A uterine-centric view of reproductive senescence: genetic insights into late-life performance in laying hens

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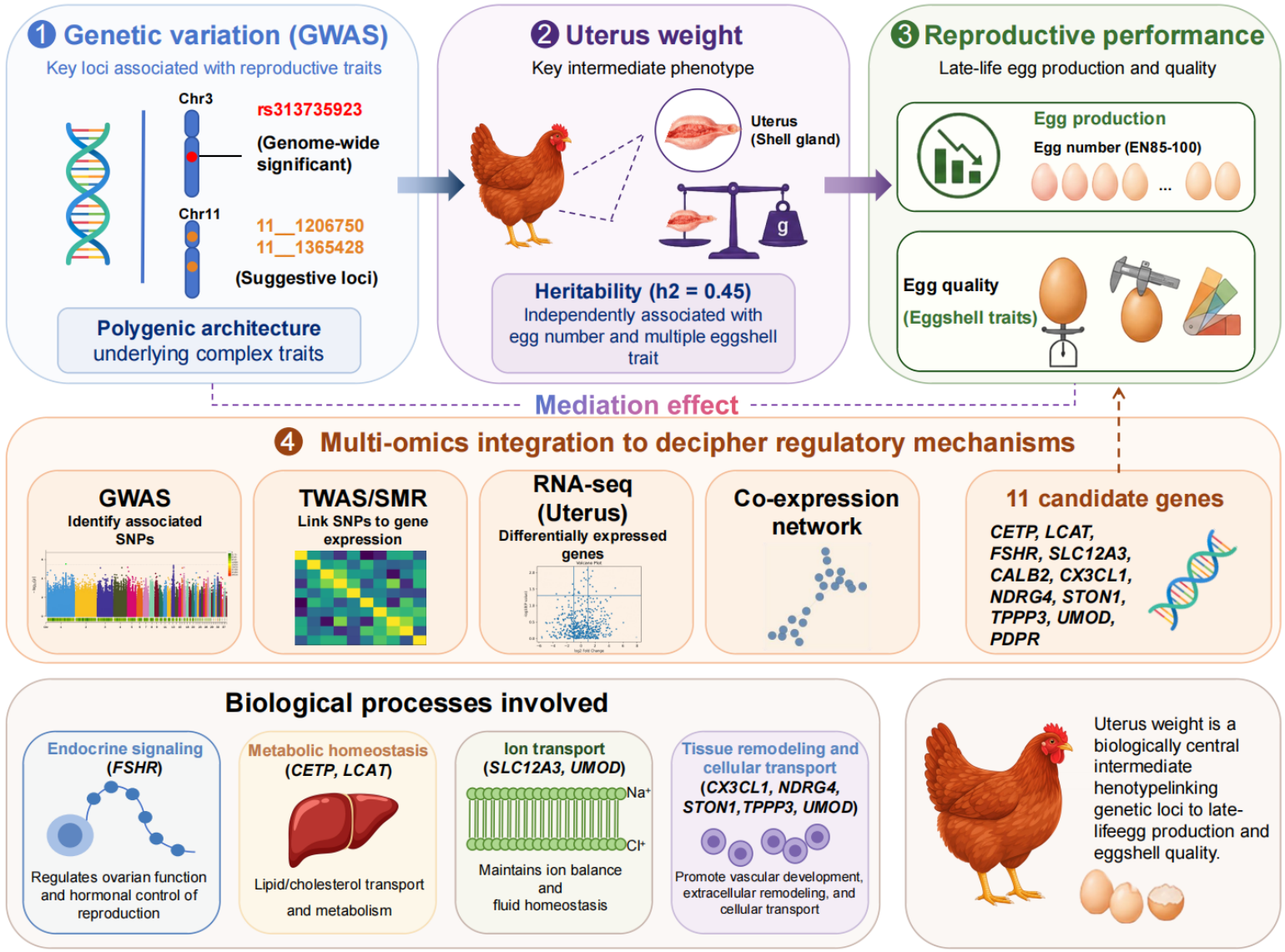
Introduction

① Background

Egg production and egg quality are the core economic traits in the laying hen industry, but both decline significantly during the later stages of lay, accompanied by a reduction in the carcass value of culled hens

