DIPARTIMENTO DI SCIENZE ANIMALI, DELLA NUTRIZIONE E DEGLI ALIMENTI FACOLTA' DI SCIENZE AGRARIE ALIMENTARI AMBIENTALI

UNIVERSITÀ CATTOLICA del Sacro Cuore

LA NUOVA LATTAZIONE INIZIA PRIMA DEL PARTO: IL SEGRETO DEL SUCCESSO NEL PERIPARTO

Convegno finale del Progetto di Grande Rilevanza Cina - MOST e Italia – MAECI

Titolo progetto "Meccanismi di comunicazione tra microbioma ruminale, fegato e sistema immunitario nella regolazione del metabolismo energetico dall'asciutta all'inizio della lattazione nelle vacche da latte"

Paesi partner: Italia Coordinatore Scientifico: Prof. Erminio Trevisi (Università Cattolica S. Cuore)
Cina Coordinatore Scientifico: Prof. Liu Guowen (Jilin University)

Ministero degli Affari Esteri e della Cooperazione Internazionale

中华人民共和国科学技术部
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Executive Programme of Scientific and Technological Cooperation between Italy and China for the years 2024-2025

PROGETTO CRUMLIS

Investigation of crosstalking between rumen microbiome, liver and immune system in regulating energy metabolism from dry off to early lactation in dairy cows.

Scientific Coordinators

for Italy: Prof. Erminio Trevisi (Università Cattolica del Sacro Cuore)

for China: Prof. Guowen Liu (Jilin University)

Jilin University is Located in Changchun, the capital city of Jilin Province in Northeast China

JILIN UNIVERSITY

COLLEGE OF VETERINARY MEDICINE

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SCOPO della nostra UO

Migliorare le conoscenze sul periodo di transizione prolungato (TP), poiché l'insorgenza di alcune malattie metaboliche come la chetosi non è ben compresa e probabilmente potrebbe iniziare prima del parto.

Lo studio dei cambiamenti metabolici e immunitari al momento dell'asciutta (DO) è fondamentale per prevedere i cambiamenti che si verificheranno all'inizio della lattazione.

La risposta infiammatoria e le alterazioni comportamentali evidenziate al momento del dry-off rappresentano un evento stressante.

Approccio multi-omico per caratterizzare i cambiamenti che avvengono dalla DO all'inizio della lattazione, concentrandoci su rumine, fegato, sistema immunitario e ghiandola mammaria.

Collaboration within two Departments

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J. Dairy Sci. 107:8629–8641
https://doi.org/10.3168/jds.2023-24485

Expression of hepatic genes involved in bile acid metabolism in dairy cows with fatty liver

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Ju et al.
Journal of Animal Science and Biotechnology (2024) 15:152
https://doi.org/10.1186/s40104-024-01110-8

Journal of Animal Science and Biotechnology

RESEARCH Open Access

Dietary supplementation with citrus peel extract in transition period improves rumen microbial composition and ameliorates energy metabolism and lactation performance of dairy cows

Lingxue Ju[1†], Qi Shao[1†], Zhiyuan Fang[1], Erminio Trevisi[2], Meng Chen[1], Yuxiang Song[1], Wenwen Gao[1], Lin Lei[1], Xinwei Li[1], Guowen Liu[1*] and Xiliang Du[1*]

Animal Research and One Health

WILEY

AROH ANIMAL RESEARCH & ONE HEALTH

ARTICLE OPEN ACCESS

Growth Hormone Promotes Lipolysis and Impairs Insulin Sensitivity by Activating the ERK/HSL Signaling Pathway in Bovine Adipocytes

Xinxing Gao[1] | Hao Yu[1] | Erminio Trevisi[2] | Cai Lin[3] | Zhiyuan Fang[1] | Xinwei Li[1] | Yuxiang Song[1] | Wenwen Gao[1] | Lin Lei[1] | Xiliang Du[1] | Guowen Liu[1]

1594 Impact of nutrient restriction at dry-off on milk somatic cell composition and transcriptome. L. Cattaneo*[1], V. Lopreiato[2], M. M. Passamonti[1], F. Piccioli Cappelli[1], M. Sfulcini[1], G. Liu[3], E. Trevisi[1], and A. Minuti[1], *[1]Department of Animal Sciences, Food and Nutrition, Università Cattolica del Sacro Cuore, Piacenza, Italy, [2]Department of Veterinary Sciences, Università di Messina, Messina, Italy, [3]Institute of Zoonosis, College of Veterinary Medicine, Jilin University, Changchun, China.*

J. Dairy Sci. Vol. 108, Suppl. 1

Programma:

9:30 Accoglienza – Caffè di benvenuto

10:00 Introduzione, Coordinatore italiano del progetto CRUMLIS, E. Trevisi

10:15 Il periodo di transizione: processi fisiologici e patologici, *A. Minuti.*

10:45 Dalla teoria ai numeri: monitorare la funzionalità epatica nel periparto, *E. Trevisi*

11:15 La messa in asciutta: pausa o opportunità? L'impatto della gestione sull'adattamento metabolico, *L. Cattaneo*

11:45 Mitigare per prevenire: strategie nutrizionali e gestionali nel periparto, *M. Mezzetti*

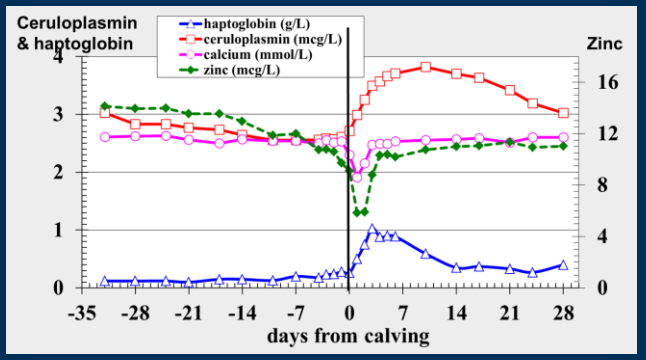
12:15 Discussione generale

12:30 Pranzo

Sono previsti i CFP per gli iscritti all'ordine dei dottori Agronomi

Inquadra il QR per iscriverti

Dalla Teoria ai Numeri: monitorare la funzionalità epatica nel periparto



Erminio Trevisi

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Summary

- **Dal Profilo Metabolico al profile Immuno-metabolico**
- **Indici utili a classificare la severità dei processi infiammatori nel periparto**
  - **LAI (Liver Activity Index)**
  - **LFI (Liver Functionality Index) & come usarlo?**
  - **Indici più rapidi di distress immunometabolico**
- **Prospettive e implicazioni**

Controlli ematici: strumento di "precision health"

PMP classico (popolazione)

Limiti:

1. Pre (-40/-15) e post parto (+30/+90 DIM)
2. costo e tempi
3. finalità principale: individuare errori alimentari

Indicatori:

- energetico, proteico, minerale, vitaminico;
- funzionalità epatica
- PMP progressivamente evoluto, ma ancora migliorabile

PMP «**precision health**» (individuo e SMART)

Limiti:

1. **costo e tempi** di valutazione (superabile …)
2. **numerosità controlli** (quanti animali? quante volte?)
3. **livelli riferimento**

Limiti relativi se:

1. Migliora salute e riduce distress
2. Riduce costo farmaci
3. Risolve domande sociali (es. ↓ uso antibiotici, ↑ welfare)
4. Si opera in precise fasi fisiologiche

Indicatori disponibili o promettenti

1. *negAPP/posAPP (es.LFI, LAI)*
2. *ROM / Antiox Glob/alb*
3. *NEFA, BHB, creatinina*
4. ottimi candidati (es. IL)

Liver response during the inflammation in the TP is crucial for many aspects

Problems are: severity and duration of these responses

Inflammation is not a negative process in se, but can cause concerns when:

