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A systems genetics approach reveals potential regulators of feed efficiency in pigs

Yuliaxis Ramayo-Caldas, Maria Ballester, Juan Pablo Sánchez, Rayner González-Prendes, Marcel Amills, Raquel Quintanilla

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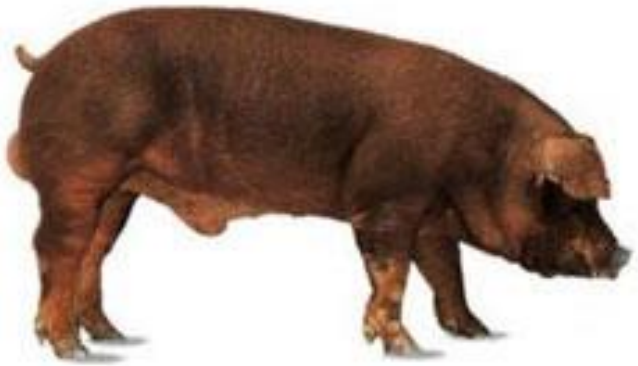
MARIE CURIE ACTIONS

OBJECTIVES

Identifying interacting genes, biological pathways and potential regulators of feed efficiency (FE) in pigs using a systems genetic approach.

Phenotypic and Genotypic data



349 Duroc pigs

LIPGEN project

QC

30,530 SNPs

FEED EFFICIENCY

- **Residual Feed Intake (RFI)**
- Food Conversion Ratio (FCR)
- Daily feed intake (DFI)

GROWTH & FAT DEPOSITION

- Daily growth (ADG)
- Back fat (BF)
- Intramuscular fat (IMF)

MEAT QUALITY

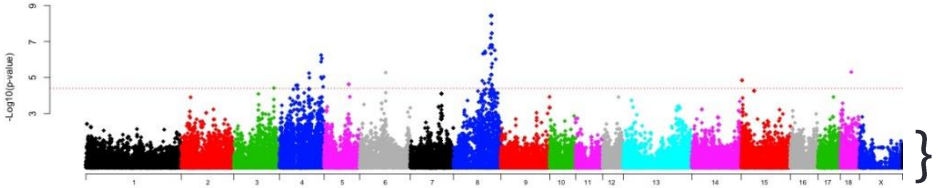
- Saturated fatty acid (SFA)
- Monounsaturated FA (MUFA)
- Polyunsaturated FA (PUFA)

Association weight matrix (AWM)

Fortes et al. 2010

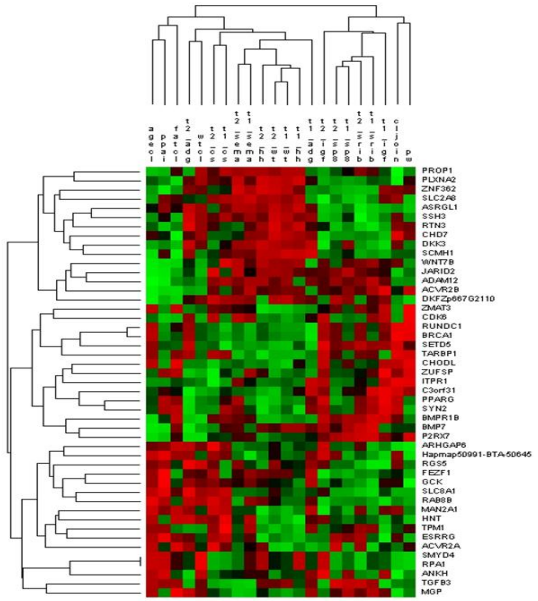
1. Exploit the power of Multivariate analysis
2. Combine the results from GWAS
3. With the knowledge of Transcription Regulators
4. In a Network Theory framework