② Questions

The physiological regulation and resource allocation during the laying period are complex, and the carcass and reproductive traits may share a common genetic basis. However, the genetic relationship among these three aspects remains unclear in aged hens



Highlights

1

Uterus weight as heritable intermediate phenotype

h^2=0.45; independently associated with late-life egg production and eggshell quality

2

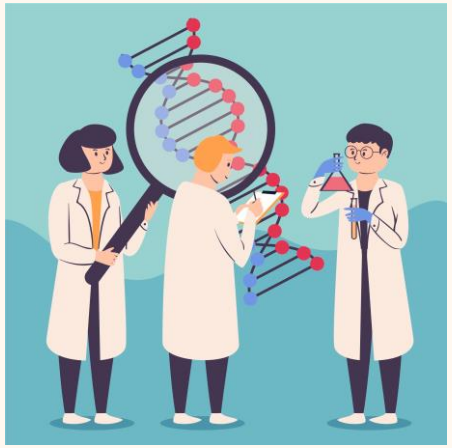
GWAS + Mediation analysis reveals genetic architecture

Genome-wide significant locuson Chr3 (*NRXN1*, *FSHR*, *LHCGR*); 403 SNPs with mediation effects on EN85-100

3

Multi tissue and omics integration identifies 11 candidate genes

Involved in pathways such as endocrine signaling, metabolic homeostasis, and tissue remodeling



