

# GENOME-WIDE ASSOCIATION STUDY OF VHS (VIRAL HEMORRHAGIC SEPTICEMIA) RESISTANCE TRAITS USING HIGH-DENSITY SNP ARRAY IN OLIVE FLOUNDER (*Paralichthys olivaceus*)

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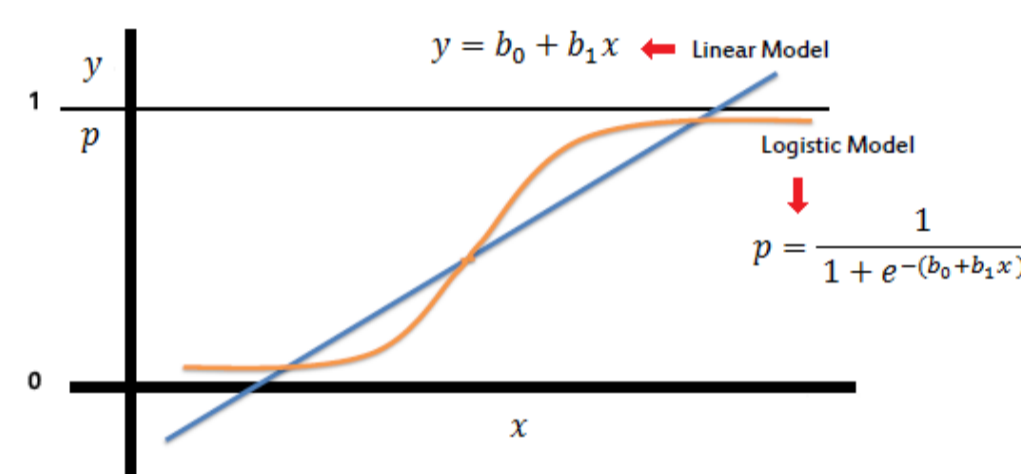
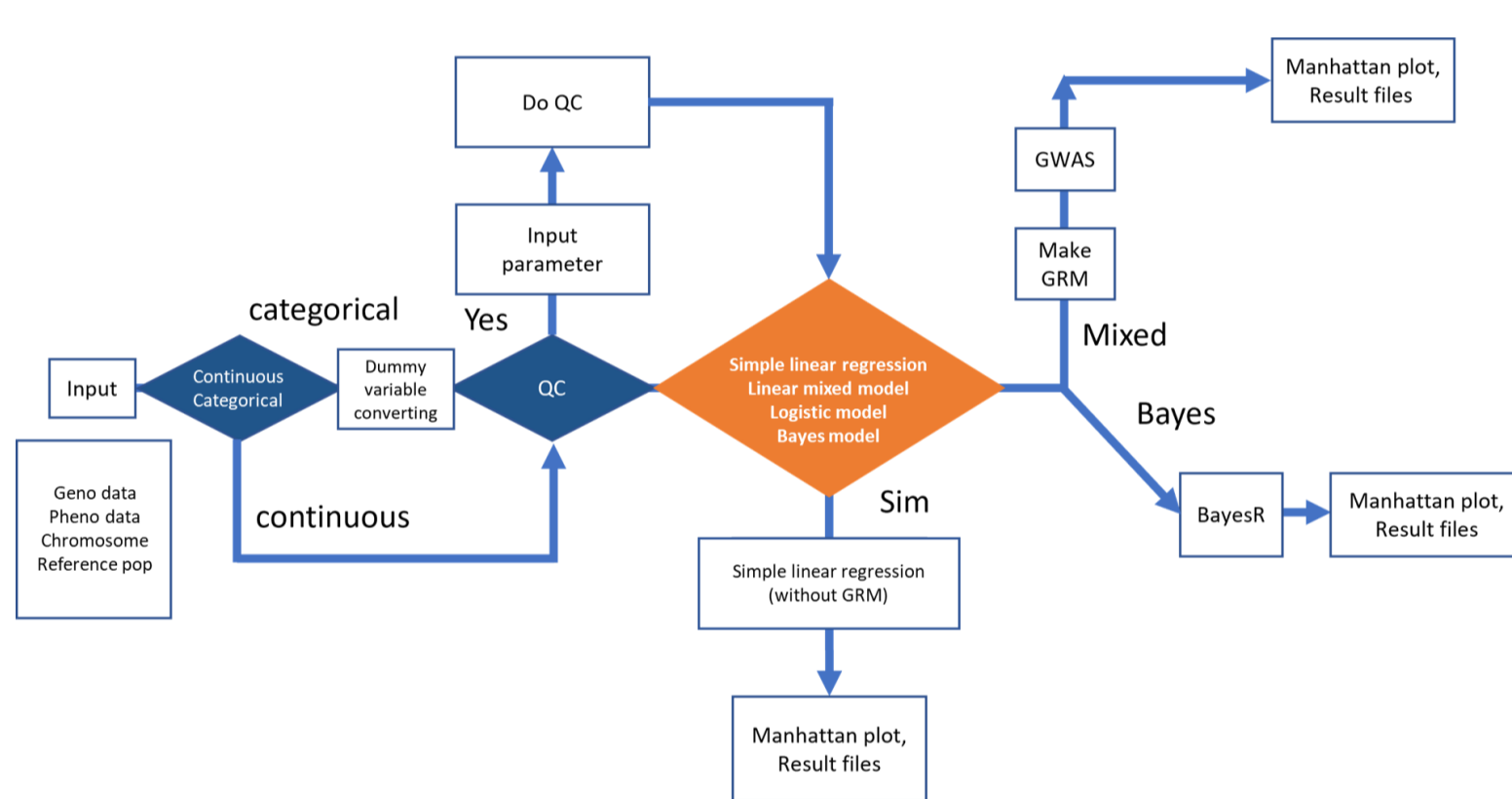
## ABSTRACT

