Uncovering the Effect of Immunoglobulin A on the Rumen Ecosystem

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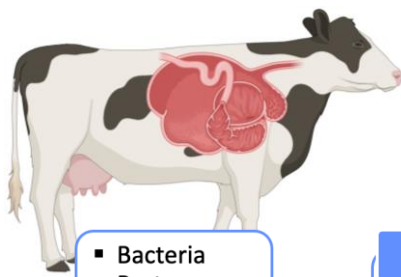
1

Rumen Microbes Play a Central Role in Ruminant Nutrition



- Bacteria
- Protozoa
- Fungi
- Archaea

Rumen microbes

Fermentation

- Fiber breakdown
- Nutrient synthesis

- Energy
- Amino acids

Benefit to the host

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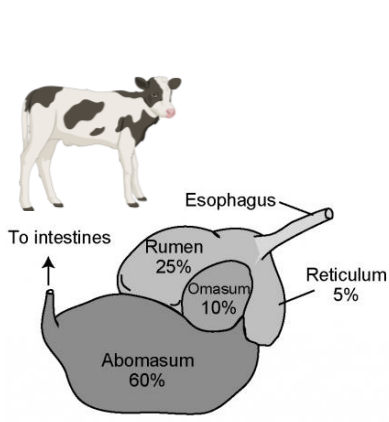
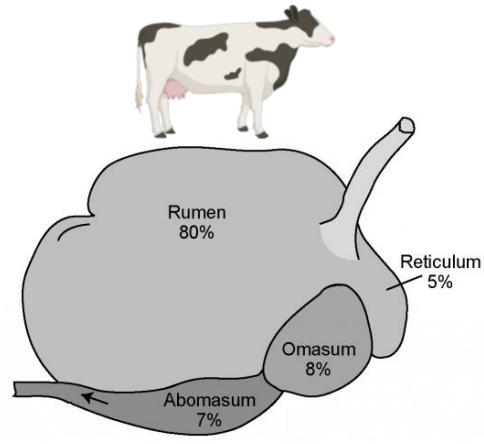
The Development of the Digestive System in Ruminants

- Rumen and reticulum: allometric growth
- Rumen development and function are closely tied to microbial establishment





CalfCare.ca

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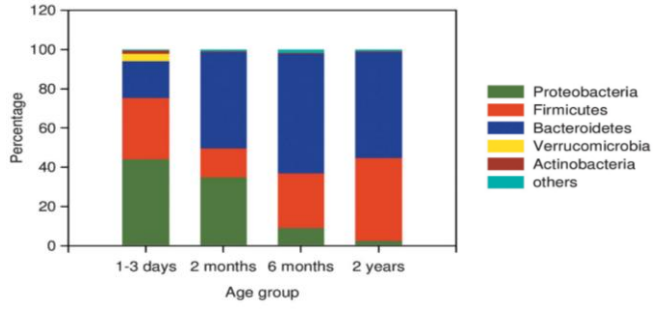
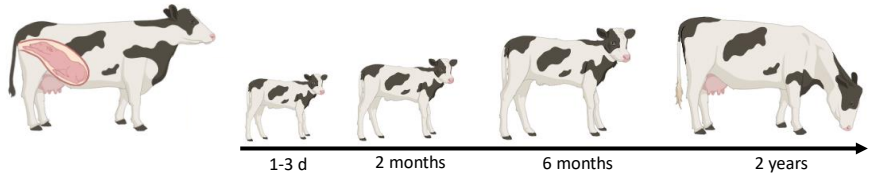
The Establishment of the Rumen Microbial Ecosystem



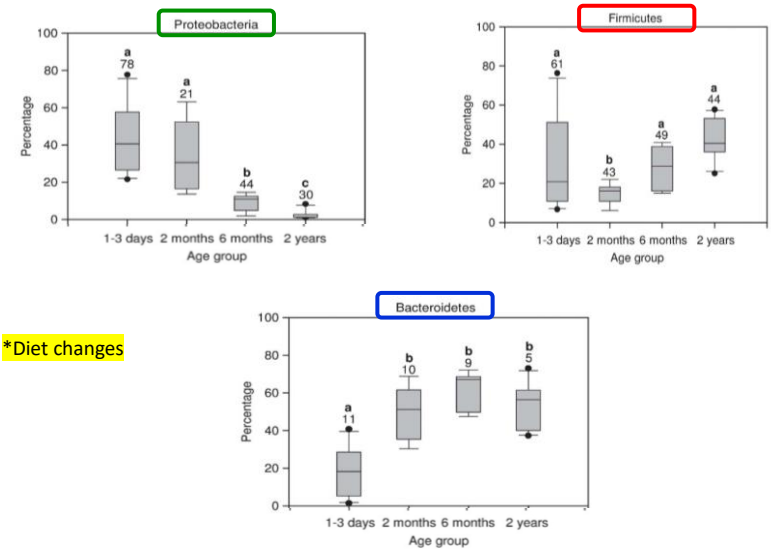
Bacterial phylum distribution in the rumen at different ages.