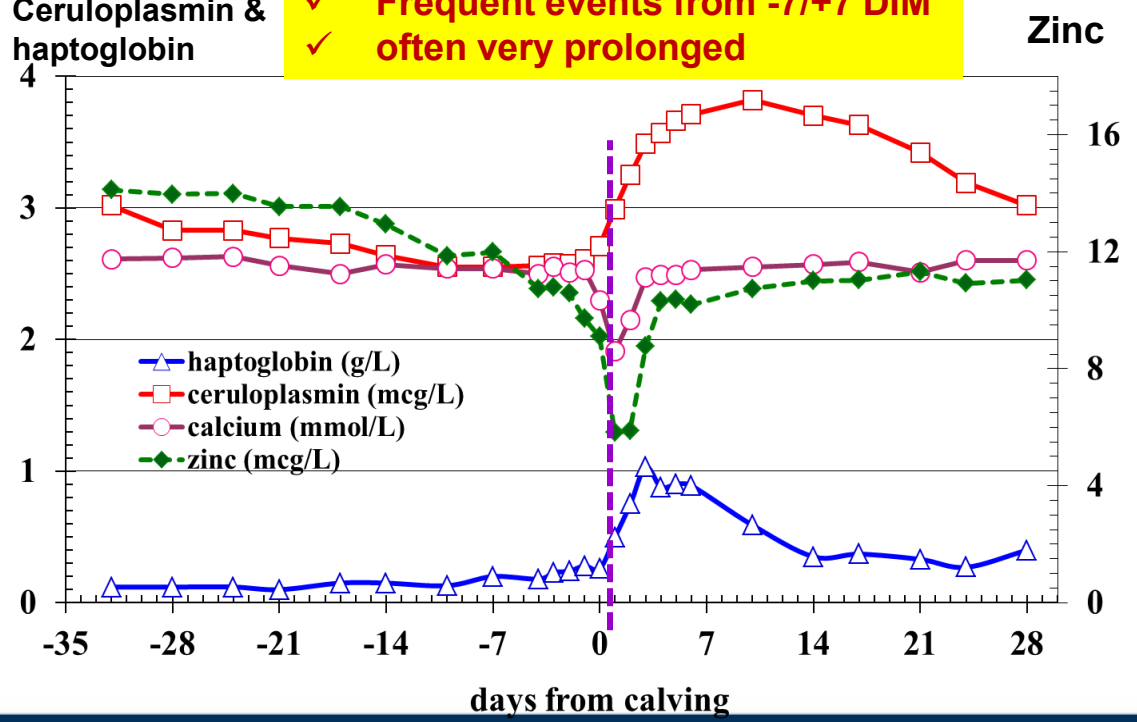
1. Excessive or uncontrolled
2. Reiterated
3. **Resolution is delayed**

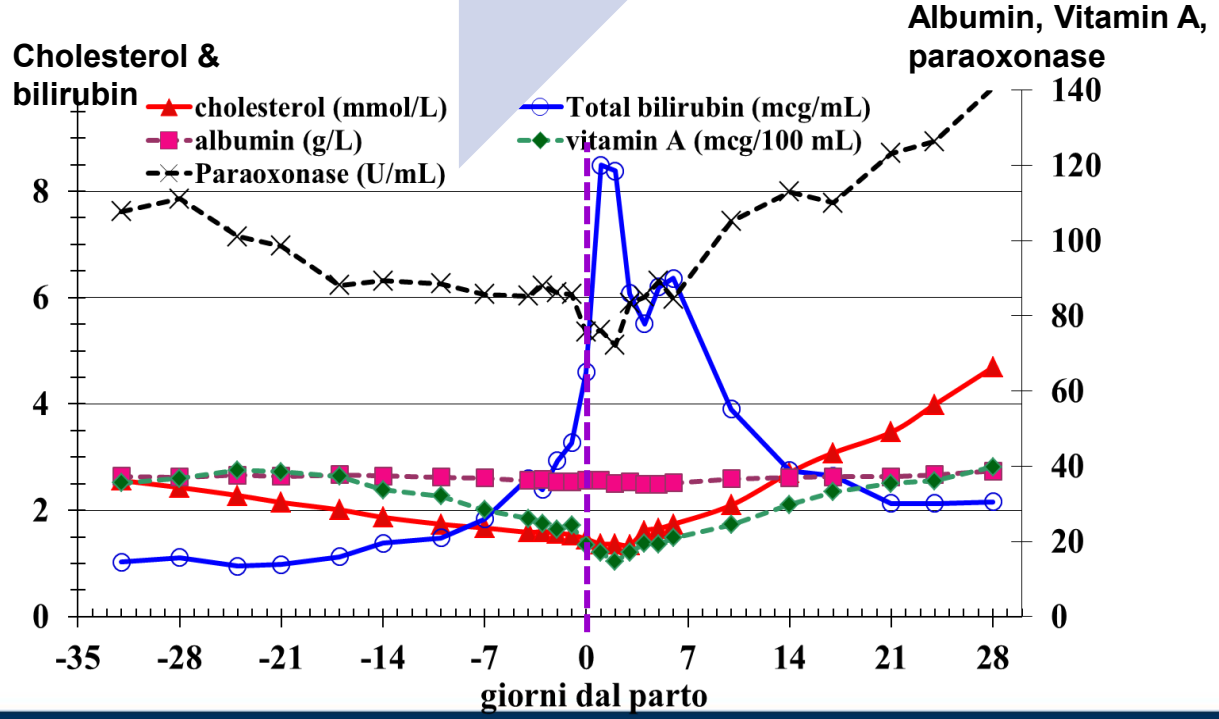
What to measure?

Inflammation presence (i.e. posAPP)?

Inflammation consequences (i.e. negAPP)?

- ✓ **Frequent events from -7/+7 DIM**
- ✓ **often very prolonged**





Assessment of the inflammation severity in TP

- **Biometric Benchmark** (es. threshold/physiological ranges of NEFA; BHB; Hp in different stages) (*Kervin et al., 2021 JDS 105:5327; Premi et al., 2021, Animals 11:1714)*
  - ✓ *strength point*: easy to identify cow at risk
  - ✓ *weakness points*: not consensus on reference ranges; methods analyses; time consuming, costly
- **Composite indices**:
  - **LAI** (Liver Activity Index; *Trevisi et al., 2001; Bertoni et al., 2008, JDS91:3300)*
  - **LFI (Liver Functionality Index;** *Bertoni et al., 2006; Trevisi et al., 2012 RVS 93:695)*
  - **PIRI** (Post-calving Inflammatory Response Index; *Trevisi et al., 2016 IJAS 12(s1):58)*
    - ✓ *strength points*: clusterize cows/herds highlighting critical (subclinical); anticipate attentions of operators
    - ✓ *weakness points*: time consuming, costly, delayed response
  - **Indexes before calving**

Summary

- **Dal Profilo Metabolico al profile Immuno-metabolico**
- **Indici utili a classificare la severità dei processi infiammatori nel periparto**
  - **LAI (Liver Activity Index)**
  - **LFI (Liver Functionality Index) & come usarlo?**
  - **Indici più rapidi di distress immunometabolico**
- **Prospettive e implicazioni**

LAI = liver activity index

Trevisi et al., 2001

parametri

3 parametri ematici, relativi a sintesi usuali del fegato:
- albumina
- colesterolo (=lipoproteine)
- vitamina A (= retinol binding protein)

calcolo

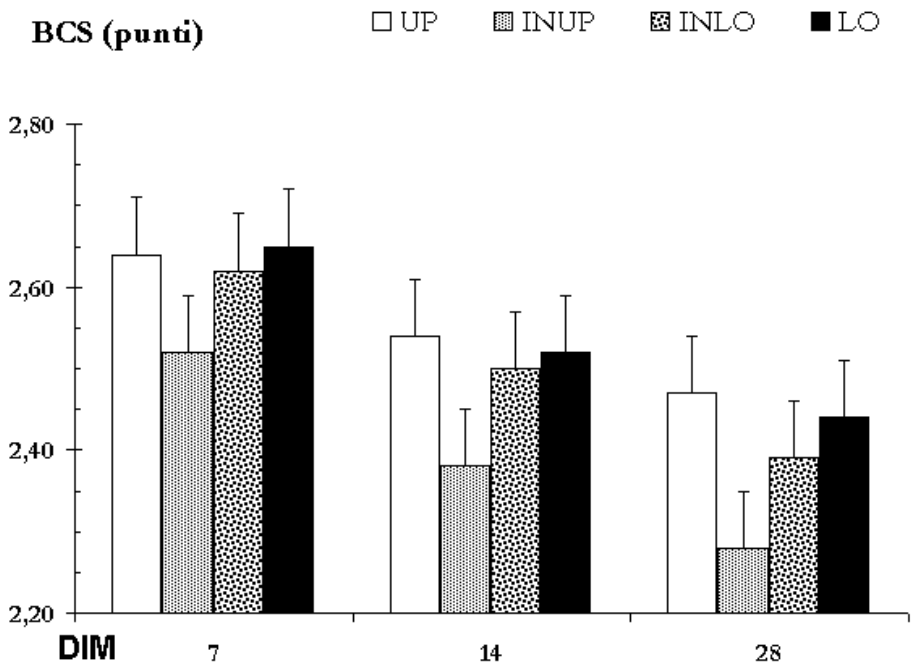
- 3 o 4 misure nel 1° mese di lattazione
- Dati ematici trasformati in unità di deviazione standard (entro ciascun allevamento per diminuire le interferenze tra i 3 parametri)

