

PHENOTYPE AND GENE NETWORKS FOR LIPID METABOLISM IN PIGS INFERRED FROM GLOBAL LIVER EXPRESSION

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INTRODUCTION

Lipid metabolism in pigs represents a complex system gathering a number of traits related to animal health, carcass performance, and nutritional and technological properties of pork.

The aim of this study is to infer **gene networks** involved in the (co)variation of ten traits related to lipid metabolism and fat deposition on the basis of global liver expression.



MATERIAL & METHODS

- **Animal material:** 350 Duroc barrows (5 half-sib families.)
- **Analysed phenotypes:** serum lipid levels (cholesterol, LDL, HDL and triglycerides), fatness (BFT and lean), intramuscular fat (IMF), and fatty acid composition (SFA, MUFA and PUFA).
- **High-density SNP data** (*Illumina PorcineSNP60 BeadChip*)
- **Expression data of 100 liver samples** (*Affymetrix GeneChip Porcine Genome® arrays*)
6919 probes after minimum fold-change filter



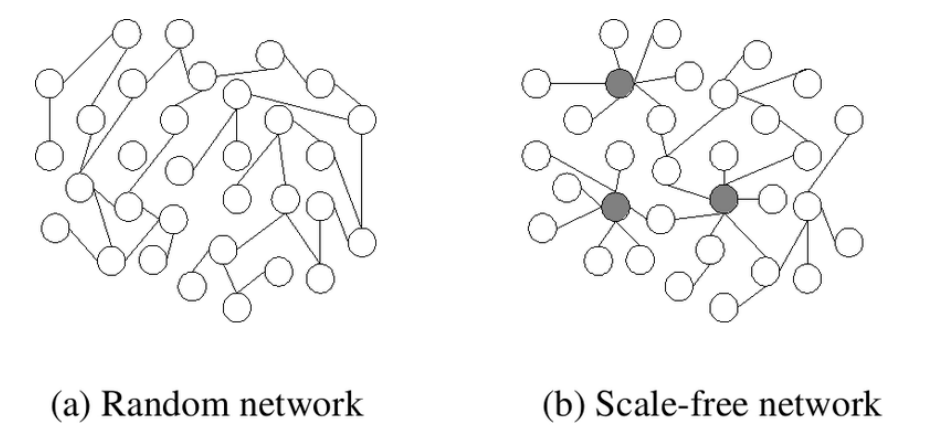
Phenotype networks from **Association Weight Matrix** (Fortes et al. 2010) and PCIT algorithm (Reverter & Chan 2008)

Weighted Gene Coexpression Network (Zhang y Horvath 2005)

1. Adjacency matrix & network construction

Considering scale free topology.