Correlation and Regression Analysis

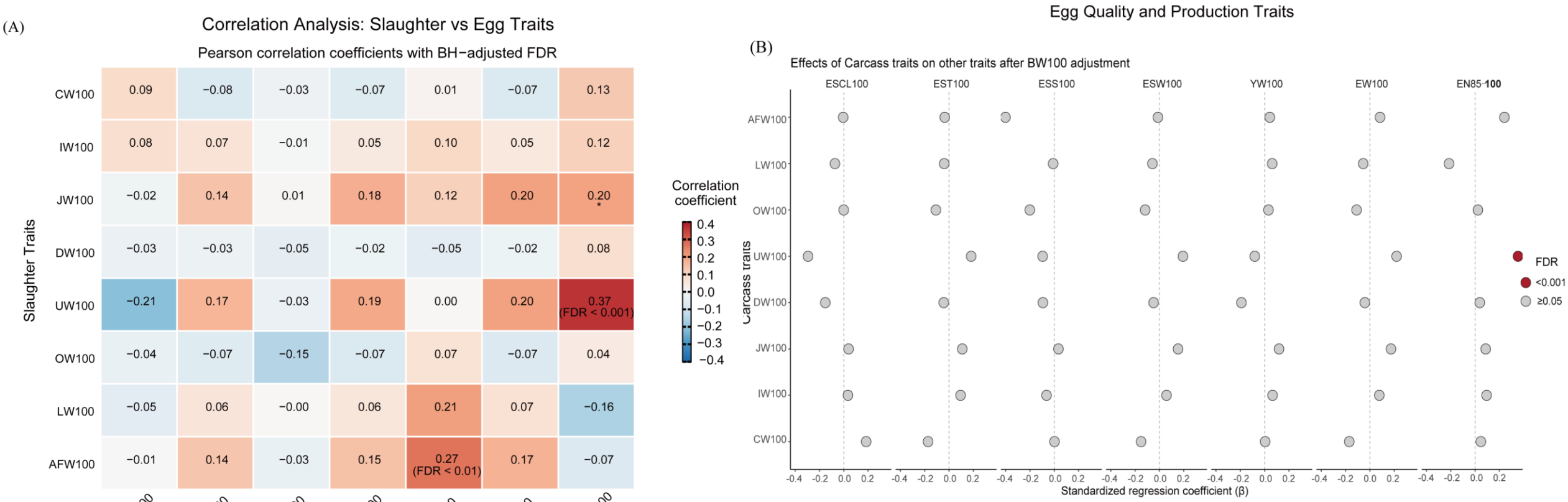
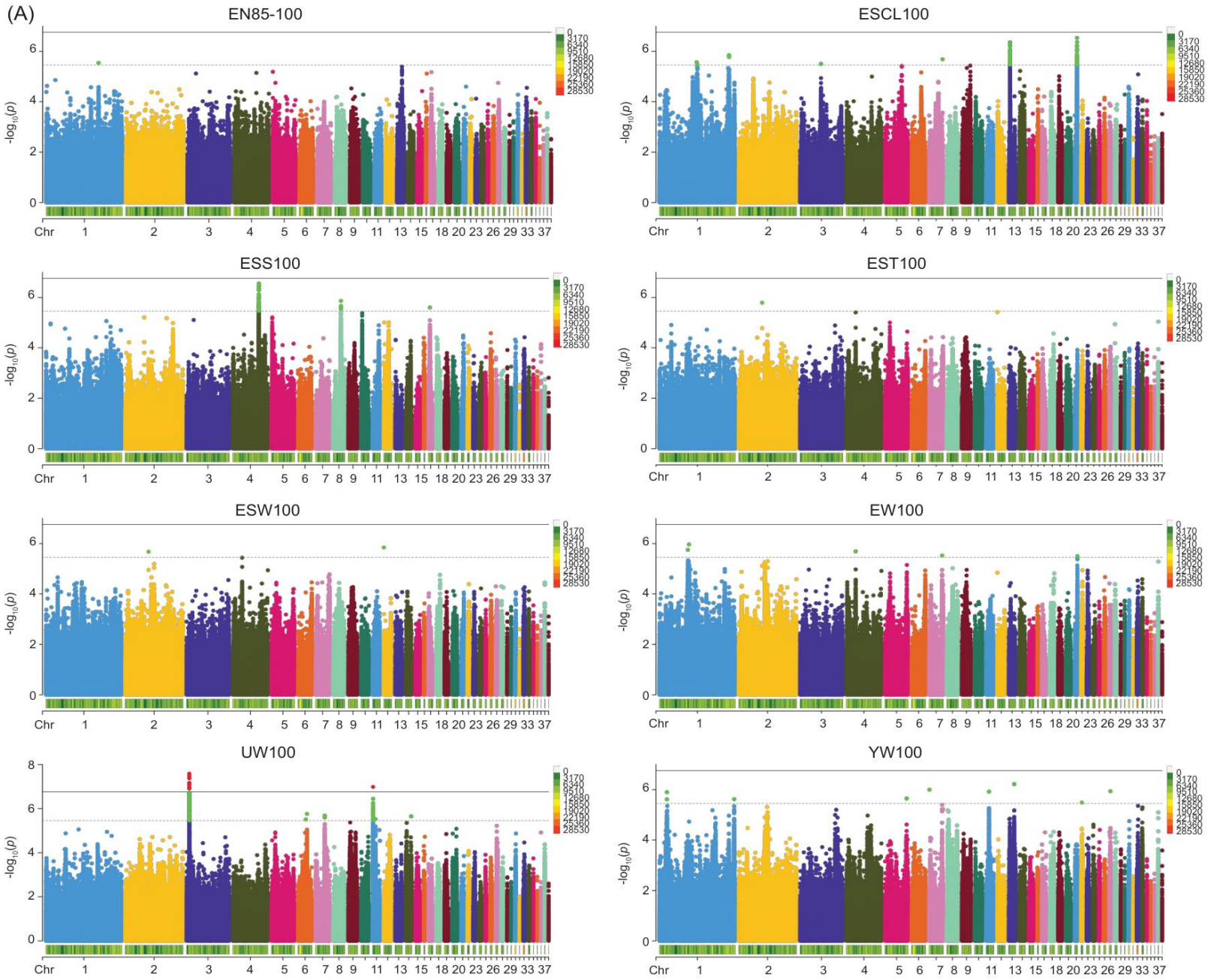


Figure 1. Phenotypic links between slaughter traits and egg production/quality traits at 100 weeks of age.

