



Estimation of Genetic Parameters and Weighted Single-Step Genome-Wide Association Studies for Fertility Traits in Holstein Cattle Using Liquid Chip

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Introduction

- The liquid chip based on Genotyping by Target Sequencing (GBTS) technology can detect a wide range of variations and offers high efficiency, low cost, broad adaptability, and flexible application.
- Fertility traits are crucial functional traits in dairy cows.
- Weighted single-step genome-wide association studies (wssGWAS) integrated phenotype, pedigree and genotype information, estimated GEBV based on ssGBLUP model, and used GEBV to invert SNP effect. Then the next round of GEBV estimation is carried out for SNP effect weight.

AIM: This study estimates genetic parameters and performs wssGWAS to identify genes associated with three fertility traits in the Chinese Holstein population: number of services for heifers (NS_H), interval from calving to first services (ICF), and calving interval (CI).

Materials and Methods

Phenotype Data

- Trait:** number of services for heifers (NS_H), interval from calving to first services (ICF), and calving interval (CI).
- Pedigree:** 522 222 individuals, born in 1969 ~ 2022
- Records:** NS_H - 134,141; ICF - 345,751; CI - 238,277

Genotype Data

- 5,545 cattle have liquid chips (166,009 SNPs + 7,518 InDels), while 18,226 have 150K chips, which were imputed to the liquid-phase chip level and merged after quality control

➡ Imputation: Beagle v5.0 ➡ Quality Control: PLINK 1.9

Individual genotype rate; MAF; H-W

13,690 individuals and 103,262 loci using analysis

Statistical model

➡ Software: blupf90 模型 $y = Xb + Za + (Wc) + e$

- A weighted single-step genome-wide association method with 20 adjacent SNPs as sliding windows was implemented

$$\frac{\text{Var}(\sum_{j=1}^n Z_j \hat{\mu}_j)}{\sigma_a^2} \times 100\%$$

- The region where the interpretive genetic variance is greater than 0.2% was selected as the target QTL region

GO and KEGG enrichment analysis

- GO and KEGG pathway enrichment analysis were performed for the significantly QTL regions using clusterProfiler, with the P-value adjusted by Bonferroni correction method, and P-value and q-value cutoffs of 0.05.

