MARIA RITA GONÇALVES DA SILVA

A META-ANALYSIS OF GENOME-WIDE ASSOCIATION STUDIES TO IDENTIFY CANDIDATE GENES FOR FEED EFFICIENCY TRAITS IN PIGS

Dissertation submitted to the Animal Science Graduate Program of the Universidade Federal de Viçosa in partial fulfillment of the requirements for the degree of *Magister Scientiae.*

Adviser: Paulo Sávio Lopes

Co-advisers: Delvan Alves da Silva
Renata Veroneze

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Assent:

Maria Rita Gonçalves da Silva

Maria Rita Gonçalves da Silva
Author

Paulo Sávio Lopes

Paulo Sávio Lopes
Adviser

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ABSTRACT

SILVA, Maria Rita Gonçalves da, M.Sc., Universidade Federal de Viçosa, April 2024. **A meta-analysis of genome-wide association studies to identify candidate genes for feed efficiency traits in pigs.** Advisor: Paulo Sávio Lopes. Co-advisors: Delvan Alves da Silva and Renata Veroneze.

The pig production industry is an activity of great importance for the economic and social scenarios of the Brazilian and world markets. The growing prominence of feed efficiency traits in production systems, due to their impact on production costs and the environment, has increased the importance given to these traits in animal breeding programs. Genome wide association studies (GWAS) have emerged as an important methodology for assessing the genetic background of complex traits, contributing to a better biological understanding of the trait under study. In this context, this study was carried out with the main objective of identifying and validating candidate genes associated with feed conversion ratio (FCR) and residual feed intake (RFI) through a systematic review and meta-analysis of GWAS in pigs. The systematic review was conducted to compile the studies that would make up the database. For the meta-analysis, information on the significant markers, including associated p-values and number of observations, was extracted from each article. The METAL software was used to implement the meta-analysis. After the meta-analysis, Bonferroni correction was applied considering an alpha of 0.05 to establish statistically significant associations for the genome-wide significance level, by dividing alpha by the number of SNPs tested in the meta-analysis. The significant SNPs in the meta-analysis were used to identify candidate genes. An enrichment analysis was conducted using the Database for Annotation, Visualization, and Integrated Discovery (DAVID). The results of the systematic review revealed 13 studies, of which 10 evaluated FCR and 6 evaluated RFI, identifying a total of 160 markers for FCR and 96 for RFI. After the meta-analysis, 145 and 90 markers were significantly associated with FCR and RFI, respectively. The gene annotation process resulted in 105 and 114 genes for FCR and RFI, respectively. The enrichment analysis for FCR resulted in 16 significant gene ontology (GO) terms, while 6 terms were identified for RFI. The *MED18, PHACTR4, ABCC2, TRHDE, FRS2, FAR2* and *FIS1* genes stand out as strong candidates for FCR, and the *ADGRL2, ASGR1, ASGR2* and *MAN2B1* genes for RFI.

Keywords: Feed conversion ratio; Residual feed intake, GWAS.

RESUMO

SILVA, Maria Rita Gonçalves da, M.Sc., Universidade Federal de Viçosa, abril 2024. **Uma meta-análise de estudos de associação genômica ampla para identificar genes candidatos para características de eficiência alimentar em suínos.** Orientador: Paulo Sávio Lopes. Co-orientadores: Delvan Alves da Silva e Renata Veroneze.

A cadeia produtiva de suínos é uma atividade de grande importância para o cenário econômico e social do mercado brasileiro e mundial. A crescente proeminência das características de eficiência alimentar nos sistemas de produção, devido ao seu impacto nos custos de produção e no ambiente, aumentou a importância dada a essas características nos programas de melhoramento animal. Os estudos de associação genômica ampla (GWAS) têm se destacado como uma importante metodologia para avaliar a arquitetura genética de características complexas, contribuindo para uma melhor compreensão biológica da caraterística em estudo. Nesse contexto, o presente estudo foi realizado com o objetivo principal de identificar e validar genes candidatos associados com a taxa de conversão alimentar (CA) e ao consumo alimentar residual (CAR) por meio de uma revisão sistemática e de uma meta-análise de GWAS em suínos. A revisão sistemática foi conduzida para compilar os estudos que comporiam o banco de dados. Para a meta-análise, foram extraídas informações dos marcadores significativos, incluindo o p-valor associado e o número de observações de cada artigo. O software METAL foi utilizado para implementar a meta-análise. Após a meta-análise, foi aplicada a correção de Bonferroni a alfa = 0,05 para estabelecer associações estatisticamente significativas para o nível de significância do genoma, dividindo alfa pelo número de SNPs testados na meta-análise. Os SNPs significativos na meta-análise foram utilizados para identificar genes candidatos. Uma análise de enriquecimento foi conduzida usando o *Database for Annotation, Visualization, and Integrated Discovery* (DAVID). Os resultados da revisão sistemática revelaram 13 estudos, dos quais 10 avaliaram CA e 6 avaliaram CAR, identificando um total de 160 marcadores para CA e 96 para CAR. Após a meta-análise, 145 e 90 marcadores foram significativamente associados com CA e CAR, respectivamente. O processo de anotação de genes resultou em 105 e 114 genes para CA e CAR, respectivamente. A análise de enriquecimento para CA resultou em 16 termos de ontologia gênica significativos, enquanto para CAR foram identificados 6 termos. Os genes MED18, PHACTR4, ABCC2, TRHDE, FRS2, FAR2 e FIS1 destacaram-se como fortes genes candidatos para CA, e para CAR, os genes ADGRL2, ASGR1, ASGR2 e MAN2B1.

Palavras-chaves: Taxa de conversão alimentar; Consumo alimentar residual; GWAS.

SUMMARY

CHAPTER 1

INTRODUCTION

The pig production chain is an activity of great importance for the economic and social scenario in Brazil and in the world. Its relevance is linked to the growing demand for pork, which has led farmers to significantly improve production (DING et al., 2017). Thus, the search for more sustainable production systems has been one of the main objectives of professionals in the pig sector.

The concept of sustainability has been gaining prominence and breaking paradigms in pig farming, which it is based on the economic, environmental and social pillars (FREITAS et al., 2022). On the economic front, pork producers face the great challenge of reducing the production costs of their systems. Among these costs, feed is the main one and can represent more than 75% of the total cost in modern production (ALI et al., 2017). Therefore, it is necessary to adopt strategies to achieve greater animal efficiency.

Improving pig efficiency can have an impact on the social aspect, since reducing production costs can contribute to reducing the final cost of pig products, and on the environmental aspect, reducing the impact related to the waste generated (SILVA et al., 2019). This environmental concern is increasingly relevant to society. More efficient animals result in reduced consumption and/or lower demand for feed production, which consequently leads to reductions in the emission of nutrients such as nitrogen and phosphorus, as well as in the emission of greenhouse gases such as methane and CO_2 (FREITAS et al., 2022). Studies such as Soleimani e Gilbert (2021) have reported improving animal efficiency as a promising strategy to reduce these environmental impacts caused by production.

Animal breeding is of great importance for identifying more efficient animals, and selection is an important strategy. Three important traits have been used to evaluate efficiency: feed conversion ratio (FCR), which is the ratio between the feed intake and weight gain; feed efficiency (FE), which is the animal's production divided by feed intake; and residual feed intake (RFI), which is the difference between real feed intake and expected feed intake (DAVOUDI et al., 2022).

Therefore, the future of pork production is centered on animals that efficiently convert feed into meat, and improving feed efficiency traits is a priority in pig breeding programs to reduce the cost per unit produced (GODINHO et al., 2018) and to reduce the environmental impact of pig production. Thus, the study of feed efficiency traits within breeding programs is highly relevant to the production chain, since it can provide permanent and cumulative gains of great importance to production systems.

An important genomic methodology is the genome-wide association study (GWAS), which allows a practical assessment of the genetic architecture of complex traits, such as efficiency traits, based on the identification of genetic markers that can be associated with genes that influence the trait (KRONENBERG, 2008; MAGALHÃES et al., 2016). The GWAS results can be used in genomic selection. However, single GWAS studies show inconsistencies between the results for the same trait, which can be attributed mainly to aspects such as population size, marker density and population genetic structure (ZHANG et al., 2012). One strategy that is gaining ground is the meta-analysis, a methodology that combines the results of several studies (UFFELMANN et al., 2021) and can be applied to improve the accuracy of GWAS results.

LITERATURE REVIEW

Pig efficiency

Improving pig efficiency is highly significant for pig farming (CARMELO et al., 2020), since it is related to animal production and feed consumption (DAVOUDI et al., 2022). In pig breeding programs, selection to improve feed efficiency results in greater efficiency in the use of food by animals in production systems, reducing the costs and the environmental impact. Efficiency can be assessed through various characteristics; in this study, we will focus on three of them, feed conversion ratio (FCR), feed efficiency (FE), and residual feed intake (RFI).

FCR can be defined as the ratio between feed intake and body weight gain, while FE is the ratio between the animal's production and feed intake. Both traits are affected by the animal's initial body weight, feed intake, and growth rate (DAVOUDI et al., 2022).

RFI was first proposed in the early 1940s as an approach related to the rearing of laying birds. Later, in 1963, it was developed for cattle (KOCH et al., 1963) and pigs (FOSTER et al., 1983). This trait can be defined as the difference between observed and predicted feed consumption based on the average requirements for growth and maintenance (CAI et al., 2008). RFI is independent of growth, and selection for low RFI can improve feed efficiency without causing correlated changes in production traits (PRAKASH et al., 2020).

In the study conducted by Do et al. (2013), populations of three breeds were used to estimate genetic parameters for feed efficient traits in pigs. The heritability estimated for RFI ranged from 0.34 to 0.40, while for FCR it ranged from 0.30 to 0.32. In addition, there was a strong genetic correlation between RFI and FCR (0.85 to 0.91). These results were corroborated by the study of Saintilan et al. (2011), in which the traits showed moderate heritability, with 0.40 and 0.47 for RFI and FCR, respectively. In addition, a genetic correlation of 0.85 was observed between the two traits.

Although studied for a long time, feed efficiency traits are complex and expensive for measuring in large scale, since it requires an automatic feeding system (FU et al, 2020). Increasing our understanding of the architecture and genetic basis behind these traits can provide important information for pig breeding programs.

Genome-wide Association Studies for feed efficiency

Genomics is a science related to the complete study of an organism's genome based on information from the DNA molecule (deoxyribonucleic acid). One of the uses of genomic information in domestic animals is to dissect the genetic architecture of traits of economic interest, determining the genes and their contribution to the phenotype expression.

Animal breeding has made great strides with the sequencing of the genomes of several domestic species and the development of single-nucleotide polymorphisms (SNPs) arrays. SNPs are a class of genetic markers, and according to Brookes (1999), they are the most abundant class of genetic variation found in eukaryotic genomes.

An important genomic methodology currently being used in several studies is genome-wide association studies (GWAS), which focus on identifying markers associated with economically important traits. Initially used to investigate complex diseases in humans, the initial milestone for this approach, as discussed by Visscher et al. (2012), was the 2007 Wellcome Trust Case Control Consortium (WTCCC) paper published in Nature. This study was the first large, well-designed GWAS for complex diseases using an SNP chip with good genome coverage. In animal breeding, the GWAS approach became more widely used when genome sequencing was carried out and high-density marker panels were developed for domestic species (ZHANG et al., 2012).

GWAS has the power to identify genetic variants associated with complex traits, providing a better biological understanding of the trait and a practical approach for evaluating its genetic architecture (KRONENBERG, 2008; MAGALHÃES et al., 2016). In recent years, several GWAS in domestic animals have been reported, addressing a variety of traits. Among these studies are those investigating feed efficiency-related traits in pigs. (HORODYSKA et al., 2017, FU et al., 2020, MIAO et al., 2020, ONTERU et al., 2013, DING et al., 2018)

For FCR, Horodyska et al. (2017) performed a GWAS and reported significant SNPs on pig chromosomes 1, 4, 6, and 15. Similarly, in the study of Fu et al. (2020), significant SNPs were identified on chromosomes 7, 13, 14, 17, and 18, whereas in the study performed by Miao et al. (2021), significant SNPs were located on chromosome 5.

GWAS has also been applied to investigate RFI in pigs. Onteru et al. (2013) reported significant SNPs on chromosomes 3, 5, 6, 7, and 13, while the study of Ding et al. (2018) reported association mainly on chromosome 1.

Despite being widely used in research, GWAS has some limitations that lead to inconsistencies among the results of different studies for the same trait. Zhang et al., (2012) point out some reasons for such inconsistences, as sample size, marker density, population genetic structure and choice of statistical models. Among these aspects, sample size has been identified as an essential factor for GWAS efficiency (FU et al., 2020). According to Korte and Farlow (2013), increasing the sample size improves the power to recover significant associations. Thus, to increase the sample size, an approach that has been widely used is the genome-wide association meta-analysis, a method that combines results from different studies for a more consistent research (UFFELMANN et al., 2021).

Meta-analysis

The term meta-analysis was coined in 1977 by Smith and Glass, who conducted a study in which they statistically aggregated the results of 375 studies on psychotherapy. However, the fundamentals of this method had been used before Smith and Glass' observations. For example, Fisher (1932) proposed a method of combining p-values, and Cochran (1954) worked on the problem of combining results from several independent experiments. Thus, it is believed that the basis of modern meta-analysis comes from these studies.

The methodology of meta-analysis finds application in various scientific fields, with its roots initially in the social sciences, education, and medicine, and later expanding to the agricultural sciences (LOVATTO et al., 2007). In recent years, the interest in the method has intensified in a wide variety of areas, driven by the need to deal with the challenge of compiling the vast volume of information being produced. In this context, meta-analysis has emerged as an effective alternative for analyzing and systematizing these data. This statistical method is characterized as a procedure that combines different studies to provide a summarized result that can be worked on, constituting a reproducible and quantifiable synthesis of the data, improving the statistical power (LOVATTO et al., 2007; EVANGELOU E IOANNIDIS, 2013).

This approach has been increasingly used, since in the process of transforming research results into usable knowledge, a single study may not be enough for an inference process, which calls into question the representativeness of the results (SAUVANT et al., 2005). Thus, using a methodology that allows results to be aggregated into an objective increases the power of the research. For this reason, the first step in carrying out a meta-analysis is to define the objective of the study, i.e. the problem you want to solve, which is essential for defining the next stages of the method, which consist of coding, filtering, weighting the data and analyzing the compiled data (SAUVANT et al., 2005).

In the field of animal breeding, meta-analysis is applied in different contexts, such as estimating genetic parameters, as shown in the studies by Felipe et al. (2021) and Giannotti et al. (2005) in cattle. In addition, this methodology has been also applied to GWAS, in the GWAS meta-analysis (DUARTE et al., 2019; TAHERKHANI et al., 2022; SELL-KUBIAK et al., 2022).

Given the possibility of single GWAS being limited due to sample size and the complexity of the traits analyzed, GWAS meta-analysis synthesizes information from independent studies, increasing the power of association and reducing false-positive results (EVANGELOU AND IOANNIDIS, 2013). The GWAS meta-analysis increases the sample size and examines more variants across the genome than each dataset alone (ZEGGINI AND IOANNIDIS, 2009). Duarte et al. (2019) explored this methodology for RFI in cattle to deepen the understanding of the genetic mechanism underlying this trait. In addition, Taherkhani et al. (2022) and Sell-Kubiak et al. (2022) used the methodology to identify candidate chromosomal regions responsible for milk yield in cows and litter traits in pigs, respectively.

REFERENCES

Ali, B. M., H. H. E. Van Zanten, P. Berentsen, J. W. M. Bastiaansen, P. Bikker, and A Oude Lansink. 2017. Environmental and economic impacts of using co-products in the diets of finishing pigs in Brazil. *Journal of Cleaner Production*. *162*:247-259. doi:10.1016/j.jclepro.2017.06.041.

Brookes, A. J. The essence of SNPs. 1999. Gene. 234:177-186. doi:10.1016/S0378-1119(99)00219-X.

Cai, W., D. S. Casey, and J. C. M. Dekkers. 2008. Selection response and genetic parameters for residual feed intake in Yorkshire swine. J. Anim. Sci. 86:287-298. doi:10.2527/jas.2007-0396.

Carmelo, V. A. O., P. Banerjee, W. J. S. Diniz, and H. N. Kadarmideen. 2020. Metabolomic networks and pathways associated with feed efficiency and related-traits in Duroc and Landrace pigs. Sci Rep. 10:255. doi:10.1038/s41598-019-57182-4.

Cochran, W. G. 1954. The combination of estimated from different experiments. Biometrics. 10:101–129.

Davoudi, P., D.N. Do, S. M. Colombo, B. Rathgeber, and Y. Miar. 2022. Application of genetic, genomic and biological pathways in improvement of swine feed efficiency. Front. Genet. 13:903733. doi:10.3389/fgene.2022.903733

Ding, R., J. Quan, M. Y. X. Wang, E. Zheng, H. Yang, D. Fu, Y. Yang, L. Yang, Z. Li, D. Liu, G. Cai, Z. Wu, and J. Yang. 2017. Genome-wide association analysis reveals genetic loci and candidate genes for feeding behavior and eating efficiency in Duroc boars. PloS One. 12:8:e0183244. doi:10.1371/journal.pone.0183244.

Ding, R., M. Yang, X. Wang, J. Quan, Z. Zhuang, S. Zhou, S. Li, Z. Xu, E. Zheng, G. Cai, D. Liu, W. Huang, J. Yang, and Z. Wu. 2018. Genetic architecture of feeding behavior and feed efficiency in a Duroc pig population. Front. Genet. 9:220. doi: 10.3389/fgene.2018.00220.

Do, D. N., A. B. Strathe, J. Jensen, T. Mark, and H. N. Kadarmideen. 2013. Genetic parameters for different measures of feed efficiency and related traits in boars of three pig breeds, J. Anim. Sci. 91: 4069–4079. doi:10.2527/jas.2012-6197.

Duarte, D. A. S., C. J. Newbold, E. Detmann, F. F. Silva, P. H. F. Freitas, R. Veroneze, M. S. Duarte. 2019. Genome-wide association studies pathway-based meta-analysis for residual feed intake in beef cattle. Anim. Genet. 50:150-153. doi:10.1111/age.12761.

Evangelou, E., and J. P. A.Ioannidis. 2013. Meta-analysis methods for genome-wide association studies and beyond. Nat Rev Genet. 14: 379–389. doi:10.1038/nrg3472.

Fávero, J. A., and E. A. P. Figueiredo. 2009. Evolução do melhoramento genético de suínos no Brasil. Revista Ceres. 56:420-427.

Felipe, E. F., N. A. M. Silva, and G. F. Moraes. 2021. Meta-análise para estimativas de herdabilidade de características ponderais em bovinos da raça nelore. Brazilian Journal of Development. 7:59365-59379. doi.org/10.34117/bjdv7n6-364

Fisher, R. A. 1935. The design of experiments. Edinbourgh: Oliver and Boyd.

Foster, W. H., D. J. Kilpatrick and I. H. Heaney. 1983. Genetic variation in the efficiency of energy utilization by the fattening pig. Animal Production. 37:387–393. doi: 10.1017/S0003356100001999

Freitas, L. S., F. Miranda, and C. Martinez. 2022. A genética do futuro: Eficiência com eficácia em um mundo sustentável. Revista Suíno Brasil.

Fu, L., Y. Jiang, C. Wang, M. Mei, Z. Zhou, Y. Jiang, H. Song, and X. Ding. 2020. A genome-wide association study on feed efficiency related traits in Landrace pigs. Front. Genet. 11:692. doi:10.3389/fgene.2020.00692.

Giannotti, J. D. G., I. U. Packer, and M. E. Z. Mercadante. 2005. Meta-análise para estimativas de herdabilidade para características de crescimento em bovinos de corte. Revista Brasileira de Zootecnia. 34: 4:1173-1180. doi:10.1590/S1516-35982005000400011.

Godinho, R. M., R. Bergsma, F. F. Silva, C. A. Sevillano, E. F. Knol, M. S. Lopes , P. S. Lopes , J. W. M. Bastiaansen, and, S. E. F. Guimarães. 2018. Genetic correlations between feed efficiency traits, and growth performance and carcass traits in purebred and crossbred pigs. J. Anim. Sci. 96:817-829. doi:10.1093/jas/skx011.

