Multiomics analysis of Feed Efficiency in Danish Breeding boars

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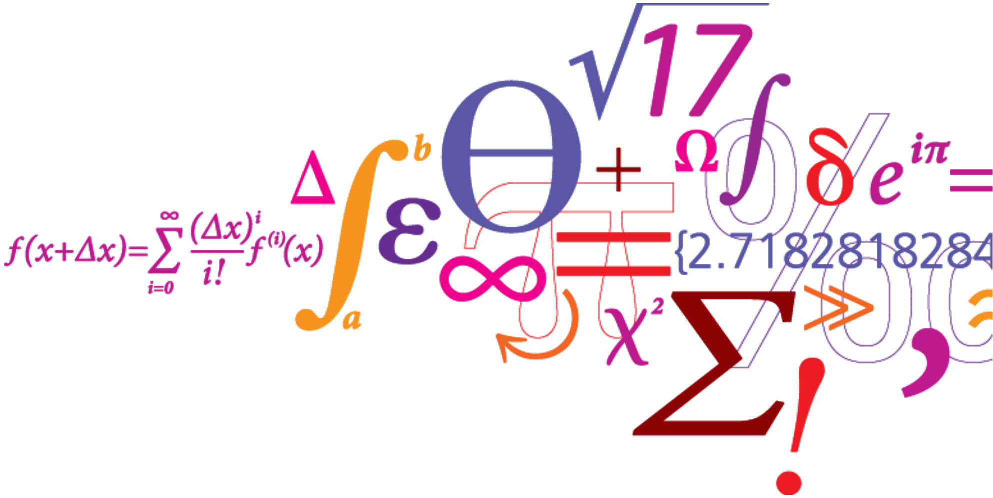


Background

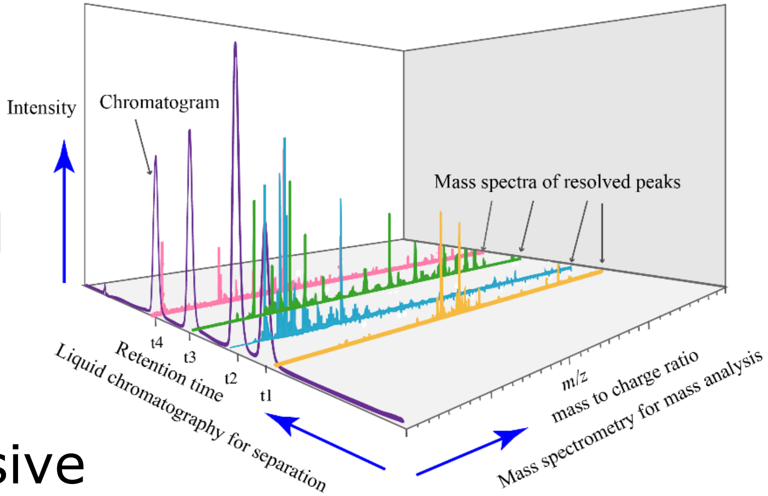
- Feed efficiency (FE) is one of the most important goals in pig production and pig breeding goals

- This study is part of the bigger project called FeedOMICS (a 4 year project) where the main objectives are to:
  - generate transcriptomic and metabolite profiles in feed efficient and inefficient pigs and identify highly predictive biomarkers of feed efficiency via systems biology methods.
  - conduct integration of genomic data with transcriptomic and metabolomic datasets, and analyse them via bioinformatics and integrative systems biology methods
  - To develop powerful prediction methods for feed efficiency in pigs and to provide accurate functionally relevant markers for highly feed efficient pigs.

LC-MS – Liquid Chromatography Mass Spectrometry

- LC is the technique for physical separation of molecules
- MS measures the masses of the molecules

Why LC-MS?



LC-MS allows a broad untargeted quantification of metabolites in our desired target.
Coupled with relatively non-invasive sampling it is a great tool for gaining functional knowledge and a possible screening tool.

