Beyond the rumen: Targeting the hindgut to improve health and performance

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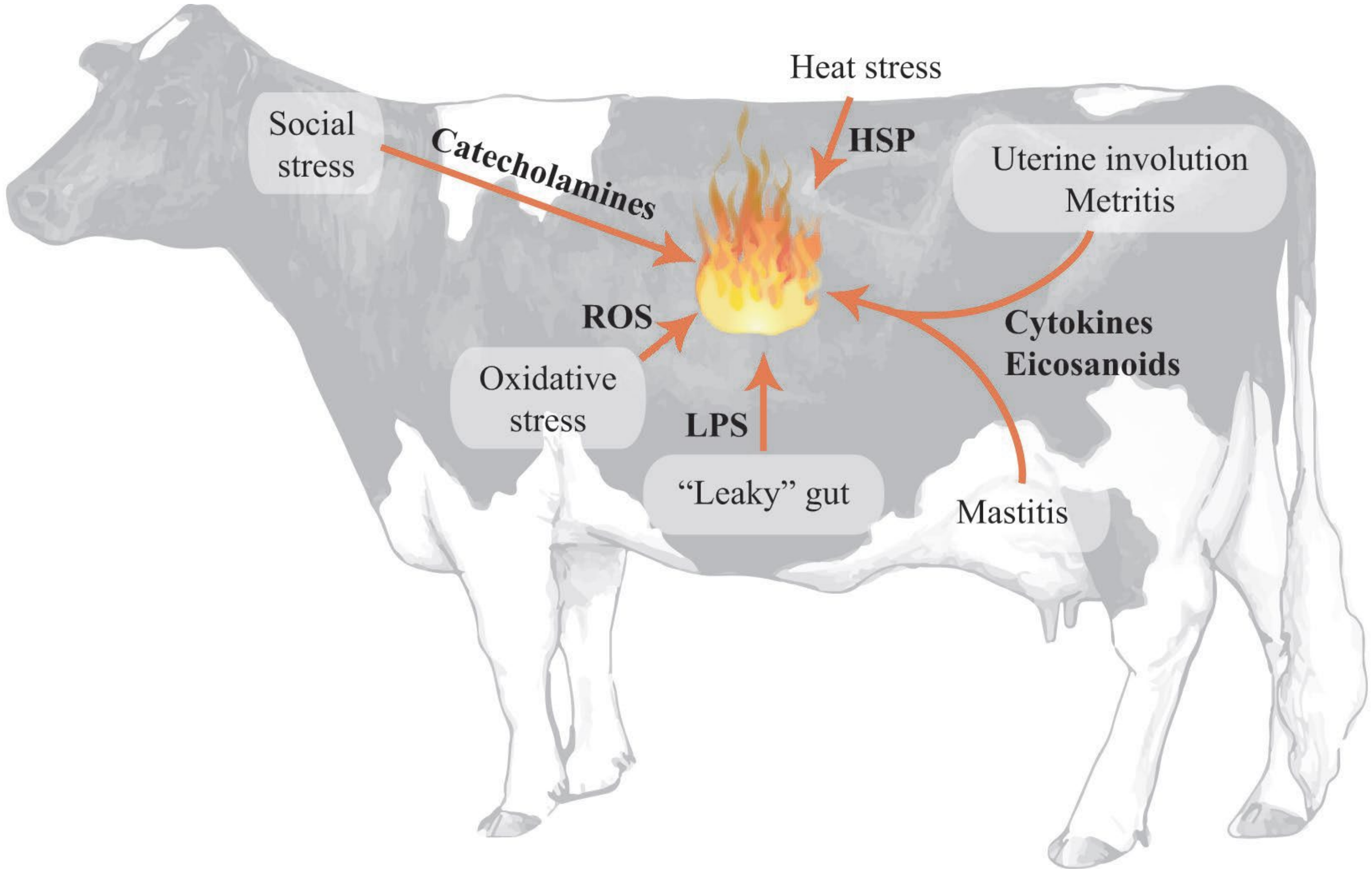
Leaky gut as a source of inflammation



HEALTHYLIFE

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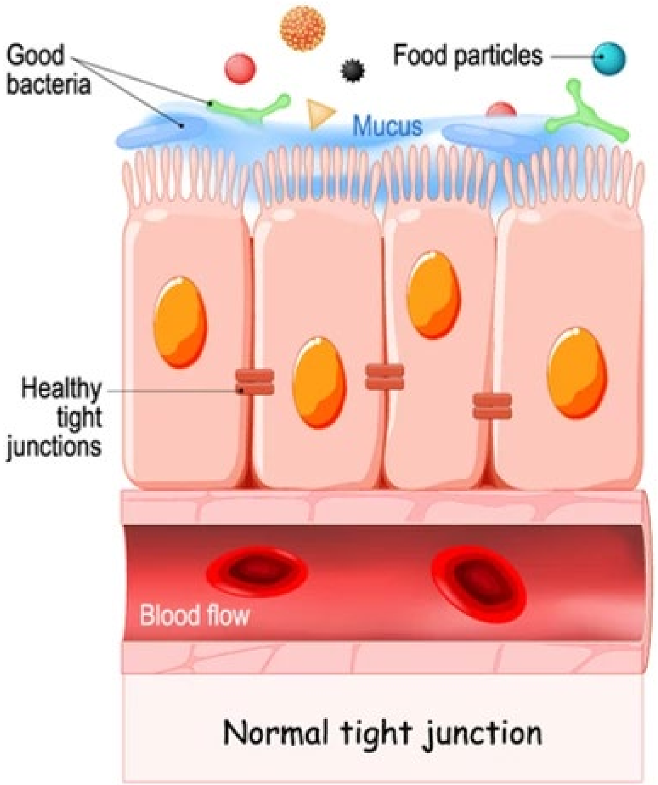
Bradford et al., 2015

Intestinal health & inflammation

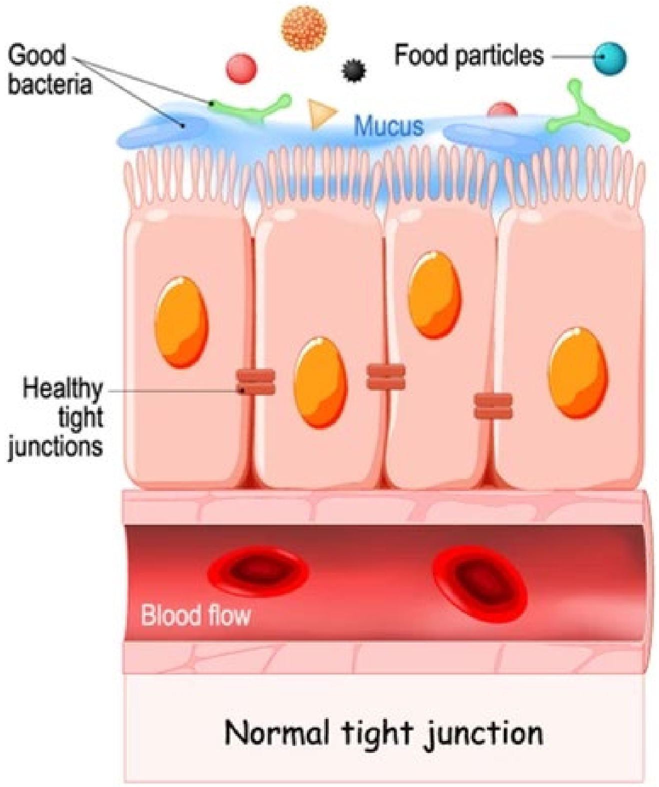
Healthy barrier



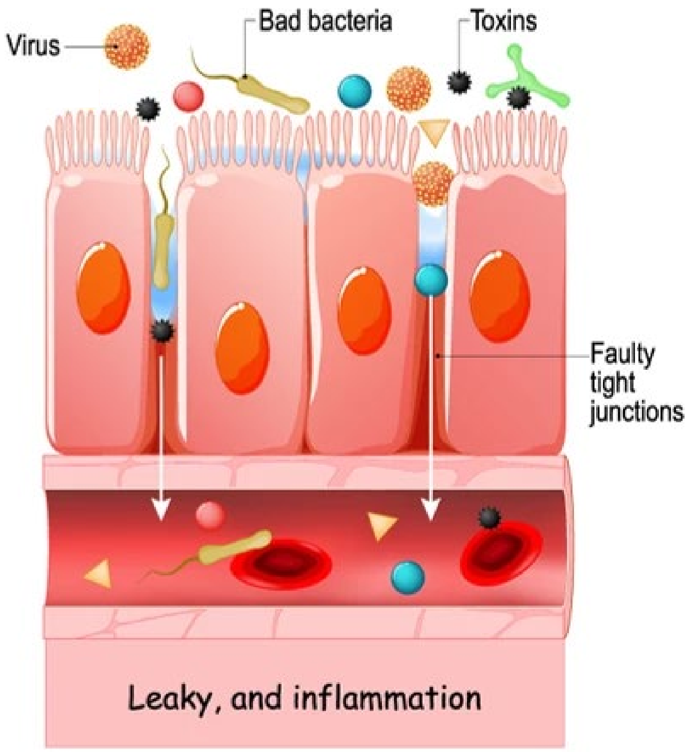
https://www.tcimedicine.com/post/leaky-gut-syndrome-may-be-the-cause-of-your-brain-health-issues

Intestinal health & inflammation

Healthy barrier



Leaky gut



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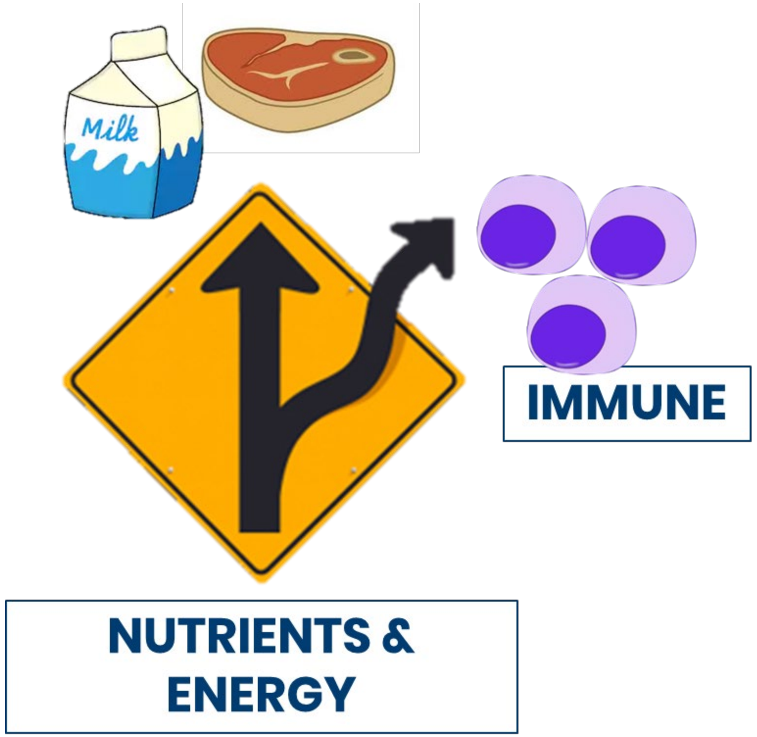
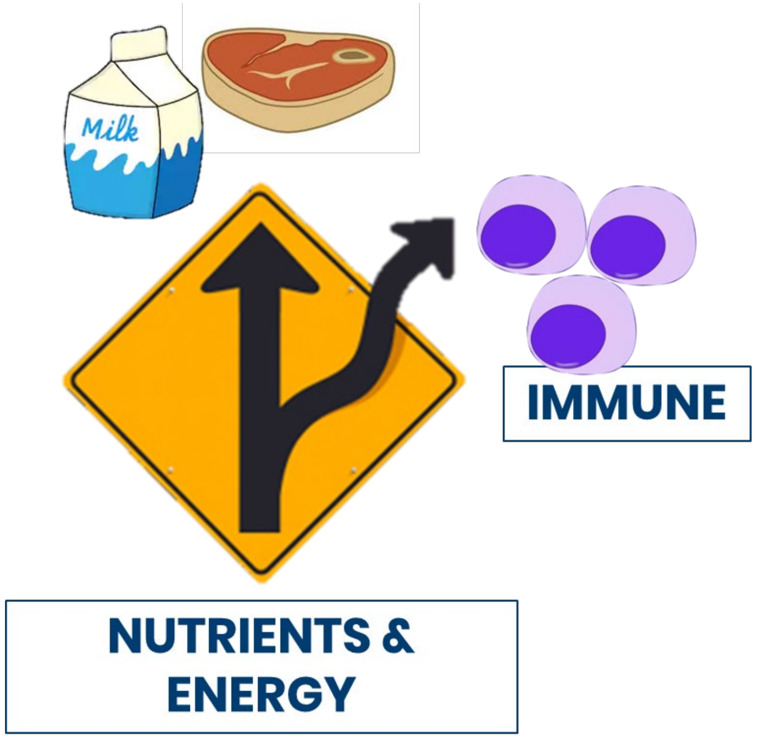
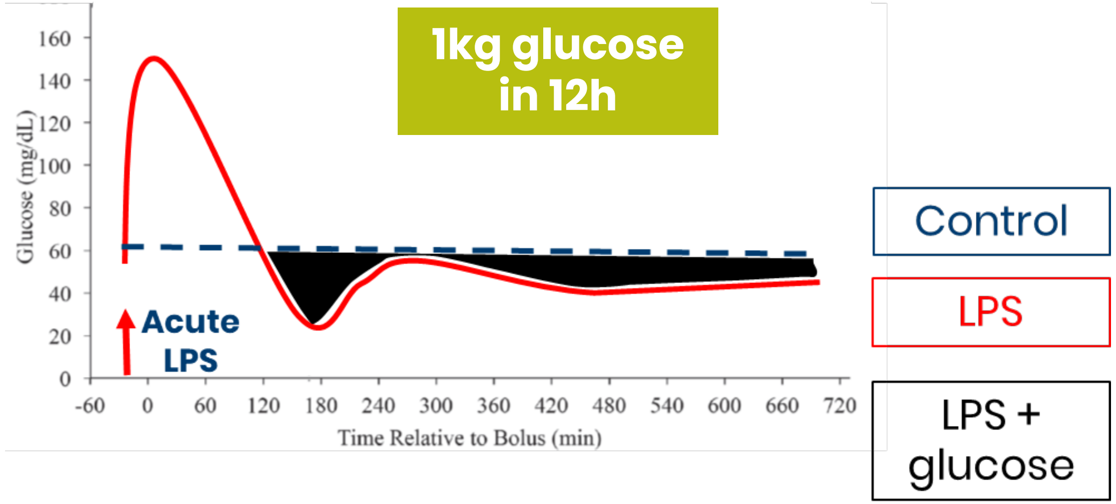
Cost of inflammation