Jami et al. (2013), *ISME J*

4

The Establishment of the Rumen Microbial Ecosystem



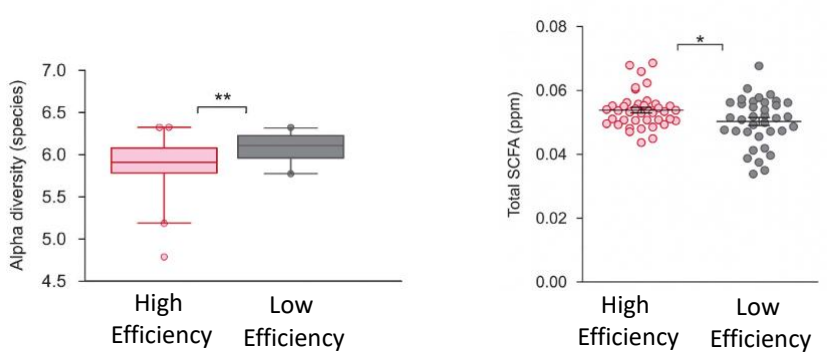
*Diet changes

Relative abundance of the three main bacterial phyla in the rumen at different ages.

Jami et al. (2013), *ISME J*

5

Rumen Microbial Composition and Activity are Associated with Production Efficiency

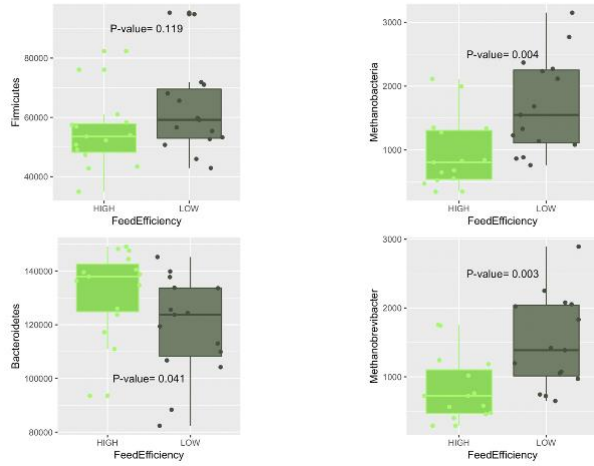


* $P < 0.05$
** $P < 0.01$

Shabat et al. (2016), *ISME J*

6

Rumen Microbial Composition and Activity are Associated with Production Efficiency



Delgado et al. (2018), *Scientific Reports*

Classification of Bacterial Species by Function

In 1953, Bryant & Burkey isolated and characterized 896 strains of bacteria from the rumen of cows fed different diets during six experiments. There fundings are summarized in table:

Classification	% of total population
Anaerobic	98
Glucose users	72
Cellobiose users	62
Xylan (hemicellulose) users	54
Starch users (amylolytics)	39
Protein users (proteolytic)	21
Cellulose users (cellulolytics)	15

The Interest in Modulating the Rumen Microbial Ecosystem has been Longstanding

Proc. Nutr. Soc. (1972), **31**, 125

PROCEEDINGS OF THE NUTRITION SOCIETY

The Two Hundred and Forty-second Scientific Meeting (Ninety-sixth Scottish Meeting) was held at the Hannah Research Institute, Ayr, on 10 March 1972

SYMPOSIUM ON
'MANIPULATION OF RUMEN FERMENTATION'

Chairman's introduction

By J. A. F. Rook, *The Hannah Research Institute, Ayr KA6 5HL*

Rook (1972), *Proc Nutr Soc*

9

Stability and Adaptability of the Ruminal Microbial Community in Mature Animals

Characteristic	Definition	Likely status in rumen
Inertia	Resistance to change	High, based on dosing studies
Resilience	Ability to restore its structure following acute or chronic disturbances	High, based on exchange studies

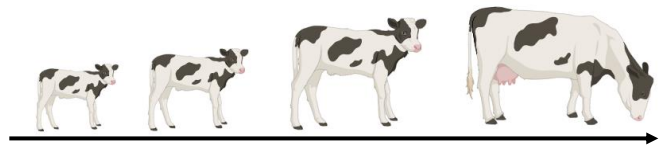
- Previous attempts to modulate the mature rumen microbiome: diet, enzymes, prebiotics, probiotics, etc.
- The effects do not persist once the insult is discontinued.

Weimer (2015), *Front Microbiol*

10

Early-life Attempts to Modulate the Rumen Microbial Ecosystem

- More recent efforts have focused on early-life strategies to modulate the assembly of the rumen microbial community.
  - Imprint a favorable microbial phenotype throughout the animals' lives.
  - Diet and inoculation.



11

Early-life Attempts to Modulate the Rumen Microbial Ecosystem

- Treatments:
  - Autoclaved rumen fluid
  - Rumen inoculum
- Administration:
  - Day 3: 100 mL
  - Day 7: 200 mL
  - Day 21: 300 mL
  - Day 42: 400 mL
  - Day 50: 500 mL
- No changes in animal performance.

