

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

Valérie Sautron^{1,2,3*}, Elena Terenina^{1,2,3}, Laure Gress^{1,2,3}, Yannick Lippi⁴, Yvon Billon⁵, Catherine Larzul^{1,2,3}, Laurence Liaubet^{1,2,3}, Nathalie Villa-Vialaneix⁶ and Pierre Mormède^{1,2,3}

¹INRA, UMR 1388 Génétique, Physiologie et Systèmes d'Élevage, F-31326 Castanet-Tolosan, France.

²Université de Toulouse INPT ENSAT, UMR 1388 Génétique, Physiologie et Systèmes d'Élevage, F-31326 Castanet-Tolosan, France. ³Université de Toulouse INPT ENVT, UMR 1388 Génétique, Physiologie et Systèmes d'Élevage, F-31076 Toulouse, France. ⁴INRA, UMR 1331 ToxAlim, F-31027 Toulouse, France. ⁵INRA, UE 1372 GenESI, F-17700 Surgères, France. ⁶INRA, UR 0875 MIAT Mathématiques et Informatique Appliquées de Toulouse, F-31326 Castanet-Tolosan, France.

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 adrenocorticotrophic 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 4 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 -value < 0.05). These genes were classified into 4 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*, *PER1*, *RGS2* and *RHOB* were shown to be connected to each other by the glucocorticoid receptor NR3C1. Most of the differentially expressed genes that encode transcription factors have not been described yet as being important in transcription networks involved in stress response. Their co-expression indicates possible co-regulation and they potentially provide new potential biomarkers of sensitivity to cortisol.

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