The Dynamic Impact Approach as a web-based platform for analysis of time-course or multiple treatments omics datasets
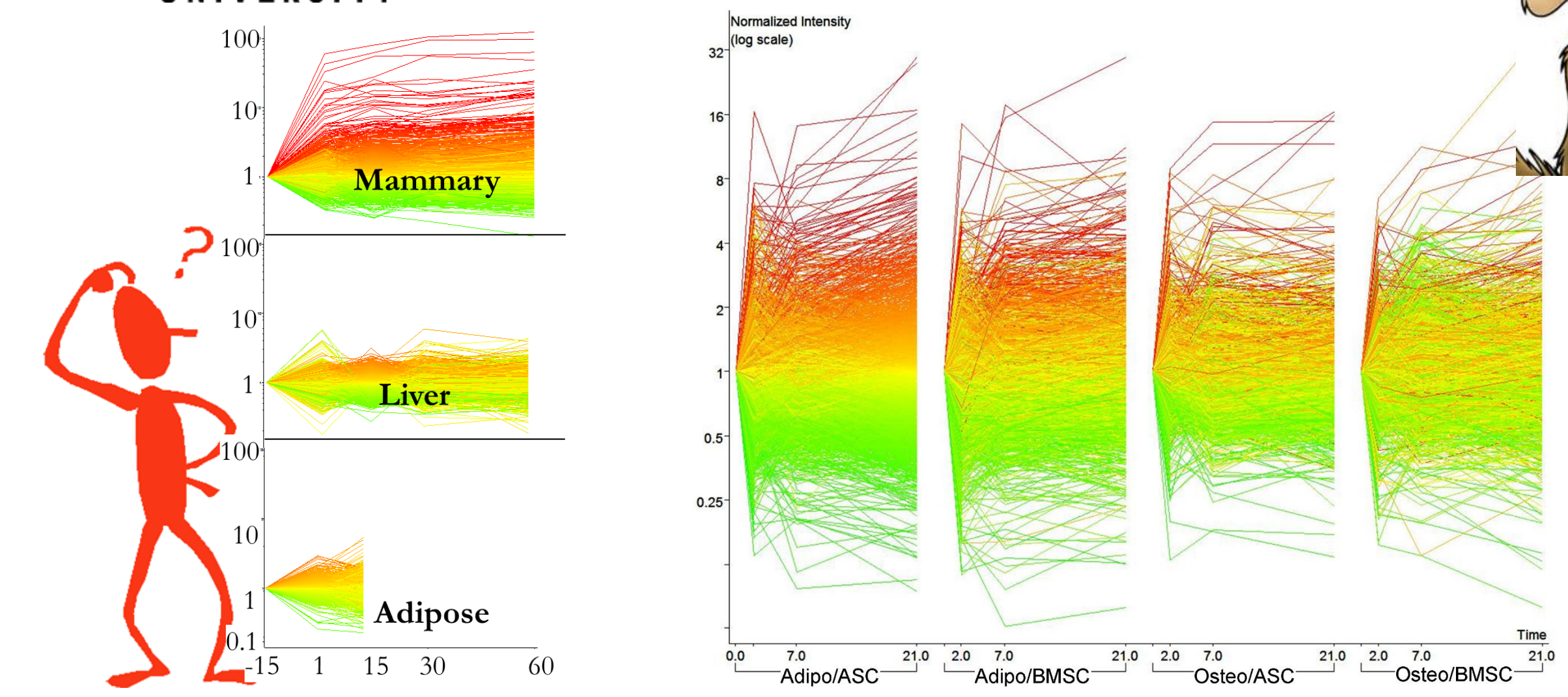
Massimo Bionaz and Austin Nguyen

Department of Animal and Rangeland Sciences, Oregon State University, Corvallis, OR, USA

