Impact of nutrition on the immune system of cattle

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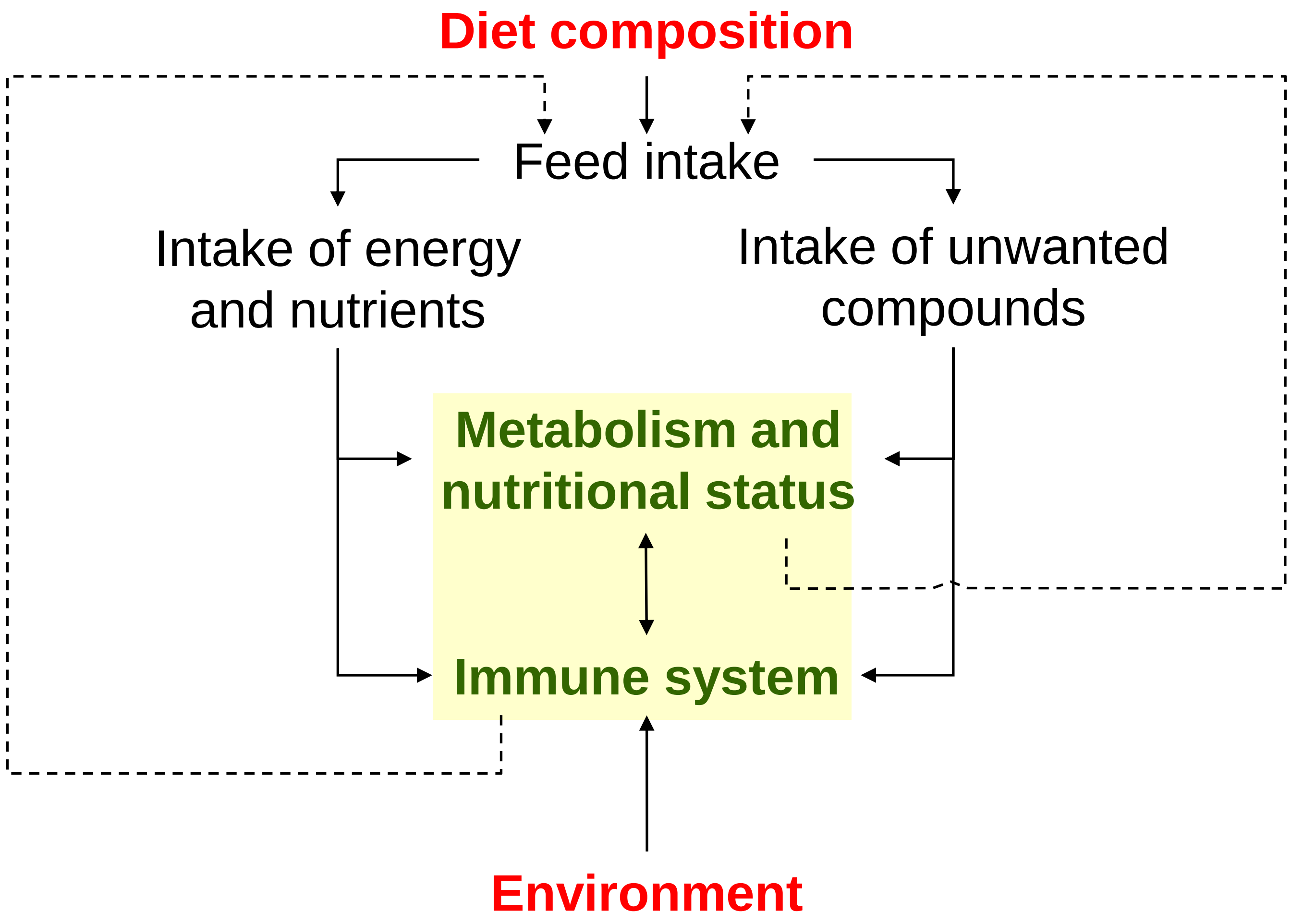
Institute of Animal Nutrition
Braunschweig

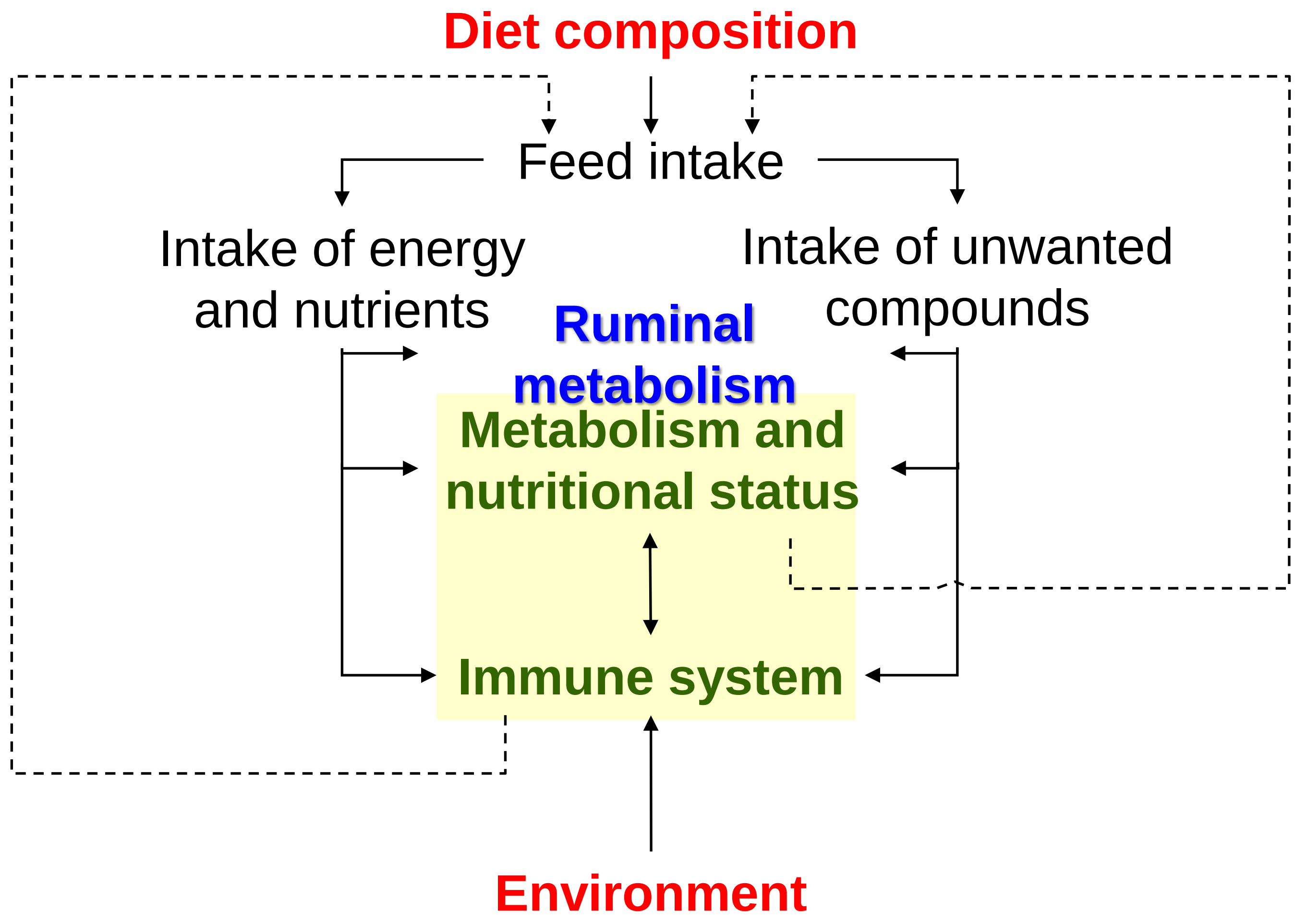




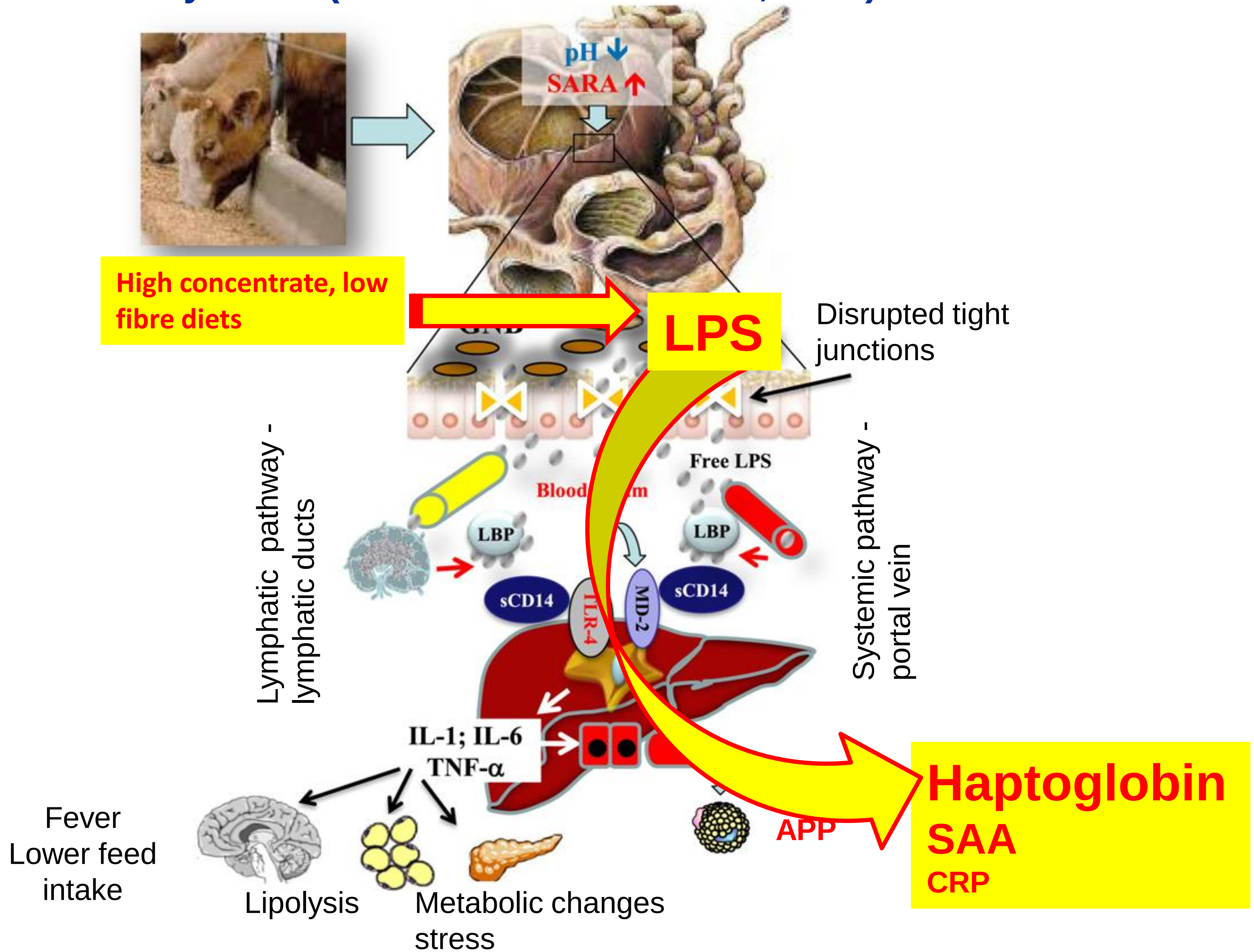
Possible implications of nutrition and other environmental factors on the functionality of the immune system



Possible implications of nutrition and other environmental factors on the functionality of the immune system



Interplay between rumen digestive disorders and diet-induced inflammation in dairy cattle (Zebeli & Metzler-Zebeli, 2012)

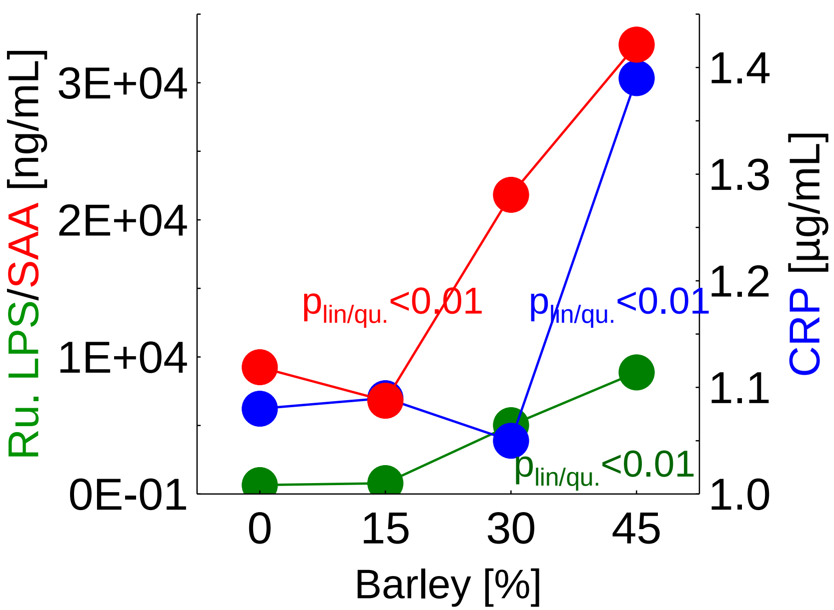


Review article: Application of acute phase protein measurements in veterinary clinical chemistry (Petersen et al., 2004)

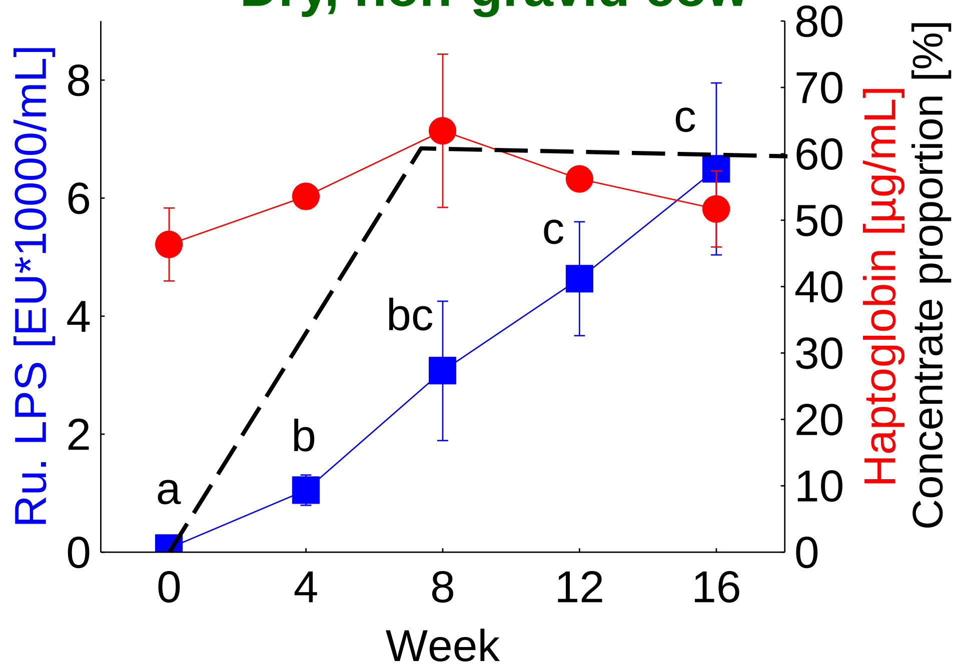
	Fold-increase in cattle
Haptoglobin • Binding hemoglobin • Bacteriostatic effect • Stimulation of angiogenesis • Role in lipid metabolism/development of fatty liver in cattle • Immunomodulatory effect • Inhibition of neutrophil respiratory burst activity	> 10
Serum amyloid A • Transport of cholesterol from dying cells to hepatocytes • Inhibitory effect on fever • Inhibitory effect on the oxidative burst of neutrophilic granulocytes • Inhibitory effect on in vitro immune response • Chemotaxic effect on monocytes, polymorphonuclear leucocytes and T-cells • Induction of calcium mobilisation by monocytes • Inhibition of platelet activation	1 - 10
C-reactive protein • Complement activation and opsonisation • Modulation of monocytes and macrophages, cytokine production • Binding of chromatin • Prevention of tissue migration of neutrophiles	0

Associations between rumen endotoxin and plasma acute phase protein concentrations in cows

