation of mouse NRs. We will first create an assembly of all known mouse SNPs in the vicinity of mouse NR genes (+-1Mbp up-or downstream). In a second step, phenotype information for genetic knockouts and genetic variation data will be included. Knockout phenotypes are available from the MGI database, while the Mouse Phenome Database provides SNPs from various mouse strains, which can be correlated to extreme phenotypes, measured in these mouse strains. The goal of this analysis is to find NR SNPs in mice that influence changes in biological parameters such as body weight, body fat and other phenotypic traits. Furthermore, we will couple these findings to phenotypes observed in mice with a targeted or spontaneous mutation of the nuclear receptor and thus provide additional indication for a putative functionality of the investigated SNPs.

Keywords

Nuclear receptors — SNPs — Gene variation

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Introduction

IntroIntroIntro

1. Methods

1.1 Nuclear receptors

49 nuclear receptors

1.2 human genome

tbd

2. Tools

2.1 MGI

Mouse Genome Informatics[1] is a database for the laboratory mouse, which makes information about integrated genetics and associated phenotypes and alleles available. The 49 nuclear receptors were searched in the MGI database to achieve an association between these nuclear receptors and phenotypes which arise from alternation in the scope of their genes.

2.2 MPD

Mouse Phenome Database[2] [1].

[1] `http://www.informatics.jax.org/`, March 9, 2015

[2] `http://phenome.jax.org/`, March 9, 2015

3. Database

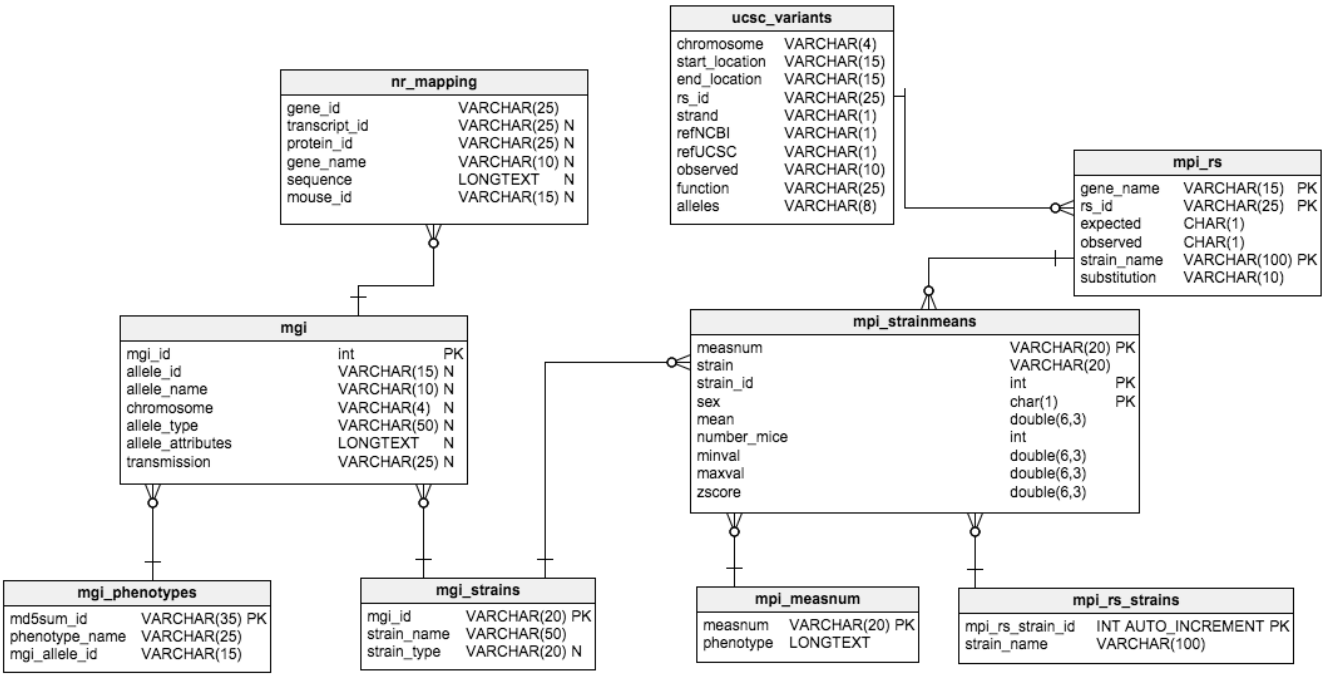

Figure 1. MGI phenotypes.
Mouse Genome Informatics phenotype distribution over the nuclear receptors.