Kvidera et al., 2017

Cost of inflammation





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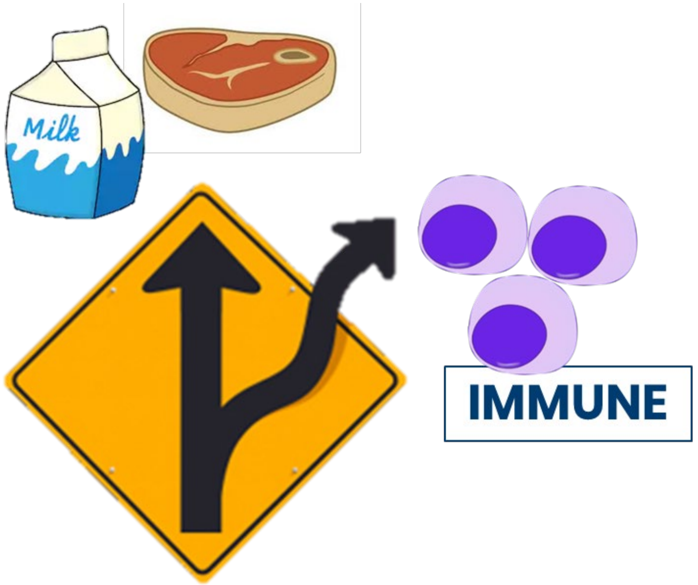
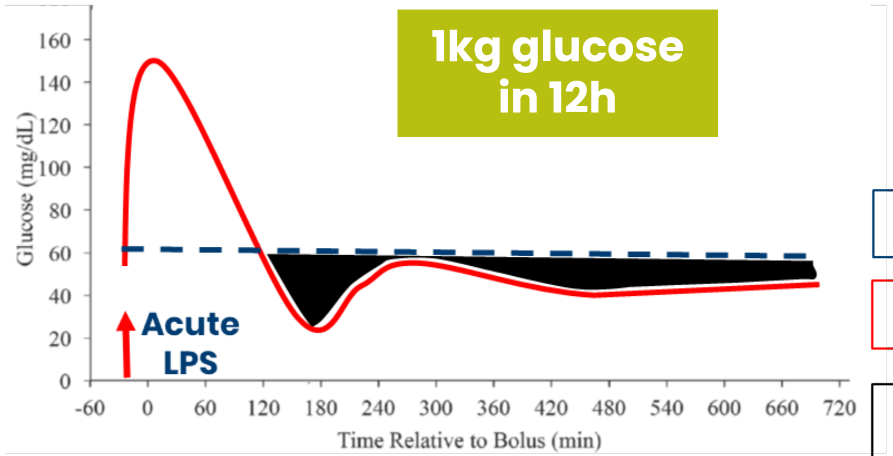
Cost of inflammation



NUTRIENTS & ENERGY



Control

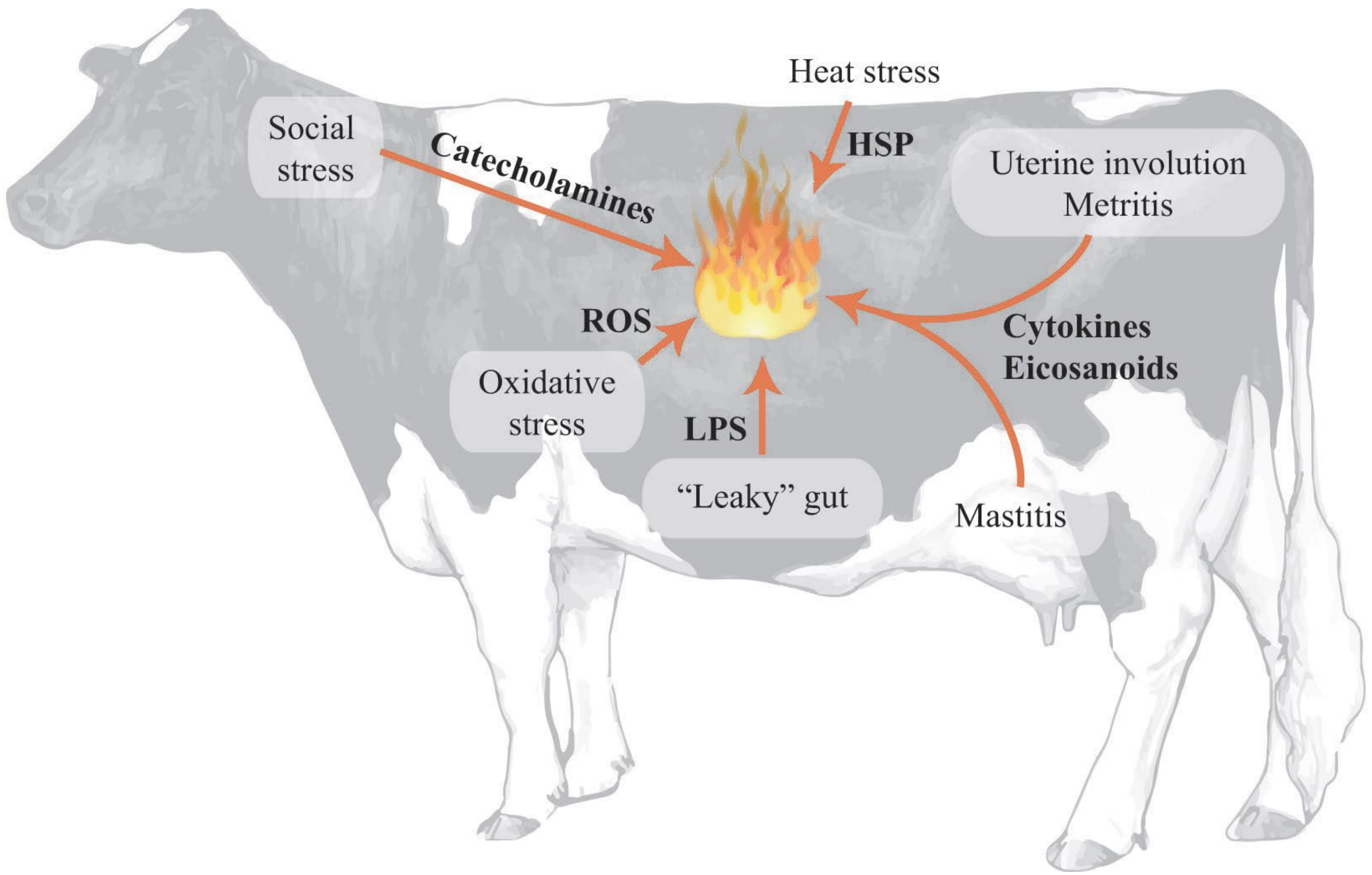
LPS

LPS + glucose

40kg milk = 3kg glucose

Kvidera et al., 2017

Leaky gut as a source of inflammation



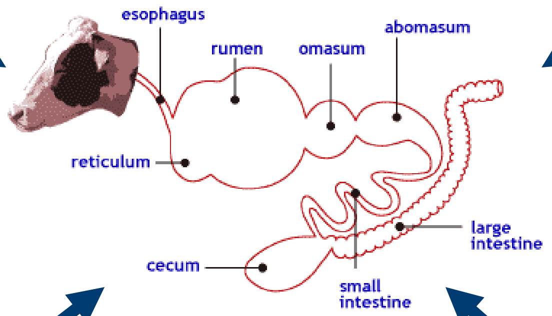
Bradford et al., 2015

Factors affecting intestinal health

Environmental stress

Feed restriction

Diet



Local/systemic inflammation

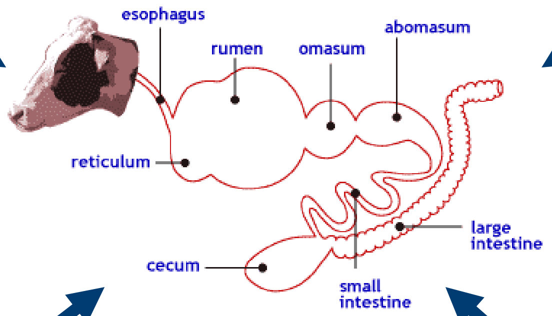
Stress

Factors affecting intestinal health

Environmental stress

Feed restriction

Diet



Local/systemic inflammation

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Factors affecting intestinal health

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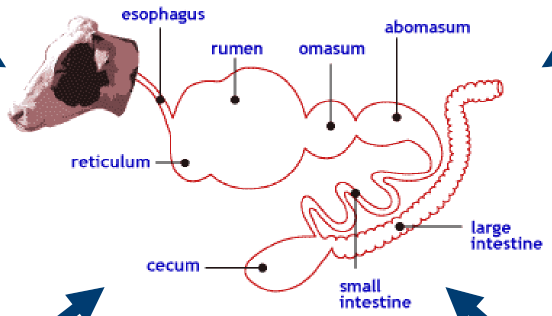


Local/systemic inflammation

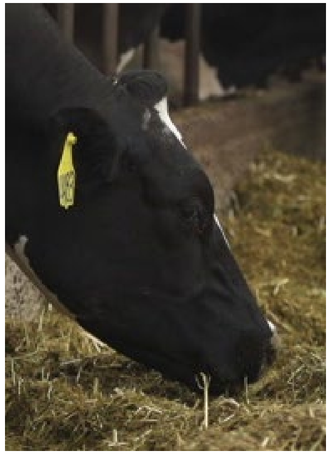
Stress

High grain diet

- Abrupt introduction
- High fermentability
  -> ↓ pH
- Microbial proliferation/lysis
  -> ↑ endotoxin

Rumen acidosis

↑↑ Grain
(↑↑ starch)



Rumen

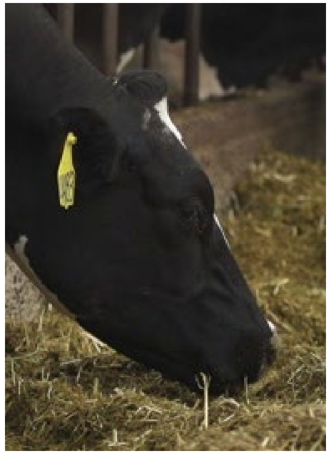
↑↑ Starch:
- ↑ fermentation
- ↓pH
- ↑microbial prolif./lysis
- ↑endotoxins/LPS

↓

ACIDOSIS
LEAKY GUT

Rumen acidosis

↑↑ Grain (↑↑ starch)



Rumen

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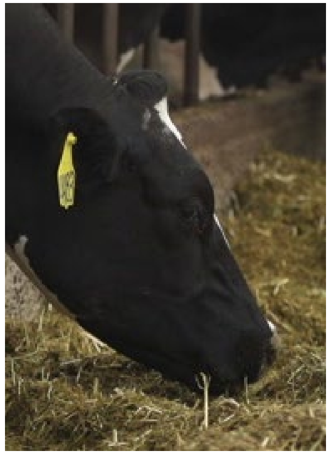
ACIDOSIS
LEAKY GUT

Small intestine

↑↑ Bypass starch

Rumen acidosis

↑↑ Grain (↑↑ starch)



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ACIDOSIS
LEAKY GUT

Small intestine

↑↑ Bypass starch

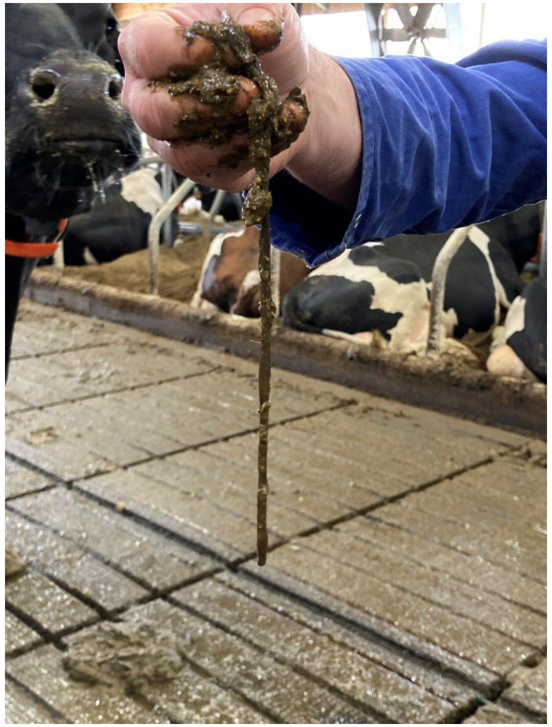
Hindgut

↑↑ Starch:
- ↑ fermentation
- ↓pH
- ↑microbial prolif./lysis
- ↑endotoxins/LPS

ACIDOSIS
LEAKY GUT

On farm: rumen acidosis = hindgut acidosis

Mucin casts



Frothy feces

Fresh blood

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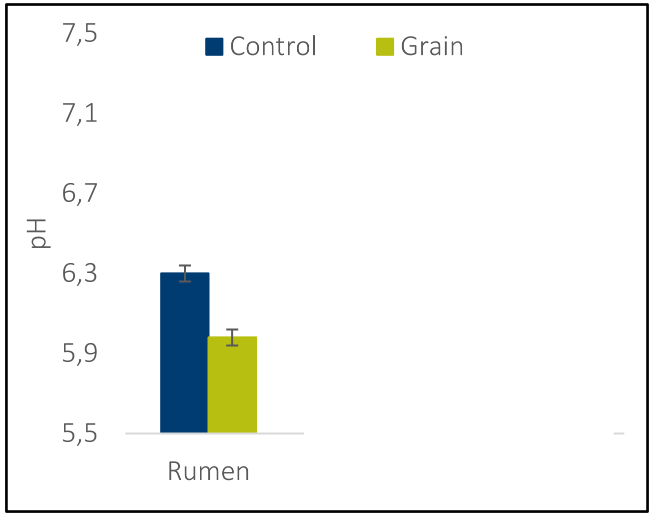
High grain diets and acidosis along the GI tract

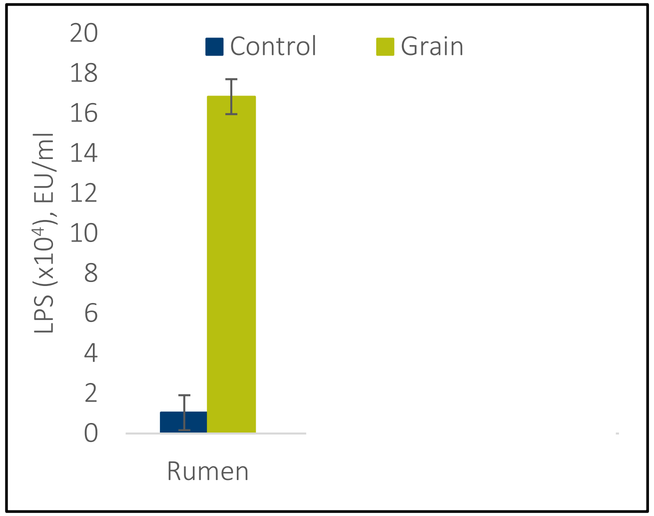
Treatments:

1. Control (↑NDF, ↓starch): 70% forage, 30% supplement
2. SARA (↓NDF, ↑starch): 36% forage, 30% wheat:barley pellet, 34% supplement

↓pH



↑LPS



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Adapted from Li et al., 2012

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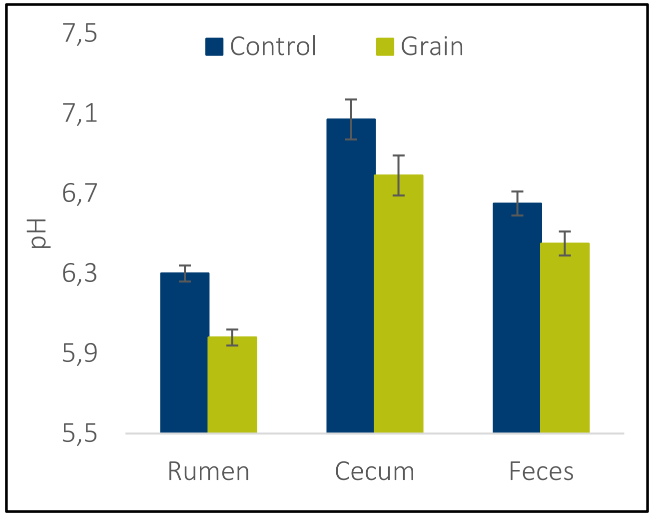
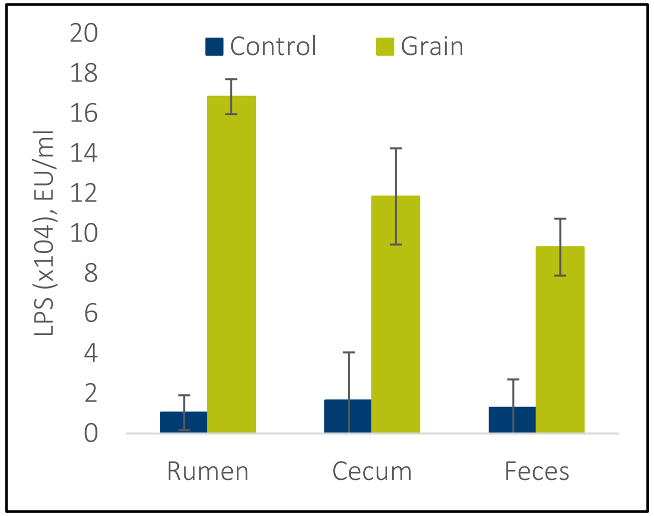


↑LPS



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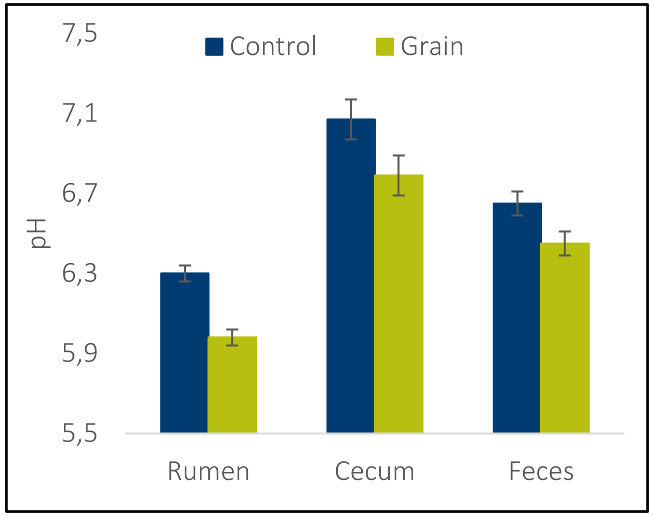
Adapted from Li et al., 2012

High grain diets and acidosis along the GI tract

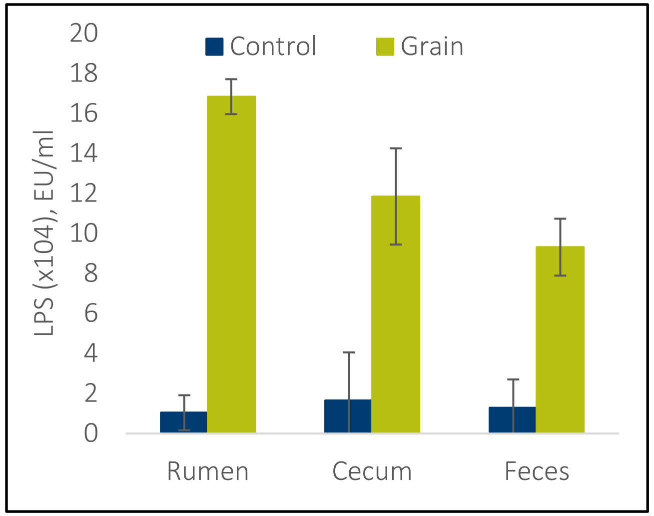
Treatments:

1. Control: 70% forage, 30% supplement
2. Subacute ruminal acidosis: 36% forage, 30% wheat:barley pellet, 34%, supplement

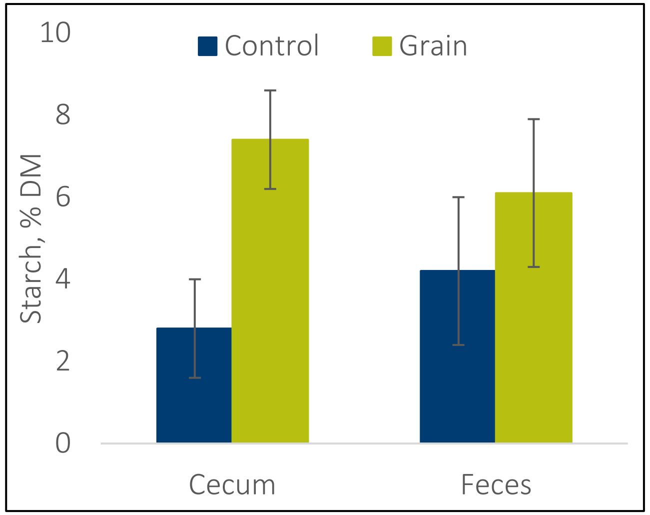
↓pH



↑LPS



↑ Starch



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Adapted from Li et al., 2012

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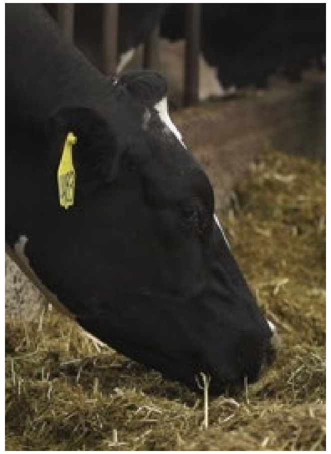
Rumen acidosis

↑↑ Grain (↑↑ starch)



Rumen

↑↑ Starch:

- ↑ fermentation
- ↓pH
- ↑microbial prolif./lysis
- ↑endotoxins/LPS

ACIDOSIS
LEAKY GUT

Small intestine

↑↑ Bypass starch

Hindgut

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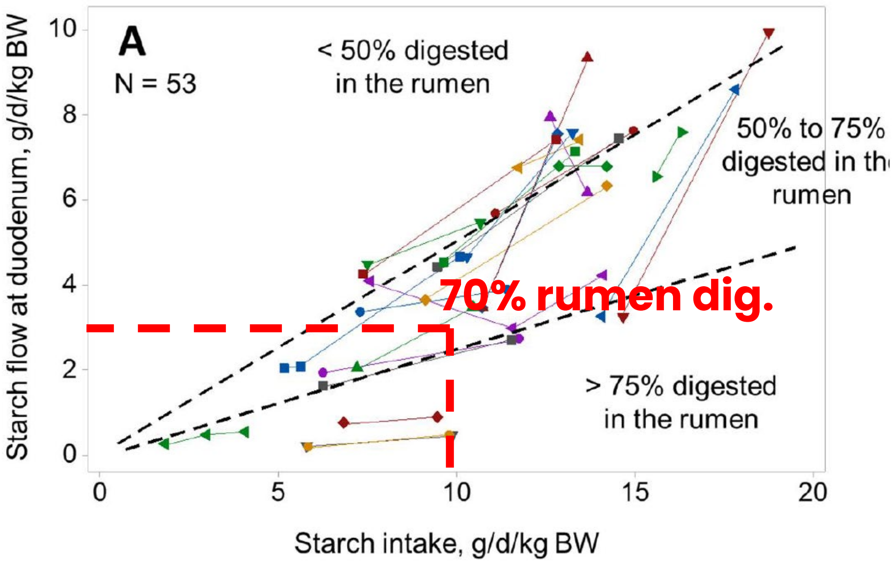
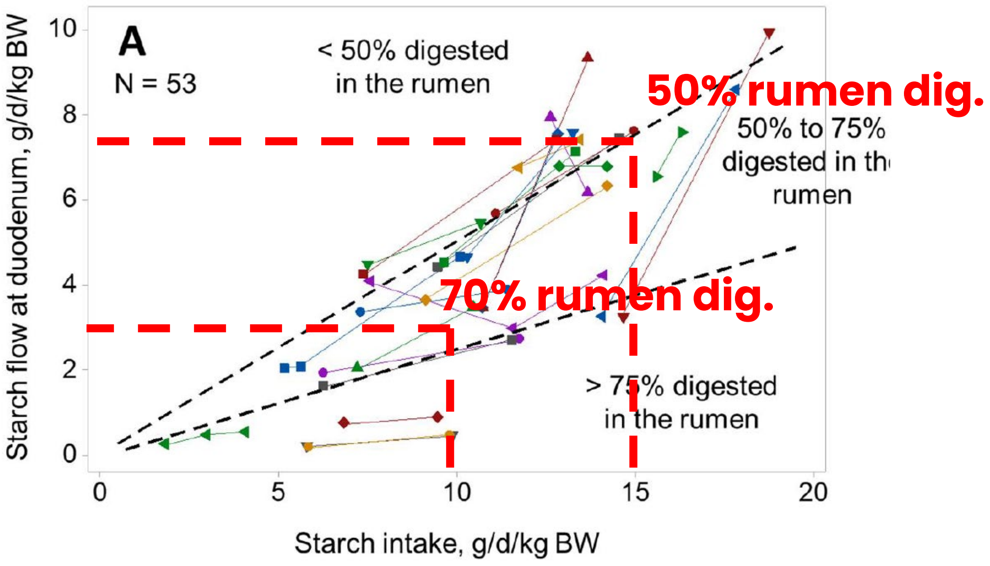
ACIDOSIS
LEAKY GUT

Postruminal starch digestion



Sanz-Fernandez et al., 2020; Offner and Sauvant, 2004

Postruminal starch digestion



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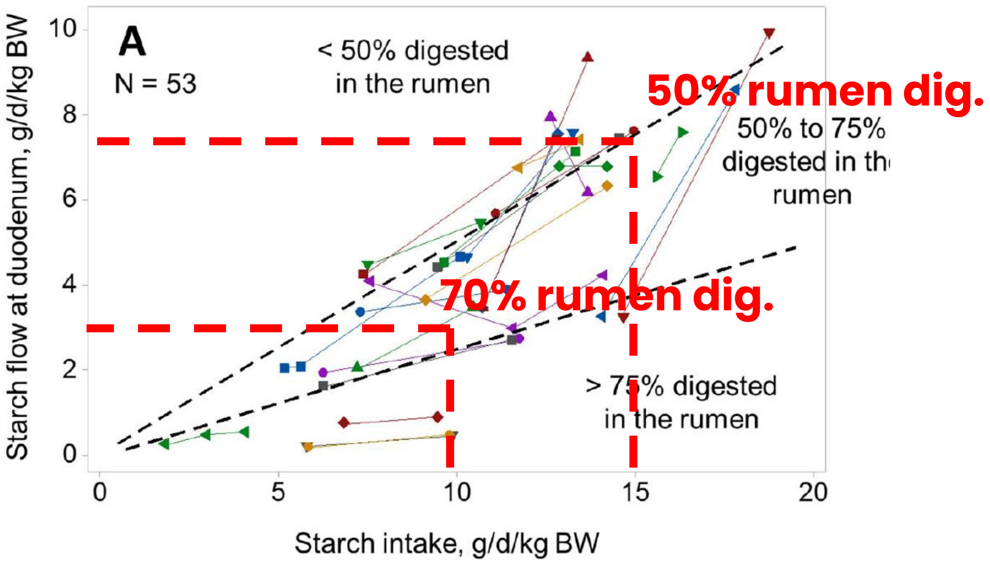
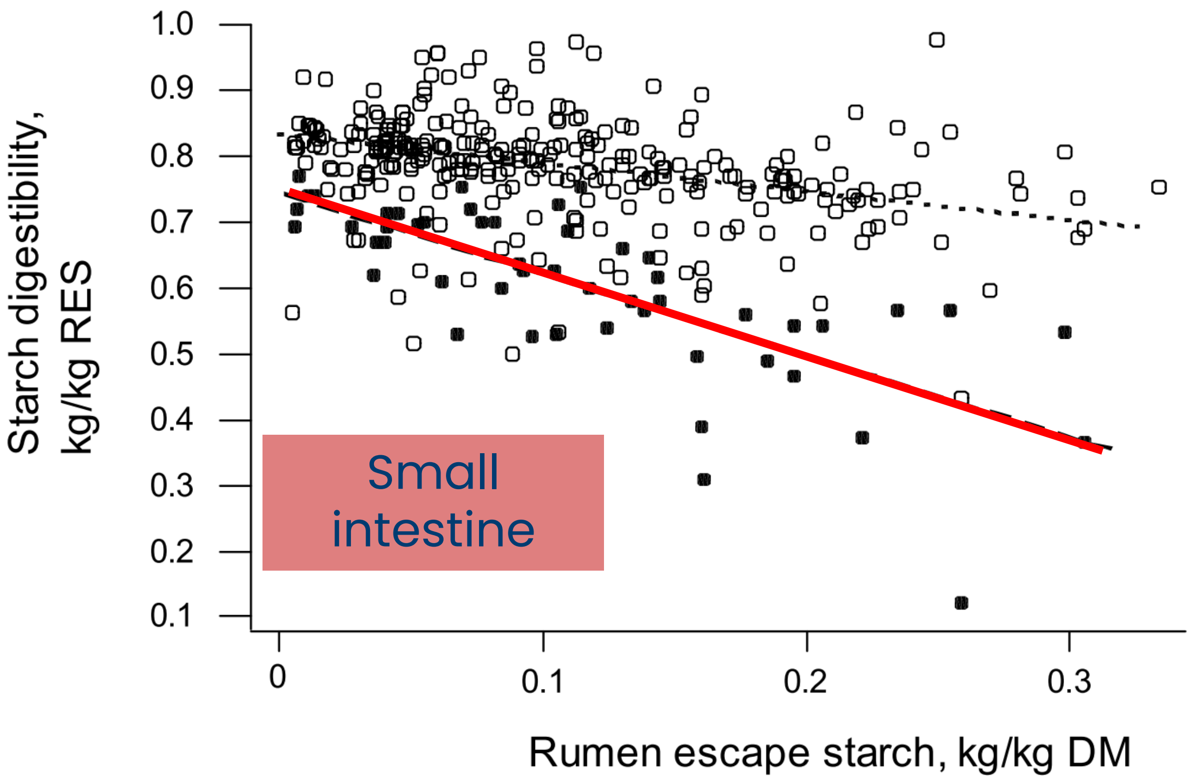
Postruminal starch digestion