Lactating cow



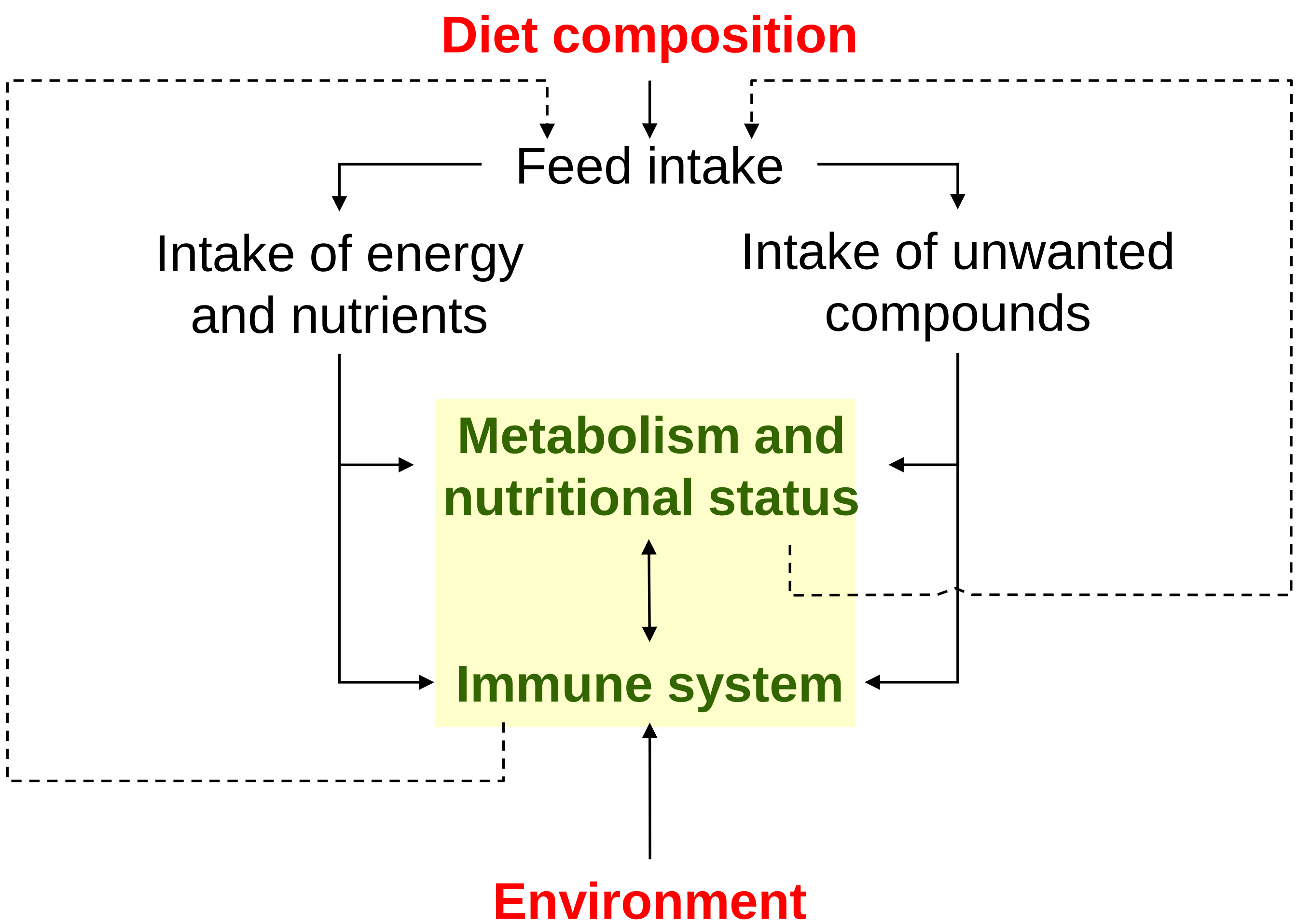
Dry, non-gravid cow



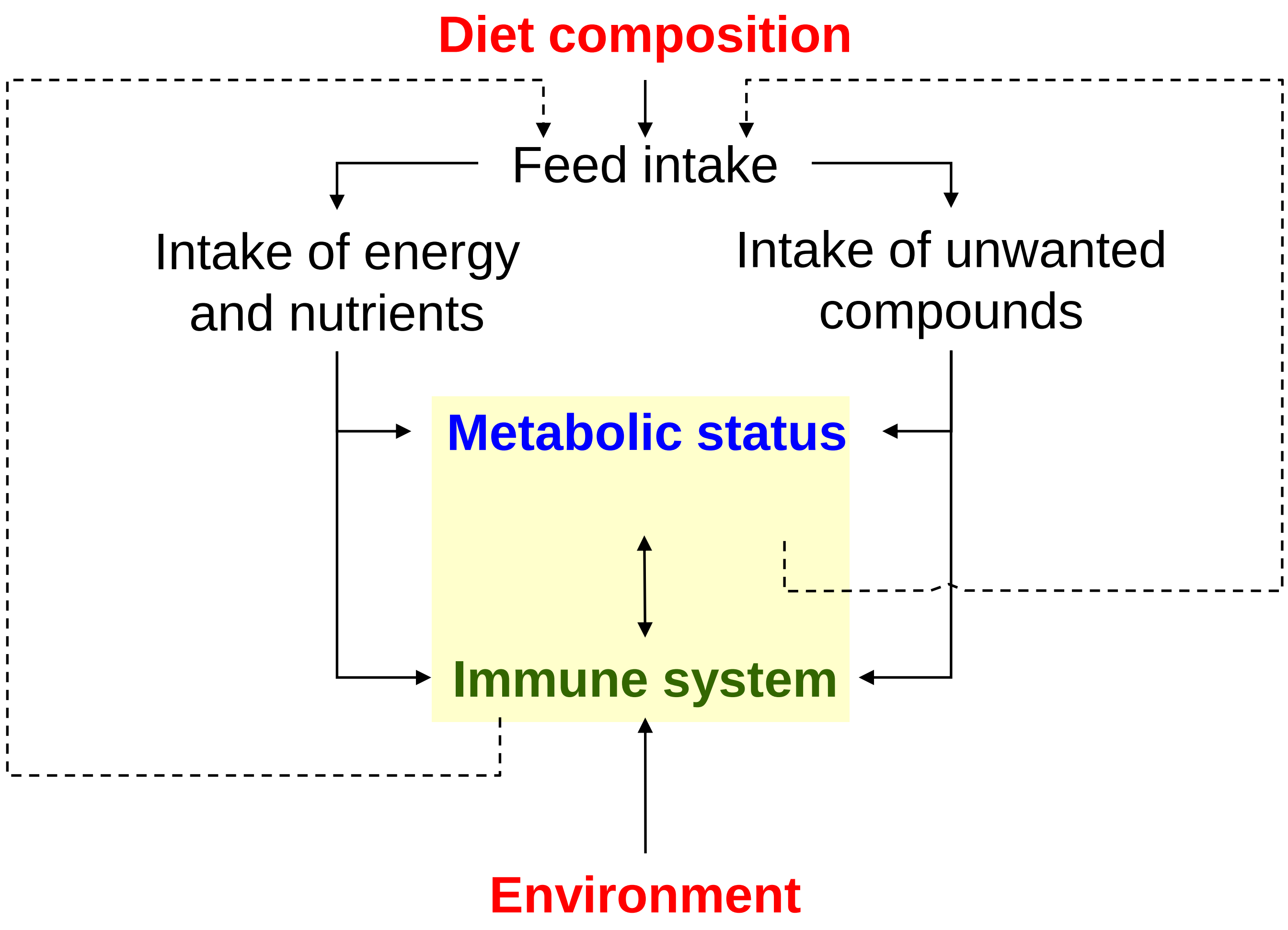
Zebeli et al. (2010)

Dänicke et al. (2014)

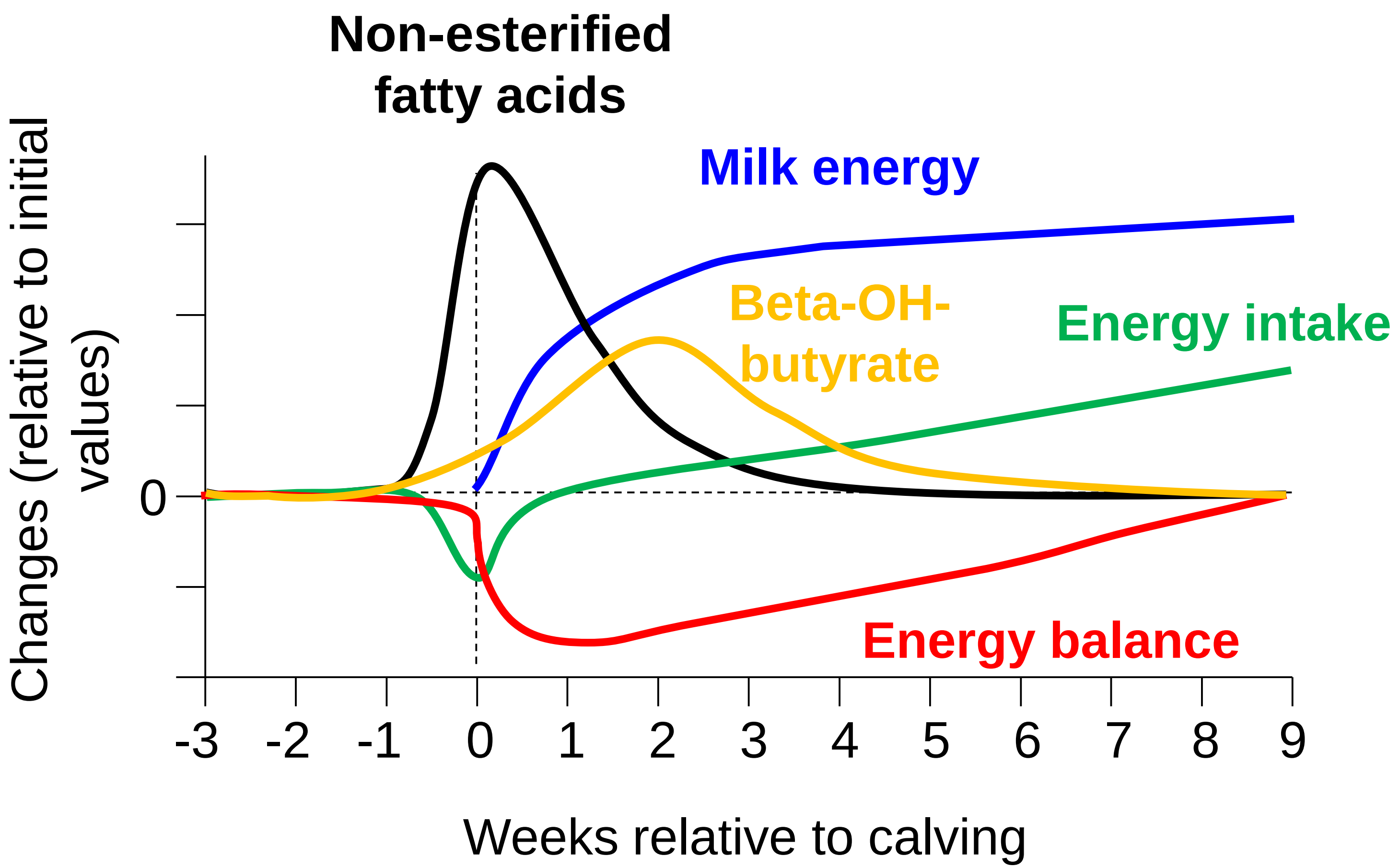
Possible implications of nutrition and other environmental factors on the functionality of the immune system



Possible implications of nutrition and other environmental factors on the functionality of the immune system

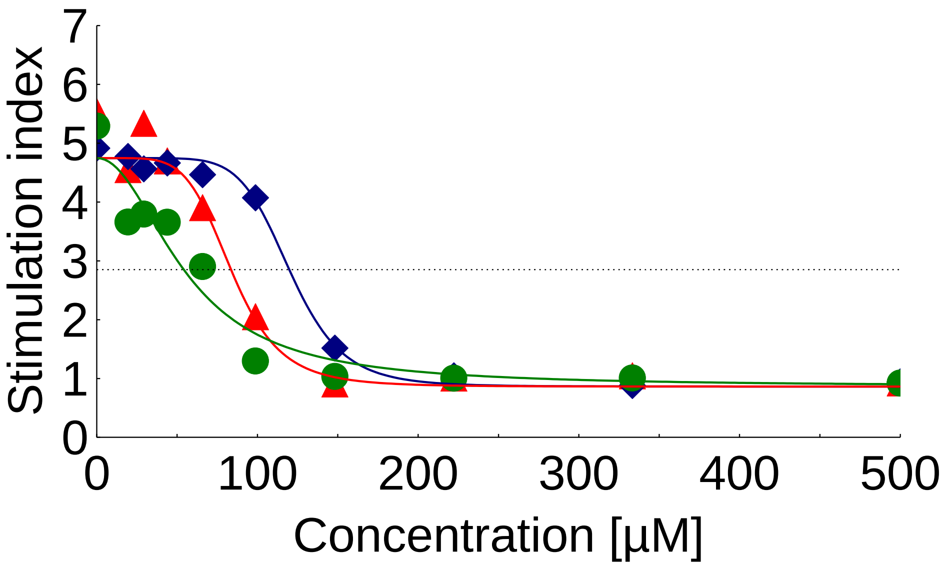


Physiological events in the transition period with relevance for metabolism and immune system



Non esterified fatty acids (NEFA) and beta-OH-butyrate (BHB) inhibit the *in vitro* proliferative response of bovine peripheral mononuclear cells dose-dependently

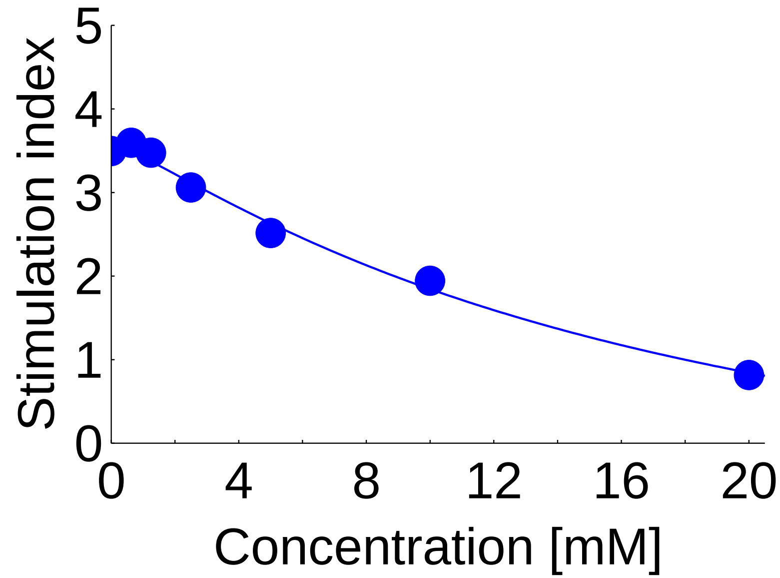
NEFA



Fatty acid	IC_{50} [µM]
cis-9, trans-11 conjugated linoleic acid	56
Linoleic acid	105
NEFA [C16:0 (29.8%), C16:1 (6.1%), C18:0 (15.6%), C18:1 (41.5%)]	81

Renner et al., 2013

BHB



IC_{50} [mM]
6.9

Schulz et al., 2015

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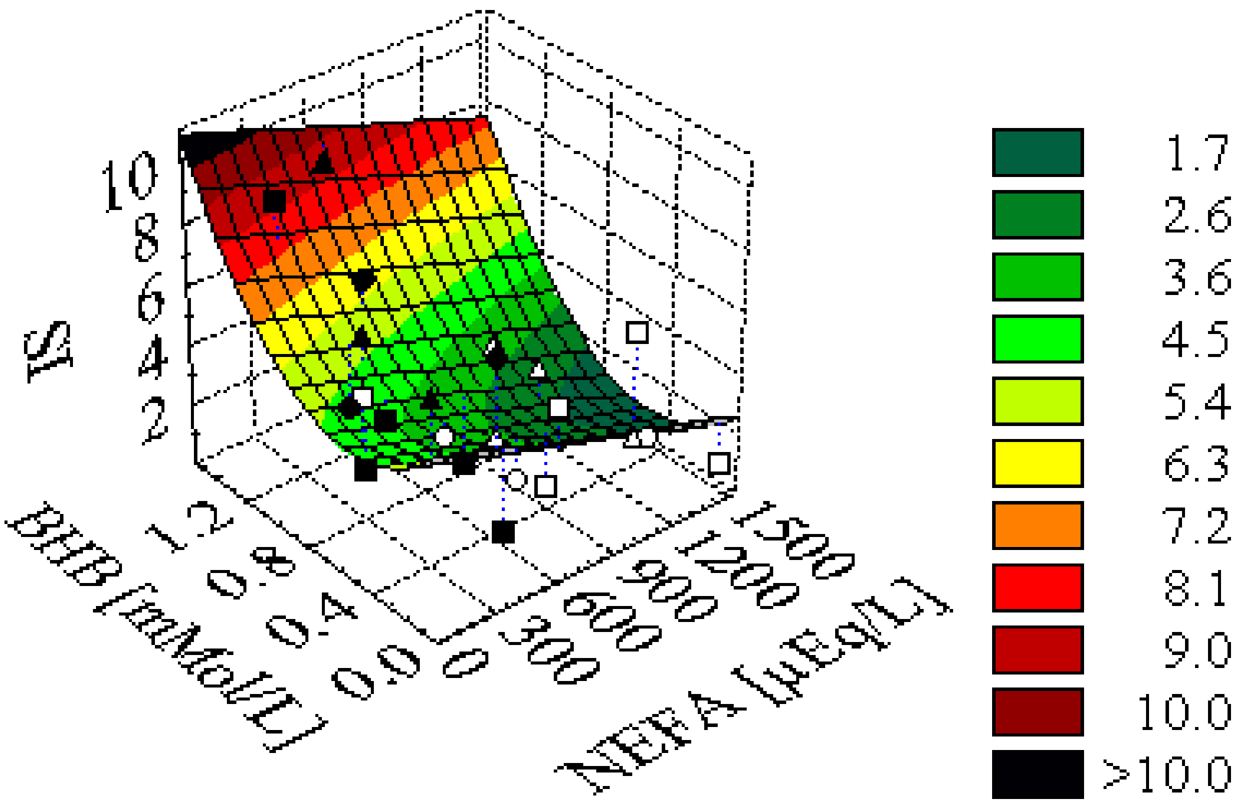
Federal Research Institute for Animal Health

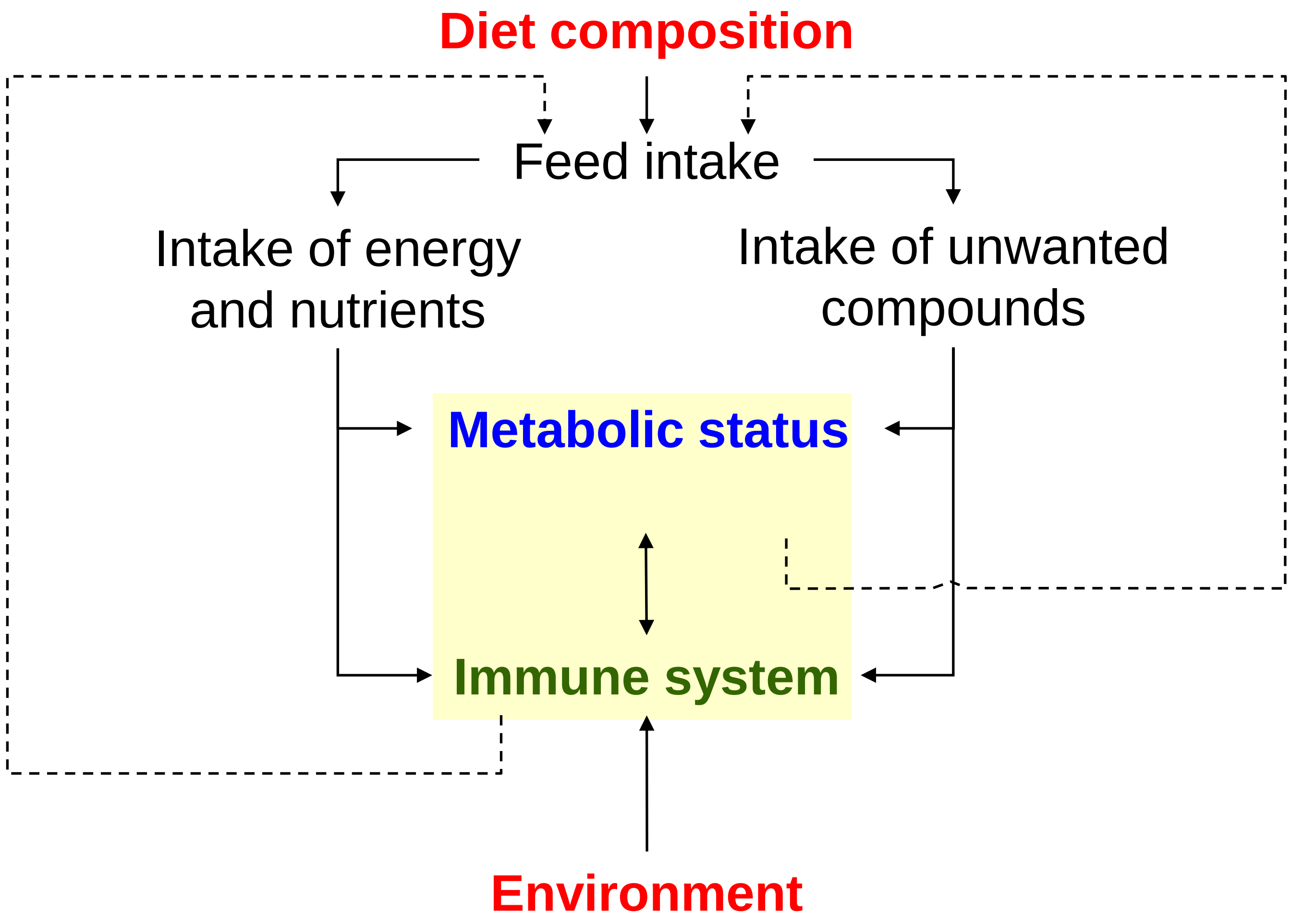
Relationship between non-esterified fatty acids (NEFA), 3-β-hydroxybutyrate (BHB) and stimulation index (SI) of cows *ex vivo* (Dänicke et al., 2012)



$SI = 6.1 - 0.002 \cdot NEFA - 6.7 \cdot BHB + 6.3 \cdot BHB^2$ ($r^2 = 0.562$, RSD=1.7)