4. Results

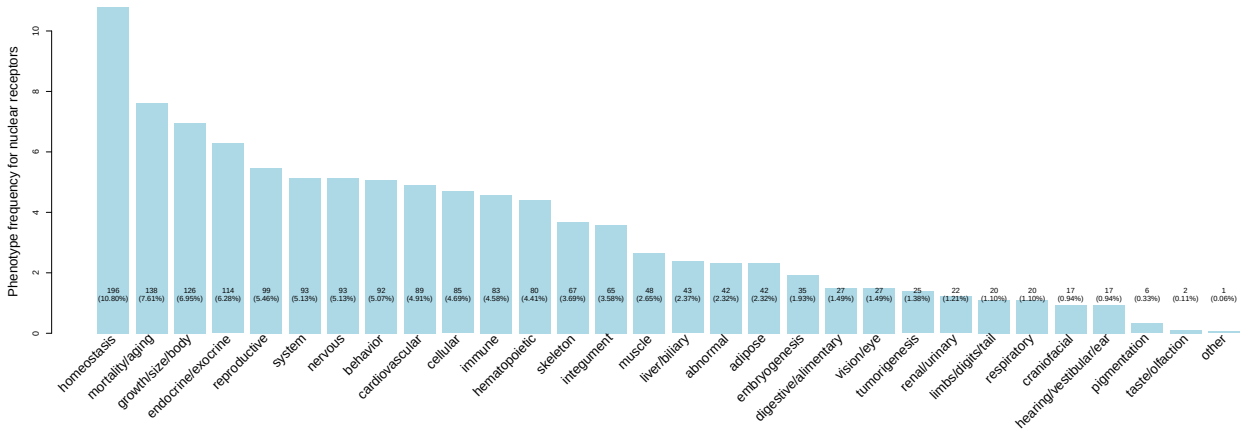

Figure 2. MGI phenotypes.
Mouse Genome Informatics phenotype distribution over the nuclear receptors.

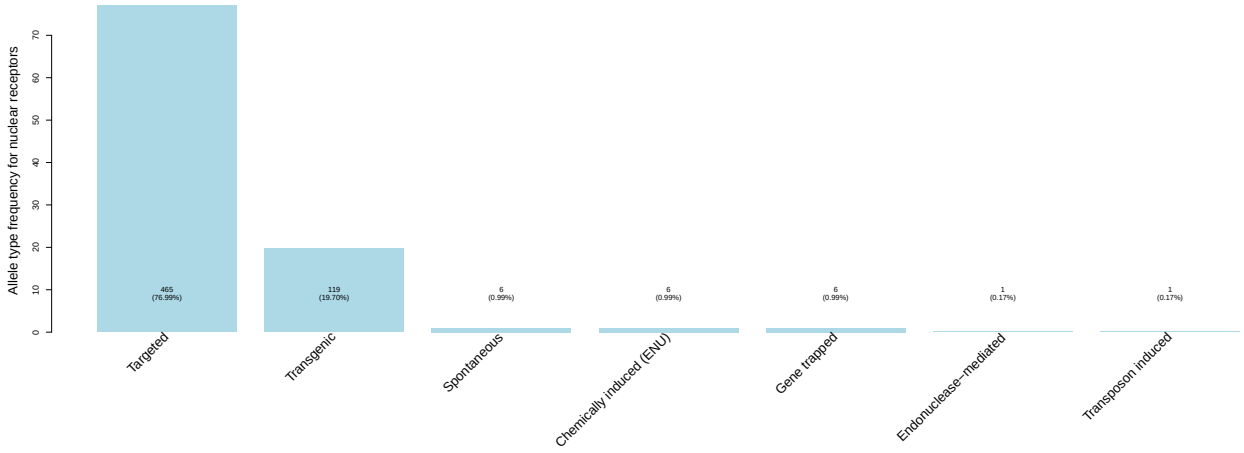

Figure 3. MGI allele types.
Mouse Genome Informatics allele type distribution over the nuclear receptors.

