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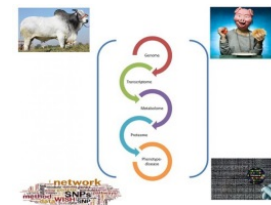
Linear and Bayesian Methods of genome mapping and pathway profiling for fatness in pigs

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Outline

➢   Background & Objectives

➢   Materials & Methods

- ▪ Data

- ▪ GWAS by linear mixed model

- ▪ Bayesian variable selection (Bayes Cπ)

➢ Results

- ▪ GWAS, Annotation, networks and pathways

➢ Conclusions and Future perspectives

BMC
Genetics

RESEARCH ARTICLE

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Genome-wide association and systems genetic analyses of residual feed intake, daily feed consumption, backfat and weight gain in pigs

Duy Ngoc Do[1], Tage Ostersen[2], Anders Bjerring Strathe[1,2], Thomas Mark[1], Just Jensen[3] and Haja N Kadarmideen[1*]

JOURNAL OF ANIMAL SCIENCE
The Premier Journal and Leading Source of New Knowledge and Perspective in Animal Science

Genetic parameters for different measures of feed efficiency and related traits in boars of three pig breeds

D. N. Do, A. B. Strathe, J. Jensen, T. Mark and H. N. Kadarmideen

frontiers in GENETICS

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*]

Journal of Animal Science
The Premier Journal and Leading Source of New Knowledge and Perspective in Animal Science

SNP annotation-based whole genomic prediction and selection: An application to feed efficiency and its component traits in pigs[1]

Duy Ngoc Do[*], Luc L. G. Janss[†], Just Jensen[†] and Haja N. Kadarmideen[2*]

PLOS ONE

Genome-Wide Association Study Reveals Genetic Architecture of Eating Behavior in Pigs and Its Implications for Humans Obesity by Comparative Mapping

Duy Ngoc Do[1], Anders Bjerring Strathe[1,2], Tage Ostersen[2], Just Jensen[3], Thomas Mark[1], Haja N Kadarmideen[1*]

QTL for Backfat in pigs

➢ QTL for BF is reported in every chromosome in pigs

➢ 243 QTL have been detected for Average Backfat Thickness (updated in April, 2015)

Top 15 QTL Traits

Traits	Number of QTL
Drip loss	1,049
Average daily gain	312
Loin muscle area	260
Average backfat thickness	243
Hematocrit	238
Mean corpuscular volume	237
Red blood cell count	221
Age at puberty	208
Backfat at last rib	203
Intramuscular fat content	180
Shear force	175
PH 24 hr post-mortem (loin)	166
Backfat at tenth rib	159
Mean corpuscular hemoglobin content	148
Backfat at rump	147

QTN for Backfat in pigs by GWAS

➤ Fontanesi et al. reported candidate genes on SSC 7 and 18 associated with Italian heavy pigs

➤ Onteru et al. reported fat metabolism genes on SSC 3, 7 and 18 for BF in Yorkshire pigs

➤ Okumura et al. reported QTL on SSC 6 for backfat thickness in Japanese Duroc pig population

➤ We (Do et al. 2014a,b) detected QTL for BF on SSC 2 in Danish pigs

Background

- ➢ Backfat thickness is one of the important traits that determine meat quality ➔ important for producer and also customers

- ➢ Identification of SNPs linked to backfat thickness can provide an alternative tool to improve carcass and meat quality traits

- ➢ Many studies used only one GWAS method

  - ➢ Association based on single method might be limited or inconsistent in results
  - ➢ Validation by several methods before functional studies - important

Objectives

Main Aims: to find

➢ Top SNPs via Linear and Bayesian mixed methods

➢ Positional candidate genes, networks and biological pathways for fatness trait via bioinformatics & systems biology
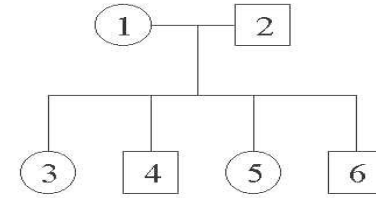
Materials and Methods: GWAS

Phenotypic records

(8.6 ±1.3 mm)