Viral Hemorrhagic Septicemia (VHS) represents a significant threat to aquaculture, causing substantial losses in olive flounder (*Paralichthys olivaceus*), a species of paramount importance in marine aquaculture of South Korea. In this study, Genome-Wide Association Study (GWAS) for VHS resistance traits (survival: SUR, days post challenge: DPC) was conducted to uncover genetic parameter and direct or indirect connection between genotype and phenotype of the target trait.

This study aimed to assess performance of 4 different GWAS models (Simple Linear Regression: SLR, Linear Mixed Model: LMM, Logistic model: Logit, Bayesian model: Bayes) for detecting significant SNPs related VHS resistance traits in olive flounder.

A total of 2,398 olive flounders, including VHS-resistant and susceptible groups, were genotyped using a 120K SNP chip designed specifically for this species. In the case of SUR trait, 4 SNPs showed significance ( $p < 1 \times 10^{-6}$ ) in the logistic regression model, while mixed logit model revealed only 1 SNP. SLR and LMM model detected 96, 80 significant SNPs associated with DPC trait respectively and the effects of SNPs using Bayes model were shown. As SLR and LMM were used for SUR trait, lambda was found to be 2.043 and 1.001, respectively. For DPC trait with the same models, lambda was confirmed as 1.207 and 0.983, respectively. Both SUR and DPC traits showed that the expected and observed p-values exhibit non-linear when using SLR, with lambda values deviating from 1 compared to results of LMM. This indicates that overestimation is relatively severe, suggesting it might not be suitable for exploring VHS resistant trait-associated variations.

## METHODS



Simple linear regression:  $Y_i = \beta_0 + \beta_1 X_i + \epsilon_i$

Logistic model:  $\ln\left(\frac{p}{1-p}\right) = \beta_0 + \beta_1 x$   
 $\Rightarrow p = \frac{e^{\beta_0 + \beta_1 x}}{1 + e^{\beta_0 + \beta_1 x}}$

Linear mixed model:  $y = X\beta + Zu + e$

Bayes model:  $p(\beta | \pi, \sigma^2) = \pi_1 \times N(0, 0 \times \sigma^2) + \pi_2 \times N(0, 10^{-3} \times \sigma^2) + \pi_3 \times N(0, 10^{-3} \times \sigma^2) + \pi_4 \times N(0, 10^{-2} \times \sigma^2)$