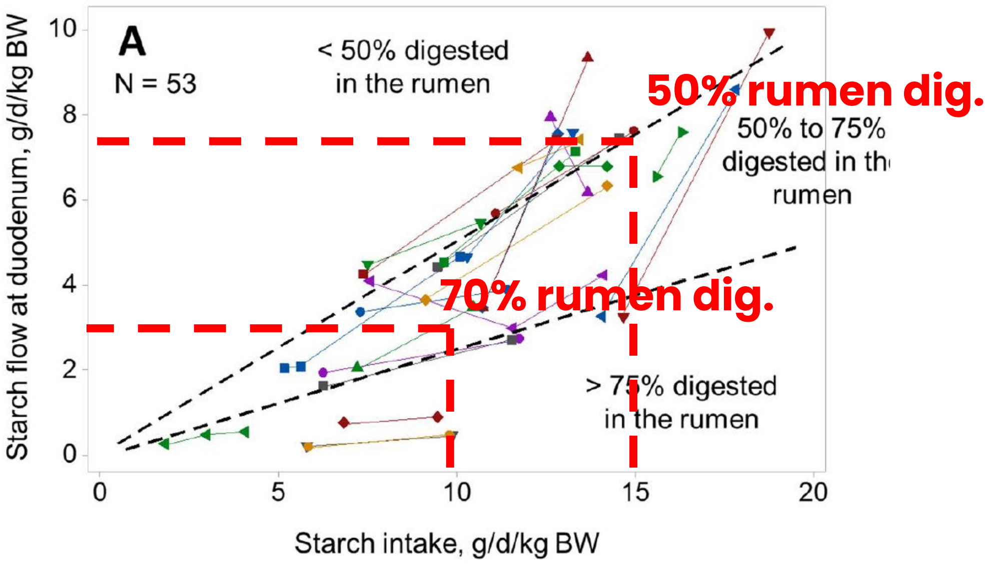


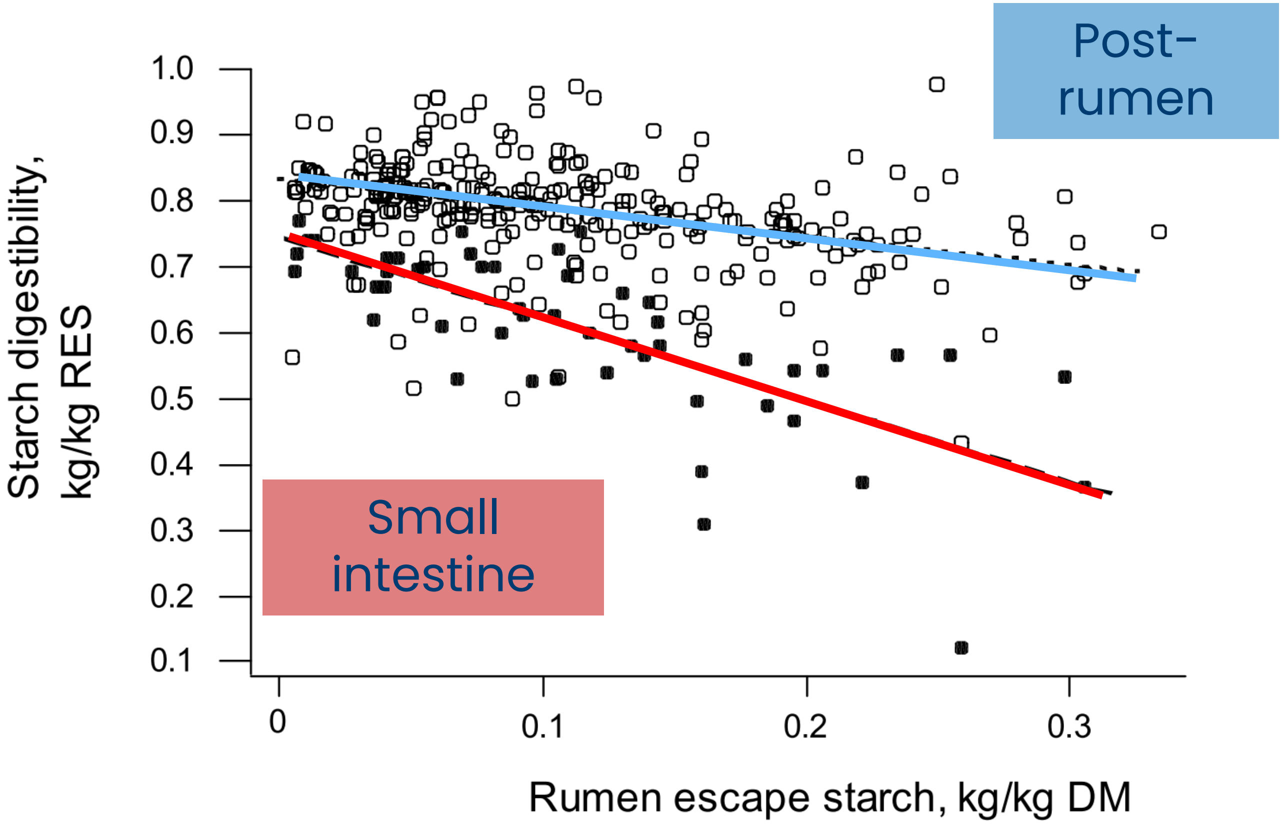


Sanz-Fernandez et al., 2020; Offner and Sauvant, 2004

Postruminal starch digestion

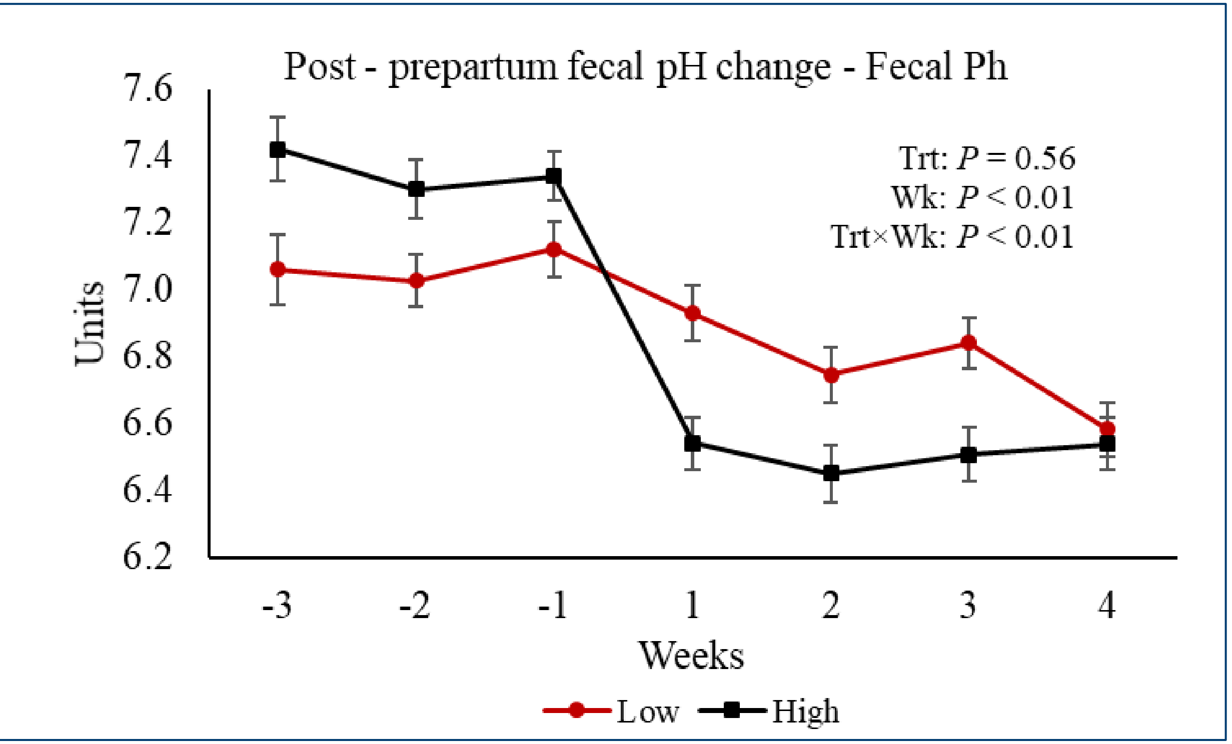
Compensatory role of the hindgut





Sanz-Fernandez et al., 2020; Offner and Sauvant, 2004

Change in fecal pH around calving



Rodriguez Jimenez et al., 2019

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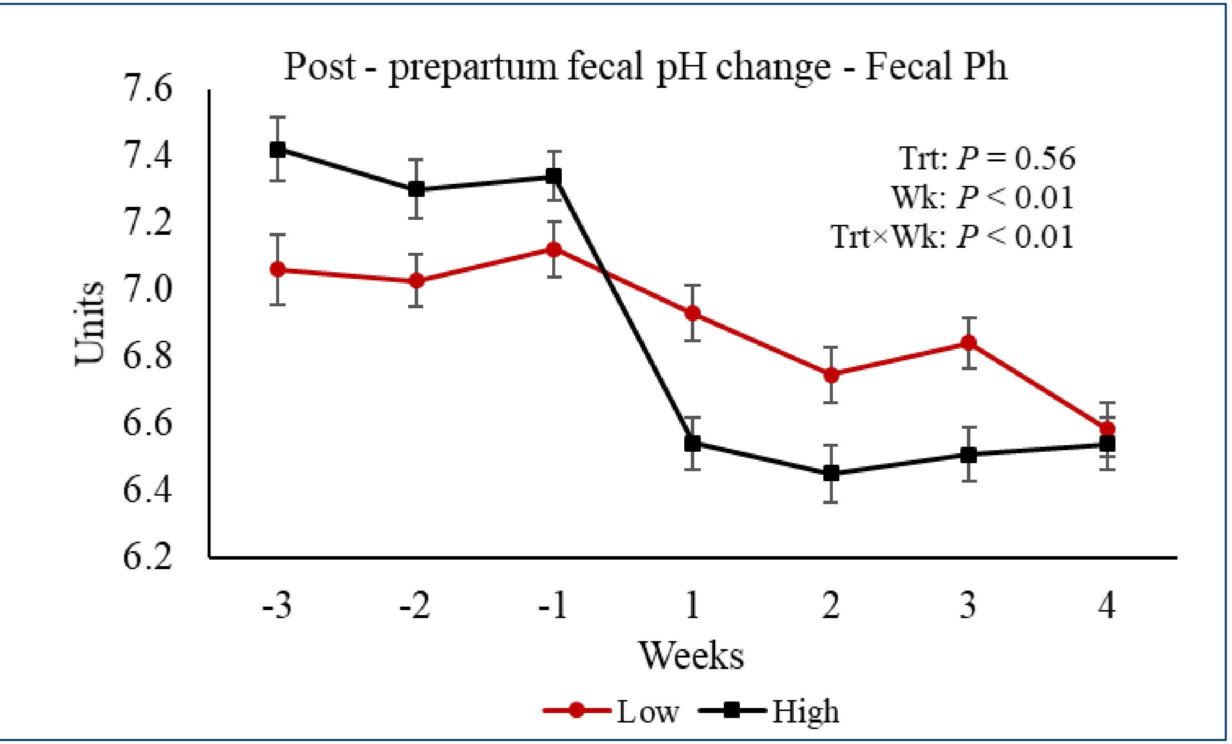

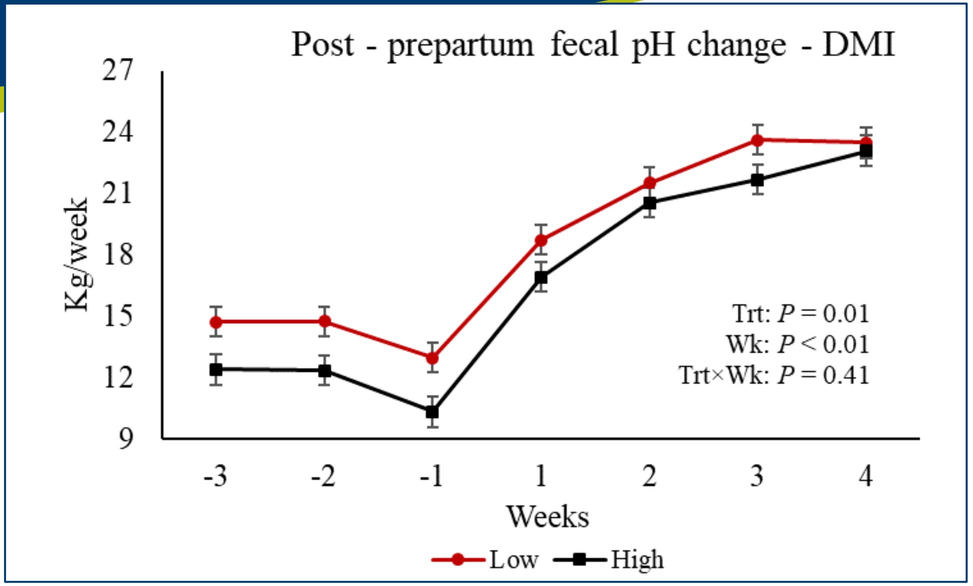

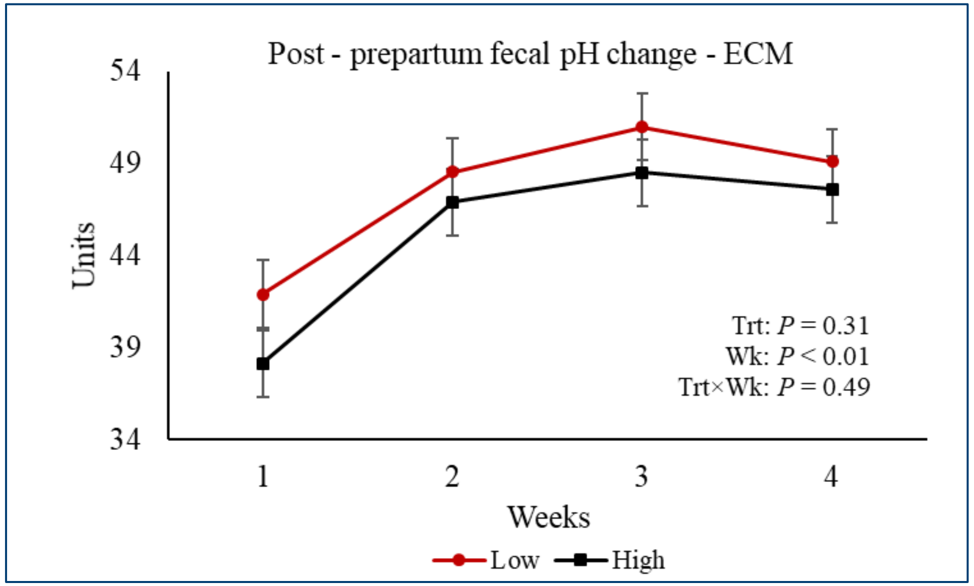

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Rodriguez Jimenez et al., 2019