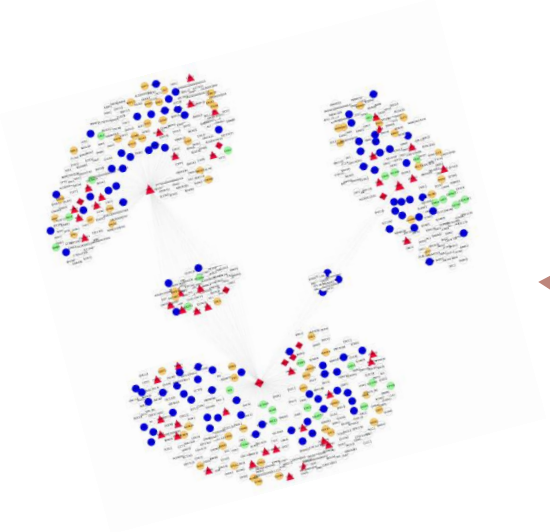
for (trait in dataset) { **GWAS** (p-value & â)

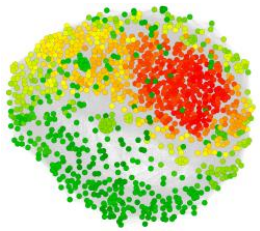


}

AWM





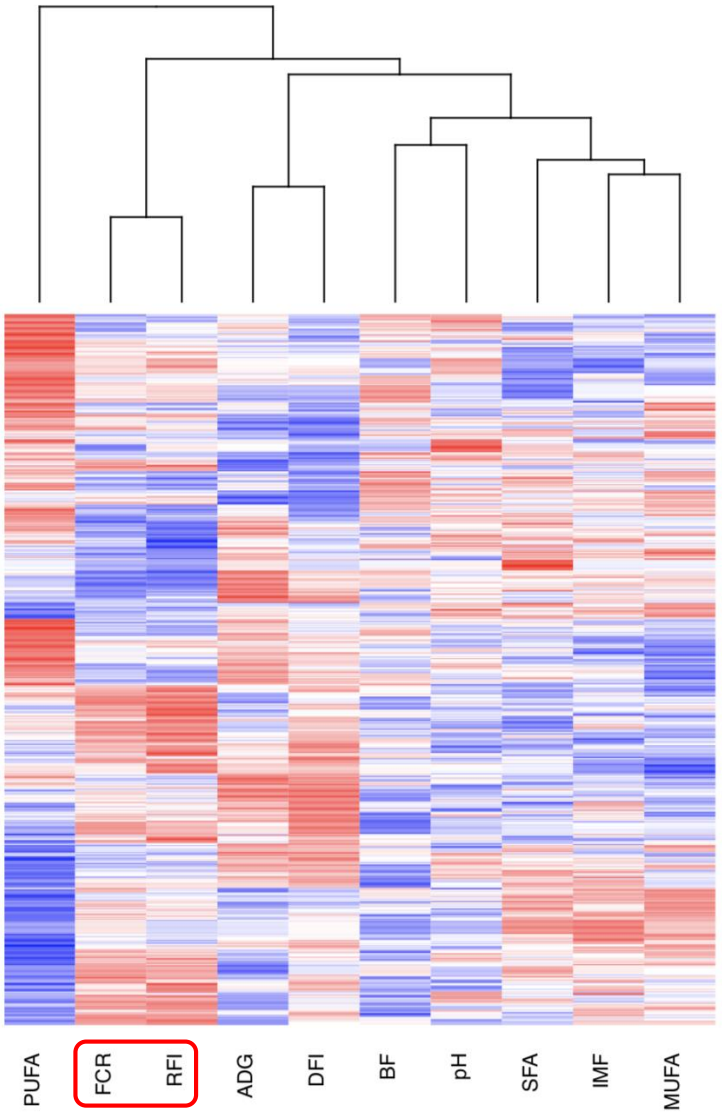


PCIT Reverter and Chan, 2008

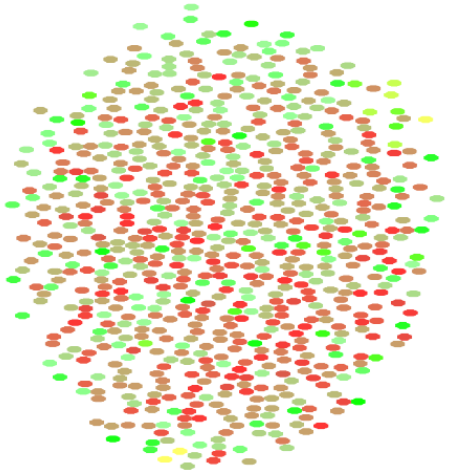
AWM for feed efficiency

- Select SNPs that may affect RFI ($P \leq 5\%$)
- On average, how many of the remaining traits are affected by these RFI-associated SNPs?
- Select SNPs with $P \leq 5\%$ in ≥ 3 traits

