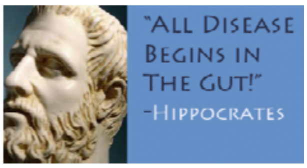
Impaired gut health: the root of systemic disorders in cattle

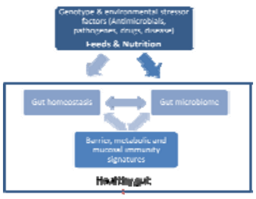
Qendrim Zebeli

An inside-outside approach to dairy cow health

University of Veterinary Medicine, Vienna (Vetmeduni Vienna)

Gut and disease





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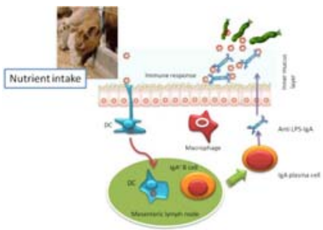
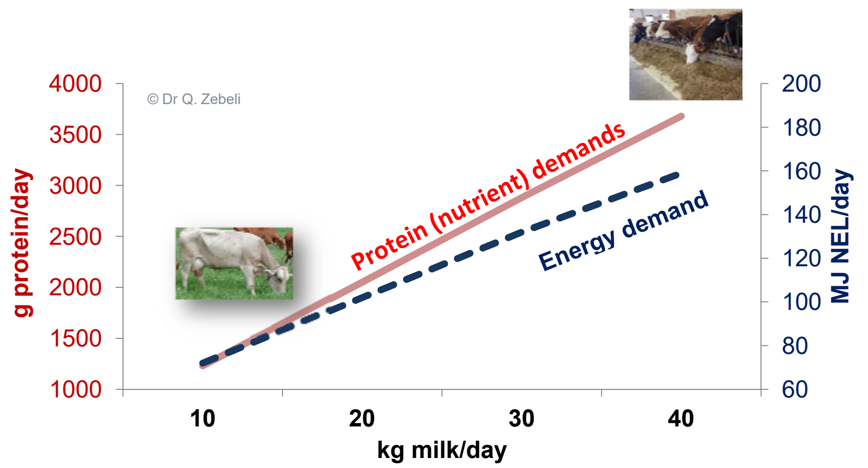


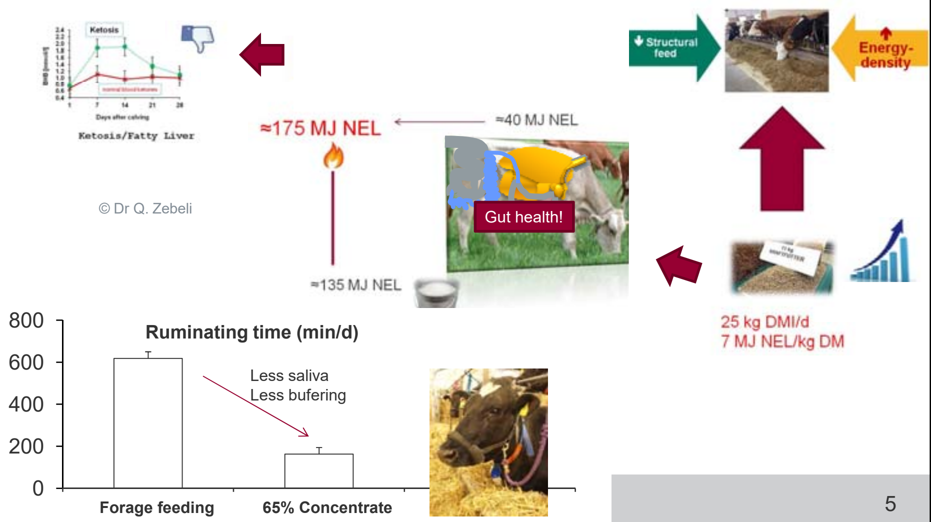
Zebeli et al. 2011 Innate Immunity

Diet for health and performance

High the performance, higher the demands!