Time-course experiments
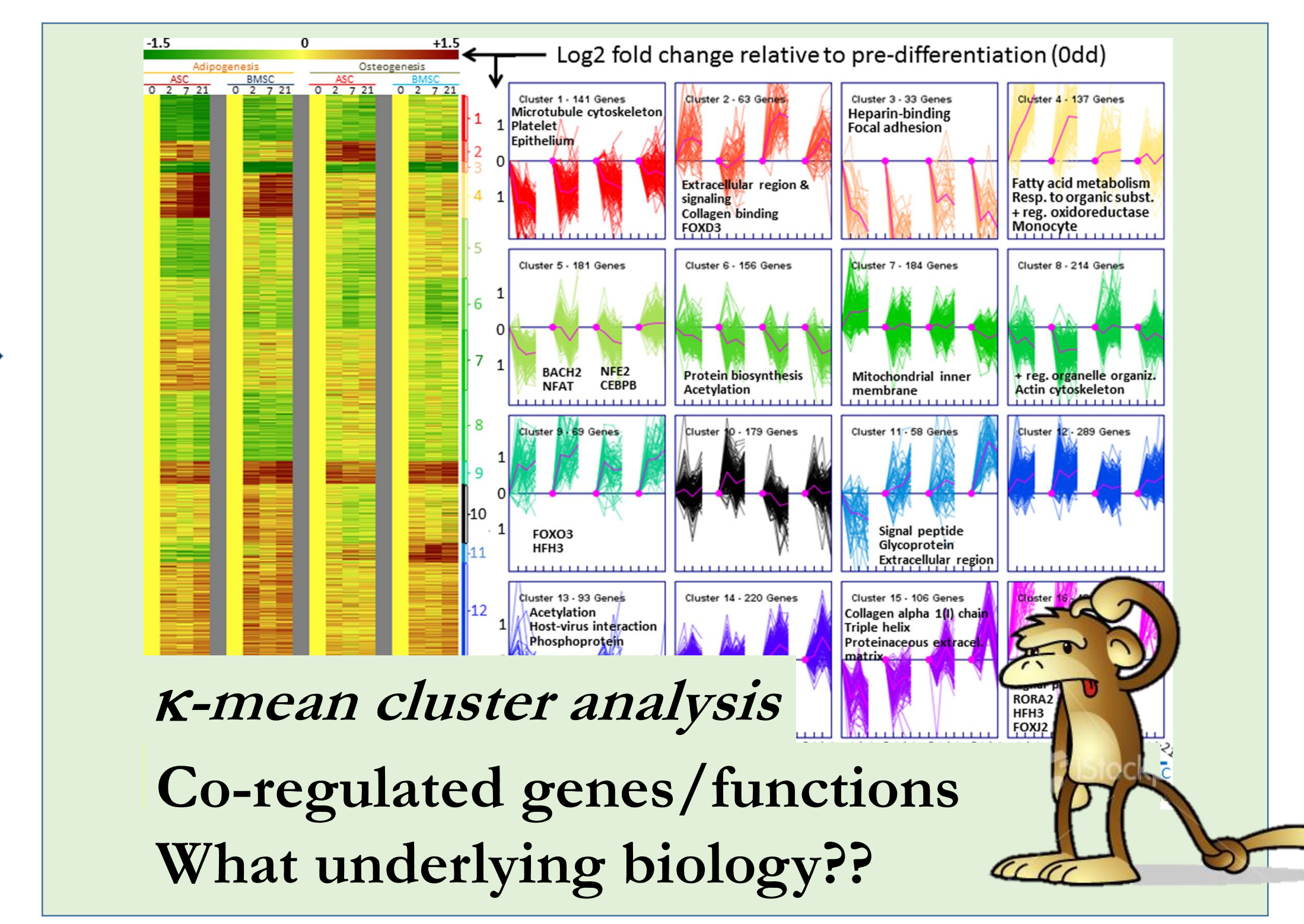
+ *multiple tissues* + *multiple treatments*