- 704 Genes as rows (via neighbouring SNP)
- 10 Traits as columns
- Each cell $\{i, j\}$ value is the normalized (z-scores) additive effect of i^{th}-SNP on the j^{th}-trait
- **49 regulators** (transcription factors)



Biological network parameters

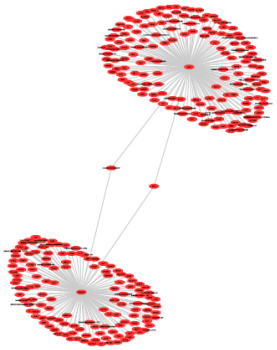


CentiScaPe: Network topology and node centralities

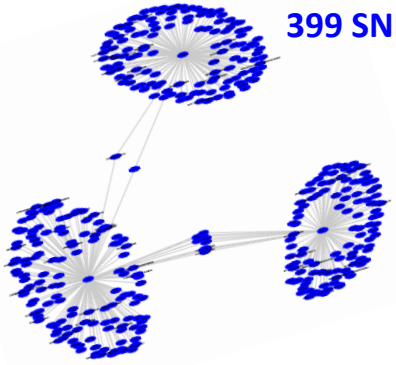
ClueGO and **IPA**: Gene ontology and pathways analysis

iRegulon: binding sites for predicted targets of key TF

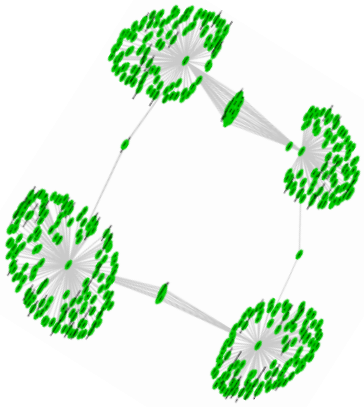
Discovering of key regulators (TF)



LHX4, POU2AF1



LHX4, POU2AF1, TCF7L2



LHX4, POU2AF1, TCF7L2, ARID1B

Literature evidence

TCFL2

Identification of genetic markers associated with residual feed intake and meat quality traits in the pig

B. Fan [a,b,c], S. Lkhagvadorj [a,b], W. Cai [a,b], J. Young [a,b], R.M. Smith [a], J.C.M. Dekkers [a,b], E. Huff-Lonergan [a], S.M. Lonergan [a], M.F. Rothschild [a,b,*]

Genome-wide association and pathway analysis of feed efficiency in pigs reveal candidate genes and pathways for residual feed intake

*Duy N. Do[1], Anders B. Strathe[1,2], Tage Ostersen[2], Sameer D. Pant[1] and Haja N. Kadarmideen[1]**

LHX4

Three Novel Missense Mutations within the *LHX4* Gene Are Associated with Variable Pituitary Hormone Deficiencies

Roland W. Pfaeffle, Chad S. Hunter, Jesse J. Savage, Mario Duran-Prado, Rachel D. Mullen, Zachary P. Neeb, Urs Eiholzer, Volker Hesse, Nadine G. Haddad, Heike M. Stobbe, Werner F. Blum, Johannes F. W. Weigel, and Simon J. Rhodes