## RESULTS

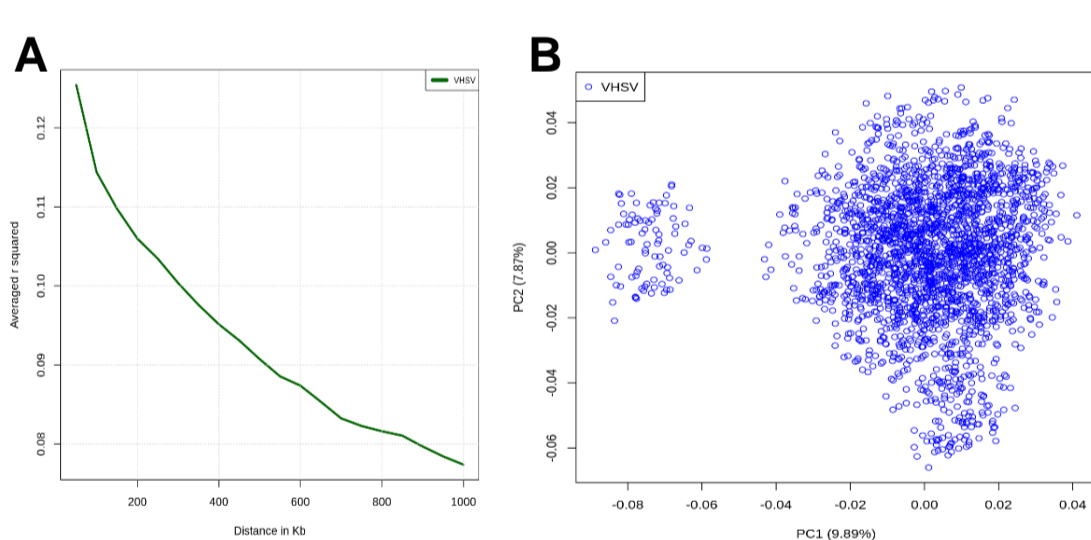


Fig. 1. Visualization of population structure. A, analysis of linkage disequilibrium. The x axis represents distance(kilobase) between SNPs, and the y axis represents average of r squared. B, principal component analysis with the first two principal components.

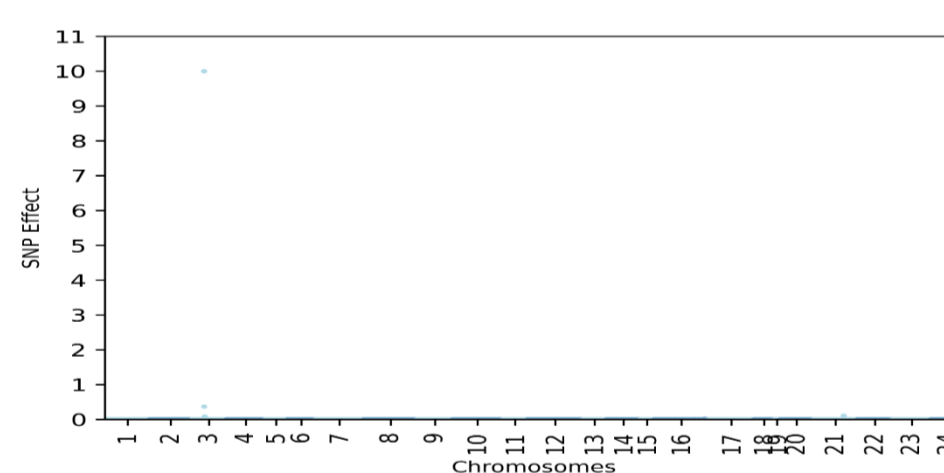


Fig. 2. Genome-wide association study of days-to-death before mortality in VHSV challenge experiment using bayesian method(Bayes).

