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The WISH network method applied to obesity in an F2 pig popolution

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High-throughput genotype (HGT) data are extensively used in genome-wide association studies (GWAS) to investigate the biological and genetic background of complex traits, such as obesity. Unfortunately, to date results explaining complete genetic variation are limited. As it has been repeatedly shown that gene x gene interactions may play a key role in complex traits, systems genetics approaches are increasingly used to elucidate more of the currently limited knowledge of complex traits. We previously published the Weighted Interaction SNP Hub (WISH) network method, which uses HGT data to detect modules of highly interconnected SNPs, potentially representing biological pathways associated with the trait under study. Here we used the WISH network method to study obesity in a porcine model for human obesity. We previously created an F2 pig population, which was extensively phenotyped and genotyped. We created an Obesity Index (OI) based on multi-trait selection indexes containing nine obesity-related phenotypes, to perform a GWAS and WISH network analysis, both followed up with pathway analysis. The GWAS revealed 404 SNPs highly associated with the OI, and functional annotation revealed several genes located in or near those SNPs related to obesity (e.g. NPC2). Furthermore, WISH network construction revealed several modules related to obesity, and pathway analysis revealed among others an overrepresentation of *purinergic receptor activity*, which has been associated before with feeding behavior. In conclusion, this study shows the potential of systems genetics methods that involve network and pathway based approaches to jointly use phenotype and high-throughput genotype data. In particular, the WISH method moves GWAS beyond its scope to detect gene x gene interactions, resulting in the detection of biologically relevant pathways in complex traits.