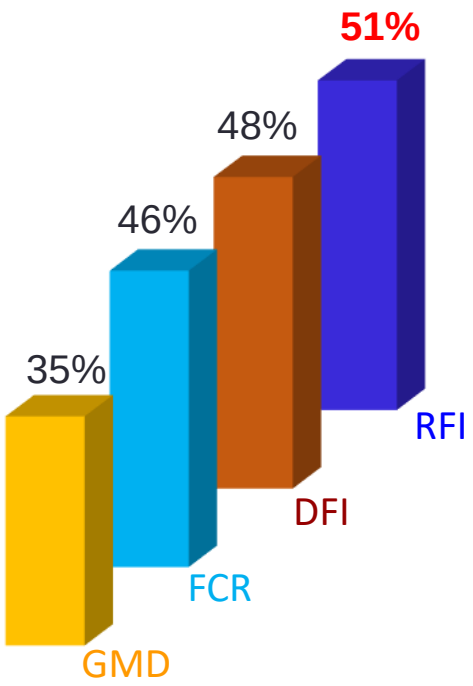
POU2AF1

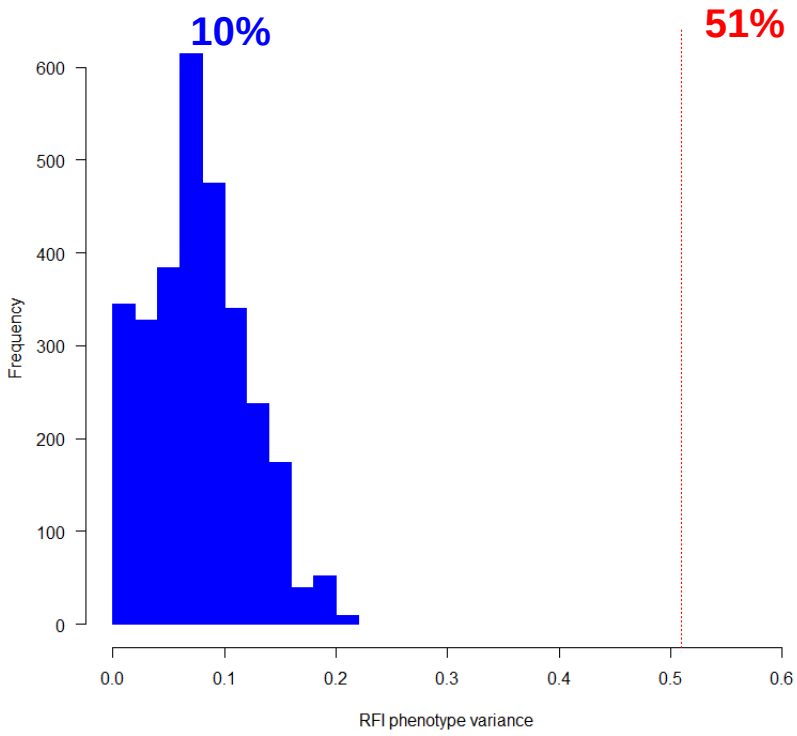
Cloning, Functional Characterization, and Mechanism of Action of the B-Cell-Specific Transcriptional Coactivator OCA-B

YAN LUO AND ROBERT G. ROEDER*

Proportion of phenotypic variance (399 SNPs)

GCTA-GREML method (Yang et al. 2010)