Results and Discussions

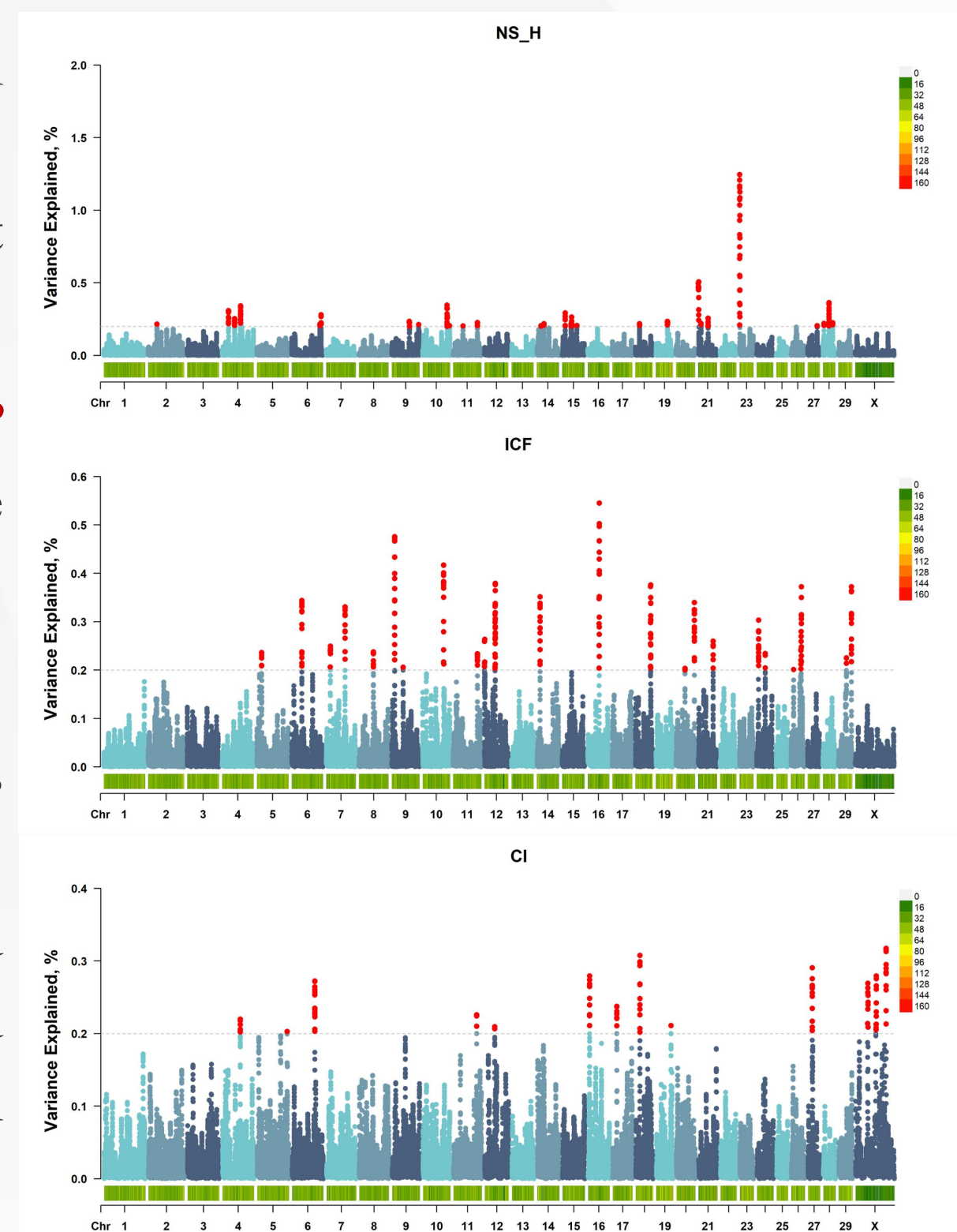
Genetic parameter estimation

Traits	Heritability	Repeatability
NS_H	0.049	-
ICF	0.029	0.073
CI	0.064	0.086

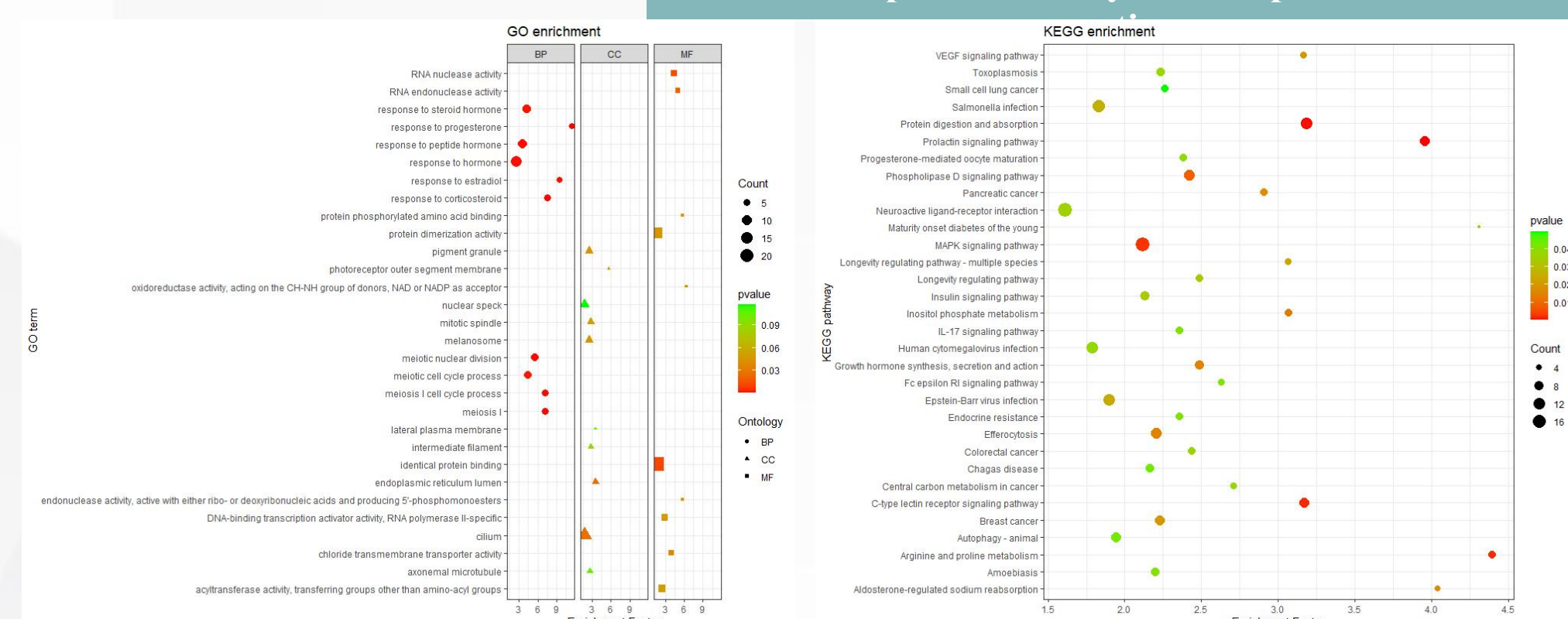
- Fertility traits are low heritability traits in dairy cattle.

Candidate genes

- The QTL region on BTA23:0.02-1.35 in NS_H explained the largest genetic variance (1.25%).
- OVOS2*, *PMEPA1*, *TEPP* were identified candidate genes relating with fertility traits.
- Three fertility traits enriched into reproductive hormone (GO) and progesterone mediated oocyte maturation pathways (KEGG).



Manhattan plot of fertility traits explained variance



The plot of GO (left) and KEGG (right) enrichment analysis

Conclusions

- Candidate genes main functional enrichment: reproduction related hormones (progesterone, steroids, estradiol, corticosteroids, etc.), progesterone mediated oocyte maturation signaling pathway and prolactin signaling pathway.
- These findings provide a foundation for future research into the genetic mechanisms underlying fertility traits, contributing to accurate genomic predictions in the Chinese Holstein population.

References

Luo H, Hu L, Brito L F, et al. Weighted single-step GWAS and RNA sequencing reveals key candidate genes associated with physiological indicators of heat stress in Holstein cattle[J]. J Anim Sci Biotechnol. 2022, 13(1): 108.