Diet balancing becomes increasingly difficult



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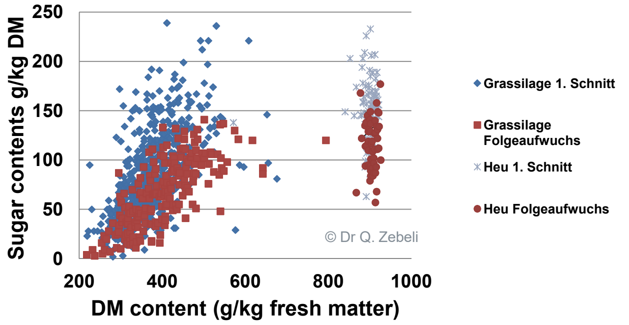
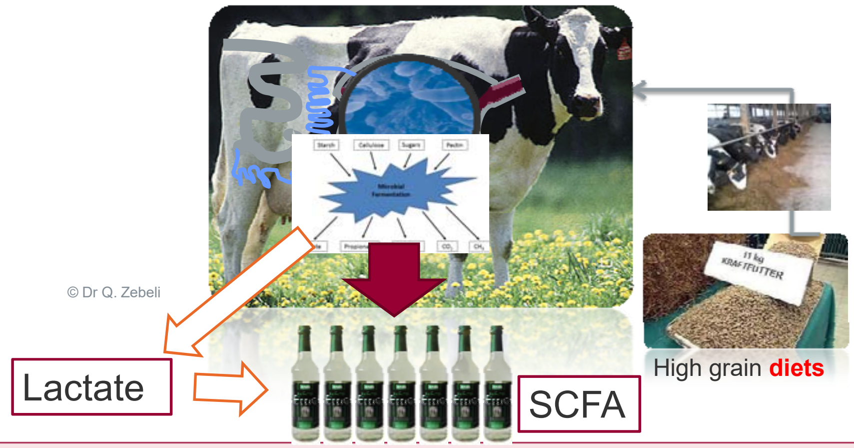
Sugars in silages and hays in AUT



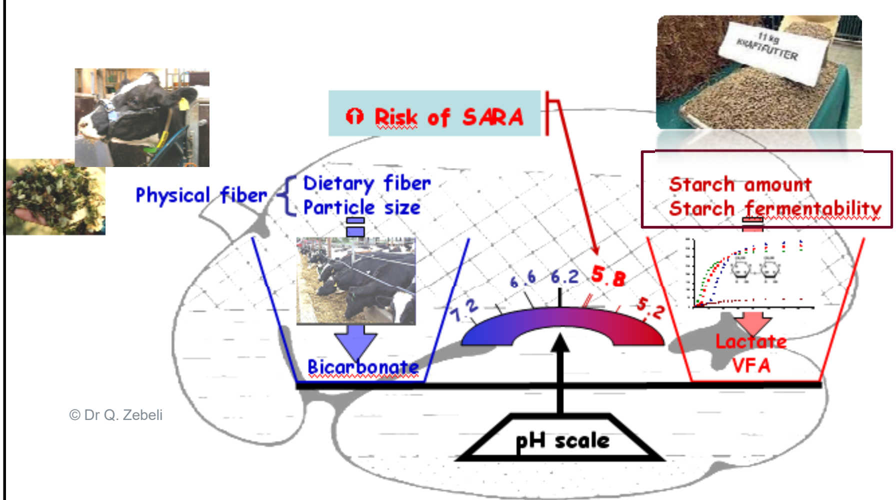
Futtermittellabor Rosenau (2017)

Rumen fermentation load

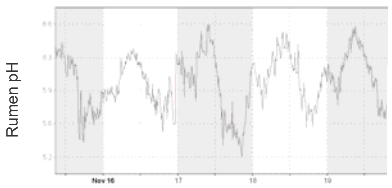


≈120 mol short-chain fatty acids (SCFA) (6-7 kg/daily):
70-75% of energy requirements

High fermentation load acidifies the rumen



Rumen pH drop



PhD work P Pourazad, Vetmeduni Vienna

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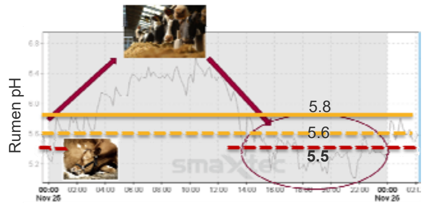


SARA thresholds

If longer than 5-6 h/day (Zebeli et al. 2008 J Dairy Sci)
If longer than 3 h/day (Plaizier et al. 2008 Vet J)

How common is SARA?

- Limited information surveys with rumenocentesis based on rumen pH (5.5 threshold)
  - Wisconsin, USA→19% (early) and 26% (mid lactation) (Garrett et al., 1997), 20.1% in early and peak lactation (Oetzel et al., 1999)
  - The Netherlands → 13.8% (0 – 38% on farms) (Kleen et al., 2009)
  - Germany → 20% (Kleen et al., 2013)
  - Italy → 33% (Morgante et al., 2007)

SARA diagnosis via ruminal pH

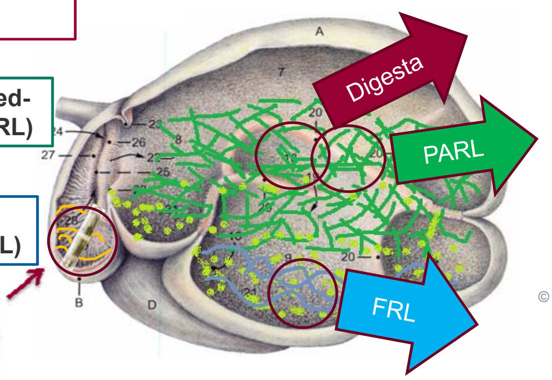
- SARA threshold: pH<5.8
  - Spot sampling
  - Stomach tubes, Rumenocentesis, Rumen cannula
  - Location: Rumen
- Diurnal pH- changes!
- Wireless pH-boli
  - In non-fistulated cows
  - Herd level
  - Continuous measurement
- Location: Reticulum!