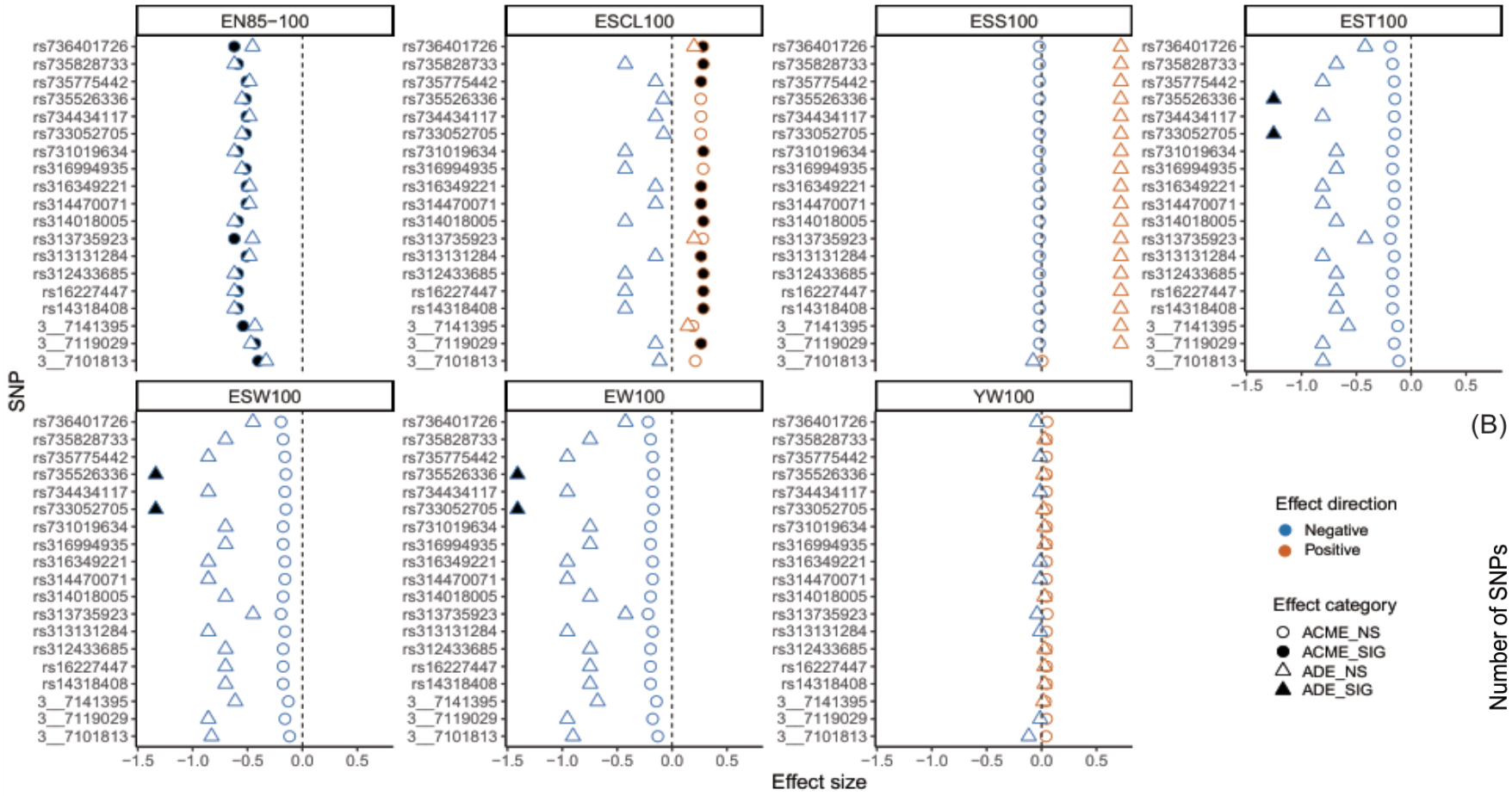
- Uterus weight (UW100) stands out with a strong positive correlation to late-lay egg number (EN85-100, r = 0.37, FDR < 0.001)
- After adjusting for body weight (BW100), the regression plot confirms that the UW100–EN85-100 association remains significant, supporting UW100 as a body-size-independent intermediate phenotype

