

Enhancer-promoter interaction maps provide insights into skeletal muscle-related traits in pig genome

Jingjin Li^{1*}, Yue Xiang^{1*}, Lu Zhang^{1*}, Xiaolong Qi¹, Zhuqing Zheng¹, Peng Zhou¹, Zhenshuang Tang¹, Jin Yi¹, Qiulin Zhao¹, Yuhua Fu¹, Yunxia Zhao¹, Xinyun Li^{1,2†}, Liangliang Fu^{1,2†}, Shuhong Zhao^{1,2†}

¹Key Laboratory of Agricultural Animal Genetics, Breeding and Reproduction of Ministry of Education & Key Lab of Swine Genetics and Breeding of Ministry of Agriculture and Rural Affairs, Huazhong Agricultural University, Wuhan 430070, P. R. China;

²The Cooperative Innovation Center for Sustainable Pig Production, Huazhong Agricultural University, Wuhan 430070, P. R. China;

*These authors contributed equally to this work.

† Corresponding author:

Correspondence and requests for materials should be addressed to Shuhong Zhao (shzhao@mail.hzau.edu.cn)

Many variants related to complex traits have been identified by Genome-wide association studies (GWAS), but translating them into target genes from a multi-omics dimension has posed a major challenge over the past decade. Here, we first present a comprehensive interaction map of nuclear dynamics of 3D chromatin-chromatin interactions (H3K27ac BL-HiChIP) and RNA-chromatin interactions (GRID-seq) to reveal genomic variants that contribute to complex skeletal muscle-associated traits. In a genome-wide scan, we provide systematic fine mapping and gene prioritization from GWAS leading signals that underlie phenotypic variability of growth rate, meat quality, and carcass performance. A set of candidate causal variants and 54 target genes previously not detected were identified, with 71% of these candidate causal variants choosing to skip over their nearest gene to regulate the target gene in a long-range manner. We further provide cohort validation for three functional variants regulating *KLF6* related to Days to 100 Kg (AGE), *MXRAB* related to Lean meat percentage (LMP), and *TAF11* related to Loin muscle depth (LMD). Moreover, we find that this multi-omics interaction map consists of functional communities that are enriched in specific biological functions, and GWAS target genes can serve as core genes for exploring

peripheral trait-relevant genes. Overall, utilizing RNA-chromatin and chromatin-chromatin interactions simultaneously and investigating their mutual effects on transcriptional regulation provide new approaches and insights for future association studies.

Keywords: H3K27ac BL-HiChIP, GRID-seq, GWAS, Skeletal Muscle, Pigs