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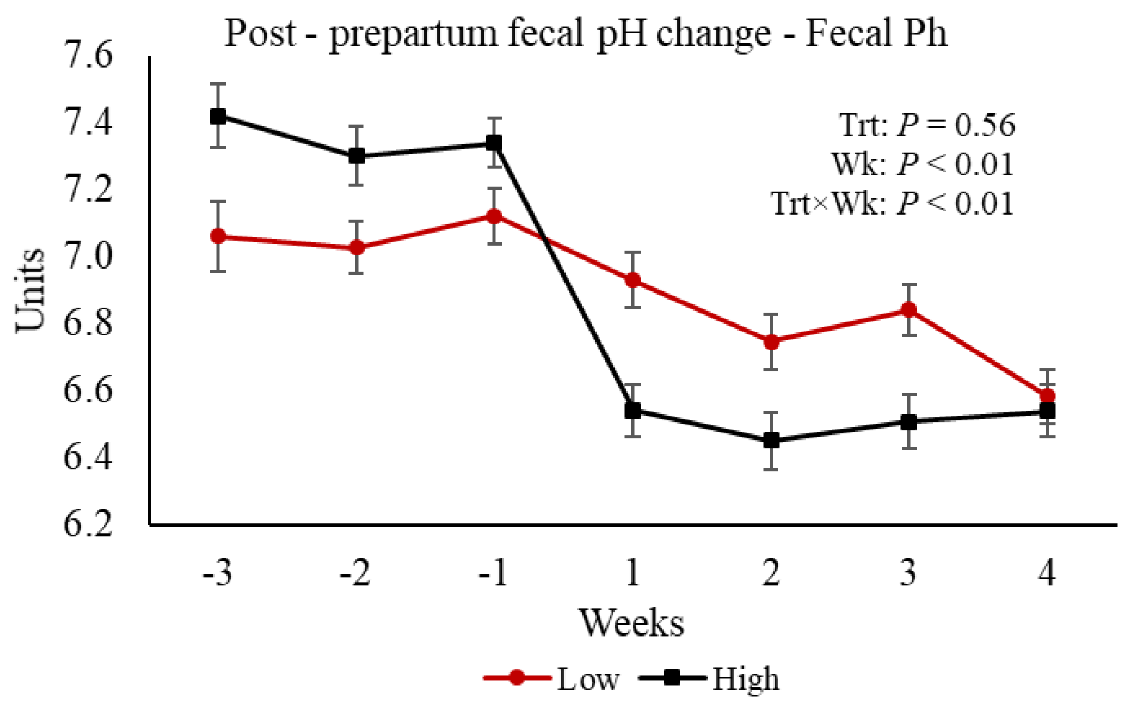

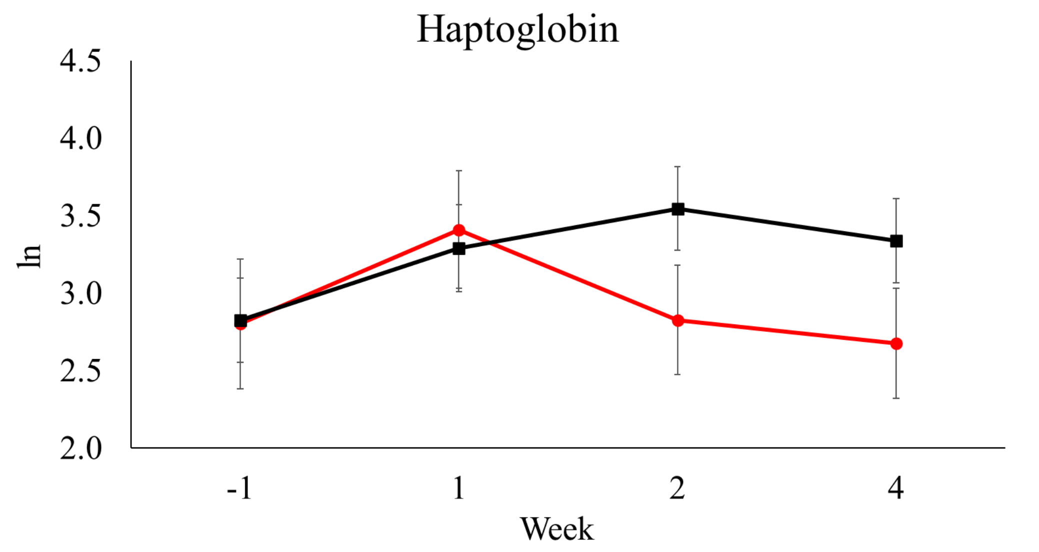

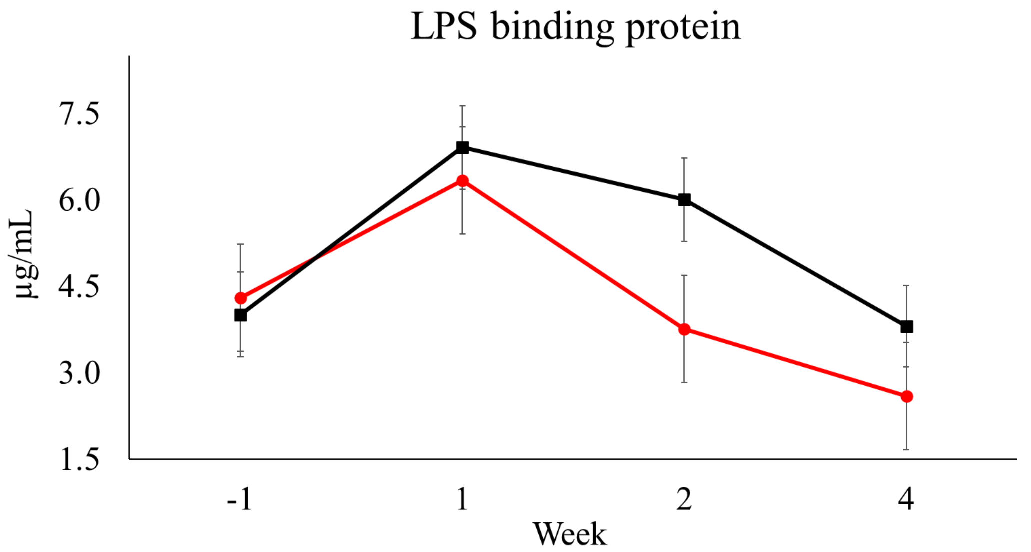

Rodriguez Jimenez et al., 2019

Hindgut acidosis and leaky gut

Saline — Starch

Period 1					Washout			Period 2				
D0	D1	D2	D3	D4	D1	D2	D3	D0	D1	D2	D3	D4

Treatments (n=4):

1. Control:

   Abomasal saline

2. Hindgut acidosis:

   Abomasal cornstarch

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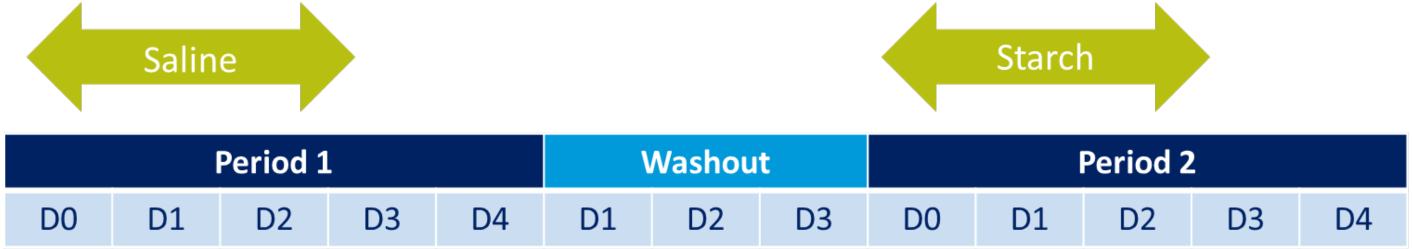
Sanz-Fernandez et al., 2023 (In press)

Hindgut acidosis and leaky gut



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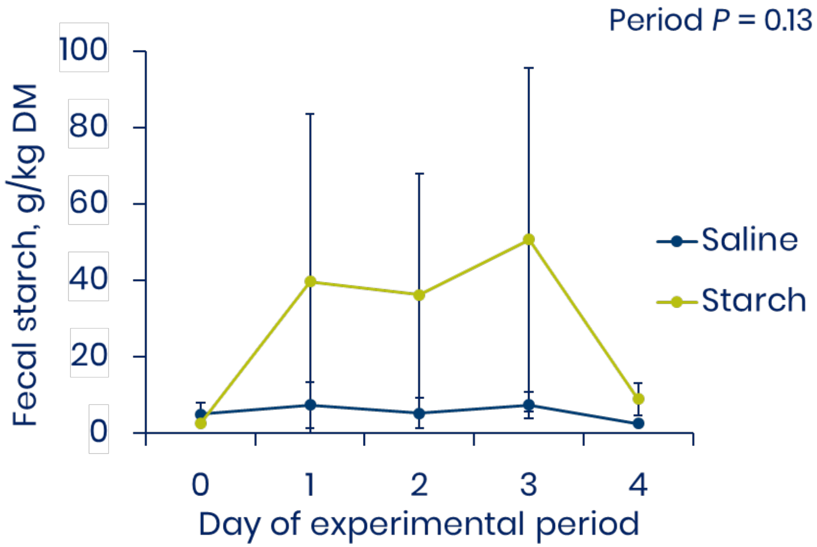

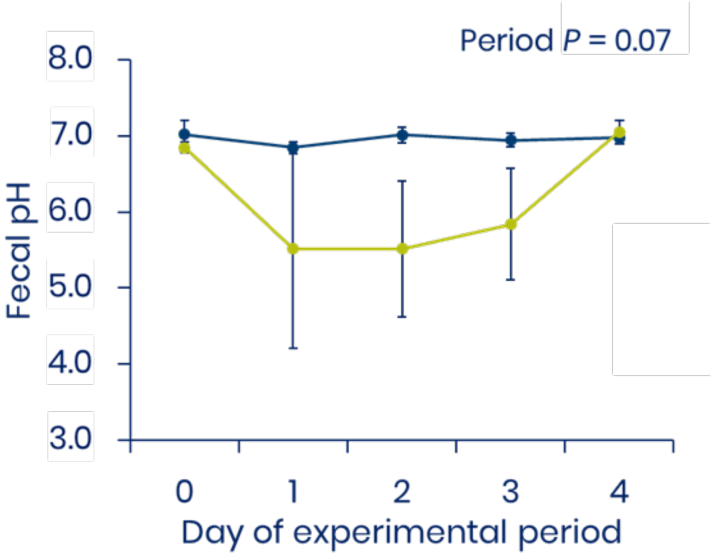

Sanz-Fernandez et al., 2023 (In press)

Hindgut acidosis and leaky gut

Saline Starch

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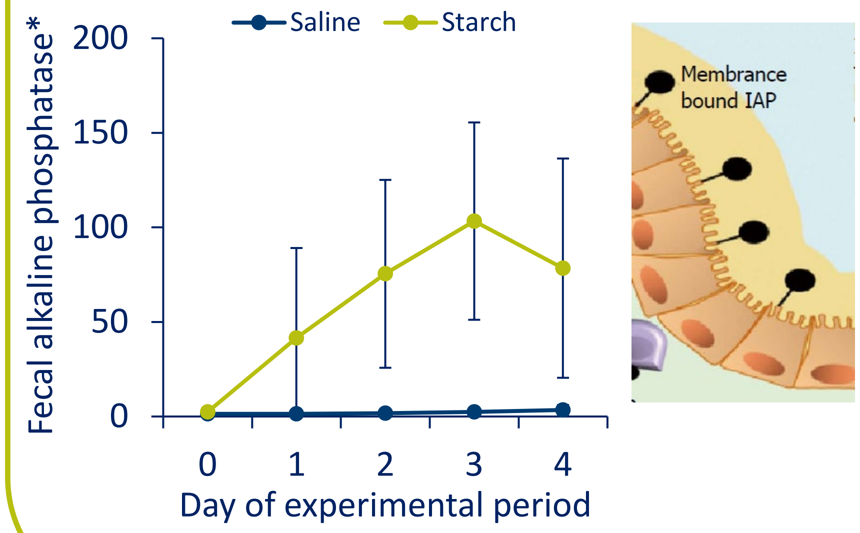
Intestinal damage



*activity, mOD 405nm/min

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Estaki et al., 2014; George et al., 2018; Sanz-Fernandez et al., 2023 (In press)

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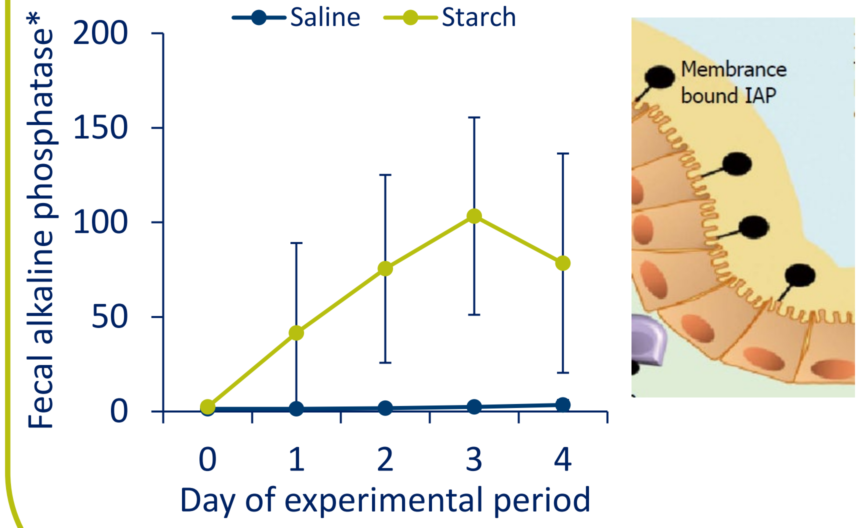
Hindgut acidosis and leaky gut