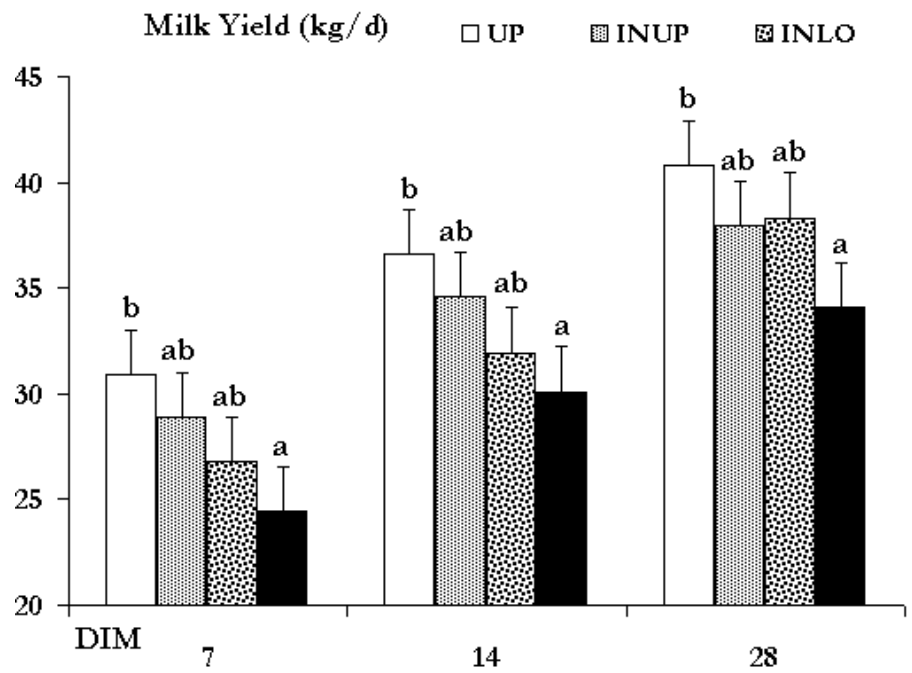
score

- Punteggio finale di ciascuna bovina è pari alla media dei 3 parametri nel 1° mese di lattazione
- Più è alto il punteggio, migliore è l'adattamento alle sollecitazioni del parto e minori sono le conseguenze negative dell'infiammazione

Trevisi et al., 2001; Bertoni *et al.*, *JDS* 2008; Bertoni & Trevisi, 2013; Loor et al., 2013

LAI & produzione





Frequenza dei principali problemi di salute in bovine raggruppate per quartile di Liver Activity Index (LAI): upper (UP), upper intermediate (INUP), lower intermediate (INLO), lower (LO).

	Gruppo				*P*-value
	UP	INUP	INLO	LO	
Problemi di salute[1]					
Al parto[2]	0.0 [a]	5.0[a]	36.9[b]	21.1[b]	<0.01
Dopo il parto[3]	5.3[a]	30.0[b]	42.2[b]	31.7[b]	0.21
Metriti	0.0[a]	5.0[a]	5.3[a]	26.3[b]	0.02

[a,b] Effetto tra i gruppi ($P < 0.05$).
[1] Frequenza dei problemi, espresso come percentuale di bovine con almeno un problema
[2] Distocia, Collasso Puerperale, Ritenzione di placenta (metriti escluse)
[3] Chetosi, zoppie, mastiti

77 bovine gravide, 3 allev. (120 capi controllati), confronto tra quartili di LAI

Bertoni et al., 2008 - JDS, 91:3300-3310m

Inflammation at calving & fertility

Bertoni et al., 2008 - JDS, 91:3300-3310

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UP-LAI group (the more productive) showed the best fertility

Item	UP n = 19	INUP n = 20	INLO n = 19	LO n = 19
Services per pregnancy* (n°)	1.65±1.3^{a}	2.04±1.6^{ab}	2.68±1.5^{b}	2.01±1.5^{ab}
Open Days* (DIM)	92.9±48^{a}	132.5±89^{b}	138.8±89^{b}	110.5±55^{ab}
Conception rate at 1st service (%)	52.6	45.0	21.0	36.8
Repeat breeders (at least 3 services)	21.0	45.0	57.9	31.6

*after logarithmic transformation

Inflammation (clinical or subclinical) affects fertility.

Less than 50% of cows in LO/INLO groups showed clinical signs.

Concentrations of –APP are more suitable to identify the metabolic distress in early lactation

Inflammation delays the resumption of cyclicity in cows

(30.0±2.5 vs 18.4±0.8 DIM in LO & HI-LAI)

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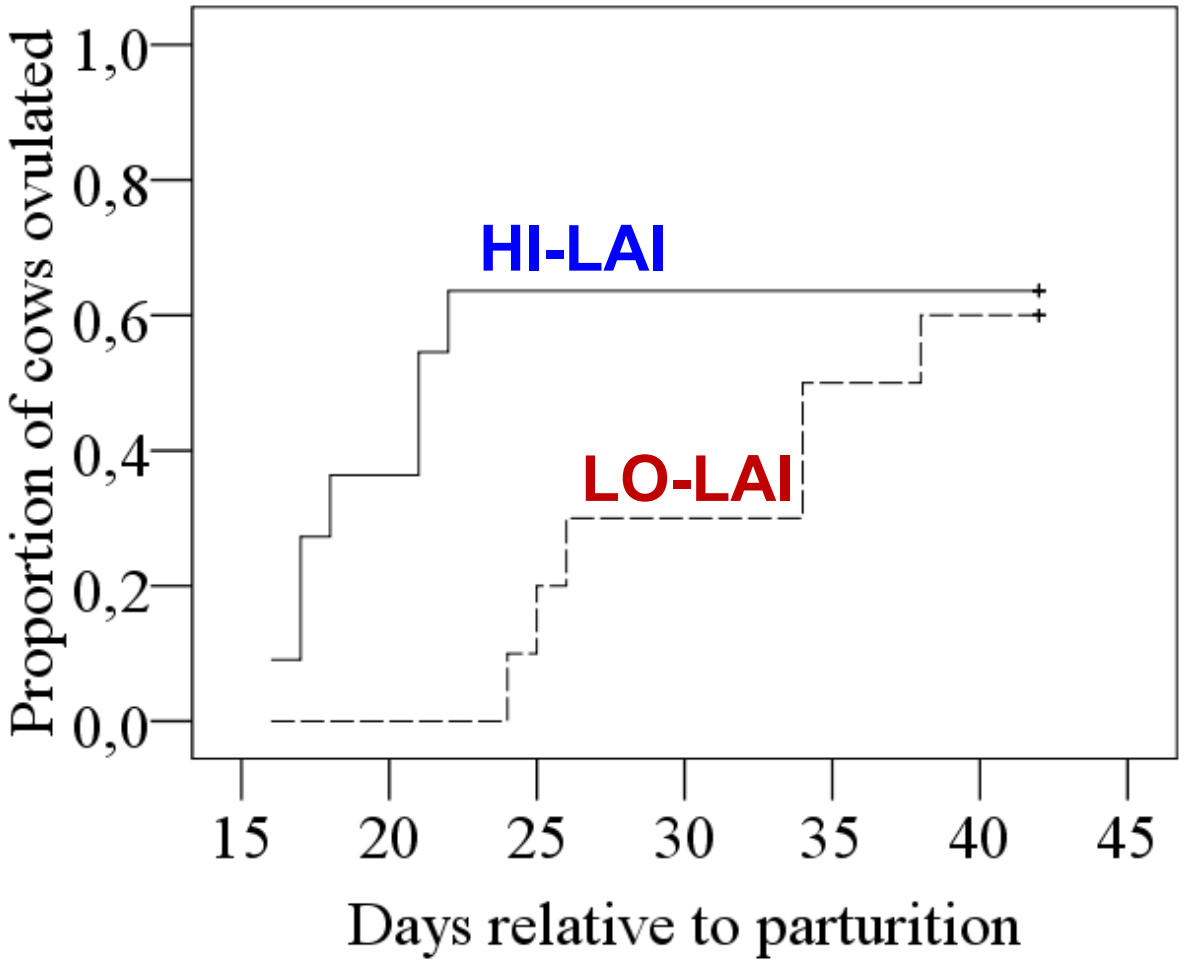
Cumulative survival chart representing the proportion of 21 high-yielding dairy cows that have ovulated during the first 42 DIM.

Cows were classified according to their LAI:
group 1 (LO-LAI, dashed line; N = 10) had a lower index value, suggestive of more pronounced inflammation, compared to
group 2 (HI-LAI, solid line; N = 11).



