

GENETIC PREDISPOSITION FOR THE DEVIATION OF OFFSPRING SEX RATIO IN TWO VARIETIES OF IBERIAN PIG

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Sex Ratio (SR)

In livestock species, gametes are crossed randomly and an equal number of males and females should be expected in the offspring^a. However, Trivers and Willard^b stand that natural selection must favor genes that adjust the sex ratio according to the condition of the female during the parental investment time (differential mortality of either sperm cells, embryos, fetuses or neonates), modulating the ability of each female to modify the offspring SR.

Farrowing and Genomic data

Pig variety	No of parities	No of sows	Pedigree	Genotyped sows ^e	PLINK ^f Quality control
Entrepelado	9,358 (2010-2019)	1,980	1,774 (114 founders)	423	39,752 SNPs
Retinto	9,663 (2009-2019)	1,915	1,786 (44 founders)	397	32,526 SNPs

Animal Linear Mixed Model

$$R_{ij} = N_{\delta ij} / (N_{\delta ij} + N_{\varnothing ij}) \quad SRV_i = (\sum_{k=1,j} D_{ij}^2 (N_{\delta ij} + N_{\varnothing ij})) / (\sum_{k=1,j} N_{\delta ij} + N_{\varnothing ij}) \quad \mathbf{y} = \boldsymbol{\mu} + \mathbf{W}\mathbf{h} + \mathbf{Z}\mathbf{a} + \mathbf{e}$$

R_{ij} sex ratio of the piglets born alive in the j th litter of the i th sow $N_{\delta ij}$, $N_{\varnothing ij}$ number of male and female offspring in the j th litter
 SRV_i across-litter weighted variance of offspring sex ratio for sow i D_{ij} deviation from the expected 50% R_{ij} ; $D_{ij} = (R_{ij} - 0.5)$
 \mathbf{y} vector of SRV phenotypes $\boldsymbol{\mu}$ population mean \mathbf{h} vector of random herd-year-season effects (>50 sows per level) \mathbf{a} vector of genetic additive effects \mathbf{e} vector of the residual effects \mathbf{W} and \mathbf{Z} incidence matrices relating phenotype to fixed and random effects

Genome-Wide Association (GWA) Analyses

Posterior mean of breeding values (\mathbf{a}) were analyzed under a linear regression-based association analysis by the software tool GCTA^g; SNP-by-SNP and accounted for $\boldsymbol{\mu}$ and the additive effect inherent to each SNP. Obtained p -values were transformed to q -values by the Benjamini and Hochberg approach for false discovery rate (FDR).