Horodyska, J., R. M. Hamill, P. F. Varley, H. Reyer, and K. Wimmers. 2017. Genome-wide association analysis and functional annotation of positional candidate genes for feed conversion efficiency and growth rate in pigs. PLoS ONE. 16:6:e0173482. doi:10.1371/journal.pone.0173482.

Koch, R. M., L. A. Swiger, D. Chambers, and K. E. Gregory. 1963. Efficiency of Feed Use in Beef Cattle. Journal Animal Science. 22:486–494.

Korte, A., and A. Farlow. 2013. The advantages and limitations of trait analysis with GWAS: a review. Plant Methods. 9:29. doi:10.1186/1746-4811-9-29.

Kronenberg, F. 2008. Genome-wide association studies in aging-related processes such as diabetes mellitus, atherosclerosis and cancer. Experimental Gerontology. 43:39–43. doi:10.1016/j.exger.2007.09.005.

Lovatto, P. A., C. R. Lehnen, I. Andretta, A. D. Carvalho, and L. Hauschil. 2007. Meta-análise em pesquisas científicas - enfoque em metodologias. Revista Brasileira de Zootecnia. 36:285-294. doi:10.1590/S1516-35982007001000026.

Magalhães, A. F. B., G. M. F. Camargo, G. A. F. Junior, D. G. M. Gordo, R. L. Tonussi, R. B. Costa, R. Espigolan, R. M. O. Silva, T. Bresolin, W. B. F. Andrade, L. Takada, F. L.B. Feitosa, F. Baldi, R. Carvalheiro, L. A. L. Chardulo, and L. G. Albuquerque. 2016. Genome-wide association study of meat quality traits in Nellore cattle. PLoS ONE. 11:6:e0157845. doi:10.1371/journal.pone.0157845.

Miao, Y. Q. Mei, C. Fu, M. Liao, Y. Liu, X. Xu, X. Li, S. Zhao, and T. Xiang. 2021. Genome-wide association and transcriptome studies identify candidate genes and pathways for feed conversion ratio in pigs. BMC Genomics. 22:294. doi:10.1186/s12864-021-07570-w

Neeteson-Van Nieuwenhoven, A. M., P. Kanap, and S. Avendaño. 2013 The role of sustainable commercial pig and poultry breeding for food security. Animal Frontiers. 3:52-57. doi:10.2527/af.2013-0008.

Onteru, S. K., D. M. Gorbach, J. M. Young, D. J. Garrick, J. C. M. Dekkers, and M. F. Rothschild. 2013. Whole genome association studies of residual feed intake and related traits in the pig. PloS One. 8:6:e61756. doi:10.1371/journal.pone.0061756

Patience, J. F., M. C. Rossoni-Serão, and N. A. Gutiérrez. 2015. A review of feed eficiency in swine: biology and application. J. Animal Sci. Biotechnol. 6(1):33. doi:10.1186/s40104-015-0031-2

Prakash, A., V. K. Sazena, and M. K. Singh. 2020. Genetic analysis of residual feed intake, feed conversion ratio and related growth parameters in broiler chicken: a review. World's Poultry Science Journal. 76: 304-317. doi:10.1080/00439339.2020.1735978

Relatório Anual. Associação Brasileira de Proteína Animal. São Paulo, 2022.

Saintilan, R., I. Mérour, S. Schwob., P. Sellier, J. P. Bidanel, and H. Gilbert. 2013. Genetic parameters and halothane genotype effect for residual feed intake in Piétrain growing pigs. Livestock Science. 142: 203-209.

Sauvant, D., P. Schmidely , and J. J. Daudin. 2005. Les méta-analyses des données expérimentales: applications en nutrition animale. INRAE Productions Animales. 18:1,:63-73. doi:10.20870/productions-animales.2005.18.1.3510

Sell-Kubiak E., J. Dobrzanski, M. F. L. Derks, M. S. Lopes, and T. Szwaczkowski. 2022. Meta-analysis of SNPs determining litter traits in pigs. Genes. 13:10. doi:10.3390/genes13101730.

Silva, E. F., M. S. Lopes, P. S. Lopes, and E. Gasparino. 2019. A genome-wide association study for feed efficiency-related traits in a crossbred pig population. Animal. 13:2447-2456. doi:10.1017/S1751731119000910

Smith, M. L., and G. V. Glass. 1977. Meta-analysis of psychotherapy outcome studies. American Psychologist. 32:752-760.

Smith, S. N., M. E. Davis, and S. Loerch. 2010. Residual feed intake of Angus beef cattle divergently selected for feed conversion ratio. Livestock Science. 132:41–47. doi:10.1016/j.livsci.2010.04.019

Soleimani, T., and H. Gilbert. 2021. An approach to achieve overall farm feed efficiency in pig production: environmental evaluation through individual life cycle assessment. Int J Life Cycle Assess. 26:455–469. doi:10.1007/s11367-020-01860-3

Taherkhani, L., M. H. Banabazi, N. EmamJomeh-Kashan, A. Noshary, and I. Imumorin. 2022. The Candidate Chromosomal Regions Responsible for Milk Yield of Cow: A GWAS Meta-Analysis. Animals. 12(5). doi:10.3390/ani12050582.

Uffelmann, E., Q. Q. Huang, N. S. Munung, J. Vries, Y. Okada, A. R. Martin, H. C. M., T. Lappalainen, and D. Posthuma. 2021. Genome-wide association studies. Nature Reviews Methods Primers. 1:59. doi:10.1038/s43586-021-00056-9.

Visscher, P. M., M. A. Brown, M. I. McCarthy, J. Yang. 2012. Five years of GWAS discovery. The American Journal of Human Genetics. 90: 7-24. doi: 10.1016/j.ajhg.2011.11.029

Zeggini, E., J. P. A. Ioannidis. 2009. A. Meta-analysis in genome-wide association studies. Future Medicine, Pharmacogenimics. 10:191-201. doi: 10.2217/14622416.10.2.191.

Zhang, H., Z. Wang, S. Wang, and H. Li. 2012. Progress of genome wide association study in domestic animals. Journal of Animal Science and Biotechnology. 3:1-10. doi.org/10.1186/2049-1891-3-26.

CHAPTER 2

INTRODUCTION

The growing prominence of feed efficiency traits in production systems, related to their impact on production costs and environment, increased the importance given to these traits in animal breeding programs. The advancement of dense genomic marker panels, coupled with the significant reduction in genotyping costs in recent years, have driven the growing application of genome-wide association studies (GWAS) in livestock. GWAS focus on identifying genetic variants associated with relevant traits, such as feed efficiency traits. Their practical approach to evaluate the genetic architecture of complex traits offers an important contribution to a better biological understanding of the trait under study, since it allows the identification of quantitative trait loci (QTL) regions (KRONENBERG, 2008; MAGALHÃES et al., 2016) and candidate genes.

Various GWAS reported SNP associations and candidate genes for feed efficiency traits (Sahana et al., 2013, Ding et al., 2017, Miao et al., 2021, Ding et al., 2018, Li et al., 2020). However, there are significant differences among them. For example, evaluating feed conversion ratio (FCR) in pigs, Sahana et al. (2013) identified significant SNPs only on chromosome 14, while in the results presented by Miao et al. (2021) and Ding et al. (2017), significant SNPs were identified on chromosomes 5 and 12, respectively. These differences were also observed in GWAS with pigs for residual feed intake (RFI). In the study of Ding et al. (2018), the significant SNPs were mainly located on chromosome 1, while Li et al. (2020) reported significant SNPS mainly on chromosome 2for this trait.

These discrepancies between studies can be explained by the fact that these traits present complex genetic architectures, leading to different identification of significant regions in GWAS reports. Additionally, these differences may be explained by the differences in the populations, marker set, and in the sample size used (KORTE et al., 2013). As indicated by Fu et al. (2020), the sample size is an essential factor for the power of GWAS, increasing the importance of using methods that integrate different studies to improve the identification of QTL. One of the main approaches to integrate data is the meta-analysis, a statistical method that combines results from different studies to provide a summarized outcome. Meta-analysis has become a popular approach for discovering of new QTL for common phenotypes (EVANGELOU & IOANNIDIS, 2013).

GWAS meta-analysis has emerged as a strategy capable of increasing the power of detecting association signals compared to individual data sets (ZEGGINI & IOANNIDIS, 2009), providing a better understanding of the genetic architecture of the traits under study. This is particularly relevant, since isolated studies have limitations in terms of statistical power and the reliability of results (TAHERKHANI et al., 2022). Thus, meta-analysis is becoming increasingly crucial in GWAS for quantitative traits (DE BAKKER et al., 2008), allowing the combination of results at low cost. In addition, meta-analysis can help identify false positives and makes the results clearer, as evidenced by Duarte et al. (2019), which linked SNPs to genes and metabolic pathways. In this context, we aimed to identify and validate candidate genes associated with feed conversion ratio (FCR) and residual feed intake (RFI) in pigs through a systematic review and meta-analysis of GWAS for these traits.

MATERIAL AND METHODS

Systematic review

A systematic review was performed to gather studies for a database building. The searches were carried out on the Web of Science, Scopus, and Pubmed websites. The search terms used were combinations of keywords with the following criteria: a) species ("pig", "swine"); b) type of association test ("genome wide association", "GWAS"); and c) term related to the trait evaluated ("feed efficiency", "feed conversion", "residual feed intake", "RFI"). We also used the Boolean Operators "and" and "or", which are conjunctions used to form combinations of keywords, to find more focused and productive results (KOUTSOS et al., 2019). We used two combinations of keywords as presented below:

- “pig” **OR** “swine” **AND** “genome wide association” **OR** “GWAS” **AND** “feed efficiency” **OR** “feed conversion”
- “pig” **OR** “swine” **AND** “genome wide association” **OR** “GWAS” **AND** “feed efficiency” **OR** “residual feed intake” **OR** “RFI”

The search was conducted by two independent people. After performing the searches, the results were added to the End Note application, so that the next steps could be carried out. Firstly, duplicate papers were excluded and then the query terms for each combination were checked to see if they appeared in the title and abstract of each paper. After this stage, the references were checked individually to analyze if the full text was available, if the specie was a pig, if the methodology adopted was GWAS for FCR and RFI, and if the SNP, its genomic coordinate (chromosome and location on the chromosome) and its p-value were provided.

After a thorough reading, those papers that did not provide sufficient information were excluded. The articles considered eligible for the research, after reviewing the full text, were included in the final set of studies to assemble the database. The following information was extracted from each paper: author, SNP chip, traits, number of observations, significant SNPs identification, the chromosome and genomic position of the significant SNPs, and the associated p-value.

An additional search was carried out using Google Scholar to find articles that had not yet been selected. The same keyword combinations and article filtering process were used.

Meta-Analysis

The genomic location of each SNP was updated using the Biomart tool available on the Ensembl website (*Sus scrofa* 11.1). After all filtering, 160 SNPs for FCR and 96 for RFI were included in the database. The meta-analysis was based on the weighted Z scores model, implemented using METAL software (WILLER et al. 2010), which is a tool for meta-analysis genome wide association scans. This method considers the p-value associated with the marker, direction of effect and the number of individuals included in each GWAS study. First, for each marker, a reference allele is selected and a z-statistic characterizing the evidence of association is calculated. The z-statistic summarizes the magnitude and the direction of the effect relative to the reference allele and all studies are aligned to the same reference allele. Next, an overall z-statistic and p-value are then calculated from a weighted sum of the individual statistics. Weights are proportional to the square-root of the number of individuals examined in each sample and selected such that the squared weights sum to 1.0 (SANNA et al., 2008; WILLER et al., 2010). However, in this study the direction of the effect was considered to be the same for all the markers, since the reference allele is not available in the papers.

After the meta-analysis, to establish statistically significant associations, the Bonferroni correction was applied at alpha = 0.05 for the genome-wide significance level, dividing alpha by the number of SNPs tested in the meta-analysis

Gene annotation and functional analyses

The significant SNPs in the meta-analysis were used to identify candidate genes. SNP - gene annotation was carried out using a window of 32kb either side of each marker using the Biomart package in the R software, following Verardo et al. (2016). Gene annotations, including gene identifiers, symbols, and locations were performed.

Enrichment analyses were then conducted using the Database for Annotation, Visualization, and Integrated Discovery (DAVID) (HUANG et al., 2009; SHERMAN et al., 2022). DAVID is a website bioinformatic database that is designed to identify the biological functions of genes or proteins. The analyses included Gene Ontology (GO) and KEGG pathways to identify biological processes, molecular functions, cellular components, and biological pathways associated with the candidate genes identified after the meta-analysis. A p-value < 0.05 was considered statistically significant.

Gene Network Analysis

The gene network analysis was carried out with GeneMANIA (WARDE-FARLEY et al., 2010) as a plug-in for Cytoscape (SHANNON et al., 2003), with the human gene annotation as a reference. This is a tool for looking for integration between genes or sets of genes and makes it possible to evaluate co-expression, physical integration, genetic integrations, shared protein domains, and co-localizations. This analysis was performed with the genes identified after the meta-analysis and only genes with complete identification and symbol information were used. Three gene networks were built: one for the genes associated with FCR, another for the genes associated with RFI and a third network combining the genes of both traits.

RESULTS

Systematic review

The systematic review resulting from the search processes made it possible to identify 208,880 scientific reports, of which 8,806 came from Pubmed, 74 from Scopus, and 200,000 from Web of Science. The paper selection process is summarized in figure 1. Among the studies found, 62,453 duplicated articles were excluded and 146,427 studies remained for the first filtering stage, in which it was checked whether the query terms for each combination appeared in the title and abstract of each paper.

At this stage, 32 references were selected after evaluating the titles, and 20 of these were selected after reading the abstracts. Thus, these 20 studies were individually full-text analyzed to determine whether or not they should be included in the database. After assessing whether the specie used was a pig, whether the methodology adopted was a GWAS for FCR and RFI, whether the SNP, its genomic coordinate and its p-value were provided, 10 articles that did not meet the eligibility criteria were excluded. Thus, at the end of the evaluation procedures, 10 studies were selected to make up the database.

An additional search on Google Scholar using the same keyword combinations was carried out. This resulted in 374 articles found, from which six articles were selected according to the same criteria used in full-text analysis. After this analysis, three studies were included in the set of studies to make up the database. Therefore, 13 studies were used to assemble the final database, of which 10 studies evaluated FCR and six were related to RFI, with Ding et al. (2018), Fu et al. (2020), and Li et al. (2020) evaluating both phenotypes. To assemble the database, the following information was extracted from each paper: author, SNPchip, traits, number of observations, significant SNP identification, the chromosome and genomic position of the SNP, and the associated p-value. The complete data collected is presented in supplementary table 1. The overview of the articles is presented in table 1.

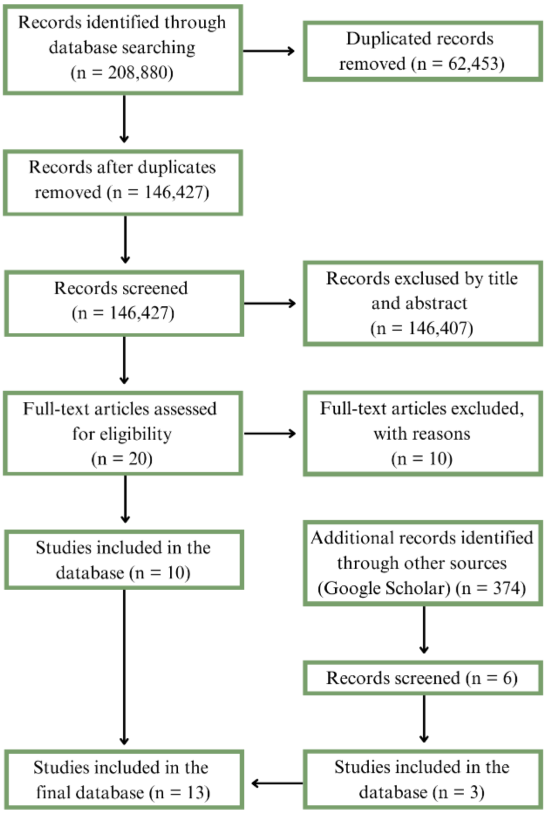

Figure 1. Flowchart of the article selection process in systematic review

Table 1. Papers selected in the systematic review

Paper	Trait	Number of individuals	Number of markers extracted - FCR	Number of markers extracted - RFI
Belous et al., 2019	FCR	715	31	-
Ding et al., 2017	FCR	338	3	-
Fu et al., 2020	FCR and RFI	296	15	21
Horodyska et al., 2017	FCR	952	10	-
Li et al., 2020	FCR and RFI	485	2	22
Miao et al., 2021	FCR	3672	60	-
Reyer et al., 2017	FCR	846	12	-
Sahana et al., 2013	FCR	3071	9	-
Wang et al., 2015	FCR	796	4	-
Bai et al., 2017	RFI	217	-	12
Ding et al., 2018	FCR and RFI	1008	14	14
Do et al., 2014	RFI	596	-	19
Onteru et al., 2013	RFI	1410	-	8
Total number of markers extracted			160	96

FCR = Feed conversion ratio
RFI = Residual feed intake

Meta-analysis

Considering the 13 papers selected in the systematic review, 160 markers for FCR and 96 markers for RFI were identified. For both FCR and RFI, no marker was recorded in more than one study. And 11 markers associated with both traits were identified (rs80795431, rs80853064, rs80872918, rs80887408, rs80897170, rs80919991, rs80939464, rs80948504, rs80976610, rs81349630, rs81349654). The genomic locations of each SNP were updated considering the position in the pig genome, Sus scrofa 11.1 (Supplementary Table 1).

The 160 SNPs for FCR were located on chromosomes (SSC) 1, 2, 3, 4, 5, 6, 7, 9, 11, 12, 13, 14, 15, and 18. The 96 SNPs for RFI were located on chromosomes 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16 and 17. SSC5 presented the highest number of SNPs for FCR, while SSC2 was the one with the highest number of SNPs for RFI. Supplementary Table 2 shows the number of SNPs on each chromosome for the two traits studied.

The meta-analysis was performed using METAL software and the Bonferroni correction was applied at $\alpha = 0.05$ for the significance level of the genome, dividing α by the number of SNPs tested in the meta-analysis. Thus, a SNP was considered significant if its p-value was less than 3.125 x $^{10-4}$ and 5.208 x $^{10-4}$ for FCR and RFI, respectively.

As a result, of the 160 markers extracted from the studies related to FCR, 145 were significantly associated with the trait. Thus, 15 markers that had been reported by other studies did not pass the significance level and could be false positives, being the SNPs rs334464676, rs336083023, rs340527699, rs345794390, rs698819984, rs80812508, rs80844227, rs80883237, rs80895086, rs80904397, rs80934608, rs81245790, rs81332374, rs81454344, rs81467760.

For RFI, of the 96 SNPs extracted, 90 were significantly associated after meta-analysis (rs333944426, rs80875559, rs81258024, rs81311244, rs81402975, rs81430022). The SNPs detected as significant for FCR and RFI by the meta-analysis and their respective p-values are shown in Supplementary table 3.

Gene annotation, functional analysis, and gene networks

The process of annotating the genes associated with the significant SNPs in the meta-analysis was carried out using a genomic window of 32 kb either side of each marker. For FCR, of the 145 significant SNPs, 22 SNPs had more than one associated gene and 33 SNPs were not associated with any gene. The total number of genes identified for FCR was 145 (regardless of duplicated genes). For RFI, 34 SNPs had more than one associated gene and 25 SNPs were not associated with any gene. The total number of genes identified for RFI was 133 (regardless of duplicated genes). Only 3 genes were identified for both traits: ENSSSCG00000054980, ENSSSCG00000056451, and ENSSSCG00000061170. The complete list of genes and their respective information are shown in supplementary table 4.

The functional enrichment analyses carried out on the identified genes revealed 27 GO terms, being 13 biological processes, six cellular components, and eight molecular functions for the genes associated with the FCR. A total of 13 GO terms were identified for RFI, being five biological processes, four cellular components, three molecular functions, and one ligand. Of the total GO identified, 16 and six were considered statistically significant ($p<0.05$) for FCR and RFI, respectively. Tables 2 e 3 show the significant terms identified, their respective p-values, and associated genes for FCR and RFI, respectively. Information on all the terms can be found in supplementary table 5.