Genotypic records
~ 600 boars

Pedigree available
from 1970s

Quality control

- 37,192 SNPs and
- 596 pigs

Association test

Functional enrichment,
Pathway profiling

- Call rate of 0.95,

- HWe (p< 0.0001)

- MAF> 0.05

Methods

Association test (linear mixed model – LMM)

Model: $y = 1\mu + \mathbf{Z}a + \mathbf{m}g + e$

y: deregressed EBV (Garrick et al, 2009)
a: random polygenic effect
g: additive effect of the SNP
e: error term

• Implemented in DMU package

Methods

Bayesian variable selection (Bayes Cπ)

$$\mathbf{y} = \mathbf{1}\mu + \mathbf{X}b + \mathbf{M}\beta + e$$

y: deregressed EBV as phenotypes

b: environmental effects: pen, herd-year-batch

β : SNP effect

➢ BayesCπ: π proportion of SNPs without effects fitted as unknown and π ~ uniform distribution; prior π = 0.995 (MCMC: 50000, Burn-in : 20000)

➢ Bayes factor = $\dfrac{p/(1-p)}{\pi/(1-\pi)}$ *(Π: prior probability, P: posterior probability)*

➢ Implemented in Bayz package (http://bayz.biz/)

➢ Find using genes in 100kb flanking regions from common SNPs detected by both LMM and BayesCπ methods - Pathway annotation in DAVID
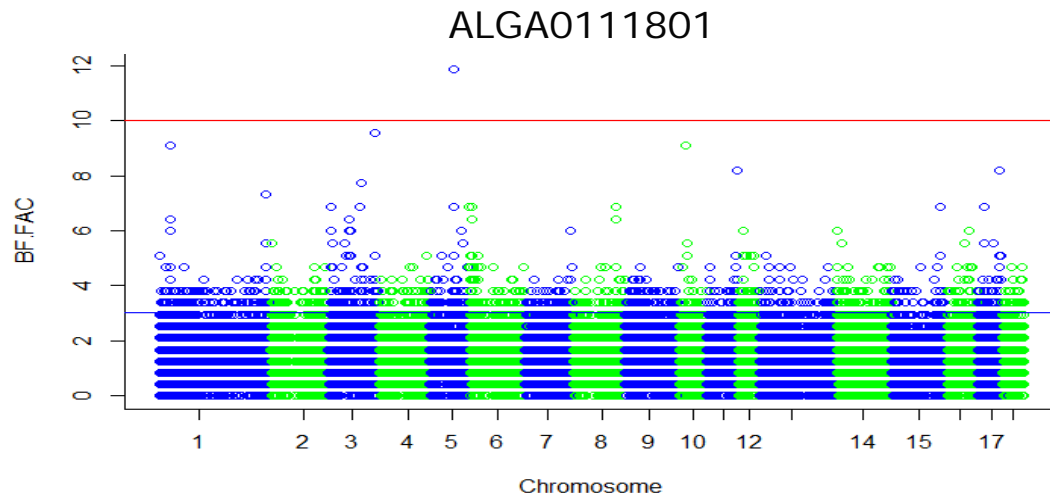
Results

Manhattan plot for P value from LMM
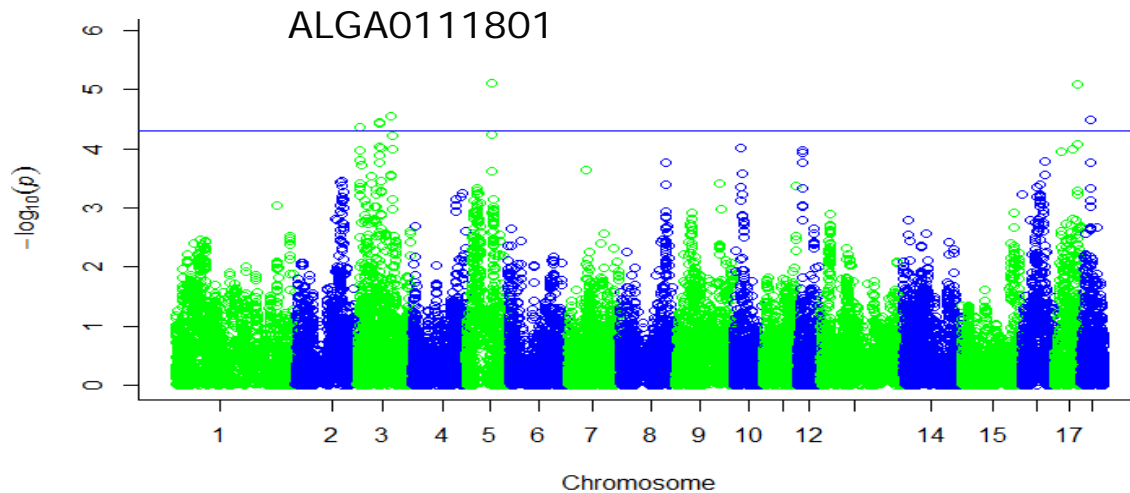
Detected 9 significant SNPs on SSC 3,5,17 and 18 (p < 5e-05)

