Integrated network multi-omics approach highlights muscle late fetal maturation process

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P3006 Integrated network multi-omics approach highlights muscle late fetal maturation process.

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While transcriptomic analysis has provided incredible insight into cell operation, an integrated multi-omics approach is crucial to gain further insights into complex biological systems. Here, we chose to develop an integrated network method of proteomic and phenotypic data, with integration of transcriptomic information, to highlight some important proteins during the end of gestation in pig skeletal muscle. Networks are increasingly used to analyze and visualize data in biology and genetics. An integrated network analysis was first developed to explore relationships between co-expression network models, built from proteomic data, and targeted biological phenotypes of interest to identify molecular signatures underlying late fetal muscle development. Second, correlation with muscle transcriptomic data was also investigated to complete and combine different layers of expression. Piglet maturation, which occurs at the end of gestation, leads to a state of full development after birth and is an important determinant of early survival. The objective of our project is an integrated global multi-omics analysis (transcriptome, proteome and targeted biological phenotypes) with a focus on skeletal muscle because of its key role in adaptation to extra-uterine life (locomotion and thermogenesis). Progeny from two extreme purebreds for maturity (Large White and Meishan) were investigated. The Large White (LW) breed is a highly selected breed with a high rate of mortality at birth, whereas the Chinese Meishan (MS) is a more robust breed exhibiting an extremely low neonatal mortality. The late fetal maturation process was analyzed on the progeny from these two breeds (LW, MS and reciprocal F1) at two developmental time points during the end of gestation (90 and 110 d of gestation). First, three targeted biological phenotypes (glycogen, MyHC adult fast and embryonic) were found as good descriptors of muscle maturity. The proteomic approach showed that proteins associated with the cytoskeleton and muscle filaments were overexpressed at 90 dg, whereas proteins involved in muscle energy metabolism were strongly up-regulated at 110 dg. The integrated network analysis revealed a high number of proteins involved in the mitochondrial oxidation/reduction metabolic process that were overexpressed at 110 dg with a higher expression in MS than in LW. In particular, CKMT2 and ATP5A1 were identified as important nodes and possible good biological markers of muscle maturity at 110 dg. Our data also showed that some of these proteins are transcriptionally regulated and that PPARGC1A could be an important transcriptional factor.

Key Words: biological data integration, muscle fetal development, pigs

P3007 Time course of the response to ACTH in pig: biological and transcriptomic study.

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The hypothalamic–pituitary–adrenal (HPA) axis plays a major role in physiological homeostasis. It is also involved in stress and adaptive response to the environment. In farm animals in general and more specifically in pigs, breeding strategies have highly favored production traits such as lean growth rate, feed efficiency and prolificacy at the cost of robustness. On the hypothesis that the HPA axis could contribute to the trade-off between robustness and production traits, we have designed this experiment to explore individual variation in the biological response to the main stress hormone, cortisol, in pigs. We used adrenocorticotropic hormone (ACTH) injections to trigger production of cortisol in 120 juvenile Large White (LW) pigs from 28 litters, and the kinetics of the response was measured with biological variables and whole blood gene expression at four time points. A multilevel statistical analysis was used to take into account the longitudinal aspect of the data.

Cortisol level reached its peak 1 h after ACTH injection. White blood cell composition was modified with a decrease of lymphocytes and monocytes and an increase of granulocytes ($FDR < 0.05$). Basal level of cortisol was correlated with birth and weaning weights. Microarray analysis identified 65 unique genes whose expression responded to the injection of ACTH (adjusted $P\text{-}value < 0.05$). These genes were classified into four clusters with distinctive kinetics in response to ACTH injection. The first cluster identified genes strongly correlated to cortisol and previously reported as being regulated by glucocorticoids. In particular, *DDIT4*, *DUSP1*, *FKBP5*, *IL7R*, *NFKBIA*,