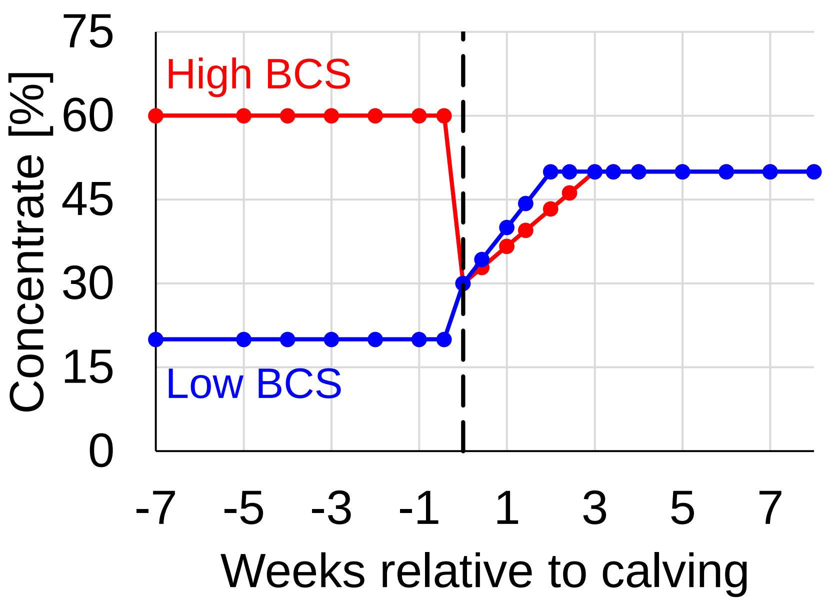
○ CON: day 0; ● CON: day 21, □ CLA50: day 0; ■CLA50: day 21; ∆ CLA100- day 0; ▲ CLA100: day 21

Possible implications of nutrition and other environmental factors on the functionality of the immune system

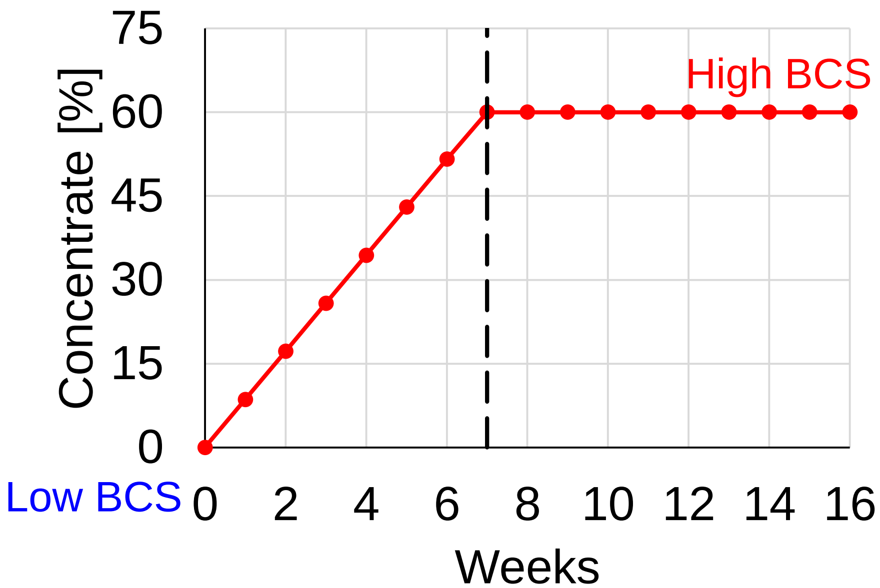


Designs for studying the role body reserves on metabolism and immune system in cows differing in physiological state

Transition cow



Dry, non-gravid cow



Energy requirement for:

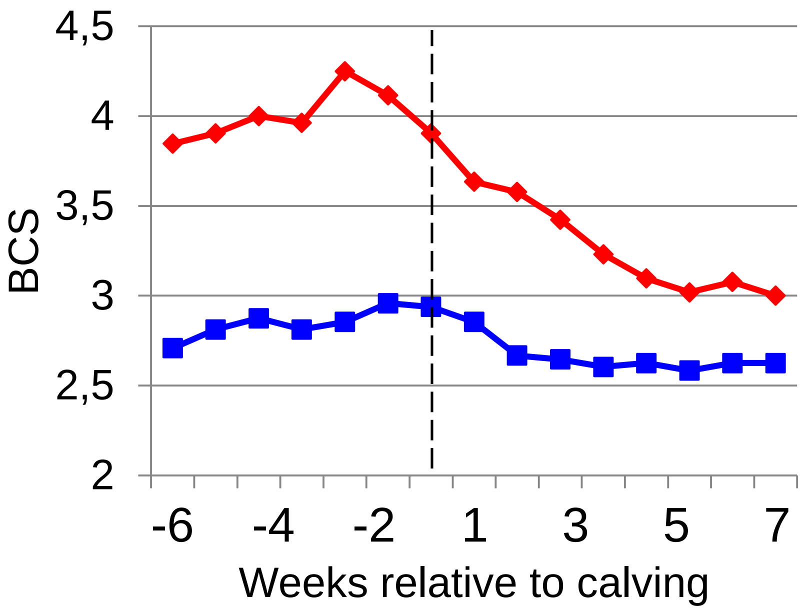
- Maintenance
- Gravidity (Fetus, body accretion)

- Maintenance
- Milk energy

- Maintenance
- Body accretion (mainly fat)

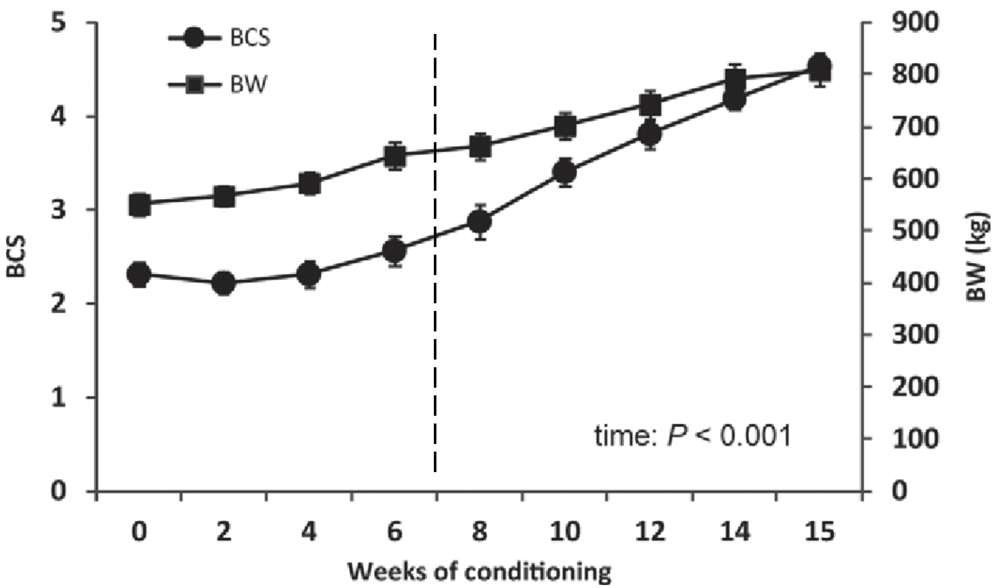
Body condition of cows differing in physiological state

Transition cow



Drong et al., 2016

Dry, non-gravid cow



Locher et al., 2015

Energy requirement for:

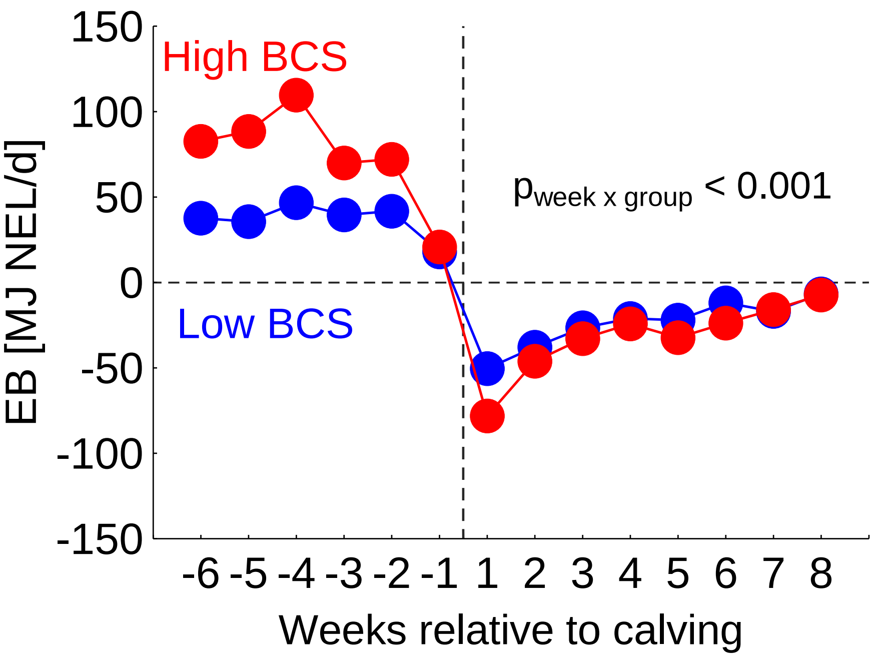
- Maintenance
- Gravidity (Fetus, body accretion)

- Maintenance
- Milk energy

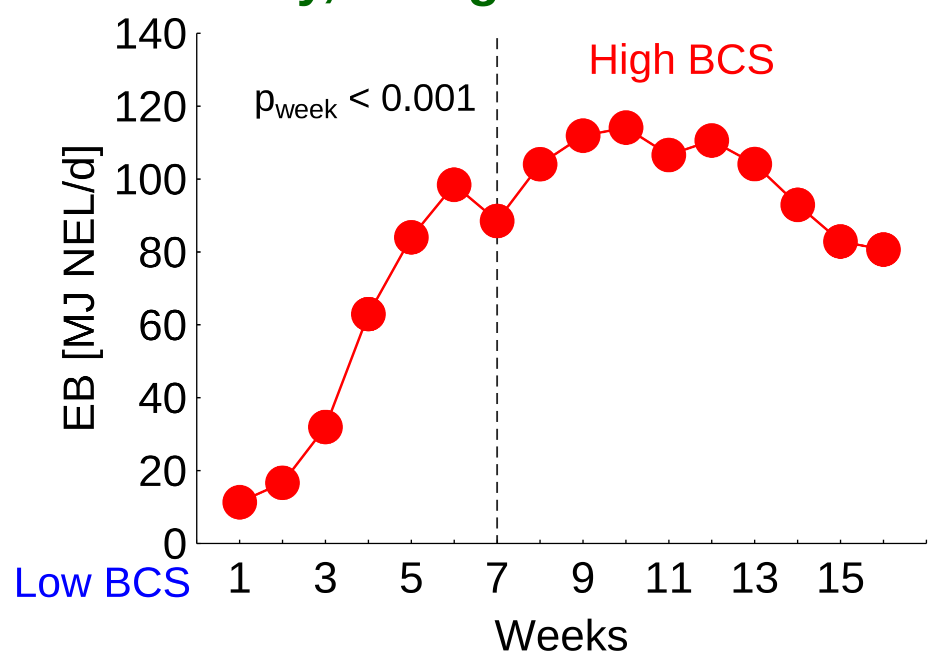
- Maintenance
- Body accretion (mainly fat)

Energy balance of cows differing in physiological state

Transition cow



Dry, non-gravid cow



Drong et al., 2016

Dänicke et al., 2016

Energy requirement for:

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- Gravidity (Fetus, body accretion)

- Maintenance
- Milk energy

- Maintenance
- Body accretion (mainly fat)

NEFA and BHB of cows differing in physiological state

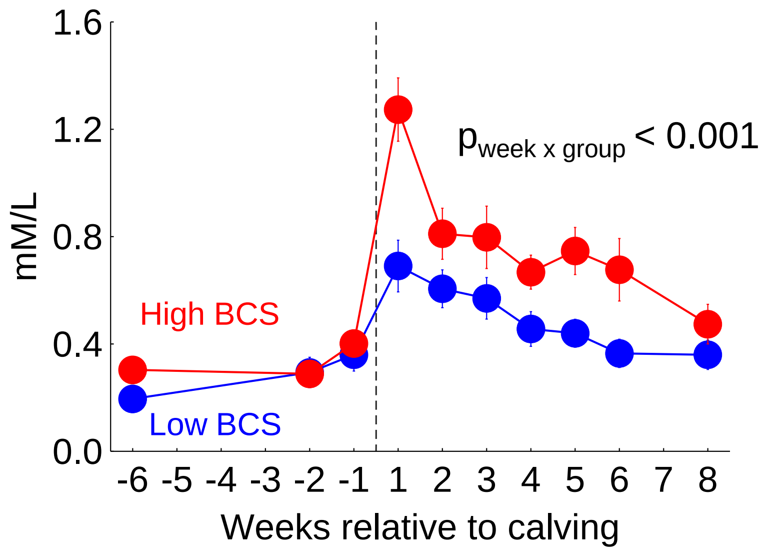
Transition cow

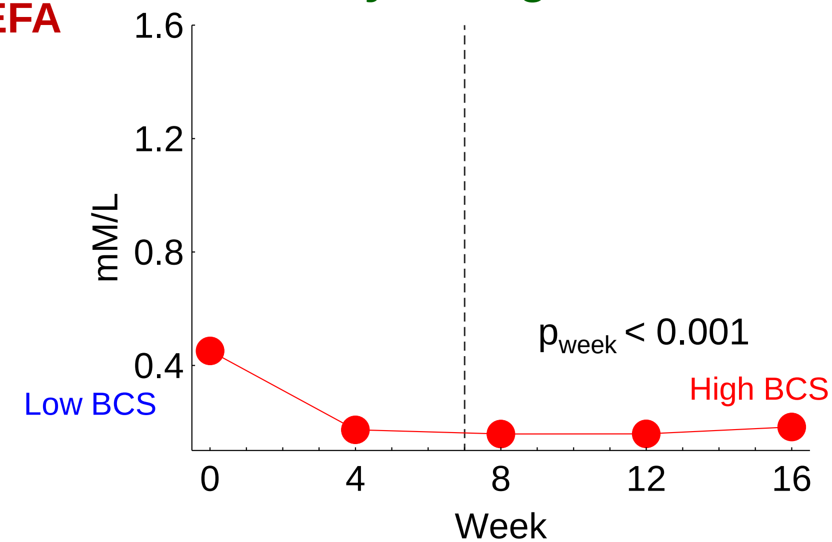
Dry, non-gravid cow

Drong et al., 2016

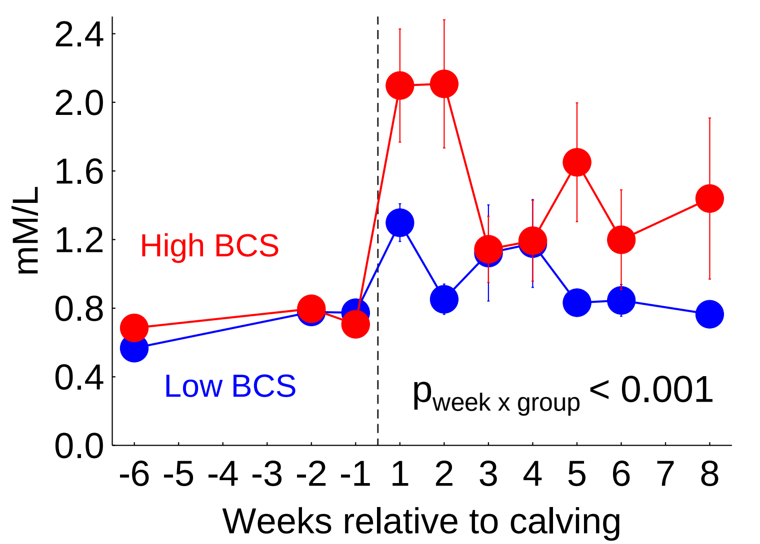
Dänicke et al., 2016

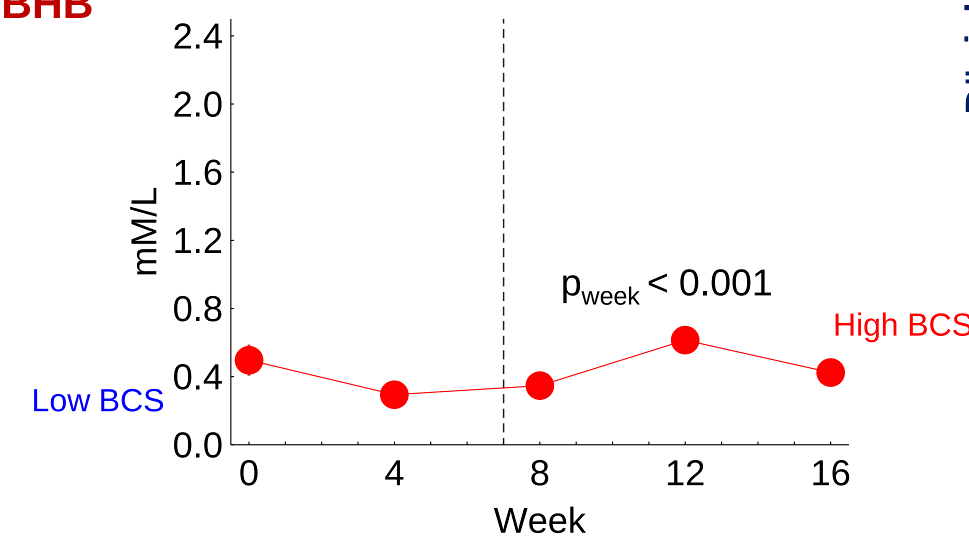
NEFA



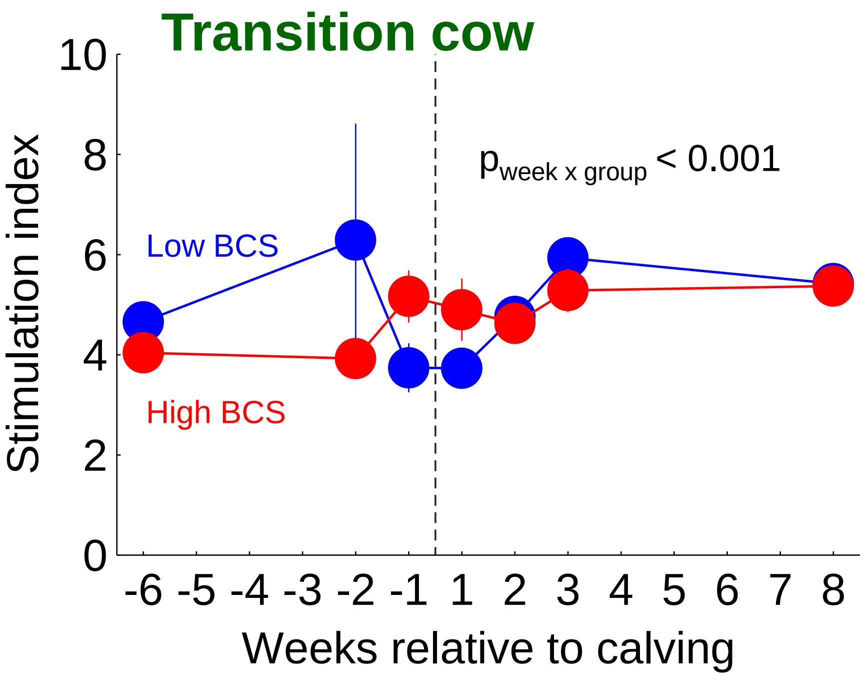


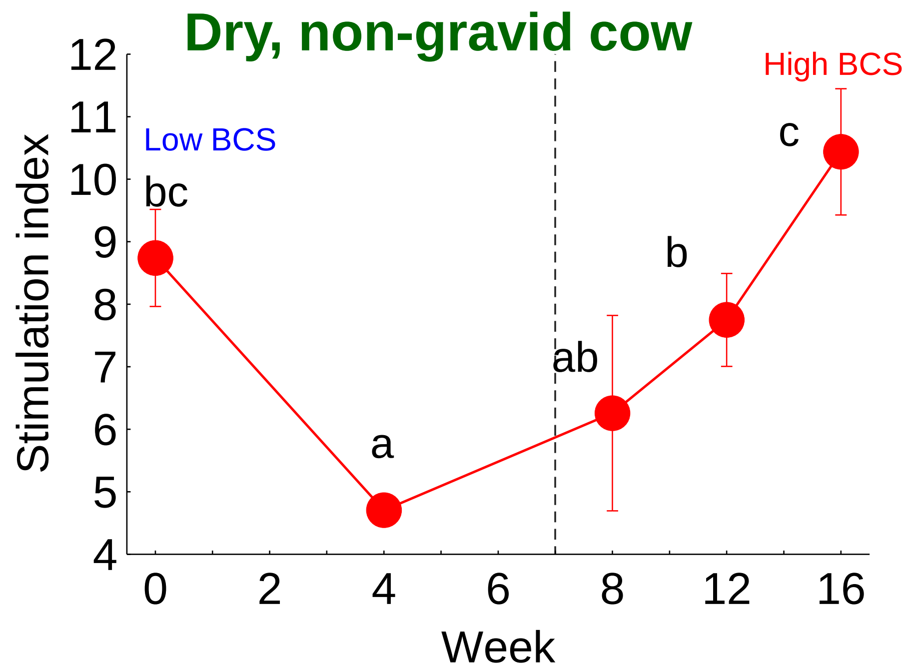
BHB





Ex vivo proliferative response of bovine peripheral mononuclear cells in dependence on physiological state