These results provide important information on the processes involved with feed efficiency in pigs, highlighting potential processes and genes for research. Furthermore, it is important to note that no GO terms were found in common for both traits, which suggests that FCR and RFI may be associated with different biological processes, despite having a high genetic correlation. This fact shows the complexity underlying feed efficiency in pigs.

Table 2. Significant results of enrichment analyses related to the feed conversion ratio (FCR)

Category	Term	Count	P-Value	Genes
GO: Biological Process	GO:0061386 closure of optic fissure	2	0.009	*MED18, PHACTR4*
GO: Biological Process	GO:2001045 negative regulation of integrin-mediated signaling pathway	2	0.012	*MED18, PHACTR4*
GO: Biological Process	GO:0033598 mammary gland epithelial cell proliferation	2	0.021	*TNFSF11, BTRC*
GO: Biological Process	GO:0043085 positive regulation of catalytic activity	2	0.045	*MED18, PHACTR4*
GO: Biological Process	GO:0048484 enteric nervous system development	2	0.045	*MED18, PHACTR4*
GO: Biological Process	GO:0001843 neural tube closure	3	0.010	*MED18, SUFU, PHACTR4*
GO: Biological Process	GO:0030036 actin cytoskeleton organization	4	0.006	*DLC1, WASF2, MED18, PHACTR4*
GO: Biological Process	GO:0051726 regulation of cell cycle	4	0.009	*MED18, YEATS4, PHACTR4, BTRC*
GO: Biological Process	GO:0007165 signal transduction	5	0.044	*DLC1, TRHDE, ARHGAP27, TCP11L1, TENM3*
GO: Cellular Component	GO:0000178 exosome (RNase complex)	2	0.034	*DIS3L2, ZFC3H1*
GO: Cellular Component	GO:0005779 integral component of peroxisomal membrane	2	0.048	*FIS1, FAR2*
GO: Cellular Component	GO:0030027 lamellipodium	3	0.045	*WASF2, MED18, PHACTR4*
GO: Cellular Component	GO:0016020 membrane	8	0.012	ENSSSCG00000056202, *DLC1*, ENSSSCG00000034739, *TRHDE, FRS2, ABCC2, TNFSF4*, ENSSSCG00000008665
GO: Molecular Function	GO:0072542 protein phosphatase activator activity	2	0.023	*MED18, PHACTR4*
GO: Molecular Function	GO:0003779 actin binding	4	0.034	ENSSSCG00000056202, *WASF2, MED18, PHACTR4*
Molecular Function	KW-0009 actin-binding	4	0.007	ENSSSCG00000056202, *WASF2, MED18, PHACTR4*

Table 3. Significant results of enrichment analyses related to the residual feed intake (RFI)

Category	Term	Count	P-Value	Genes
GO: Biological Process	GO:0000724 double-strand break repair via homologous recombination	3	0.020	*SAMHD1, RAD51B, ZFYVE26*
GO: Biological Process	GO:0030520 intracellular estrogen receptor signaling pathway	2	0.037	*SAFB, POU4F2*
GO: Biological Process	GO:0050684 regulation of mRNA processing	2	0.041	*SAFB, SAFB2*
GO: Cellular Component	GO:0005736 DNA-directed RNA polymerase I complex	2	0.035	*POLR1D, LOC106505238*
GO: Molecular Function	GO:0030246 carbohydrate binding	5	0.001	*ASGR1, ASGR2, MAN2B1,* ENSSSCG00000040377, *ADGRL2*
GO: Molecular Function	GO:0003677 DNA binding	9	0.031	*HIPK1,* ENSSSCG00000013715, *ILF3, RAD51B, NFIX, POLR1D, PHTF1, RFX2, LOC106505238*

Gene interaction networks were constructed using GeneMANIA as a plug-in for Cytoscape. These analyses aimed to investigate the interactions between genes related to the traits studied in our research, since this knowledge is fundamental to the understanding of the biological underlying mechanisms.

To build the gene networks, only the genes associated with the significant SNPs after the meta-analysis and with complete identification and symbol information were used. Three gene networks were built: one for the genes associated with the significant SNPs related to FCR, another for the genes associated with the significant SNPs related to RFI, and a third combining the genes of both traits.

For the network associated with FCR, 62 genes were used. The network was made up of 82 nodes, which represent the individual genes. This is because 20 other functionally similar genes (in gray) have been identified by the software in previously published papers. The network also showed 1,066 edges, which represent the interactions or relationships between the genes. Of these, 924 are co-expression, 10 physical interactions, five predicted, 18 co-localization and 109 genetic interactions, as shown in figure 2. All the genes included in the network interacted with each other.

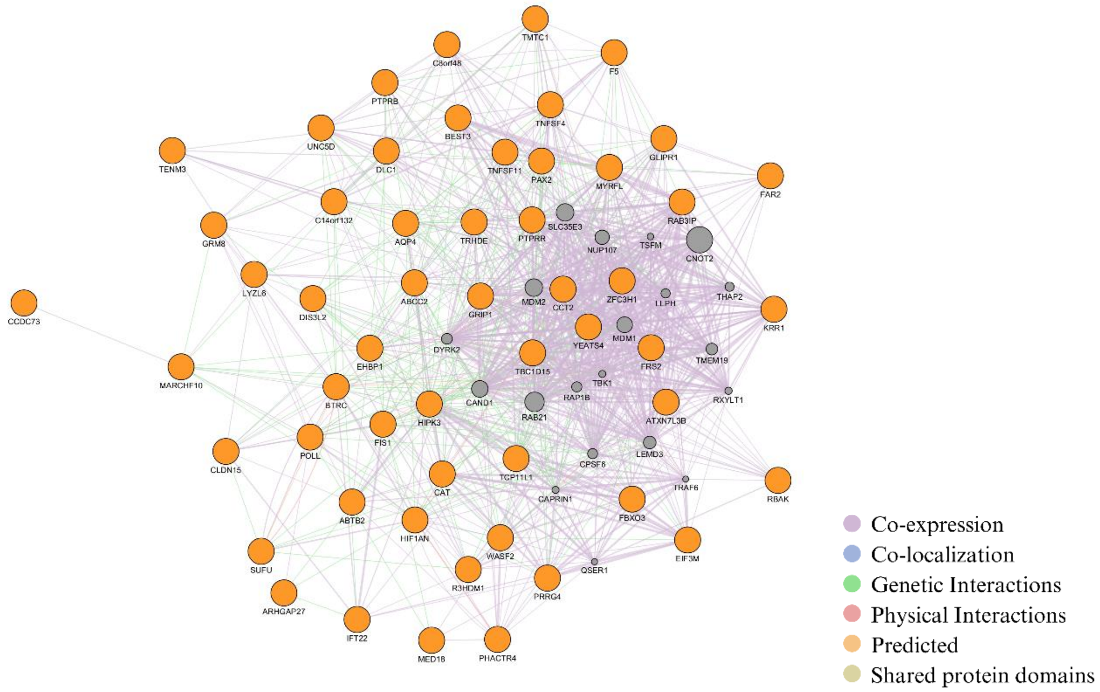

Figure 2. Gene network analysis for feed conversion ratio (FCR)

The gene network associated with RFI was built with a total of 74 nodes, 54 genes associated with significant SNPs after meta-analysis, and 20 other functionally similar genes (in gray). This network showed 962 edges, 766 of which were co-expression, 10 physical interactions, 173 genetic interactions, one co-localization, three predicted, and nine shared protein domains (figure 3). In this network, most of the genes showed some kind of interaction with another gene, but the *TINCR* and *SP9* genes were not linked to any other gene.

The third network constructed combined the 62 and 54 genes associated with FCR and RFI, respectively, as well as 20 other functionally similar genes, resulting in 136 nodes in the network and 2,531 edges, of which 1902 were co-expression, 18 physical interaction, 520 genetic interaction, 47 co-localization, 5 predicted and 39 shared protein domains (Figure 4). Most of the genes identified for RFI and FCR were connected in the network, only the *TINCR* gene, which is associated with RFI, was not connected with any other gene.

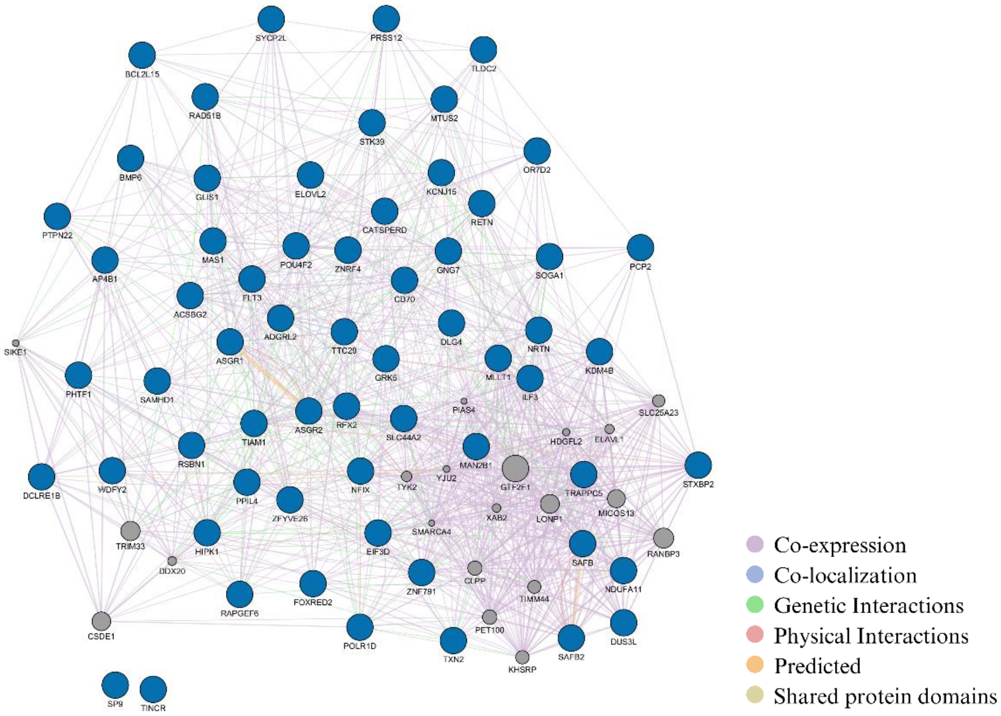

Figure 3. Gene network analysis for residual feed intake (RFI)

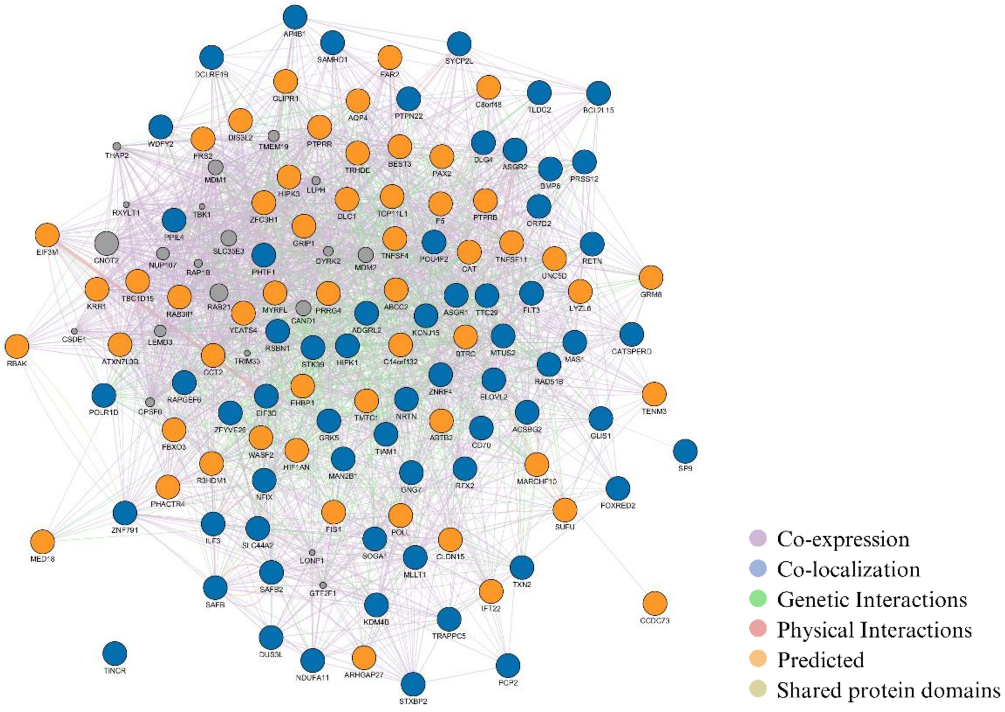

Figure 4. Gene network analysis for both feed conversion ratio (FCR) and residual feed intake (RFI) traits

DISCUSSION

The systematic review carefully followed the eligibility criteria for articles. Only those that contained all the necessary information were selected for inclusion in our database. Therefore, this selection process resulted in a significant reduction in the number of articles removed from the search platforms throughout the filtering process.

A genomic meta-analysis and an enrichment analysis for FCR and RFI traits were carried out according to the results of 10 studies for FCR and 6 studies for RFI. This study aimed to evaluate existing knowledge about the genomic regions associated with the traits, with the main objective of identifying and validating genes associated with them.

After extracting the significant SNPs from each study, a total of 160 SNPs for FCR were identified. A descriptive analysis of this data revealed that there was no significant SNPs in common between different studies, showing a possible inconsistency across studies, which may be an indication of the interference of the population and sample size used. For RFI, 96 significant SNPs were extracted from the papers, and similar to FCR, there was no significant SNPs in common between studies.

Authors such as Fu et al. (2020) and Uffelmann et al. (2021) point to sample size as an essential factor for the success of a GWAS, which generally requires large sample sizes to identify significant and reproducible associations across the entire genome. In the present review, the sample size varied from 296 to 3,672 observations, reflecting a wide range of sample sizes in the studies considered in the systematic review. It is important to note that many of these studies have relatively small sample sizes (Table 1), which may contribute to the inconsistencies observed in the results.

This lack of overlap between markers within each trait can also be influenced by other factors. An example of this is the type of panel used to genotype the animals in each study, since different panels can contain different markers, resulting in the capture of different SNPs related to the trait in question. In addition, it is possible that SNPs that could be common between the studies were eliminated during the quality control process that is carried out before the GWAS analysis. Another possible explanation for this inconsistency is the difference in the correction methods used in each study, since some methods are more rigorous than others.

When comparing the significant markers extracted for both traits, only 11 SNPs were present in the two databases, however, they were extracted from the same study, Ding et al. (2018), which carried out the GWAS for both traits, i.e. the database used and the number of observations were the same for both traits. This suggests, once again, an inconsistency in the GWAS results, which may be due to aspects such as differences in the genetic composition of the populations studied and sample size. In this sense, although there are several studies on these traits and despite significant progress, they have relatively small sample sizes. This disparity in sample sizes highlights the need for caution when interpreting the results, since studies with small sample sizes may be more susceptible to this variability. It is therefore recommended that future studies seek to increase the sample size in order to obtain results that are more applicable.

The meta-analysis identified 145 significant SNPs for FCR and 90 for RFI, which were found in different regions of the pig genome, covering a variety of chromosomes. Of these, the 11 markers that were present in both databases were significant for both traits, all of them located on chromosome 1 and belonging to the study of Ding et al. (2018), as previously described. However, given the high genetic correlation between FCR and RFI, a greater overlap in the markers identified for both traits was expected. This lack of overlap may suggest greater complexity in the genetic mechanisms underlying these traits.

The process of annotating genes associated with the significant SNPs in the meta-analysis resulted in a total of 145 genes for FCR, and after removing those that appeared in more than one SNP, the total was 105 genes. For RFI, 133 genes were identified, and after removing the duplicates, 114 genes remained. It is important to note that 33 and 25 significant markers after the meta-analysis did not have any genes associated for FCR and RFI, respectively. A notable and important aspect to highlight is that, when examining the duplicated genes within each trait, we found that when a gene appeared more than once, it was associated with SNPs taken from the same study. In other words, we did not find any genes that were associated with markers from different studies.

Another important point to note is that, of the 105 for FCR and 114 RFI genes annotated, only 62 and 54 genes, respectively, had complete identification and symbol information. This scenario can be attributed to the lack of complete information on the pig genome, highlighting the need for further research to elucidate these genes in a more comprehensive manner.

The annotated gene sets were used to carry out enrichment analyses and to build gene networks. For the FCR, the enrichment analysis resulted in 16 significant terms, and of the genes that were used in the enrichment analysis for FCR, 19 of them contributed to the significance of these GO terms. The *MED18* and *PHACTR4* genes were associated with 11 GO terms. In the gene networks constructed to investigate interactions between genes, *MED18* and *PHACTR4* had a co-expression interaction, i.e. expression levels were similar between conditions in gene expression studies.

The *MED18* gene, a component of the mediator complex, has already been reported in the literature as a candidate gene for FCR (BELOUS et al., 2019), in which it has been linked to the regulation of transcription. Mediator modules are required for the regulation of different subsets of genes, where *MED18* is required for the formation of a stable initiation complex, for efficient basal transcription, and for activated transcription (LARIVIÈRE et al., 2008). This may explain its association with several GO terms since it can influence the expression of other genes.

PHACTR4 has also been reported in the literature for FCR (BELOUS et al., 2019). Its functions include participation in the proliferation of nerve cells, as well as interaction with muscle actin, being involved in the motility of different types of cells. This gene is present in the biological process related to the organization of the actin cytoskeleton (GO_BP:0030036). It is known that the actin cytoskeleton plays a fundamental role in cell movement, which is essential for several physiological processes, including cell growth and proliferation (SVITKINA, 2018). Changes in organization of the actin cytoskeleton can have an impact on these biological processes.

These two genes were also associated with the positive regulation of catalytic activity (GO_BP:0043085), the molecular function of actin-binding (KW-0009 and GO_MF:0003779), the regulation of the cell cycle (GO_BP:0051726), closure of optic fissure (GO_BP:0061386), neural tube closure (GO_BP:0001843), negative regulation of integrin-mediated signaling pathway (GO_BP:2001045), protein phosphatase activator activity (GO_MF:0072542), to the cellular component lamellipodium (GO_CC:0030027) and3 enteric nervous system development (GO_BP:0048484). Therefore, *MED18* and *PHACTR4* genes play roles in various processes that have been associated with FCR.

The membrane-associated *ABCC2* gene (GO_CC:0016020) is expressed in the main physiological barriers, such as in intestinal cells (JEMNITZ et al., 2010). The gastrointestinal epithelium functions as a selective barrier to absorb nutrients, electrolytes, and water. *ABCC2* encodes a membrane transporter involved in the transportation of various substances and is important for the intestinal barrier as well as its regulation (ARANA et al., 2016). Thus, alterations in its expression or activity can affect the absorption of nutrients or the excretion of diet-related metabolites, influencing the animals' feed efficiency.

Other genes also associated with the membrane (GO_CC:0016020) were *TRHDE* and *FRS2*, which are genes already reported in the literature as candidates for FCR (MIAO et al., 2021). *TRHDE* is an extracellular peptidase that specifically degrades thyrotropin-releasing hormone (TRH) to regulate appetite and metabolism (SCHOMBURG et al., 1999; FREUDENBERG et al., 2011). *FRS2* is involved in fibroblast growth factor 21 (FGF21) signaling with AMP-activated protein kinase (AMPK) and thus related to energy metabolism (VIDELA et al., 2018). FGF21 regulates whole-body energy metabolism (SALMINEN et al., 2016) and AMPK is an important metabolic energy sensor in cells, regulating energy production by stimulating the breakdown of glucose and lipids (LAGE et al., 2008; HARDIE et al., 2012). Thus, the *TRHDE* and *FRS2* are shown to be promising candidate genes for FCR, given their participation in important processes for the trait and highlighting the importance of these genes in understanding the genetic mechanisms underlying feed efficiency in pigs.