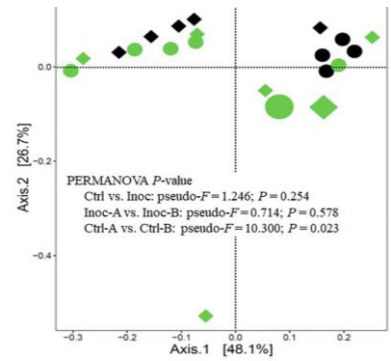


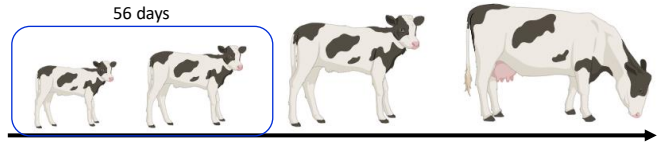
FIGURE 1 | PCoA plot showing the overall comparison of the rumen prokaryotic microbiota. Large green circle, Inoc-A donor; small green circles, Inoc-A calves; large diamond, Inoc-B donor; small green diamonds, Inoc-B calves; small black circles, Ctrl-A calves; small black diamonds, Ctrl-B calves Data of the donors for the control calves were not shown.

Bu et al. (2020), *Front Microbiol*

12

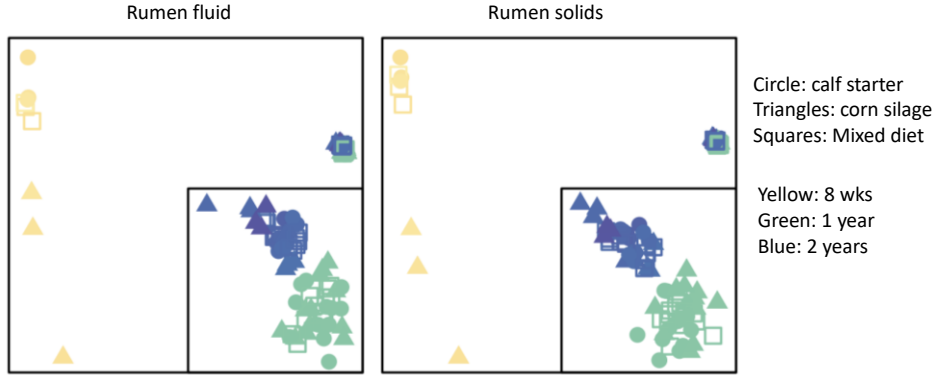
Early-life Attempts to Modulate the Rumen Microbial Ecosystem

- Treatments:
  - Calf starter
  - Corn silage
  - Mixed diet (25% calf starter, 75% corn silage)



Dill-McFarland et al. (2018), Appl Environ Microbiol

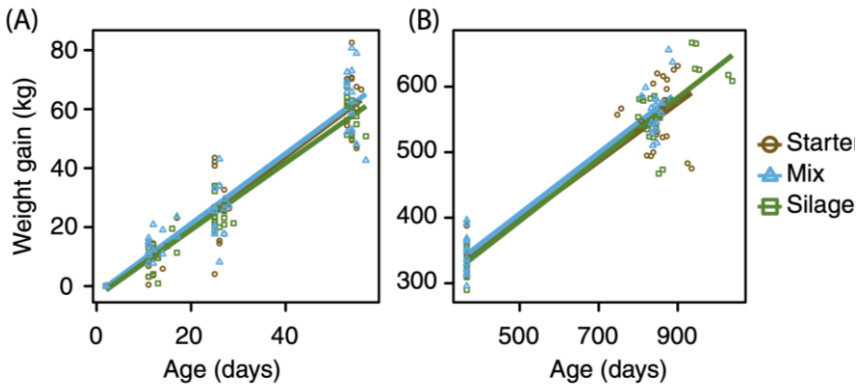
Early-life Attempts to Modulate the Rumen Microbial Ecosystem



NMDS plots of Bray-Curtis diversity index values for bacteria.

Dill-McFarland et al. (2018), Appl Environ Microbiol

Early-life Attempts to Modulate the Rumen Microbial Ecosystem



Calf diet effect on weight gain.

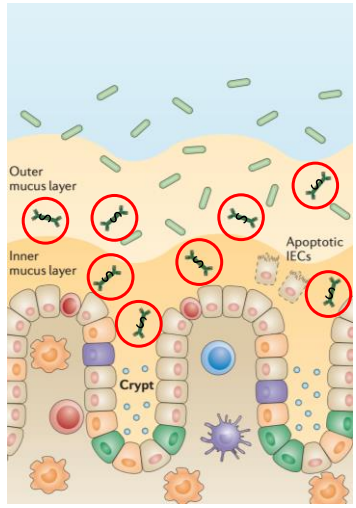
Dill-McFarland et al. (2018), Appl Environ Microbiol

Modulatory Effect of Antibodies on Gastrointestinal Microorganisms

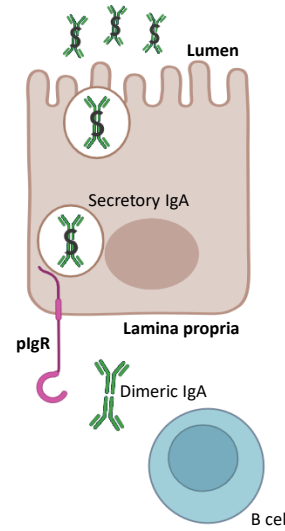
- The lack of response to diet and inoculum in early-life trials indicates that host-dependent mechanisms may contribute to rumen homeostasis.
- Immune system >> antibodies
  - Secretory immunoglobulin A (SIgA)