Drong et al., 2016

Dänicke et al., 2016

Energy requirement for:

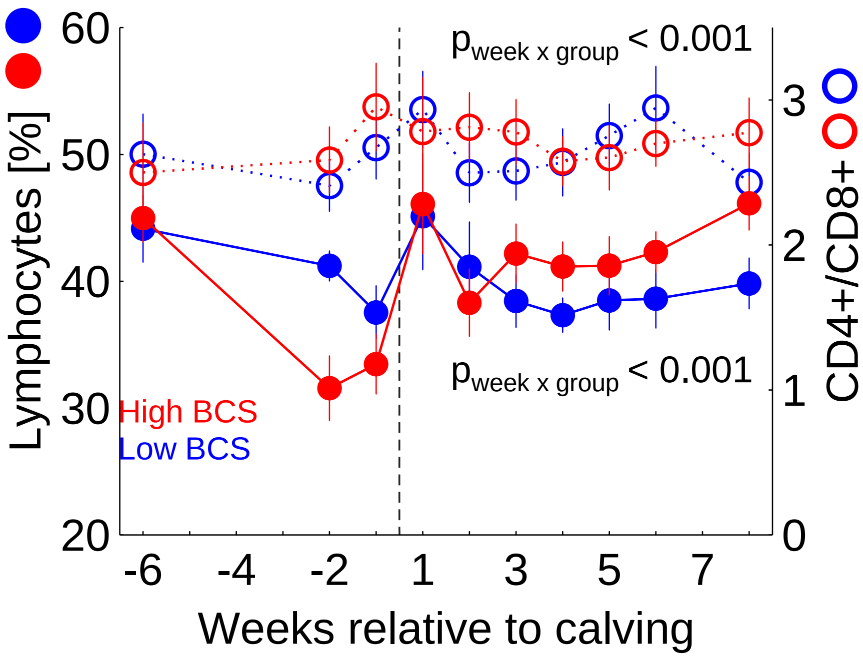
- Maintenance
- Gravidity (Fetus, body accretion)

- Maintenance
- Milk energy

- Maintenance
- Body accretion (mainly fat)

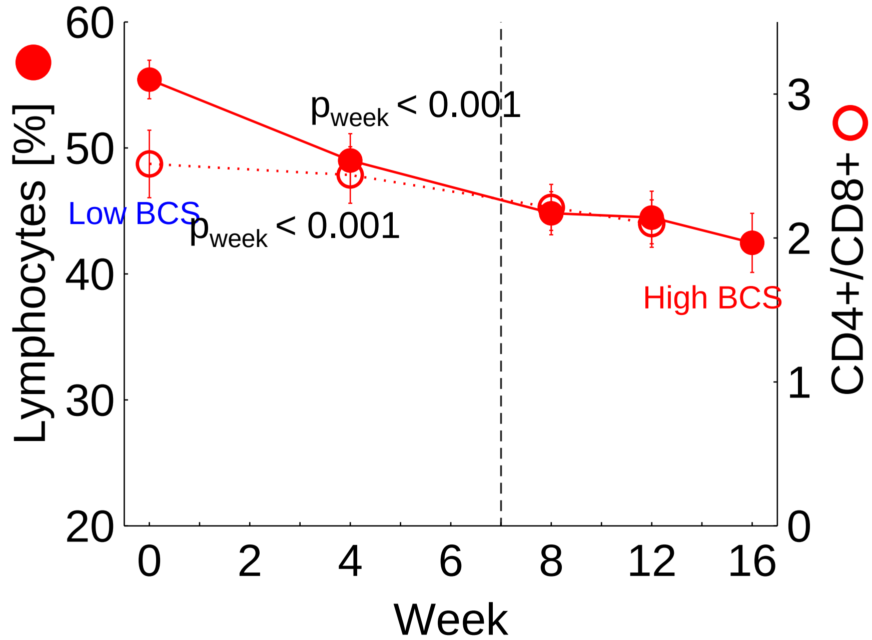
Lymphocyte proportion and CD4+ to CD8+ ratio in dependence on physiological state

Transition cow



Drong et al., 2016

Dry, non-gravid cow



Dänicke et al., 2016

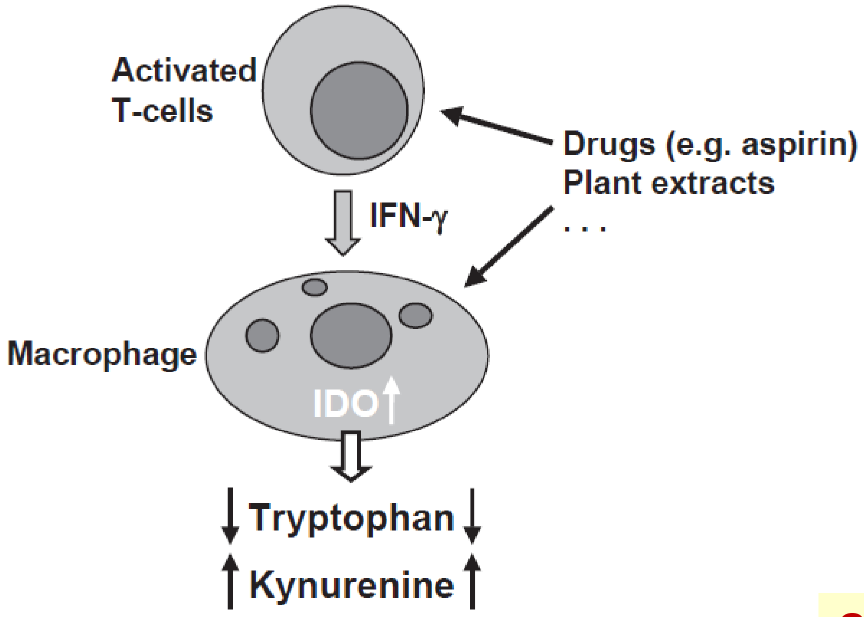
Energy requirement for:

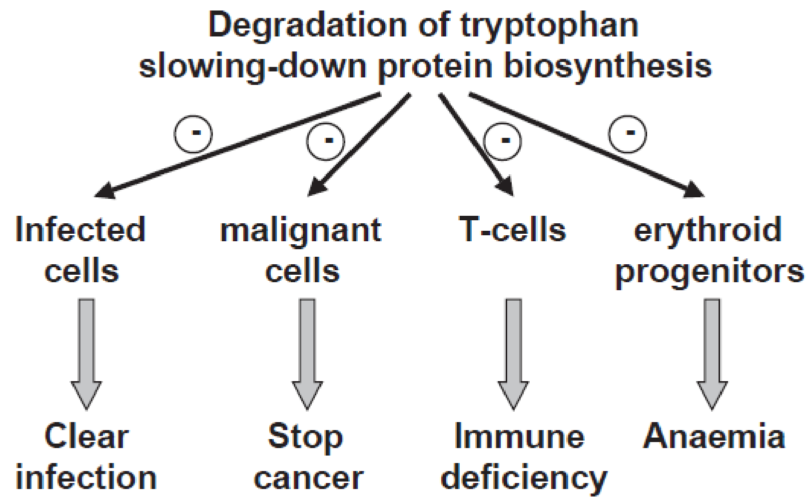
- Maintenance
- Gravidity (Fetus, body accretion)

- Maintenance
- Milk energy

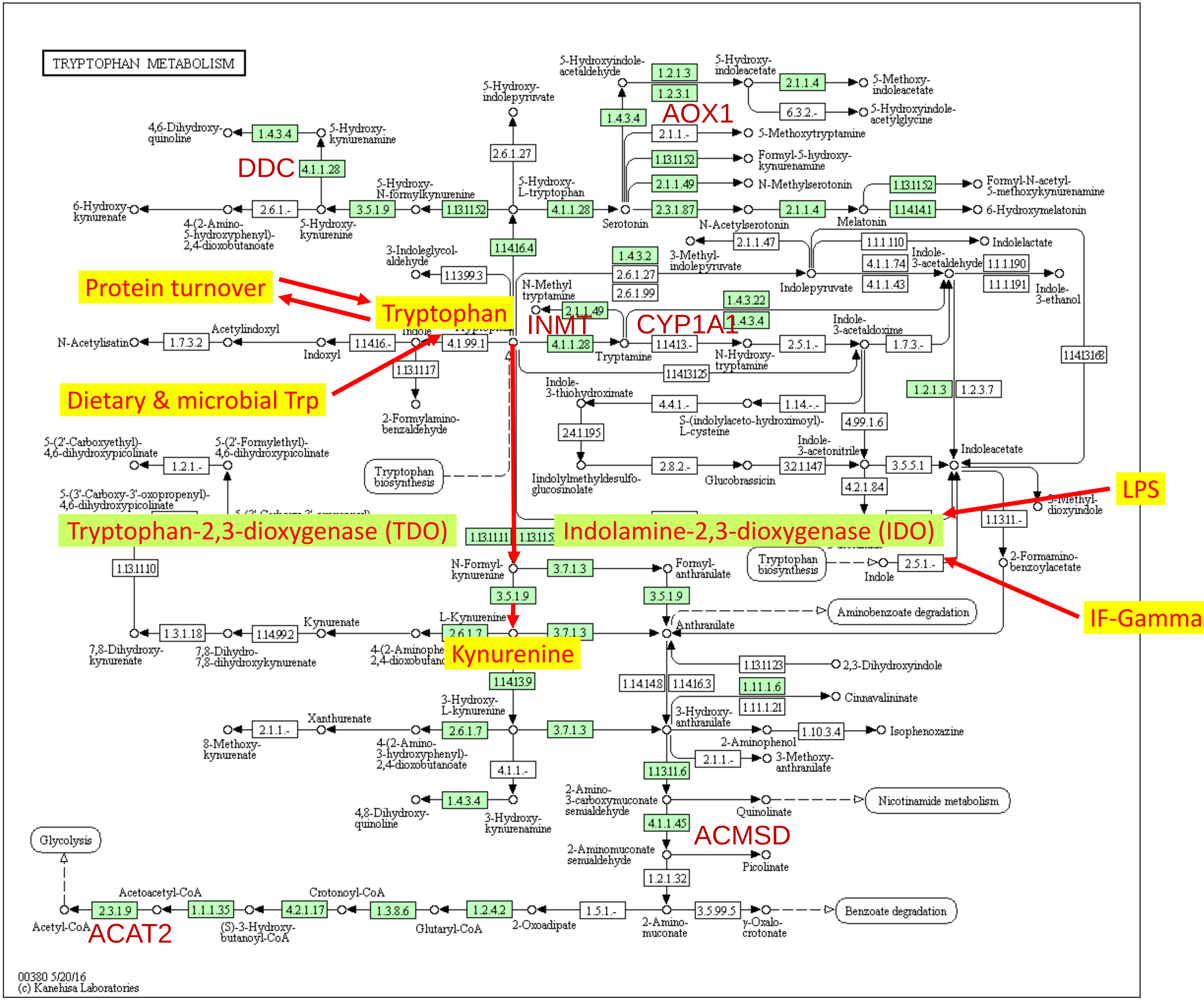
- Maintenance
- Body accretion (mainly fat)

Activation of indolamine- 2, 3-dioxygenase (IDO) and its consequences (Schröcksnadel et al., 2006)

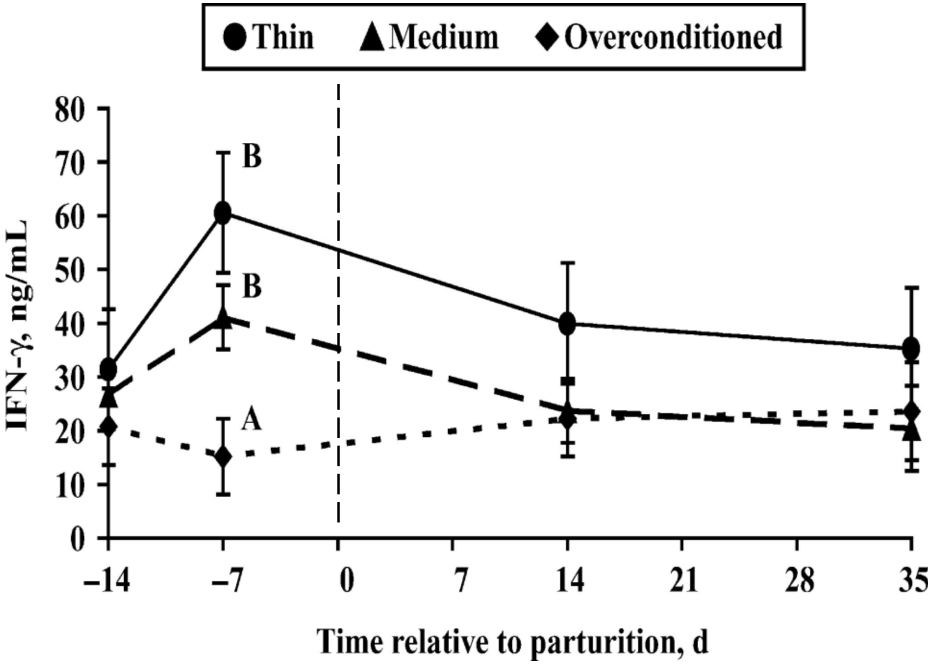




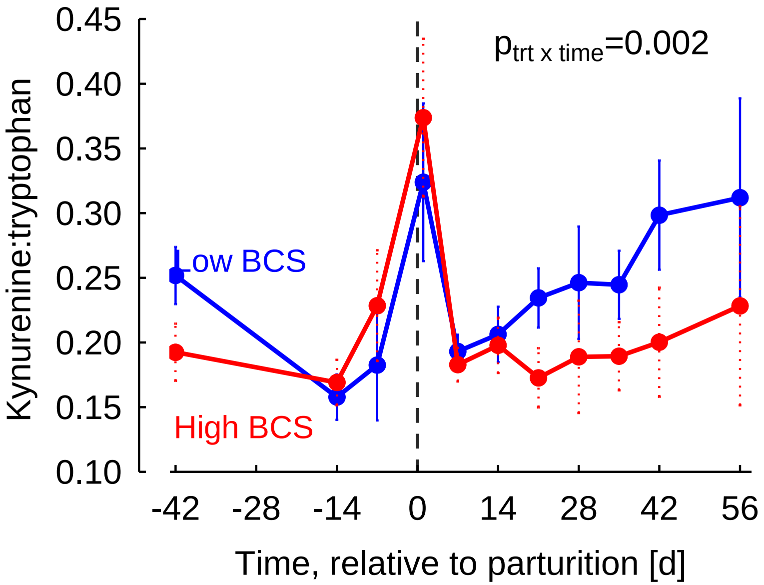
Cattle:
Induction of endometrial IDO-mRNA-expression together with a locally increased kynurenine/tryptophan ratio (=IDO-activity) was suggested as an immunological mechanism to establish embryo tolerance (Groebner et al., 2011).


TRYPTOPHAN METABOLISM
Protein turnover
Tryptophan
Dietary & microbial Trp
INMT
CYP1A1
AOX1
DDC
Tryptophan-2,3-dioxygenase (TDO)
Indolamine-2,3-dioxygenase (IDO)
LPS
IF-Gamma
Kynurenine
ACMSD
ACAT2
Serotonin
Melatonin
N-Acetylserotonin
Tryptamine
Indolepyruvate
Indoleacetate
Anthranilate
3-Hydroxy-L-kynurenine
3-Hydroxy-anthranilate
Quinolinate
Picolinate
Kynurenate
Xanthurenate
Acetyl-CoA
Glycolysis
Nicotinamide metabolism
Benzoate degradation
Aminobenzoate degradation
Tryptophan biosynthesis
00380 5/20/16
(c) Kanehisa Laboratories

Interferon-γ (IFN-γ) secretion in ConA-stimulated PBMC in dependence on BCS (Lacetera et al., 2005)



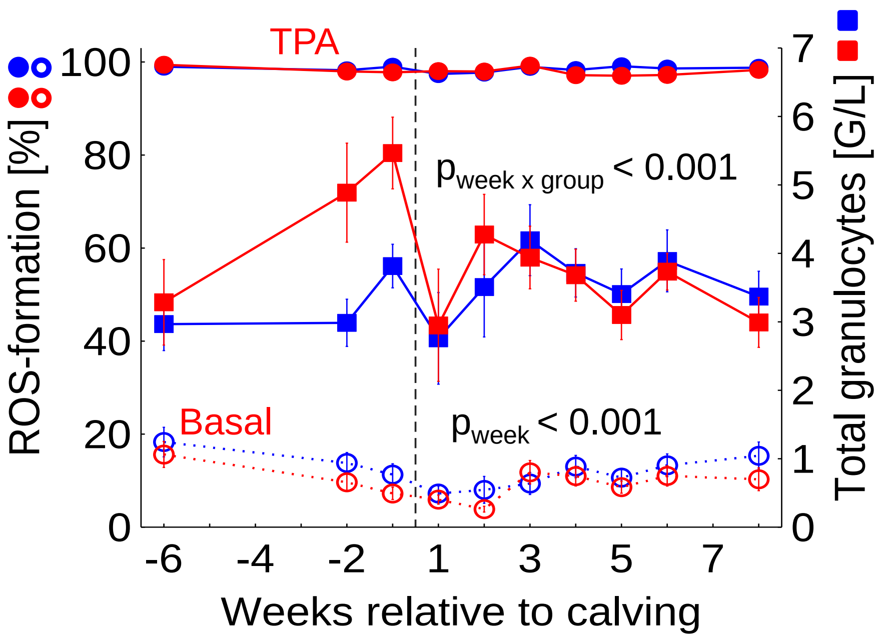
Tryptophan catabolism in dependence on BCS (Hüther et al., 2016)



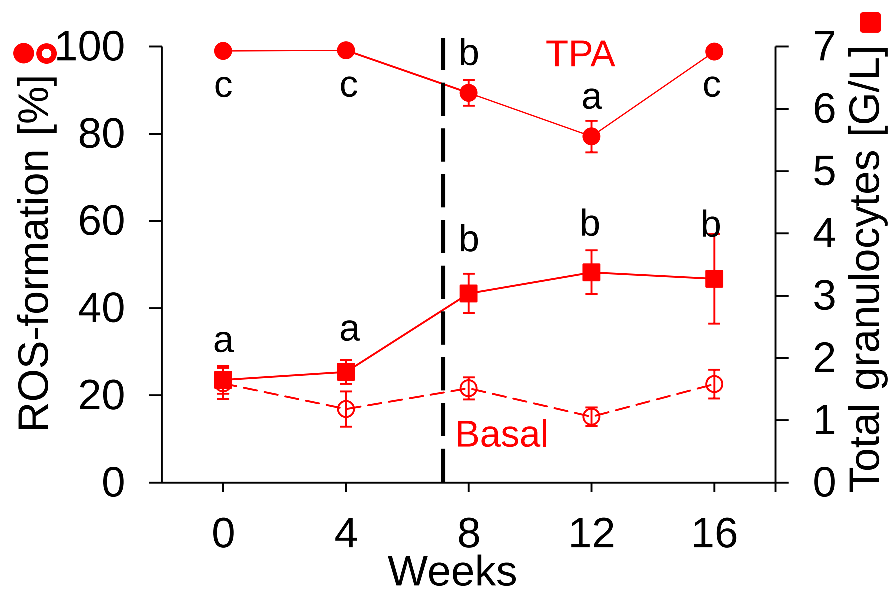
A higher kynurenine to tryptophan ratio indicates a higher IDO/TDO activity and suggests a lower immuno-reactivity