Osservations on cows of Bossaert et al.,
Vet. J. 2011, 192(2):222-225

LFI = Liver Functionality Index

Bertoni et al., 2006 57th EAAP Meeting, 17-20 Sept, Antalya, Turkey, pp 325
Bertoni & Trevisi 2013. Vet. Clin. North Am. Food Anim. 29(2):413–431

parameters

3 plasma biomarkers routinely synthesized by the liver:
albumin
cholesterol (= lipoproteins)
total bilirubin (= indirect measure of enzymes needed for clearance)

calculation

- **2 measurements in the 1st month of lactation** (3 and 28 DIM)
- I step: index of each biomarker: for albumin & cholesterol= 50% VI + 50% I; for bilirubin = 67% VI + 33% R (VI = value at 3 DIM; I = increase from 3 to 28 DIM; R = reduction from 3 to 28 DIM)
- II step: Normalization of indices obtained in the I step, with reference values (X± SD) obtained from healthy cows and good performances (Bertoni et al., 2008)

$$LFI = \frac{albumins\ index - 17{,}71}{1{,}08} + \frac{cholesterol\ index - 2{,}57}{0{,}43} - \frac{bilirubin\ index - 6{,}08}{2{,}17}$$

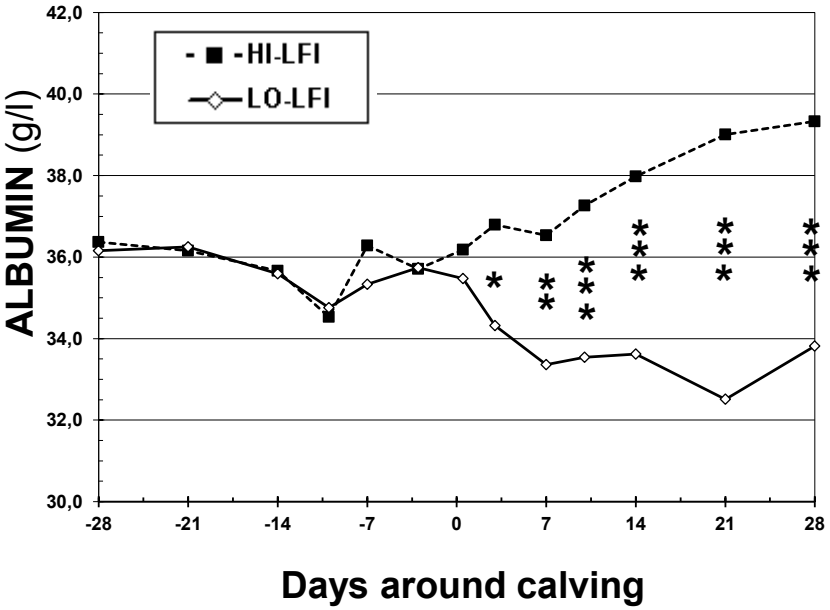
score

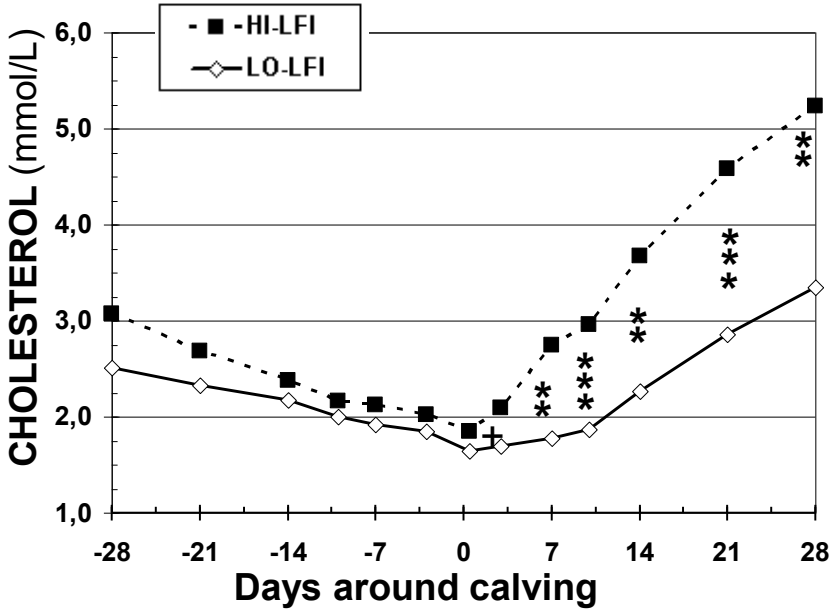
- **Final score of each cow is the sum of the normalized indices**
- The individual value can be compared within herd (clustering cows), across herds (ranking farms) …
- **More is high the LFI score and better is the adaptation** (with lower consequences due to inflammation)

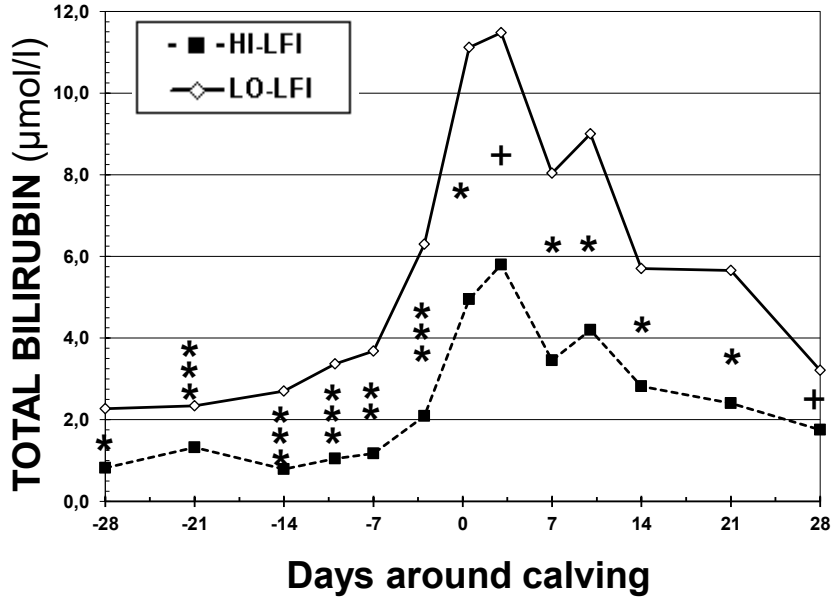
LAI e LFI: r = 0.87; P<0.001 (Trevisi et al., 2010)

LFI = Liver Functionality Index
(levels & evolution of biomarkers in TP)

Direct (albumin, cholesterol) and indirect (bilirubin) indices of negAPP response in plasma samples of periparturient cows with high (**HILFI**) and low (**LOLFI**) LFI.
(*Trevisi et al., 2012 Res Vet Sci 93:695-704*)







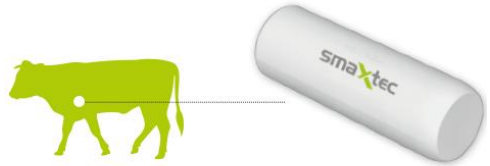
Detection inflammation before calving: body temperature

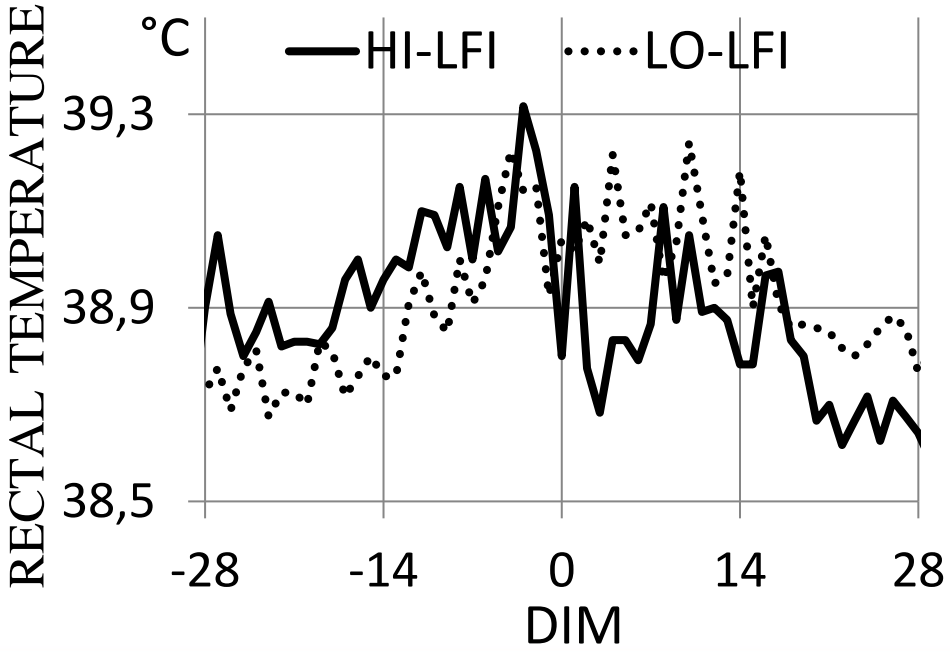
Low vs high LFI (*Trevisi et al., 2010 - 3rd EAAP ISEP – PR*):