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Bøgildsgård
Core
Testing Facility

5000 Males per year from 28 breeders

Arrival at 4 weeks age

7kg

5 week acclimatization 30kg

60-70 days test phase

100kg

Slaughter or Breeding program

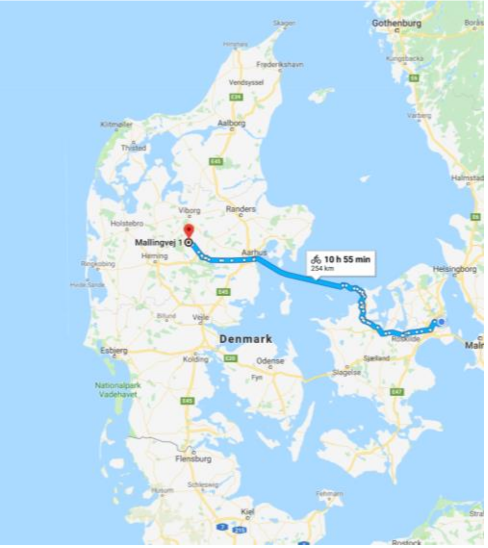

Photo by Markus Drag

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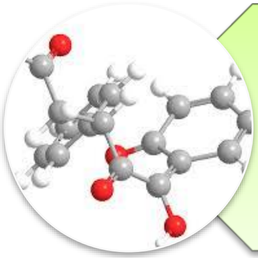


Blood Metabolites – 2 time points

Phenotypes and data

Weight data

Raw feed intake

Feed Efficiency Index

Pedigree Information

Photo by Markus Drag

Data Description

Total Duroc Sampled: 59 (x2)

Total Landrace Sampled: 50 (x2)

218 Blood Samples

LC-MS

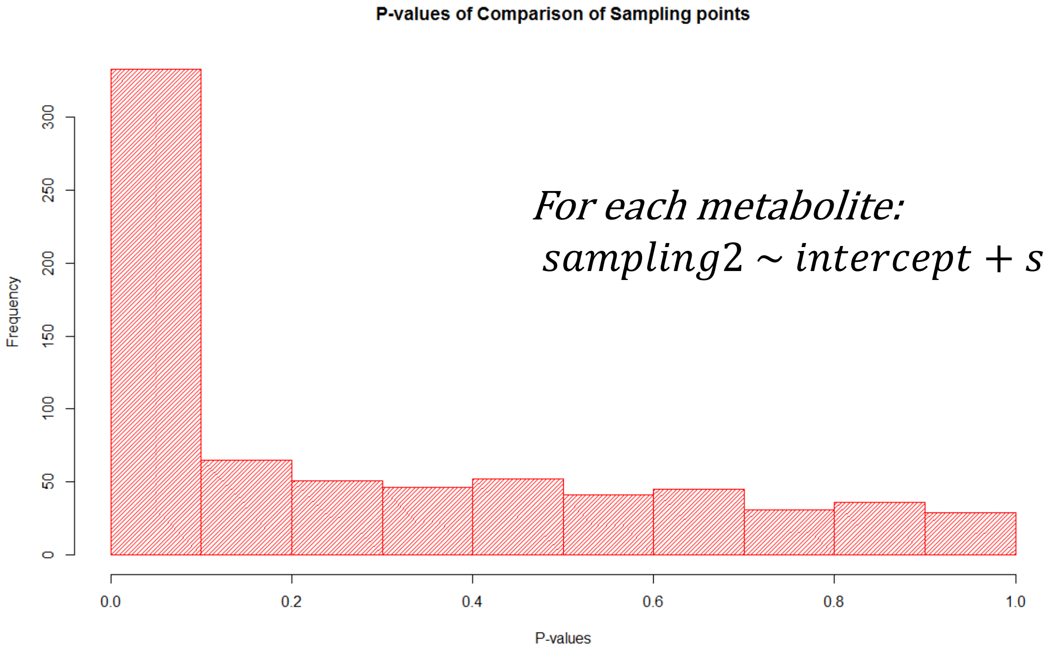
729 Metabolites Detected

Quantile Normalization

Example Compounds: Nucleic Acids, Amino Acids, Other Acids, Vitamins and many uncharacterized compounds (polar compounds in general)

