Tenzin Nyima[1]*, Michael Müller[2], Guido Hooiveld[2], Marco Scotti[1], Melissa J Morine[1]
[1]The Microsoft Research – University of Trento Centre for Computational and Systems Biology, Rovereto, Italy
[2]Netherlands Nutrigenomics Centre, Top Institute Food and Nutrition, Wageningen, The Netherlands
*nyima@cosbi.eu

Gene expression in mouse intestine is modulated by dietary fat intake

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Introduction

High caloric diet, in conjunction with lower levels of physical activity, promotes obesity. Obesity has been linked with numerous chronic diseases such as diabetes, cardiovascular diseases and cancer. Many studies are available regarding the relation between dietary fat and the aetiology of obesity, but most focus mainly on tissues like liver, muscle and white adipose. Considering the indispensable role of small intestine in the absorption and digestion of dietary lipids, our study focuses specifically on the dose-dependent effects of dietary fat concentrations on differential gene expression in the proximal, middle and distal sections of the small intestine in C57Bl/6J mice.

Objectives

1. To assess dose-dependent effects of dietary fat consumption ranging from 10% to 45% of total energy intake on gene expression in the proximal, middle and distal sections of the murine small intestine.
2. Identification of biological pathways enriched with differentially expressed genes related to increased fat consumption, by considering both up-regulated as well as down-regulated genes.

Materials and Methods

Microarrays were hybridized with intestinal RNA (proximal, middle or distal section) following a 4-week diet consisting of 10%, 20%, 30% or 45% kcal intake from fat; ten biological replicates were assigned to each diet (total n=120).
The microarray platform used for this study is Affymetrix NuGO mouse array (nugomm1a520177) containing 16,269 probesets. Microarray data were analyzed using R, along with libraries from Bioconductor. Careful quality assessment and filtering resulted in a final data set of 13,110 probesets. The limma library was used to identify the differentially expressed genes ($p < 0.05$; adjusted for multiple testing) as a function of dietary fat % in each segment of the small intestine. Functional classification of the differentially expressed genes was assessed using the DAVID functional enrichment tool. (http://david.abcc.ncifcrf.gov).

Results

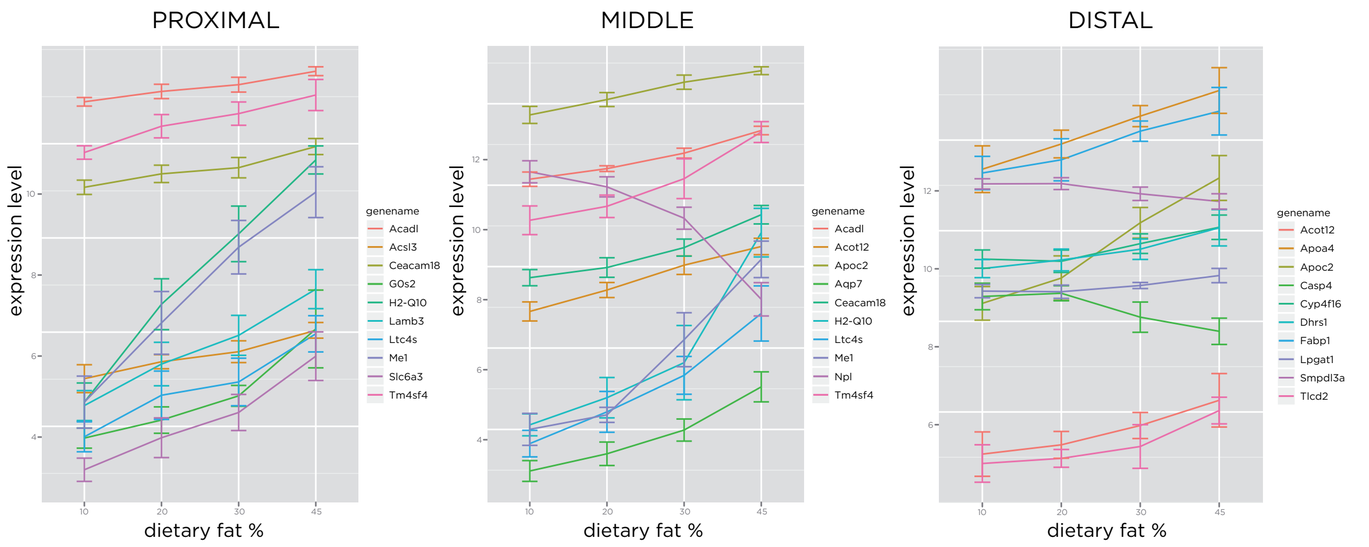

Figure 1. Expression levels of the top ten differentially regulated genes in each section of the small intestine.