The *FAR2* gene is a key gene for β-oxidation of fatty acids and translocation of acetyl-CoA (MIAO et al., 2021). In addition, *FAR2* has been associated with insulin resistance (BURGHARDT et al., 2016). This gene is associated with integral components of the peroxisomal membrane (GO_CC:0005779). Peroxisomes are specialized cellular structures involved in various metabolic functions, including lipid metabolism (PÉRICHON et al., 1998). Previous studies, such as that of Xu et al. (2018), have reported that lipid metabolism can explain variation in FCR, so this gene could be a candidate gene for the trait.

The *FIS1* gene, also associated with integral components of the peroxisomal membrane (GO_CC:0005779), is known to play a role in mitochondrial dynamics (ONOUE et al., 2013). Studies, such as Kobayashi et al. (2007), have also shown a possible relationship of *FIS1* with peroxisomes. So, the gene may be related to the morphology and division of peroxisomes in mammalian cells.

The three genes that were associated with the membrane (*ABCC2*, *TRHDE*, and *FRS2*) and the two associated with integral components of the peroxisomal membrane (*FAR2* and *FIS1*), showed interaction in the gene network. *ABCC2* had a co-expression interaction with *FRS2*, *FAR2* and *FIS1*. *TRHDE* also had a co-expression interaction with *FRS2* and *FAR2*. This co-expression between these genes means that two genes are linked when their expression levels are similar between different conditions in a gene expression study, showing a possible functional interaction between them and their participation in similar processes.

The enrichment analysis for RFI resulted in 6 significant GO terms: GO_MF:0030246 (carbohydrate binding); GO_BP:0000724 (double-strand break repair via homologous recombination); GO_MF:0003677 (DNA binding); GO_CC:0005736 (DNA-directed RNA polymerase I complex); GO_BP:0030520 (intracellular estrogen receptor signaling pathway); GO_BP:0050684 (regulation of mRNA processing). Of the set of genes used, 15 genes contributed to the significance of these GO terms.

Carbohydrates are biomolecules involved in many vital processes. To deal with this multiplicity of functions, several carbohydrate-active proteins have acquired non-catalytic modules that interact very specifically with mono, oligo, and polysaccharides. These modules allow these proteins to recognize and bind specifically to carbohydrates, facilitating their various biological functions. These can be found, for example, in proteins that recognize polysaccharides such as cellulose, chitin, β-glucans, starch, glycogen, and in active enzymes. Invariably, the main role of these binding modules is to recognize and bind specifically to carbohydrates, resulting in different biological consequences (HASHIMOTO, 2006; GUILLÉN et al., 2010; ARMENTA et al., 2017).

In the context of RFI, this carbohydrate-binding capacity may be related to the interaction between proteins or enzymes and the carbohydrates present in food, as this may be an important event for processes related to the metabolism of these important components of the animal diet (GUILLÉN et al., 2010). For example, in the study of Bueren & Boraston (2007), the authors point out that the recognition of starch by these binding modules is important for the activity of starch-degrading enzymes. This shows an important molecular function associated with this trait.

Genes such as *ADGRL2*, *ASGR1*, *ASGR2*, and *MAN2B1* were associated in this molecular function of carbohydrate binding, making them important and promising candidate genes for RFI. They also showed interactions in the gene networks: *ADGRL2* and *MAN2B1* had co-expression interactions with *ASGR1* and *ASGR2*, which means that, in gene expression studies, their expression levels were similar; and *AGR1* interacted with *AGR2* through co-expression, physical interaction and prediction, which are predicted functional relationships between genes.

ADGRL2 encodes a protein that belongs to the family of G protein-coupled receptors (HAMANN et al., 2015). *ASGR1* is a transmembrane protein that plays a critical role in serum glycoprotein homeostasis (BAI et al., 2017). *ASGR1* encodes asialoglycoprotein receptor 1 and is highly expressed in the liver; *ASGR2* encodes receptor 2, and both genes mediate the removal of this glycoconjugate, which is potentially hazardous to health (SOUKHAREV et al., 2000; HARRIS et al., 2012). The *MAN2B1* gene encodes the α-D-mannosidase enzyme, which acts in the degradation of N-linked oligosaccharides and therefore plays an important role in mannose metabolism for mammals (KHAN & RANGANATHAN, 2009).

The biological process of repairing DNA double strand breaks through homologous recombination (GO_BP:0000724) is an important way of repairing DNA damage caused by double strand breaks, which are considered a major disruption to genetic integrity (ARNAUDEAU et al., 2001). Efficient DNA repair is essential to guarantee the integrity and stability of the genome. Another important factor for genome integrity is the molecular function of DNA-binding proteins (GO_MF:0003677), which play essential roles in biological processes such as gene expression and DNA repair (CORONA & GUO, 2016). In this context of gene expression, the biological process of regulating the processing of messenger RNA (GO_BP:0050684) is also important. The genes that have been associated with these biological processes and molecular functions are: *RAD51B, SAMHD1, ZFYVE26, HIPK1, ILF3, NFIX, PHTF1, POLR1D, RFX2, SAFB, SAFB2*. Although they have no direct link to RFI, they may be influencing the expression of genes associated with the trait.

Interestingly, there was no overlap between the FCR and RFI traits in terms of enrichment analysis and only 3 genes were identified for both traits, but none of these genes were associated with processes or functions in the enrichment analysis. However, due to the high genetic correlation between FCR and RFI in pigs, it was expected that there would be a greater sharing of markers and genes between them. The lack of overlap may indicate the complexity of the feed efficiency measures studied. This complexity makes it challenging to identify the same genes or processes associated with both traits, despite the undeniable relationship between them. It is possible that the genetic background of the traits is affected by different genomic regions, reflecting the genetic diversity underlying them. In addition, it is important to consider the possibility of limitations in the analyses, mainly due to the inconsistencies found in the results extracted from each single GWAS.

CONCLUSIONS

Our meta-analysis of the results of genome-wide association studies helped identify possible false positive markers that had been reported in single studies, considering that of the 160 and 96 significant SNPs extracted for feed conversion ratio and residual feed intake, respectively, 15 and 6 of them were not significant after meta-analysis. The most interesting candidate genes for FCR were *MED18, PHACTR4, ABCC2, TRHDE, FRS2, FAR2* and *FIS1*, whereas for RFI, the genes were *ADGRL2, ASGR1, ASGR2 and MAN2B1*.

REFERENCES

Arana, M. R., G. N. Tocchetti, J. P. Rigalli, A. D. Mottino, and S. S. Villanueva. 2016. Physiological and pathophysiological factors affecting the expression and activity of the drug transporter MRP2 in intestine. Impact on its function as membrane barrier. Pharmacol Res. 109:32-44. doi: 10.1016/j.phrs.2016.04.014.

Armenta, S., S. Moreno-Mendieta, Z. Sánchez-Cuapio, S. Sánchez, and R. Rodríguez-Sanoja. 2017. Advances in molecular engineering of carbohydrate-binding modules. Proteins. 85(9):1602-1617. doi: 10.1002/prot.25327.

Arnaudeau, C., C. Lundin, and T. Helleday. 2001. DNA double-strand breaks associated with replication forks are predominantly repaired by homologous recombination involving an exchange mechanism in mammalian cells. J Mol Biol. 307(5):1235-45. doi: 10.1006/jmbi.2001.4564.

Bai, C., Y. Pan, D. Wang, F. Cai, S. Yan, Z. Zhao, and B. Sun. 2017. Genome-wide association analysis of residual feed intake in Junmu No. 1 White pigs. Anim Genet. 48(6):686-690. doi: 10.1111/age.12609.

Belous, A. A., A. A. Sermyagin, O.V. kostyunina, G. Brem, and N.A. Zinovieva. 2019. Study of genetic architecture of feed conversion rate in duroc young boars (sus scrofa) based on the genome-wide snp analysis. Agricultural Biology. 54:705-712. doi: 10.15389/agrobiology.2019.4.705rus

Bueren, A. L. V., and A. B. Boraston. 2007. The structural basis of α-glucan recognition by a family 41 carbohydrate-binding module from thermotoga maritima. J Mol Biol. 365(3):555-60. doi: 10.1016/j.jmb.2006.10.018.

Burghardt, K. J., J. M. Goodrich, D. C. Dolinoy, and V. L. Ellingrod. 2016. Gene-specific DNA methylation may mediate atypical antipsychotic-induced insulin resistance. Bipolar Disord. 18(5):423-32. doi: 10.1111/bdi.12422.

Corona, R. I., and J. T. Guo. 2016. Statistical analysis of structural determinants for protein-DNA-binding specificity. Proteins. 84(8):1147-61. doi: 10.1002/prot.25061.

De Bakker, P. I., M. A. Ferreira, X. Jia, B. M.Neale, S. Raychaudhuri, and B. F. Voight. 2008. Practical aspects of imputation-driven meta-analysis of genome-wide association studies. Hum Mol Genet. 17(R2):R122-8. doi: 10.1093/hmg/ddn288.

Ding, R., J. Quan, M. Y. X. Wang, E. Zheng, H. Yang, D. Fu, Y. Yang, L. Yang, Z. Li, D. Liu, G. Cai, Z. Wu, and J. Yang. 2017. Genome-wide association analysis reveals genetic loci and candidate genes for feeding behavior and eating efficiency in Duroc boars. PloS One. 12:8:e0183244. doi:10.1371/journal.pone.0183244.

Ding, R., M. Yang, X. Wang, J. Quan, Z. Zhuang, S. Zhou, S. Li, Z. Xu, E. Zheng, G. Cai, D. Liu, W. Huang, J. Yang, and Z. Wu. 2018. Genetic Architecture of Feeding Behavior and Feed Efficiency in a Duroc Pig Population. Front. Genet. 9:220. doi: 10.3389/fgene.2018.00220.

Do, D. N., A. B. Strathe, J. Jensen, T. Mark, and H. N. Kadarmideen. 2013. Genetic parameters for different measures of feed efficiency and related traits in boars of three pig breeds, *J. Anim. Sci. 91:* 4069–4079. doi:10.2527/jas.2012-6197.

Duarte, D. A. S., C. J. Newbold, E. Detmann, F. F. Silva, P. H. F. Freitas, R. Veroneze, and M. S. Duarte. 2019. Genome-wide association studies pathway-based meta-analysis for residual feed intake in beef cattle. Anim. Genet. 50:150-153. doi:10.1111/age.12761.

Evangelou, E., and J. P. A. Ioannidis. 2013. Meta-analysis methods for genome-wide association studies and beyond. Nat Rev Genet. 14: 379–389. doi:10.1038/nrg3472.

Freudenberg, J., H. S. Lee, B. G. Han, H. D. Shin, Y. M. Kang, Y. K. Sung, S. C. Shim, C. B. Choi, A. T. Lee, P. K. Gregersen, and S. C. Bae. 2011. Genome-wide association study of rheumatoid arthritis in Koreans: population-specific loci as well as overlap with European susceptibility loci. Arthritis Rheum. 63(4):884-93. doi: 10.1002/art.30235.

Fu, L., Y. Jiang, C. Wang, M. Mei, Z. Zhou, Y. Jiang, H. Song, and X. Ding. 2020. A genome-wide association study on feed efficiency related traits in Landrace pigs. Front. Genet. 11:692. doi:10.3389/fgene.2020.00692.

Guillén, D., S. Sánchez, and R. Rodríguez-Sanoja. 2010. Carbohydrate-binding domains: multiplicity of biological roles. Appl Microbiol Biotechnol. 85(5):1241-9. doi: 10.1007/s00253-009-2331-y.

Hamann, J., G. Aust, D. Araç, F. B. Engel, C. Formstone, R. Fredriksson, R. A. Hall, B. L. Harty, C. Kirchhoff, B. Knapp, A. Krishnan, I. Liebscher, H. H. Lin, D. C. Martinelli, K. R. Monk, M. C. Peeters, X. Piao, S. Prömel, T. Schöneberg, T. W. Schwartz, K. Singer, M. Stacey, Y. A. Ushkaryov, M. Vallon, U. Wolfrum, M. W. Wright, L. Xu, T. Langenhan, and H. B. Schiöth. 2015. International Union of Basic and Clinical Pharmacology. XCIV. Adhesion G protein-coupled receptors. Pharmacol Rev. 67(2):338-67. doi: 10.1124/pr.114.009647.

Hardie, D. G., F. A. Ross, and S. A. Hawley. 2012. AMPK: a nutrient and energy sensor that maintains energy homeostasis. Nat Rev Mol Cell Biol. 13(4):251-62. doi: 10.1038/nrm3311.

Harris, R. L., C. W. Van den Berg, and D. J. Bowen. 2012. ASGR1 and ASGR2, the genes that encode the asialoglycoprotein receptor (ashwell receptor), are expressed in peripheral blood monocytes and show interindividual differences in transcript profile. Mol Biol Int. 2012:283974. doi: 10.1155/2012/283974.

Hashimoto, H. 2006. Recent structural studies of carbohydrate-binding modules. Cell Mol Life Sci. 63(24):2954-67. doi: 10.1007/s00018-006-6195-3.

Horodyska, J., R. M. Hamill, P. F. Varley, H. Reyer, and K. Wimmers. 2017. Genome-wide association analysis and functional annotation of positional candidate genes for feed conversion efficiency and growth rate in pigs. PLoS ONE. 16:6:e0173482. doi:10.1371/journal.pone.0173482.

Huang, W., B. T. Sherman, and R. A. Lempicki. 2009. Systematic and integrative analysis of large gene lists using DAVID bioinformatics resources. Nat Protoc. 4(1):44-57. doi: 10.1038/nprot.2008.211.

Jemnitz, K., K. Heredi-Szabo, J. Janossy, E. Ioja, L. Vereczkey, and P. Krajcsi. 2010. ABCC2/Abcc2: a multispecific transporter with dominant excretory functions. Drug Metab Rev. 42(3):402-36. doi: 10.3109/03602530903491741

Khan, J. M., and S. Ranganathan. 2009. A multi-species comparative structural bioinformatics analysis of inherited mutations in α-D-Mannosidase reveals strong genotype-phenotype correlation. BMC Genomics. 10:S33. doi:10.1186/1471-2164-10-S3-S33

Kobayashi, S., A. Tanaka, and Y. Fujiki. 2007. Fis1, DLP1, and Pex11p coordinately regulate peroxisome morphogenesis. Exp Cell Res. 313(8):1675-86. doi: 10.1016/j.yexcr.2007.02.028.

Korte, A., A. Farlow. 2013. The advantages and limitations of trait analysis with GWAS: a review. Plant Methods. 9:29. doi:10.1186/1746-4811-9-29

Koutsos, T. M., G. C. Menexes, and C. A. Dordas. 2019. An efficient framework for conducting systematic literature reviews in agricultural sciences. Sci Total Environ. 682:106-117. doi: 10.1016/j.scitotenv.2019.04.354.

Kronenberg, F. 2008. Genome-wide Association Studies in Aging-Related Processes Such as Diabetes Mellitus, Atherosclerosis and Cancer. Experimental Gerontology. 43:39–43. doi:10.1016/j.exger.2007.09.005.

Lage, R., C. Diéguez, A. Vidal-Puig, and M. López. 2008. AMPK: a metabolic gauge regulating whole-body energy homeostasis. Trends Mol Med. 14(12):539-49. doi: 10.1016/j.molmed.2008.09.007.

Larivière, L., M. Seizl, S. van Wageningen, S. Röther, L. van de Pasch, H. Feldmann, K. Strässer, S. Hahn, F. C. Holstege, and P. Cramer. 2008. Structure-system correlation identifies a gene regulatory Mediator submodule. Genes Dev. 22(7):872-7. doi: 10.1101/gad.465108.

Li, W., Z. Wang, S. Luo, J. Wu, L. Zhou, and J. Liu. 2022. Genome-wide association analysis and genetic parameters for feed efficiency and related traits in Yorkshire and Duroc pigs. Animals. 12(15):1902. doi: 10.3390/ani12151902.

Magalhães, A. F. B., G. M. F. Camargo, G. A. F. Junior, D. G. M. Gordo, R. L. Tonussi, R. B. Costa, R. Espigolan, R. M. O. Silva, T. Bresolin, W. B. F. Andrade, L. Takada, F. L.B. Feitosa, F. Baldi, R. Carvalheiro, L. A. L. Chardulo, and L. G. Albuquerque. 2016. Genome-wide association study of meat quality traits in Nellore cattle. PLoS ONE. 11:6:e0157845. doi:10.1371/journal.pone.0157845.

Miao, Y. Q. Mei, C. Fu, M. Liao, Y. Liu, X. Xu, X. Li, S. Zhao, and T. Xiang. 2021. Genome-wide association and transcriptome studies identify candidate genes and pathways for feed conversion ratio in pigs. BMC Genomics. 22:294. doi:10.1186/s12864-021-07570-w

Onteru, S. K., D. M. Gorbach, J. M. Young, D. J. Garrick, J. C. M. Dekkers, M. F. Rothschild. 2013. Whole genome association studies of residual feed intake and related traits in the pig. PloS One. 8:6:e61756. doi:10.1371/journal.pone.0061756

Périchon, R., J. M. Bourre, J. F. Kelly, and G. S. Roth. 1998. The role of peroxisomes in aging. Cell Mol Life Sci. 54(7):641-52. doi: 10.1007/s000180050192.

Reyer, H., M. Shirali, S. Ponsuksili, E. Murani, P. F. Varley, J. Jensen, and K. Wimmers. 2017. Exploring the genetics of feed efficiency and feeding behaviour traits in a pig line highly selected for performance characteristics. Mol Genet Genomics. 292(5):1001-1011. doi: 10.1007/s00438-017-1325-1.

Sahana, G., V. Kadlecová, H. Hornshøj, B. Nielsen, and O. F. Christensen. 2013. A genome-wide association scan in pig identifies novel regions associated with feed efficiency trait. J Anim Sci. 91(3):1041-50. doi: 10.2527/jas.2012-5643.

Salminen, A., A. Kauppinen, and K. Kaarniranta. 2017. FGF21 activates AMPK signaling: impact on metabolic regulation and the aging process. J Mol Med (Berl). 95(2):123-131. doi: 10.1007/s00109-016-1477-1.

Sanna, S., A. U. Jackson, R. Nagaraja, C. J. Willer, W. M. Chen, L. L. Bonnycastle, H. Shen, N. Timpson, G. Lettre, G. Usala, P. S. Chines, H. M. Stringham, L. J Scott, M. Dei, S. Lai, G. Albai, L. Crisponi, S. Naitza, K. F. Doheny, E. W. Pugh, Y. Ben-Shlomo, S. Ebrahim, D. A. Lawlor, R. N. Bergman, R. M. Watanabe, M. Uda, J. Tuomilehto, J. Coresh, J. N. Hirschhorn, A. R. Shuldiner, D. Schlessinger, F. S. Collins, G. Davey Smith, E. Boerwinkle, A. Cao, M. Boehnke, G. R. Abecasis, and K. L. Mohlke. 2008. Common variants in the GDF5-UQCC region are associated with variation in human height. Nat Genet. 40(2):198-203. doi: 10.1038/ng.74.

Schomburg, L., S. Turwitt, G. Prescher, D. Lohmann, B. Horsthemke, and K. Bauer. 1999. Human TRH-degrading ectoenzyme cDNA cloning, functional expression, genomic structure and chromosomal assignment. Eur J Biochem. 265(1):415-22. doi: 10.1046/j.1432-1327.1999.00753.x.

Shannon, P., A. Markiel, O. Ozier, N. S. Baliga, J. T. Wang, D. Ramage, N. Amin, B. Schwikowski, and T. Ideker. Cytoscape: a software environment for integrated models of biomolecular interaction networks. Genome Res. 13(11):2498-504. doi: 10.1101/gr.1239303.

Sherman, B. T., M. Hao, J. Qiu, X. Jiao, M. W. Baseler, H. C. Lane, T. Imamichi, and W. Chang. 2022. DAVID: a web server for functional enrichment analysis and functional annotation of gene lists (2021 update). Nucleic Acids Res. 50(W1):W216-W221. doi: 10.1093/nar/gkac194.

Soukharev, S., W. Berlin, J. A. Hanover, B. Bethke, and B. Sauer. 2000. Organization of the mouse ASGR1 gene encoding the major subunit of the hepatic asialoglycoprotein receptor. Gene. 241(2):233-40. doi: 10.1016/s0378-1119(99)00493-x.