Sensorex, Stanton, CA

LRCpH system, Dascor, Escondido, CA

Reticular vs. ruminal pH

- **Particles of rumen mat (Digesta)**
- **Particle-associated-rumen liquid (PARL)**
- **Ventral sac: Free rumen liquid (FRL)**



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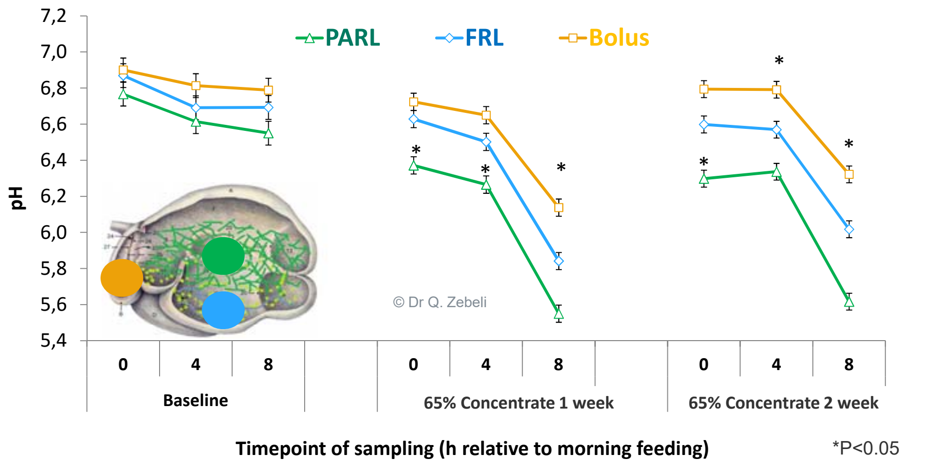
pH at different locations



Neubauer et al 2018 J Anim Physiol Anim Nutr

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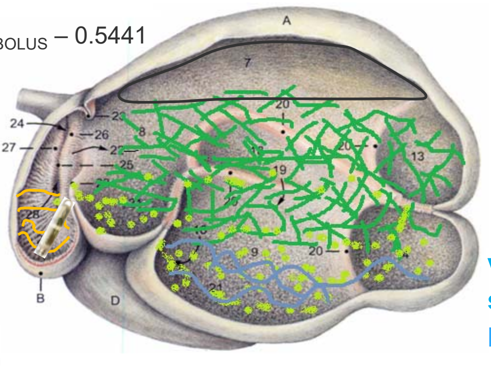
Reticular vs. ruminal pH during high-concentrate feeding

SARA threshold **reticulum**: **pH < 6.0 for > 5-6 h/d**

Prediction equation for SARA phases:
$pH_{FRL} = 1.0509 \times pH_{BOLUS} - 0.5441$



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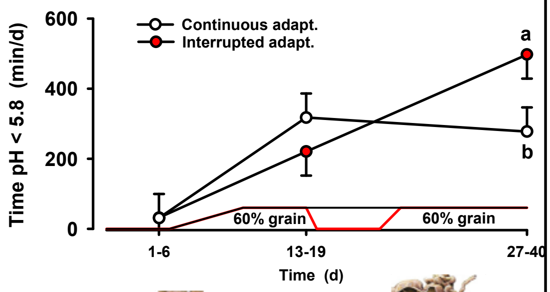
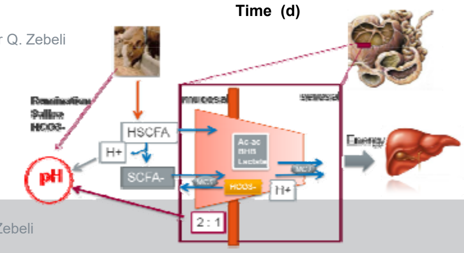
Luminal SCFA absorption and pH regulation





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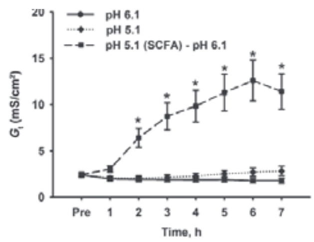
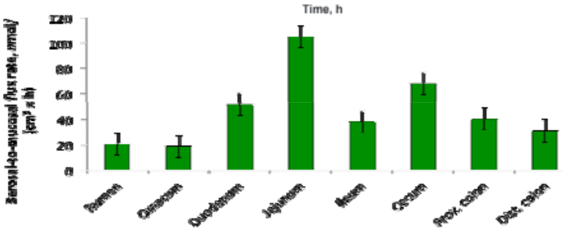
pH drop/SCFA make GIT „leaky“