Granulocyte numbers, unstimulated (basal) and stimulated ROS formation of granulocytes in dependence on physiological state

Transition cow



Dry, non-gravid cow



Drong et al., 2016

Dänicke et al., 2016

Energy requirement for:

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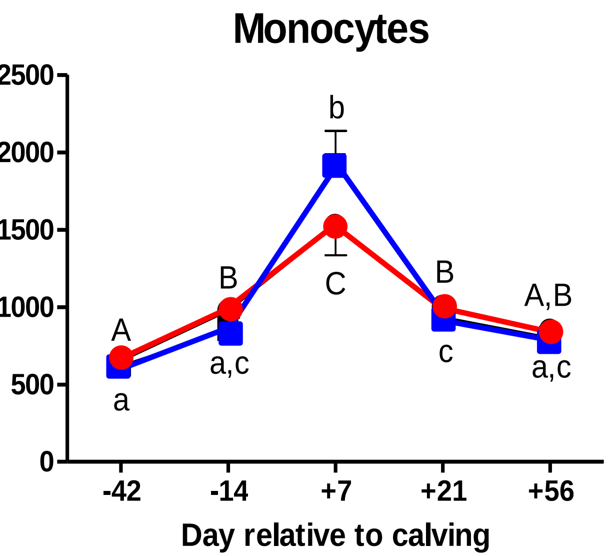
- Gravidity (Fetus, body accretion)

- Maintenance
- Milk energy

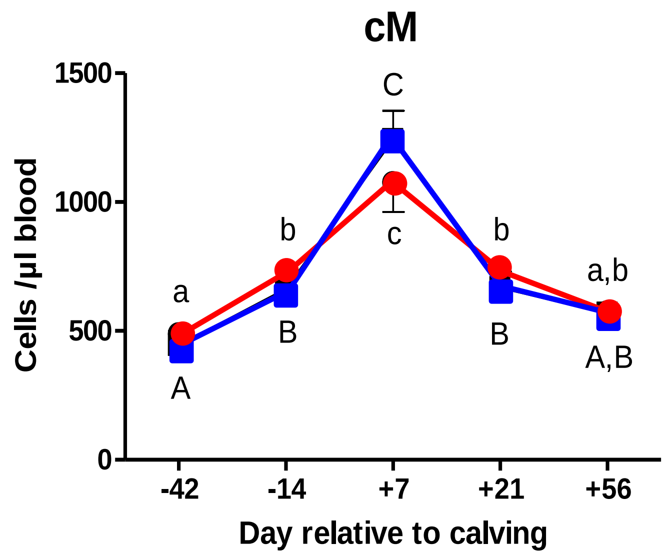
- Maintenance
- Body accretion (mainly fat)

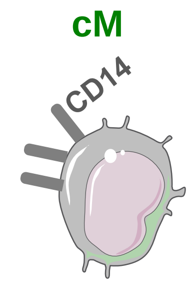
Monocyte numbers in dependence on body condition and physiological state (Eger et al., 2015)



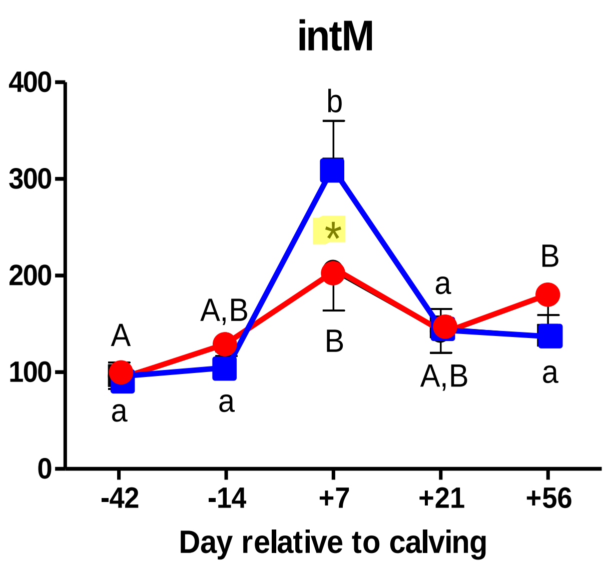
Significant differences:
A,B,C: BCS high
a,b,c : BCS low
*: between groups

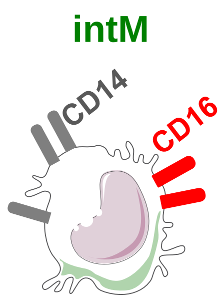
BCS high
BCS low



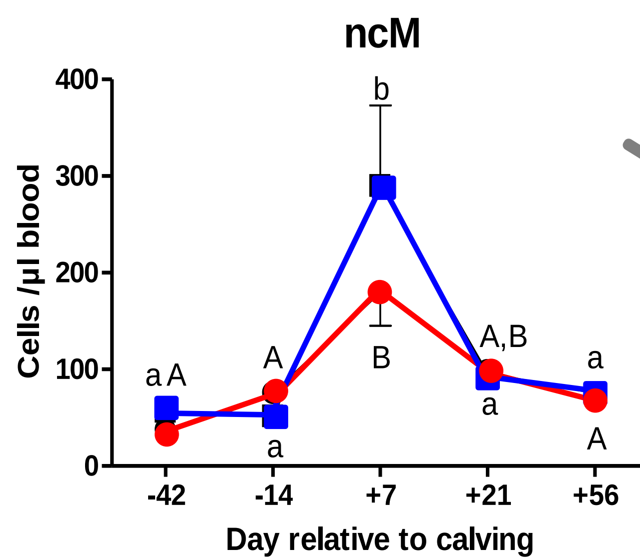


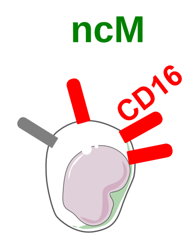
high phago-
cytic activity,
most abundant





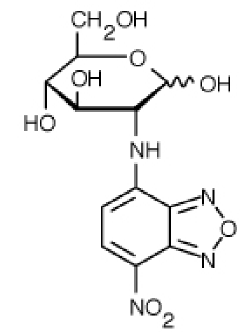
high ROS for-
mation, pro-
inflammatory



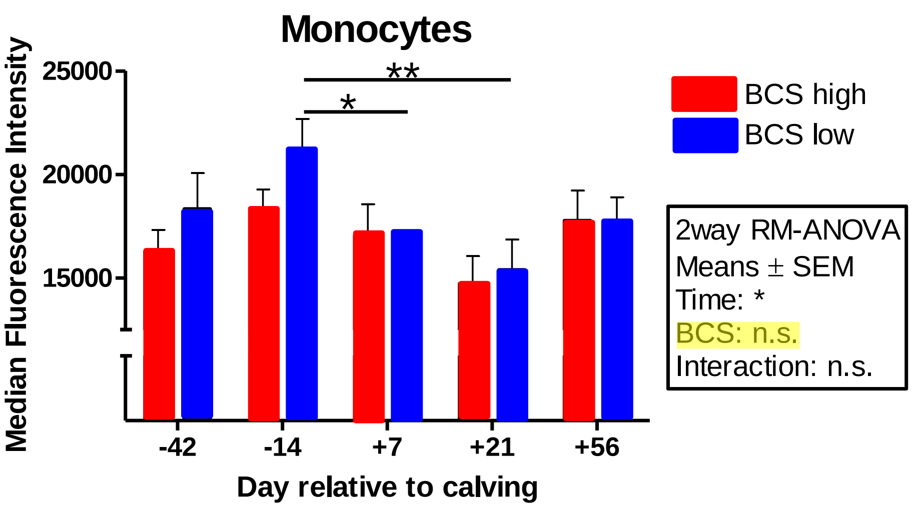


high phagocytic
activity,
patrolling?

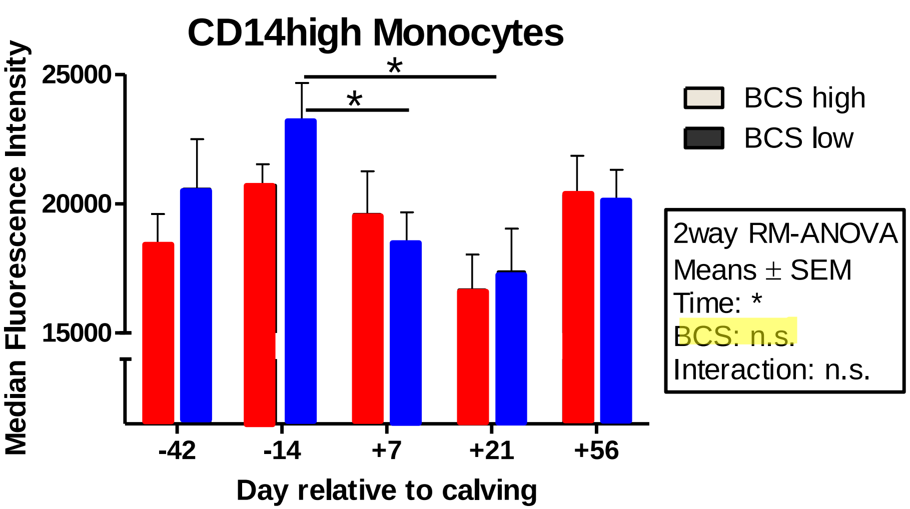
Flow cytometric assessment of glucose uptake of monocytes from cows differing in body condition (Eger et al., 2016)

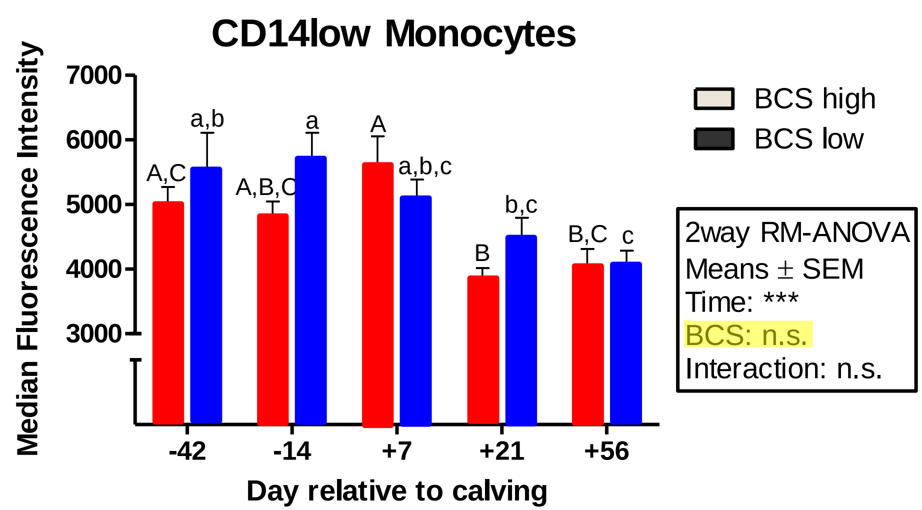


2-(*N*-(7-Nitrobenz-2-oxa-1,3-diazol-4-yl)Amino)-2-Deoxyglucose
Ex. max.: 465 nm
Em. max.: 540 nm

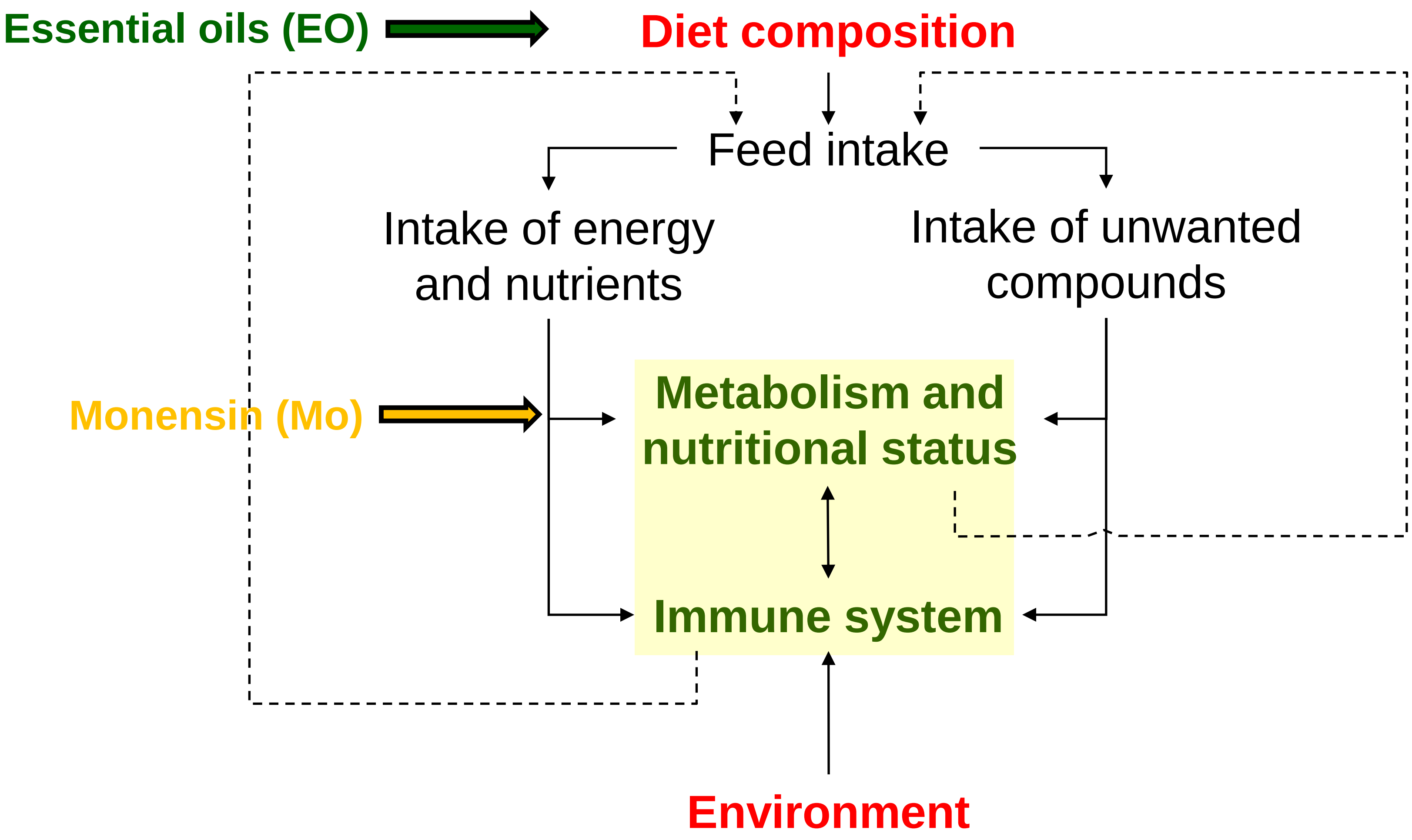


➡ Glucose uptake of all monocytes decreased after parturition





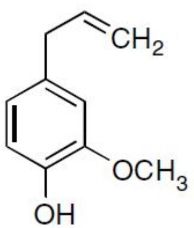
Possible implications of nutrition and other environmental factors on the functionality of the immune system



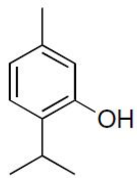
Substances with potential effects on ruminal microbiota