Svitkina, T. 2018. The actin cytoskeleton and actin-based motility. Cold Spring Harb Perspect Biol. 10(1):a018267. doi: 10.1101/cshperspect.a018267.

Taherkhani L., M. H. Banabazi, N. EmamJomeh-Kashan, A. Noshary, and I. Imumorin. 2022. The candidate chromosomal regions responsible for milk yield of cow: A GWAS meta-analysis. Animals. 12(5). doi:10.3390/ani12050582.

Uffelmann, E., Q. Q. Huang, N. S. Munung, J. Vries, Y. Okada, A. R. Martin, H. C. M., T. Lappalainen, and D. Posthuma. 2021. Genome-wide association studies. Nature Reviews Methods Primers. 1:59. doi:10.1038/s43586-021-00056-9.

Verardo, L. L., M. S. Lopes, S. Wijga, O. Madsen, F. F. Silva, M. A. Groenen, E. F. Knol, P. S. Lopes, andS. E. Guimarães. 2016. After genome-wide association studies: Gene networks elucidating candidate genes divergences for number of teats across two pig populations. J Anim Sci. 94(4):1446-58. doi: 10.2527/jas.2015-9917.

Videla, L. A., R. Vargas, B. Riquelme, J. Fernández, and V. Fernández. 2018. Thyroid Hormone-Induced Expression of the Hepatic Scaffold Proteins Sestrin2, β-Klotho, and FRS2α in Relation to FGF21-AMPK Signaling. Exp Clin Endocrinol Diabetes. 126(3):182-186. doi: 10.1055/s-0043-115533.

Wang, K., D. Liu, J. Hernandez-Sanchez, J. Chen, C. Liu, Z. Wu, M. Fang, and N. Li. 2015. Genome wide association analysis reveals new production trait genes in a male Duroc population. PLoS One. 10(9):e0139207. doi: 10.1371/journal.pone.0139207.

Warde-Farley, D., S. L. Donaldson, O. Comes, K. Zuberi, R. Badrawi, P. Chao, M. Franz, C. Grouios, F. Kazi, C. T. Lopes, A. Maitland, S. Mostafavi, J. Montojo, Q. Shao, G. Wright, G. D. Bader, and Q. Morris. 2010. The GeneMANIA prediction server: biological network integration for gene prioritization and predicting gene function. Nucleic Acids Res. 38:214-220. doi: 10.1093/nar/gkq537.

Willer, C. J., Y. Li, and G. R. Abecasis. 2010. METAL: fast and efficient meta-analysis of genomewide association scans. Bioinformatics. 26(17):2190-1. doi: 10.1093/bioinformatics/btq340.

Xu Y., X. Qi, M. Hu, R. Lin, Y. Hou, Z. Wang, H. Zhou, Y. Zhao, Y. Luan, S. Zhao, and X. Li. 2018. Transcriptome analysis of adipose tissue indicates that the cAMP signaling pathway affects the feed efficiency of pigs. Genes. 9(7):336. doi: 10.3390/genes9070336.

Zeggini, E., and J. P. A. Ioannidis. 2009. A. Meta-analysis in genome-wide association studies. Future Medicine, Pharmacogenimics. 10:191-201. doi: 10.2217/14622416.10.2.191.

ADDITIONAL FILES

Table S1. Single Nucleotide Polymorphisms (SNP) extracted from each paper

Author	SNPchip	Trait	Number of observations	SNP	CHR	Genomic position	P-value
Belous et al., 2019	Illumina Porcine SNP60 BeadChip	FCR	715	rs322861732	2	28160205	0.00000319
Belous et al., 2019	Illumina Porcine SNP60 BeadChip	FCR	715	rs332408271	2	27690713	0.000002
Belous et al., 2019	Illumina Porcine SNP60 BeadChip	FCR	715	rs341847211	2	28107543	0.00000319
Belous et al., 2019	Illumina Porcine SNP60 BeadChip	FCR	715	rs342013568	2	26610361	0.00000257
Belous et al., 2019	Illumina Porcine SNP60 BeadChip	FCR	715	rs81317829	2	27916909	0.00000432
Belous et al., 2019	Illumina Porcine SNP60 BeadChip	FCR	715	rs81330735	2	26792270	0.00000284
Belous et al., 2019	Illumina Porcine SNP60 BeadChip	FCR	715	rs81356589	2	27133981	0.00000392
Belous et al., 2019	Illumina Porcine SNP60 BeadChip	FCR	715	rs81356686	2	28291546	0.00000201
Belous et al., 2019	Illumina Porcine SNP60 BeadChip	FCR	715	rs81356693	2	28404691	0.00000328
Belous et al., 2019	Illumina Porcine SNP60 BeadChip	FCR	715	rs81356722	2	28370069	0.00000172
Belous et al., 2019	Illumina Porcine SNP60 BeadChip	FCR	715	rs81363704	2	119547373	0.00000373
Belous et al., 2019	Illumina Porcine SNP60 BeadChip	FCR	715	rs334331384	3	4404919	0.00000183
Belous et al., 2019	Illumina Porcine SNP60 BeadChip	FCR	715	rs335445826	3	8959142	0.00000456
Belous et al., 2019	Illumina Porcine SNP60 BeadChip	FCR	715	rs81327212	3	4544334	0.00000103
Belous et al., 2019	Illumina Porcine SNP60 BeadChip	FCR	715	rs81369032	3	8142551	0.00000224
Belous et al., 2019	Illumina Porcine SNP60 BeadChip	FCR	715	rs81375722	3	110100507	0.000000414
Belous et al., 2019	Illumina Porcine SNP60 BeadChip	FCR	715	rs332555715	4	128397522	0.0000044
Belous et al., 2019	Illumina Porcine SNP60 BeadChip	FCR	715	rs329632313	6	85493952	0.00000722
Belous et al., 2019	Illumina Porcine SNP60 BeadChip	FCR	715	rs333263885	6	85385407	0.00000722
Belous et al., 2019	Illumina Porcine SNP60 BeadChip	FCR	715	rs336409671	6	86345973	0.00000157
Belous et al., 2019	Illumina Porcine SNP60 BeadChip	FCR	715	rs81343499	6	86401903	0.00000157
Belous et al., 2019	Illumina Porcine SNP60 BeadChip	FCR	715	rs81389224	6	86333941	0.00000117
Belous et al., 2019	Illumina Porcine SNP60 BeadChip	FCR	715	rs81389246	6	86282384	0.00000157
Belous et al., 2019	Illumina Porcine SNP60 BeadChip	FCR	715	rs81476027	6	86273741	0.00000987

Belous et al., 2019	Illumina Porcine SNP60 BeadChip	FCR	715	rs80887364	7	102851360	0.00000798
Belous et al., 2019	Illumina Porcine SNP60 BeadChip	FCR	715	rs344609508	12	16010788	0.00000647
Belous et al., 2019	Illumina Porcine SNP60 BeadChip	FCR	715	rs80859153	15	62211674	0.0000102
Belous et al., 2019	Illumina Porcine SNP60 BeadChip	FCR	715	rs80938723	15	63541092	0.00000918
Belous et al., 2019	Illumina Porcine SNP60 BeadChip	FCR	715	rs80956594	15	62234985	0.00000918
Belous et al., 2019	Illumina Porcine SNP60 BeadChip	FCR	715	rs81291577	15	30615152	0.00000369
Belous et al., 2019	Illumina Porcine SNP60 BeadChip	FCR	715	rs81301069	15	43810887	0.00000254
Ding et al., 2017	Porcine SNP60 Beadchip llumina	FCR	338	rs81228724	12	18089508	0.0000164
Ding et al., 2017	Porcine SNP60 Beadchip llumina	FCR	338	rs81244225	12	17862124	0.0000144
Ding et al., 2017	Porcine SNP60 Beadchip llumina	FCR	338	rs81319708	12	18094410	0.0000164
Ding et al., 2018	Geneseek Porcine 50K SNP Chip	FCR	1.008	rs80795431	1	172286374	0.000026
Ding et al., 2018	Geneseek Porcine 50K SNP Chip	FCR	1.008	rs80853064	1	173801989	0.0000161
Ding et al., 2018	Geneseek Porcine 50K SNP Chip	FCR	1.008	rs80872918	1	173241334	0.0000174
Ding et al., 2018	Geneseek Porcine 50K SNP Chip	FCR	1.008	rs80887408	1	173838073	0.0000161
Ding et al., 2018	Geneseek Porcine 50K SNP Chip	FCR	1.008	rs80897170	1	173749334	0.0000163
Ding et al., 2018	Geneseek Porcine 50K SNP Chip	FCR	1.008	rs80919991	1	173146830	0.00000872
Ding et al., 2018	Geneseek Porcine 50K SNP Chip	FCR	1.008	rs80939464	1	174008560	0.0000221
Ding et al., 2018	Geneseek Porcine 50K SNP Chip	FCR	1.008	rs80948504	1	174142217	0.0000161
Ding et al., 2018	Geneseek Porcine 50K SNP Chip	FCR	1.008	rs80976610	1	173858164	0.0000161
Ding et al., 2018	Geneseek Porcine 50K SNP Chip	FCR	1.008	rs81349630	1	172353082	0.000026
Ding et al., 2018	Geneseek Porcine 50K SNP Chip	FCR	1.008	rs81349654	1	173699271	0.0000161
Ding et al., 2018	Geneseek Porcine 50K SNP Chip	FCR	1.008	rs81314854	3	92925143	0.0000189
Ding et al., 2018	Geneseek Porcine 50K SNP Chip	FCR	1.008	rs80889405	11	73310954	0.00000228

Ding et al., 2018	Geneseek Porcine 50K SNP Chip	FCR	1.008	rs80997384	17	17867190	0.0000299
Fu et al., 2020	PorcineSNP50 BeadChip	FCR	296	rs80883237	7	45856658	0.000411
Fu et al., 2020	PorcineSNP50 BeadChip	FCR	296	rs80895086	7	45828581	0.000562
Fu et al., 2020	PorcineSNP50 BeadChip	FCR	296	rs345794390	13	3655526	0.00035
Fu et al., 2020	PorcineSNP50 BeadChip	FCR	296	rs80812508	14	40548521	0.000708
Fu et al., 2020	PorcineSNP50 BeadChip	FCR	296	rs80904397	14	40507969	0.000682
Fu et al., 2020	PorcineSNP50 BeadChip	FCR	296	rs330850570	17	1636763	0.000213
Fu et al., 2020	PorcineSNP50 BeadChip	FCR	296	rs335751907	17	1152272	0.000078
Fu et al., 2020	PorcineSNP50 BeadChip	FCR	296	rs342832896	17	1935638	0.000223
Fu et al., 2020	PorcineSNP50 BeadChip	FCR	296	rs344116455	17	1956407	0.00017
Fu et al., 2020	PorcineSNP50 BeadChip	FCR	296	rs698819984	17	2346395	0.00068
Fu et al., 2020	PorcineSNP50 BeadChip	FCR	296	rs80821766	17	1703513	0.000117
Fu et al., 2020	PorcineSNP50 BeadChip	FCR	296	rs337939758	18	20961153	0.000205
Fu et al., 2020	PorcineSNP50 BeadChip	FCR	296	rs81245790	18	20484602	0.000631
Fu et al., 2020	PorcineSNP50 BeadChip	FCR	296	rs81467760	18	23538749	0.000733
Fu et al., 2020	PorcineSNP50 BeadChip	FCR	296	rs334464676	17	2686699	0.000536
Horodyska et al., 2017	PorcineSNP60 BeadChip	FCR	952	rs80892627	1	75408202	0.000239883
Horodyska et al., 2017	PorcineSNP60 BeadChip	FCR	952	rs80847745	4	81479518	0.000000145
Horodyska et al., 2017	PorcineSNP60 BeadChip	FCR	952	rs80848071	4	81493481	0.000000123
Horodyska et al., 2017	PorcineSNP60 BeadChip	FCR	952	rs80903322	4	79331939	0.0000005495
Horodyska et al., 2017	PorcineSNP60 BeadChip	FCR	952	rs80996243	4	80728673	0.00000001096
Horodyska et al., 2017	PorcineSNP60 BeadChip	FCR	952	rs81382168	4	79493443	0.00000033884
Horodyska et al., 2017	PorcineSNP60 BeadChip	FCR	952	rs81389211	6	84705728	0.00000036308
Horodyska et al., 2017	PorcineSNP60 BeadChip	FCR	952	rs81389383	6	86804762	0.00000037154
Horodyska et al., 2017	PorcineSNP60 BeadChip	FCR	952	rs80896554	15	132562815	0.00000003981
Horodyska et al., 2017	PorcineSNP60 BeadChip	FCR	952	rs81326442	15	134782929	0.00000053703
Li et al., 2020	CAU50K	FCR	485	rs81383976	5	43879295	0.000000736

Li et al., 2020	CAU50K	FCR	485	rs81383984	5	44464360	0.0000267
Miao et al., 2021	Illumina PorcineSNP60 BeadChip	FCR	3672	rs342109728	3	79049546	0.00000102
Miao et al., 2021	Illumina PorcineSNP60 BeadChip	FCR	3672	rs322002490	5	38864890	0.0000013
Miao et al., 2021	Illumina PorcineSNP60 BeadChip	FCR	3672	rs323754097	5	36346640	0.000000975
Miao et al., 2021	Illumina PorcineSNP60 BeadChip	FCR	3672	rs324415971	5	37876819	0.00000102
Miao et al., 2021	Illumina PorcineSNP60 BeadChip	FCR	3672	rs332237334	5	33842149	0.000000479
Miao et al., 2021	Illumina PorcineSNP60 BeadChip	FCR	3672	rs334378193	5	38853109	0.00000143
Miao et al., 2021	Illumina PorcineSNP60 BeadChip	FCR	3672	rs339913443	5	35929672	0.000000661
Miao et al., 2021	Illumina PorcineSNP60 BeadChip	FCR	3672	rs345043801	5	33871482	0.000000603
Miao et al., 2021	Illumina PorcineSNP60 BeadChip	FCR	3672	rs80785563	5	33946621	0.000000603
Miao et al., 2021	Illumina PorcineSNP60 BeadChip	FCR	3672	rs80786392	5	33912700	0.000000451
Miao et al., 2021	Illumina PorcineSNP60 BeadChip	FCR	3672	rs80811321	5	30820701	0.00000126
Miao et al., 2021	Illumina PorcineSNP60 BeadChip	FCR	3672	rs80816650	5	34256405	0.000000492
Miao et al., 2021	Illumina PorcineSNP60 BeadChip	FCR	3672	rs80827728	5	38080702	0.0000011
Miao et al., 2021	Illumina PorcineSNP60 BeadChip	FCR	3672	rs80832154	5	34967936	0.000000701
Miao et al., 2021	Illumina PorcineSNP60 BeadChip	FCR	3672	rs80833936	5	34933883	0.000000701
Miao et al., 2021	Illumina PorcineSNP60 BeadChip	FCR	3672	rs80835055	5	34189654	0.0000007
Miao et al., 2021	Illumina PorcineSNP60 BeadChip	FCR	3672	rs80837106	5	33991092	0.000000451

Miao et al., 2021	Illumina PorcineSNP60 BeadChip	FCR	3672	rs80841312	5	33897913	0.000000439
Miao et al., 2021	Illumina PorcineSNP60 BeadChip	FCR	3672	rs80841410	5	34303955	0.000000492
Miao et al., 2021	Illumina PorcineSNP60 BeadChip	FCR	3672	rs80845463	5	34022700	0.000000451
Miao et al., 2021	Illumina PorcineSNP60 BeadChip	FCR	3672	rs80850598	5	34747588	0.000000493
Miao et al., 2021	Illumina PorcineSNP60 BeadChip	FCR	3672	rs80881700	5	37422475	0.00000121
Miao et al., 2021	Illumina PorcineSNP60 BeadChip	FCR	3672	rs80892229	5	34769398	0.000000744
Miao et al., 2021	Illumina PorcineSNP60 BeadChip	FCR	3672	rs80896133	5	37322781	0.00000124
Miao et al., 2021	Illumina PorcineSNP60 BeadChip	FCR	3672	rs80911792	5	41078366	0.00000142
Miao et al., 2021	Illumina PorcineSNP60 BeadChip	FCR	3672	rs80938383	5	40804197	0.00000146
Miao et al., 2021	Illumina PorcineSNP60 BeadChip	FCR	3672	rs80942282	5	35093967	0.000000741
Miao et al., 2021	Illumina PorcineSNP60 BeadChip	FCR	3672	rs80943228	5	35016164	0.000000701
Miao et al., 2021	Illumina PorcineSNP60 BeadChip	FCR	3672	rs80953078	5	38079753	0.00000102
Miao et al., 2021	Illumina PorcineSNP60 BeadChip	FCR	3672	rs80955114	5	34990669	0.000000701
Miao et al., 2021	Illumina PorcineSNP60 BeadChip	FCR	3672	rs80957248	5	37397149	0.00000121
Miao et al., 2021	Illumina PorcineSNP60 BeadChip	FCR	3672	rs80957355	5	38185708	0.0000011
Miao et al., 2021	Illumina PorcineSNP60 BeadChip	FCR	3672	rs80958876	5	40434314	0.0000015
Miao et al., 2021	Illumina PorcineSNP60 BeadChip	FCR	3672	rs80964107	5	38960519	0.0000013
Miao et al., 2021	Illumina PorcineSNP60 BeadChip	FCR	3672	rs80964888	5	33934311	0.000000472

Miao et al., 2021	Illumina PorcineSNP60 BeadChip	FCR	3672	rs80989003	5	33669222	0.000000439
Miao et al., 2021	Illumina PorcineSNP60 BeadChip	FCR	3672	rs80989707	5	33970407	0.000000635
Miao et al., 2021	Illumina PorcineSNP60 BeadChip	FCR	3672	rs80994480	5	35036218	0.000000701
Miao et al., 2021	Illumina PorcineSNP60 BeadChip	FCR	3672	rs81000718	5	34677764	0.000000701
Miao et al., 2021	Illumina PorcineSNP60 BeadChip	FCR	3672	rs81212454	5	38794710	0.00000146
Miao et al., 2021	Illumina PorcineSNP60 BeadChip	FCR	3672	rs81230832	5	38880761	0.0000013
Miao et al., 2021	Illumina PorcineSNP60 BeadChip	FCR	3672	rs81287625	5	34177721	0.000000525
Miao et al., 2021	Illumina PorcineSNP60 BeadChip	FCR	3672	rs81303224	5	38033697	0.00000105
Miao et al., 2021	Illumina PorcineSNP60 BeadChip	FCR	3672	rs81319635	5	34221053	0.000000552
Miao et al., 2021	Illumina PorcineSNP60 BeadChip	FCR	3672	rs81323542	5	44096325	0.00000137
Miao et al., 2021	Illumina PorcineSNP60 BeadChip	FCR	3672	rs81331039	5	44127767	0.00000149
Miao et al., 2021	Illumina PorcineSNP60 BeadChip	FCR	3672	rs81331835	5	44121830	0.00000149
Miao et al., 2021	Illumina PorcineSNP60 BeadChip	FCR	3672	rs81344478	5	33838344	0.000000479
Miao et al., 2021	Illumina PorcineSNP60 BeadChip	FCR	3672	rs81383574	5	30276591	0.000000879
Miao et al., 2021	Illumina PorcineSNP60 BeadChip	FCR	3672	rs81383707	5	34122773	0.000000454
Miao et al., 2021	Illumina PorcineSNP60 BeadChip	FCR	3672	rs81383732	5	35634440	0.00000101
Miao et al., 2021	Illumina PorcineSNP60 BeadChip	FCR	3672	rs81383754	5	36197319	0.00000103
Miao et al., 2021	Illumina PorcineSNP60 BeadChip	FCR	3672	rs81383786	5	36903934	0.00000126