$$A=[a_{ij}] ; a_{ij}=|r(\text{exp}_i, \text{exp}_j)|^\beta$$



2. Co-expression module detection

- Topological overlap matrix
- Dissimilarity measure
- Hierarchical clustering

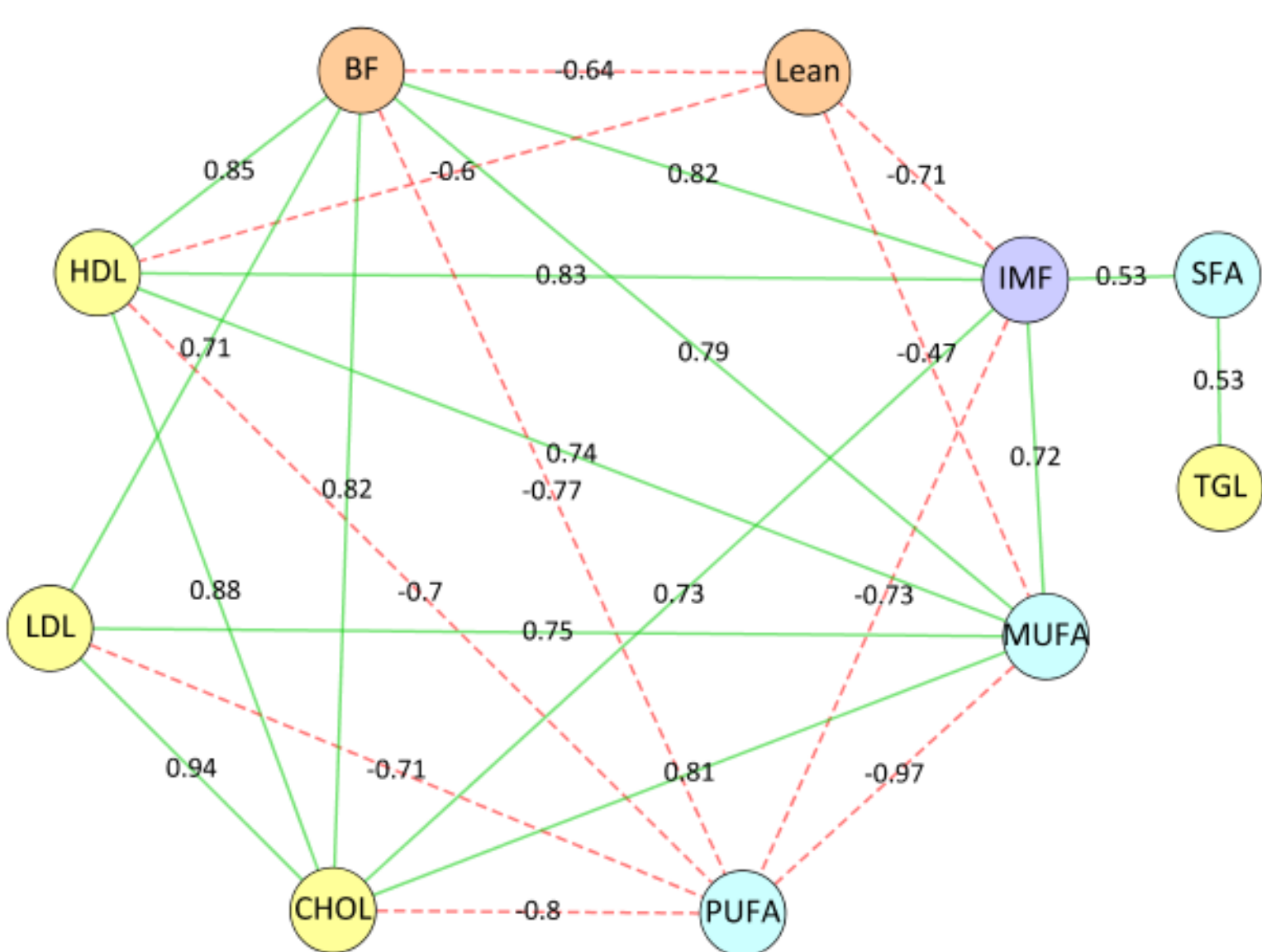
3. Selecting the modules most related to phenotypes