- Higher frequency of diseases
- Higher body temperature in early lactation
- Higher CuCp before calving and slower recovery of physiological levels of +APP in the postpartum

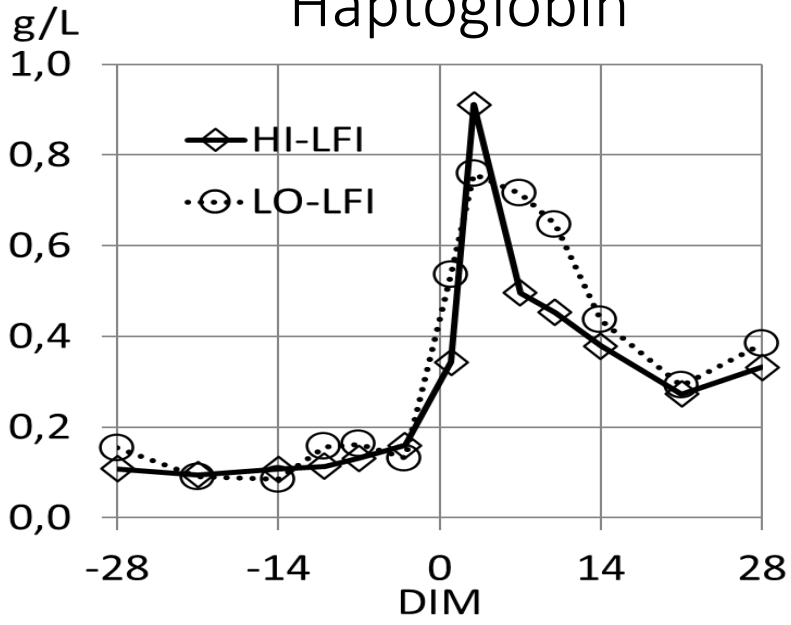
PLF

T° in line
(i.e. rumen sensors)

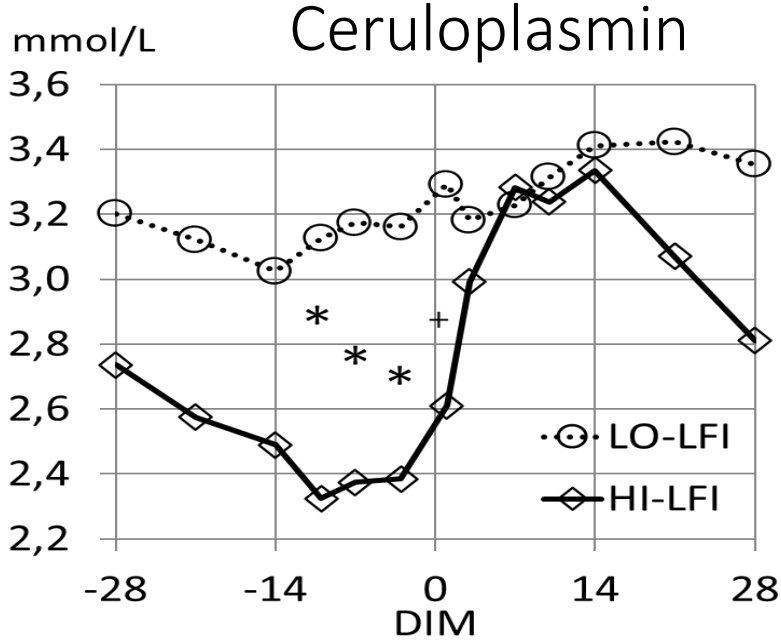




Haptoglobin



Ceruloplasmin



LFI e stato salute

Table 1 - Frequency of main health problems observed in the first month of lactation in multiparous dairy cows, belonging to two herds ranked in tertiles of Liver Functionality Index (LFI): low (LOLFI), intermediate (INLFI), high (HILFI) LFI. Different subscripts among groups of LFI within each herd indicate statistical differences (P<0.05).

Herd	groups of LFI	cows	LFI		RP	MET	KET	MAST	LAM	Fever	Other	Overall health problems	Disease/ cow	Cows without clinical signs
		n.	*average*	*st dev*	*n.*	*n.*	*n.*	*n.*	*n.*	*n.*	*n.*	*n.*	*n./cow*	*n.*
1	**LOLFI**	7	-3,02^{a}	1,50	3	1	1	3	0	2	3	**13**	**1,86^{c}**	**2**
	INLFI	6	-0,54^{b}	0,52	1	0	1	2	0	1	1	**6**	**1,00^{ab}**	**1**
	HILFI	7	1,27^{c}	0,57	0	0	0	1	0	1	0	**2**	**0,29^{a}**	**5**
2	**LOLFI**	11	-3,76^{a}	1,37	1	2	2	1	0	6	9	**21**	**1,91^{c}**	**2**
	INLFI	12	-1,13^{b}	0,80	0	4	1	1	1	4	2	**13**	**1,08^{ab}**	**5**
	HILFI	11	1,94^{c}	1,24	0	2	0	1	1	2	2	**8**	**0,73^{a}**	**4**
1+2		54	-0,91	2,39	5	9	5	9	2	16	17	63	1,17	19

Note: LFI = Liver Functionality Index; RP = retained placenta; MET = metritis; KET = ketosis; MAST = mastitis; LAM = lameness; Fever = rectal temperature > 39.5°C (also without additional clinical signs); Other = other health problems with clinical signs

Trevisi et al. 2014. RVS 96(2):229-233

LFI e spese per farmaci

Table 2 - Average costs (euro/cow) for the drug treatments in the first month of lactation in multiparous dairy cows, belonging to two herds ranked in tertiles of Liver Functionality Index (LFI): low (LOLFI), intermediate (INLFI), high (HILFI) LFI. Different subscripts among groups of LFI within each herd indicate statistical differences (P<0.05).

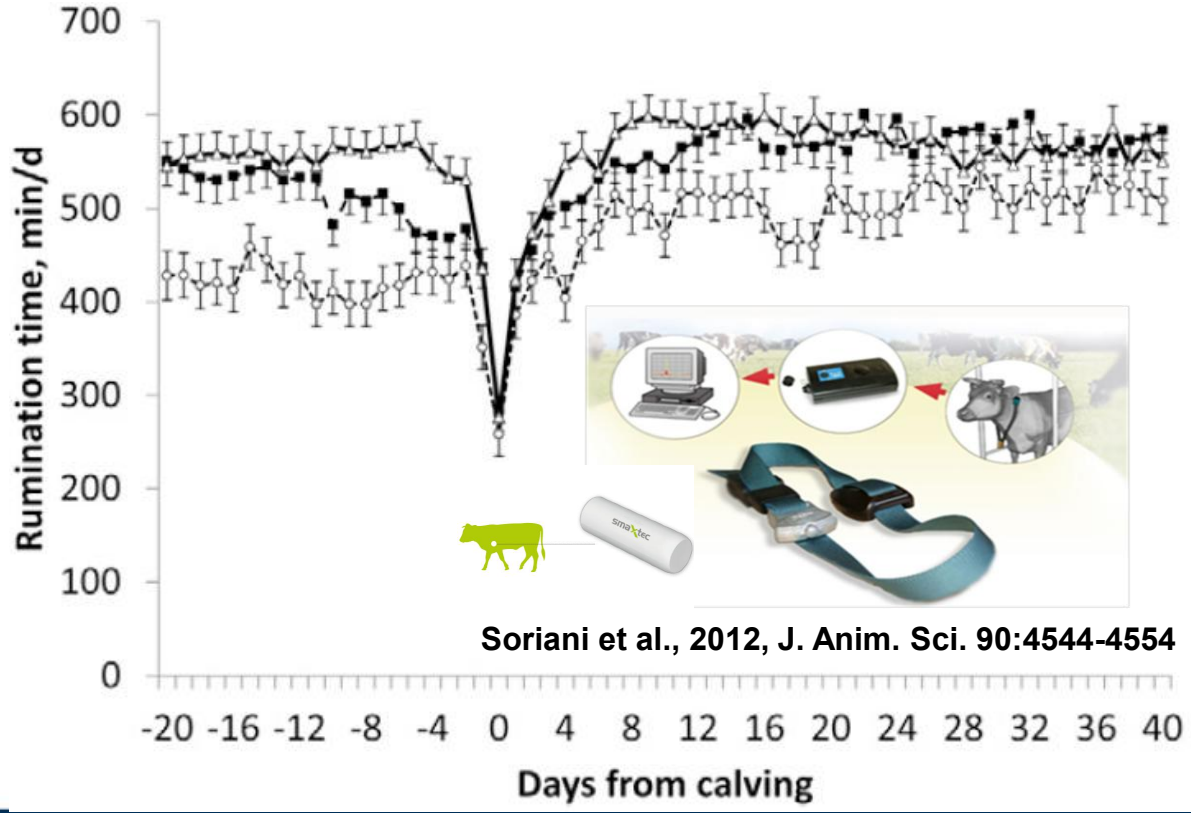
Herd	grup of LFI	cows	antibiotics (1)		other drugs (2)	galenic (3)	overall
			treatments		cost		
		n.	*n./cows*		*euro/cow*		
1	LOLFI	7	1,71^{b}	53,9^{b}	47,06^{b}	15,65^{b}	**116,6^{b}**
	INLFI	6	0,50^{a}	8,6^{a}	10,45^{a}	10,63^{ab}	**29,7^{a}**
	HILFI	7	0,29^{a}	8,5^{a}	17,37^{a}	1,22^{a}	**27,1^{a}**
2	LOLFI	11	0,73	11,9	17,6	23,7	**53,2**
	INLFI	12	0,58	13,6	12,0	20,6	**46,1**
	HILFI	11	0,36	10,0	5,1	14,2	**29,3**
Overall		54	0,66	16,5	16,8	15,7	**49,0**