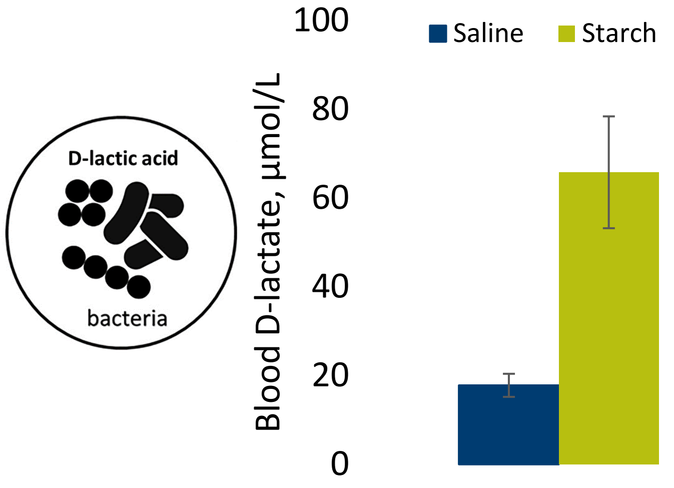
Period 1					Washout			Period 2				
D0	D1	D2	D3	D4	D1	D2	D3	D0	D1	D2	D3	D4

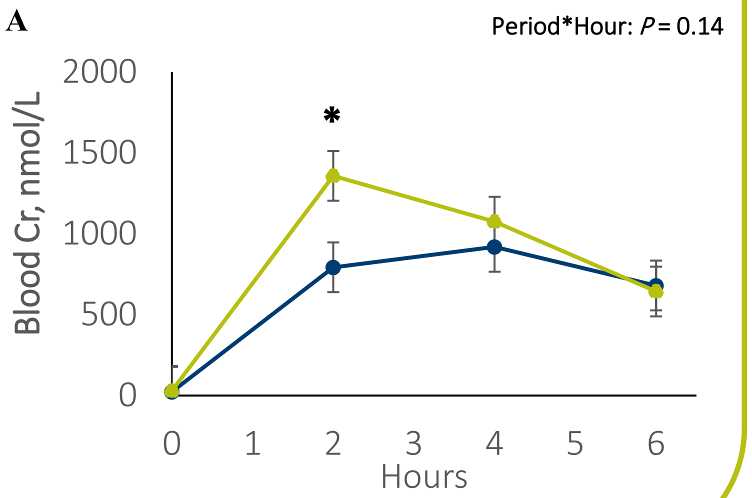
Intestinal damage



*activity, mOD 405nm/min

Increased intestinal permeability





Does hindgut acidosis trigger systemic inflammation?

- Experimentally inducing SARA (with a high grain diet) results in systemic inflammation

  (e.g., Gozho et al., 2005 & 2007; Khafipour et al., 2009; Li et al., 2012; Abeyta et al. 2023)

- Postruminal infusion of starch fails to induce systemic inflammation.

  (e.g., Sanz-Fernandez et al., unpublished; Abeyta et al. 2023a,b,c; van Gastelen et al. 2021a,b)

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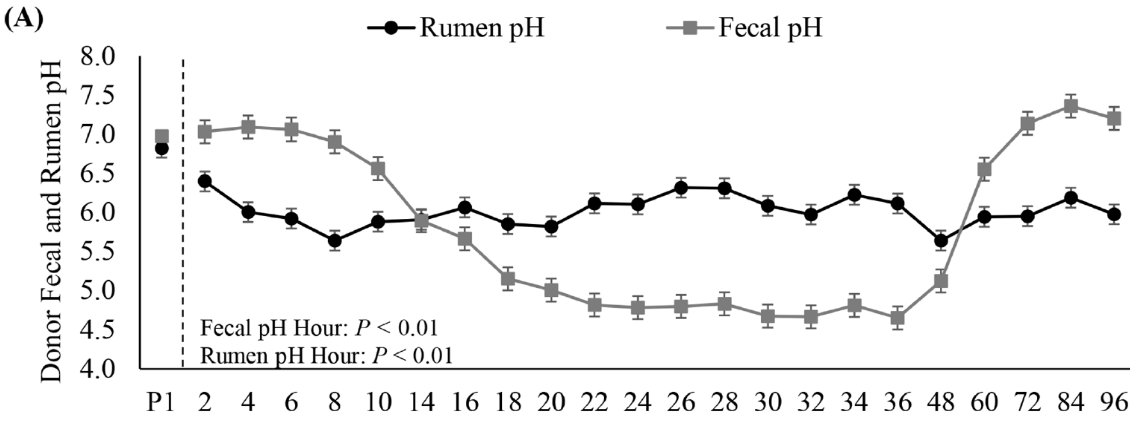
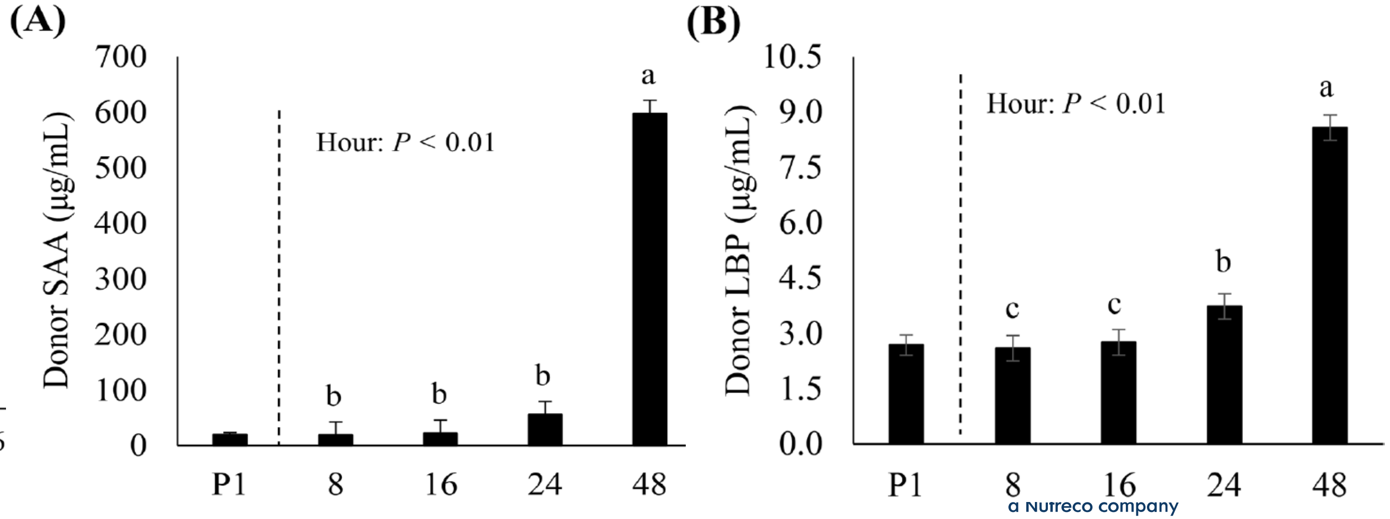
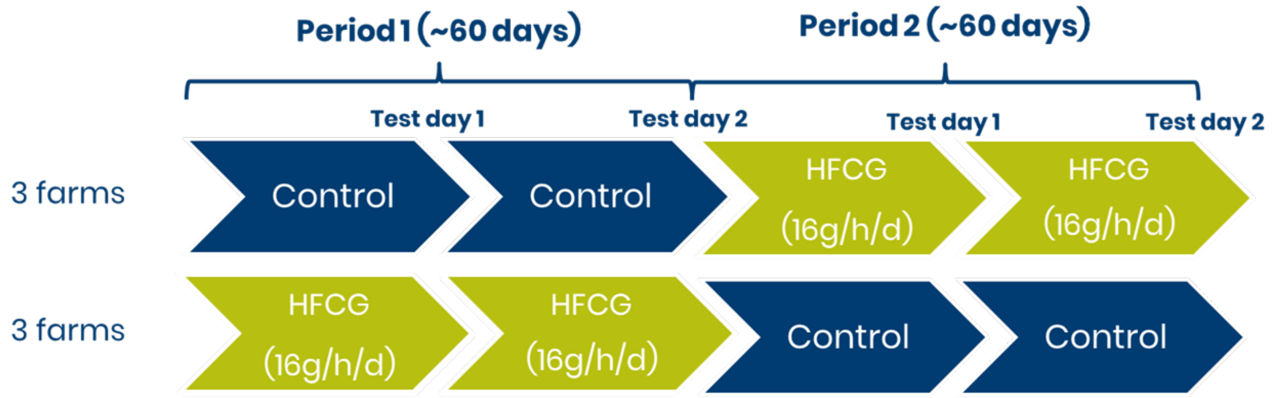
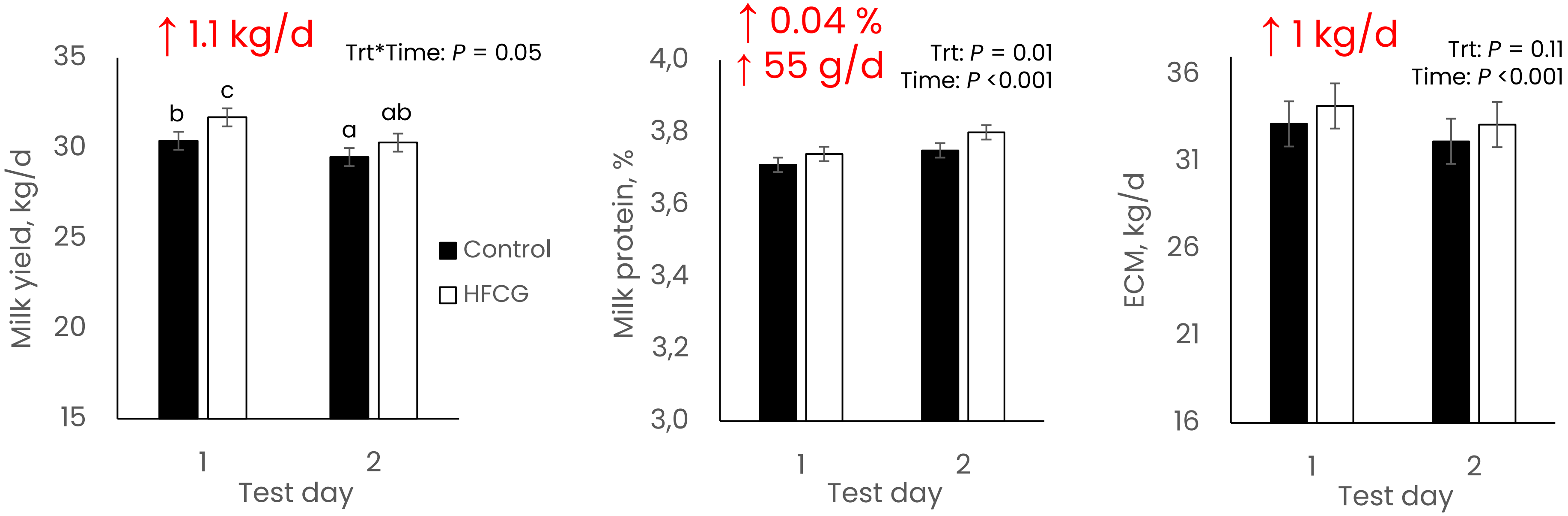
SARA inductions: 2.75% BW ground corn after 16 h of 75% feed restriction (Abeyta et al., 2023)





Postrumen prebiotic improves milk performance in dairy





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Sanz Fernandez and Seymour et al., 2023 (In press)

Targeting the hindgut

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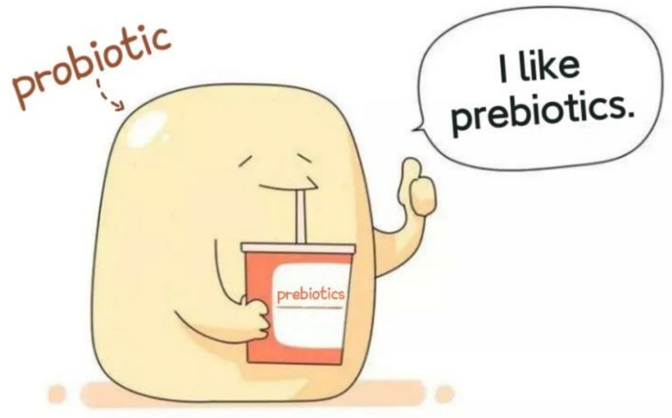
(Postrumen) prebiotics

"Prebiotics are nondigestible food ingredients that beneficially affect host health by selectively stimulating the growth and/or activity of bacteria in the gastrointestinal tract"



- Prebiotics are particularly well suited for postruminal applications

Chow et al., 2006; Gaggia et al., 2010; Sanders et al., 2019

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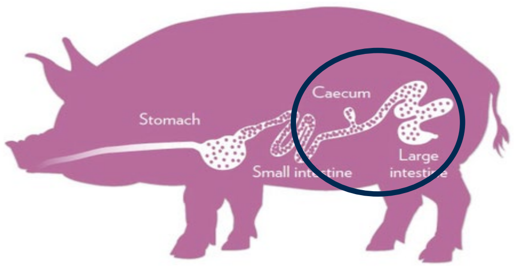
Gluconic acid and its salts



- In swine, gluconate improves performance and VFA production.