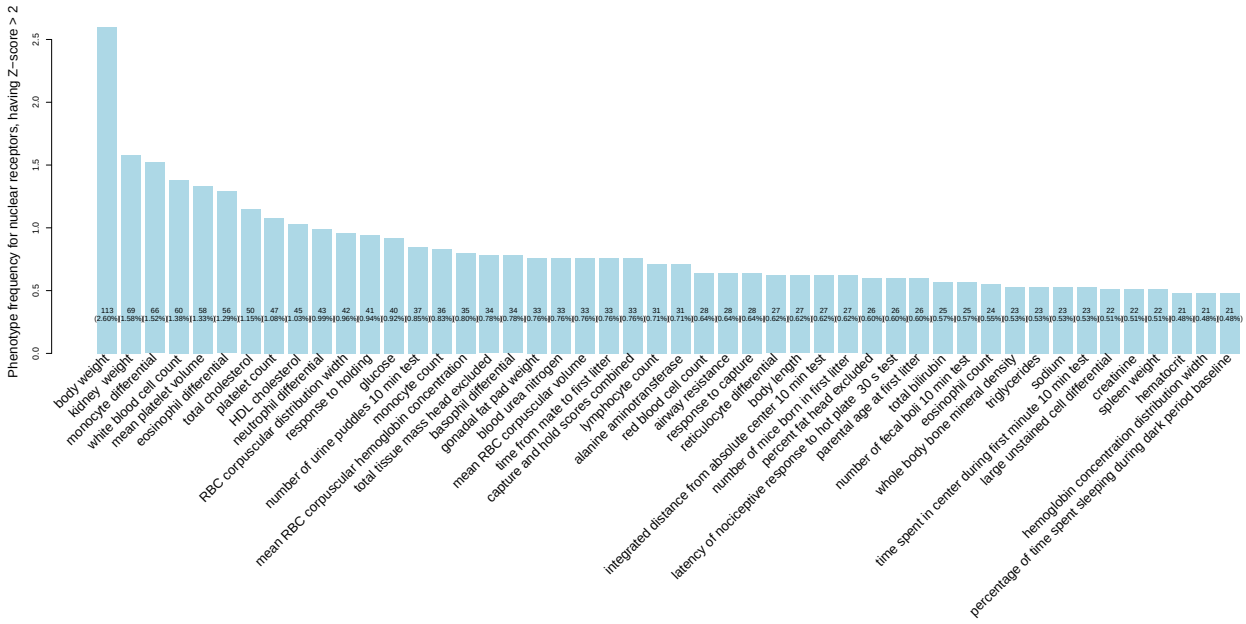

Figure 4. MPD phenotypes, having Z-score > 2.
Mouse Phenotype Database phenotype distribution over the nuclear receptors, having Z-score > 2

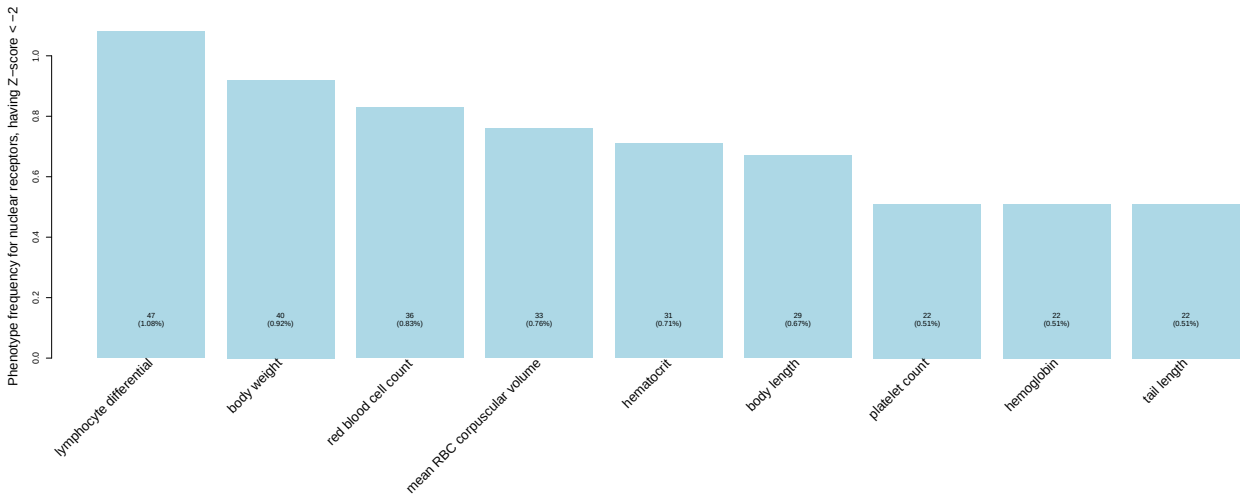

Figure 5. MPD phenotypes, having Z-score $<$ -2.
Mouse Phenotype Database phenotype distribution over the nuclear receptors, having Z-score $<$ -2