Dr G Penner (Univ. Saskatchewan)

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The Reference in Prevention for Animal Health

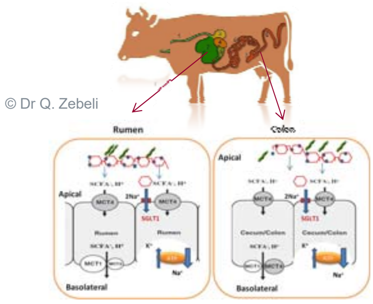
Hindgut acidosis

RUMINANT NUTRITION SYMPOSIUM: Productivity, digestion, and health responses to hindgut acidosis in ruminants[1]

T. F. Gressley,*[1] M. B. Hall,† and L. E. Armentano‡

*Department of Animal and Food Science, University of Delaware, Newark 19716;
†Agricultural Research Service, USDA, US Dairy Forage Research Center, Madison, WI 53706;
and ‡Department of Dairy Science, University of Wisconsin, Madison 53706

Too much fermentable substrates escaping the rumen!!



Hingut acidosis vs. Rumen acidosis

Anaerobe
Molecular biology, genetics and biotechnology

Grain-rich diets differently alter ruminal and colonic abundance of microbial populations and lipopolysaccharide in goats

Barbara U. Metzler-Zebeli, Stephan Schmitz-Esser, Fenja Klevenhusen, Leopold Podstatzky-Lichtenstein, Martin Wagner, Qendrim Zebeli

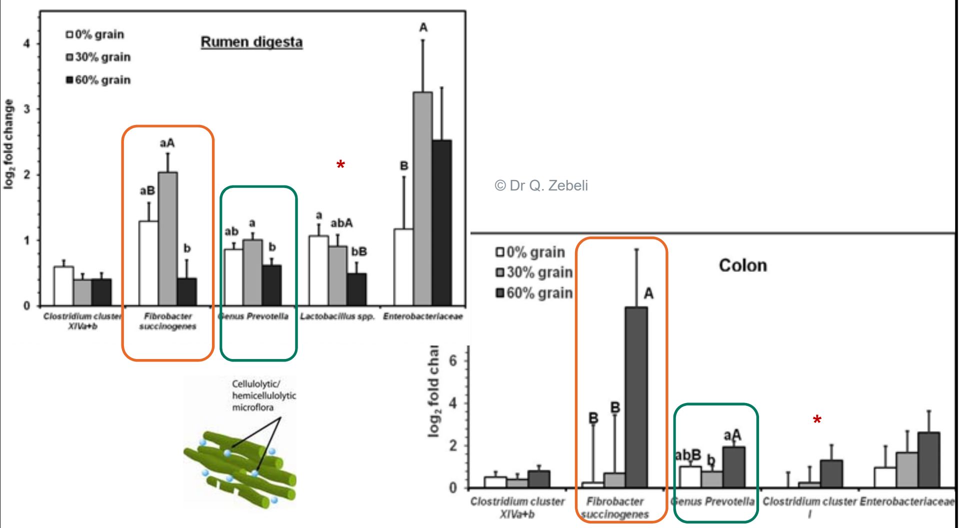
Table 3
pH and total SCFA concentration in rumen filtrate and colon digesta of goats fed diets containing 0, 30 and 60% barley grain.

Item	% Grain			Pooled SEM	P-value contrast			
	0	30	60		Linear	Quadratic	0 Versus 30 + 60% grain	0 + 30 versus 60% grain
pH								
Rumen	6.4	6.0	5.5	0.13	<0.001	0.726	0.003	0.001
Colon	8.5	8.1	7.0	0.27	0.006	0.248	0.034	0.005
Total SCFA								
Rumen (μmol/ml)	113	120	129	5.48	0.105	0.920	0.162	0.128
Colon (μmol/g)	20	26	78	15.83	0.039	0.338	0.156	0.015

Values are least squares means ± pooled standard error of the mean (SEM); $n = 5$ for 0% grain diet; $n = 6$ for 30 and 60% barley grain diet.