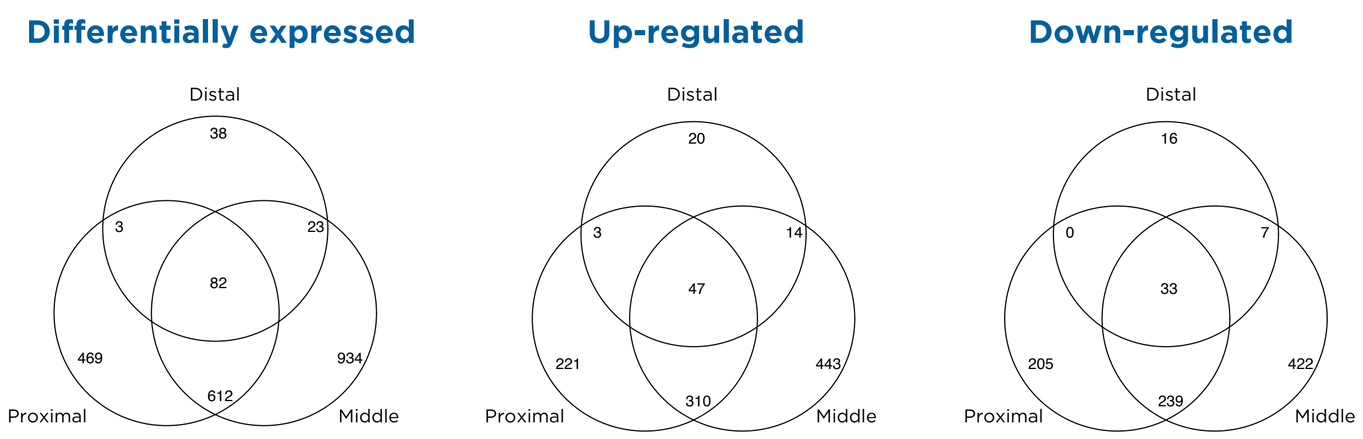

Figure 2. Total number of differentially expressed genes in each section is shown using Venn diagrams, followed by unique plots for the up- and down-regulated genes.

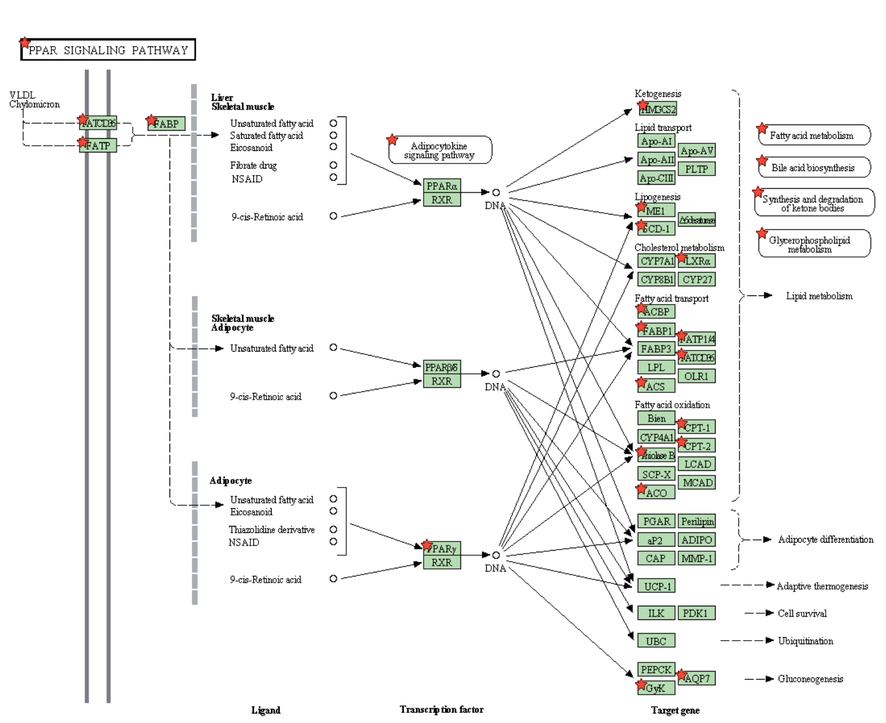

Figure 3. The PPAR signaling pathway, illustrating significantly up-regulated genes in the proximal section of the intestine (shown with red stars). Image obtained from the DAVID functional enrichment tool.

Conclusions

Microarray analysis identified genes that responded in a dose-dependent manner to dietary fat intake in proximal, middle and distal sections of the small intestine (Figure 1). Moreover, intestinal transcriptomic response to dietary fat intake is unique in each section (Figure 2). The number of differentially expressed genes were higher in the middle and proximal sections of the intestine, with respect to the distal section. There were considerable differences among the up- and the down-regulated genes with few genes commonly regulated by fat intake in all the sections.
Functional enrichment analysis of the differentially expressed genes highlighted the PPAR signaling pathway as significantly up-regulated by fat intake in all sections of the small intestine (results from proximal section shown in Figure 3).