Secretion of SIgA by the Gastrointestinal Tract

Large intestine



Adapted from Mowat & Agace (2014), *Nat Rev Immunol*

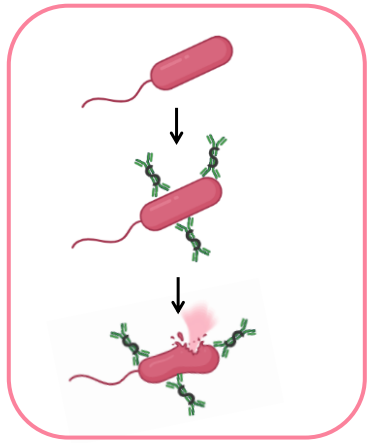


Adapted from Johansen & Kaetzel (2011), *Mucosal Immunol*

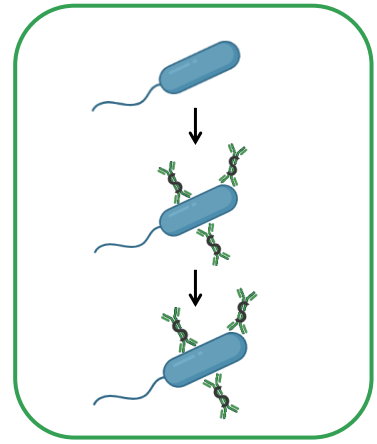
17

Roles of SIgA in Gastrointestinal Microorganisms

1. Neutralization of pathogens



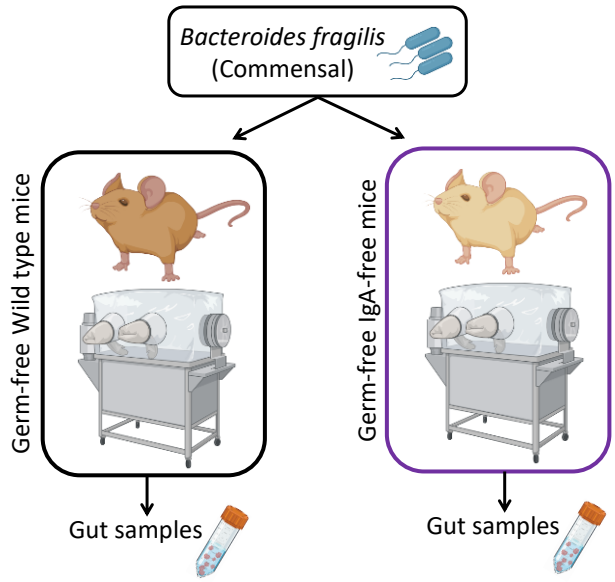
2. Maintenance of commensal bacteria



Adapted from Gutzeit et al. (2014), *Immunol Rev*

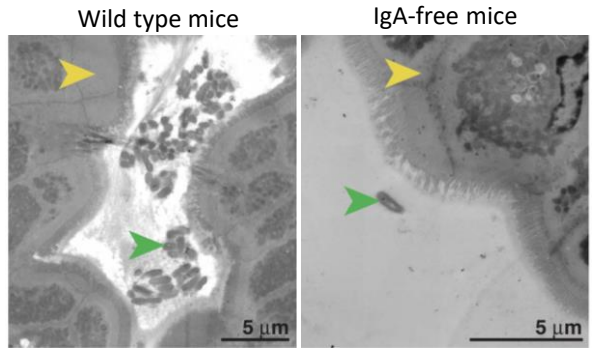
18

SIgA Favors Gut Colonization by Commensal Bacteria in Mice

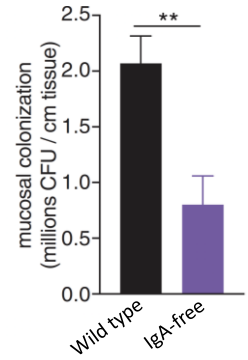


Donaldson et al. (2018), *Science*

SIgA Favors Gut Colonization by Commensal Bacteria in Mice



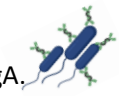
Transmission electron microscopy images of the colon (yellow arrowhead denotes epithelial cell) in mice colonized with *B. fragilis* (green arrowhead).



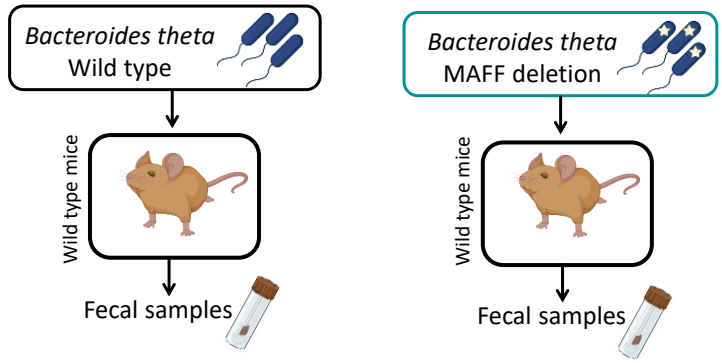
- SIgA is essential for the colonization of commensal bacteria in the gut.
- SIgA plays a role in establishing host-microbial symbiosis.