Essential oils

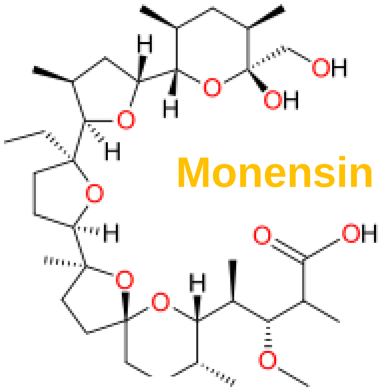
Eugenol



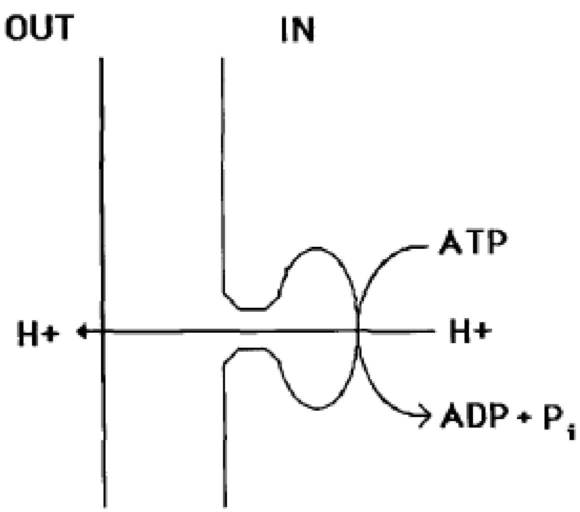
Thymol

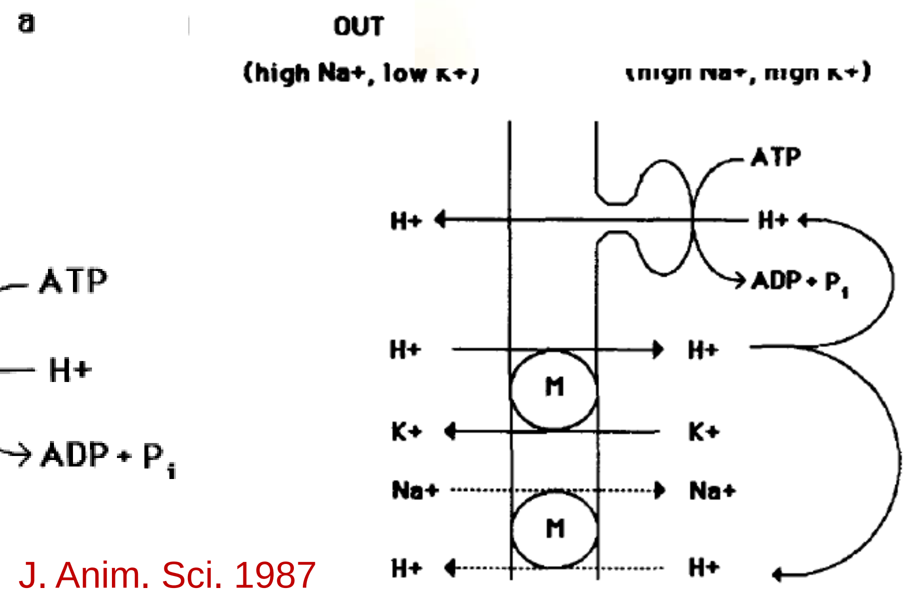


Antibiotic



Monensin A

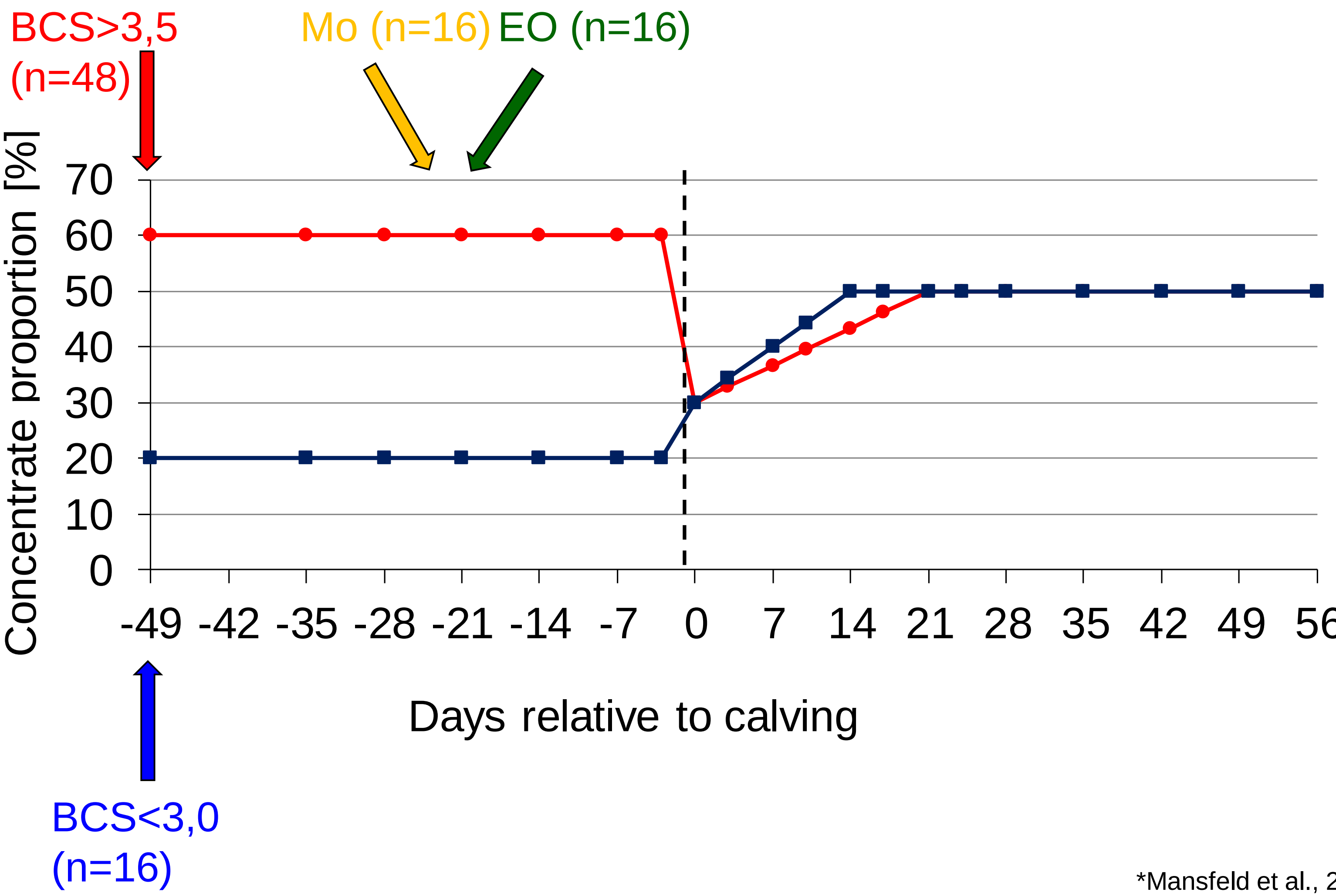




Russell J. Anim. Sci. 1987

Design for investigation of the effects of essential oils (EO) as additive and Monensin (Mo) as slow release intraruminal bolus for ketosis prevention in pre-disposed cows (Drong et al., 2015)

BCS=4*



BCS=2*

*Mansfeld et al., 2000

Rumen microbiome analysis by using the 16S Ilumina MiSeq-technique (Schären et al., 2017)

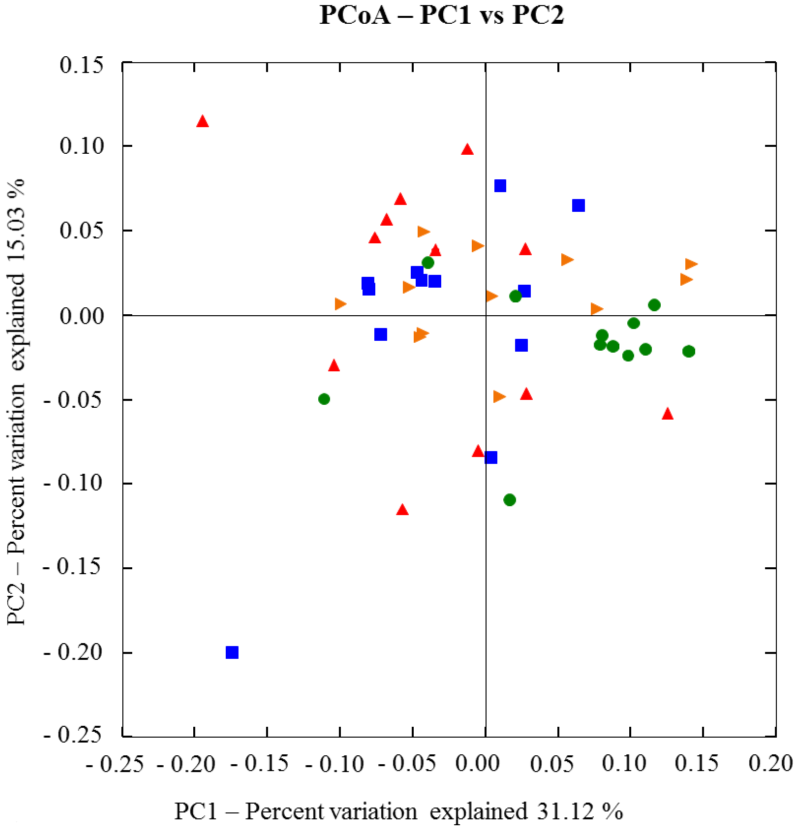
Similarity among samples

→ Significant difference between microbiome of **HC/MO** animals compared to others. (*P* < 0.001)
→ No difference between **HC/EO** and control (**LC, HC**).

Sample diversity / alpha-diversity variables

Significantly lower species diversity in **HC/MO** samples:

→ only 162 vs. 170 species detected!

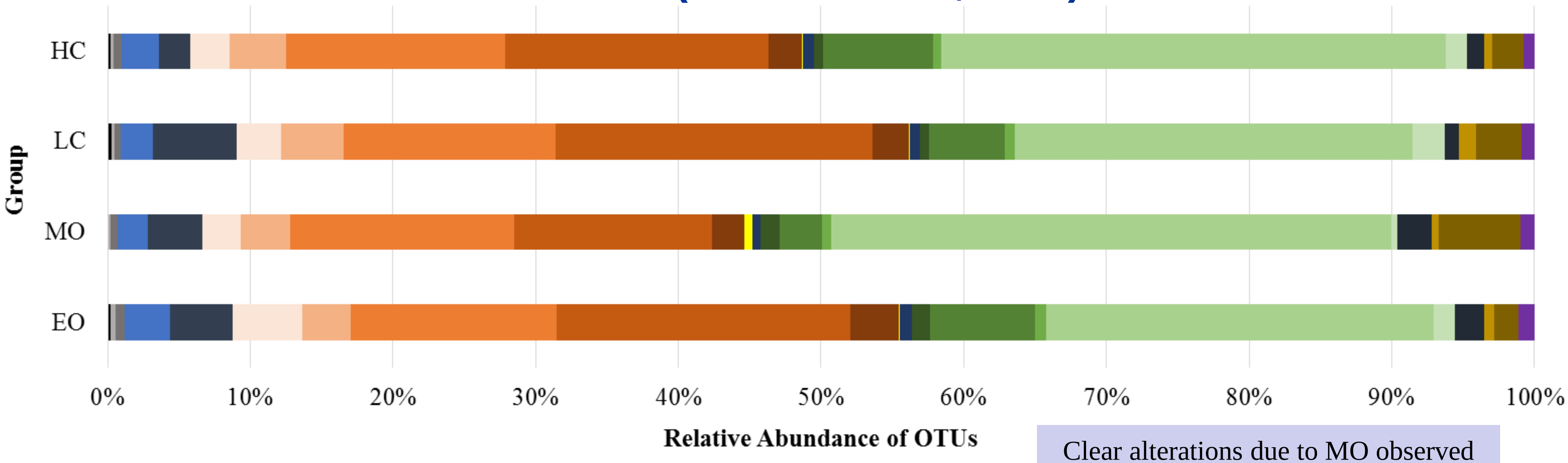


Variable[2]	Group[3] HC	LC	MO	EO	Significance[4]
Chao1	171.3 / 2.2	172.4 / 4.3	166.8 / 5.7	171.0 / 7.5	0.323
Observed species	171.0 / 4.5 [a]	170.5 / 4.0 [a]	162.5 / 4.0 [b]	170.5 / 8.5 [a]	0.015
Shannon index	4.41 / 0.23 [a]	4.43 / 0.16 [a]	4.20 / 0.13 [b]	4.39 / 0.37 [ab]	0.020

Blue = **LC**; Green =**HC/MO**; Red= **HC/EO**; Orange = **HC**

Oral rumen liquid samples collected at 56 DIM.

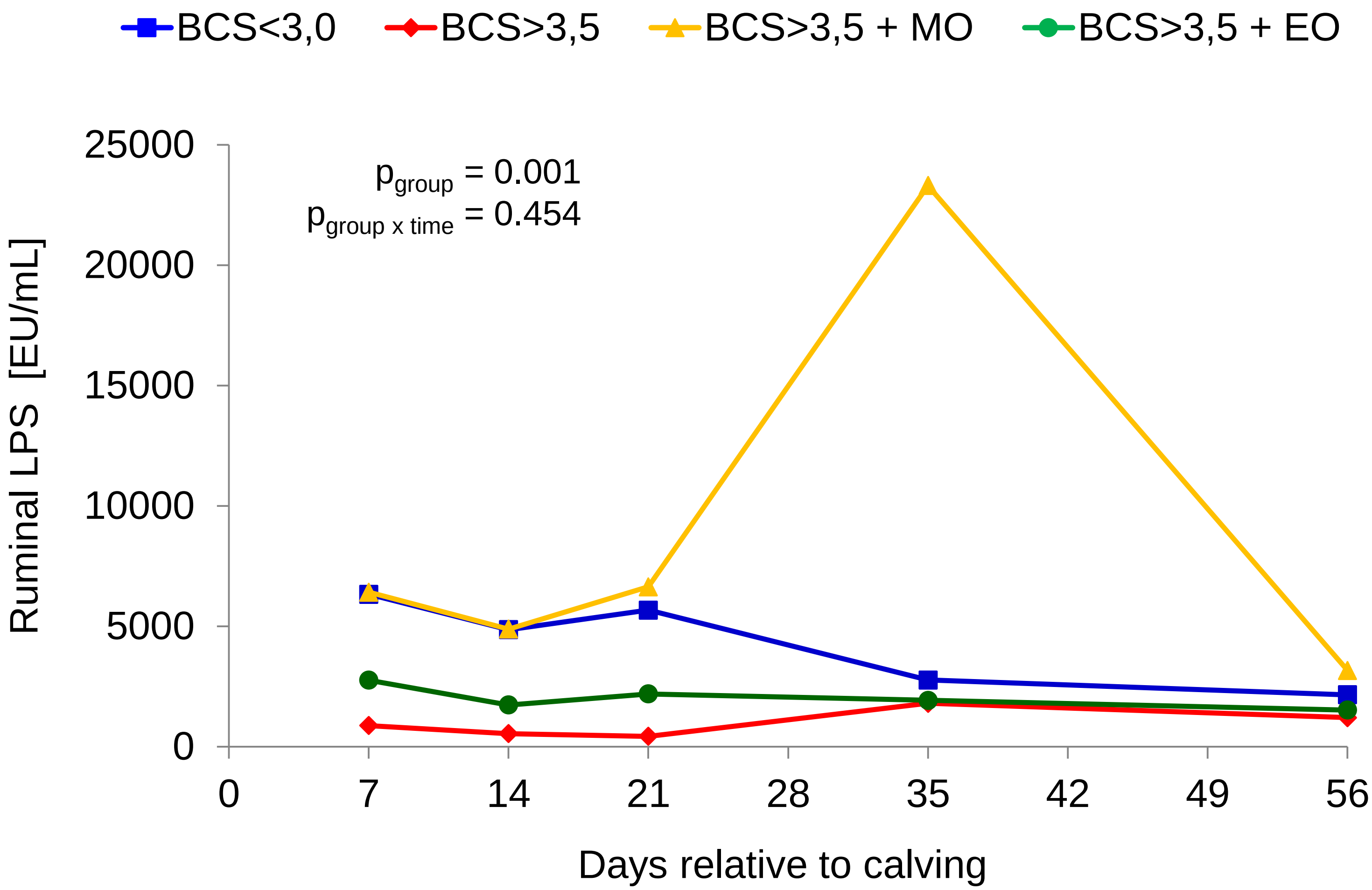
Differences between groups in rumen microbiota on family level (Schären et al., 2017)



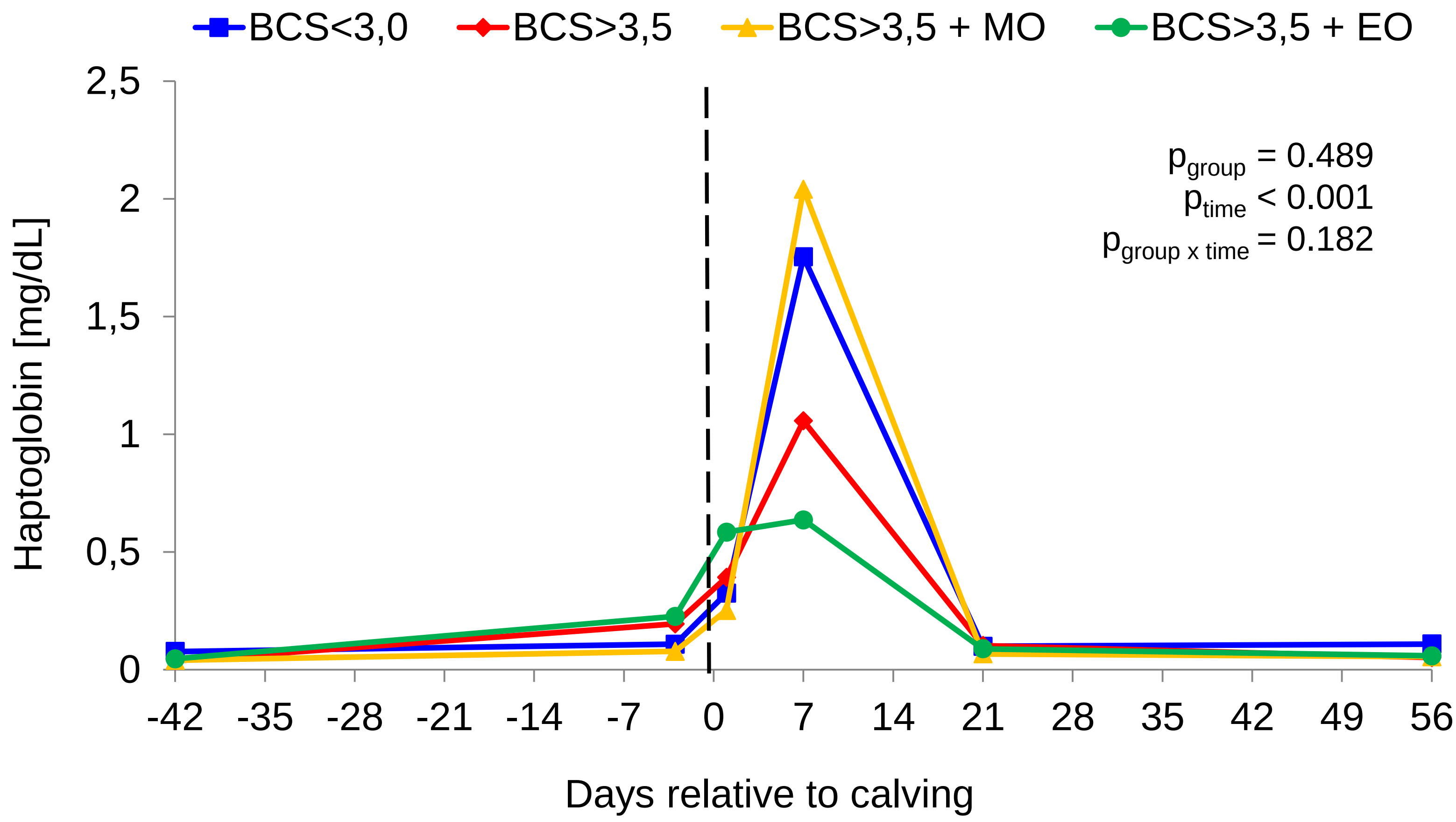
Clear alterations due to MO observed on family level

Taxonomy	*P*-value						
	Global	EO:LC	EO:HC	EO:MO	LC:HC	MO:LC	MO:HC
Archaea - Euryarchaeota - Methanobacteria - Methanobacteriales – Methanobacteriaceae	0.846	-	-	-	-	-	-
Bacteria - Actinobacteria - Bifidobacteriales - Bifidobacteriaceae - Bifidobacterium	0.141	-	-	-	-	-	-
Bacteria - Actinobacteria - Bifidobacteriales - Bifidobacteriaceae - uncultured and other	0.229	-	-	-	-	-	-
Bacteria - Actinobacteria - Coriobacteriia - Coriobacteriales - Coriobacteriaceae	0.025	0.610	0.913	0.425	0.937	0.024	0.108
Bacteria - Bacteroidetes - Bacteroidia - Bacteroidales - BS11 gut group	0.001	0.839	0.998	0.029	0.915	0.001	0.012
Bacteria - Bacteroidetes - Bacteroidia - Bacteroidales - Prevotellaceae	0.050	1.000	0.316	0.049	0.316	0.049	0.818
Bacteria - Bacteroidetes - Bacteroidia - Bacteroidales - RF16	0.779	-	-	-	-	-	-
Bacteria - Bacteroidetes - Bacteroidia - Bacteroidales - Rikenellaceae	0.000	0.807	1.000	0.001	0.778	0.026	0.000
Bacteria - Bacteroidetes - Bacteroidia - Bacteroidales - S24-7	0.064	0.948	0.978	0.227	0.999	0.063	0.082
Bacteria - Candidate division TM7	0.440	-	-	-	-	-	-
Bacteria - Cyanobacteria - SHA-109	0.001	0.970	1.000	0.001	0.982	0.006	0.001
Bacteria - Firmicutes - Clostridia - Clostridiales - Family XIII Incertae Sedis	0.342	-	-	-	-	-	-
Bacteria - Firmicutes - Clostridia - Clostridiales - Lachnospiraceae	0.007	0.948	0.825	0.006	0.991	0.043	0.085
Bacteria - Firmicutes - Clostridia - Clostridiales - Ruminococcaceae	0.981	-	-	-	-	-	-
Bacteria - Firmicutes - Clostridia - Clostridiales - Veillonellaceae	0.476	-	-	-	-	-	-
Bacteria - Firmicutes - Erysipelotrichi - Erysipelotrichales - Erysipelotrichaceae	0.151	-	-	-	-	-	-
Bacteria - Proteobacteria - Gammaproteobacteria - Aeromonadales - Succinivibrionaceae	0.183	-	-	-	-	-	-
Bacteria - Spirochaetes - Spirochaetales - Spirochaetaceae - Treponema	0.193	-	-	-	-	-	-
Bacteria - Tenericutes - Mollicutes - Anaeroplasmatales - Anaeroplasmataceae	0.192	-	-	-	-	-	-
Bacteria - Tenericutes - Mollicutes - RF9	0.729	-	-	-	-	-	-
Unassigned	0.000	0.908	1.000	0.001	0.911	0.000	0.000