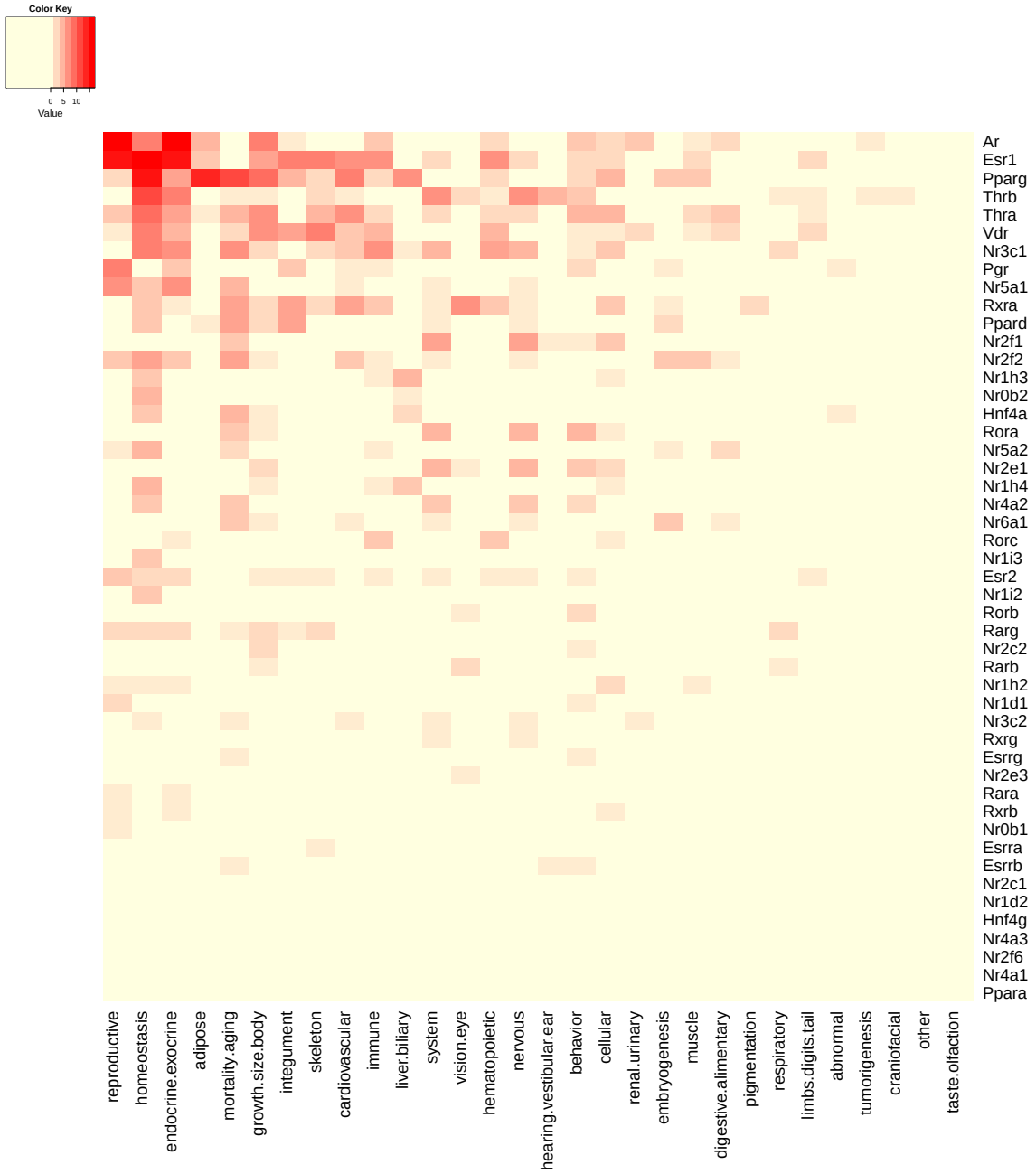

Figure 6. MGI phenotype - nuclear receptor associations.
Mouse Genome Informatics phenotype occurrence frequency among the nuclear receptors.