How to extrapolate the biological meaning?
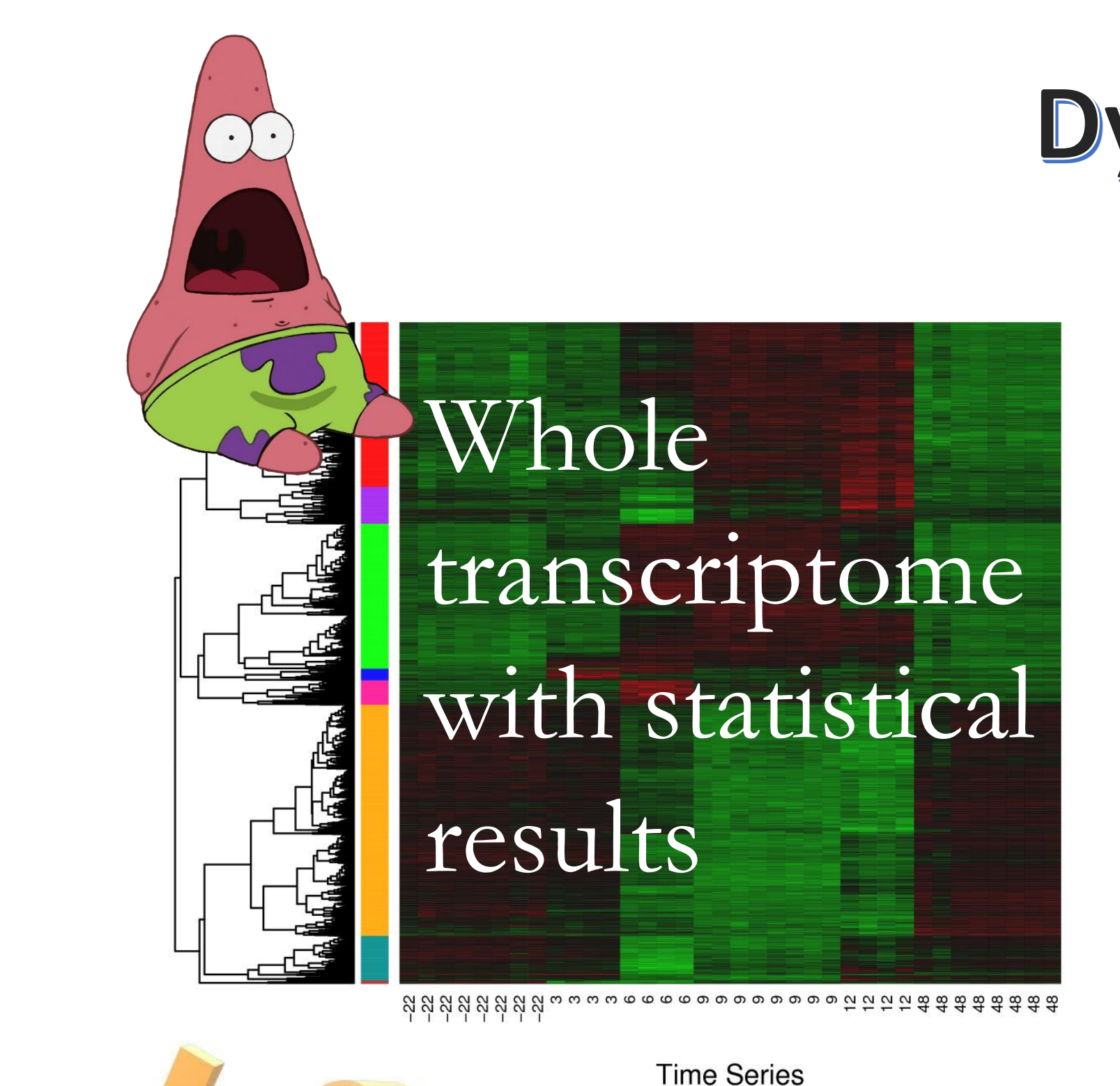
Enrichment/ overrepresented approaches?

OK!

No!

Systems biology / overall view of biological adaptation

κ-mean cluster analysis
Co-regulated genes/functions
What underlying biology??

Solution?

Dynamic Impact Approach (DIA)

Whole transcriptome with statistical results

Specific Impact = [% Differentially Expressed Genes (DEG)] ×[mean $\log_2$ expression ratio]×[mean $-\log_{10}$ p-value]