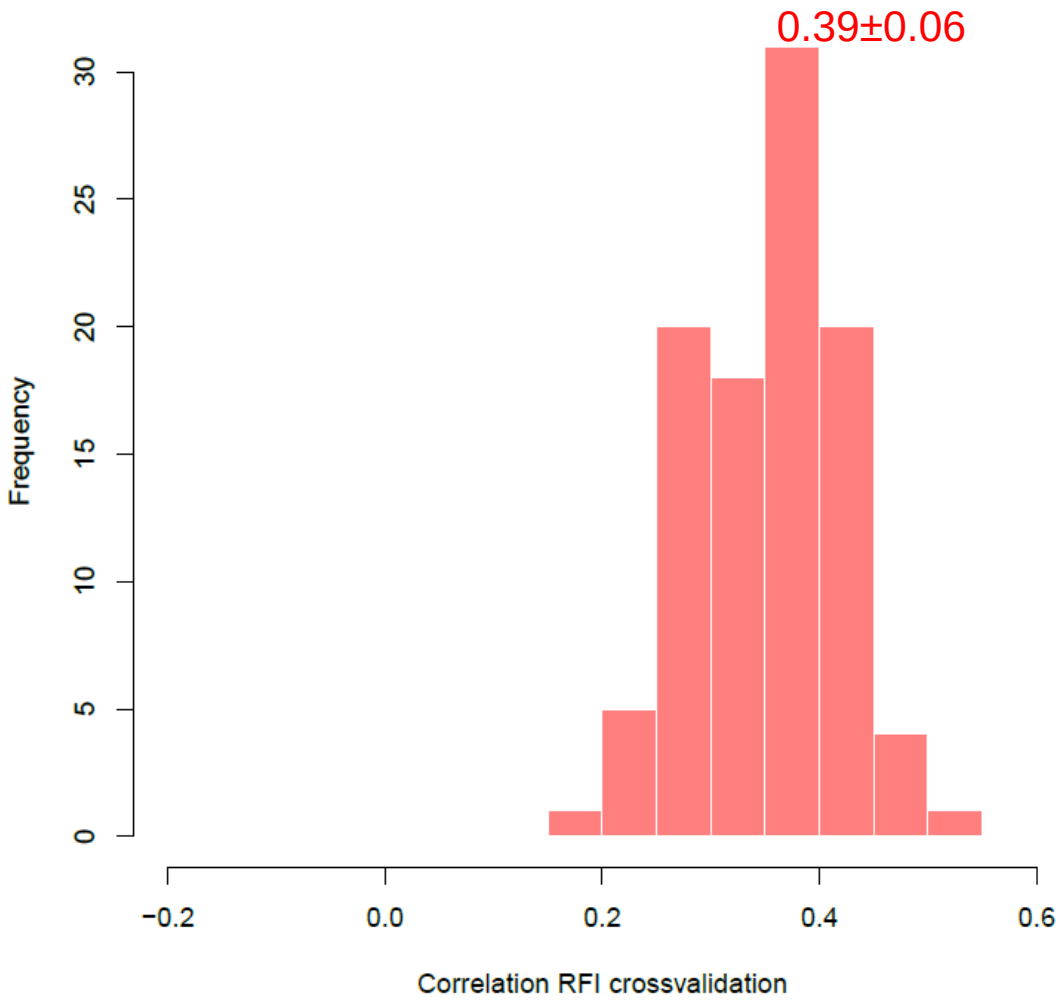


Explained by the network regulated by *LHX4, POU2AF1, TCF7L2*

RFI phenotype variance explained by 399 randomly selected SNPs (3,000 replicates)

Accuracy of RFI prediction (399 SNPs)

Crossvalidation (BGLR; de los Campos and Perez, 2013)



