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Session 02 Theatre 6

A dynamic mathematical model to study the flexibility of energy reserves in adipose and muscle cells

M. Taghipoor, J. Van Milgen and F. Gondret
INRA, UMR1348 Pegase, Domaine de la Prise, 35590 Saint Gilles, France; florence.gondret@rennes.inra.fr

Animals need energy for their basal metabolism and productive functions. When dietary energy intake exceeds energy expenditure, the excess is stored as glycogen and triacylglycerols (TG) in cells. The dynamics of uptake, oxidation and storage of nutrients at the cellular level are very important to understand tissue composition and to predict the effects of different sources of energy supply to animals. A dynamic model was developed to investigate the plasticity of energy stores into a generic cell. This model was based on a system of coupled ordinary differential equations, with each equation representing a single biochemical reaction or successive transformations of intermediate metabolites. Reaction rates were regulated by the activities of enzymes involved in the reactions. The ATP/ADP ratio was assumed to be the main intracellular signal to switch between storage and oxidation pathways. Cellular uptake of glucose and free fatty acids was modeled in a continuous or discontinuous phenomenon during the day. Simulations included the time-dependent evolution of glycogen and TG in the cell. Because of its generic aspect, the model can be used to study muscle or adipocyte metabolism by changing the basic parameters. Further development would include hormone signals regulating the partitioning of nutrients between muscle and adipose cells, and the coupling between hypertrophy and hyperplasia in tissue development. In conclusion, the model provides a dynamic framework to investigate relevant hypotheses in farm animal production, including the postprandial metabolism (fast dynamics) and flexibility of energy reserves in response to changes in feed intake, physical activity or growth (slow dynamics).

Session 02 Theatre 7

Adipose tissue hypoxia is related to increased mtDNA copies and decreased VEGF-A in fat dairy cows

L. Laubenthal[1], L. Locher[2], J. Winkler[3], U. Meyer[3], J. Rehage[2], S. Dänicke[3], H. Sauerwein[1] and S. Häussler[1]
[1]University of Bonn, Institute of Animal Science, Katzenburgweg 7-9, 53115 Bonn, Germany, [2]University for Veterinary Medicine, Clinic for Cattle, Bischofsholer Damm 15, 30173 Hannover, Germany, [3]Friedrich-Loeffler-Institute, Institute of Animal Nutrition, Bundesallee 50, 38116 Braunschweig, Germany; lilian.laubenthal@uni-bonn.de

Due to the potentially inadequate vascularization, as previously indicated by the pro-angiogenic vascular endothelial growth factor A (VEGF-A) in adipose tissue (AT) of overconditioned cows, we hypothesized that cell oxygen supply is insufficient and will increase the hypoxia-inducible-factor-1α (HIF-1α) indicating local hypoxia. We aimed to examine whether mitochondrial DNA (mtDNA) copy numbers, reflecting the abundance of mitochondria and thus the energetic status of a cell, are related to HIF-1α. Non-pregnant, non-lactating cows (n=8) were fed diets with increasing concentrate feed proportions during the first 6 weeks of the trial until a proportion of 60% was reached, which was maintained for another 9 weeks. Body weight and condition score increased from 540±20 to 792±29 kg and from 2.31±0.12 to 4.53±0.14 throughout the trial, respectively. Subcutaneous AT biopsies from the beginning and after 15 weeks of trial were immunohistochemically evaluated for HIF-1α-positive cells or analyzed for mtDNA copy number and VEGF-A protein expression via multiplex qPCR and semi-quantitative Western blot, respectively. Data were analyzed using the pairwise Student´s t-test (HIF-1α) and the Wilcoxon test (mtDNA, VEGF-A; SPSS). HIF-1α-positive cells tended to be increased 3.3-fold throughout the trial ($P=0.065$) and were correlated to mtDNA copies ($\rho=0.55$, $P=0.034$), and to VEGF-A amounts ($r=-0.654$, $P=0.008$). Decreasing VEGF-A together with excessive fat accumulation indicates inadequate angiogenesis leading to local hypoxia in AT of overconditioned cows. The increase of mtDNA copies might be a compensatory reaction to prolong adipocyte life in face of hypoxic conditions.