Photos by Markus Drag

Metabolite Data stability



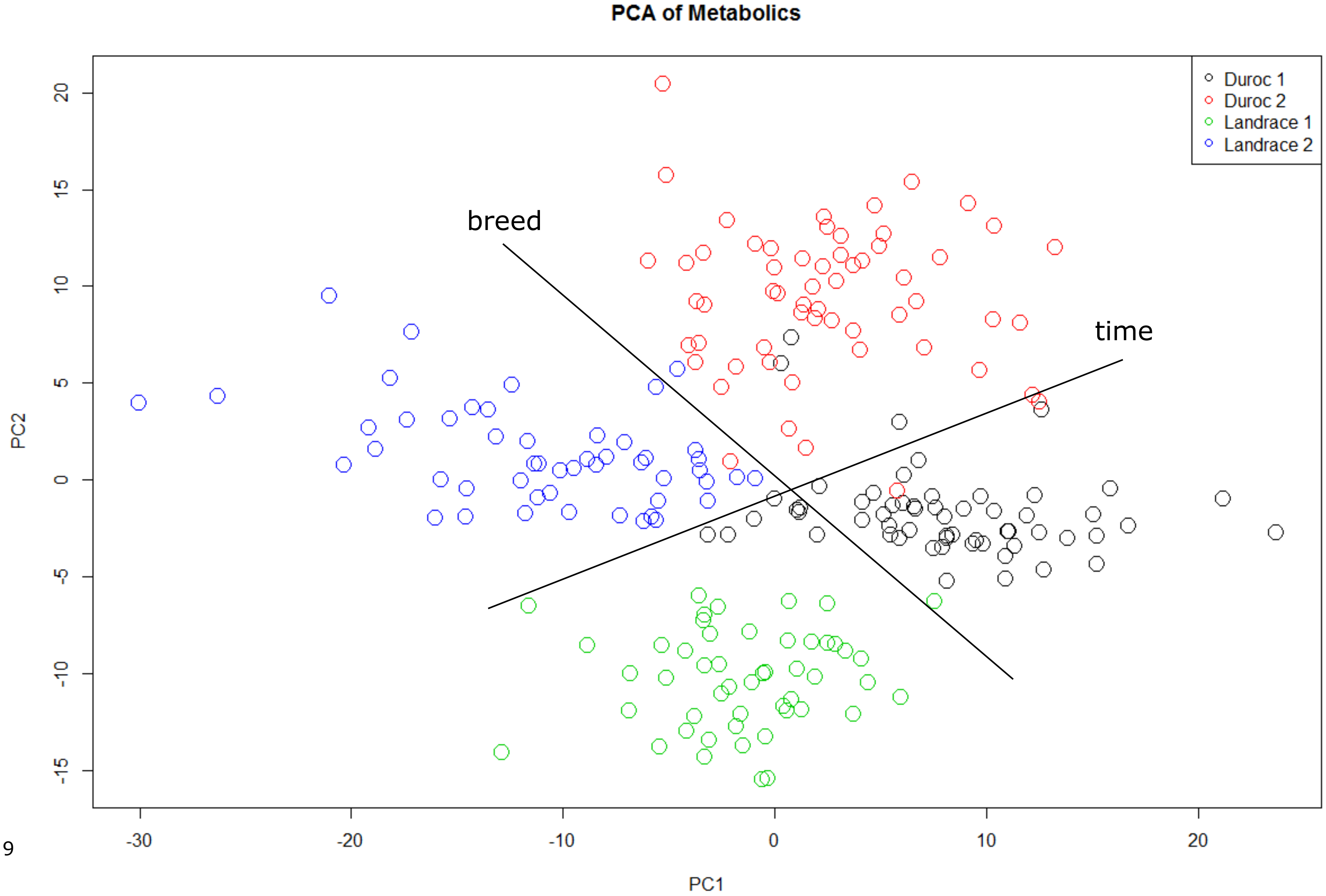
For each metabolite:

$$sampling2 \sim intercept + sampling1 + breed$$

Relationship between sample points is significant for most metabolites

This indicates blood metabolites is a stable phenotype

Data Overview



Linear Modelling

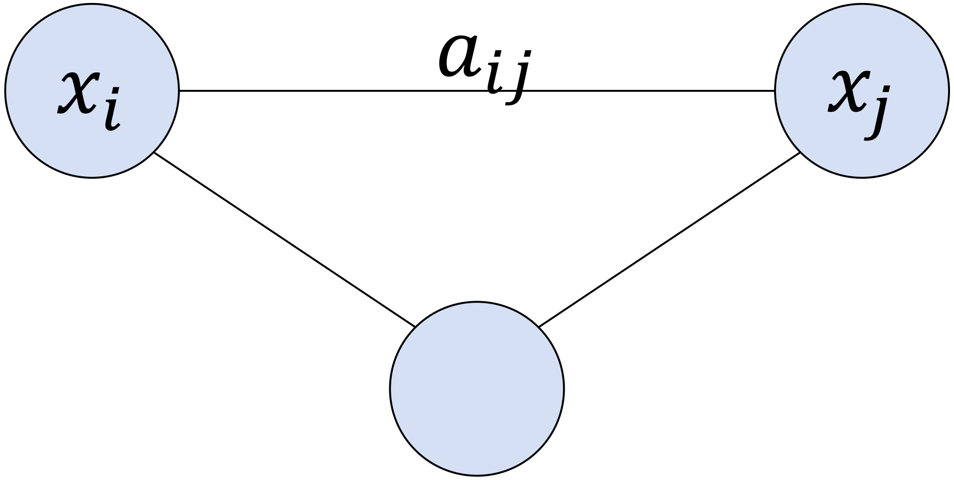
- To asses the relation between individual metabolites and FE, each metabolite was fit using a linear model to FE.

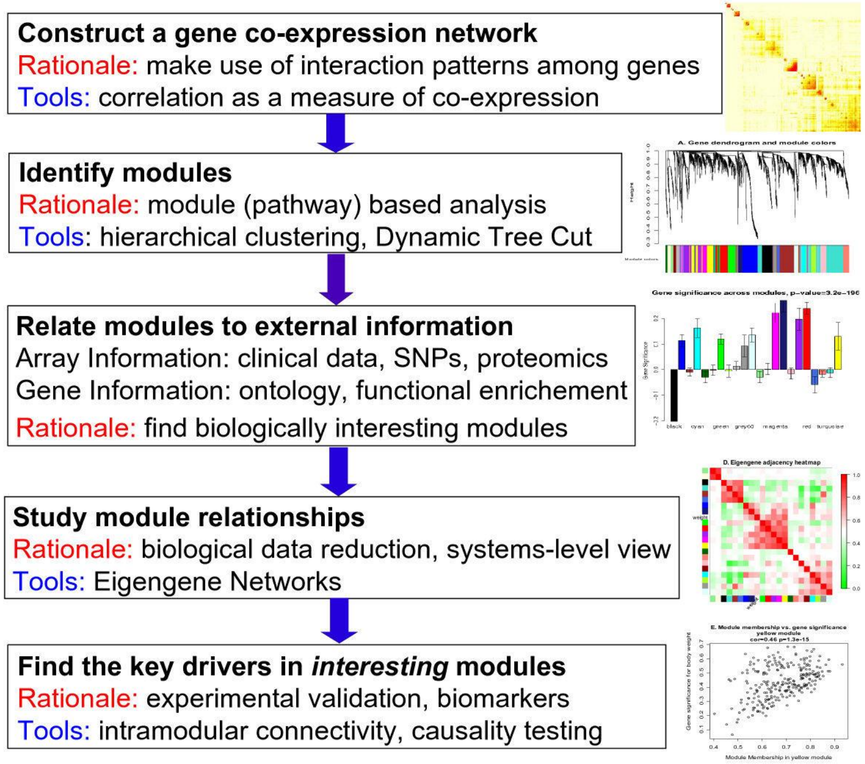
	DD 1	DD 2	DD 1+2	LL 1	LL 2	LL 1+2
P < 0.05	71	64	71	90	76	89
Bootstrap P value	$<10^{-6}$	$<10^{-5}$	$<10^{-6}$	$<10^{-7}$	$<10^{-6}$	$<10^{-7}$

