Role of the gut microbiome in reducing antimicrobial use in swine

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“...the ecological community of commensal, **symbiotic** and **pathogenic** microorganisms that literally share our body space”

Roles of the Microbiome

Absorption, Metabolism and Storage of Calories

Development and Regulation of Immunity

Protective Barrier Function
Gut Microbiome and Respiratory Infections

Infectious respiratory disease is a leading cause of morbidity and antimicrobial use in swine

Gut-lung axis

Influenza virus
Endogenous gut microbiota
(Wu et al., 2013)

Streptococcus pneumoniae
Microbiome diversity in gut
(Schuijt et al., 2016)

Mycobacterium tuberculosis
Helicobacter species in gut
(Arnold et al., 2015)

Respiratory syncytial virus
Lactobacillus johnsonii in gut
(Fujimura et al., 2014)
Human Infectious Respiratory Disease

Weight

Microbiome

Immunity

Porcine Respiratory Disease Complex
Porcine Respiratory Disease Complex Co-infection Model

Porcine reproductive and respiratory syndrome virus (PRRSV) + Porcine circovirus type 2 (PCV2)
Are there microbiome characteristics associated with outcome after PRRSV/PCV2 co-infection?
Fecal microbiota transplantation (FMT): Transplanting the feces from a healthy donor into a diseased or young individual

- Increased **microbial diversity**, enhanced **beneficial microbes**, modulation of systemic and mucosal **immunity**

Can **prophylactic microbiome modulation** improve outcome to PRRSV/PCV2 co-infection?
Experimental Design

3-week-old littermates

Control Group
- Oral Transplant
- $n = 10$

Fecal Group
- Fecal Microbiota Transplant
- $n = 10$

PRRSV/PCV2d Challenge

Niederwerder et al., 2018
Disease Outcome

- 60% Reduction in Antimicrobials
- 70% Reduction in Mortality

Niederwerder et al., 2018
Lung Lesions and Immunity

Niederwerder et al., 2018

Lung Weight to Body Weight Ratio

PRRSV Antibody

PCV2d Antibody

Niederwerder et al., 2018
Characteristics of Improved Outcome

- ↑ Diversity
- ↑ Veillonellaceae
- ↑ Ruminococcaceae
- ↑ Streptococcaceae
- ↑ Lachnospiraceae
- ↑ Escherichia coli
- ↑ Average Daily Gain
- ↓ Methanobacteriaceae
- ↓ Clinical Disease
- ↑ Antibodies
- ↓ Antimicrobials
- ↓ Interstitial Pneumonia
- ↓ Virus Replication
- ↓ Mortality

Niederwerder et al., 2016; Ober et al., 2017; Niederwerder et al., 2018
FMT: Beneficial for Diseases in Humans

- Indications for Fecal microbial transplantation (FMT)
  - Approved indications
  - Recurrent Clostridium difficile infection
  - Gastrointestinal disease:
    - Inflammatory bowel disease
    - Irritable bowel syndrome
    - Pouchitis
  - Metabolic syndrome
  - Neuropsychiatric disease:
    - Multiple sclerosis
    - Myoclonus dystonia
    - Autism
  - Hematologic disease:
    - Immune thrombocytopenic purpura
    - Acute graft versus host disease
  - Sepsis
  - Eradication of resistant microbes

- Novel Indications
  - Gastrointestinal disease:
    - Hepatic encephalopathy
    - Chronic Hepatitis B

**REVIEW**

Fecal microbial transplantation as a therapeutic option in patients colonized with antibiotic resistant organisms

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<table>
<thead>
<tr>
<th>Species</th>
<th>Disease/Pathogen/Condition</th>
<th>Effect of Transplantation</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Swine</td>
<td><em>Mycoplasma hyopneumoniae</em></td>
<td>Reduced <strong>coughing</strong> frequency, delayed coughing onset, decreased <strong>lung lesions</strong>, more rapid <strong>seroconversion</strong></td>
<td>(Schachtschneider et al., 2013)</td>
</tr>
<tr>
<td>Swine</td>
<td>Intestinal structure, immunity, growth</td>
<td>Higher <strong>weight gain</strong>, reduced <strong>diarrhea</strong> incidence</td>
<td>(Hu et al., 2017)</td>
</tr>
<tr>
<td>Swine</td>
<td>Acute colitis</td>
<td>Resistance to <strong>colitis</strong>, lower <strong>clinical scores</strong>, less severe <strong>colonic bleeding</strong></td>
<td>(Xiao et al., 2017)</td>
</tr>
<tr>
<td>Swine</td>
<td>Porcine epidemic diarrhea virus (PEDV)</td>
<td>Reduced <strong>diarrhea</strong> and <strong>mortality</strong> in piglets, less virus in intestine</td>
<td>(Goede et al., 2015)</td>
</tr>
<tr>
<td>Chicken</td>
<td><em>Salmonella infantis</em></td>
<td>Reduced prevalence of <strong>Salmonella carriers</strong> and level of <strong>colonization</strong></td>
<td>(Nurmi and Rantala, 1973)</td>
</tr>
<tr>
<td>Chicken</td>
<td>Feed efficiency</td>
<td>Increased <strong>total feed intake</strong> and <strong>weight gain</strong> in females</td>
<td>(Siegerstetter et al., 2018)</td>
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<tr>
<td>Sheep</td>
<td>Ruminal acidosis and atony, inappetence</td>
<td>Appetite normalized, resolution of <strong>clinical signs</strong></td>
<td>(Jasmin et al., 2011)</td>
</tr>
<tr>
<td>Cattle</td>
<td>Left-displaced abomasum (post-surgical)</td>
<td>Increased <strong>feed intake</strong>, greater <strong>milk production</strong>, less <strong>ketonuria</strong></td>
<td>(Rager et al., 2004)</td>
</tr>
<tr>
<td>Cattle</td>
<td>Unthriftiness, poor growth in experimental calves</td>
<td>Smoother coats, improved <strong>growth rates</strong> and condition</td>
<td>(Pounden and Hibbs, 1949)</td>
</tr>
<tr>
<td>Cattle</td>
<td>Transportation stress</td>
<td>Increased <strong>feed intake</strong></td>
<td>(Leo-Penu et al., 2016)</td>
</tr>
<tr>
<td>Cattle</td>
<td>Feed efficiency</td>
<td>Increased <strong>feed intake</strong> and <strong>nitrogen digestibility</strong></td>
<td>(Ribeiro et al., 2017)</td>
</tr>
</tbody>
</table>
FMT: Potential Applications

Administered PRIOR to high risk of pathogen exposure or disease onset → PROPHYLACTIC → Administered to improve feed efficiency, prevent infection or disease

Administered AFTER pathogenic infection or disease onset → THERAPEUTIC
Administered to treat clinical signs or resolve disease

Administered to stimulate pathogen-specific immunity THROUGH exposure → IMMUNOGENIC
Administered to increase immunoglobulin transfer to neonate

Niederwerder, 2018
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