Miao et al., 2021	Illumina PorcineSNP60 BeadChip	FCR	3672	rs81383847	5	37889695	0.00000102
Miao et al., 2021	Illumina PorcineSNP60 BeadChip	FCR	3672	rs81383849	5	37914858	0.00000102
Miao et al., 2021	Illumina PorcineSNP60 BeadChip	FCR	3672	rs81383856	5	37997338	0.00000102
Miao et al., 2021	Illumina PorcineSNP60 BeadChip	FCR	3672	rs81383857	5	38009941	0.00000146
Miao et al., 2021	Illumina PorcineSNP60 BeadChip	FCR	3672	rs81383866	5	38110593	0.00000141
Miao et al., 2021	Illumina PorcineSNP60 BeadChip	FCR	3672	rs81383891	5	38815027	0.00000158
Miao et al., 2021	Illumina PorcineSNP60 BeadChip	FCR	3672	rs329844461	15	16281234	0.0000011
Reyer et al., 2017	Porcine SNP60 Beadchips	FCR	846	rs81270901	6	104183387	0.000002570
Reyer et al., 2017	Porcine SNP60 Beadchips	FCR	846	rs81310751	6	101311106	0.000000028
Reyer et al., 2017	Porcine SNP60 Beadchips	FCR	846	rs81344722	6	111400426	0.000000083
Reyer et al., 2017	Porcine SNP60 Beadchips	FCR	846	rs81389928	6	95114962	0.000020893
Reyer et al., 2017	Porcine SNP60 Beadchips	FCR	846	rs80838208	7	117217668	0.000075858
Reyer et al., 2017	Porcine SNP60 Beadchips	FCR	846	rs81266686	9	111867248	0.000008511
Reyer et al., 2017	Porcine SNP60 Beadchips	FCR	846	rs81332374	9	135187034	0.003162278
Reyer et al., 2017	Porcine SNP60 Beadchips	FCR	846	rs81346296	9	109802987	0.000003802
Reyer et al., 2017	Porcine SNP60 Beadchips	FCR	846	rs81416088	9	115687227	0.000002570
Reyer et al., 2017	Porcine SNP60 Beadchips	FCR	846	rs80878204	11	24524578	0.000001549
Reyer et al., 2017	Porcine SNP60 Beadchips	FCR	846	rs80844227	14	98677304	0.002089296
Reyer et al., 2017	Porcine SNP60 Beadchips	FCR	846	rs81453027	15	50628285	0.0000676083
Sahana et al., 2013	Illumina Porcine SNP60 BeadChip	FCR	3071	rs80807306	14	112353593	0.0000000214
Sahana et al., 2013	Illumina Porcine SNP60 BeadChip	FCR	3071	rs80840893	14	111758839	0.0000002037
Sahana et al., 2013	Illumina Porcine SNP60 BeadChip	FCR	3071	rs80853351	14	110994066	0.0000008204
Sahana et al., 2013	Illumina Porcine SNP60 BeadChip	FCR	3071	rs80882443	14	111671437	0.0000001972

Sahana et al., 2013	Illumina Porcine SNP60 BeadChip	FCR	3071	rs80898194	14	112271963	0.0000000161
Sahana et al., 2013	Illumina Porcine SNP60 BeadChip	FCR	3071	rs80938302	14	113642045	0.0000000927
Sahana et al., 2013	Illumina Porcine SNP60 BeadChip	FCR	3071	rs80955217	14	112646857	0.0000000090
Sahana et al., 2013	Illumina Porcine SNP60 BeadChip	FCR	3071	rs80976779	14	111896310	0.0000002716
Sahana et al., 2013	Illumina Porcine SNP60 BeadChip	FCR	3071	rs80987116	14	112381190	0.0000000129
Wang et al., 2015	Illumina Porcine SNP60 BeadChip	FCR	796	rs336083023	4	96632994	0.044
Wang et al., 2015	Illumina Porcine SNP60 BeadChip	FCR	796	rs340527699	4	102036416	0.0313
Wang et al., 2015	Illumina Porcine SNP60 BeadChip	FCR	796	rs80934608	15	112225927	0.0451
Wang et al., 2015	Illumina Porcine SNP60 BeadChip	FCR	796	rs81454344	15	112052254	0.0451
Bai et al., 2017	Illumina PorcineSNP60v2 BeadChip	RFI	217	rs80782607	1	23143307	0.000000038
Bai et al., 2017	Illumina PorcineSNP60v2 BeadChip	RFI	217	rs80928833	1	23100880	0.000000380
Bai et al., 2017	Illumina PorcineSNP60v2 BeadChip	RFI	217	rs81367118	2	146148111	0.000000365
Bai et al., 2017	Illumina PorcineSNP60v2 BeadChip	RFI	217	rs81367093	2	146286826	0.000000976
Bai et al., 2017	Illumina PorcineSNP60v2 BeadChip	RFI	217	rs81303936	10	64664567	0.000000744
Bai et al., 2017	Illumina PorcineSNP60v2 BeadChip	RFI	217	rs81314967	10	66885948	0.000000243
Bai et al., 2017	Illumina PorcineSNP60v2 BeadChip	RFI	217	rs81225502	10	66864936	0.000000149
Bai et al., 2017	Illumina PorcineSNP60v2 BeadChip	RFI	217	rs81335643	12	52538083	0.000000962
Bai et al., 2017	Illumina PorcineSNP60v2 BeadChip	RFI	217	rs80890689	13	194871653	0.000000711
Bai et al., 2017	Illumina PorcineSNP60v2 BeadChip	RFI	217	rs81270180	13	46617497	0.000000147
Bai et al., 2017	Illumina PorcineSNP60v2 BeadChip	RFI	217	rs81243930	13	46647842	0.000000328
Bai et al., 2017	Illumina PorcineSNP60v2 BeadChip	RFI	217	rs80810051	15	1770319	0.000000460

Ding et al., 2018	Geneseek Porcine 50K SNP Chip	RFI	1008	rs81349630	1	172353082	0.00000163
Ding et al., 2018	Geneseek Porcine 50K SNP Chip	RFI	1008	rs80976610	1	173858164	0.00000121
Ding et al., 2018	Geneseek Porcine 50K SNP Chip	RFI	1008	rs80919991	1	173146830	0.00000065
Ding et al., 2018	Geneseek Porcine 50K SNP Chip	RFI	1008	rs80853064	1	173801989	0.00000121
Ding et al., 2018	Geneseek Porcine 50K SNP Chip	RFI	1008	rs81349654	1	173699271	0.00000121
Ding et al., 2018	Geneseek Porcine 50K SNP Chip	RFI	1008	rs80897170	1	173749334	0.00000125
Ding et al., 2018	Geneseek Porcine 50K SNP Chip	RFI	1008	rs80948504	1	174142217	0.00000121
Ding et al., 2018	Geneseek Porcine 50K SNP Chip	RFI	1008	rs343652685	1	174156779	0.00000467
Ding et al., 2018	Geneseek Porcine 50K SNP Chip	RFI	1008	rs80939464	1	174008560	0.00000153
Ding et al., 2018	Geneseek Porcine 50K SNP Chip	RFI	1008	rs80887408	1	173838073	0.00000121
Ding et al., 2018	Geneseek Porcine 50K SNP Chip	RFI	1008	rs80795431	1	172286374	0.00000163
Ding et al., 2018	Geneseek Porcine 50K SNP Chip	RFI	1008	rs80872918	1	173241334	0.00000128
Ding et al., 2018	Geneseek Porcine 50K SNP Chip	RFI	1008	rs344942807	1	170064540	0.00002370
Ding et al., 2018	Geneseek Porcine 50K SNP Chip	RFI	1008	rs337007455	7	17415915	0.00002250
Do, 2014	PorcineSNP60 Illumina	RFI	596	rs81258794	1	7525648	0.000100
Do, 2014	PorcineSNP60 Illumina	RFI	596	rs81373421	3	89283831	0.000100
Do, 2014	PorcineSNP60 Illumina	RFI	596	rs80965843	7	91581930	0.000054
Do, 2014	PorcineSNP60 Illumina	RFI	596	rs80928116	7	17849496	0.000025
Do, 2014	PorcineSNP60 Illumina	RFI	596	rs81343022	8	81954795	0.00003600
Do, 2014	PorcineSNP60 Illumina	RFI	596	rs81401867	8	82021406	0.00000780
Do, 2014	PorcineSNP60 Illumina	RFI	596	rs81401869	8	82005379	0.00002500
Do, 2014	PorcineSNP60 Illumina	RFI	596	rs81307920	8	81966981	0.00002600
Do, 2014	PorcineSNP60 Illumina	RFI	596	rs81301816	8	26573019	0.000090

Do, 2014	PorcineSNP60 Illumina	RFI	596	rs81324693	9	129675437	0.000042
Do, 2014	PorcineSNP60 Illumina	RFI	596	rs81477738	10	40418554	0.000081
Do, 2014	PorcineSNP60 Illumina	RFI	596	rs80920844	14	129218494	0.000100
Do, 2014	PorcineSNP60 Illumina	RFI	596	rs81453514	15	73900108	0.00009700
Do, 2014	PorcineSNP60 Illumina	RFI	596	rs80983703	15	74462028	0.00009100
Do, 2014	PorcineSNP60 Illumina	RFI	596	rs81455122	15	122718113	0.000027
Do, 2014	PorcineSNP60 Illumina	RFI	596	rs81266609	15	80306098	0.000084
Do, 2014	PorcineSNP60 Illumina	RFI	596	rs80909494	17	40099823	0.000110
Fu et al., 2020	PorcineSNP50 BeadChip	RFI	296	rs327236185	1	16417185	0.000373000
Fu et al., 2020	PorcineSNP50 BeadChip	RFI	296	rs327329163	4	106658684	0.000472000
Fu et al., 2020	PorcineSNP50 BeadChip	RFI	296	rs324132912	4	106826499	0.000389000
Fu et al., 2020	PorcineSNP50 BeadChip	RFI	296	rs80875559	5	94558952	0.000593000
Fu et al., 2020	PorcineSNP50 BeadChip	RFI	296	rs81251279	5	11256612	0.000475000
Fu et al., 2020	PorcineSNP50 BeadChip	RFI	296	rs81393578	6	158658647	0.000496000
Fu et al., 2020	PorcineSNP50 BeadChip	RFI	296	rs81402975	8	102999435	0.000560000
Fu et al., 2020	PorcineSNP50 BeadChip	RFI	296	rs81311244	8	102881678	0.000563000
Fu et al., 2020	PorcineSNP50 BeadChip	RFI	296	rs81262025	10	40140575	0.000128000
Fu et al., 2020	PorcineSNP50 BeadChip	RFI	296	rs81431225	11	5379554	0.000214000
Fu et al., 2020	PorcineSNP50 BeadChip	RFI	296	rs81430068	11	16074356	0.000169000
Fu et al., 2020	PorcineSNP50 BeadChip	RFI	296	rs80983830	11	6366025	0.000334000
Fu et al., 2020	PorcineSNP50 BeadChip	RFI	296	rs81430022	11	16032696	0.000628000
Fu et al., 2020	PorcineSNP50 BeadChip	RFI	296	rs81430119	11	16080206	0.000189000
Fu et al., 2020	PorcineSNP50 BeadChip	RFI	296	rs319450828	16	7078401	0.000280000
Fu et al., 2020	PorcineSNP50 BeadChip	RFI	296	rs327697767	2	133780841	0.000177000
Fu et al., 2020	PorcineSNP50 BeadChip	RFI	296	rs81371975	3	68298863	0.000347000
Fu et al., 2020	PorcineSNP50 BeadChip	RFI	296	rs340095665	6	131840097	0.000262000
Fu et al., 2020	PorcineSNP50 BeadChip	RFI	296	rs81403088	8	105105852	0.000290000

Fu et al., 2020	PorcineSNP50 BeadChip	RFI	296	rs81258024	9	102094613	0.000527000
Fu et al., 2020	PorcineSNP50 BeadChip	RFI	296	rs333944426	9	112313852	0.000550000
Fu et al., 2020	PorcineSNP50 BeadChip	RFI	296	rs341948420	9	112285807	0.000390000
Fu et al., 2020	PorcineSNP50 BeadChip	RFI	296	rs329448606	11	5092611	0.000476000
Li et al., 2020	CAU50K	RFI	880	rs320237095	2	73217053	0.000001850
Li et al., 2020	CAU50K	RFI	880	rs320243411	2	66008692	0.000002510
Li et al., 2020	CAU50K	RFI	880	rs322933932	2	66729446	0.000002510
Li et al., 2020	CAU50K	RFI	880	rs324255146	2	72934295	0.000029700
Li et al., 2020	CAU50K	RFI	880	rs329056098	2	73818550	0.000001850
Li et al., 2020	CAU50K	RFI	880	rs330639556	2	66849146	0.000001750
Li et al., 2020	CAU50K	RFI	880	rs331867151	2	71484107	0.000002860
Li et al., 2020	CAU50K	RFI	880	rs333725490	2	67397353	0.000013400
Li et al., 2020	CAU50K	RFI	880	rs335984226	2	73428891	0.000001850
Li et al., 2020	CAU50K	RFI	880	rs336484525	2	71484462	0.000002860
Li et al., 2020	CAU50K	RFI	880	rs340791819	2	72523054	0.000020600
Li et al., 2020	CAU50K	RFI	880	rs343447412	2	69408667	0.000025800
Li et al., 2020	CAU50K	RFI	880	rs344662679	2	76061262	0.000017300
Li et al., 2020	CAU50K	RFI	880	rs345488861	2	73162496	0.000029700
Li et al., 2020	CAU50K	RFI	880	rs693098203	2	73817678	0.000001850
Li et al., 2020	CAU50K	RFI	880	rs712612698	2	73232214	0.000029700
Li et al., 2020	CAU50K	RFI	880	rs792542846	2	73363418	0.000001850
Li et al., 2020	CAU50K	RFI	880	rs81223451	2	72820932	0.000029700
Li et al., 2020	CAU50K	RFI	880	rs81225998	2	73477969	0.000029700
Li et al., 2020	CAU50K	RFI	880	rs81272049	2	66370420	0.000028900
Li et al., 2020	CAU50K	RFI	485	rs345393699	8	89446476	0.000032600
Li et al., 2020	CAU50K	RFI	880	rs338952192	15	119660194	0.000028400

Onteru et al., 2013	Illumina PorcineSNP60 BeadChip	RFI	1410	rs81343873	3	75985820	0.000005300
Onteru et al., 2013	Illumina PorcineSNP60 BeadChip	RFI	1410	rs80836254	5	60462452	0.000000994
Onteru et al., 2013	Illumina PorcineSNP60 BeadChip	RFI	1410	rs81317745	6	8535032	0.000005300
Onteru et al., 2013	Illumina PorcineSNP60 BeadChip	RFI	1410	rs81398306	7	89226744	0.000000233
Onteru et al., 2013	Illumina PorcineSNP60 BeadChip	RFI	1410	rs80864749	7	7655911	0.000000092
Onteru et al., 2013	Illumina PorcineSNP60 BeadChip	RFI	1410	rs81001871	7	5050865	0.000002240
Onteru et al., 2013	Illumina PorcineSNP60 BeadChip	RFI	1410	rs80848608	13	201881431	0.000000053
Onteru et al., 2013	Illumina PorcineSNP60 BeadChip	RFI	1410	rs81256772	13	115052269	0.000007210

CHR = chromosome

FCR = feed conversion ratio

RFI = Residual feed intake

Table S2. Number of Single Nucleotide Polymorphisms (SNPs) per chromosome

CHR Number	No. SNPs on CHR - FCR	No. SNPs on CHR - RFI
1	12	18
2	11	23
3	7	3
4	8	2
5	60	3
6	13	3
7	4	7
8	0	10
9	4	4
10	0	5
11	2	6
12	4	1
13	2	5
14	12	1
15	11	6
16	0	1
17	12	1
18	5	0

CHR = chromosome

FCR = feed conversion ratio

RFI = Residual feed intake

Table S3. Single Nucleotide Polymorphisms (SNPs) detected as significant by the meta-analysis

Trait	SNP	P-value
FCR	rs80881700	0.00000121
FCR	rs80896554	0.00000003981
FCR	rs336409671	0.00000157
FCR	rs81383707	0.000000454
FCR	rs80898194	0.0000000161
FCR	rs81356589	0.00000392
FCR	rs81383754	0.00000103
FCR	rs81343499	0.00000157
FCR	rs80994480	0.000000701
FCR	rs81270901	0.00000257
FCR	rs81383786	0.00000126
FCR	rs81327212	0.00000103
FCR	rs332408271	0.000002
FCR	rs342013568	0.00000257
FCR	rs80957248	0.00000121
FCR	rs81331039	0.00000149
FCR	rs334331384	0.00000183
FCR	rs80850598	0.000000493
FCR	rs80976779	0.000000272
FCR	rs81383732	0.00000101

FCR	rs81326442	0.000000537
FCR	rs80938302	0.0000000927
FCR	rs80989003	0.000000439
FCR	rs329844461	0.0000011
FCR	rs339913443	0.000000661
FCR	rs80887408	0.0000161
FCR	rs80882443	0.000000197
FCR	rs80919991	0.00000872
FCR	rs81000718	0.000000701
FCR	rs80786392	0.000000451
FCR	rs80838208	0.00007586
FCR	rs81344722	0.00000008318
FCR	rs342832896	0.000223
FCR	rs80795431	0.000026
FCR	rs80847745	0.0000001445
FCR	rs81323542	0.00000137
FCR	rs81319635	0.000000552
FCR	rs80987116	0.00000001285
FCR	rs323754097	0.000000975
FCR	rs81375722	0.000000414
FCR	rs345043801	0.000000603
FCR	rs80835055	0.0000007
FCR	rs335445826	0.00000456
FCR	rs81344478	0.000000479
FCR	rs81453027	0.00006761
FCR	rs81383857	0.00000146
FCR	rs329632313	0.00000722
FCR	rs80948504	0.0000161
FCR	rs80872918	0.0000174
FCR	rs81301069	0.00000254
FCR	rs80848071	0.000000123
FCR	rs80976610	0.0000161
FCR	rs81416088	0.00000257
FCR	rs322861732	0.00000319
FCR	rs81266686	0.000008511
FCR	rs81349630	0.000026
FCR	rs81317829	0.00000432
FCR	rs341847211	0.00000319
FCR	rs80878204	0.000001549
FCR	rs80816650	0.000000492
FCR	rs80942282	0.000000741
FCR	rs80853351	0.0000008204
FCR	rs81383574	0.000000879
FCR	rs80785563	0.000000603
FCR	rs80827728	0.0000011
FCR	rs80964107	0.0000013
FCR	rs80892627	0.0002399
FCR	rs81319708	0.0000164
FCR	rs81383891	0.00000158
FCR	rs80845463	0.000000451
FCR	rs80938383	0.00000146
FCR	rs80896133	0.00000124

FCR	rs80997384	0.0000299
FCR	rs337939758	0.000205
FCR	rs81314854	0.0000189
FCR	rs80939464	0.0000221
FCR	rs81389383	0.000000372
FCR	rs80943228	0.000000701
FCR	rs81331835	0.00000149
FCR	rs81230832	0.0000013
FCR	rs81228724	0.0000164
FCR	rs81383984	0.0000267
FCR	rs332237334	0.000000479
FCR	rs81389246	0.00000157
FCR	rs324415971	0.00000102
FCR	rs80887364	0.00000798
FCR	rs81389211	0.000000363
FCR	rs80938723	0.00000918
FCR	rs81383866	0.00000141
FCR	rs81382168	0.0000003388
FCR	rs81310751	0.00000002818
FCR	rs80821766	0.000117
FCR	rs80859153	0.0000102
FCR	rs333263885	0.00000722
FCR	rs80955114	0.000000701
FCR	rs81369032	0.00000224
FCR	rs81356686	0.00000201
FCR	rs80903322	0.0000005495
FCR	rs81330735	0.00000284
FCR	rs81383849	0.00000102
FCR	rs81389928	0.00002089
FCR	rs80832154	0.000000701
FCR	rs80811321	0.00000126
FCR	rs80837106	0.000000451
FCR	rs81363704	0.00000373
FCR	rs80897170	0.0000163
FCR	rs80957355	0.0000011
FCR	rs81212454	0.00000146
FCR	rs81244225	0.0000144
FCR	rs344609508	0.00000647
FCR	rs330850570	0.000213
FCR	rs81383976	0.000000736
FCR	rs334378193	0.00000143
FCR	rs80911792	0.00000142
FCR	rs80841410	0.000000492
FCR	rs81383856	0.00000102
FCR	rs81291577	0.00000369
FCR	rs80853064	0.0000161
FCR	rs80889405	0.00000228
FCR	rs332555715	0.0000044
FCR	rs80964888	0.000000472
FCR	rs80989707	0.000000635
FCR	rs335751907	0.000078
FCR	rs80892229	0.000000744

