

## **SUPPLEMENTAL MATERIALS AND METHODS**

### **Gene cluster visualization**

Mapping of the direction of gene regulation on the network was based on the direction of the regulation of the genes belonging to each of the clusters. If all regulated genes were regulated in one direction, the same direction was assigned to the gene cluster. However, if genes in the same cluster were regulated in opposite directions, the cluster was marked as “regulated in both directions”. Clusters containing no genes differentially expressed in a specific model were marked as “non-regulated”. To each type of cluster regulation, we assigned a colour: red and green for up- and down-regulation respectively, grey – for regulation in both directions and white with black contour – for lack of regulation.

### **Preprocessing animal datasets**

Samples profiled on Affymetrix Mouse Genome 430 2.0 arrays were preprocessed by using frozen Robust Multi-array Analysis (fRMA). This procedure normalizes each of the samples to a large external cohort of samples profiled on the same arrays. Such approach leads to the same intensity range across all samples normalized with this procedure, thus removing some of the technical variation across different datasets. In order to perform the fRMA procedure, we used “frma” package in R.

To combine all mouse datasets we used Distance-Weighted Discrimination (DWD) method, a procedure that removes technical variation across batches (datasets). Since DWD requires pair-wise combination of datasets, we first combined datasets for each platform separately, and only then combined the obtained groups into a large collection, starting with larger groups. In order to perform the DWD procedure, we used a MatLab package (URL: <http://www.unc.edu/depts/stat-or/miscellaneous/marron/Matlab7Software/BatchAdjust/>).

### **Network analysis**

Networks were constructed by using Reactome FI plugin in Cytoscape software, a plugin designed to examine network patterns, biological processes and pathways related to gene lists of interest. More specifically, we used “Gene Set/Mutation Analysis” option, without the linker genes. The networks were then analysed for presence of significant gene clusters (also termed “clusters” or “modules”), by using the “Cluster FI Network” option. The resulted clusters were examined for pathway enrichment and Gene Ontology, by using “Analyze Module Functions”: “Pathway Enrichment” and “GO Cell Component”, “GO Molecular Function”, and “GO Biological Process”, respectively.

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