Note: (1) includes antibiotics used intramuscolar (i.m), endovenous(e.v.), intramammary, intrauterine; (2) includes antiinflammatories and other drugs which require the discard of milk after their use; (3) vitamins and minerals supplied orally, i.m. or e.v. (without withdrawal time)

Trevisi et al. 2014. RVS 96(2):229-233

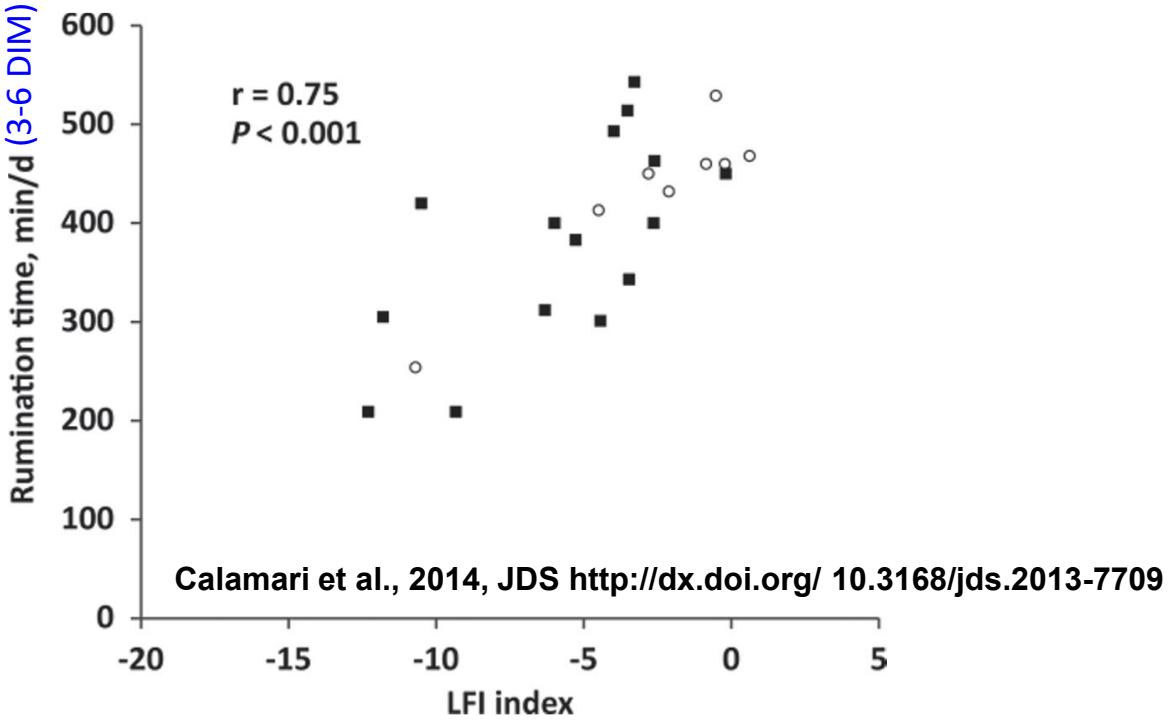
Detection of inflammation before calving: Rumination time

Daily behavior of rumination time (least squares means and SEM) during the transition period in **cows categorized according to the rumination time before calving** *(dotted line with open circles: short rumination time; dashed line with solid squares: middle rumination time; solid line with open triangles: long rumination time).*



Soriani et al., 2012, J. Anim. Sci. 90:4544-4554

The rumination time before and after the calving is negatively associated with LFI score

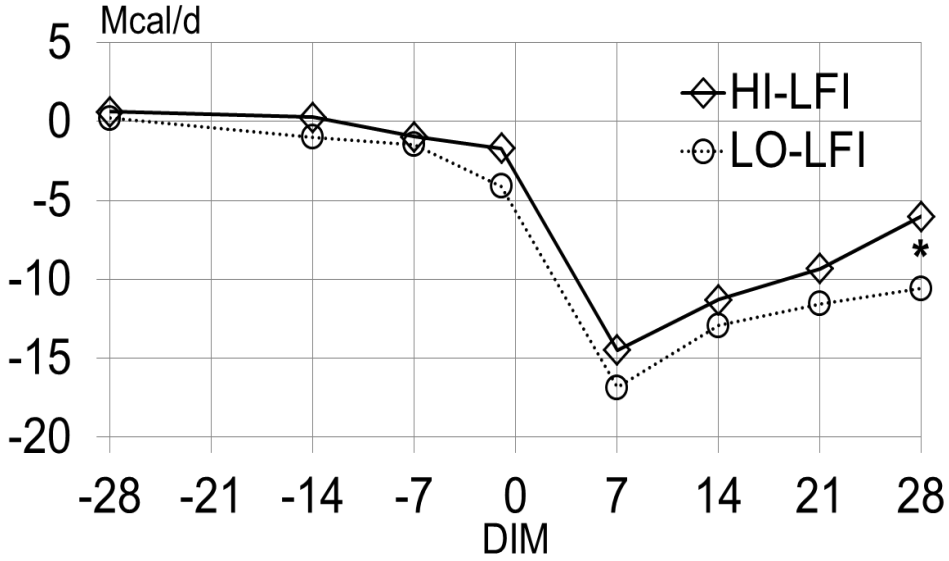


Calamari et al., 2014, JDS http://dx.doi.org/ 10.3168/jds.2013-7709

Low rumination (<450 min/d) before calving &/or **severe reductions** (before or after calving) are strictly related to worsen immunometabolic conditions and predict poor performances in TP

LFI, bilancio energetico ed efficienza nel TP

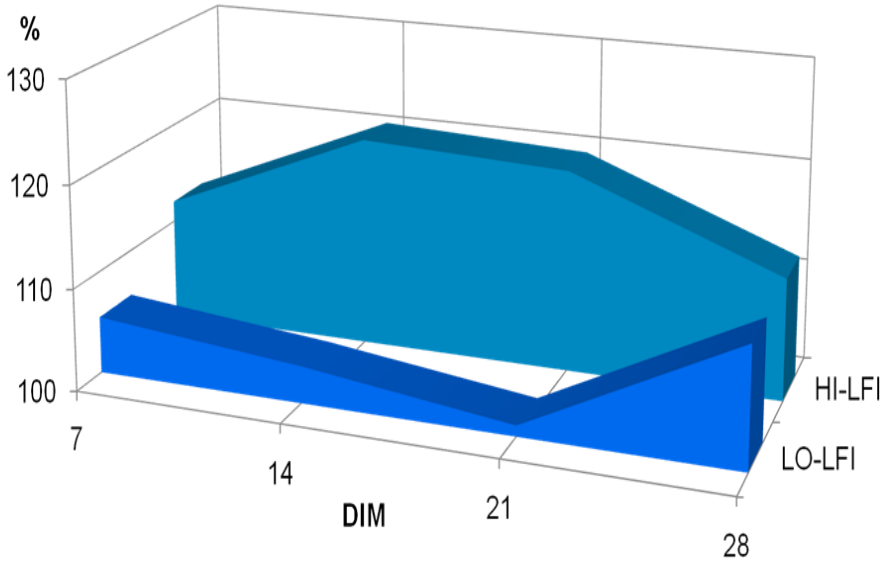
ENERGY BALANCE



stronger NEB in LO-LFI in the 1st month of lactation (P<0.10)