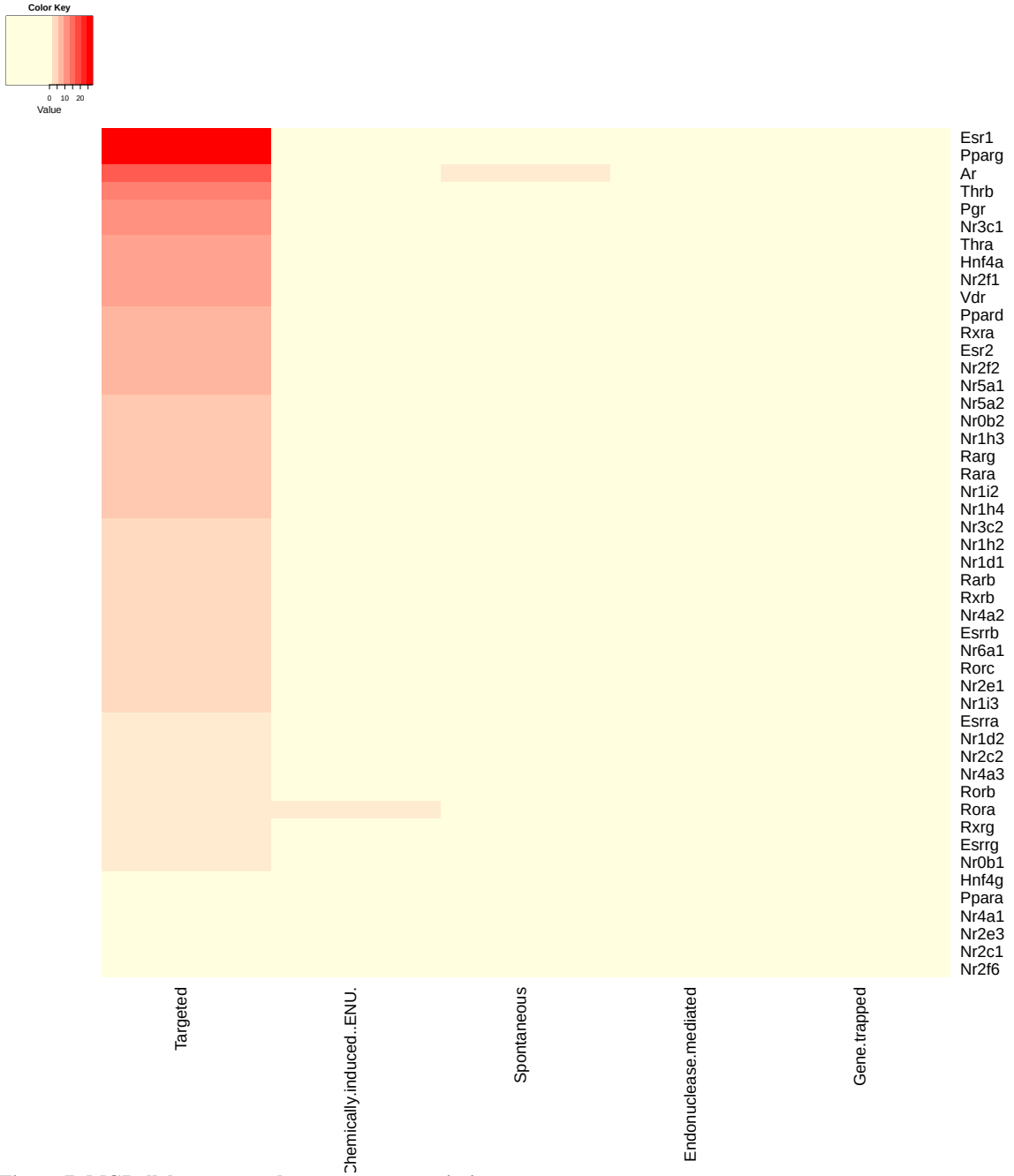

Figure 7. MGI allele type - nuclear receptor associations.
Mouse Genome Informatics allele type occurrence frequency among the nuclear receptors.