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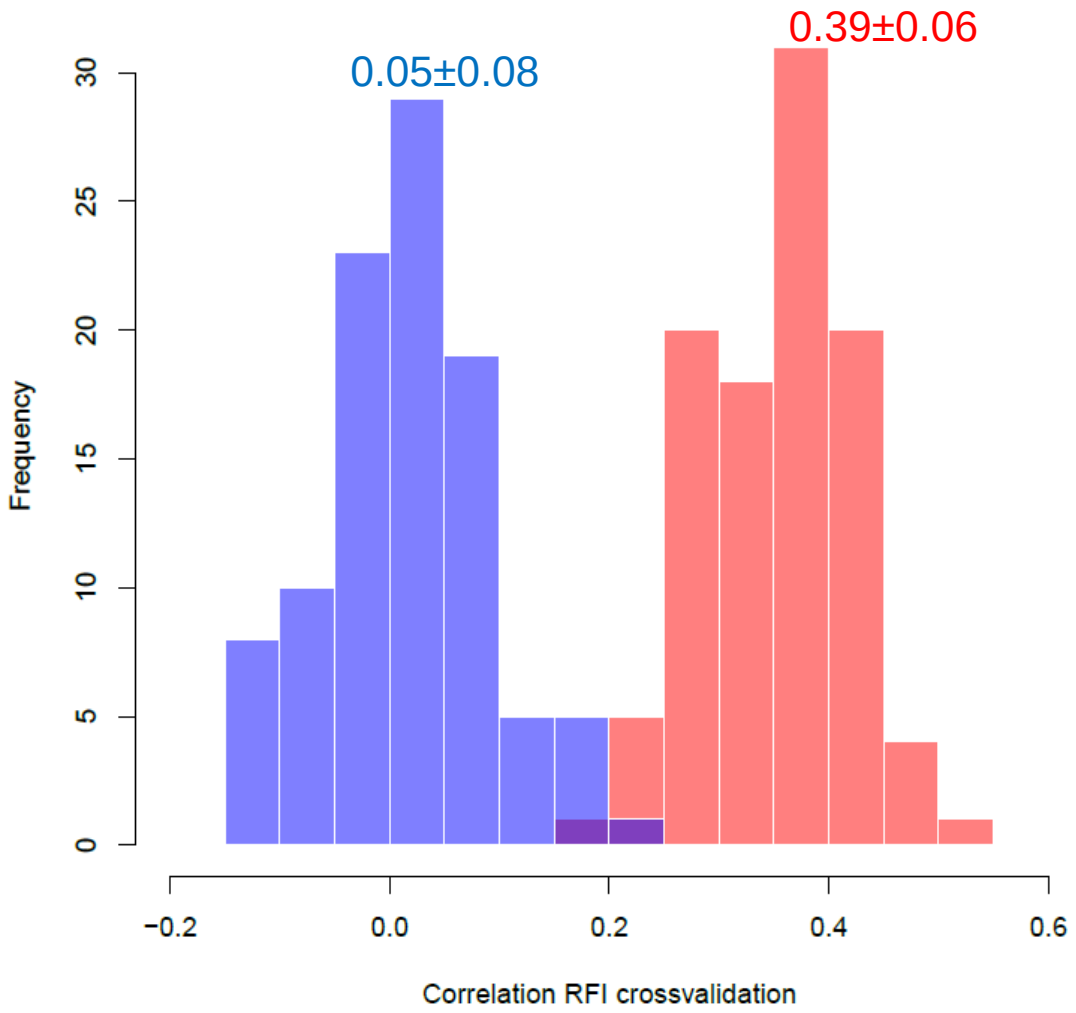