Quantitatively, the fermentation is less intensive in the hingut

Microbiota in the rumen and colon due to SARA

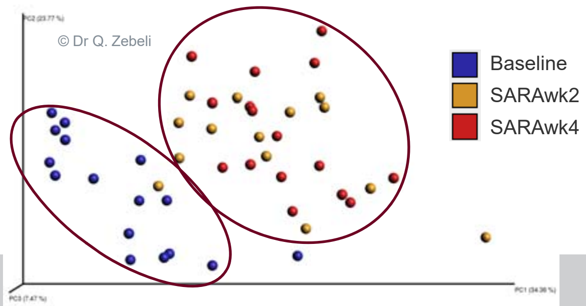


Metzler-Zebeli et al. 2013 Anaerobe

Grain feeding affects bacterial diversity and community structure

Index	Baseline	SARA wk2	SARA wk4	SEM	*P*-value
observed OTU's	1623[a]	1439[b]	1389[b]	30.6	<0.001
Chao1 (richness estimator)	2787[a]	2402[b]	2381[b]	51.8	<0.001
Shannon (count, abundance)	8.88[a]	8.21[b]	8.20[b]	0.070	<0.001
Simpson (abundance)	0.993[a]	0.982[b]	0.984[b]	0.001	<0.001

Diversity, richness



Neubauer et al Journal of Dairy Science 101(3)
DOI: 10.3168/jds.2017-13565

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Feeding affects bacterial community in hindgut

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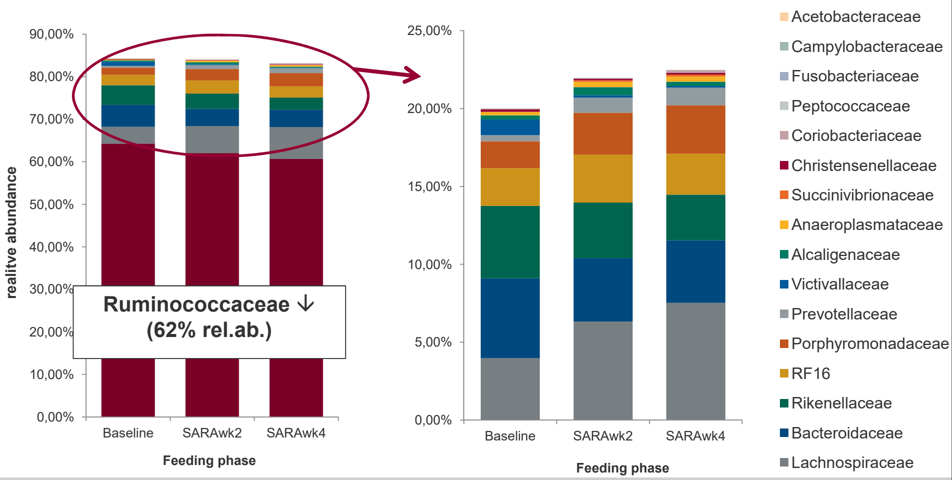

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$P < 0.05$

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SARA depletes rumen epithelia protective factors

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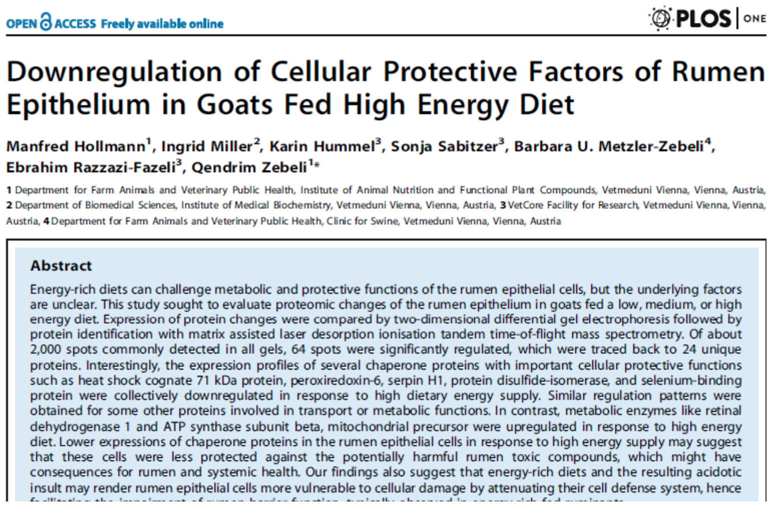
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Downregulation of Cellular Protective Factors of Rumen Epithelium in Goats Fed High Energy Diet

Manfred Hollmann[1], Ingrid Miller[2], Karin Hummel[3], Sonja Sabitzer[3], Barbara U. Metzler-Zebeli[4], Ebrahim Razzazi-Fazeli[3], Qendrim Zebeli[1]*

1 Department for Farm Animals and Veterinary Public Health, Institute of Animal Nutrition and Functional Plant Compounds, Vetmeduni Vienna, Vienna, Austria, 2 Department of Biomedical Sciences, Institute of Medical Biochemistry, Vetmeduni Vienna, Vienna, Austria, 3 VetCore Facility for Research, Vetmeduni Vienna, Vienna, Austria, 4 Department for Farm Animals and Veterinary Public Health, Clinic for Swine, Vetmeduni Vienna, Vienna, Austria