Examples: Sorbitol, Monosaccharide, Riboflavine, Nicotine, Guanosine, Uridine, Arginine

Metabolic Network Construction - WGCNA

$$a_{ij} = \left|cor(x_i, x_j)\right|^{\beta}$$





Construct a gene co-expression network
Rationale: make use of interaction patterns among genes
Tools: correlation as a measure of co-expression

Identify modules
Rationale: module (pathway) based analysis
Tools: hierarchical clustering, Dynamic Tree Cut

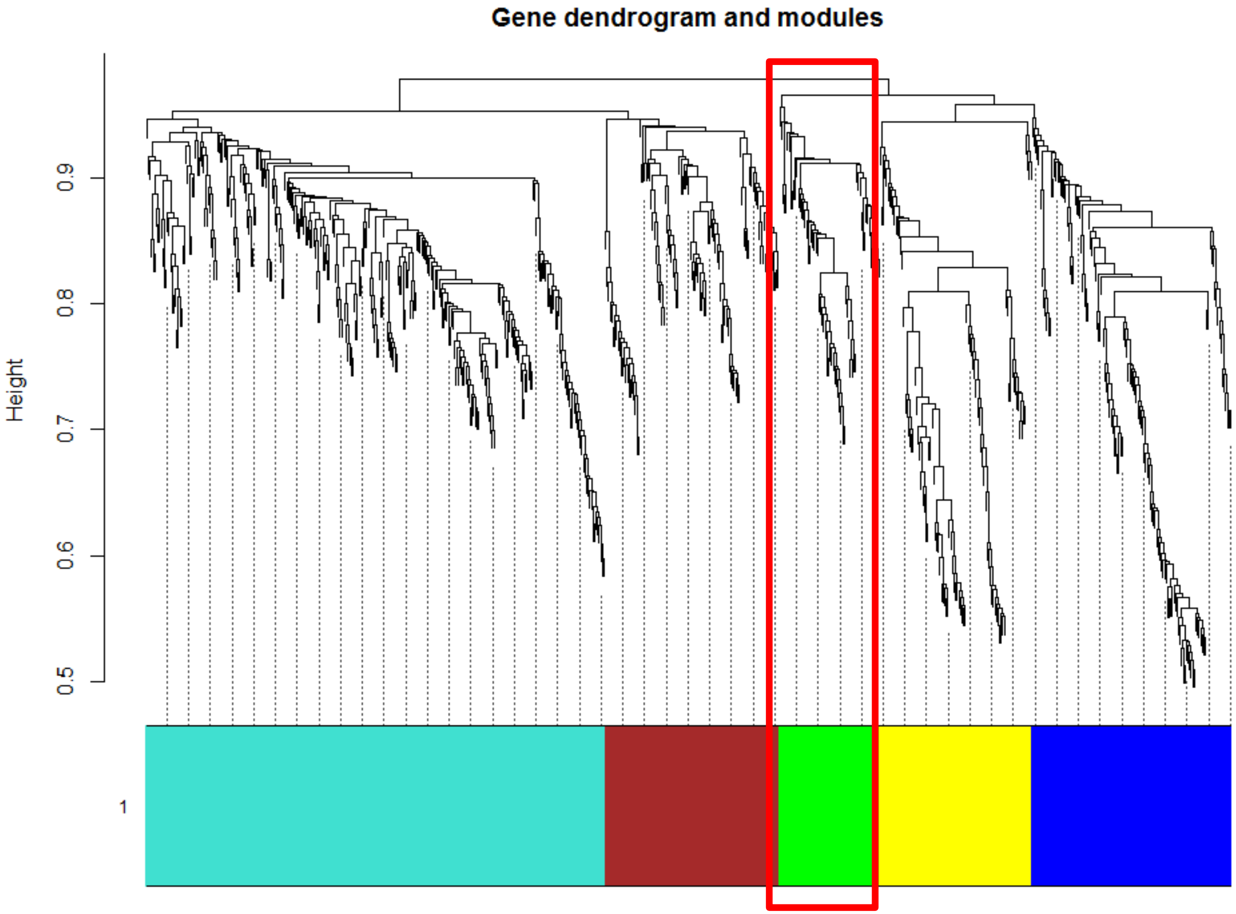
Relate modules to external information
Array Information: clinical data, SNPs, proteomics
Gene Information: ontology, functional enrichement
Rationale: find biologically interesting modules