Impact = Specific Impact of DEG with a <u>positive</u> effect on the biological term + Specific Impact of DEG with a <u>negative</u> effect on the biological term.
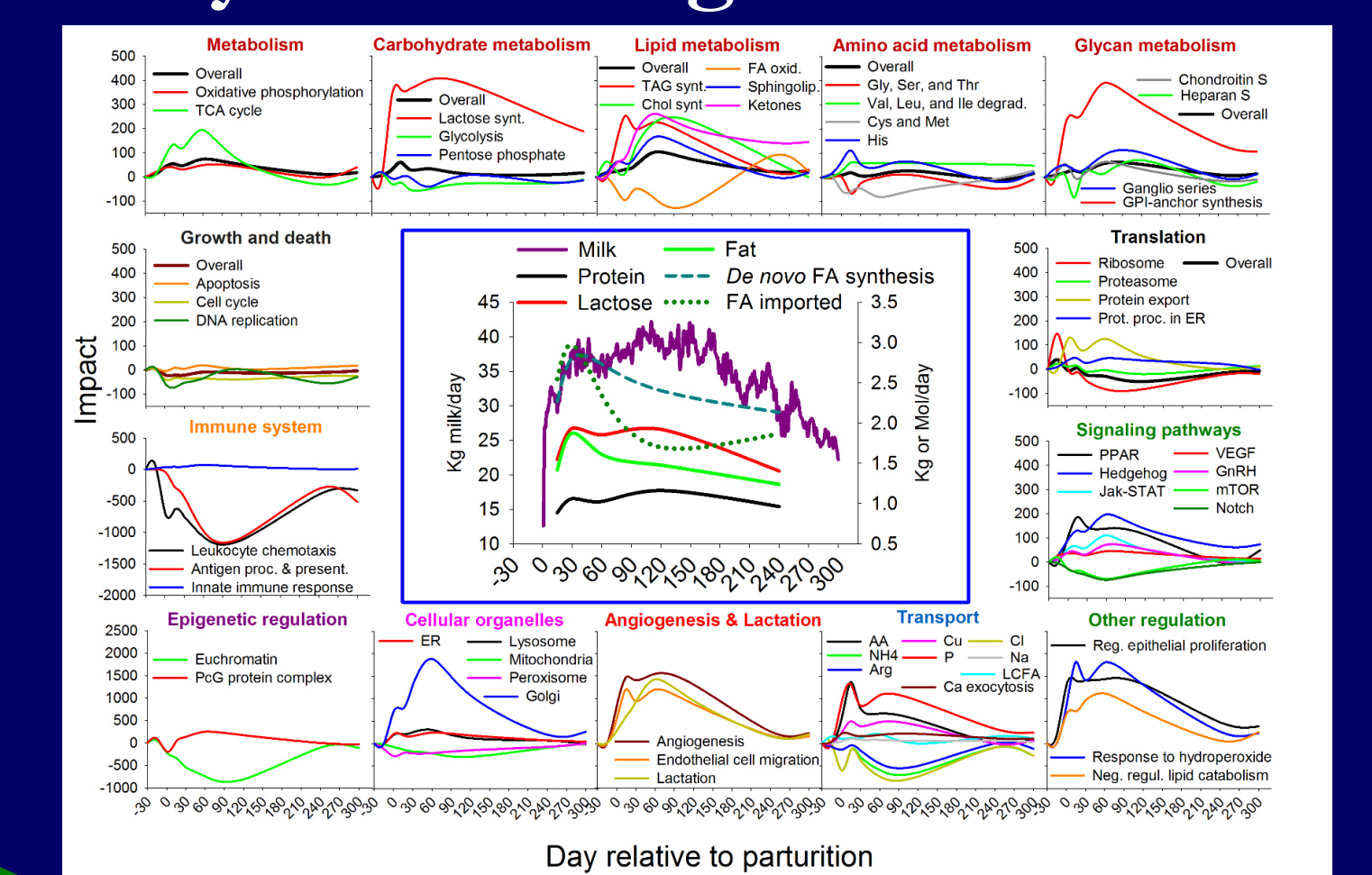
Direction of the Impact = Impact of DEG with a <u>positive</u> effect on the biological term − Impact of DEG with a <u>negative</u> effect on the biological term