Abstract

Energy-rich diets can challenge metabolic and protective functions of the rumen epithelial cells, but the underlying factors are unclear. This study sought to evaluate proteomic changes of the rumen epithelium in goats fed a low, medium, or high energy diet. Expression of protein changes were compared by two-dimensional differential gel electrophoresis followed by protein identification with matrix assisted laser desorption ionisation tandem time-of-flight mass spectrometry. Of about 2,000 spots commonly detected in all gels, 64 spots were significantly regulated, which were traced back to 24 unique proteins. Interestingly, the expression profiles of several chaperone proteins with important cellular protective functions such as heat shock cognate 71 kDa protein, peroxiredoxin-6, serpin H1, protein disulfide-isomerase, and selenium-binding protein were collectively downregulated in response to high dietary energy supply. Similar regulation patterns were obtained for some other proteins involved in transport or metabolic functions. In contrast, metabolic enzymes like retinal dehydrogenase 1 and ATP synthase subunit beta, mitochondrial precursor were upregulated in response to high energy diet. Lower expressions of chaperone proteins in the rumen epithelial cells in response to high energy supply may suggest that these cells were less protected against the potentially harmful rumen toxic compounds, which might have consequences for rumen and systemic health. Our findings also suggest that energy-rich diets and the resulting acidotic insult may render rumen epithelial cells more vulnerable to cellular damage by attenuating their cell defense system, hence

HIPRA
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SARA depletes rumen epithelia protective factors

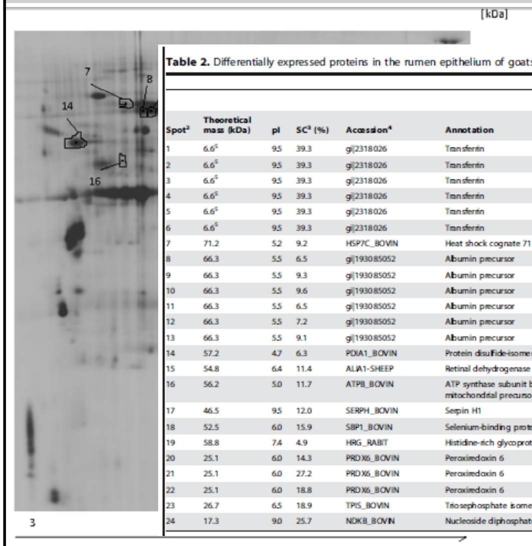
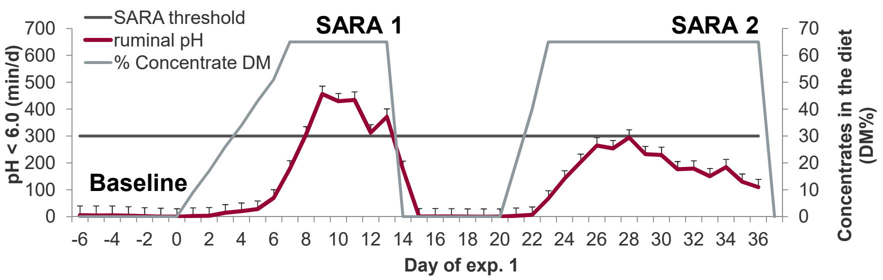


Table 2. Differentially expressed proteins in the rumen epithelium of goats fed diets differing in the energy supply[1].

