Amino Acid Balancing for the Transition Cow: Old and New Stories from a Molecular Perspective

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Peripartal or Transition period

Cow in negative energy balance

Body fat and protein mobilization

Peripartal protein mobilization

Metabolizable protein and amino acids likely limiting around calving

Energy balance
Body condition score
Energy intake

4% Fat corrected milk

Tissue mobilization

NEFA
TG
NE
Epi
Insulin
NEFA
NEFA
CO2
Propionate
Ketone bodies
Mitochondria
Glucose
AA, Lactate and Glycerol

Feed Intake

TG

VLDL

Milk Fat

Modified from Drackley, 1999

Decrease
Increase

Fat Protein

10.4 17.8 8.4 6.9 6.7 7.8 6.2 5.4

0 50 100 150 200 250 300

Fat Protein

8 22 5 27 68 32 16 78 78 78 78 78 78

0 50 100 150 200 250 300

Week relative to parturition

3 47

Metabolizable protein

(Feed Intake)

Methylhistidine (μM)

Proteolysis 3-Methylhistidine

Metabolizable Protein

0 50 100 150 200 250

Period from calving (d)

Bell et al. (2000)

Needed for milk protein, glucose synthesis, synthesis of other compounds (e.g. SAM, glutathione, taurine)
Net liver uptake of Methionine and Histidine increases after calving

Net uptake of Met by liver can be enhanced by supplemental RP-Met also prevents decrease in blood Met postpartum (Dalbach et al., 2011)

Methionine and the Peripartal Period

<table>
<thead>
<tr>
<th>Dietary component</th>
<th>Osorio et al., 2013</th>
<th>Zhou et al., 2016</th>
<th>Batistel et al., 2017</th>
</tr>
</thead>
<tbody>
<tr>
<td>CP, % of DM</td>
<td>17.4</td>
<td>17.2</td>
<td>17.7</td>
</tr>
<tr>
<td>MP supplied (g/d)</td>
<td>1.563</td>
<td>1.840</td>
<td>2.090</td>
</tr>
<tr>
<td>MP balance (g/d)</td>
<td>-574</td>
<td>-616</td>
<td>-434</td>
</tr>
<tr>
<td>Lys (% of MP)</td>
<td>6.17</td>
<td>6.07</td>
<td>6.33</td>
</tr>
<tr>
<td>Met (% of MP)</td>
<td>1.81</td>
<td>2.15</td>
<td>1.79</td>
</tr>
<tr>
<td>lys:Met</td>
<td>3.43:1</td>
<td>2.82:1</td>
<td>3.54:1</td>
</tr>
</tbody>
</table>

Milk yield & Performance

Antioxidant Liver function DNA & Histone methylation Reduced immunosuppression

Liver Function

Fatty liver on milk yield

n = 100 transition cows

Actual TG mean:
- Mild = 3.3 ± 1.0
- Moderate = 6.5 ± 1.5
- Severe = 11.1 ± 0.9

Actual Milk yield:
- Mild = 41.9 ± 0.84
- Moderate = 41.6 ± 1.5
- Severe = 36.9 ± 2.9

Correlation:
- r = -0.2
- P = 0.06
**Methionine plays several roles in liver**

- **Phospholipid synthesis**
- **Apolipoprotein synthesis**
- **Glutathione**
- **Taurine** (antioxidants)
- **Amino acids (Met, et al.)**
- **Albumin** (major secretory protein synthesized by liver)

**Liver function**

- **Carnitine metabolism**
- **Apolipoprotein synthesis**
- **Esterification**

**Inflammatory response**

- **Metritis**
- **Mastitis**
- **Acute Phase Proteins**
- **Liver**
- **Potential Pathogen Infection**

Adapted from Osorio et al., 2013

Adapted from Sun et al., 2016
Fat or Adipose Tissue

Liver

Inflammatory response

Acute Phase Proteins

Albumin

Inflammatory Response Signal

Potential Pathogen Infection

Liver

Cow in negative energy balance

Fat or Adipose Tissue

NEFA

TG

Liver

Insulin, Epi

NEFA

(modified from Drackley, 1999)

Cow in negative energy balance

Inflammatory Response

Metritis

Mastitis

Liver

Potential Pathogen Infection

Liver

Dietary methyl-donors in dairy cows

Methionine supplementation alters the liver transcriptome

2,663 genes with diet × time effect

Glutathione Priming Effect

Methionine

Glutathione

Liver function

Day relative to parturition

Diet, P = 0.28
Time, P = 0.04
D × T, P = 0.20
Control, P = 0.15

Bertoni et al., 2008. J Dairy Sci

Osorio et al., 2014

MS = Metasmart
SM = Smartamine M

Liver function

Milk yield +6.5 kg/d in Upper

Osorio et al., 2012

Batistel et al., 2018

Zhou et al., 2016

Zom et al., 2011

Cooke et al., 2007

Diet, P = 0.28
Time, P = 0.04
D × T, P = 0.20
Control, P = 0.15

Glutathione (mM)

CON
MS
SM

Glutathione

P = 0.04

Glutathione Priming Effect

Methionine

Glutathione

Liver

Gene expression

2,663 genes with diet × time effect

Osorio et al., 2012

Control

Methionine
Methionine and Gene Regulation

Central Dogma of Molecular Biology

Epigenetic Mechanisms

DNA Methylation

Histone Modification

Non-coding RNA

Methionine and Nutrigenomics

Histone Methylation

Control

Active/Open

125 uM Met

500 uM Met

Relative Histone Methylation

Inactive/close

Histone Methylation

Methionine cycle

Enzymes

Histone Methylation

Methionine cycle

Enzymes

Histone Methylation

Methionine cycle

Enzymes
Histone Methylation

Relative Histone Methylation

Milk protein

Total protein

0 0.2 0.4 0.6 0.8 1

0 24 6 8 10 12 14 16 18 20 22 24 26 28 30

Relative Histone Methylation

Control

125 uM

250 uM

500 uM

Fernanda Bionaz et al., 2012; PLoS ONE 7:333268

Conclusions

Methionine

Prepartum

Postpartum

Histone Methylation

Model

Gene Regulation

Performance

Histone Methylation

Enzymes

Microbes

Gene expression

Thanks!

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Histone Methylation

Dietary Methionine?

Euchromatin

Heterochromatin

Epigenetic regulation

Bionaz et al. 2012; PLoS ONE 7:333268
METHIONINE
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