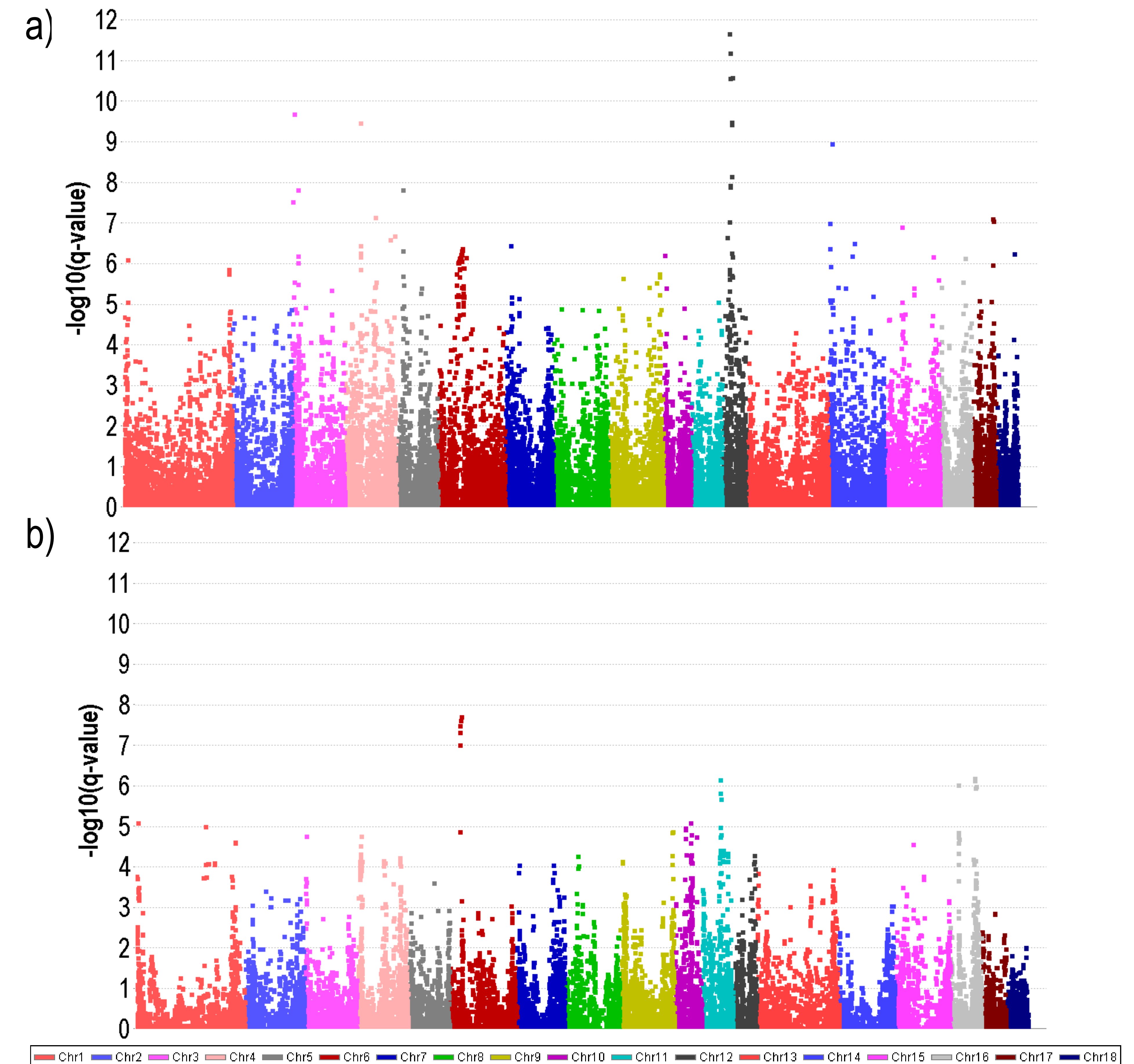
Candidate Gene Search

Candidate genes were searched with flanking regions of 1.0 Mb upstream or downstream SNPs with q -values <0.001 using Sus scrofa Build 11.1.99. Candidate genes shared by both pig varieties were studied for the identification of biology function by the PANTHER Classification System^h and GeneCardsⁱ.

Results

Pig variety	mean SRV	σ_a^2	σ_h^2	σ_e^2	h^2
Entrepelado	0.0290±0.0008	0.027 (0.002-0.093)	0.047 (0.018-0.094)	0.894 (0.822-0.966)	0.028 (0.002-0.095)
Retinto	0.0287±0.0008	0.042 (0.006-0.042)	0.028 (0.009-0.060)	0.828 (0.757-0.899)	0.048 (0.006-0.123)

Mean SRV (piglets²), posterior mean (95% credibility interval) of variance components (×1,000) and heritability for variability in offspring SR. σ_a^2 : additive genetic variance; σ_h^2 : herd-year-season variance; σ_e^2 : residual variance; h^2 : heritability.



Manhattan plot of $-\log_{10}$ q-values for the SNPs across the autosomic chromosomes ignoring pairwise comparisons of markers >500 kb apart for Entrepelado (a) and Retinto (b) Iberian pig varieties.

Conclusions

Additive genetic background of variability in the sow ability to depart offspring SR in pigs has been found with heritabilities within the range of regular heritabilities for reproductive traits in pig. Within the most significant regions in the GWA study, candidate genes reported to be essential for proper placentation (*IGFBP4*), early age development (*ESRP2*, *PARD6A*) and death when knockout (*FGF23*, *TOP2A*) plus regulation of important development pathways like BMP and Hh (*PSMB10*, *SMPD3*, *SMURF1*) were detected. These could be candidate genes for sex-biased embryological death which subsequently could influence SRV in litters.

^a Fisher RA. 1930. The genetical theory of natural selection. The Clarendon Press, Oxford, United Kingdom

^b Trivers RL, Willard D. 1973. Natural selection of parental ability to vary the sex ratio of offspring. Science 179, 90–92

^c INVITEK Molecular GmbH, Berlin, Germany

^d Thermo Fisher Scientific, Waltham, MS, USA

^e Genesee Genomic Profiler Porcine HD,

illumina, Inc., San Diego, CA, USA

^f Purcell S., et al. 2007. PLINK: a tool set for whole-genome association and population-based linkage analyses. American Journal of Human Genetics. 2007 Sep;81(3):559-75

^g v1.93.2beta ;Yang et al., 2011

^h Thomas et al., 2003

ⁱ https://www.genecards.org/; Weizmann Institute of Science, Rehovot, Israel)