						Av. Ratio		
Spot[2]	Theoretical mass (kDa)	pI	SC[3] (%)	Accession[4]	Annotation	L vs. M	M vs. H	L vs. H
1	6.6[5]	9.5	39.3	gi|2318026	Transferrin	−1.18	−1.30	−1.53**
2	6.6[5]	9.5	39.3	gi|2318026	Transferrin	−1.22	−1.39	−1.69**
3	6.6[5]	9.5	39.3	gi|2318026	Transferrin	−1.23	−1.46	−1.79**
4	6.6[5]	9.5	39.3	gi|2318026	Transferrin	−1.24	−1.24	−1.54*
5	6.6[5]	9.5	39.3	gi|2318026	Transferrin	−1.28	−1.42	−1.82**
6	6.6[5]	9.5	39.3	gi|2318026	Transferrin	−1.33	−1.54	−2.06**
7	71.2	5.2	9.2	HSP7C_BOVIN	Heat shock cognate 71 kDa protein	−1.04	−1.26*	−1.31*
8	66.3	5.5	6.5	gi|193085052	Albumin precursor	−1.15	−1.16	−1.33*
9	66.3	5.5	9.3	gi|193085052	Albumin precursor	−1.41	−1.48	−2.09**
10	66.3	5.5	9.6	gi|193085052	Albumin precursor	−1.47*	−1.31	−1.92**
11	66.3	5.5	6.5	gi|193085052	Albumin precursor	−1.41	−1.36	−1.92*
12	66.3	5.5	7.2	gi|193085052	Albumin precursor	−1.52	−1.38	−2.10**
13	66.3	5.5	9.1	gi|193085052	Albumin precursor	−1.57	−1.22	−1.91*
14	57.2	4.7	6.3	PDIA1_BOVIN	Protein disulfide-isomerase	+1.48*	−1.82*	−1.23
15	54.8	6.4	11.4	ALIA1-SHEEP	Retinal dehydrogenase 1	+1.38	+1.13	+1.56*
16	56.2	5.0	11.7	ATPB_BOVIN	ATP synthase subunit beta, mitochondrial precursor	−1.00	+1.73*	+1.72*
17	46.5	9.5	12.0	SERPH_BOVIN	Serpin H1	+1.35	−1.86**	−1.38
18	52.5	6.0	15.9	SBP1_BOVIN	Selenium-binding protein 1	−1.07	−1.92*	−2.06*
19	58.8	7.4	4.9	HRG_RABIT	Histidine-rich glycoprotein	−1.57	+1.76*	+1.12
20	25.1	6.0	14.3	PRDX6_BOVIN	Peroxiredoxin 6	+1.02	−1.59	−1.56*
21	25.1	6.0	27.2	PRDX6_BOVIN	Peroxiredoxin 6	+1.19	−1.50	−1.30*
22	25.1	6.0	18.8	PRDX6_BOVIN	Peroxiredoxin 6	+1.03	−1.54	−1.50**
23	26.7	6.5	18.9	TPIS_BOVIN	Triosephosphate isomerase	−1.10	−1.27	−1.39**
24	17.3	9.0	25.7	NDKB_BOVIN	Nucleoside diphosphate kinase B	−1.23	−1.55	−1.91*

Ruminal pH < 6.0 (min/d) during 2 SARA



Neubauer et al Journal of Dairy Science 101(3)
DOI: 10.3168/jds.2017-13565

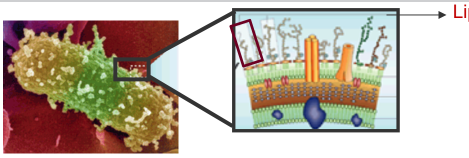
SARA and rumen metabolomic changes

Variable	Phase[1]			SEM	P-value
	Baseline	SARA1	SARA2		
LPS	14,581[c]	131,209[b]	168,285[a]	25,722	<0.01
Ethanolamine	3.76[c]	9.82[a]	6.45[b]	0.597	<0.01
Methylamine	37.3[ab]	33.6[b]	46.0[a]	5.67	0.07
Isopropylamine	7.50[b]	17.4[a]	16.2[a]	2.65	<0.01
Pyrrolidine	6.68[c]	12.6[a]	9.41[b]	1.257	<0.01
Putrescine	14.0[b]	32.2[a]	30.7[a]	3.65	<0.01
Cadaverine	15.9[z]	24.2[yz]	24.3[y]	5.12	0.13
Histamine	2.06[b]	13.0[a]	5.19[b]	3.326	<0.01
Tyramine	1.00[z]	1.61[yz]	2.14[y]	0.614	0.18
Spermidine	8.62[b]	14.9[a]	17.0[a]	2.417	<0.01
Spermine	0.70	1.09	1.10	0.431	0.40

[a,b,c]Indicate significant ($P \leq 0.05$) changes or a trend (y,z) ($0.05 < P < 0.10$) between the feeding phases.
[1]SARA1 = 65% concentrate for 1 wk; SARA2 = 65% concentrate for 2 wk.

Impaired gut health: the root of systemic disorders in cattle – Dr Zebeli

Main pro-inflammatory agents in the rumen



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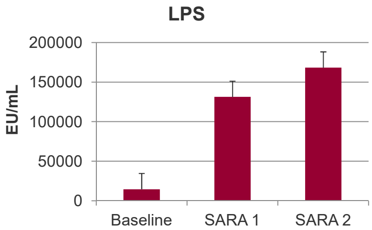