FCR	rs81303224	0.00000105
FCR	rs81356693	0.00000328
FCR	rs81287625	0.000000525
FCR	rs344116455	0.00017
FCR	rs81383847	0.00000102
FCR	rs80807306	0.00000002138
FCR	rs80841312	0.000000439
FCR	rs80958876	0.0000015
FCR	rs80956594	0.00000918
FCR	rs342109728	0.00000102
FCR	rs81389224	0.00000117
FCR	rs81346296	0.000003802
FCR	rs80840893	0.0000002037
FCR	rs322002490	0.0000013
FCR	rs81356722	0.00000172
FCR	rs80996243	0.00000001096
FCR	rs81476027	0.00000987
FCR	rs80955217	0.000000009036
FCR	rs80953078	0.00000102
FCR	rs80833936	0.000000701
FCR	rs81349654	0.0000161
RFI	rs81324693	0.000042
RFI	rs81367093	0.000000976
RFI	rs80890689	0.000000711
RFI	rs345393699	0.0000326
RFI	rs81262025	0.000128
RFI	rs341948420	0.00039
RFI	rs80939464	0.00000153
RFI	rs337007455	0.0000225
RFI	rs81251279	0.000475
RFI	rs81401869	0.000025
RFI	rs81317745	0.0000053
RFI	rs81453514	0.000097
RFI	rs81256772	0.00000721
RFI	rs81225998	0.0000297
RFI	rs340095665	0.000262
RFI	rs81343873	0.0000053
RFI	rs81403088	0.00029
RFI	rs693098203	0.00000185
RFI	rs80983703	0.000091
RFI	rs329448606	0.000476
RFI	rs81272049	0.0000289
RFI	rs81477738	0.000081
RFI	rs80920844	0.0001
RFI	rs81393578	0.000496
RFI	rs80848608	0.0000000525
RFI	rs327236185	0.000373
RFI	rs338952192	0.0000284
RFI	rs80928116	0.000027
RFI	rs80909494	0.00011
RFI	rs320237095	0.00000185
RFI	rs80887408	0.00000121

RFI	rs335984226	0.00000185
RFI	rs80919991	0.00000065
RFI	rs80897170	0.00000125
RFI	rs330639556	0.00000175
RFI	rs81243930	0.000000328
RFI	rs324132912	0.000389
RFI	rs81430119	0.000189
RFI	rs340791819	0.0000206
RFI	rs80983830	0.000334
RFI	rs329056098	0.00000185
RFI	rs81373421	0.0001
RFI	rs80782607	0.000000038
RFI	rs80795431	0.00000163
RFI	rs81401867	0.0000078
RFI	rs81301816	0.00009
RFI	rs81258794	0.0001
RFI	rs81223451	0.0000297
RFI	rs80853064	0.00000121
RFI	rs81335643	0.000000962
RFI	rs81430068	0.000169
RFI	rs712612698	0.0000297
RFI	rs81371975	0.000347
RFI	rs344662679	0.0000173
RFI	rs81431225	0.000214
RFI	rs80810051	0.00000046
RFI	rs81225502	0.000000149
RFI	rs80864749	0.0000000924
RFI	rs81303936	0.000000744
RFI	rs81314967	0.000000243
RFI	rs343447412	0.0000258
RFI	rs81001871	0.00000224
RFI	rs80948504	0.00000121
RFI	rs792542846	0.00000185
RFI	rs331867151	0.00000286
RFI	rs80872918	0.00000128
RFI	rs333725490	0.0000134
RFI	rs336484525	0.00000286
RFI	rs80976610	0.00000121
RFI	rs81367118	0.000000365
RFI	rs319450828	0.00028
RFI	rs81343022	0.000036
RFI	rs320243411	0.00000251
RFI	rs345488861	0.0000297
RFI	rs327329163	0.000472
RFI	rs80836254	0.000000994
RFI	rs344942807	0.0000237
RFI	rs80965843	0.000054
RFI	rs81349630	0.00000163
RFI	rs81455122	0.000027
RFI	rs343652685	0.00000467
RFI	rs81270180	0.000000147
RFI	rs81266609	0.000084

RFI	rs327697767	0.000177
RFI	rs324255146	0.0000297
RFI	rs80928833	0.00000038
RFI	rs81307920	0.000026
RFI	rs81398306	0.000000233
RFI	rs322933932	0.00000251
RFI	rs81349654	0.00000121

FCR = feed conversion ratio

RFI = Residual feed intake

Table S4. Genes associated with significant Single Nucleotide Polymorphisms (SNPs) after meta-analysis

Trait	SNP	Gene Ensembl	CHR	Gene start	Gene end	Symbol
FCR	rs322002490	ENSSSCG00000057485	5	38837753	38837855	*U6*
FCR	rs322861732	ENSSSCG00000026433	2	28081234	28259323	*CCDC73*
FCR	rs323754097	ENSSSCG00000000515	5	36274165	36658701	*TRHDE*
FCR	rs324415971	-	-	-	-	-
FCR	rs329632313	ENSSSCG00000028973	6	85412134	85528715	*PHACTR4*
FCR	rs329844461	ENSSSCG00000015692	15	16230922	16413990	*R3HDM1*
FCR	rs329844461	ENSSSCG00000019503	15	16273551	16273659	*MIR128-1*
FCR	rs330850570	ENSSSCG00000006970	17	1170208	1637114	*DLC1*
FCR	rs330850570	ENSSSCG00000006972	17	1610565	1611374	*C8orf48*
FCR	rs330850570	ENSSSCG00000006970	17	1170208	1637114	*DLC1*
FCR	rs330850570	ENSSSCG00000006972	17	1610565	1611374	*C8orf48*
FCR	rs332237334	ENSSSCG00000000493	5	33725444	33849953	*FRS2*
FCR	rs332408271	ENSSSCG00000013312	2	27580129	27685843	*HIPK3*
FCR	rs332555715	ENSSSCG00000062868	4	128363200	128371734	NA
FCR	rs332555715	ENSSSCG00000060113	4	128367448	128370694	NA
FCR	rs332555715	ENSSSCG00000053026	4	128414054	128418482	NA
FCR	rs333263885	ENSSSCG00000053664	6	85352219	85355380	NA
FCR	rs333263885	ENSSSCG00000044404	6	85384080	85392291	*MED18*
FCR	rs333263885	ENSSSCG00000028973	6	85412134	85528715	*PHACTR4*
FCR	rs334331384	ENSSSCG00000052755	3	4381265	4385481	NA
FCR	rs334331384	ENSSSCG00000031365	3	4391504	4409570	NA
FCR	rs334331384	ENSSSCG00000008668	3	4422784	4439945	*RBAK*
FCR	rs334378193	ENSSSCG00000057485	5	38837753	38837855	*U6*
FCR	rs335445826	ENSSSCG00000038901	3	8931097	8937184	*CLDN15*
FCR	rs335445826	ENSSSCG00000038938	3	8937453	8946955	*FIS1*
FCR	rs335445826	ENSSSCG00000046214	3	8958056	8971572	NA
FCR	rs335445826	ENSSSCG00000054316	3	8976306	8981510	*IFT22*
FCR	rs335751907	ENSSSCG00000006970	17	1170208	1637114	*DLC1*
FCR	rs335751907	ENSSSCG00000006970	17	1170208	1637114	*DLC1*
FCR	rs336409671	-	-	-	-	-
FCR	rs337939758	ENSSSCG00000022865	18	20951003	21758568	*GRM8*
FCR	rs337939758	ENSSSCG00000022865	18	20951003	21758568	*GRM8*
FCR	rs339913443	ENSSSCG00000000512	5	35827473	35908385	*TBC1D15*

FCR	rs341847211	ENSSSCG00000013313	2	28062626	28081249	*PRRG4*
FCR	rs341847211	ENSSSCG00000026433	2	28081234	28259323	*CCDC73*
FCR	rs342013568	ENSSSCG00000013302	2	26487653	26581452	*CAT*
FCR	rs342109728	ENSSSCG00000008372	3	78907317	79257760	*EHBP1*
FCR	rs342832896	ENSSSCG00000055908	17	1867481	2012144	NA
FCR	rs342832896	ENSSSCG00000055908	17	1867481	2012144	NA
FCR	rs344116455	ENSSSCG00000055908	17	1867481	2012144	NA
FCR	rs344609508	ENSSSCG00000017299	12	15969769	16052680	*MARCHF10*
FCR	rs345043801	ENSSSCG00000000493	5	33725444	33849953	*FRS2*
FCR	rs80785563	ENSSSCG00000000499	5	33904975	33956637	*BEST3*
FCR	rs80786392	ENSSSCG00000062156	5	33892659	33895175	NA
FCR	rs80795431	ENSSSCG00000061170	1	172288465	172294994	NA
FCR	rs80807306	-	-	-	-	-
FCR	rs80811321	ENSSSCG00000000478	5	30697040	31020901	*GRIP1*
FCR	rs80816650	ENSSSCG00000045667	5	34221371	34239952	NA
FCR	rs80821766	ENSSSCG00000057452	17	1674893	1679916	NA
FCR	rs80821766	ENSSSCG00000057452	17	1674893	1679916	NA
FCR	rs80827728	-	-	-	-	-
FCR	rs80832154	ENSSSCG00000025969	5	34794977	35047818	*PTPRR*
FCR	rs80833936	ENSSSCG00000025969	5	34794977	35047818	*PTPRR*
FCR	rs80835055	ENSSSCG00000023936	5	34067941	34218520	*MYRFL*
FCR	rs80837106	ENSSSCG00000000500	5	34003180	34053896	*RAB3IP*
FCR	rs80838208	ENSSSCG00000033807	7	117242760	117290347	*C14orf132*
FCR	rs80840893	ENSSSCG00000058770	14	111733993	111737342	NA
FCR	rs80841312	ENSSSCG00000000496	5	33858572	33873523	*CCT2*
FCR	rs80841410	ENSSSCG00000053428	5	34275314	34279339	NA
FCR	rs80841410	ENSSSCG00000047171	5	34300826	34305005	NA
FCR	rs80845463	ENSSSCG00000000500	5	34003180	34053896	*RAB3IP*
FCR	rs80845463	ENSSSCG00000044473	5	34008711	34013040	NA
FCR	rs80847745	ENSSSCG00000006289	4	81403274	81485066	*F5*
FCR	rs80848071	ENSSSCG00000006289	4	81403274	81485066	*F5*
FCR	rs80850598	ENSSSCG00000000504	5	34659964	34794289	*PTPRB*
FCR	rs80853064	-	-	-	-	-
FCR	rs80853351	ENSSSCG00000010543	14	110955633	111037537	*ABCC2*
FCR	rs80859153	-	-	-	-	-
FCR	rs80872918	-	-	-	-	-
FCR	rs80878204	ENSSSCG00000052062	11	24468110	24505477	*TNFSF11*
FCR	rs80881700	-	-	-	-	-
FCR	rs80882443	ENSSSCG00000010555	14	111636376	111650318	*HIF1AN*
FCR	rs80887364	-	-	-	-	-
FCR	rs80887408	-	-	-	-	-
FCR	rs80889405	-	-	-	-	-
FCR	rs80892229	ENSSSCG00000000504	5	34659964	34794289	*PTPRB*
FCR	rs80892229	ENSSSCG00000025969	5	34794977	35047818	*PTPRR*
FCR	rs80892627	ENSSSCG00000004415	1	75323639	75431569	NA
FCR	rs80896133	-	-	-	-	-
FCR	rs80896554	ENSSSCG00000022177	15	132540829	132906232	*DIS3L2*
FCR	rs80897170	-	-	-	-	-
FCR	rs80898194	ENSSSCG00000048585	14	112216732	112284224	NA
FCR	rs80903322	-	-	-	-	-

FCR	rs80911792	-	-	-	-	-
FCR	rs80919991	ENSSSCG00000054980	1	173163633	173168800	NA
FCR	rs80938302	ENSSSCG00000010586	14	113500842	113626003	*SUFU*
FCR	rs80938383	-	-	-	-	-
FCR	rs80938723	ENSSSCG00000055550	15	63509039	63515648	NA
FCR	rs80939464	-	-	-	-	-
FCR	rs80942282	ENSSSCG00000061118	5	35103369	35109892	NA
FCR	rs80943228	ENSSSCG00000025969	5	34794977	35047818	*PTPRR*
FCR	rs80948504	-	-	-	-	-
FCR	rs80953078	-	-	-	-	-
FCR	rs80955114	ENSSSCG00000025969	5	34794977	35047818	*PTPRR*
FCR	rs80955217	ENSSSCG00000010564	14	112606196	112617319	*POLL*
FCR	rs80956594	ENSSSCG00000062812	15	62258573	62263424	NA
FCR	rs80957248	-	-	-	-	-
FCR	rs80957355	ENSSSCG00000059069	0	38166996	38172360	NA
FCR	rs80957355	ENSSSCG00000055514	5	38201574	38205697	NA
FCR	rs80958876	ENSSSCG00000026719	5	40416335	40423016	NA
FCR	rs80958876	ENSSSCG00000052150	5	40439087	40445620	NA
FCR	rs80958876	ENSSSCG00000038998	5	40454713	40455240	NA
FCR	rs80964107	-	-	-	-	-
FCR	rs80964888	ENSSSCG00000000499	5	33904975	33956637	*BEST3*
FCR	rs80976610	ENSSSCG00000056451	1	173876267	173876400	NA
FCR	rs80976779	ENSSSCG00000010556	14	111823308	111913969	*PAX2*
FCR	rs80987116	ENSSSCG00000010563	14	112398868	112588037	*BTRC*
FCR	rs80989003	ENSSSCG00000037845	5	33626818	33649627	*YEATS4*
FCR	rs80989707	ENSSSCG00000000499	5	33904975	33956637	*BEST3*
FCR	rs80994480	ENSSSCG00000025969	5	34794977	35047818	*PTPRR*
FCR	rs80996243	ENSSSCG00000060616	4	80713074	80718352	NA
FCR	rs80997384	-	-	-	-	-
FCR	rs81000718	ENSSSCG00000052508	5	34656469	34659775	NA
FCR	rs81000718	ENSSSCG00000000504	5	34659964	34794289	*PTPRB*
FCR	rs81212454	ENSSSCG00000000519	5	38766998	38815597	*GLIPR1*
FCR	rs81212454	ENSSSCG00000033524	5	38809854	38821731	*KRR1*
FCR	rs81228724	ENSSSCG00000017328	12	18037138	18082348	*ARHGAP27*
FCR	rs81230832	-	-	-	-	-
FCR	rs81244225	ENSSSCG00000017321	12	17839555	17847014	*LYZL6*
FCR	rs81266686	ENSSSCG00000063285	9	111843860	111848763	NA
FCR	rs81270901	ENSSSCG00000054338	6	104187469	104192996	NA
FCR	rs81287625	ENSSSCG00000023936	5	34067941	34218520	*MYRFL*
FCR	rs81291577	-	-	-	-	-
FCR	rs81301069	ENSSSCG00000015774	15	43540375	44399711	*TENM3*
FCR	rs81303224	-	-	-	-	-
FCR	rs81310751	ENSSSCG00000054462	6	101290436	101294483	NA
FCR	rs81314854	-	-	-	-	-
FCR	rs81317829	ENSSSCG00000030326	2	27855471	27899766	*TCP11L1*
FCR	rs81319635	ENSSSCG00000023936	5	34067941	34218520	*MYRFL*
FCR	rs81319635	ENSSSCG00000045667	5	34221371	34239952	NA
FCR	rs81319708	ENSSSCG00000017328	12	18037138	18082348	*ARHGAP27*
FCR	rs81323542	ENSSSCG00000027447	5	43913693	44218049	*TMTC1*
FCR	rs81326442	-	-	-	-	-

FCR	rs81327212	ENSSSCG00000008665	3	4516510	4518684	NA
FCR	rs81330735	ENSSSCG00000013303	2	26548852	26782172	*ABTB2*
FCR	rs81331039	ENSSSCG00000027447	5	43913693	44218049	*TMTC1*
FCR	rs81331835	ENSSSCG00000027447	5	43913693	44218049	*TMTC1*
FCR	rs81343499	-	-	-	-	-
FCR	rs81344478	ENSSSCG00000000493	5	33725444	33849953	*FRS2*
FCR	rs81344478	ENSSSCG00000000496	5	33858572	33873523	*CCT2*
FCR	rs81344722	ENSSSCG00000035965	6	111407639	111422109	*AQP4*
FCR	rs81346296	ENSSSCG00000034739	9	109740516	109971611	NA
FCR	rs81349630	-	-	-	-	-
FCR	rs81349654	-	-	-	-	-
FCR	rs81356589	ENSSSCG00000013308	2	27146444	27184181	*FBXO3*
FCR	rs81356686	ENSSSCG00000013315	2	28256591	28282770	*EIF3M*
FCR	rs81356693	ENSSSCG00000022291	2	28376901	28377003	*U6*
FCR	rs81356722	ENSSSCG00000022291	2	28376901	28377003	*U6*
FCR	rs81363704	ENSSSCG00000041901	2	119479189	119652531	NA
FCR	rs81369032	ENSSSCG00000007645	3	8114146	8119841	NA
FCR	rs81375722	ENSSSCG00000044640	3	110068909	110102823	NA
FCR	rs81382168	ENSSSCG00000057091	4	79396516	79575525	NA
FCR	rs81383574	-	-	-	-	-
FCR	rs81383707	ENSSSCG00000023936	5	34067941	34218520	*MYRFL*
FCR	rs81383732	ENSSSCG00000000509	5	35617266	35671149	*ZFC3H1*
FCR	rs81383754	ENSSSCG00000046209	5	36178799	36186854	NA
FCR	rs81383754	ENSSSCG00000054375	5	36203856	36206902	NA
FCR	rs81383754	ENSSSCG00000058044	5	36209019	36215483	NA
FCR	rs81383754	ENSSSCG00000059743	5	36225751	36228763	NA
FCR	rs81383786	-	-	-	-	-
FCR	rs81383847	ENSSSCG00000053636	5	37919473	37925514	NA
FCR	rs81383849	ENSSSCG00000053636	5	37919473	37925514	NA
FCR	rs81383856	ENSSSCG00000054160	5	37978739	37982422	*ATXN7L3B*
FCR	rs81383857	ENSSSCG00000054160	5	37978739	37982422	*ATXN7L3B*
FCR	rs81383866	ENSSSCG00000055893	5	38129967	38135594	NA
FCR	rs81383891	ENSSSCG00000000519	5	38766998	38815597	*GLIPR1*
FCR	rs81383891	ENSSSCG00000033524	5	38809854	38821731	*KRR1*
FCR	rs81383891	ENSSSCG00000057485	5	38837753	38837855	*U6*
FCR	rs81383976	ENSSSCG00000052538	5	43866554	43866838	NA
FCR	rs81383984	ENSSSCG00000000541	5	44381129	44559374	*FAR2*
FCR	rs81389211	ENSSSCG00000003577	6	84622800	84697429	*WASF2*
FCR	rs81389224	ENSSSCG00000049560	6	86304429	86305250	NA
FCR	rs81389246	ENSSSCG00000049560	6	86304429	86305250	NA
FCR	rs81389383	-	-	-	-	-
FCR	rs81389928	ENSSSCG00000056202	6	95070466	95114648	NA
FCR	rs81416088	ENSSSCG00000015488	9	115550569	115659263	*TNFSF4*
FCR	rs81453027	ENSSSCG00000015830	15	50201404	50802668	*UNC5D*
FCR	rs81476027	ENSSSCG00000049560	6	86304429	86305250	NA
RFI	rs327236185	ENSSSCG00000028867	1	16400983	16446854	*PPIL4*
RFI	rs327236185	ENSSSCG00000028867	1	16400983	16446854	*PPIL4*
RFI	rs343652685	-	-	-	-	-
RFI	rs344942807	ENSSSCG00000059984	1	170034359	170039195	NA
RFI	rs80782607	-	-	-	-	-

