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Whole-genome resequencing analysis of 49 Ossabaw pigs for the definition of thrifty genotype-associated gene loci

Yaolei Zhang[1, 2, 3, 4, 5], Guangyi Fan[2, 3, 4], Xin Liu[2, 3, 4], Kerstin Skovgaard[1], Peter M.H. Heegaard[1, 5, 6]

[1]Department of Biotechnology and Biomedicine, Technical University of Denmark, Lyngby, Denmark; [2]BGI-Qingdao, BGI-Shenzhen, Qingdao 266555, China; [3]BGI-Shenzhen, Shenzhen 518083, China; [4]China National GeneBank, BGI-Shenzhen, Shenzhen, 518120, China; [5]Department of Health Technology, Technical University of Denmark, Lyngby, Denmark; [6]presenting author

The markedly thrifty phenotype of the Ossabaw pig makes it extremely prone to obesity and the metabolic syndrome when subjected to prolonged high-energy dieting. Thus, the Ossabaw pig is an outstanding human translatable animal model for obesity-related metabolic disorders and disease.

We recently published the first full, high quality genome of the Ossabaw pig breed based on DNA from a single Ossabaw sow. Based on this genome we in the present study performed a whole-genome resequencing analysis of 49 individual Ossabaw pigs and compared genomes to published genome data from five other pig breeds (comprising 44 individual pig genomes). The aim was to further investigate and define the unique genetics of this obesity prone pig breed compared to lean type pig breeds to establish a robust 'genetic blueprint for obesity'.

Approximately 3.6 Tb of new sequencing data was generated, covering ~27.4-fold of the reference pig genome. We identified 12,678,637 SNPs in the Ossabaw population, of which 3,688,878 were shared among all 49 Ossabaw individuals. Of these shared SNPs 463,195 were novel, i.e. not described in the Ensembl pig dbSNP (release-104) database. These novel, shared Ossabaw SNPs are potential candidate loci associated with the Ossabaw specific "thrifty genotype" and other Ossabaw specific features. Of the 463,195 SNPs, ~65.86% were located in intergenic regions, while ~34.14% were located in gene regions. For the latter, ~2.42% (3,835) were found in exon regions, whereof 1,815 were non-synonymous mutations that lead to changes in amino acids of a total of 849 gene products. A striking example is *LEP* (leptin) having two new, i.e. Ossabaw-specific, non-synonymous mutations.

We also identified genomic selective-sweep regions of the Ossabaw population harboring genes crucial to lipid metabolism. Evaluating the inbreeding event for all pigs, Ossabaw individuals were found to have a much higher number of homozygosity fragments with 27 high-frequency runs of homozygosity (ROH) regions which contained important genes such as *POMC*, *PPARGC1A*, *CD36*, *AQP3*, and *AQP7*, which are closely related to obesity, insulin resistance and diabetes. Along with the 849 genes mentioned above, these genes are candidate genetic markers for obesity and comorbidities.