Asano et al., 1994 & 1997; Biagi et al., 2006; Michiels et al., 2020; Tsukahara et al., 2002 & 2006; Lopez-Siles et al., 2017

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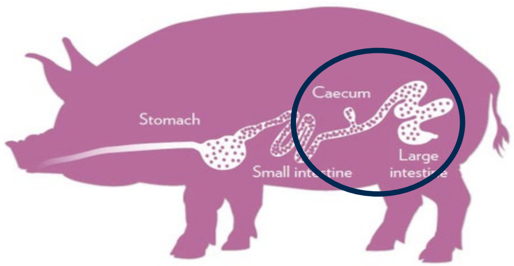

Lactic acid bacteria (LAB)
Bifidobacterium pseudocatenulatum
Bifidobacterium catenulatum
Bifidobacterium dentium
Lactobacillus reuteri
Lactobacillus mucosae
Mitsuokella multiacida

Acid-utilizing bacteria
Megasphaera elsdenii
Faecalibacterium prausnitzii

Asano et al., 1994 & 1997; Biagi et al., 2006; Michiels et al., 2020; Tsukahara et al., 2002 & 2006; Lopez-Siles et al., 2017

Gluconic acid and its salts

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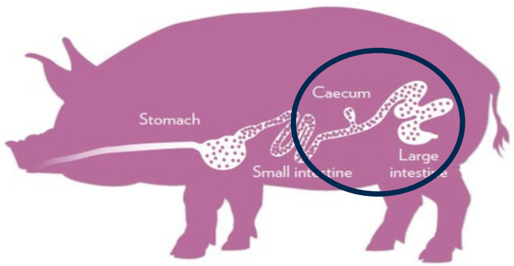

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Bifidobacterium pseudocatenulatum
Bifidobacterium catenulatum
Bifidobacterium dentium
Lactobacillus reuteri
Lactobacillus mucosae
Mitsuokella multiacida

Acid-utilizing bacteria
Megasphaera elsdenii
Faecalibacterium prausnitzii

- Metabolic substrate and signaling molecules

  Main energy source for colonocytes and ligand of G-protein coupled receptor

- Intestinal barrier function enhancement and repair

  Enhance mucin production, tight junctions expression, colonocyte proliferation and migration

- Intestinal mucosal immunity modulation

  Anti-inflammatory effects, regulation of immune cell proliferation and migration

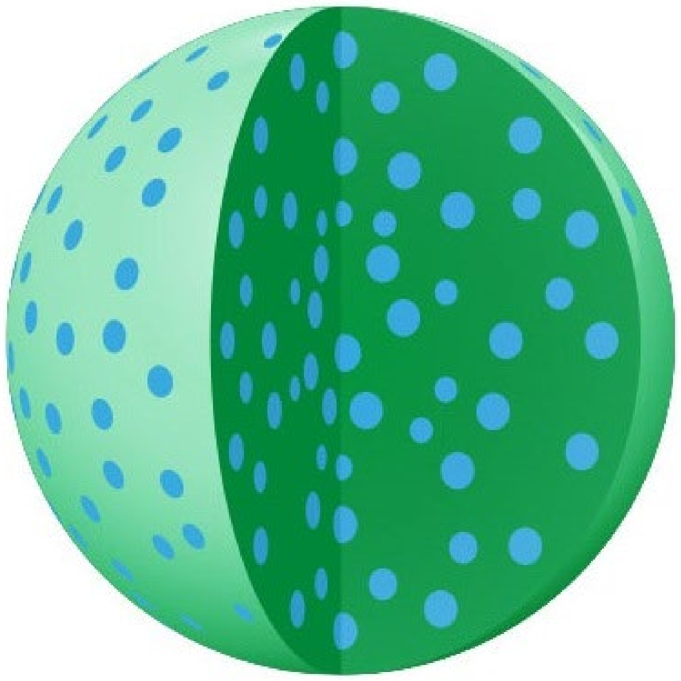
- Antimicrobial activity

Asano et al., 1994 & 1997; Biagi et al., 2006; Michiels et al., 2020; Tsukahara et al., 2002 & 2006; Lopez-Siles et al., 2017

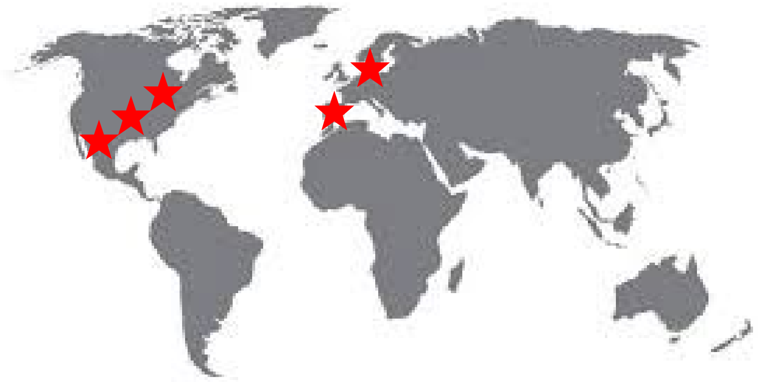
Postruminal prebiotic: gluconate

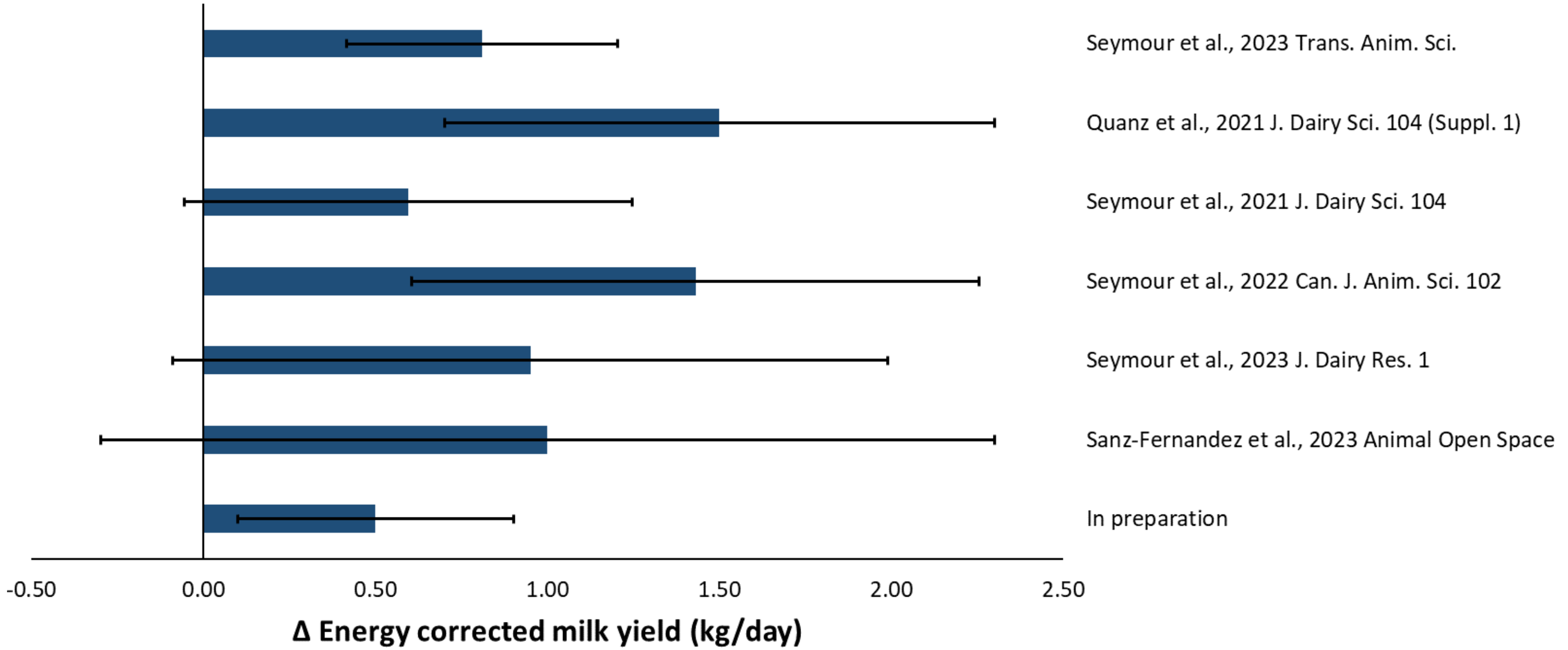
Hydrogenated fat embedded calcium gluconate (HFCG; Selko Lactibute)

- Fat matrix is digested in the small intestine facilitating gluconate delivery to the hindgut
- Recommended dose: 16g/cow/d (40% calcium gluconate)



Gluconate improves milk performance in dairy





	No. studies
Milk yield, kg/d	↑↑
Milk fat, %	↑↑
Milk fat, g/d	↑↑↑↑
Milk protein, %	↑
Milk protein, g/d	↑↑↑
ECM / FCM	↑↑↑↑↑
Feed efficiency	↑

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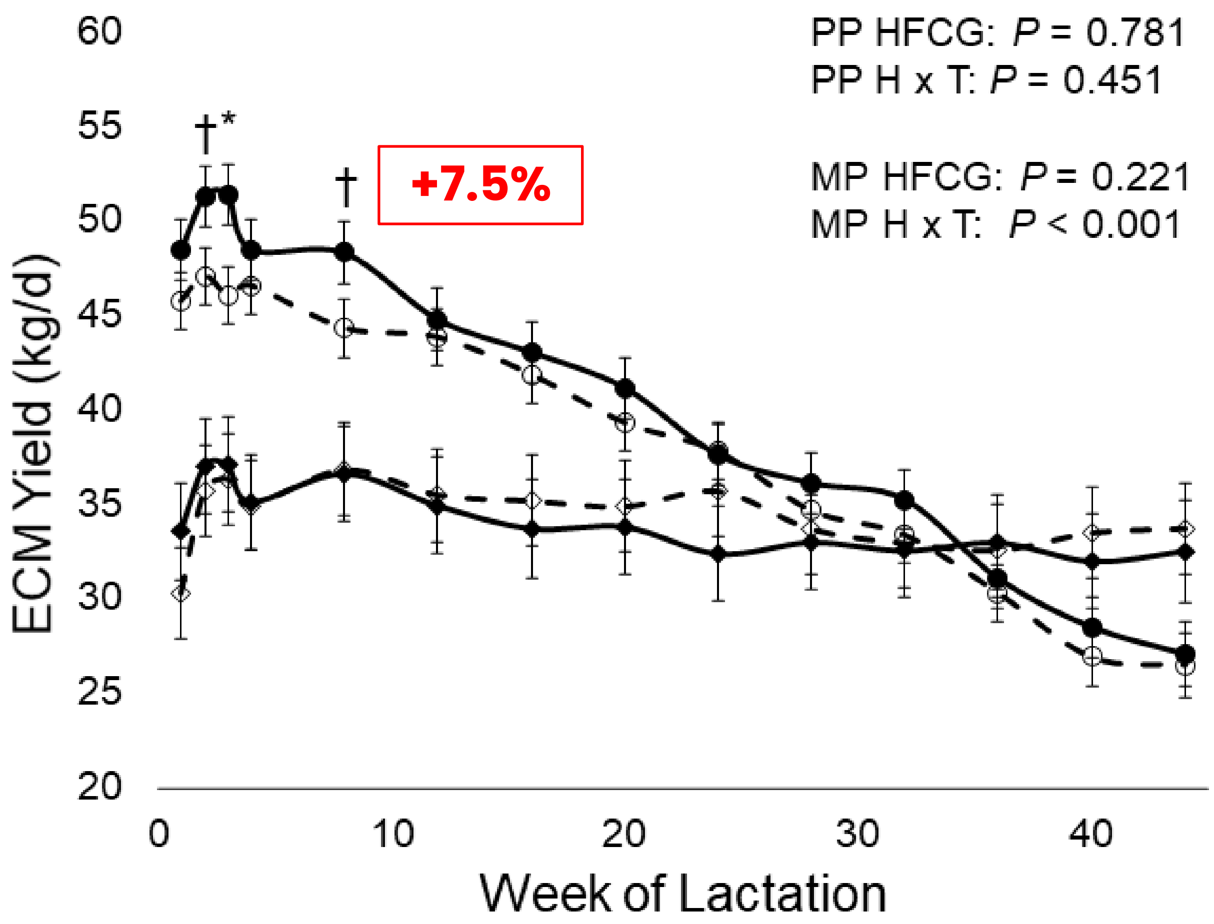
Gluconate improves milk performance in dairy

Burford, Canada

Supplementation:

Close-up + full lactation

Both primi- and multi-parous



Seymour et al., 2022

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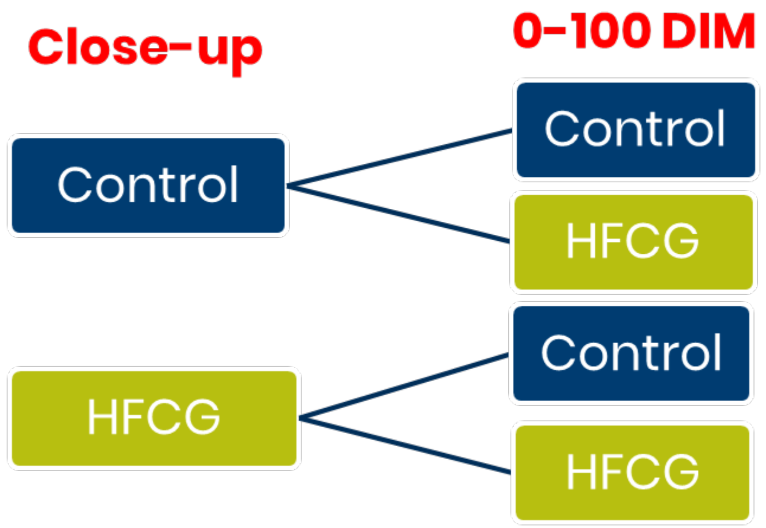
Gluconate improves milk performance in dairy

- Granja Madero, Mexico
- Multiparous



Seymour et al., 2023 (In press)

Gluconate improves milk performance in dairy

- Granja Madero, Mexico
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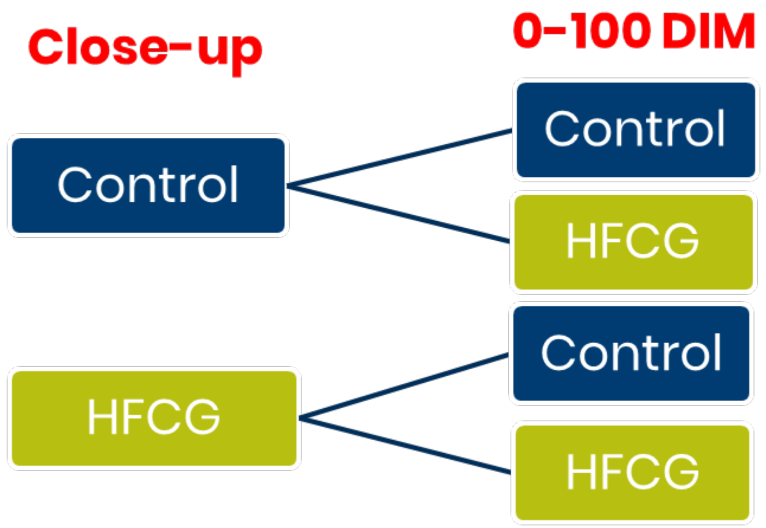

Parameter	Post CON	Post HFCG	% Change	SED	*P*-value
Milk protein content (%)	3.12	3.18	**+ 0.06**	0.038	0.125
Milk fat yield (g/d)	845	888	**+ 5.1**	23.1	0.068
Milk protein yield (g/d)	859	906	**+ 5.5**	26.2	0.077
Energy-corrected milk yield (kg/d)	24.1	25.2	**+ 4.7**	0.67	0.095

Seymour et al., 2023 (In press)

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Gluconate improves milk performance in dairy