GWAS and Mediation Analysis



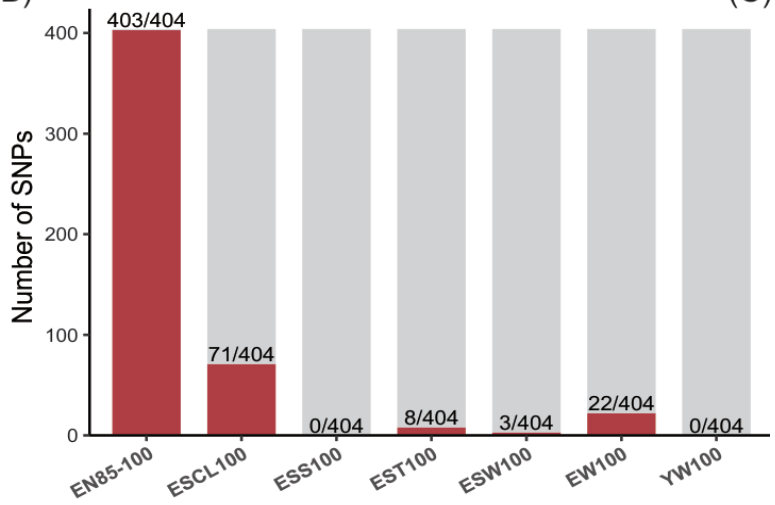
- A pronounced genome-wide significant peak for uterus weight on chromosome 3 near hormone-regulating genes including *FSHR* and *LHCGR*, whereas egg production

GWAS and Mediation Analysis



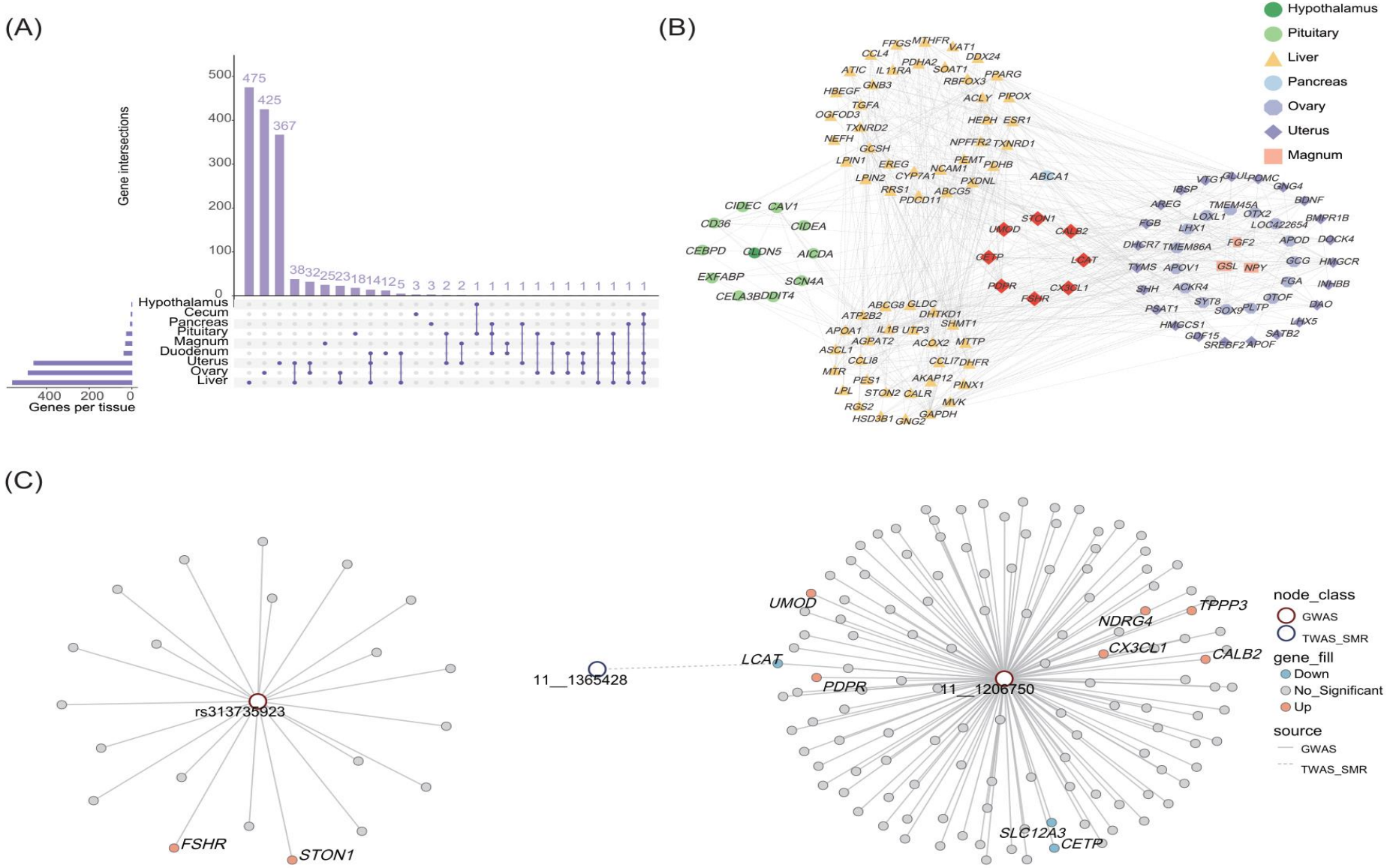
(B)