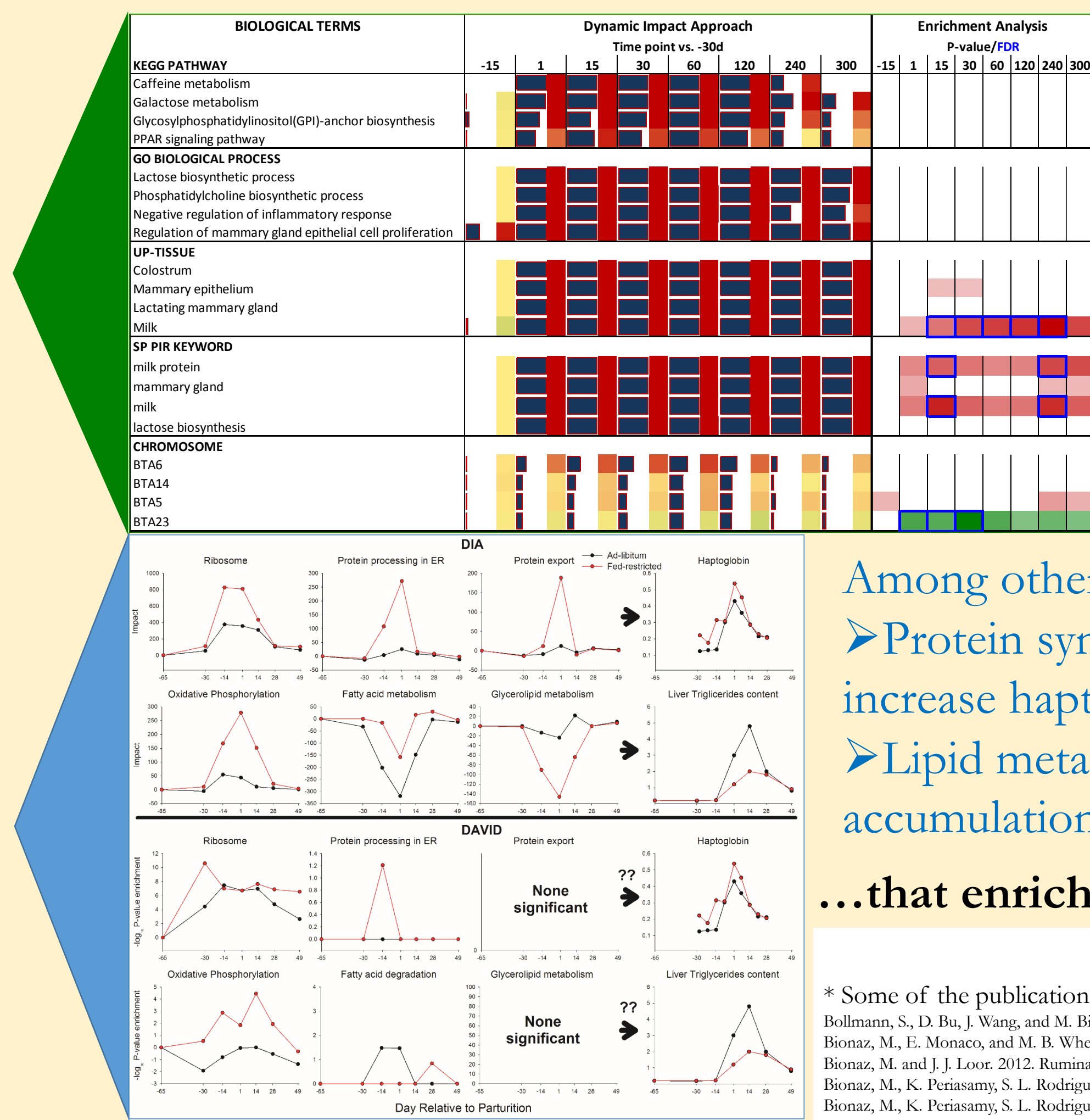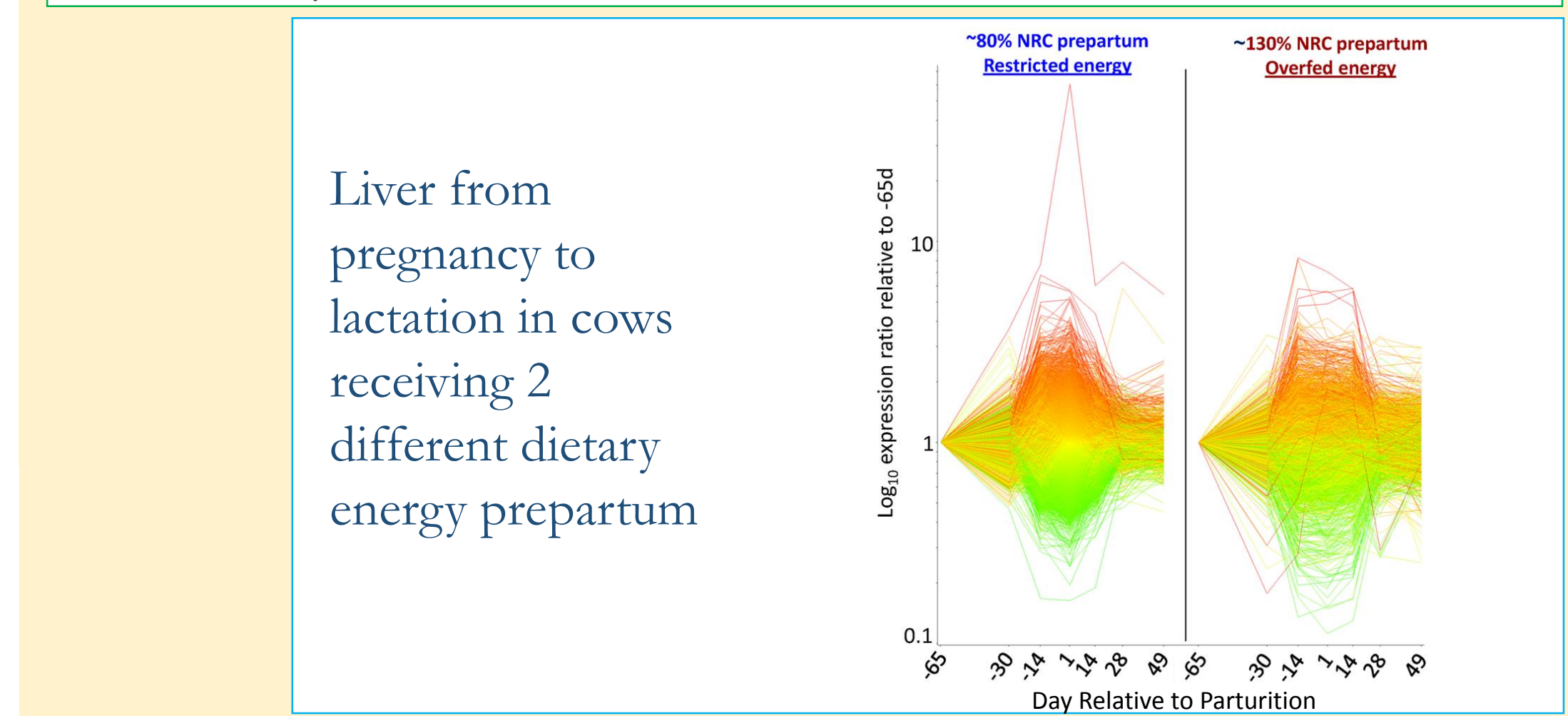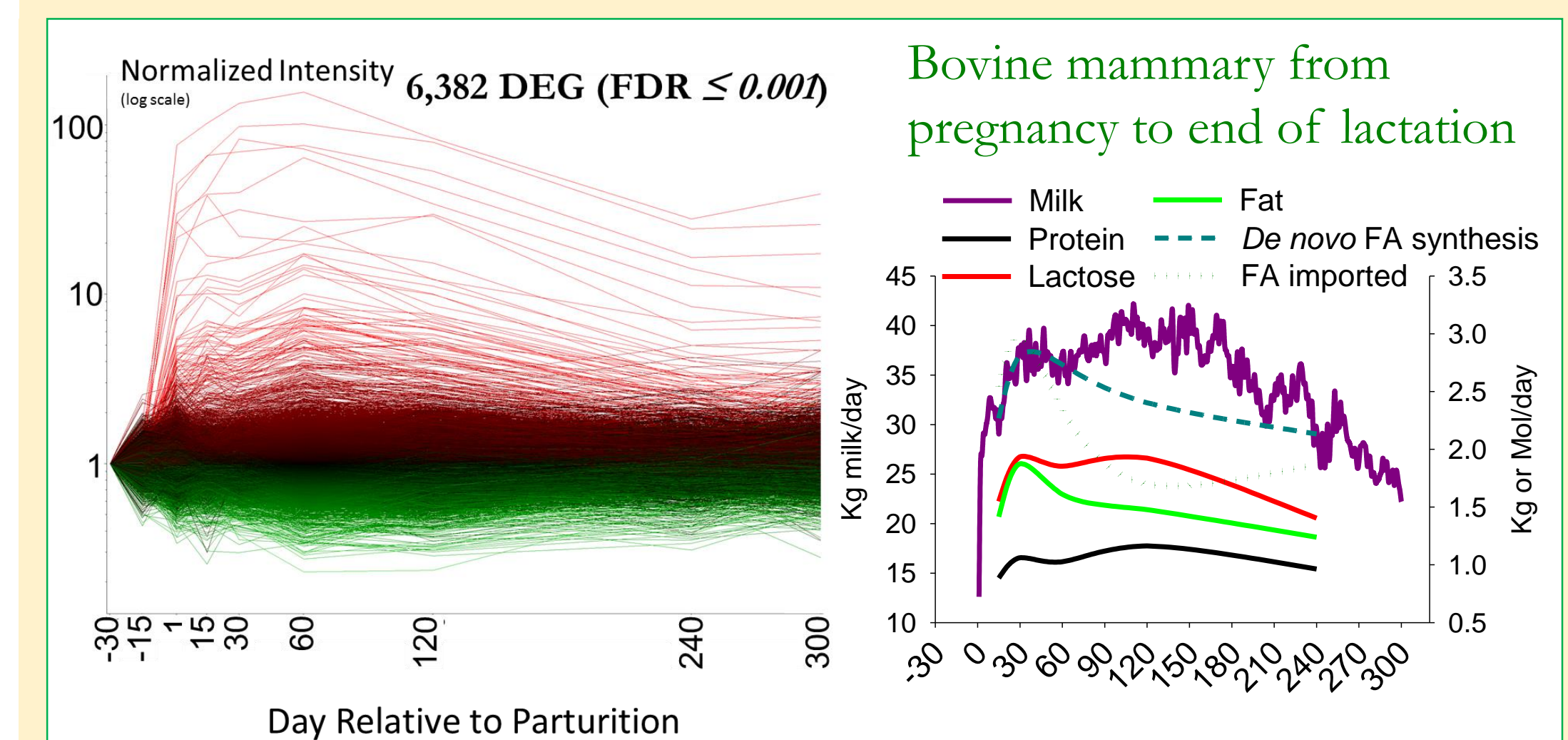
Absolute values!
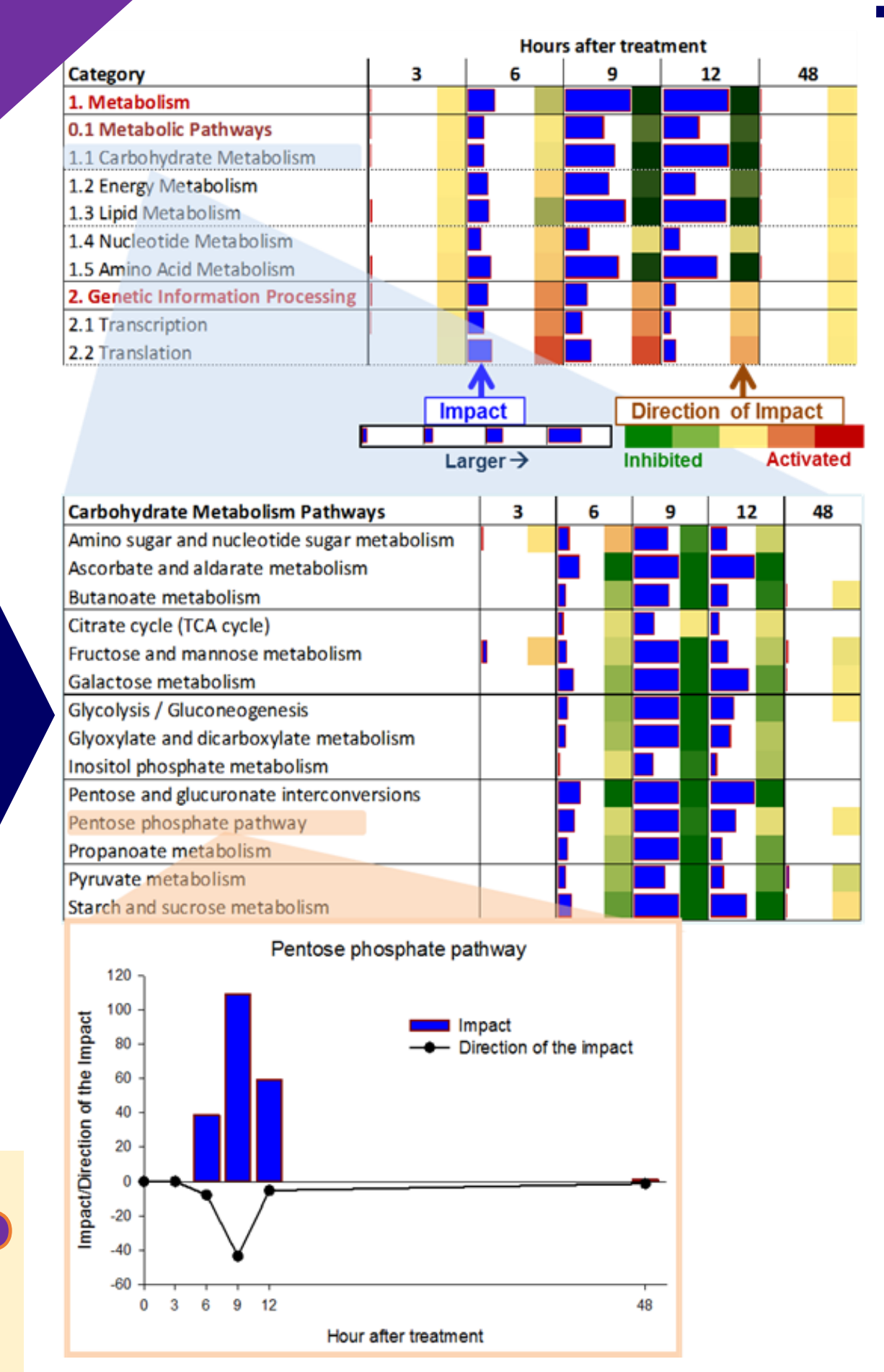
- Use of any database (e.g., KEGG pathways, Gene Ontology, up-stream regulators)
- Overview/summary of results
- Easy visualization and integration of biological dynamic changes