- Granja Madero, Mexico
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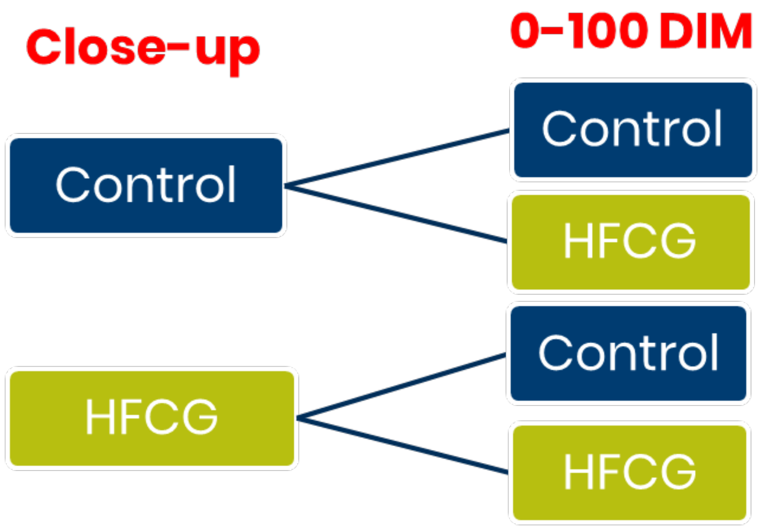

Parameters	Pre CON	Pre HFCG	Diff., d	*P*-value
Days to first observed heat	42	41		0.82
Days to first service	78	75	**-3**	**0.09**
Days to confirmed pregnancy	94	79	**-15**	**0.05**

Seymour et al., 2023 (In press)

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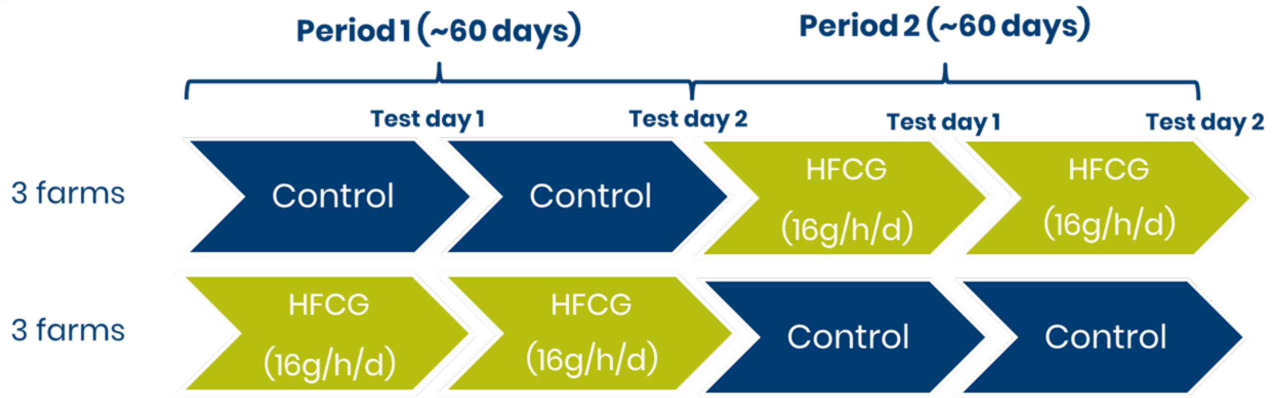
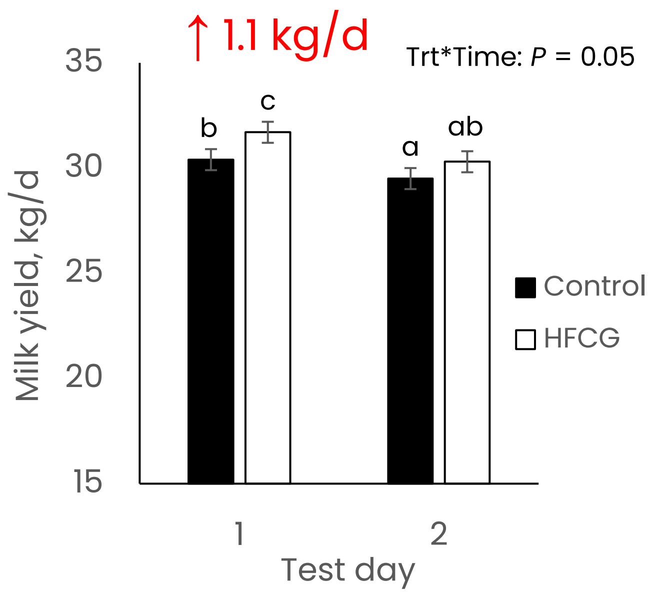
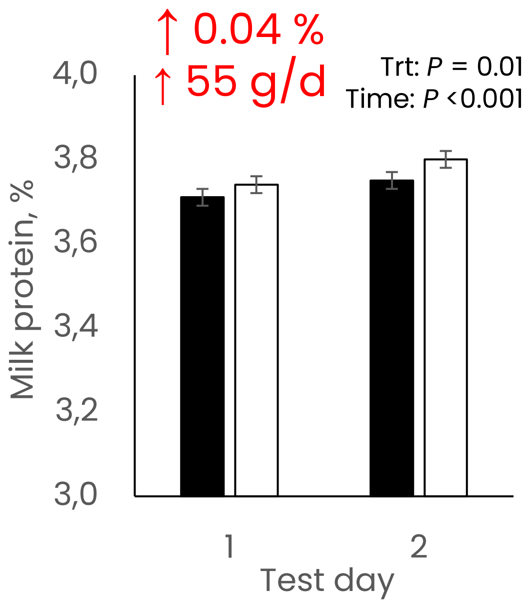
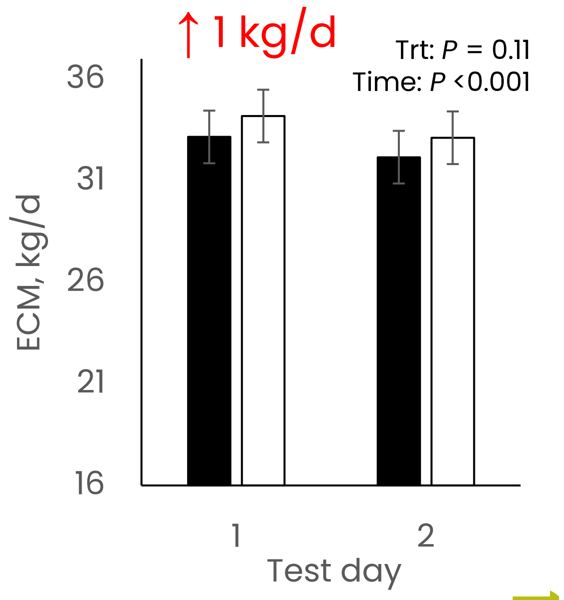
Gluconate improves milk performance in dairy









Sanz Fernandez and Seymour et al., 2023 (In press)

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Gluconate: mode of action

- Changes in fermentation patterns
- Increased VFA production

Volatile fatty acids (VFAs)		GIT sections			
		Rumen	Cecum	Colon	Rectum
Acetate	LAC	56.17	79.7^{a}	56.4	52.7^{a}
	CON	57.63	61.8^{b}	35.6	32.0^{b}
	P -value	0.88	**0.01**	0.08	**0.02**
	SEM	4.67	3.52	6.01	4.49
Propionate	LAC	41.5	28.97^{a}	21.2^{a}	18.6^{a}
	CON	42.3	17.86^{b}	11.3^{b}	9.09^{b}
	P -value	0.9	**0.02**	**0.05**	**0.01**
	SEM	2.92	2.43	2.53	1.79
Butyrate	LAC	8.8	14.1	9.13	6.82
	CON	10.68	13.1	4.9	6.85
	P - value	0.55	0.78	0.098	0.99
	SEM	1.50	1.66	1.28	1.26
Total VFA	LAC	115.57	125.41^{a}	98.29	79.97^{a}
	CON	121.44	95.55^{b}	58.97	49.22^{b}
	P - value	0.715	**0.01**	0.07	**0.02**
	SEM	7.70	6.38	9.66	6.91

Koyun et al. ADSA 2022

Gluconate: mode of action

- Changes in fermentation patterns
- Increased VFA production
- Changes in microbiome

	Rumen	Cecum	Colon	Rectum
Bacterial Richness & Diversity Indexes	- No significant difference was observed in either Chao1 index, or in the number of Observed Features of microbial communities from GIT sections of steers fed CON (un-supplemented) or LAC (Calcium gluconate-supplemented) rations - Shannon and Simpson diversity indices were numerically greater in all samples collected from GIT sections of Angus steers fed LAC (Calcium gluconate-supplemented) rations - There was no significant difference in Good's Coverage Index			
Phylum level	No significant change	Firmicutes & Actinobacteria increased, and Bacteroidetes decreased	Actinobacteria decreased	No significant change
Family level	Bifidobacteriaceae & Family_XII increased Succinivibrionaceae decreased	**Erysipelotrichaceae**, Atopobiaceae, **Peptostreptococcaceae**, **Clostridiaceae**, **Clostridiaceae_1**, & Eggerthellaceae increased Rikenellaceae & Muribaculaceae decreased	**Ruminococcaceae** & **Muribaculaceae** increased Lachnospiraceae, Erysipelotrichaceae, Atopobiaceae, Peptostreptococcaceae, Clostridiaceae_1 & Eggerthellaceae decreased	Rikenellaceae increased
Genus level	Lachnospiraceae_NK3A20_group increased	**Romboutsia**, **Clostridium** Clostridium_sensu_stricto_1, & **Turicibacter** increased Rikenellaceae_RC9_gut_group, Paeniclostridium & Eubacterium]_coprostanoli-genes_group decreased	Eubacterium]_coprostanoligenes_group increased Clostridium_sensu_stricto_1 & Turicibacter decreased	No significant change

Koyun et al. ADSA 2022

Gluconate: mode of action

- Changes in fermentation patterns
- Increased VFA production
- Changes in microbiome

	Rumen	Cecum	Colon	Rectum
Bacterial Richness & Diversity Indexes	- No significant difference was observed in either Chao1 index, or in the number of Observed Features of microbial communities from GIT sections of steers fed CON (un-supplemented) or LAC (Calcium gluconate-supplemented) rations - Shannon and Simpson diversity indices were numerically greater in all samples collected from GIT sections of Angus steers fed LAC (Calcium gluconate-supplemented) rations - There was no significant difference in Good's Coverage Index			
Phylum level	No significant change	Firmicutes & Actinobacteria increased, and Bacteroidetes decreased	Actinobacteria decreased	No significant change
F	Succinivibrionaceae decreased	Rikenellaceae & Muribaculaceae decreased	**Ruminococcaceae** & … Atopobiaceae, Peptostreptococcaceae, Clostridiaceae_1 & Eggerthellaceae decreased	
Genus level	Lachnospiraceae_NK3A20_group increased	**Romboutsia**, **Clostridium** Clostridium_sensu_stricto_1, & **Turicibacter** increased Rikenellaceae_RC9_gut_group, Paeniclostridium & Eubacterium]_coprostanoli-genes_group decreased	Eubacterium]_coprostanoligenes_group increased Clostridium_sensu_stricto_1 & Turicibacter decreased	No significant change

Ca Gluconate impacted selected beneficial bacteria with roles in butyrate production and gut health

Koyun et al. ADSA 2022

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Publications

J. Dairy Sci. 102:1274–1280
https://doi.org/10.3168/jds.2018-15148

Postruminal infusion of calcium gluconate increases milk fat production and alters fecal volatile fatty acid profile in lactating dairy cows

John Doelman,[1*] Leslie L. McKnight,[1] Michelle Carson,[1] Kelly Nichols,[2] Douglas F. Waterman,[1] and John A. Metcalf[1]
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1
NRC Research Press
ARTICLE

Feeding and postruminal infusion of calcium gluconate to lactating dairy cows

Leslie L. McKnight, John Doelman, Michelle Carson, Douglas F. Waterman, and John A. Metcalf

J. Dairy Sci. 104:7845–7855
https://doi.org/10.3168/jds.2020-20003

Effects of supplemental calcium gluconate embedded in a hydrogenated fat matrix on lactation, digestive, and metabolic variables in dairy cattle

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Canadian Journal of Animal Science
OPEN ACCESS | Article

Effect of hydrogenated fat-embedded calcium gluconate on lactation performance in dairy cows

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Research Article

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Supplementation of hydrogenated fat-embedded calcium gluconate improves milk fat content and yield in multiparous Holstein dairy cattle

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Research article

Effects of hydrogenated fat-embedded calcium gluconate on lactation performance in multiple commercial dairy herds

M.V. Sanz-Fernandez *,[1], D.J. Seymour [1], J.B. Daniel, J. Doelman, J. Martín-Tereso
Trouw Nutrition R&D, P.O. Box 299, 3800 AG, Amersfoort, the Netherlands

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Evaluating lactation performance of multiparous dairy cattle to prepartum and/or postpartum supplementation of fat-embedded calcium gluconate

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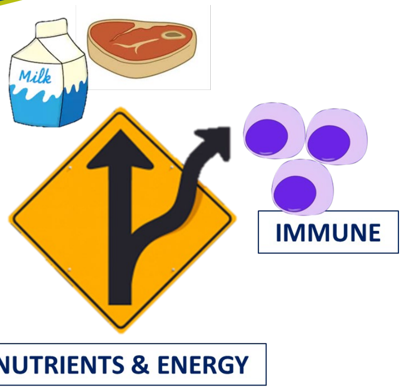
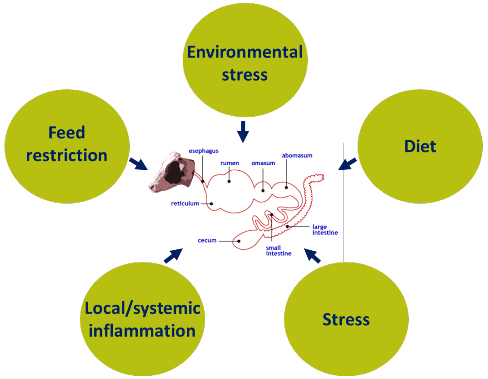
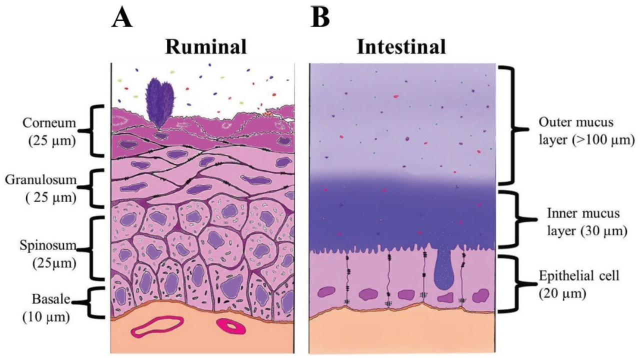
Conclusions

- Gastrointestinal health is challenged by multiple factors during the productive cycle
  - Leaky gut is a source of systemic inflammation
  - Inflammation is a costly process from an energy and nutrient point of view
- The hindgut is affected by similar factors as compared to the rumen
  - The hindgut is a source of systemic inflammation?
  - Poor hindgut health represent an energetic burden for the cows
- Supporting postrumen health is an opportunity to improve performance and health







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Thank you

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