Results

Manhattan plot for Bayes Factor using BVS methods

ALGA0111801

- ➢ ALGA0111801 has a Bayes factor > 10(significant level)

- ➢ 74 SNPs with BF > 5 (suggestive level)

- ➢ QTL region on SSC1, 2, and 10 reported in BVS method

Results

28 common SNPs among two methods (in top 100 SNPs)

snp	chr	position	P value	Bay.Fac	Regions
ASGA0013249	3	9410336	4.3E-05	6.86	intron
H3GA0008606	3	9491312	1.9E-04	5.54	upstream
ASGA0014717	3	58240635	3.6E-05	5.98	downstream
ALGA0019149	3	58257265	3.8E-05	6.42	intergenic
ASGA0014869	3	62638741	5.3E-04	5.10	intron
ASGA0015248	3	90696439	2.9E-05	6.86	intron
ALGA0113932	3	91605127	6.0E-05	7.75	intergenic
ALGA0101441	5	66015525	5.7E-05	5.10	intron
ALGA0111801	**5**	**66156897**	**7.8E-06**	**11.86**	**intergenic**
H3GA0016495	5	66327153	2.5E-04	6.86	upstream
DIAS0003118	10	19853519	9.6E-05	9.10	synonymous
ASGA0046875	10	20259974	4.5E-04	5.10	intergenic
CASI0009135	10	21907460	6.0E-04	5.54	upstream