Study module relationships
Rationale: biological data reduction, systems-level view
Tools: Eigengene Networks

Find the key drivers in *interesting* modules
Rationale: experimental validation, biomarkers
Tools: intramodular connectivity, causality testing

Figure from Langfelder et al, BMC Bioinformatics 2008 9:559

Metabolic Network Construction - WGCNA

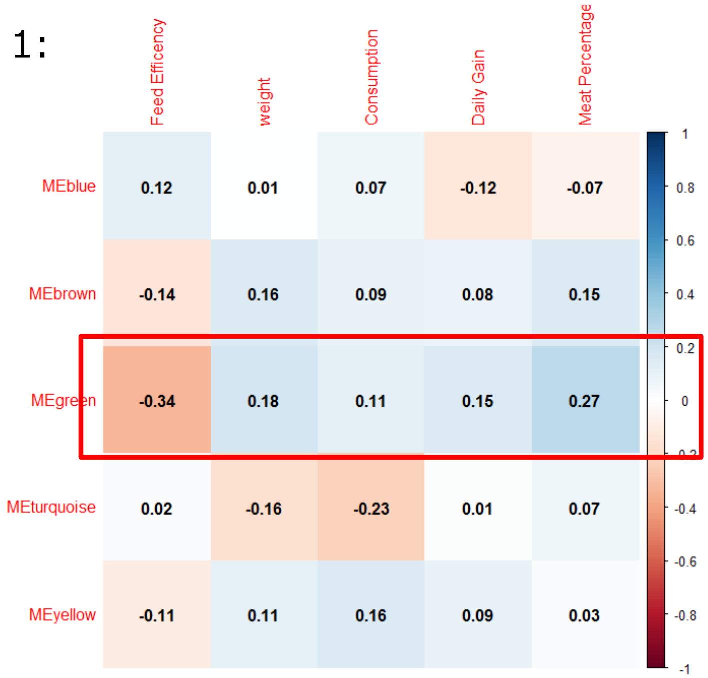


- Network Generated from DD 30 kg sampling
- Green module has a correlation of -0.339 with FE
- P-value of correlation is 0.008

Metabolic Network Summary Results

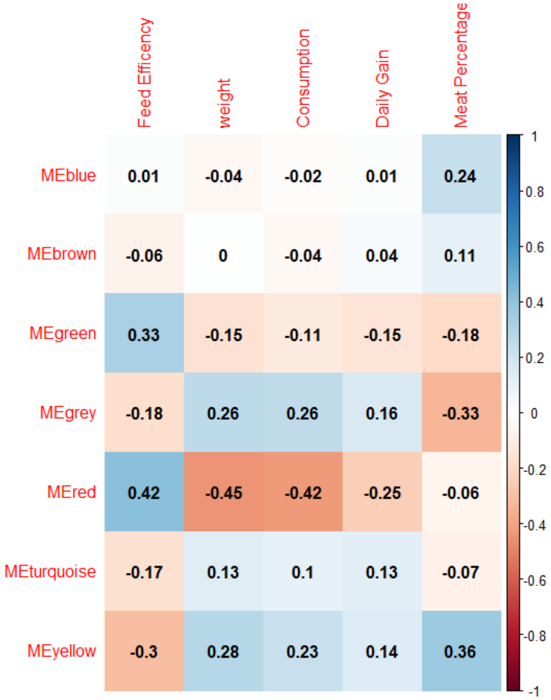
Sampling	DD 1	DD 2	LL 1	LL 2
N modules	5	7	7	5
Significant modules for Feed Efficiency	1	1	3	1