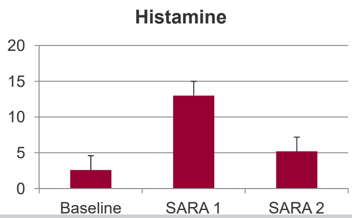

Humer et al 2018 J Dairy Sci

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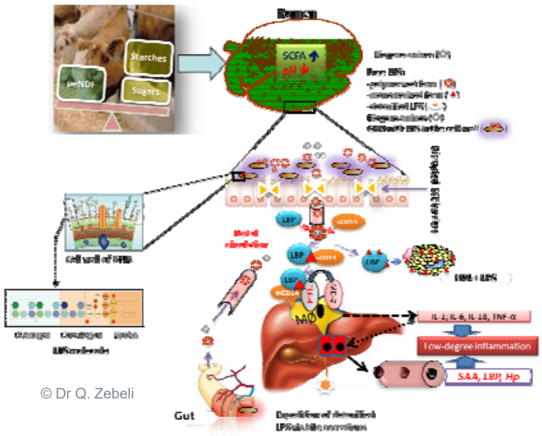
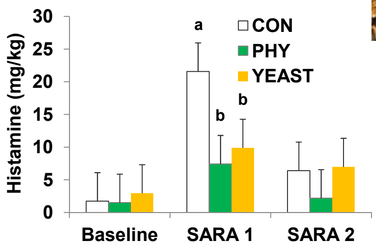
Proposed mechanism for SARA induced inflammation



AY and PHY affect ruminal Histamine



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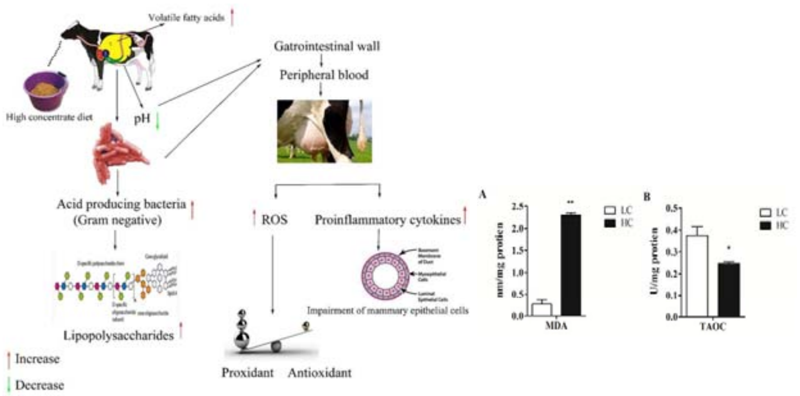
Systemic effects



Meena Arif Memon et al. 2019 Microbial Pathogenesis 128, 268-275

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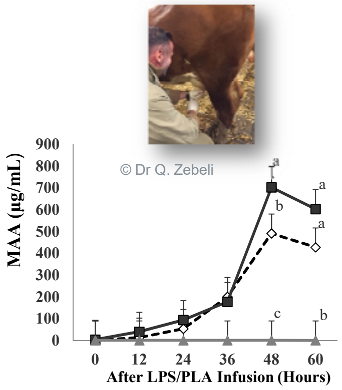
Udder health



Prolonged udder inflammation due to SARA

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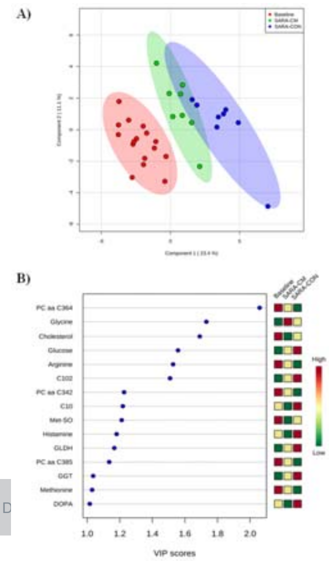
Supplementing a clay-based mineral product improves health


Supplementation of a clay mineral-based product modulates plasma metabolomic profile and liver enzymes in cattle fed grain-rich diets

E. Humer, I. Kröger, V. Neubauer, N. Reisinger and Q. Zebeli



CM = Diet intervention

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Fix the cause or treat the symptoms?

Dietary target

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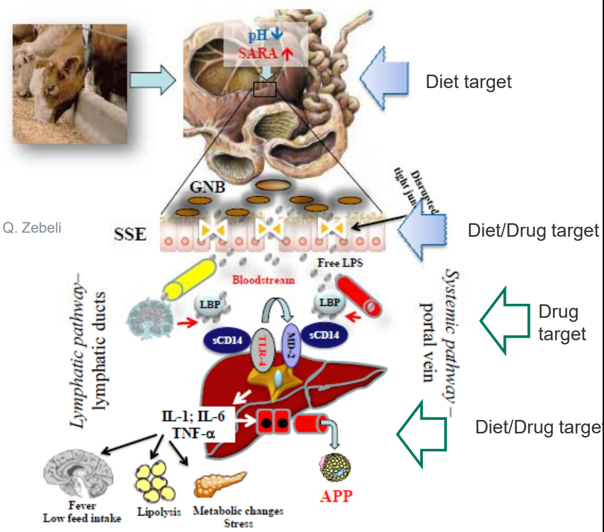

Diet target

Diet/Drug target

Drug target

Diet/Drug targe

Zebeli & Metzler-Zebeli 2012. Res. Vet. Sci. doi:10.1016/j.rvsc.2012.02.004

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