

INTEGRATION OF DIFFERENT OMICS LAYERS WITH SNP-SNP INTERACTION NETWORKS ASSOCIATED WITH METHANE EMISSION IN NELORE CATTLE

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Abstract:

Complex traits are often determined by the small effects of many SNPs interactions. This interaction, known as epistasis, is one of the non-additive effects present when a trait-related variant is affected by other variants in the genome. Previously, weighted SNP correlation network analysis identified many modules of SNPs associated with residual methane emission (RME) in Nelore cattle. Here, we reported the impact of these interactions in other omics layers (*i.e.*, microorganisms and metabolites profile in the rumen and stool, and mRNA and miRNA expression in the rumen tissue). The experimental population consisted of 52 animals genotyped using the GGP 50k chip. RME was measured as the difference between methane emission and individual dry matter intake (DMI, kg/d). The epistatic interactions for RME in Nelore cattle were calculated using the WISH-R package, considering the default parameters. The epistatic signed weighted networks were constructed, and genomic interaction modules were created based on the WGCNA pipeline. Clustering the SNPs after LD pruning, a total of four SNP-SNP modules ($r > 0.4$ and $p\text{-value} \leq 0.01$) were identified. Two modules showed a negative correlation (-RME), while the other two were positively associated with the RME trait (+RME). Analysis between RME-associated modules showed a significant correlation with eight different archaeal amplicon sequence variants (ASVs), three in the stool and five in the rumen. Stool archaeal ASVs were in general unassigned. Only one (ASV_1471), classified as *Methanobrevibacter gottschalkii*, was positively associated with a -RME module. Four ruminal archaeal ASVs were classified as *Methanobrevibacter*: *Methanobrevibacter ruminantium* and *Methanobrevibacter gottschalkii*. All of the four ASVs were positively associated with +RME modules. A total of 30 bacterial ASVs were related to the RME-associated modules. Ten bacterial ASVs in the stool, classified mainly as *Ruminococcaceae* and *Bacteroides*, and twenty ruminal bacterial ASVs (*e.g.*, *Treponema* and *Prevotellaceae*) were related to the RME modules-associated. The ASV_3873, classified as *Solobacterium*, was correlated with all four RME-associated modules. While the ASV_85, classified as *Alistipes*, was positively associated with -RME modules in the stool. Consistently, both ASVs were associated with RME in the same population. The xanthine metabolite was positively associated with two -RME modules in the stool. In addition, the modules associated with the RME trait showed significant correlations with gene expression. A total of 27 mRNAs (*e.g.*, *CHMP4*, *CFI*, *THBS1*, and *ITGA5*) and two miRNAs (bta-mir-2443 and bta-mir-7) were associated with RME modules. These genes are involved in glutathione metabolism, hypoxia and oxidative stress response, and interleukin-7-mediated signaling processes. The following steps are to investigate in detail the genes and SNPs found in this study. These results identify a series of genes and metabolic profiles correlated with methane emission and provide new targets for mitigation of this phenotype at the levels of microbiota composition and transcriptional regulation.

Palavras-chave: multi-omics; epistasis; biological networks; ;

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