Strengthening Gut Barrier Function in Pigs

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To make money from pig farming ......

the digestive system needs to be very efficient
The challenge:
Manage health and performance in intensive farming systems
But stressors have a negative effect on Sows and Piglets

Are antibiotics and zinc oxide THE solution?

- Feed transition
- Birth
- Weaning
- Climate
- Digestion
- Diseases
Your observation as a customer!!!

A lot of solutions, a lot of questions

Non proven concepts

Preventive treatments

High levels of single additives
Our strategies to gain animal performance
2 Directions

1) HEALTH

Microbiota

Healthy gut

Intestinal barrier

Damaged gut

2) METABOLIC EFFICIENCY
Gut feeling... cross talk between intestinal microbiota and host
Impact microbiota demonstrated by ‘fecal transplantation’ studies

Bacteria from slim people could help treat obesity, study finds
Experiments show microbes from thin or fat people’s intestines can cause mice to lose or gain weight.

Ian Sample, science correspondent
The Guardian, Thursday 5 September 2013 19:10 BST
Jump to comments (470)
The gut barrier function is the interface between microbiota and host.
Impaired gut barrier function in **weaned piglets**
Teaming up in *Life Science*

**Nutreco’s Nutrition & Health Science & Technology Platform**

- Microbiology
- Immunology
- Physiology & Metabolism
- Ingredient Discovery
- Pigs
- Poultry
- Ruminants
- Fish

8 PhD’s

Shared brains, Shared facilities, Shared network
Design intervention strategy to strengthen Gut Barrier Function

**Desired Features**

- Steer composition, activity *microbiota*
- Enforce integrity and function of *enterocytes*
- Stabilize immune-response by modulation of *immune cells*
Semi-high throughput testing of candidates *in vitro*

**In vitro screening methods**

- **Microbial activity screen**
- **Cell integrity screen**
- **Immunemodulation screen**

50-100 Candidates

Selection Process

*In Vivo* Proof of Efficacy

Trend: New Molecular Assays in the OMICs area
Into the world of the microbiota with pyrosequencing

Source: NIZO Food Research
Composition microbiota in piglets

Bacterial Phylum
- Actinobacteria
- Bacteroidetes
- Firmicutes
- Proteobacteria

Bacterial Species
- Actinomyces denticolens
- Lactobacillus fermentum
- Lactobacillus gasserii
- Lactobacillus jensenii
- Lactobacillus pontis
- Lactobacillus reuteri
- Streptococcus f eros
- Streptococcus hyointestinalis
- Streptococcus ortsratti
- Streptococcus suis
- Streptococcus thermophilus
- Subdoligranulum variabile
- Escherichia coli
- Escherichia fergusononii
Weaning changed diversity; signs of dysbiosis

<table>
<thead>
<tr>
<th></th>
<th>Pre-weaning</th>
<th>Post-weaning</th>
</tr>
</thead>
<tbody>
<tr>
<td>Jejunum</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Colon</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Higher proportion of *Lactobacillus reuteri* post-weaning

Reduced diversity

Nutreco R&D, 2011
Microbiota targets in weaned piglets

Number bacteria small intestine ↓
To reduce the bacterial ‘pressure’
Reduction of 0.5 log will already contribute

Bacterial diversity index ↑
Diversity is associated with a more robust microbiota

Microbiota composition
Beneficial bacteria ↑
Potential pathogens ↓
### Challenge study (MAMO) examining microbiota

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>Presan</th>
</tr>
</thead>
<tbody>
<tr>
<td>Body weight (D 35)</td>
<td>16.4</td>
<td>16.5</td>
</tr>
<tr>
<td>ADFI (D 0-35)</td>
<td>406</td>
<td>392</td>
</tr>
<tr>
<td>ADG (D 0-35)</td>
<td>304.8</td>
<td>308.2</td>
</tr>
<tr>
<td>FE (D0-35)</td>
<td>0.75 $^a$</td>
<td>0.79 $^b$</td>
</tr>
</tbody>
</table>

#### Feed efficiency during 5 weeks post weaning under dirty conditions

- **P<0.01**
- 5% improvement

#### Effect on diarrhoea incidence during 5 weeks post weaning in dirty conditions

- **P=0.06**
- 35% reduction

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Nutreco R&D, 2011
*Presan* lowered bacterial numbers in small intestine

**Total bacterial count in duodenum/jejunum**

- **Control**: 9.5 log copies/g digesta
- **Presan™**: 8 log copies/g digesta

* p<0.05

**Total bacterial count in Ileum**

- **Control**: 10 log copies/g digesta
- **Presan™**: 7 log copies/g digesta
Presan improved diversity in jejunum

Representative Pyrosequencing profiles from group on D7

Control

Presan™

Observed species in jejunum

Preweaning | Control D7 | Presan™ D7

480 | a | a
470
460
450
440
430
420
410
400
390
380
370

a, b
Design intervention strategy to strengthen Gut Barrier Function

**Desired Features**

- Steer composition, activity *microbiota*
- Enforce integrity and function of *enterocytes*
- Stabilize immune-response by modulation of *immune cells*
Heat stress weakens the gut barrier function

Heat Stress

- Feed Intake ↓
- Nutrient supply ↓
- Blood Flow ↓
- Oxygen supply ↓
- Oxidative stress ↑
- Inflammation ↑
- Atrophy villi ↓
Heat stress challenge study

Treatments, piglet received feeds from weaning to end experiment
1. Control
2. Presan, 2 kg / ton

<table>
<thead>
<tr>
<th>Pre-challenge day 0-6</th>
<th>Day 6</th>
<th>Day 8</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age piglets start 50 days</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adaptation to room</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Experimental diets</td>
<td><strong>Start Heat Stress</strong></td>
<td></td>
</tr>
<tr>
<td>40°C 10 h</td>
<td></td>
<td></td>
</tr>
<tr>
<td>28°C during night</td>
<td><strong>End Heat Stress</strong></td>
<td></td>
</tr>
<tr>
<td>n = 12 / treatment</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Histological examination</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Presan reduced impact short term heat stress in piglets

No significant differences in mucous cell area, expression tight junction proteins (INRA).

