

# Finding differential gene expression responsible for susceptibility to obesity and diabetes between two mouse strains

Timo Vehviläinen<sup>1</sup>, Yoichi Yamada<sup>2</sup>

<sup>1</sup>Department of Electrical and Computer Engineering, Faculty of Science and Engineering, Kanazawa University, Kanazawa, 920-1192, Japan

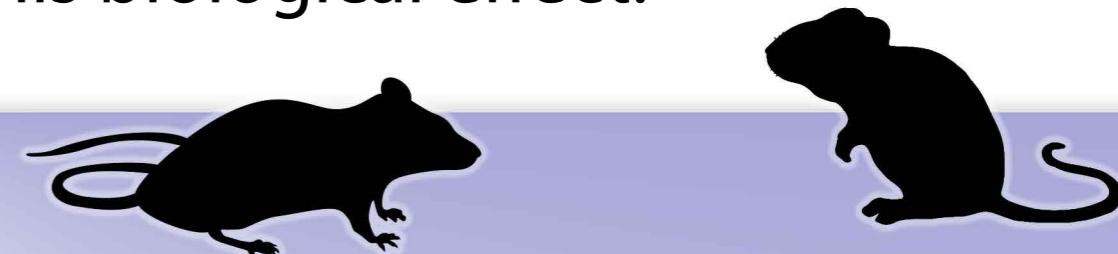
<sup>2</sup>Faculty of Electrical and Computer Engineering, Institute of Science and Engineering, Kanazawa University, Kanazawa, 920-1192, Japan

## INTRODUCTION

The Japanese Fancy mouse strain 1 (JF1, inbred from *Mus musculus molossinus*) has been found to be more susceptible to obesity and diabetes than the common C57BL/6 strain (B6, inbred from *Mus musculus domesticus*) when fed a high fat diet. Differential gene expression analysis is a process which uses differences in count data from two RNA-sequencing datasets to determine relative up- and downregulation of specific genes between samples.

The goal of this study was to find relevant differences in substrain-specific gene expression using Next Generation RNA Sequencing tools on liver samples from the JF1 and B6 strains to explain this biological effect.

## METHODS



The genomes for JF1 and B6 were constructed from the C57B6NJ (B6NJ) reference genome, downloaded from the UCSC database. Using information about the genomic differences to this reference in both B6 (downloaded from the Sanger Mouse Genome Project database) and JF1 (provided by NIG Mouse Genome Database), we were able to modify the B6NJ reference to obtain the substrain genomes. This was done using a combination of a custom perl-script and g2gtools.

Two sets of RNA-sequencing reads from both substrains were mapped to the obtained substrain-references using Bowtie 2, after which gene expression counts were generated with HTSeq. These counts were analyzed for differential expression with DESeq. The expression data was analyzed using the online GOrilla enrichment tool.