Results: Genes nearby ALGA0111801 for average backfat thickness on SSC 5


BF QTL on SSC5

Ensembl genes
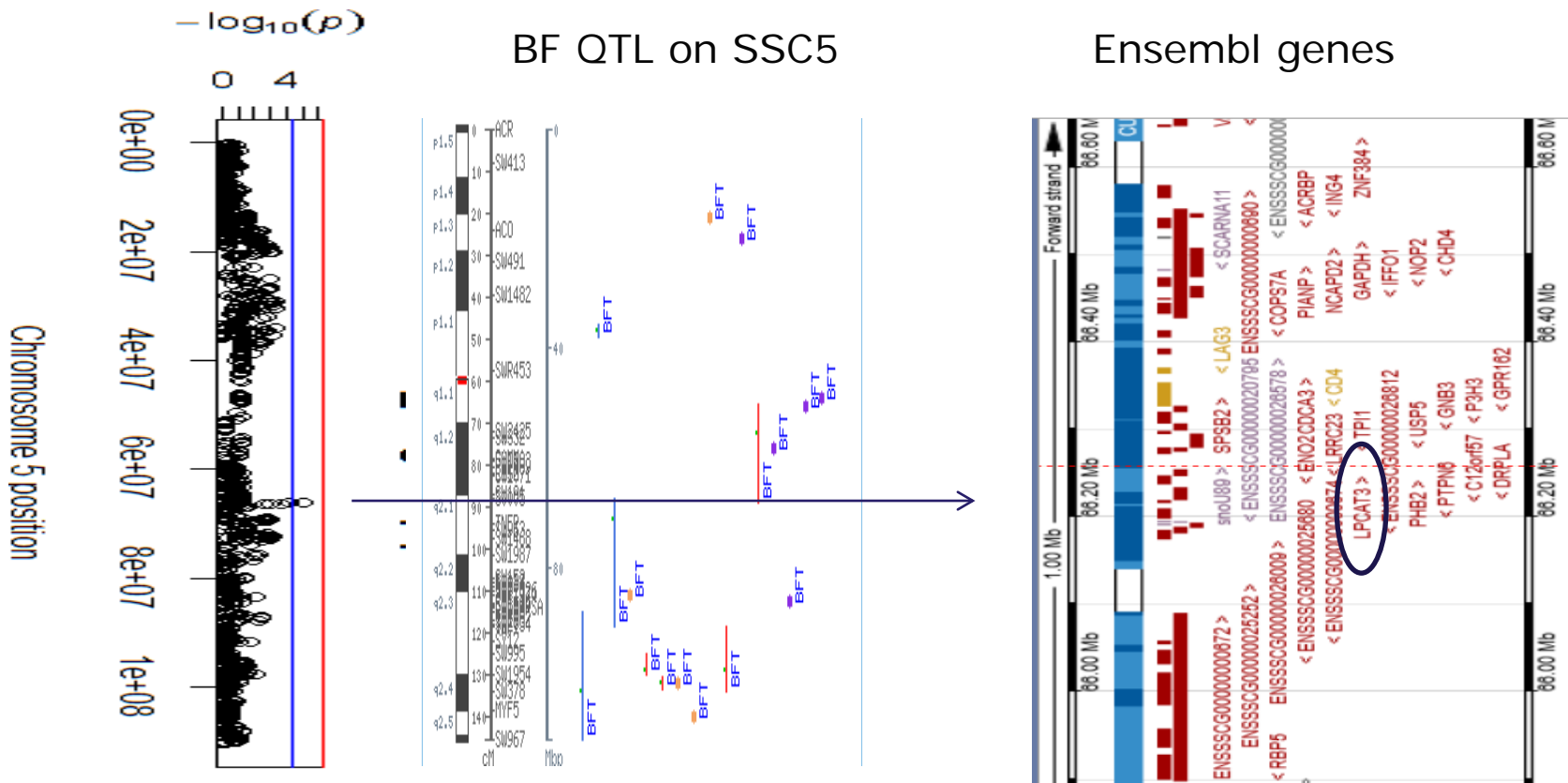
Results: Overlapped and Novel QTNs for average backfat thickness on SSC 3
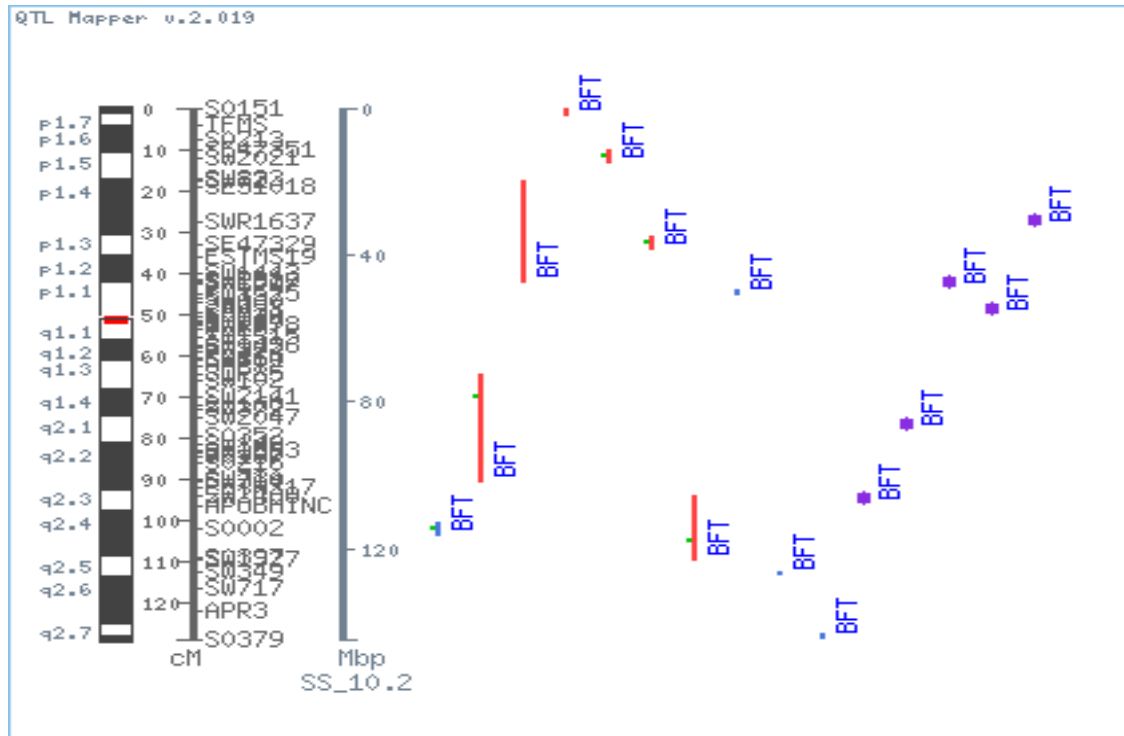
Results: Potential candidate genes