4. GO analysis and gene sub-network construction

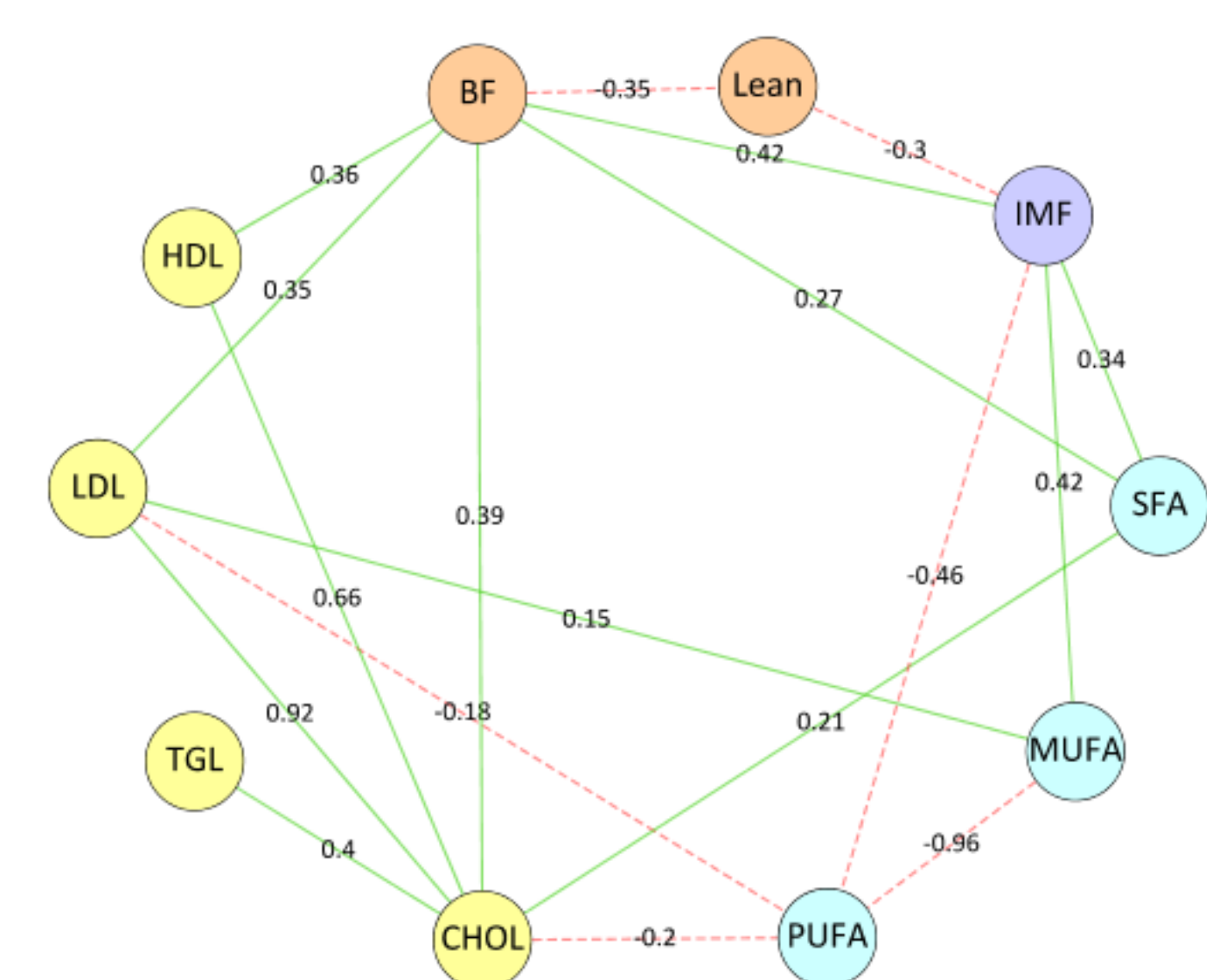
RESULTS & DISCUSSION

PHENOTYPE NETWORKS

Inferred from gene expression data



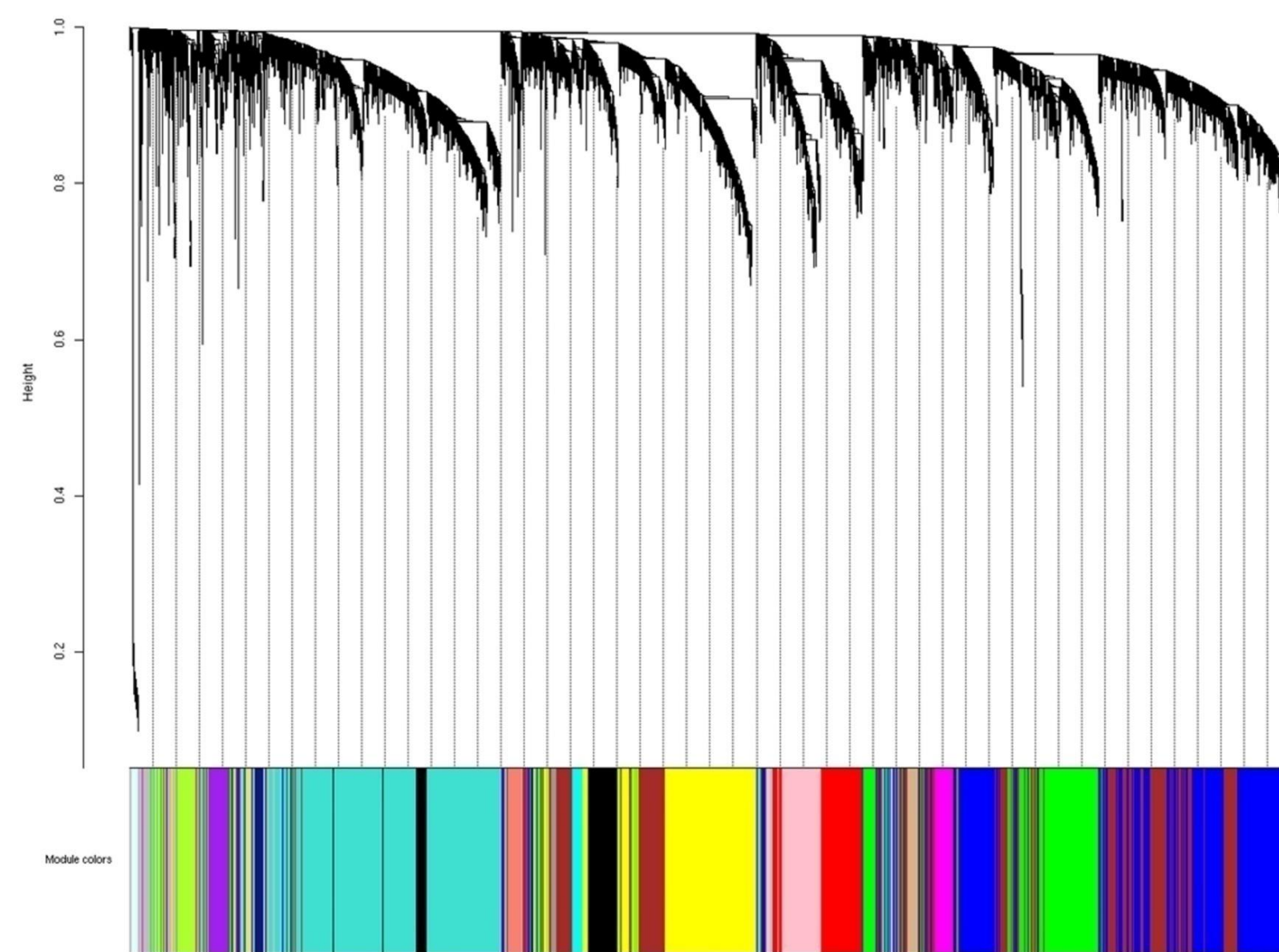