DD 1:



	Feed Efficency	weight	Consumption	Daily Gain	Meat Percentage
MEblue	0.12	0.01	0.07	-0.12	-0.07
MEbrown	-0.14	0.16	0.09	0.08	0.15
MEgreen	-0.34	0.18	0.11	0.15	0.27
MEturquoise	0.02	-0.16	-0.23	0.01	0.07
MEyellow	-0.11	0.11	0.16	0.09	0.03

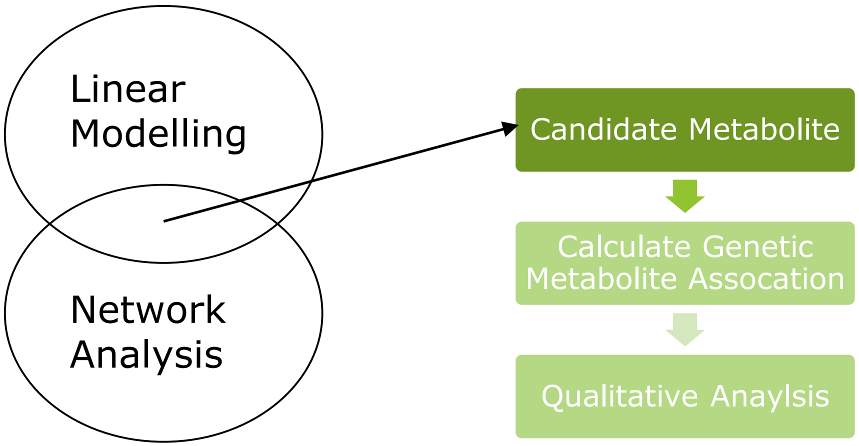
LL 1:

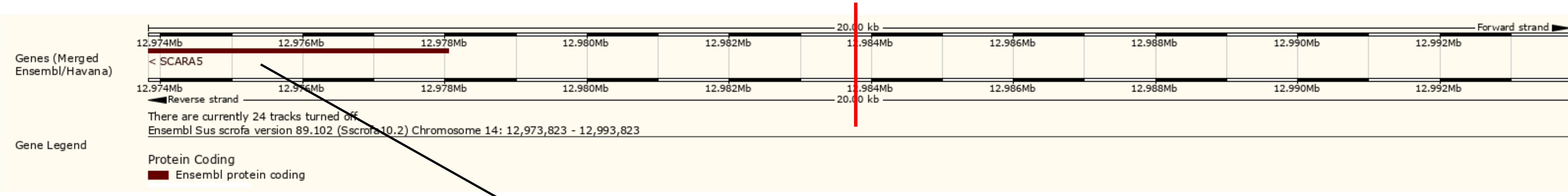


	Feed Efficency	weight	Consumption	Daily Gain	Meat Percentage
MEblue	0.01	-0.04	-0.02	0.01	0.24
MEbrown	-0.06	0	-0.04	0.04	0.11
MEgreen	0.33	-0.15	-0.11	-0.15	-0.18
MEgrey	-0.18	0.26	0.26	0.16	-0.33
MEred	0.42	-0.45	-0.42	-0.25	-0.06
MEturquoise	-0.17	0.13	0.1	0.13	-0.07
MEyellow	-0.3	0.28	0.23	0.14	0.36

Metabolite Annotation

- Many Metabolites are uncharacterized
- Functional Characterization is still possible
- Uncharacterized compounds can still be used for screening
- Further laboratory analysis can identify properties of unknown compounds





There are currently 24 tracks turned off

Ensembl Sus scrofa version 89.102 (Sscrofa10.2) Chromosome 14: 12,973,823 - 12,993,823

SCARA5 Gene, iron transport gene that has is related to cell development

Conclusions

- We have shown methods to identify relation between blood metabolites and feed efficiency
- Results reveal that the metabolites are related to feed efficiency using both network approaches and linear modelling
- This has implications for the functional background of feed efficiency
- Metabolites can be a potential screening tool for feed efficiency

Acknowledgments

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Questions?

Than you for listening!