Donaldson et al. (2018), *Science*

SIgA Alters the Composition and Metabolic Function of the Gut Microbiome in Mice



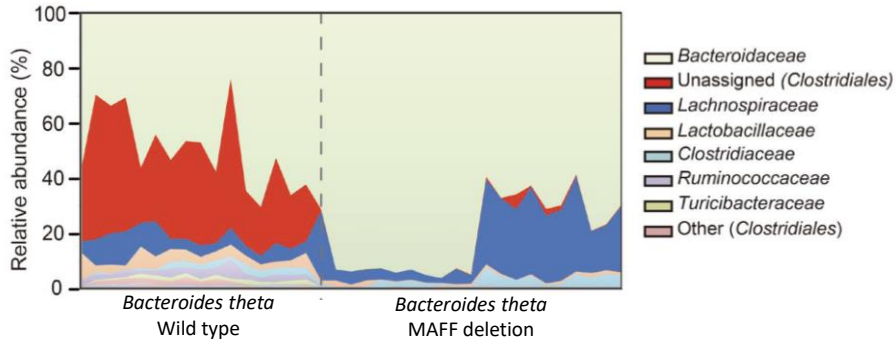
- In mice, *Bacteroides theta* (commensal) were heavily coated with SIgA.
- SIgA influenced the expression of mucus-associated functional factors (MAFF).



Nakajima et al. (2018), *J Exp Med*

21

SIgA Alters the Composition and Metabolic Function of the Gut Microbiome in Mice

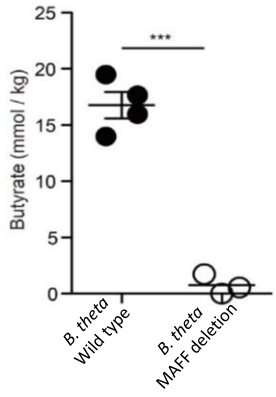


Relative abundance of bacterial families identified with 16S rRNA analysis in the cecum.

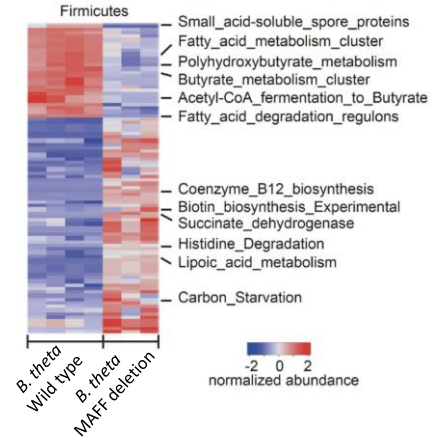
Nakajima et al. (2018), *J Exp Med*

22

SIgA Alters the Composition and Metabolic Function of the Gut Microbiome in Mice



Concentration of butyrate in cecal samples.

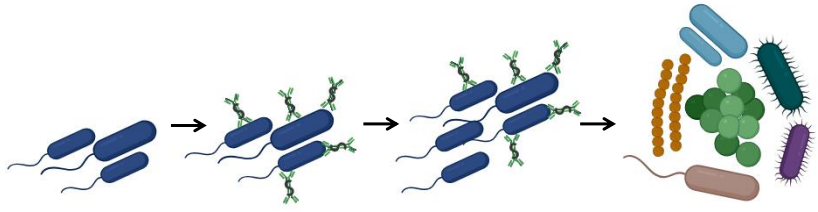


Gene expression of Firmicutes from cecal samples.

Nakajima et al. (2018), *J Exp Med*

23

SIgA Alters the Composition and Metabolic Function of the Gut Microbiome in Mice



B. theta

B. theta SIgA$^+$

Increase *B. theta* metabolic activity

Modulates microbial composition and metabolic activity

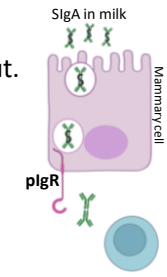
- SIgA directly and indirectly affects gut microbial composition and metabolic activity.

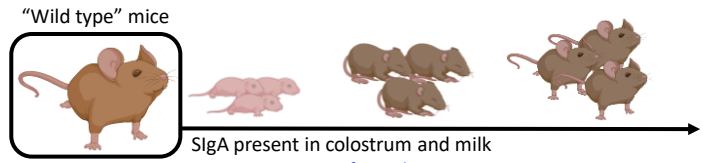
Nakajima et al. (2018), *J Exp Med*

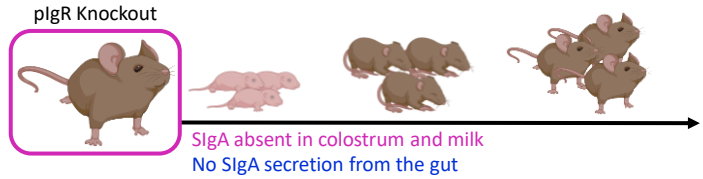
24

Milk SIgA Promotes Long-Lasting Changes in the Gut Microbiome of Mice

- SIgA is secreted into milk similarly to its secretion into the gut.



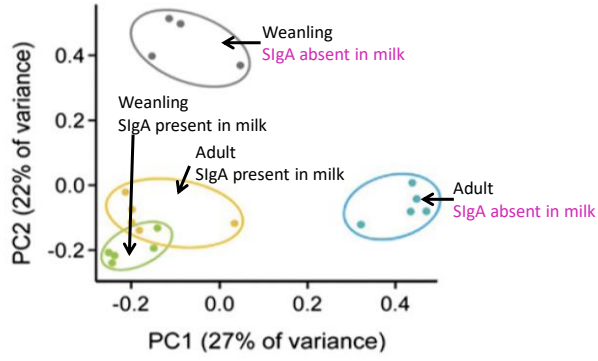




Rogier et al. (2014), *Proc Natl Acad Sci*

25

Milk SIgA Promotes Long-Lasting Changes in the Gut Microbiome of Mice



PCoA illustrating bacterial community structures.