➢ Approximately 17kb apart from ALGA0111801 (p = 7.77e-06 and BF = 11.86) is the **LPCAT3** gene

➢ **LPCAT3** mediates the conversion of lysophosphatidylcholine into phosphatidylcholine in the phospholipid metabolism process

➢ Interaction with the SOAT1 and SOAT2 genes

are important for cholesterol regulation –

Fatness trait.

➢ No functional studies of LPCAT3 gene

in pigs so far but may be recommended
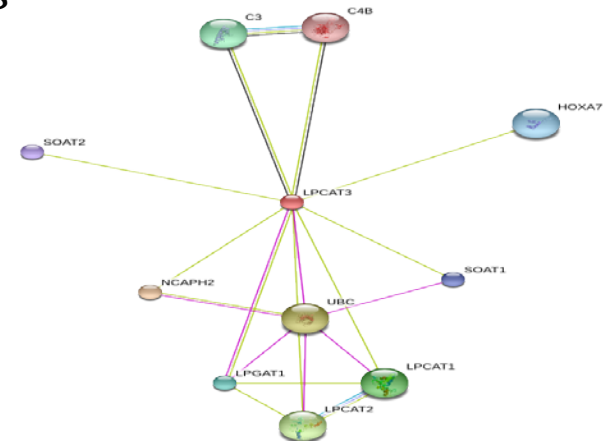
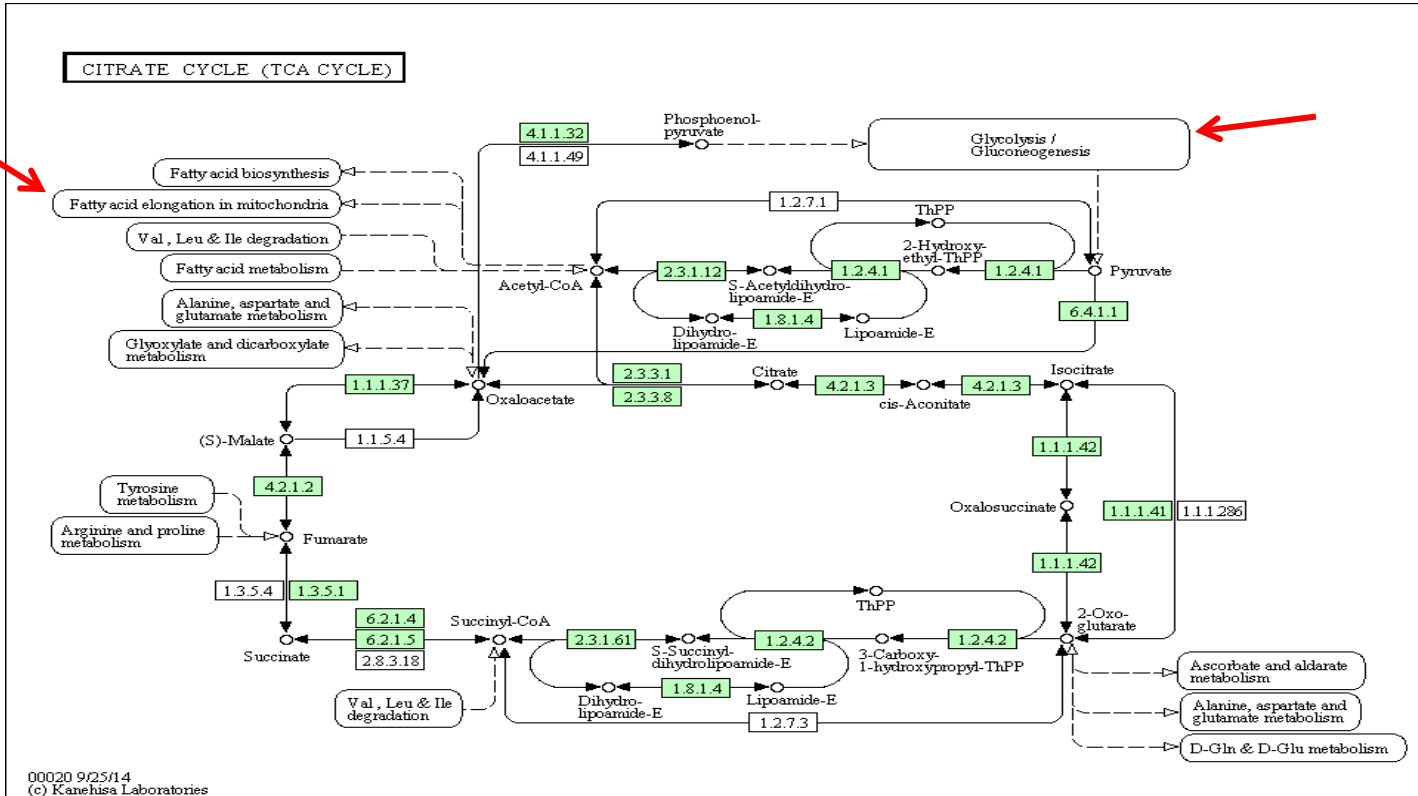# Results: Positional candidate genes around 50kb of ALGA0111801