Dynamic integrated model

Is DIA superior to enrichment analysis tools for time-course experiment?
Plenty of Evidence*. Here just two examples….

Normalized Intensity (log scale) 6,382 DEG (FDR ≤ *0.001*)

Bovine mammary from pregnancy to end of lactation

Milk / Protein / Lactose / Fat / *De novo* FA synthesis / FA imported

DIA got:

➢↑ lactose synthesis
➢↑ fat synthesis
➢Importance of BTA6

Liver from pregnancy to lactation in cows receiving 2 different dietary energy prepartum

~80% NRC prepartum **Restricted energy**   ~130% NRC prepartum **Overfed energy**

Among others…
➢Protein synthesis and export → increase haptoglobin
➢Lipid metabolism → ↑ liver fat accumulation

…that enrichment analysis tool did not!

Now DIA online web-tool! (http://104.236.163.18:3838/dia/)

* Some of the publications….
Bollmann, S, D. Bu, J. Wang, and M. Bionaz. 2015. Unmasking Upstream Gene Expression Regulators with miRNA-corrected mRNA Data. Bioinformatics and biology insights 9(Suppl 4):33-48.
Bionaz, M., E. Monaco, and M. B. Wheeler. 2015. Transcription Adaptation during In Vitro Adipogenesis and Osteogenesis of Porcine Mesenchymal Stem Cells: Dynamics of Pathways, Biological Processes, Up-Stream Regulators, and Gene Networks. PloS one 10(9):e0137644.
Bionaz, M. and J. J. Loor. 2012. Ruminant metabolic systems biology: reconstruction and integration of transcriptome dynamics underlying functional responses of tissues to nutrition and physiological state. Gene regulation and systems biology 6:109-125.
Bionaz, M., K. Periasamy, S. L. Rodriguez-Zas, R. E. Everts, H. A. Lewin, W. L. Hurley, and J. J. Loor. 2012. Old and new stories: revelations from functional analysis of the bovine mammary transcriptome during the lactation cycle. PloS one 7(3):e33268.
Bionaz, M., K. Periasamy, S. L. Rodriguez-Zas, W. L. Hurley, and J. J. Loor. 2012. A novel dynamic impact approach (DIA) for functional analysis of time-course omics studies: validation using the bovine mammary transcriptome. PloS one 7(3):e32455.