- Milk SIgA induces enduring alterations in the gut microbiome of mice.

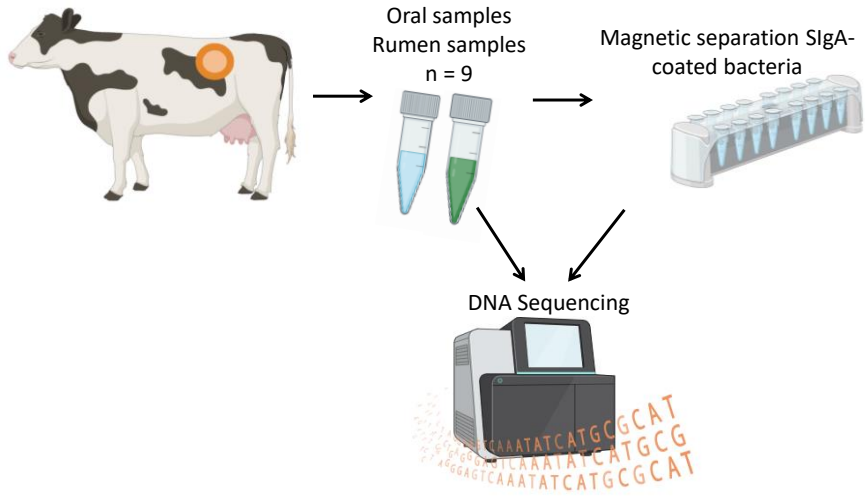
Rogier et al. (2014), *Proc Natl Acad Sci*

26

Summary SIgA Results in Mice

- SIgA modulates gut colonization by commensal bacteria.
- SIgA alters the microbial composition and metabolic function of the microbiome.
- SIgA promotes long-lasting changes in the gut microbiome.

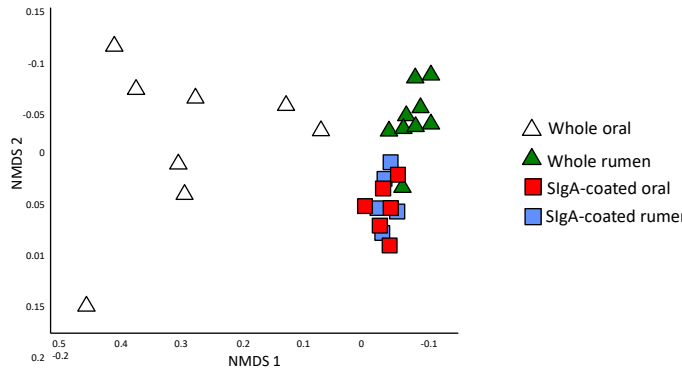
SIgA-coated Oral Microbiome is Correlated with SIgA-coated Rumen Microbiome



Fouhse et al. (2017), *Front Microbiol*

29

SIgA-coated Oral Microbiome is Correlated with the SIgA-coated Rumen Microbiome



Non-parametric multidimensional scaling (NMDS) ordination plot illustrating bacterial community structures.

- The correlation between the SIgA-coated oral microbiome and the SIgA-coated rumen microbiome suggests a host-derived mechanism impacting commensal colonization.

Fouhse et al. (2017), *Front Microbiol*

30

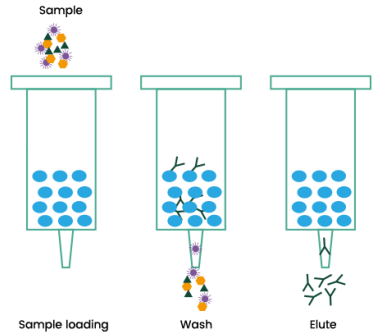
But Correlation Does Not Imply Causation…

31

Effect of Colostrum SIgA on Rumen Bacterial Growth

- We hypothesized that exposure of rumen bacteria to colostrum SIgA would favor bacterial growth.

1st step: Validated a protocol for isolating and purifying SIgA from from colostrum.



32

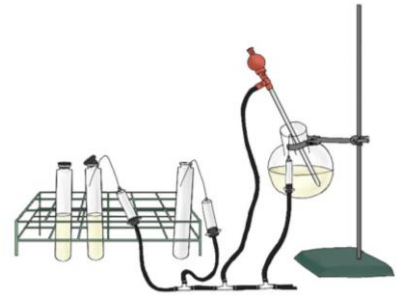
Effect of Colostrum SIgA on Rumen Bacterial Growth

- We hypothesized that exposure of rumen bacteria to colostrum SIgA would favor bacterial growth.

2nd step: The Hungate anaerobic technique was used to investigate the effect of SIgA on pure culture bacteria.