(C)



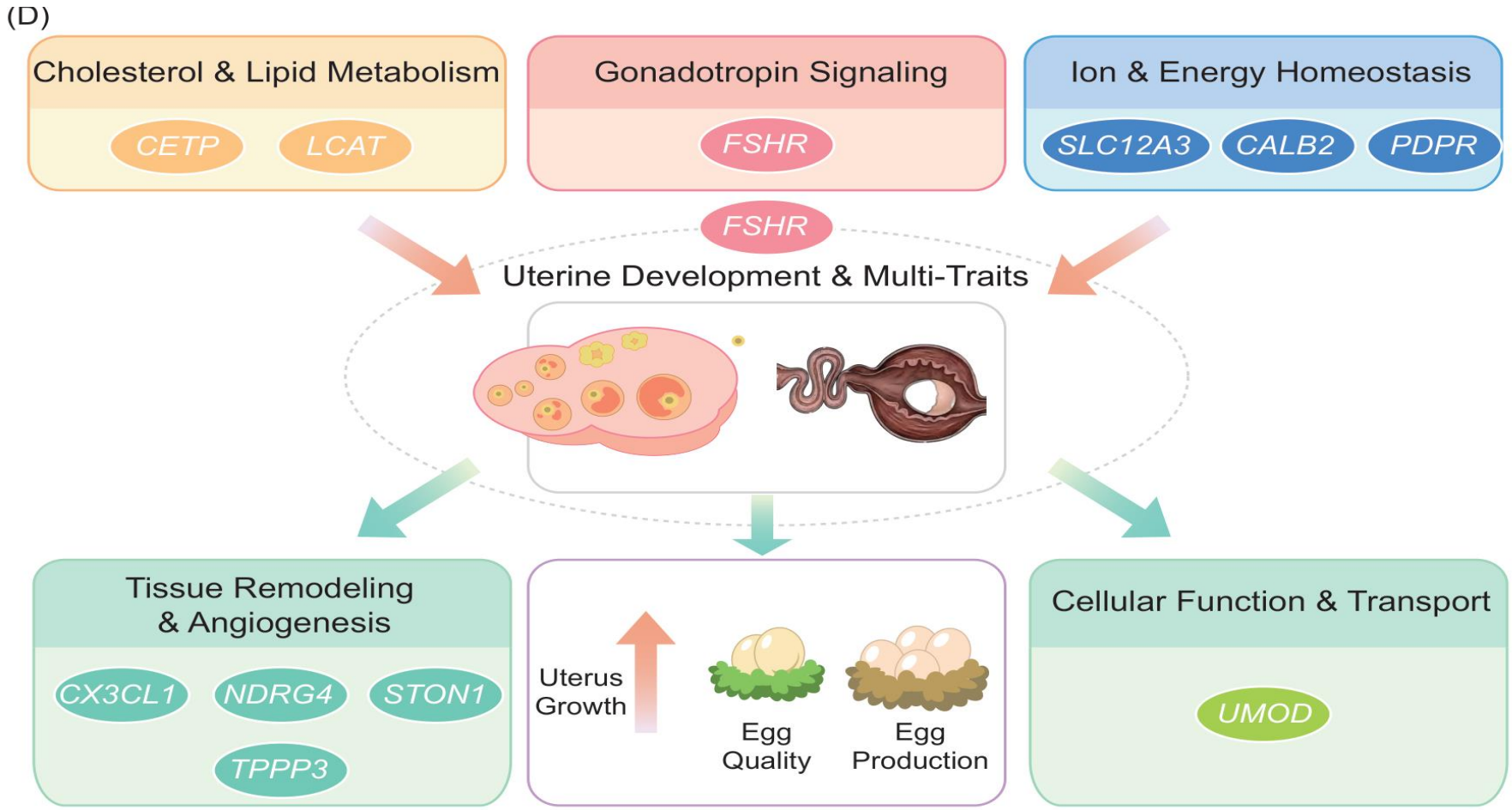
- Mediation analysis further reveals that 403 of 404 suggestive SNPs significantly affect EN85-100
- For chromosome 3 significant variants, most of them are proved to effect EN85-100 by uterus weight