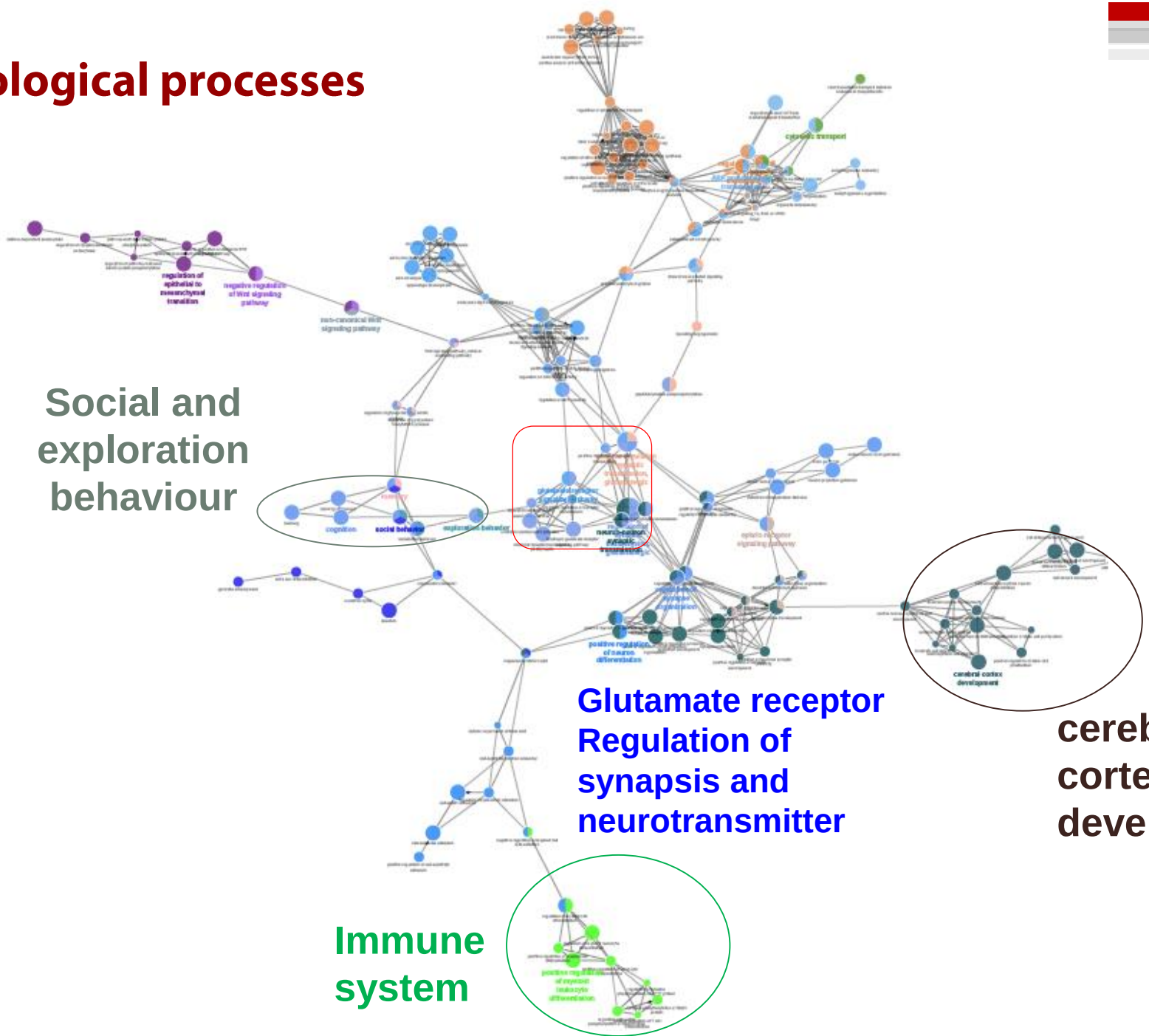
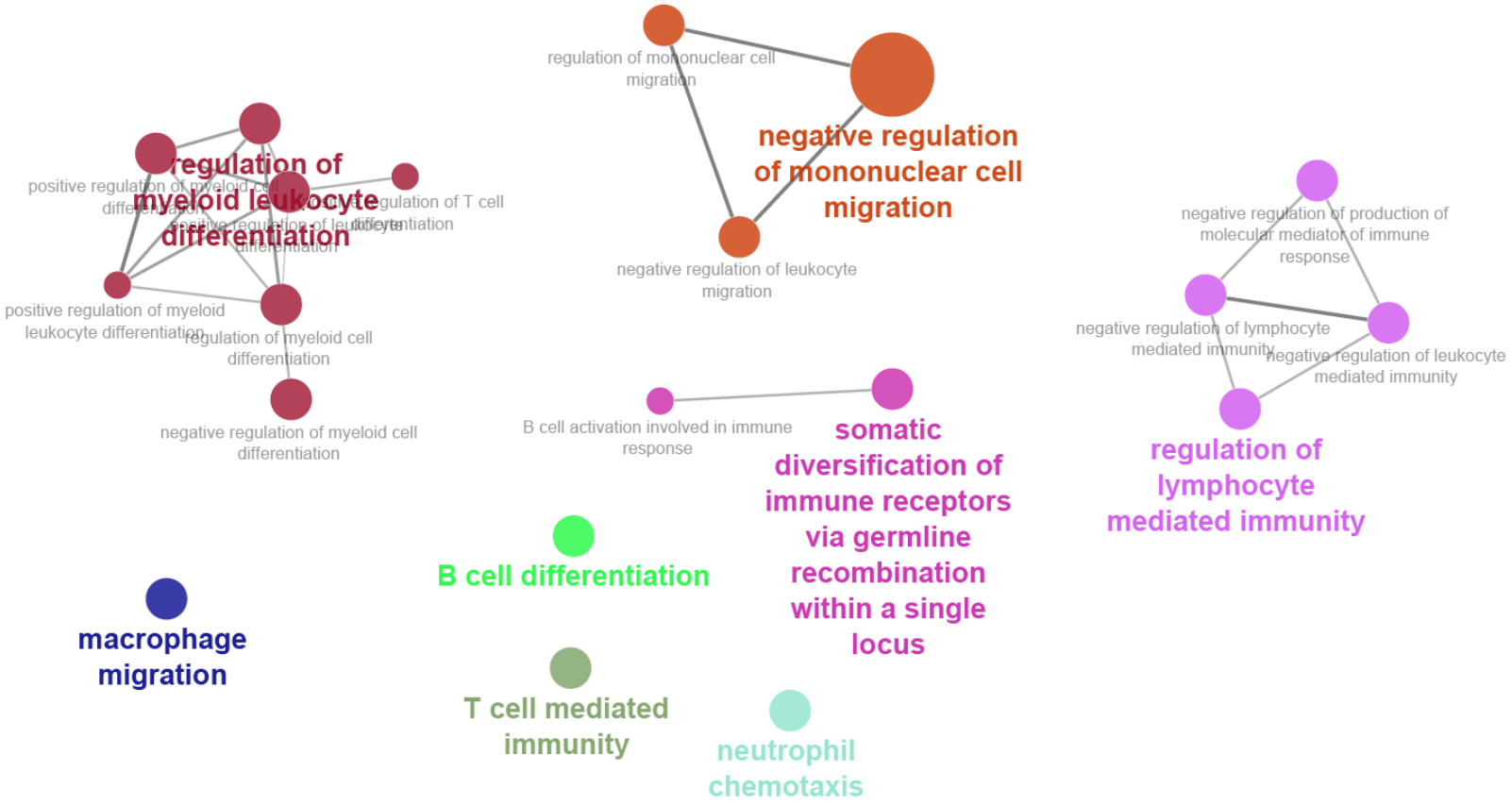