Treatments:

1. Water
2. 10 µg SIgA/mL
3. 20 µg SIgA/mL
4. 30 µg SIgA/mL
5. 30 µg autoclaved SIgA/mL



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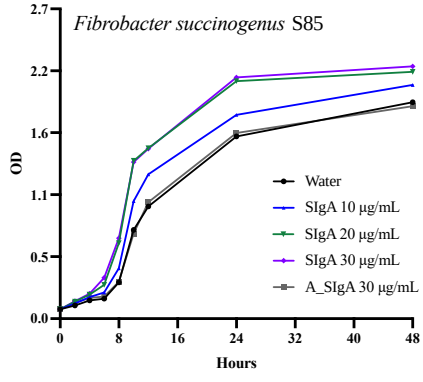
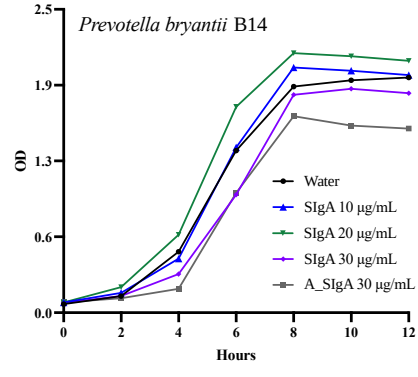
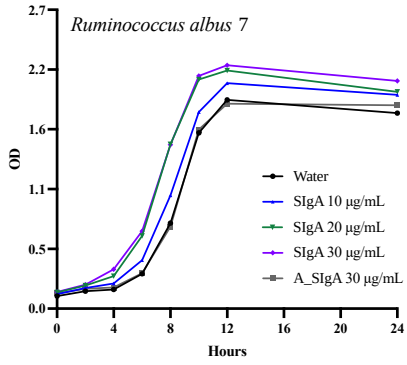
Rumen Bacterial Growth is Induced by Colostrum SIgA

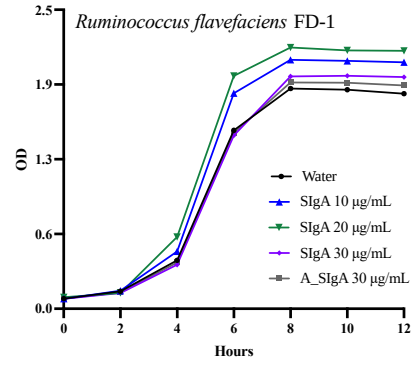




34

Rumen Bacterial Growth is Induced by Colostrum SIgA





- SIgA derived from bovine colostrum promotes the growth of fiber-digesting bacteria.

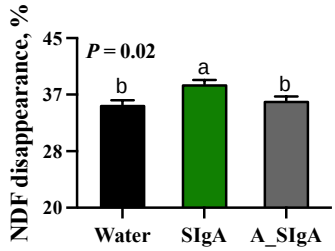
35

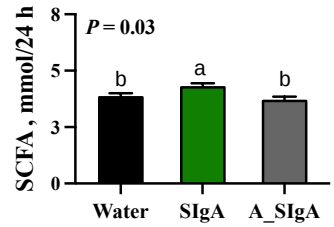
Effect of Colostrum SIgA on Rumen Fermentation

- We hypothesized that SIgA would favor rumen fermentation.
  - Batch culture technique
  - Treatments:
    1. Water
    2. 20 µg SIgA/mL
    3. 20 µg autoclaved SIgA/mL

36

Colostrum-derived SIgA Improves Fiber Digestion and SCFA Production *In Vitro*



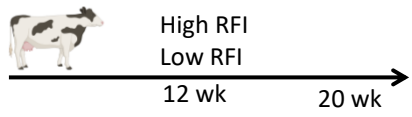


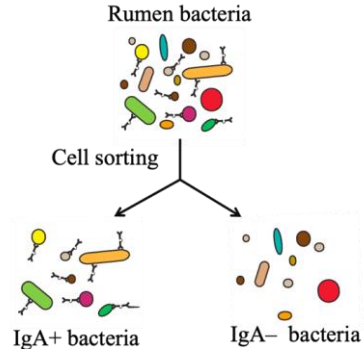
- SIgA derived from bovine colostrum influences the modulation of rumen fermentation.

37

Effect of SIgA-coated Bacteria on Feed Efficiency

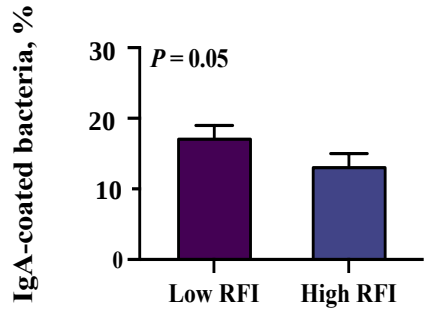
- We hypothesized that feed efficiency is positively associated with the proportion of rumen SIgA-coated bacteria.