Multi Tissue Analysis and Candidate Genes Identification



- The overlapping genes among different tissues are relatively few, indicating that the regulatory mechanisms related to uterine weight mainly have tissue specificity

Multi Tissue Analysis and Candidate Genes Identification



- Through GWAS, TWAS/SMR, differential expression and WGCNA, including *FSHR*, *CETP*, *LCAT* and *SLC12A3*, etc. were identified,, and a SNP-gene network was formed
- These genes are closely related to endocrine signal transduction, cholesterol/lipid metabolism, ion and energy homeostasis and other functions

Summary

- Uterus weight is a heritable (h^2=0.45), body weight-independent intermediate phenotype that links genetic variation with late-life egg production and eggshell quality
- GWAS revealed a genome-wide significant locus on chromosome 3 (*NRXN1*, *FSHR*, *LHCGR*); mediation analysis uncovered 403 SNPs with indirect effects through uterus weight
- Integrative multi-omics (TWAS/SMR + DESeq2 + WGCNA) prioritized 11 candidate genes spanning endocrine signaling, lipid metabolism, ion transport, and tissue remodeling

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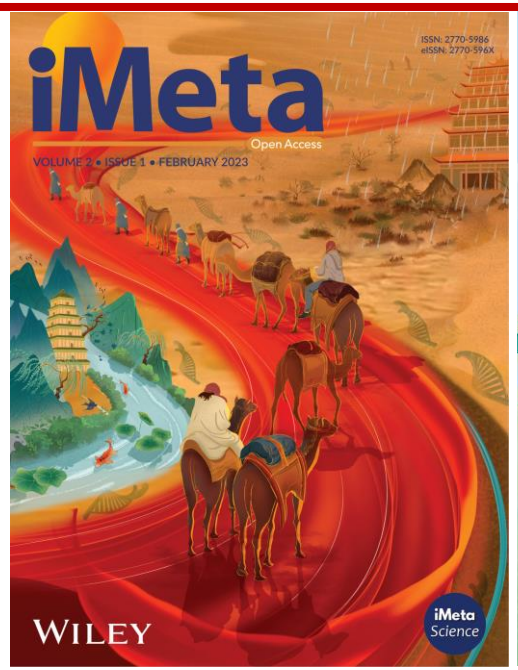

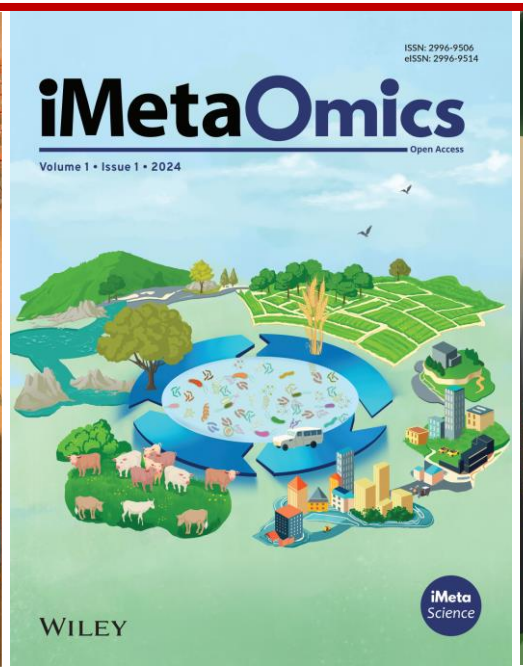

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