Proceedings of the Nutrition Society (2015), **74 (OCE5)**, E278 doi:10.1017/S0029665115003250

Summer Meeting, 6–9 July 2015, The future of animal products in the human diet: health and environmental concerns

Skeletal muscle hypertrophy in pigs is associated with an increased expression of serine biosynthetic pathway genes along with genes associated with an endoplasmic reticulum stress response

T. Parr[1], K. Ryan[1], H. Williams[1], D. Harris[4], D. Brown[1], M. Mareko[1], R. Emes[2], T. Giles[2], J. Wattis[3], I. Dryden[3], C. Lu[1], C. Hodgman[1] and J. Brameld[1]

[1]*Schools of Biosciences,* [2]*Veterinary Medicine and Science,* [3]*Mathematical Sciences, University of Nottingham, Sutton Bonington Campus, Loughborough, LE12 5RD UK and* [4]*VMRD Global Therapeutics Research, Zoetis, Kalamazoo, MI, 49007, USA*

This abstract was presented as the Cellular and Molecular Nutrition Theme highlight.

This study sought to investigate the mechanisms by which Beta-adrenergic agonists (BA) and Growth Hormone (GH) mediate their muscle hypertrophy effects[1] in pigs treated for 27 days, by examining the changes in skeletal muscle transcriptome and blood metabolome.

Duroc × (Landrance × Large White) gilts (85 kg) were all fed a high protein/ energy diet *ad-libitum,* with the GH group receiving an intramuscular injection of porcine GH (10 mg, Reporcin, Zamira, Australia) every other day, the BA group receiving Ractopamine (Eli Liley, USA) at 20 mg/kg feed, and control group (C) simply had *ad-libitum* feed. Pigs were slaughtered at 1, 3, 7, 13 and 27 days of treatment (n = 10 per treatment per slaughter day, with n = 15 on day 27) and plasma as well as samples of the *Longissimus dorsi* (LD) were collected. The relative mRNA expression of the adult myosin heavy chain isoforms were determined[2]. Metabolomic analysis of plasma samples was carried out by Metabolon Inc (USA). The effect of treatments on the LD transcriptome was assessed using the Agilent pig microarray followed by gene cluster analysis using a modified maSigPro methodology[3]. Verification of differentially expressed genes and proteins in LD was by quantitative RT-PCR and western blotting, respectively.

BA, but not GH, significantly ($P < 0{\cdot}05$) increased muscle weights and inducing a switch to faster muscle fiber types, as assessed by expression of myosin heavy chain isoforms ($P < 0{\cdot}05$), indicating a transition to fast-glycolytic muscle fibre types. In the plasma, BA increased the concentrations of more fatty acids than GH (within 1 day of treatment), only GH increased glucose and there was no effect of either GH or BA on lactate. Both GH and BA decreased certain plasma amino acids, such as lysine, but only GH decreased the concentrations for others, such as serine and glycine. Within 3 days of treatment, BA (but not GH) increased mRNA expression of genes involved in glycolysis but decreased expression of genes in the TCA cycle. The predominant effect of BA was an early (peak at day 3) co-ordinate increase ($P < 0{\cdot}05$) in the expression of serine synthesis pathway genes; phosphoglycerate dehydrogenase (PHGDH), phosphoserine-aminotransferase (PSAT) and phosphoserine phosphatase (PSPH), along with a significant increase in PHGDH protein level with BA. Co-ordinate regulation of gene expression for the serine synthesis pathway has been shown to be mediated via transcription factors associated with the endoplasm reticulum-mediated amino acid response (AAR), such as ATF4[4]. Asparagine synthetase (ASNS) and cationic amino acid transporter CAT-1 (SLC7A1) are characteristic genes upregulated in response to AAR[5] and they were also increased ($P < 0{\cdot}05$) over the time course in BA-treated pigs, similar to the serine synthesis genes.

BA had a stronger muscle hypertrophic effect than GH and this appears to be mediated through its effect on muscle biosynthetic pathways. We show for the first time, that BA induced muscle growth is associated with an early upregulation of the serine biosynthetic pathway and increased expression of other genes characteristic of the AAR. GH appears to have wider effects on whole body metabolism, whereas BA has a much stronger effect on both muscle metabolism and growth which, in part, appear to be mediated via an endoplasm reticulum-mediated amino acid response.

This work was supported by the Biotechnology and Biological Sciences Research Council (BBSRC)

1. Bell AW, Bauman DE, Beermann DH *et al.* (1998) *J Nutr* **128**, 360S–363S.
2. Hemmings K, Parr T, Daniel ZC *et al.* (2009) *J Anim Sci* **87**, 3915–3922.
3. Conesa A, Nueda MJ, Ferrer A & Talón (2006) *Bioinformatics* **22**, 1096–1102.
4. Adams CM (2007) *JBC* **282**, 16744–16753.
5. Kilberg MS, Shan J, & Su N (2009) *Trends in Endo & Met* **20**, 436–443.

Proceedings of the Nutrition Society

https://doi.org/10.1017/S0029665115003250 Published online by Cambridge University Press