Biological processes



Immune response



RESEARCH ARTICLE Open Access

A transcriptome multi-tissue analysis identifies biological pathways and genes associated with variations in feed efficiency of growing pigs

Florence Gondret[1*], Annie Vincent[1], Magalie Houée-Bigot[2], Anne Siegel[3], Sandrine Lagarrigue[1], David Causeur[2], Hélène Gilbert[4] and Isabelle Louveau[1]

Integrative approach using liver and duodenum RNA-Seq data identifies candidate genes and pathways associated with feed efficiency in pigs

Yuliaxis Ramayo-Caldas[1], Maria Ballester[1], Juan Pablo Sánchez[1], Olga González-Rodríguez[1], Manuel Revilla[2,3], Henry Reyer[4], Klaus Wimmers[4,5], David Torrallardona[6] & Raquel Quintanilla[1]

CONCLUSIONS

- *LHX4*, *POU2AF1* and *TCF7L2* may mediate a highly inter-connected regulatory cascade that seems pivotal for FE in pigs.

- **Immune response** appears consistently involved in FE related traits.

- **Social behaviour**, **neurotransmitte**r and circadian entrainment were also overrepresented biological processes.

PERSPECTIVES

GWAS

Gene expression

Liver and *Gluteus medius*

AWM

sPLS-DA

DE

rCCA

Candidates genes

eGWAS

Candidates SNPs

Genomic prediction

Thank you for your attention

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SELECCIÓN BATALLÉ

LIPGEN projects:

AGL2013-48742-C2-2-R

AGL2007-66707-C02-01

European Commission

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P-SPHERE

Your

Matters

Resume proportion of RFI phenotypic variance and predictions

	AWM	AWM_rand	399 SNPs	399_rand
RFI variance	0.56±0.06	0.10±0.01	0.51±0.07	0.10±0.03
RFI predictions	0.42±0.06	0.04±0.08	0.39±0.06	0.05±0.08