Modulation of the redox state in pigs differing in feed efficiency as revealed by a proteomic analysis

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EAAP 2014: Appetite control – mechanisms and comparative aspects
Animal feed efficiency (FE): a trait with a large economic impact for producers

Typical calculation of FE: **feed intake/average daily gain**

Residual feed intake (RFI): observed feed intake – expected feed intake

- Feed composition
- Feed availability
- Feed palatability

**Management factors**
- Disease
- Environment

**Physiology & genetics**
- BW^{0.60} ; ADG ; Backfat
  - maintenance  production

RFI: ~ one third to half of the total variation in feed intake in growing pigs

*(Knapp, 2009; Young & Dekkers, 2012)*

• Context
Variations in residual feed intake (RFI):

Feed consumption & behavior (number of visits, duration of meal intake, time spent eating, etc...)

Young et al., 2011  Meunier-Salaün et al., 2012

Digestion and utilization of nutrients

Barea et al., 2010

**Organ physiology**: thermoregulation
basal metabolic rate
energy efficiency of mitochondria
protein turnover rate
immunity, etc.

Le Naou et al., 2012; Gabler et al., 2013; Grubbs et al., 2013
The liver is a complex and unique organ responsible for a breadth of functions that are crucial for sustaining life.

We propose to use a proteomic differential approach to identify the modulation of hepatic metabolic processes participating to feed efficiency.
6th generation of a **divergent selection for RFI in pigs**

Large White pure genotype 10 wks of age (30 kg BW)

- **RFI-** (low feed intake, high FE)
- **RFI+_R** (pair-fed to RFI- pigs)
- **RFI+** (high feed intake, low FE)

Slaughtered at the same BW (115 kg) (n = 8 / group)

2D-electrophoresis of soluble proteins + MS/MS identification of differentially-abundant spots

- Experimental design
-19% of the voluntary feed intake

Results: Animal performance

RFI corresponded to a biologically imposed feed restriction
A total of 50 protein spots in the liver had a differential abundance between pigs. Proteins were included in pathways related to AA metabolism, glycolysis/gluconeogenesis, ion binding, purine binding, and oxido-reduction.

11 unique proteins belong to a top cluster related to cell oxido-reduction processes (enrichment score = 2.92)

- **Response to oxidative stress**: PRDX2, PRDX4, PRDX5, PRDX6, SOD1
- **Cell redox homeostasis**: PRDX2, PRDX4, PRDX5, PRDX6, PDIA3, PDIA6, GSTO1
- **Oxidation reduction**: PRDX2, PRDX4, PRDX5, PRDX6, SOD1, HAAO, DMGDH, ETFA

• Results: differential proteins in liver
Liver mitochondria and Reactive Oxygen Species (ROS) production

- Tricarboxylic acids (TCA) cycle
- Fatty acid oxidation

Oxidation of reducing equivalents

Transfer of electrons along the respiratory chain

oxidation to $H_2O$

ATP ↓

ROS ↑

- Liver mitochondria are a main site of ROS production
Results: greater anti-oxidant enzymes in low RFI pigs.

Levels in feed-restricted high RFI pigs were similar or intermediary to levels observed in low RFI pigs.

A lower abundance in the electron transfer flavoprotein (ETFA) is considered as leading to ROS elevation.

Levels in feed-restricted high RFI pigs were similar or intermediary to levels observed in low RFI pigs.
A low abundance of ETFA signs a low activity of the respiratory chain

A severe inhibition of the respiratory chain is considered as inhibiting lipid oxidation process in rats (Pande, 1971)

Monitoring oxidative enzyme activities in the 3 groups

**Fatty acid oxidation**

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<th>RFI-</th>
<th>RFI+</th>
<th>RFI+R</th>
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<tbody>
<tr>
<td>β-HAD</td>
<td>a</td>
<td>b</td>
<td>b</td>
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<tr>
<td>nM/min/mg proteins</td>
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\[ P = 0.01 \]

**TCA cycle**

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<th>RFI-</th>
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<th>RFI+R</th>
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<tr>
<td>Citrate synthase</td>
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<td>nM/min/mg proteins</td>
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\[ P = 0.11 \]

Lower fatty acid oxidation in the low RFI pigs, independently of feed intake

- Results: lower lipid oxidation pathway in low RFI pigs
Balance in labile methyl groups (methionine, betaine, choline) is involved in maintaining normal lipid functions and health (Mato et al., 2008)

- Results: homocysteine/methionine/betaine equilibrium?
Pigs selected for a low residual feed intake had eaten less during the growing period.

Higher anti-oxidant capacities in the liver of the most efficient pigs, due to (?) greater ROS generation.

Consequences on the redox state of the animals remains to be determined (other tissues).

Levels of anti-oxidants were lower with feed restriction.

Relationships between feed intake and oxidative stress/redox metabolism in pigs deserve further studies.

Caloric restriction in aging mice decreased hydrogen peroxide production from the mitochondria.
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