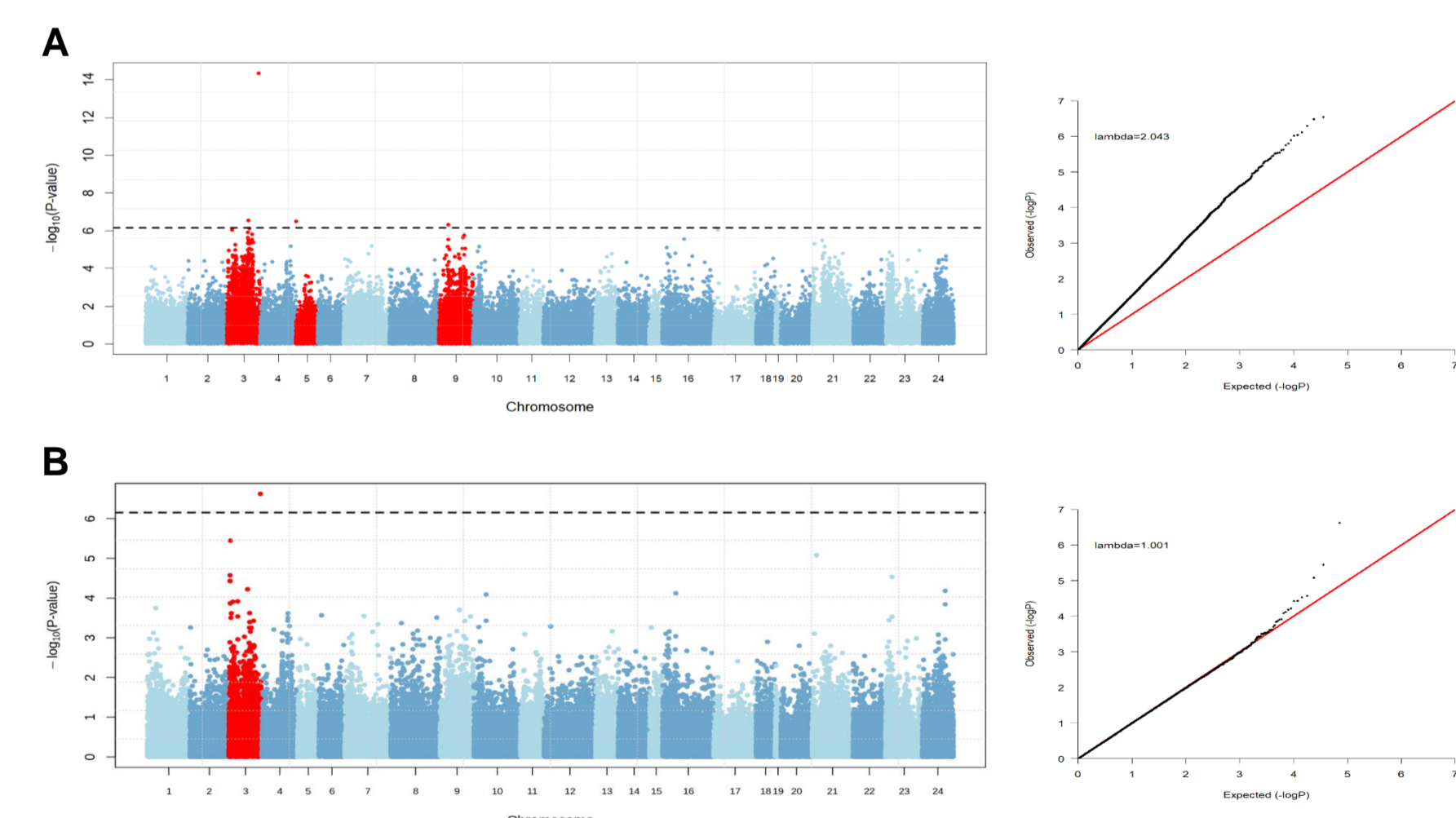


Fig. 3. Manhattan plot and qq plot for A, survival status in VHSV challenge experiment using logistic simple regression analysis and B, survival status in VHSV challenge experiment using mixed logit model. Bonferroni's cutoff was used as threshold and chromosomes with significant SNPs are indicated by red. Lambda( $\lambda$ ) were 2.043 and 1.001 respectively. As using logistic simple regression model, the expected and observed p-values deviated from 1. This indicates that overestimation is relatively severe and unsuitable for exploring traits-associated variants.