Inferred from dense SNP maps



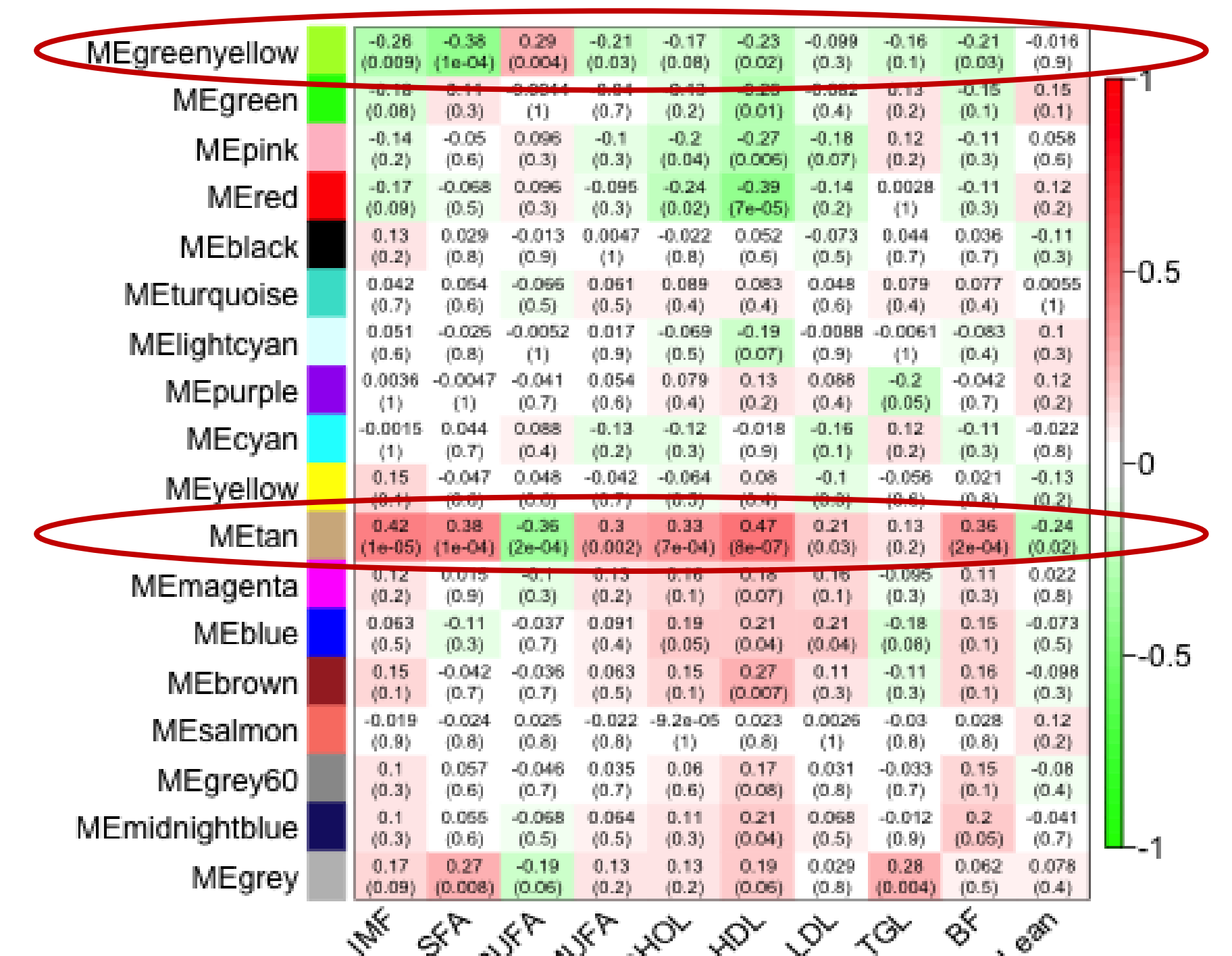
Serum lipid levels concentrations (mg/dl): **CHOL**-total cholesterol; **LDL**-low density lipoproteins; **HDL**-high density lipoproteins; **TGL**-triglycerides.
Fatness: **Lean**-%carcass lean; **BF**-backfat thickness.
Muscle: **IMF**-% intramuscular fat content; **SFA**-saturated fatty acids; **MUFA**-monounsaturated fatty acids; **PUFA**-polyunsaturated fatty acids.