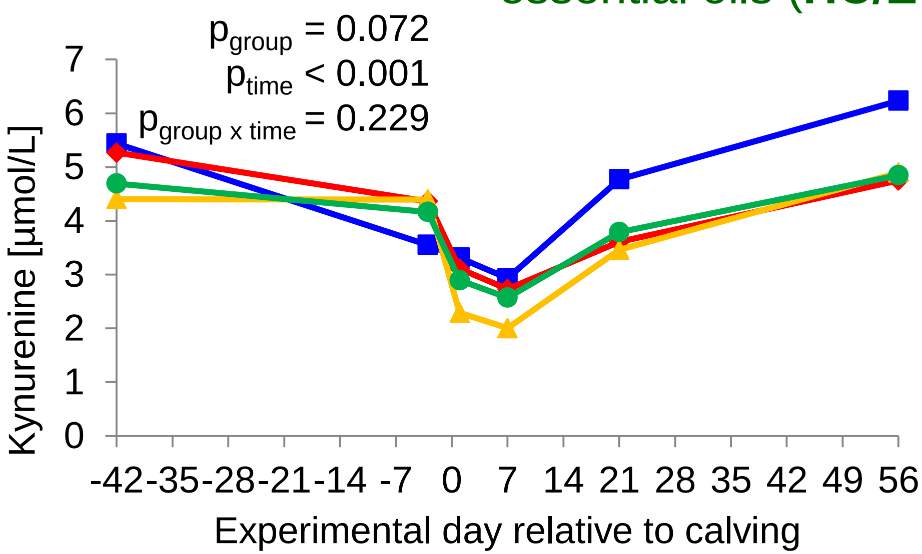
LPS concentration in rumen fluid in dependence on BCS (**LC**, **HC**), Monensin (**HC/MO**) oder essential oils (**HC/EO**) (Drong et al., 2016)

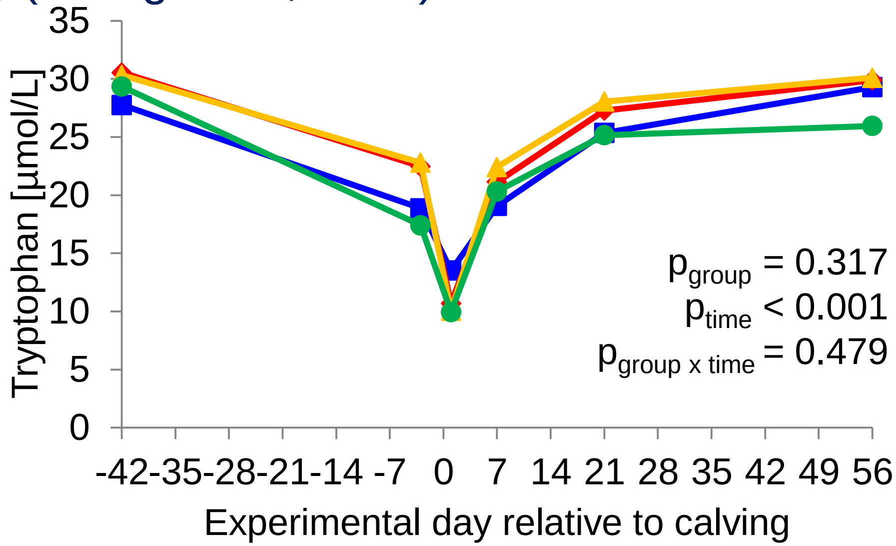


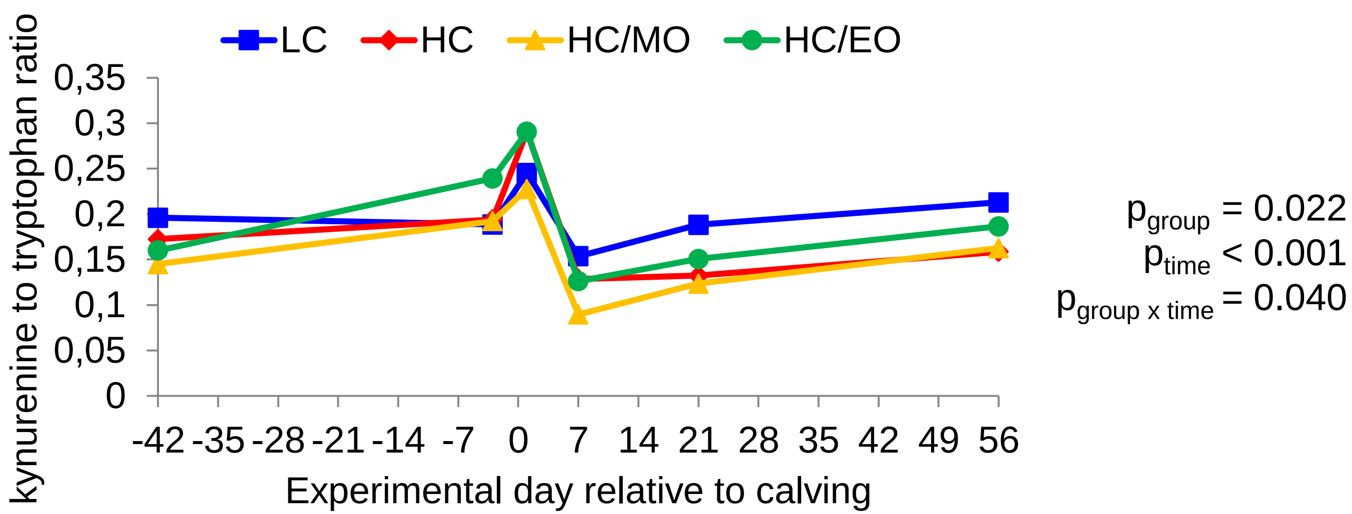
Haptoglobin in blood in dependence on BCS, Monensin (Mo) or essential oils (EO) (Drong et al., 2016)



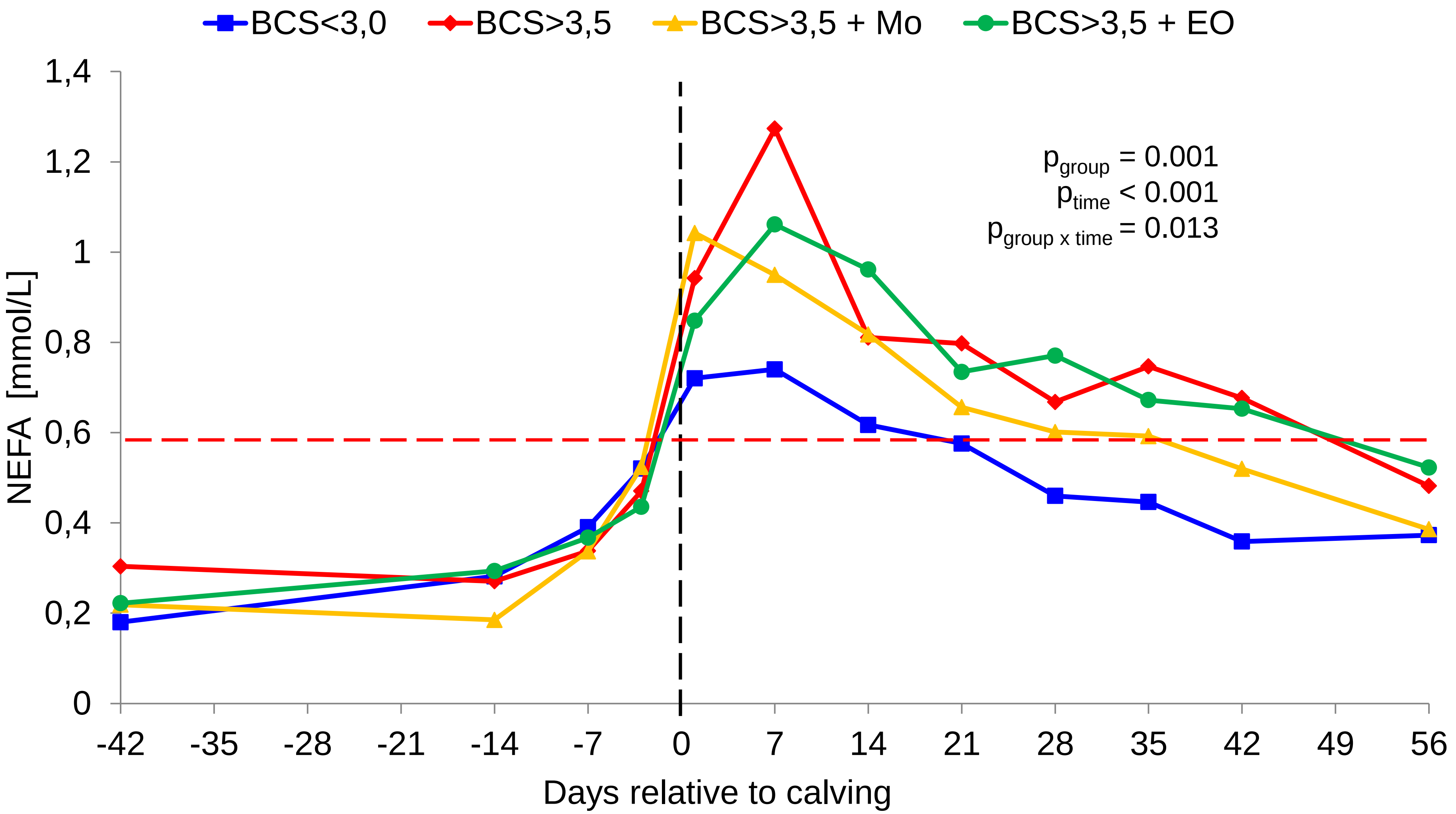
Tryptophan metabolism in dependence on BCS (**LC**, **HC**), Monensin (**HC/MO**) or essential oils (**HC/EO**) (Drong et al., 2016)



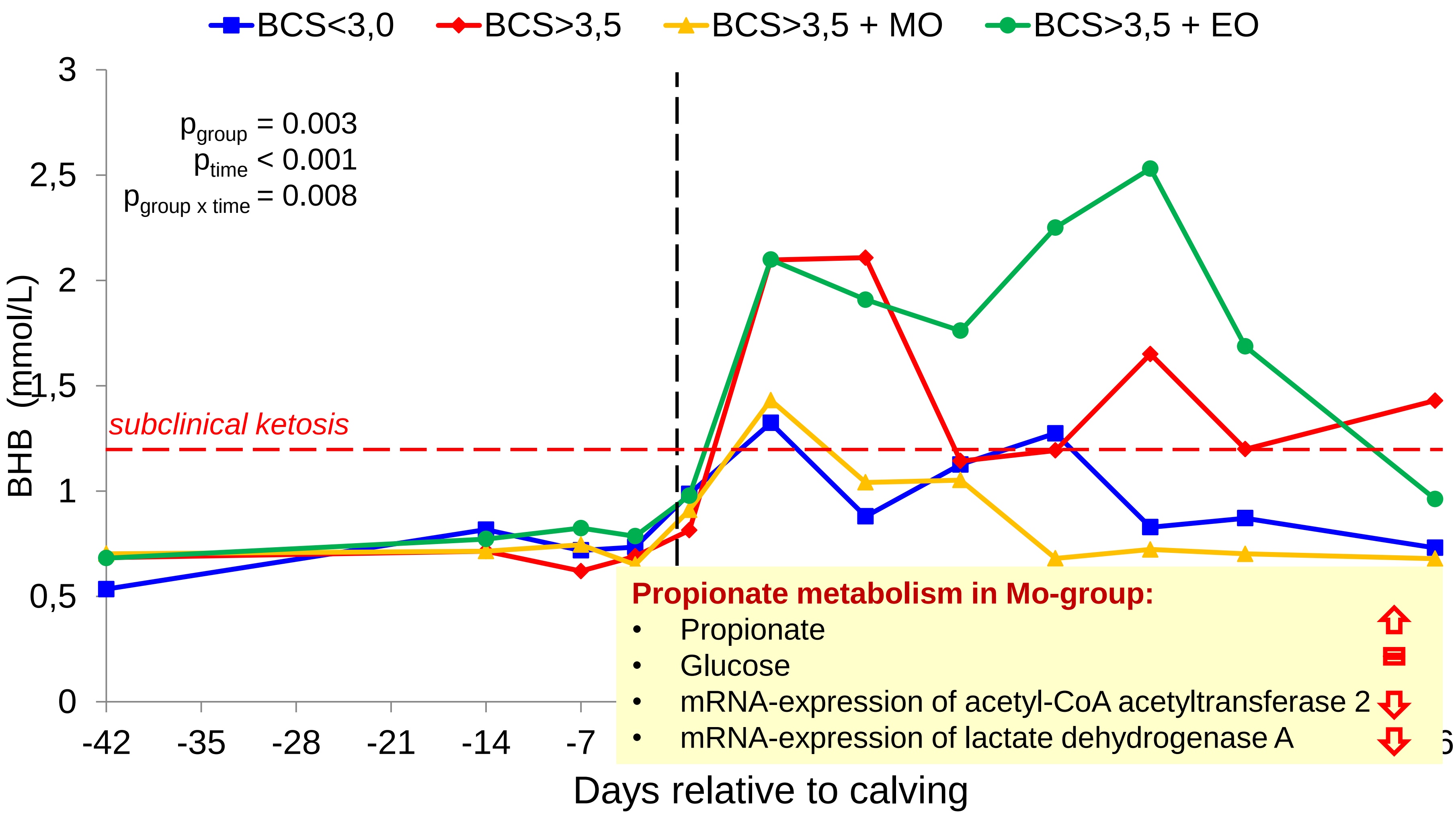




Non-esterified fatty acids (NEFA) in blood in dependence on BCS, Monensin (Mo) or essential oils (EO) (Drong et al., 2015)



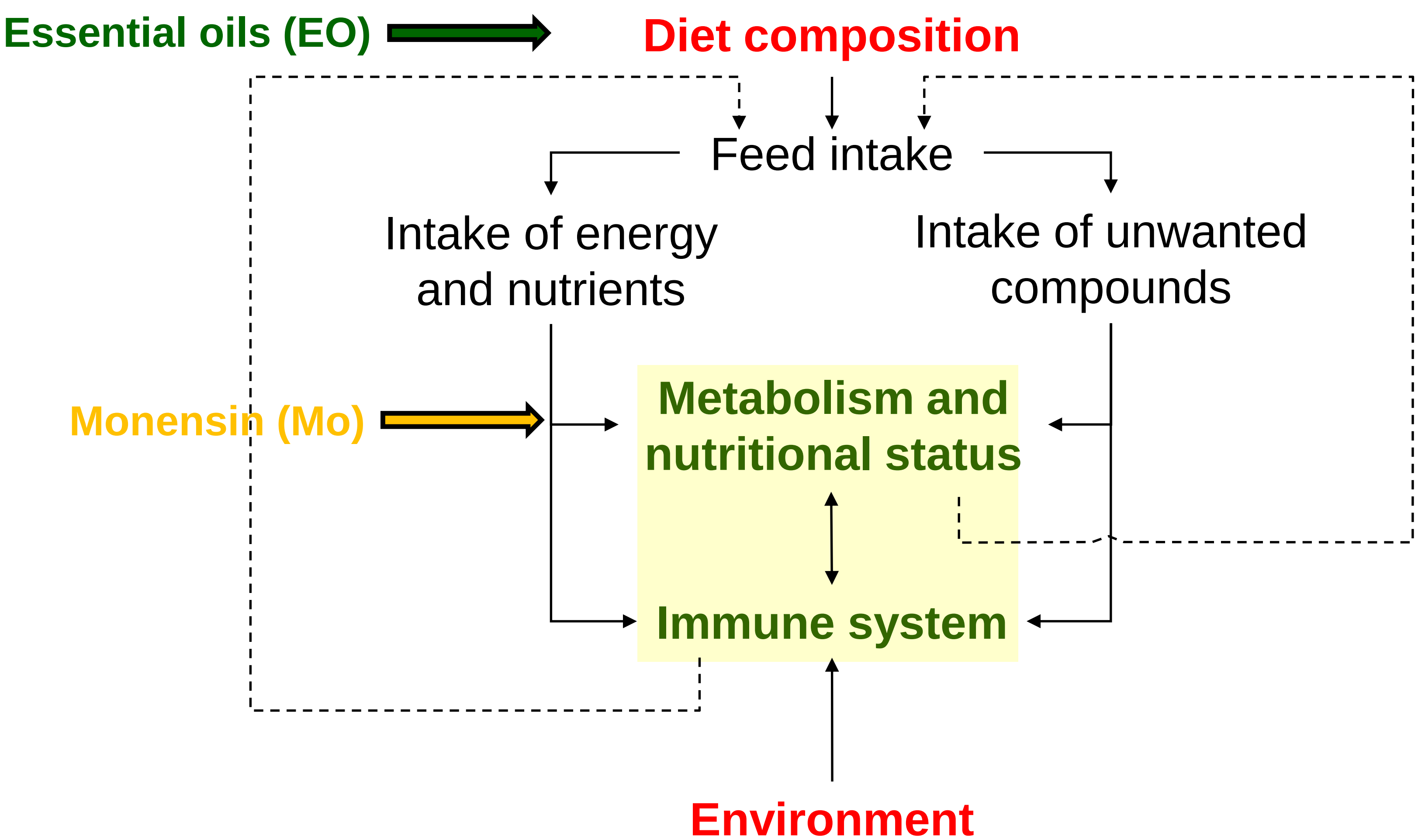
β- hydroxybutyrate (BHB) in blood in dependence on BCS, Monensin (Mo) or essential oils (EO) (Drong et al., 2015)



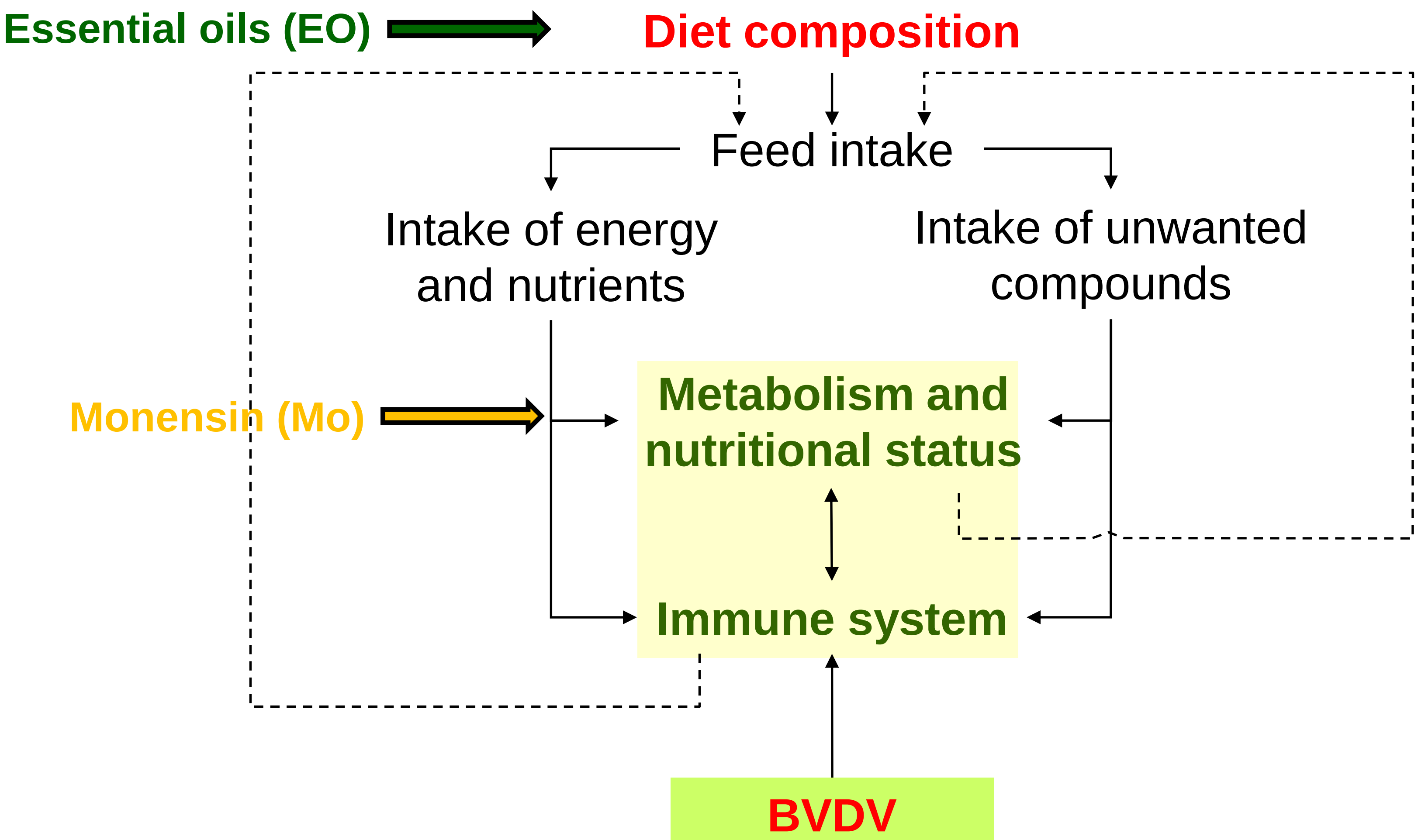
Propionate metabolism in Mo-group:

- Propionate ⇧
- Glucose =
- mRNA-expression of acetyl-CoA acetyltransferase 2 ⇩
- mRNA-expression of lactate dehydrogenase A ⇩

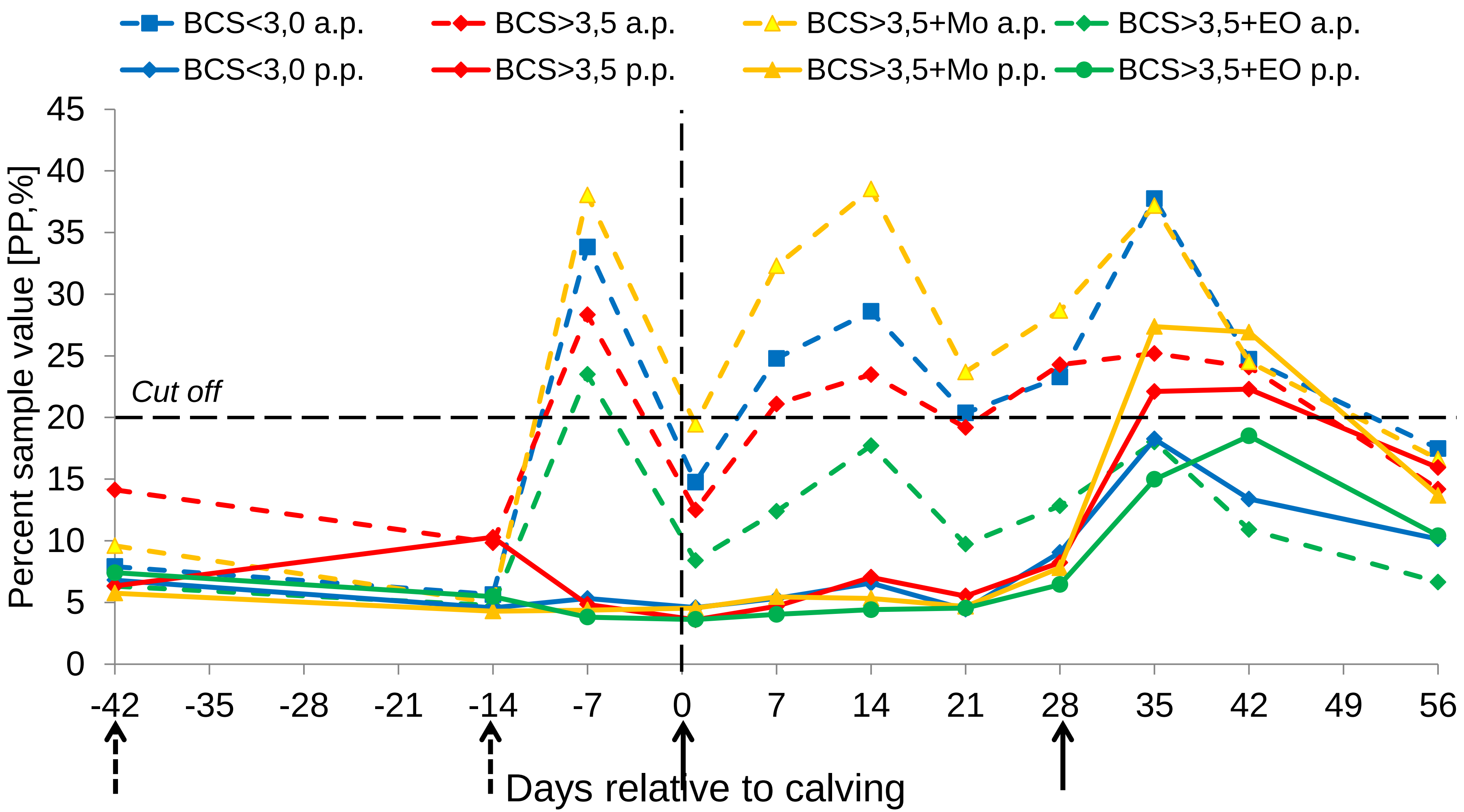
Possible implications of nutrition and other environmental factors on the functionality of the immune system



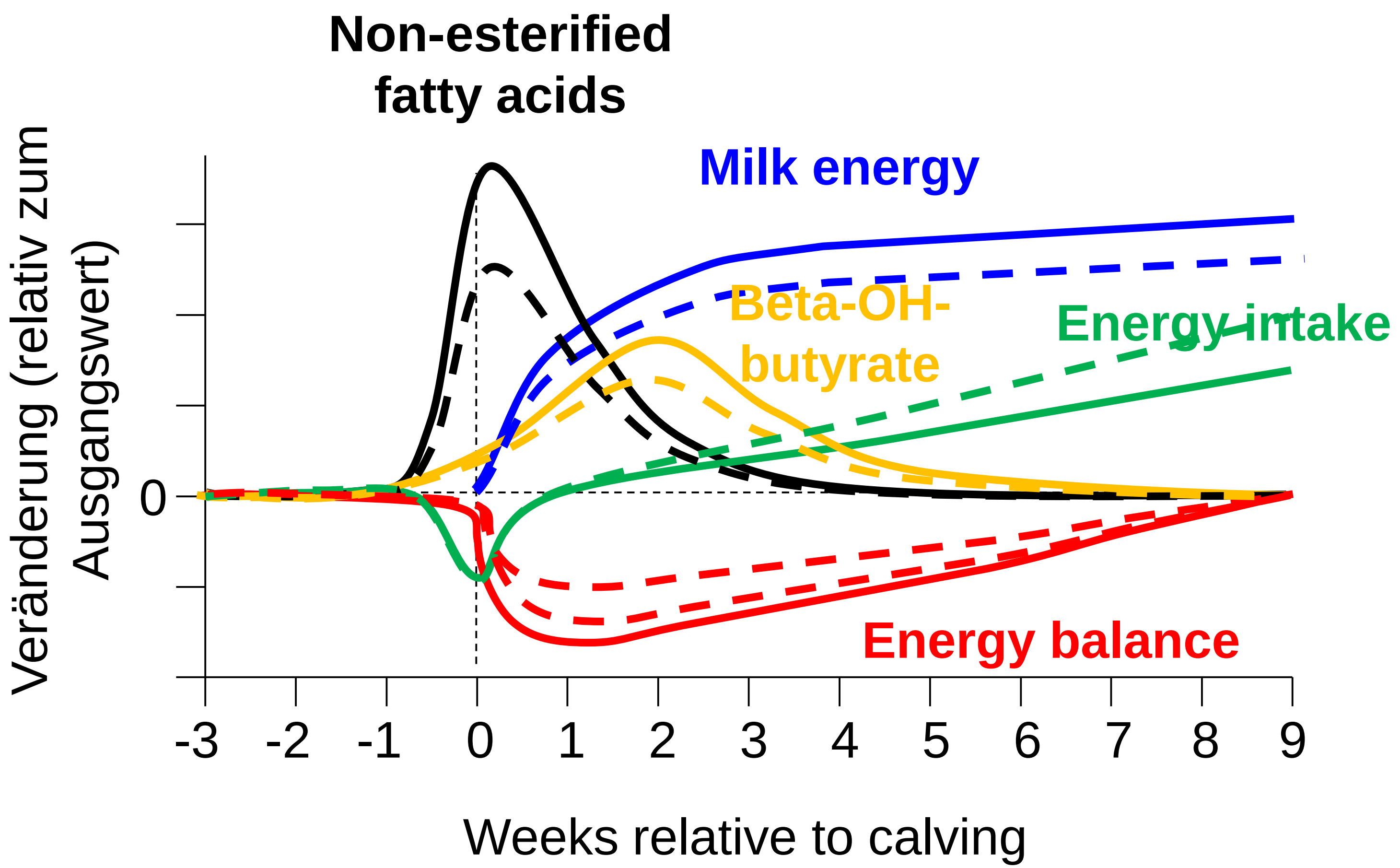
Possible implications of nutrition and other environmental factors on the functionality of the immune system



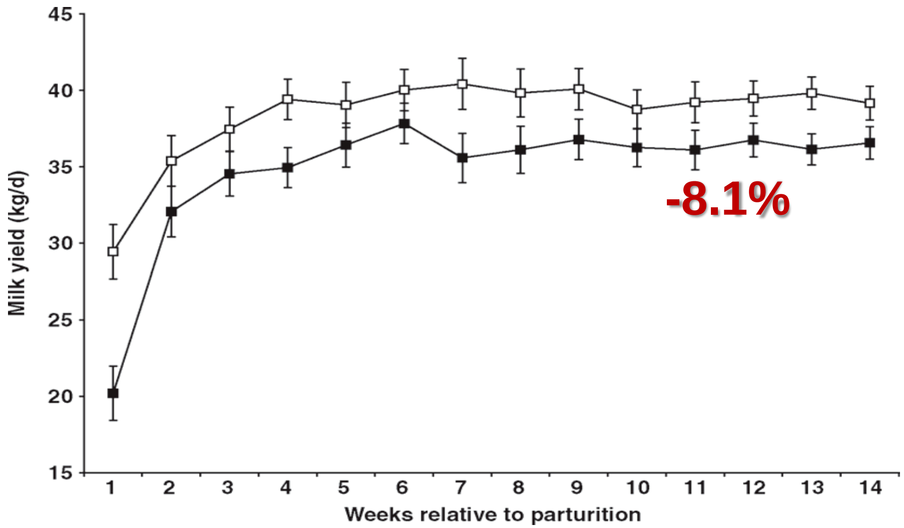
BVDV-antibody detection after BVDV-vaccination prioor to (a.p.↑) or adter (p.p.↑) calving in dependence on BCS, Monensin (Mo) or essential oils (EO) (Drong et al., 2016)

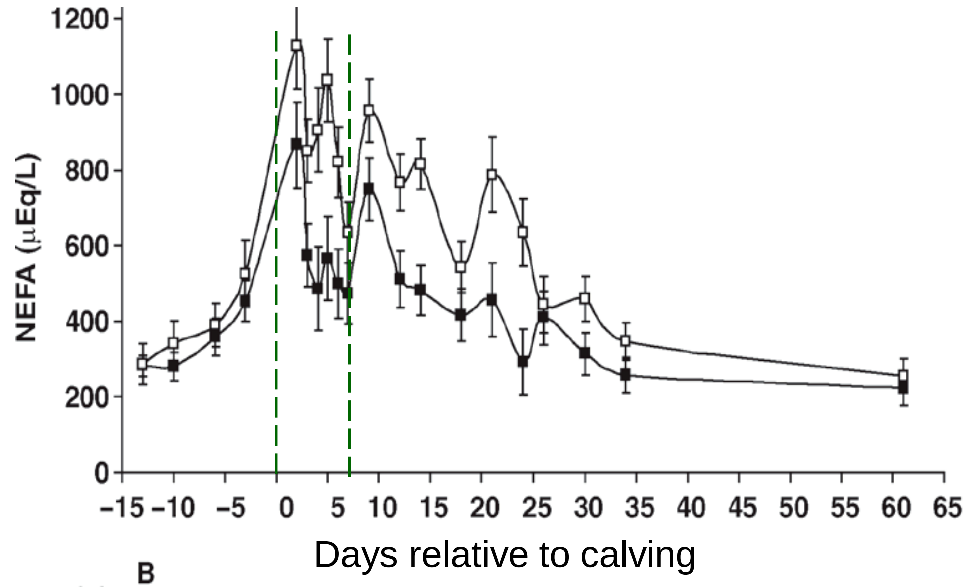


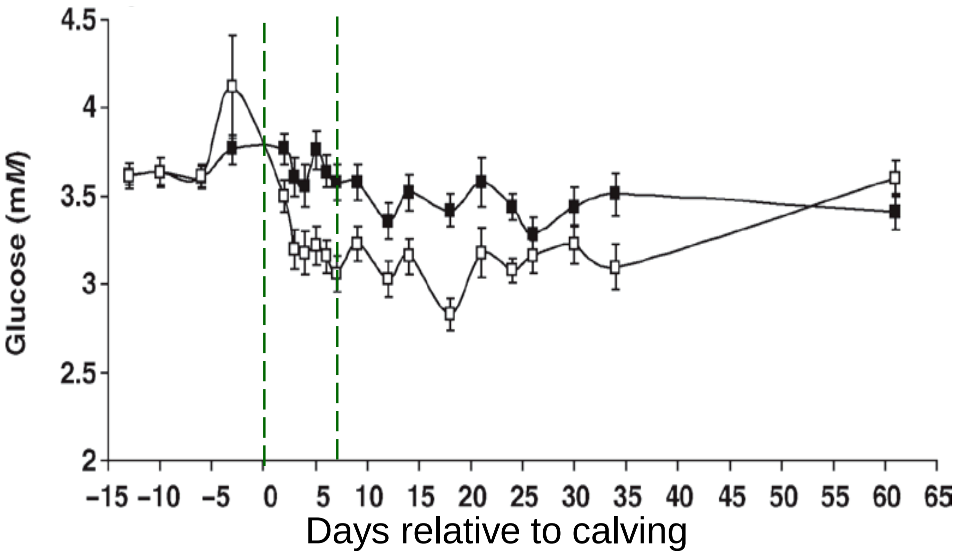
Physiological events in the transition period with relevance for metabolism and immune system

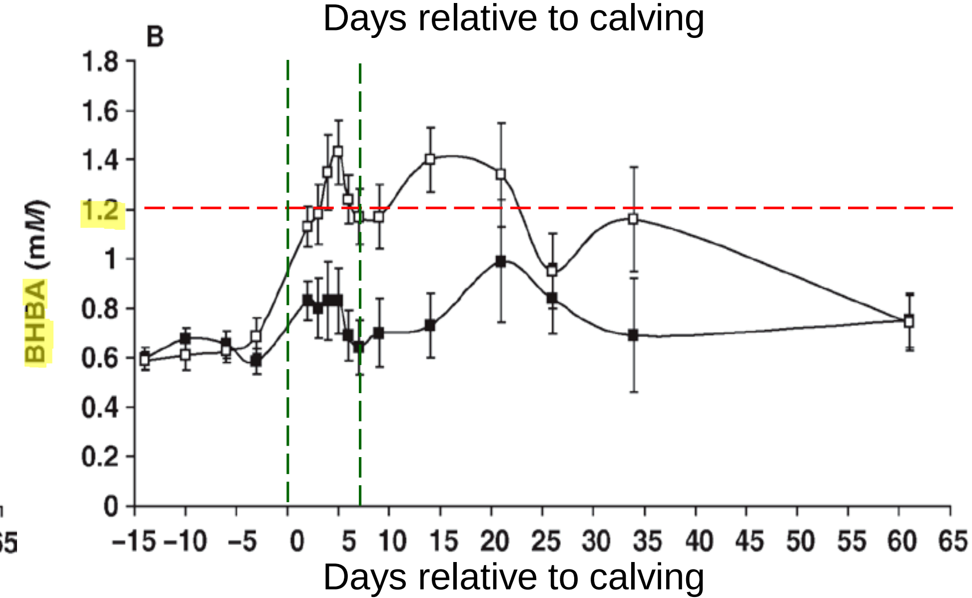


Effects of a decreasing milking frequency from 2 x daily (□) to 1 x daily (■) during the first 7 days *post partum* on milk yield and energy status (Loiselle et al. 2009)

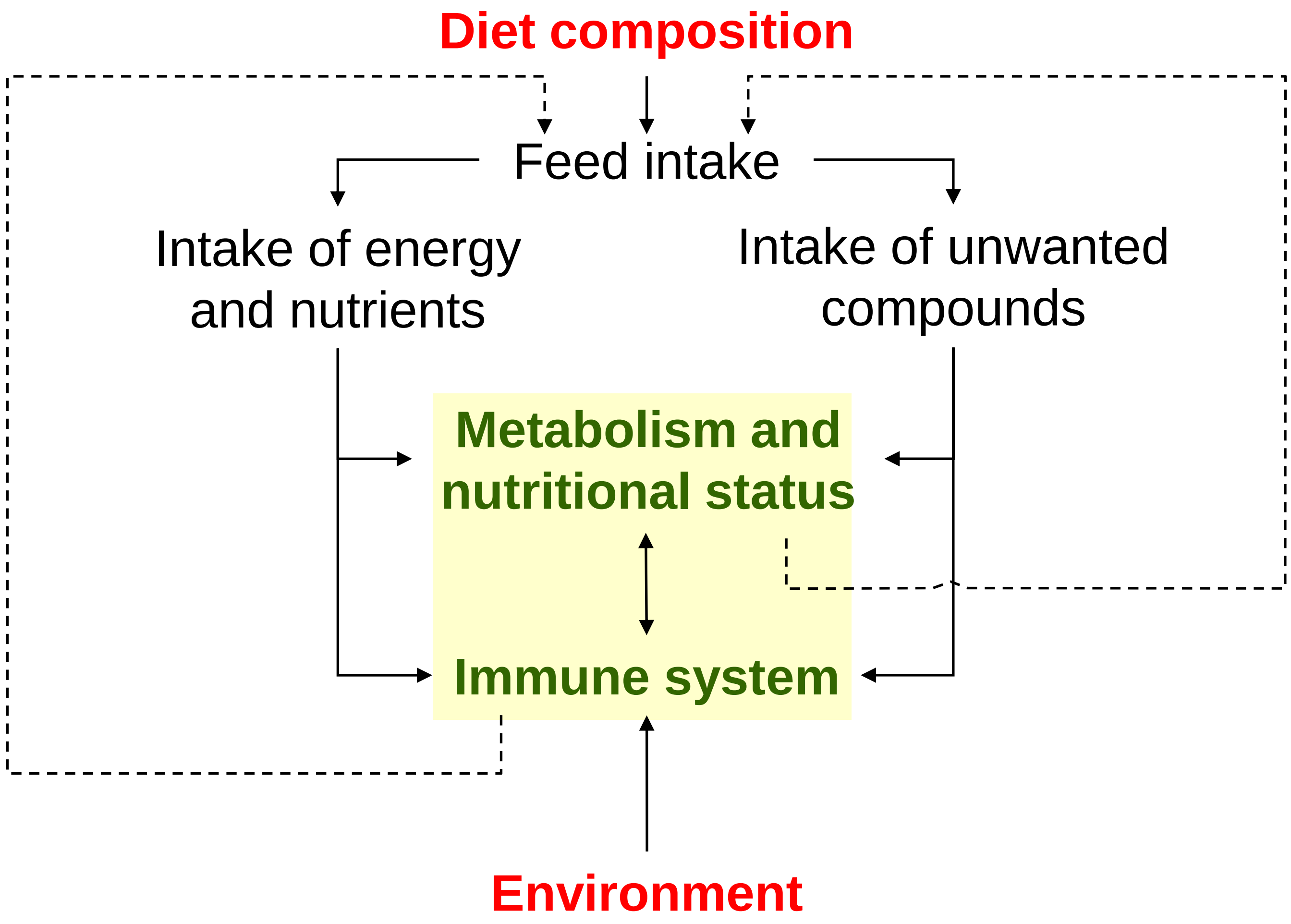








Possible implications of nutrition and other environmental factors on the functionality of the immune system



Many thanks for your attention!