NEB started earlier in LO-LFI

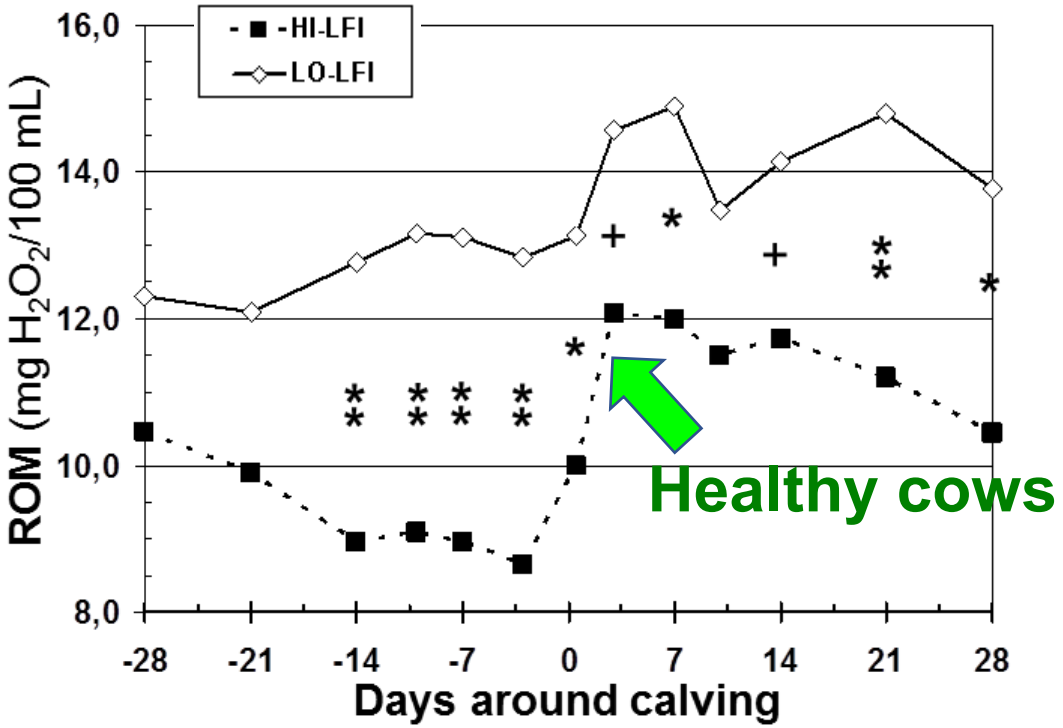
NET ENERGY EFFICIENCY



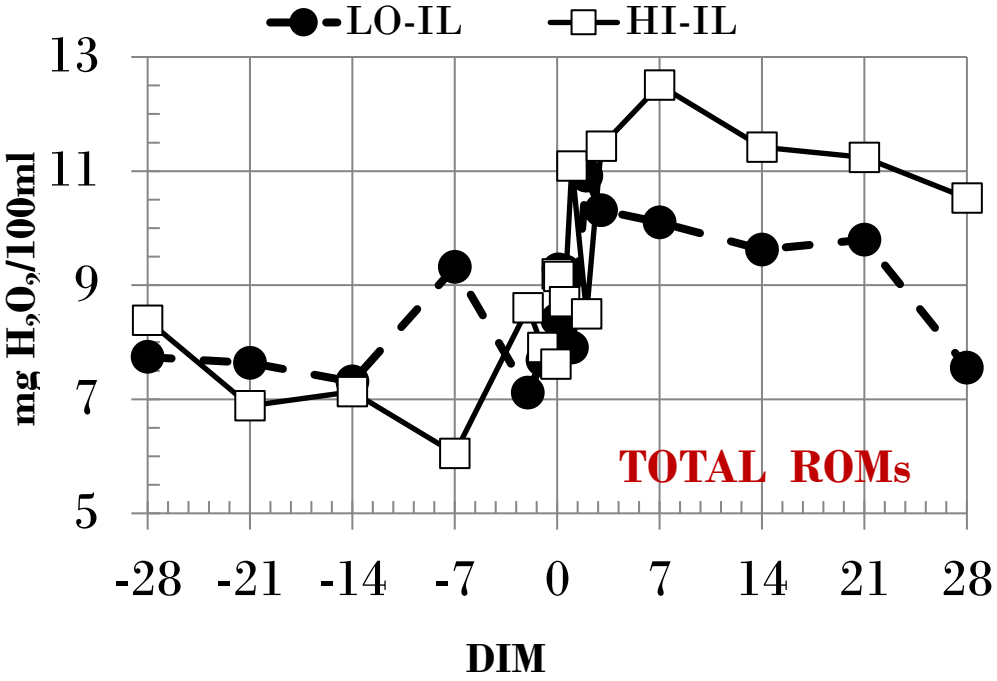
Higher efficiency in HI-LFI (+15% vs LO-LFI)

Trevisi et al., 2010 - 3rd EAAP ISEP - PR

LFI (e IL) & stress ossidativo



*Pattern of changes of ROMs during the transition period in cows with **low** (LO-LFI) or **high** (HI-LFI) **Liver Inflammatory Index** (Trevisi et al., 2012 Res Vet Sci 93:695-704)*



*Variations of ROMs (Reactive Metabolites of Oxygen) during TP in cows with **low** (LO-IL) or **high** (HI-IL) **plasma IL-6 levels during the last month of pregnancy** (Trevisi et al., 2011 IJAS,10:S1:105)*

LFI & amino acids

- **Retrospective grouping of cows with LFI level**

- Cows were ranked retrospectively and assigned to 4 groups regardless of methionine (MET) or choline (CHOL) supplementation
  - **L**: Low group (LFI<0);
  - **ML:** Medium-low group (0 < LFI < 1.5);
  - **MH:** Medium-high group (1.5 < LFI < 3);
  - **H:** High group (LFI > 3);

Most (13/20) MET cows fell into the MH and H groups
CHOL cows were evenly distributed across the 4 LFI groups.

Better production performance in cows with higher LFI

DMI, Milk yield and components

Zhou et al., 2016 JDS

Parameter	LFI L	LFI ML	LFI MH	LFI H	SEM[1]	*P*-value LFI	*P*-value Day	*P*-value LFI×Day
Prepartum								
DMI (kg/d) ↑	11.59^{d}	13.54^{c}	14.67^{bc}	15.87^{ab}	0.70	< 0.01	< 0.01	0.43
Postpartum								
DMI (kg/d) ↑	16.14^{cd}	17.86^{c}	21.26^{ab}	21.78^{a}	0.82	< 0.01	< 0.01	0.70
Milk yield ↑	36.24^{d}	41.89^{c}	48.04^{ab}	49.54^{a}	2.03	< 0.01	< 0.01	< 0.01
Milk fat yield	1.35^{b}	1.62^{a}	1.56^{ab}	1.58^{ab}	0.09	0.11	< 0.01	0.07
Milk protein yield ↑	1.09^{d}	1.35^{c}	1.49^{bc}	1.61^{ab}	0.06	< 0.01	< 0.01	< 0.01
Milk components								
Fat	3.90^{d}	4.02^{cd}	3.33^{a}	3.27^{ab}	0.18	< 0.01	< 0.01	0.78
Protein ↑	3.12	3.35	3.19	3.35	0.11	0.34	< 0.01	0.10
SCC[6]	1.86	2.02	1.74	1.81	0.13	0.36	0.02	0.89
Lactose	4.61	4.67	4.76	4.77	0.05	0.07	< 0.01	0.85
Total solids	12.25^{b}	12.97^{a}	12.11^{b}	12.28^{b}	0.24	0.04	<0.01	0.35
Other solids ↑	5.52	5.60	5.68	5.70	0.05	0.06	<0.01	0.93
MUN	13.65^{ac}	12.04^{bd}	14.04^{a}	12.16^{cd}	0.57	0.02	0.29	0.46