## RESULTS

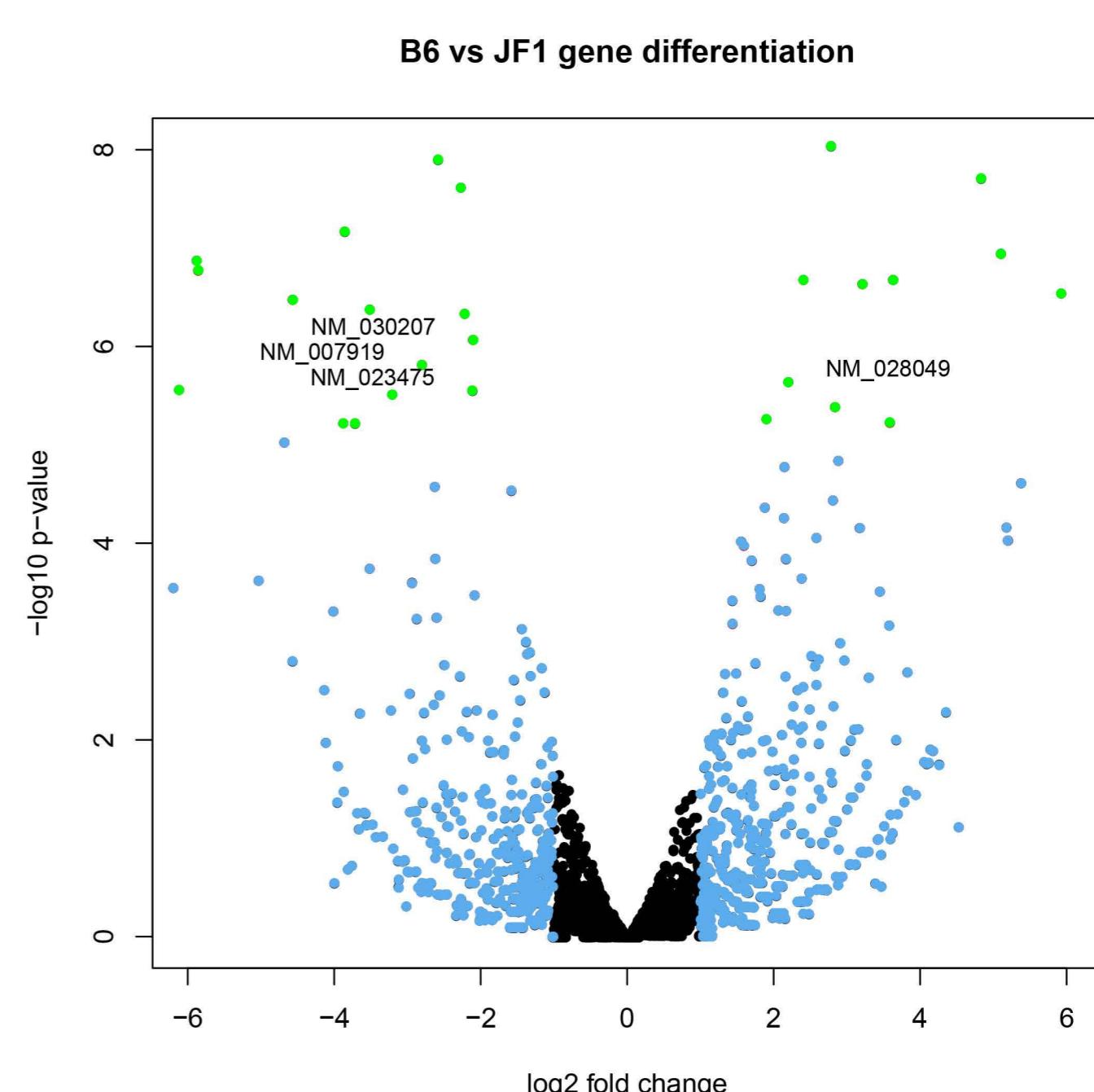
Going into enrichment analysis, we had a background set of 35,972 genes and a target set of 90 genes rated to be differentially expressed with a FDR less than 0.01 as calculated by DESeq. Differentiation analysis results are shown in Plot 1.

GOrilla uniquely recognized 21,326 and 79 genes, respectively. 13 genes were found to be differentially expressed with a p-value of less than 0.001, out of which nine had ontology relevant for our research goals. These are depicted in Table 1.

Out of these, three are associated with metabolic processes (Cyp2a4, Cyp2c37, Cyp2c39), five are associated with water homeostasis (Nlrp6, Selp, Prlr, Cela2a, Tmem79), and one is associated with both (Scd1).

Gene	Chromosome	Fold	Function	Ontology
Nlrp6	7	3.2		
Selp	1	-2.2		
Prlr	15	2.1		
Cela2a	4	-2.8	Body fluid level regulation	Water homeostasis
Tmem79	3	-5.0	Water homeostasis	
Scd1	19	-2.9	Transepidermal water loss, Unsaturated fatty acids	
Cyp2c37	19	-4.2		
Cyp2c39	19	4.5	Epoxigenase P450 pathway, Unsaturated fatty acids	Metabolic processes
Cyp2a4	7	3.6		

**Table 1** Table of the discovered nine ontologically relevant and differentially expressed genes (with  $p < 0.001$ ), along with their chromosome, fold change ( $\log_2$ ), function and gene ontology. The other four (not shown here) were associated with notch signaling pathways.



**Plot 1** A volcano plot depicting significantly differentially expressed genes. Genes with fold change  $> 1$  are colored with blue. The subset of those with  $p$ -value  $< 0.001$  are colored green, with a few examples named.

## CONCLUSIONS

We found that the majority of significantly differentially expressed genes between B6 and JF1 are related to metabolic and water homeostatic regulation, which concurs existing literature. In addition to diabetes and obesity both being primarily metabolic disorders, obesity is linked to lower body water percentages. Stearoyl-Coenzyme desaturase 1 (Scd1) has also been linked to insulin hypersensitivity, confirming our findings. These results could be further cross-examined with metabolic and other clinical measurements from the two mouse strains.