GENE CO-EXPRESSION MODULES

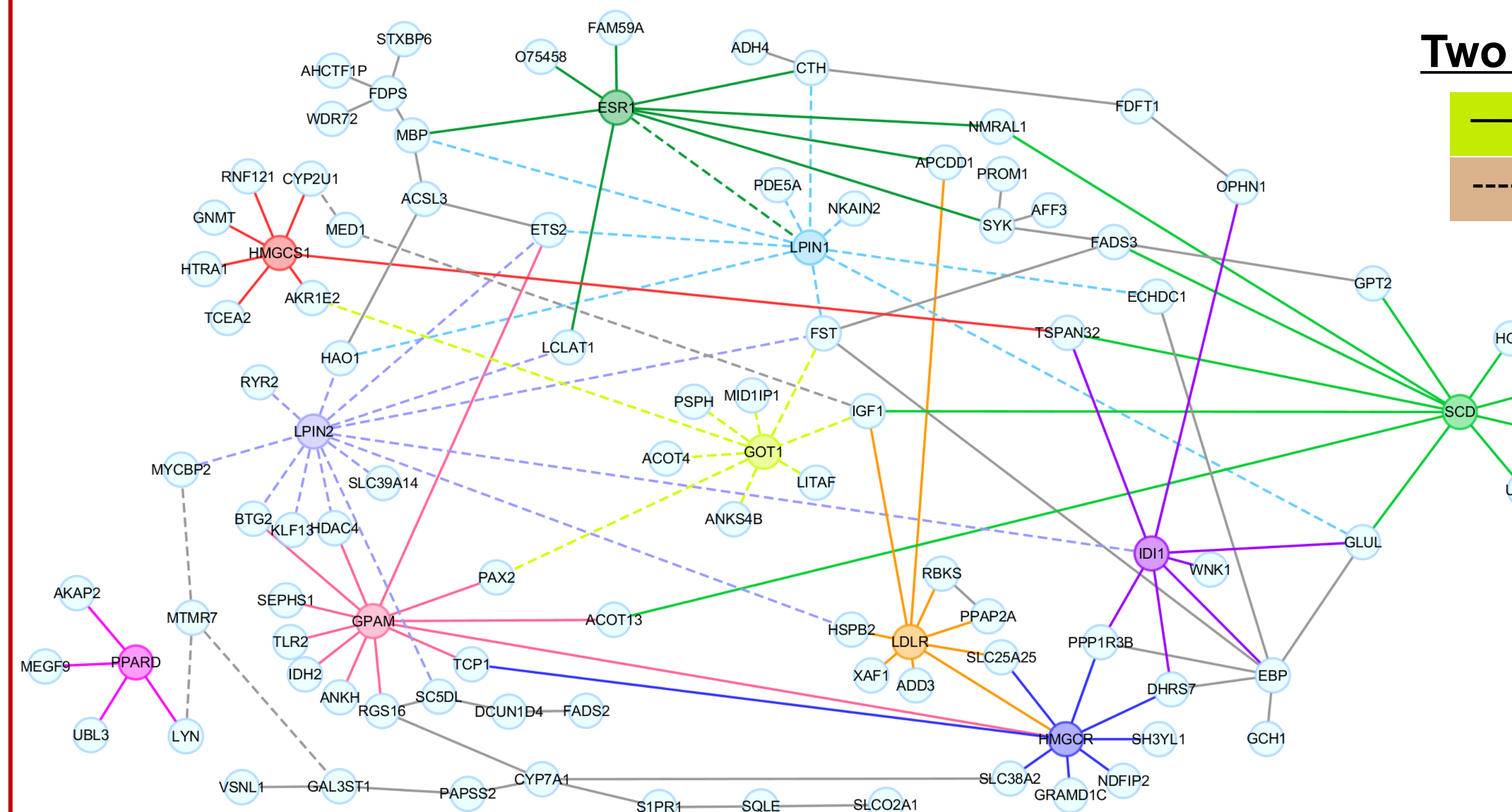
Hierarchical clustering dendrogram



MODULE-PHENOTYPE CORRELATION



GENE CO-EXPRESSION SUB-NETWORK ASSOCIATED TO PHENOTYPES



Two modules (denoted with different line patterns):

- GreenYellow module: 91 genes
- Tan module: 68 genes

GO analysis: 104 (out of 158) genes were direct or indirectly associated to lipid metabolism.

Candidate to be key regulators:

- 11 hubs or highly connected genes (denoted with different colours).
- Transcription Factors or Genes connecting several hubs: *EST2*, *IGF1*, *FST*, *GLUL*, *TSPAN32*.

CONCLUSIONS

The Weighted Gene Co-expression Network procedure allowed us identifying two co-expression modules that were significantly associated with ten lipid-metabolism and fatness phenotypes. The gene co-expression sub-network constructed with genes belonging to these modules showed several hubs (highly connected genes) and/or transcription factors candidate to be key regulators. Future studies involving eQTL mapping will allow going far beyond and identify regulatory elements modulating the gene network topology.