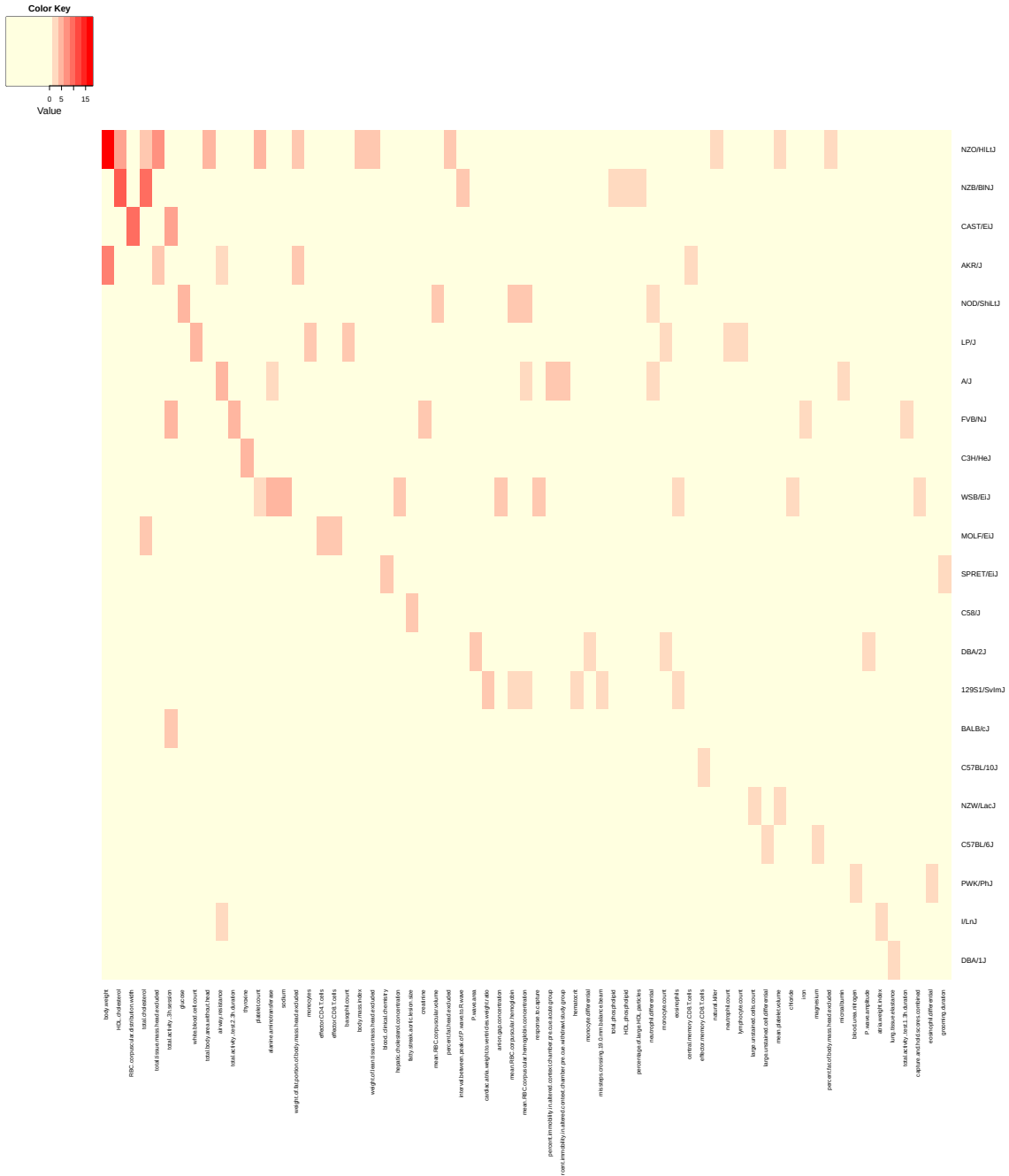

Figure 8. MPD phenotype - strain associations, having Z-score $>$ 2.
Mouse Phenome Database phenotype occurrence frequency among the strains associated with the nuclear receptors, having Z-score $>$ 2