Gene Name	SSC	Start Position	Gene Description
ABCA4	4	134846031	ATP-binding cassette, sub-family A (ABC1), member 4
CCDC88A	3	90623418	coiled-coil domain containing 88A
CDCA3	5	66295034	cell division cycle associated 3
COA5	3	58229625	cytochrome c oxidase assembly factor 5-like
LPCAT3	5	66174538	lysophosphatidylcholine acyltransferase 3
MGAT4A	3	58112127	mannosyl (alpha-1,3-)-glycoprotein beta-1,4-N-acetylglucosaminyltransferase, isozyme A
MTIF2	3	90740359	mitochondrial translational initiation factor 2
PRKRIP1	3	9518708	PRKR interacting protein 1 (IL11 inducible)
TUBGCP3	11	85779294	tubulin, gamma complex associated protein 3

Results: Function enrichment on biological process and pathways

Sublist	Category	Term	RT	Genes	Count	%	P-Value
☐	GOTERM_BP_ALL	transport	RT	▮	7	0.4	2.2E-2
☐	GOTERM_BP_ALL	establishment of localization	RT	▮	7	0.4	2.2E-2
☐	GOTERM_BP_ALL	localization	RT	▮	7	0.4	2.5E-2
☐	GOTERM_BP_ALL	system process	RT	▮	3	0.2	3.5E-2
☐	PANTHER_PATHWAY	P00043:Muscarinic acetylcholine receptor 2 and 4 signaling pathway	RT	▮	2	0.1	8.3E-2
☐	KEGG_PATHWAY	Citrate cycle (TCA cycle)	RT	▮	2	0.1	8.7E-2
☐	GOTERM_BP_ALL	synaptic transmission	RT	▮	2	0.1	9.4E-2

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Results: Pathway profiling: Citrate pathway

➢ An important aerobic pathway for the oxidation of carbohydrates and fatty acids.

Conclusion

- ✓ Identification of several novel regions that might be important for fatness traits in pigs

- ✓ Various GO terms found to be associated with fatness traits

- ✓ More functional validation for positional candidate genes are needed

- ✓ Some of the top SNPs may be considered in QTN-based Genomic Selection (BLUP|GA, sgBLUP)

Acknowledgements

- Danish Pig Research Center

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THANK YOU

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