Combined transcriptomics and metabolomics in the whole blood to depict feed efficiency in pigs

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The need to get deeper insights into feed efficiency variations in growing pigs

- Pig production is facing several issues related to competition with feed resources, and competitiveness due to global trade
- The increase in size of pig farm led to environmental issues related to storage, treatment and use of effluents
- Feed represents between 60 and 70 % of the total cost of pork production

Feed efficiency

- The ability of pigs to turn feed nutriments into lean growth rate
  → while maintaining physiological functions and health
  → by reducing effluent discharge

The need to get deeper insights into feed efficiency variations in growing pigs

↗ Feed efficiency

- A research priority to support sustainable meat production
- But a complex trait that integrates multiple biological pathways orchestrated in and by various tissues

Primary avenues for exploration

- -omics technologies: produce large amount of data without a priori
- blood samples: minimally invasive way to summarize the activities of various tissues within the body

Strategy: From single omics to multi omics analysis

The modalities are not independent

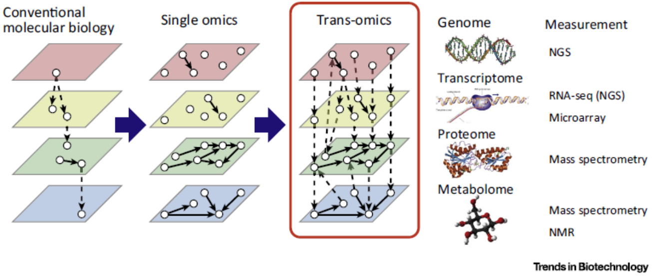


Fig. Linking the different levels of biological organization allows for a holistic view of biological entities (source: K. Yuri et al.)

Considering different levels of omics as a whole will help to understand biological systems, especially by considering the cascade of events and the interactions between entities

Objectives

Starting hypothesis

Key drivers of the phenotypic divergence in feed efficiency can be better defined by

- considering the different levels of organization between biological entities
- integrating experimental data and knowledge bases

In this study, we have

- collected in 47 Large White pigs (132d of age) divergently selected for Residual Feed Intake:
  - transcriptomic data in the whole blood (60k porcine microarray)
  - metabolomic data in plasma (1H-NMR analysis and target gas chromatography)
  - phenotypic data (feed conversion ratio, body composition)
- access to pathways knowledgebase (Reactome)

Identifying modules of co-expressed genes related to feed efficiency

Objective: Build modules of co-expressed genes correlated with variations in feed efficiency and related traits

Method: Weighted Genes Co-expression Network Analysis (WGCNA) **Results**:

- 33 modules of co-expressed genes in the whole blood (13 to 2,491 unique genes)
- The eigengenes of 8 modules were significantly/tend to be correlated with:
  - Feed Conversion Ratio (FCR, on-farm measure of feed efficiency)
  - most of them were correlated with growth rate (ADG) and %loin muscle
- The eigengene of 1 module was significantly correlated with Daily Feed Intake
- Modules were enriched in ~ 3 different biological pathways (GO terms)

Relationships between transcriptomic and metabolomic levels

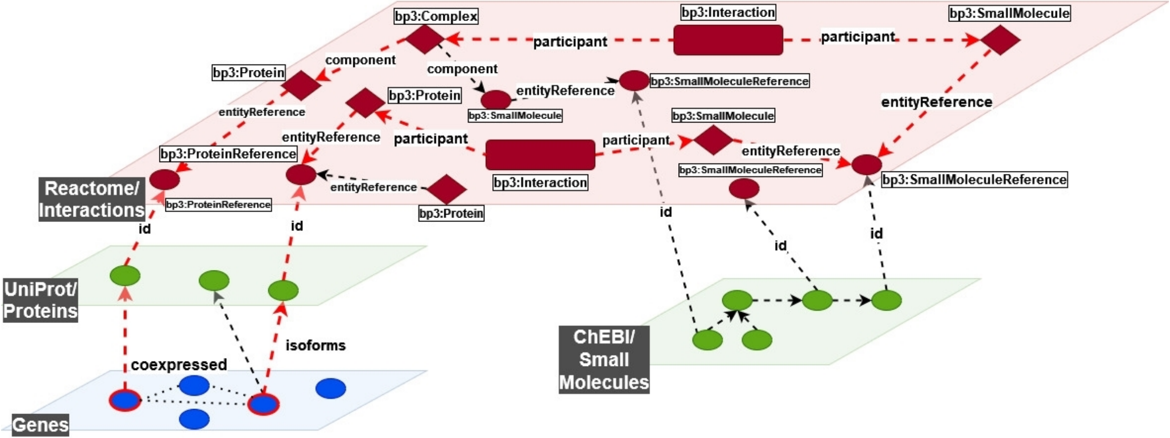
Objective: Determine lipids and metabolites profiles

Method: Construct lipids and metabolites profiles using PCA, calculate coefficient correlations between dimensions of the PCA and WGCNA eigengene modules

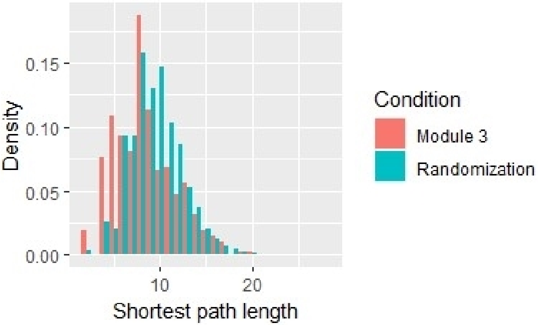
Results:

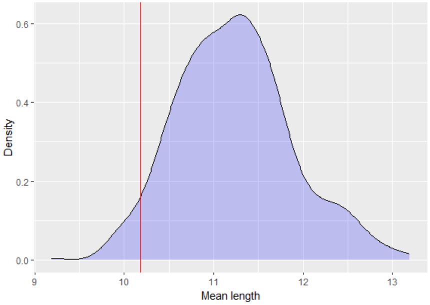
- There were few significant associations between the two -omics levels
- Example of significant association: the module Royalblue (81 genes)
- Co-expressed genes mainly involved in immunity (T and β cells signaling) and cell development — polyunsaturated fatty acids (omega-6 and omega-3) concentrations

Integration of -omics levels on a same Reactome graph to explore connections using Web Semantic technologies on public databases and ontologies



Graph traversal results on the Royalblue module





	Royalblue module	Random modules (*)
Average shortest path length	8,5	9,7
Proportion of paths with biochemical reaction encompassed	41,5%	38,3%
Proportion of paths with small molecule encompassed	41,2%	25,0%

(*) same number of genes - average for 500 randomizations

Conclusion: Insights on feed efficiency in pigs

- Identifying co-expressed and co-regulated gene modules (patterns with different structures than random) related to feed efficiency: architecture of the trait
- These modules also regulate lean growth rate
- Among the biological processes over-represented within the modules, several are linked to immunity (+ cell development and protein localization)
- Interconnecting these modules with metabolic profiles suggests links between immunity and fatty acid % concentrations (relevant for future nutritional recommendations to obtain good synergy between production and health)
- Further methodological work is needed to better understand and identify key regulators of these networks thanks to knowledge graph

additional informations in : `https://doi.org/10.21203/rs.3.rs-2946807/v1`

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contact: camille.juigne@inrae.fr

github: cjuigne/multiomics_and_feed_efficiency

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