Nutreco R&D, 2012
Reduced proinflammatory cytokines in heat stressed piglets

Inflammation ↓ ↔ Feed Intake ↑

Nutreco R&D, 2012
Presan consistently improved ADG and feed efficiency in piglets

- **Meta-analyses** of 9 controlled R&D studies
- Presan versus control diet without antibiotics, ZnO
- Data of in total 3244 piglets included
- No bias, all studies are included

<table>
<thead>
<tr>
<th>ADG, g/day</th>
<th>Feed intake, g/day</th>
<th>Feed Conversion Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>+ 5%</td>
<td>+ 4%</td>
<td>- 2%</td>
</tr>
<tr>
<td><em>p</em> &lt; 0.001</td>
<td><em>p</em> = 0.029</td>
<td><em>p</em> &lt; 0.001</td>
</tr>
</tbody>
</table>

### Notes on Figures

- The figures depict the results of the meta-analyses with box plots showing the distribution of ADG, feed intake, and feed conversion ratio across different studies.
- The box plots illustrate the variability and central tendency of the data for each parameter.
**Presan** fits in strategy to reduce zinc oxide

### Controlled R&D study at commercial farm in Spain, 2012

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Weaning-D8</th>
<th>D9-20</th>
<th>D21-40</th>
</tr>
</thead>
<tbody>
<tr>
<td>Practiced ZnO</td>
<td>3100 ppm ZnO</td>
<td>3100 ppm ZnO</td>
<td>3100 ppm ZnO</td>
</tr>
<tr>
<td>Reduced ZnO</td>
<td>3100 ppm ZnO</td>
<td>1550 ppm ZnO + 2 kg Presan</td>
<td>No ZnO + 2 kg Presan</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Treatment</th>
<th>High ZnO</th>
<th>Reduced ZnO + 2 kg <em>Presan</em></th>
<th>Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>ADG, g/day</td>
<td>400 $^a$</td>
<td>467 $^b$</td>
<td>+17%</td>
</tr>
<tr>
<td>FCR</td>
<td>1,53 $^a$</td>
<td>1,43 $^b$</td>
<td>-7%</td>
</tr>
</tbody>
</table>

Nutreco R&D, 2012
Is there a need to strengthen gut barrier function in sows?

Changes in feed intake around farrowing

Significant physiological changes during farrowing - Stress

Dysbiosis in sows?
Higher feed intake lactation with *Presan*

**Presan-FX increases lactation-feed intake**

<table>
<thead>
<tr>
<th>Days after Farrowing</th>
<th>Sow feed intake (kg/d)</th>
<th>Control</th>
<th>Presan-FX</th>
</tr>
</thead>
<tbody>
<tr>
<td>7</td>
<td>+ 2.5%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>+ 3.6%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>+ 4.3%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>+ 3.5%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>11</td>
<td>+ 6.2%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>12</td>
<td>+ 10.1%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>13</td>
<td>+ 9.5%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>14</td>
<td>+ 8.9%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>15</td>
<td>+ 8.7%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>16</td>
<td>+ 6.7%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>17</td>
<td>+ 7.4%</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Nutreco R&D, 2013
Higher feed intake results in reduced weight and backfat loss

- Meta-analyses of 3 controlled R&D studies
- Results of in total 1096 sows included in the data

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>Presan 1 kg</th>
<th>Presan 2 kg</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Feed intake</td>
<td>6.49</td>
<td>6.94</td>
<td>6.75</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Backfat loss, mm</td>
<td>2.6</td>
<td>1.9</td>
<td>2.0</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Weight loss, kg</td>
<td>9.8</td>
<td>7.8</td>
<td>6.8</td>
<td>0.079</td>
</tr>
</tbody>
</table>

Hypothesis → Improved reproduction in subsequent cycle. To be validated.

More studies in progress
Trend of heavier piglets at weaning with *Presan*

P<0.05

**Piglet weaning weight categories**

- **<4.0**
- **4.0-5.0**
- **5.0-6.0**
- **6.0-7.0**
- **>7.0**

Percentage per litter

- **Control**
- **Presan-FX**

Nutreco R&D, 2013
Support gut barrier function during critical transitions
Maximum Return On Intestine

Profitable animal performance
- Boosts gut wall integrity
- Inhibits microbial overgrowth
- Suppresses harmful bacteria throughout small intestine
- Reduces use of antibiotics
Presan: strong team with Selacid and Selko®-pH

Gut stabiliser and barrier booster

Support digestion + safe feed

Clean water, support digestion
Effect of Presan on Sows and Piglets

- Reduces inflammation
- Reduces oxidative stress
- Improves gut wall integrity
- Inhibit microbial overgrowth
- Decreases Infection pressure
- Improve performance
Value for the pig industry
- Farmers / Integrators & Feed millers
Presan value for the pig Industry

ROI > 4
Up to € 0,64/piglet

ROI > 15
Up to € 1,21/piglet

Performance Sows & Piglet

Additive cost reduction

Antibiotic & Zinc Oxide reduction

Feed cost reduction

Savings up to € 5,64/mt feed

Trails in preparation

* Data based on statistical significant trails, but outcome varies per situation
* Economical data based on local feed & swine prices
Take home message

Value for the pig industry
Proven by science

Performance
Sows & Piglet

Antibiotic & Zinc Oxide reduction

Additive cost reduction

Feed cost reduction