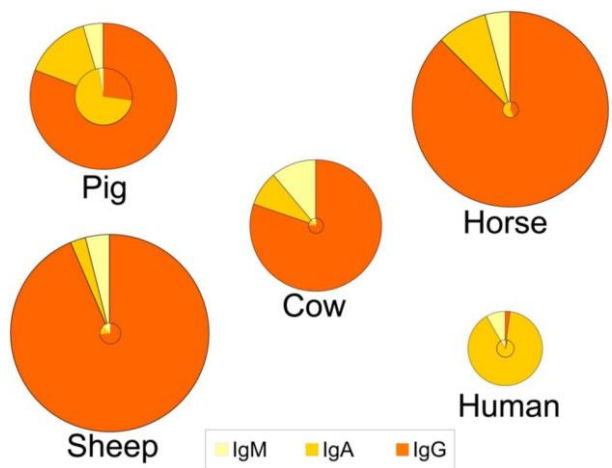
38

There Seems to be an Association Between Feed Efficiency and the Proportion of Rumen Siga-coated Bacteria in Dairy Cattle



39

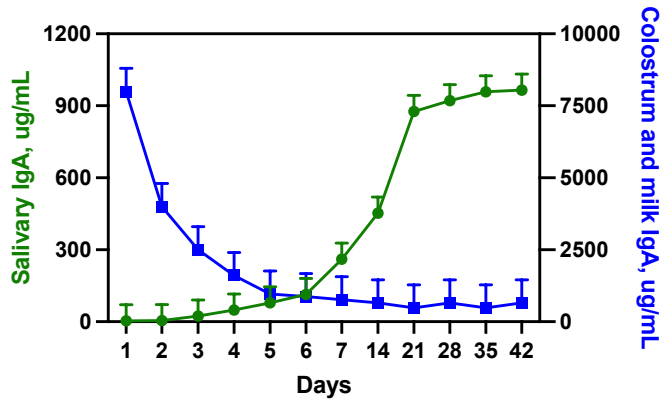
Milk is the Primary Source of SIgA Entering the Rumen During Calves' Early Life



Hurley & Theil. (2011), *Nutrients*

40

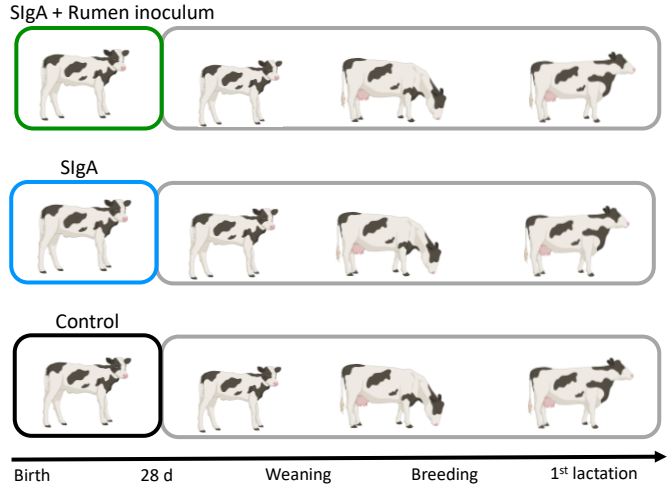
Milk is the Primary Source of SIgA Entering the Rumen During Calves' Early Life



SIgA levels in the saliva of newborn calves and in the colostrum and milk of early-lactating dairy cows.

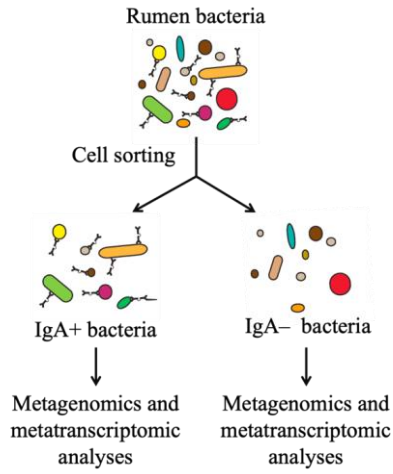
41

Determine the effects of SIgA supply during early life on the rumen microbial ecosystem and animal performance



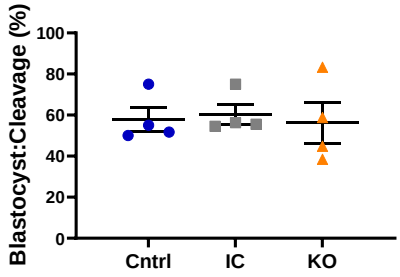
42

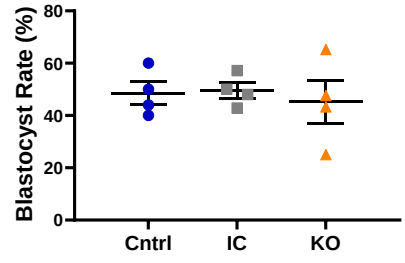
Determine the effects of SIgA supply during early life on the rumen microbial ecosystem and animal performance



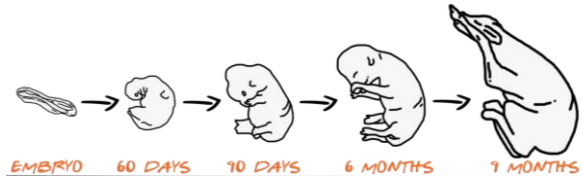
43

We wish to be able to create a bovine pIgR knockout…





- pIgR is not required for blastocyst development.



44

Preliminary Conclusions

- SIgA derived from bovine colostrum promotes the growth of fiber-digesting bacteria.
- SIgA derived from bovine colostrum influences the modulation of rumen fermentation.
- There seems to be an association between feed efficiency and the proportion of rumen SIgA-coated bacteria in dairy cattle.
- Milk is the primary source of SIgA to young dairy calves.
- Future: We expect to demonstrate that milk SIgA modulated the rumen microbial ecosystem.

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Thank you!

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