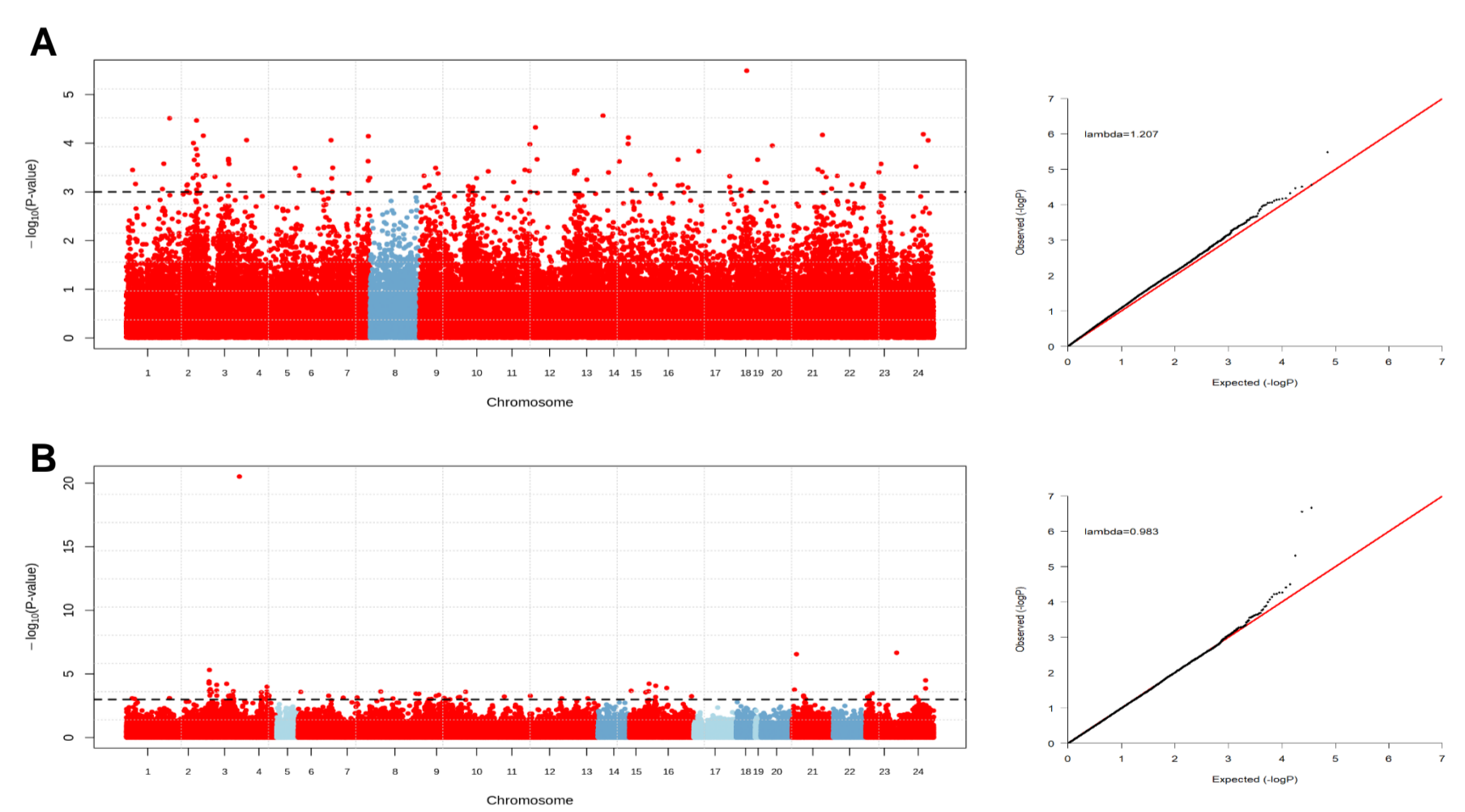


Fig. 3. Manhattan plot and qq plot for A, days-to-death before mortality in VHSV challenge experiment using simple linear regression model(SLR) and B, days-to-death before mortality in VHSV challenge experiment using liner mixed model(LMM). Bonferroni's cutoff was used as threshold and chromosomes with significant SNPs are indicated by red. Lambda( $\lambda$ ) in qq plot were 1.207 and 0.983 respectively.

## Conclusion

The findings from this study not only enhance our understanding of the genetic background of disease resistance in olive flounder but also provide valuable markers for selective breeding programs aimed at improving VHS resistance in this species.

## Acknowledgement

This work was supported by the National Institute of Fisheries Science, Ministry of Oceans and Fisheries, Korea (R2024032).



Ministry of Oceans and Fisheries  
National Institute of Fisheries Science  
Genetics and Breeding Research Center