RFI	rs80795431	ENSSSCG00000061170	1	172288465	172294994	NA
RFI	rs80853064	-	-	-	-	-
RFI	rs80872918	-	-	-	-	-
RFI	rs80887408	-	-	-	-	-
RFI	rs80897170	-	-	-	-	-
RFI	rs80919991	ENSSSCG00000054980	1	173163633	173168800	NA
RFI	rs80928833	-	-	-	-	-
RFI	rs80939464	-	-	-	-	-
RFI	rs80948504	-	-	-	-	-
RFI	rs80976610	ENSSSCG00000056451	1	173876267	173876400	NA
RFI	rs81258794	ENSSSCG00000059431	1	7527861	7528838	*MAS1*
RFI	rs81349630	-	-	-	-	-
RFI	rs81349654	-	-	-	-	-
RFI	rs320237095	ENSSSCG00000033413	2	73173926	73188129	*NRTN*
RFI	rs320237095	ENSSSCG00000040968	2	73197669	73204977	*DUS3L*
RFI	rs320237095	ENSSSCG00000013527	2	73207273	73265866	*CATSPERD*
RFI	rs320237095	ENSSSCG00000061996	2	73248723	73248829	*U6*
RFI	rs320243411	ENSSSCG00000013742	2	65954811	66056567	*NFIX*
RFI	rs320243411	ENSSSCG00000048273	2	65978081	65979528	NA
RFI	rs322933932	ENSSSCG00000036608	2	66732673	66767673	NA
RFI	rs324255146	ENSSSCG00000013536	2	72879252	72920468	*ACSBG2*
RFI	rs324255146	ENSSSCG00000035403	2	72950056	73051180	*RFX2*
RFI	rs327697767	ENSSSCG00000014267	2	133708266	133951433	*RAPGEF6*
RFI	rs329056098	ENSSSCG00000024570	2	73747669	73889866	*KDM4B*
RFI	rs330639556	ENSSSCG00000051836	2	66824440	66827161	NA
RFI	rs330639556	ENSSSCG00000013715	2	66829154	66853255	NA
RFI	rs330639556	ENSSSCG00000054319	2	66855191	66861292	NA
RFI	rs330639556	ENSSSCG00000042811	2	66859134	66861618	NA
RFI	rs330639556	ENSSSCG00000035663	2	66872671	66890769	NA
RFI	rs331867151	ENSSSCG00000040377	2	71454141	71468141	NA
RFI	rs331867151	ENSSSCG00000013573	2	71470445	71472549	*TRAPPC5*
RFI	rs331867151	ENSSSCG00000037188	2	71471417	71519421	*PCP2*
RFI	rs331867151	ENSSSCG00000033183	2	71473389	71476640	NA
RFI	rs331867151	ENSSSCG00000013575	2	71484169	71485616	*RETN*
RFI	rs331867151	ENSSSCG00000013576	2	71504569	71513422	*STXBP2*
RFI	rs333725490	ENSSSCG00000058023	2	67372510	67373355	*OR7D2*
RFI	rs333725490	ENSSSCG00000053037	2	67398730	67399668	NA
RFI	rs335984226	ENSSSCG00000042523	2	73401028	73411574	*TINCR*
RFI	rs335984226	ENSSSCG00000052254	2	73427459	73432361	NA
RFI	rs335984226	ENSSSCG00000054618	2	73433556	73439111	NA
RFI	rs336484525	ENSSSCG00000040377	2	71454141	71468141	NA
RFI	rs336484525	ENSSSCG00000013573	2	71470445	71472549	*TRAPPC5*
RFI	rs336484525	ENSSSCG00000037188	2	71471417	71519421	*PCP2*
RFI	rs336484525	ENSSSCG00000033183	2	71473389	71476640	NA
RFI	rs336484525	ENSSSCG00000013575	2	71484169	71485616	*RETN*
RFI	rs336484525	ENSSSCG00000013576	2	71504569	71513422	*STXBP2*
RFI	rs340791819	ENSSSCG00000024275	2	72500149	72500463	NA
RFI	rs340791819	ENSSSCG00000060067	2	72515064	72515366	NA
RFI	rs340791819	ENSSSCG00000031115	2	72528400	72532951	*CD70*
RFI	rs343447412	ENSSSCG00000013639	2	69365012	69399081	*SLC44A2*

RFI	rs343447412	ENSSSCG00000013638	2	69413982	69443214	*ILF3*
RFI	rs344662679	ENSSSCG00000033949	2	76039656	76083555	*GNG7*
RFI	rs345488861	ENSSSCG00000027307	2	73130403	73137916	*NDUFA11*
RFI	rs345488861	ENSSSCG00000013530	2	73152510	73171605	NA
RFI	rs345488861	ENSSSCG00000033413	2	73173926	73188129	*NRTN*
RFI	rs693098203	ENSSSCG00000024570	2	73747669	73889866	*KDM4B*
RFI	rs712612698	ENSSSCG00000040968	2	73197669	73204977	*DUS3L*
RFI	rs712612698	ENSSSCG00000013527	2	73207273	73265866	*CATSPERD*
RFI	rs712612698	ENSSSCG00000061996	2	73248723	73248829	*U6*
RFI	rs792542846	ENSSSCG00000013522	2	73300632	73334494	*SAFB*
RFI	rs792542846	ENSSSCG00000013523	2	73334561	73392846	*SAFB2*
RFI	rs81223451	ENSSSCG00000013534	2	72781121	72847685	*MLLT1*
RFI	rs81223451	ENSSSCG00000021577	2	72803981	72804092	*U6*
RFI	rs81225998	ENSSSCG00000059446	2	73481337	73486347	*ZNRF4*
RFI	rs81272049	ENSSSCG00000013720	2	66329045	66348056	*MAN2B1*
RFI	rs81272049	ENSSSCG00000029347	2	66396671	66430405	*ZNF791*
RFI	rs81367093	-	-	-	-	-
RFI	rs81367118	ENSSSCG00000055331	2	146126813	146131979	NA
RFI	rs81343873	ENSSSCG00000045708	3	75808213	76031291	NA
RFI	rs81371975	ENSSSCG00000054413	3	68305451	68311385	NA
RFI	rs81373421	-	-	-	-	-
RFI	rs324132912	ENSSSCG00000030154	4	106758836	106806863	*RSBN1*
RFI	rs324132912	ENSSSCG00000006766	4	106809391	106876846	*PHTF1*
RFI	rs327329163	ENSSSCG00000006760	4	106572755	106627418	*HIPK1*
RFI	rs327329163	ENSSSCG00000006761	4	106646011	106656452	*DCLRE1B*
RFI	rs327329163	ENSSSCG00000006762	4	106656809	106672639	*AP4B1*
RFI	rs327329163	ENSSSCG00000038970	4	106674728	106681014	*BCL2L15*
RFI	rs327329163	ENSSSCG00000006764	4	106686604	106758099	*PTPN22*
RFI	rs80836254	ENSSSCG00000059349	5	60443978	60448396	NA
RFI	rs81251279	ENSSSCG00000000141	5	11213312	11229158	*EIF3D*
RFI	rs81251279	ENSSSCG00000000142	5	11233902	11254064	*FOXRED2*
RFI	rs81251279	ENSSSCG00000000144	5	11264645	11283395	*TXN2*
RFI	rs340095665	ENSSSCG00000003761	6	131727084	132113933	*ADGRL2*
RFI	rs81317745	ENSSSCG00000061282	6	8499657	8503193	NA
RFI	rs81317745	ENSSSCG00000047139	6	8513967	8520769	NA
RFI	rs81317745	ENSSSCG00000062307	6	8515868	8520769	NA
RFI	rs81317745	ENSSSCG00000060996	6	8525289	8530556	NA
RFI	rs81317745	ENSSSCG00000053839	6	8527353	8530534	NA
RFI	rs81393578	ENSSSCG00000003846	6	158537465	158763551	*GLIS1*
RFI	rs337007455	-	-	-	-	-
RFI	rs80864749	ENSSSCG00000051558	7	7574372	7640989	*SYCP2L*
RFI	rs80864749	ENSSSCG00000001045	7	7651601	7774018	*ELOVL2*
RFI	rs80928116	ENSSSCG00000053498	7	17826219	17834852	NA
RFI	rs80928116	ENSSSCG00000056854	7	17881151	17885041	NA
RFI	rs80928116	ENSSSCG00000053498	7	17826219	17834852	NA
RFI	rs80928116	ENSSSCG00000056854	7	17881151	17885041	NA
RFI	rs80965843	ENSSSCG00000002298	7	91518452	91590449	*ZFYVE26*
RFI	rs80965843	ENSSSCG00000028877	7	91592424	92345294	*RAD51B*
RFI	rs81001871	ENSSSCG00000001027	7	5058817	5210270	*BMP6*
RFI	rs81398306	-	-	-	-	-

RFI	rs345393699	-	-	-	-	-
RFI	rs81301816	-	-	-	-	-
RFI	rs81307920	ENSSSCG00000040272	8	81746489	81982760	*TTC29*
RFI	rs81307920	ENSSSCG00000062405	8	81987429	81988108	*NA*
RFI	rs81343022	ENSSSCG00000040272	8	81746489	81982760	*TTC29*
RFI	rs81401867	ENSSSCG00000026015	8	82043643	82047675	*POU4F2*
RFI	rs81401867	ENSSSCG00000026015	8	82043643	82047675	*POU4F2*
RFI	rs81401869	ENSSSCG00000040272	8	81746489	81982760	*TTC29*
RFI	rs81401869	ENSSSCG00000062405	8	81987429	81988108	NA
RFI	rs81403088	ENSSSCG00000009114	8	105121529	105197141	*PRSS12*
RFI	rs333944426	ENSSSCG00000045606	9	112341044	112341993	NA
RFI	rs333944426	ENSSSCG00000053411	9	112335391	112476074	NA
RFI	rs341948420	-	-	-	-	-
RFI	rs81324693	ENSSSCG00000050221	9	129605449	129771888	NA
RFI	rs81324693	ENSSSCG00000059720	9	129648871	129654529	NA
RFI	rs81324693	ENSSSCG00000041374	9	129704083	129870858	NA
RFI	rs81225502	ENSSSCG00000036117	10	66741291	66971746	NA
RFI	rs81262025	-	-	-	-	-
RFI	rs81303936	ENSSSCG00000047628	10	64673925	64732648	NA
RFI	rs81314967	ENSSSCG00000036117	10	66741291	66971746	NA
RFI	rs81477738	-	-	-	-	-
RFI	rs329448606	ENSSSCG00000009310	11	5044329	5089766	*POLR1D*
RFI	rs80983830	ENSSSCG00000025996	11	6197740	6532924	*MTUS2*
RFI	rs81430068	ENSSSCG00000040538	11	16092698	16195134	*WDFY2*
RFI	rs81430119	ENSSSCG00000040538	11	16092698	16195134	*WDFY2*
RFI	rs81431225	ENSSSCG00000009316	11	5353438	5363070	NA
RFI	rs81431225	ENSSSCG00000009314	11	5370496	5455358	*FLT3*
RFI	rs81335643	ENSSSCG00000017932	12	52464689	52506574	*ASGR2*
RFI	rs81335643	ENSSSCG00000024926	12	52536738	52544791	*ASGR1*
RFI	rs81335643	ENSSSCG00000024285	12	52550141	52575143	*DLG4*
RFI	rs80848608	ENSSSCG00000012066	13	201894420	201939789	*KCNJ15*
RFI	rs80890689	ENSSSCG00000012034	13	194774497	195005089	*TIAM1*
RFI	rs81243930	-	-	-	-	-
RFI	rs81256772	ENSSSCG00000055040	13	115049159	115055443	NA
RFI	rs81270180	-	-	-	-	-
RFI	rs80920844	ENSSSCG00000010683	14	129113603	129347152	*GRK5*
RFI	rs338952192	-	-	-	-	-
RFI	rs80810051	ENSSSCG00000055275	15	1735194	1739851	NA
RFI	rs80810051	ENSSSCG00000057828	15	1773529	1778620	NA
RFI	rs80983703	ENSSSCG00000057227	15	74438156	74442246	NA
RFI	rs80983703	ENSSSCG00000022496	15	74447787	74758122	*STK39*
RFI	rs81266609	ENSSSCG00000044710	15	80295752	80296165	NA
RFI	rs81266609	ENSSSCG00000055609	15	80312149	80317626	NA
RFI	rs81266609	ENSSSCG00000036172	15	80325377	80329020	*SP9*
RFI	rs81453514	ENSSSCG00000043455	15	73772848	73973673	NA
RFI	rs81453514	ENSSSCG00000056096	15	73885211	73889201	NA
RFI	rs81453514	ENSSSCG00000048454	15	73889813	73894913	NA
RFI	rs81453514	ENSSSCG00000058820	15	73920295	73925727	NA
RFI	rs81455122	-	-	-	-	-
RFI	rs319450828	-	-	-	-	-

RFI	rs80909494	ENSSSCG00000007324	17	40020440	40099001	*SOGA1*
RFI	rs80909494	ENSSSCG00000027806	17	40107462	40171878	*SAMHD1*
RFI	rs80909494	ENSSSCG00000031690	17	40109210	40120399	*TLDC2*

CHR = chromosome

FCR = feed conversion ratio

RFI = Residual feed intake

Table S5. Functional analysis of the genes annotated after the meta-analysis.

Trait	Category	Term	Count	P-Value	Genes
FCR	Biological Process	KW-0524 neurogenesis	2	0.093	*MED18, PHACTR4*
FCR	GO: Biological Process	GO:0061386 closure of optic fissure	2	**0.009**	*MED18, PHACTR4*
FCR	GO: Biological Process	GO:2001045 negative regulation of integrin-mediated signaling pathway	2	**0.012**	*MED18, PHACTR4*
FCR	GO: Biological Process	GO:0033598 mammary gland epithelial cell proliferation	2	**0.021**	*TNFSF11, BTRC*
FCR	GO: Biological Process	GO:0043085 positive regulation of catalytic activity	2	**0.045**	*MED18, PHACTR4*
FCR	GO: Biological Process	GO:0048484 enteric nervous system development	2	**0.045**	*MED18, PHACTR4*
FCR	GO: Biological Process	GO:0003281 ventricular septum development	2	0.054	*FRS2, SUFU*
FCR	GO: Biological Process	GO:0051497 negative regulation of stress fiber assembly	2	0.060	*DLC1, WASF2*
FCR	GO: Biological Process	GO:0001755 neural crest cell migration	2	0.097	*MED18, PHACTR4*
FCR	GO: Biological Process	GO:0001843 neural tube closure	3	**0.010**	*MED18, SUFU, PHACTR4*
FCR	GO: Biological Process	GO:0030036 actin cytoskeleton organization	4	**0.006**	*DLC1, WASF2, MED18, PHACTR4*
FCR	GO: Biological Process	GO:0051726 regulation of cell cycle	4	**0.009**	*MED18, YEATS4, PHACTR4, BTRC*

FCR	GO: Biological Process	GO:0007165 signal transduction	5	**0.044**	*DLC1, TRHDE, ARHGAP27, TCP11L1, TENM3*
FCR	GO: Cellular Component	GO:0000178 exosome (RNase complex)	2	**0.034**	*DIS3L2, ZFC3H1*
FCR	GO: Cellular Component	GO:0005779 integral component of peroxisomal membrane	2	**0.048**	*FIS1, FAR2*
FCR	GO: Cellular Component	GO:0070847 core mediator complex	2	0.059	*MED18, PHACTR4*
FCR	GO: Cellular Component	GO:0005778 peroxisomal membrane	2	0.070	*FAR2, CAT*
FCR	GO: Cellular Component	GO:0030027 lamellipodium	3	**0.045**	*WASF2, MED18, PHACTR4*
FCR	GO: Cellular Component	GO:0016020 membrane	8	**0.012**	ENSSSCG00000056202, *DLC1*, ENSSSCG00000034739, *TRHDE, FRS2, ABCC2, TNFSF4*, ENSSSCG00000008665
FCR	GO: Molecular Function	GO:0072542 protein phosphatase activator activity	2	**0.023**	*MED18, PHACTR4*
FCR	GO: Molecular Function	GO:0008157 protein phosphatase 1 binding	2	0.062	*MED18, PHACTR4*
FCR	GO: Molecular Function	GO:0005164 tumor necrosis factor receptor binding	2	0.076	*TNFSF11, TNFSF4*
FCR	GO: Molecular Function	GO:0005096 GTPase activator activity	3	0.086	*DLC1, TBC1D15, ARHGAP27*
FCR	GO: Molecular Function	GO:0003779 actin binding	4	**0.034**	ENSSSCG00000056202, *WASF2, MED18, PHACTR4*
FCR	Molecular Function	KW-0217 developmental protein	3	0.093	*MED18, SUFU, PHACTR4*
FCR	Molecular Function	KW-9996 developmental protein	3	0.093	*MED18, SUFU, PHACTR4*
FCR	Molecular Function	KW-0009 actin-binding	4	**0.007**	ENSSSCG00000056202, *WASF2, MED18, PHACTR4*

RFI	GO: Biological Process	GO:0000724 double-strand break repair via homologous recombination	3	**0.020**	*SAMHD1, RAD51B, ZFYVE26*
RFI	GO: Biological Process	GO:0030520 intracellular estrogen receptor signaling pathway	2	**0.037**	*SAFB, POU4F2*
RFI	GO: Biological Process	GO:0050684 regulation of mRNA processing	2	**0.041**	*SAFB, SAFB2*
RFI	GO: Biological Process	GO:0006357 regulation of transcription from RNA polymerase II promoter	8	0.088	*SP9, GLIS1, SAFB, POU4F2, NFIX,* ENSSSCG00000035663, *ZNF791, RFX2*
RFI	GO: Cellular Component	GO:0005736 DNA-directed RNA polymerase I complex	2	**0.035**	*POLR1D, LOC106505238*
RFI	GO: Cellular Component	GO:0005666 DNA-directed RNA polymerase III complex	2	0.052	*POLR1D, LOC106505238*
RFI	GO: Molecular Function	GO:0030246 carbohydrate binding	5	**0.001**	*ASGR1, ASGR2, MAN2B1,* ENSSSCG00000040377, *ADGRL2*
RFI	GO: Molecular Function	GO:0003677 DNA binding	9	**0.031**	*HIPK1,* ENSSSCG00000013715, *ILF3, RAD51B, NFIX, POLR1D, PHTF1, RFX2, LOC106505238*
RFI	GO: Molecular Function	GO:0051213 dioxygenase activity	2	0.096	*RSBN1, KDM4B*
RFI	Biological Process	KW-0051 Antiviral defense	2	0.073	*SAMHD1, ILF3*
RFI	GO: Cellular Component	KW-9994 DNA-directed RNA polymerase	2	0.067	*POLR1D, LOC106505238*
RFI	GO: Cellular Component	KW-0240 DNA-directed RNA polymerase	2	0.067	*POLR1D, LOC106505238*
RFI	Ligand	KW-0430 Lectin	3	0.090	*ASGR1, ASGR2,* ENSSSCG00000040377

FCR = feed conversion ratio

RFI = Residual feed intake

FINAL CONSIDERATIONS

Feed conversion ratio and residual feed intake are traits that play a key role in sustainable production systems, highlighting the importance of a thorough understanding of their genetic basis. The meta-analysis approach has emerged as a crucial solution to overcome the limitations found in individual genome-wide association studies, allowing for better identification of false positives and providing a more accurate and comprehensive view of genetic associations.

However, when conducting this study, some limitations were observed. For example, the lack of complete information in GWAS studies, such as the absence of data on the reference allele used in each paper and the lack of access to the complete database of the markers used in the analyses. This information would have the potential to enrich and expand our study. In addition, it was difficult to define the size of the window to be used in gene annotation, since there is no consensus in the literature on this definition.

This meta-analysis opens up space for further research into the genes identified as possible candidates, offering prospects for future investigations and practical applications in pig farming. This can result in significant advances in the efficiency, sustainability and productivity of pig production. It is also worth highlighting the importance of future meta-analyses on the subject, since the feed conversion rate and residual feed consumption have proved to be complex characteristics that require further studies to gain a better understanding.