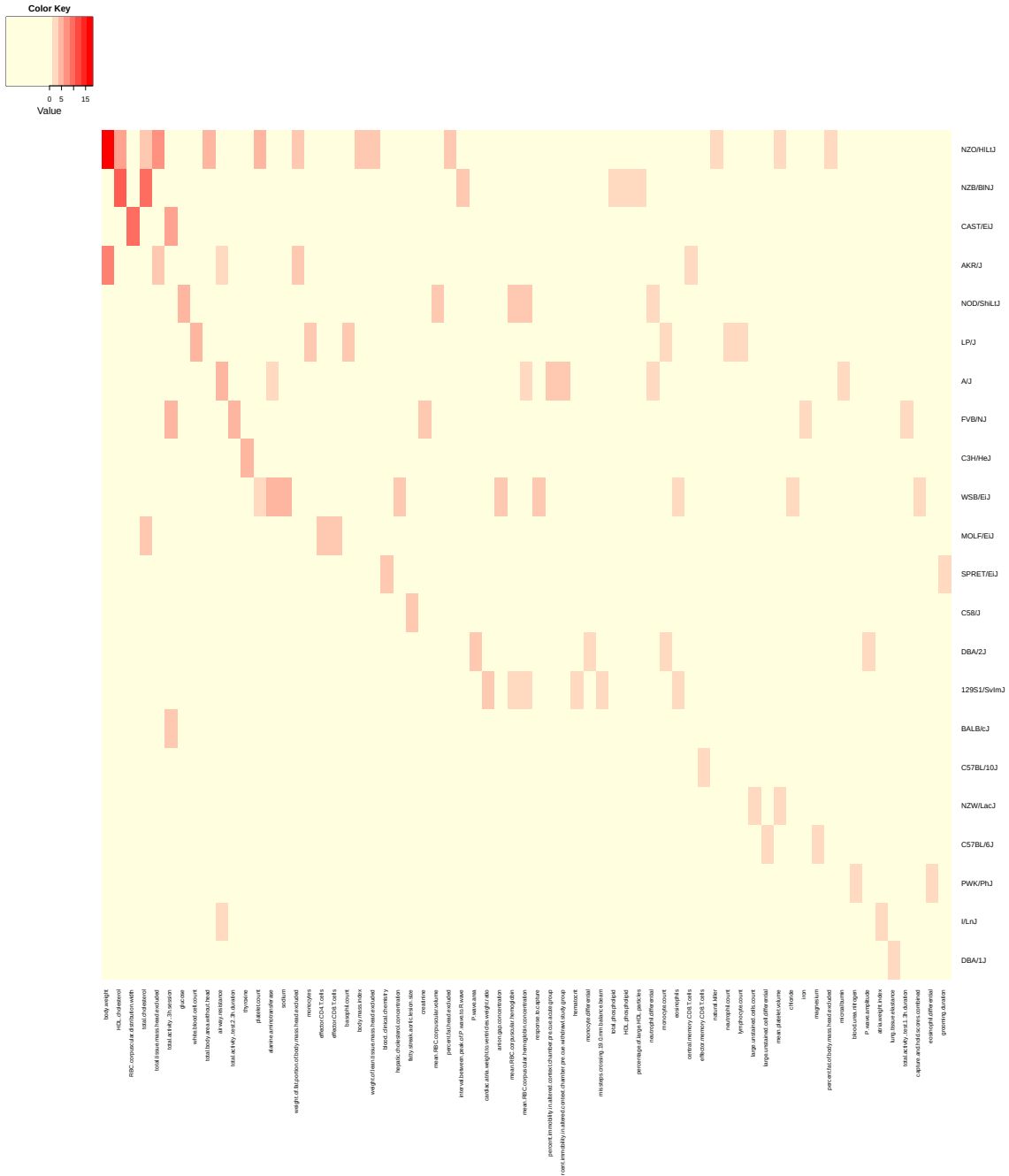

Figure 9. MPD phenotype - strain associations, having Z-score $<$ -2.
Mouse Phenome Database phenotype occurrence frequency among the strains associated with the nuclear receptors, having Z-score $<$ -2

5. Discussion and Outlook

Blabla

6. Acknowledgments

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References

[1] Terry P. Maddatu, Stephen C. Grubb, Carol J. Bult, and Molly A. Bogue. Mouse phenome database (mpd). 2011.