Greater BCAA concentrations in cows with higher LFI

Plasma BCAA concentrations

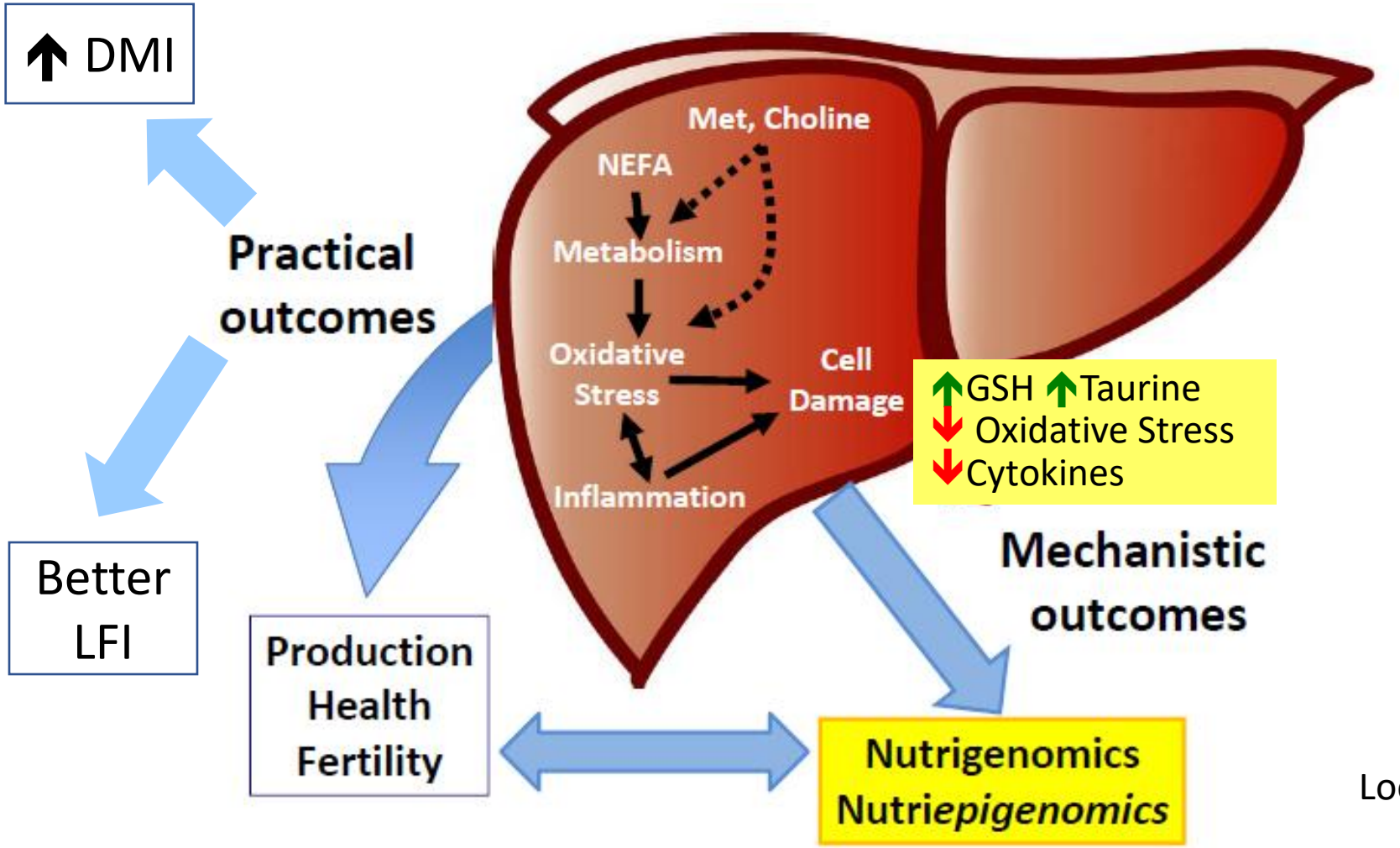
Amino acids (μmol/L) ↑	LFI					*P*-value		
	L	ML	MH	H	SEM[1]	LFI	Day	LFI×Day
Valine	230.29^{b}	229.29^{b}	238.15^{b}	278.86^{a}	13.25	0.03	< 0.01	0.88
Leucine	159.01^{b}	154.46^{b}	157.19^{b}	187.28^{a}	9.31	0.05	< 0.01	0.76
Isoleucine	94.46^{b}	98.19^{b}	101.43^{b}	120.47^{a}	5.97	0.02	< 0.01	0.56
BCAA	484.27^{b}	482.63^{b}	495.65^{b}	586.64^{a}	26.76	0.02	< 0.01	0.82

- **BCAA absolutely essential for lymphocytes to synthesize protein, RNA, DNA. During LPS stimulation their concentration severely decreased (Calder, 2006).**
- **In mice, dietary BCAA restriction impairs several aspects of the immune function and increases the susceptibility to pathogens (Tsukishiro et al., 2000).**

Increased availability of all 3 BCAAs may be beneficial to protein synthesis in immune cells & help mounting an optimal immune response.

Zhou et al., 2016 JDS

Effects of rumen-protected methyl donors in the liver



Loor, 2015 (modified)

Research in Veterinary Science 106 (2016) 84–88

Contents lists available at ScienceDirect

Research in Veterinary Science

journal homepage: www.elsevier.com/locate/rvsc

Reduction of liver function delays resumption of postpartum ovarian activity and alters the synthesis of acute phase proteins in dairy cows

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ARTICLE INFO

Article history:
Received 27 March 2015
Received in revised form 9 February 2016
Accepted 21 February 2016

Keywords:
Liver Functionality Index
Ovarian activity
Haptoglobin
Paraoxonase
Albumin

ABSTRACT

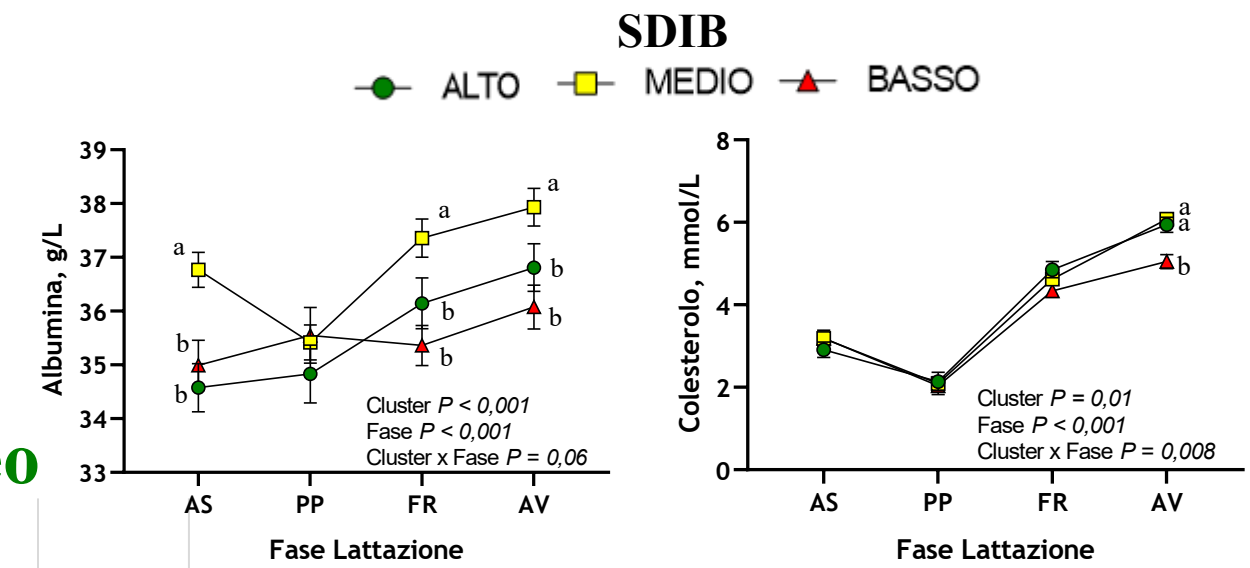
The aim of this study was to evaluate the concentration of acute phase proteins, milk production, and resumption of postpartum ovarian activity of clinically healthy dairy cows in a semi-extensive system with different Liver Functionality Index (LFI) values. The animals were divided into two groups: Low LFI (LLFI: −7 to −12; n: 10) and High LFI (HLFI: −7 to −4; n: 10). Animals with LLFI had lower paraoxonase activity and lower albumin concentration in the pre- and postpartum periods ($P < 0.05$), higher non-esterified fatty acids prepartum ($P < 0.005$), and higher haptoglobin concentration postpartum ($P < 0.01$). The LLFI group showed lower resumption of ovarian activity until 44 days postpartum (29%; $P < 0.05$) than HLFI (86%). Milk production did not differ between groups. Therefore, this study suggests that the LFI is an important biomarker of synthesis of acute phase proteins and the first ovulation interval, and it can be used to improve the production and reproductive performance.

A better LFI means better fertility & confirms our data

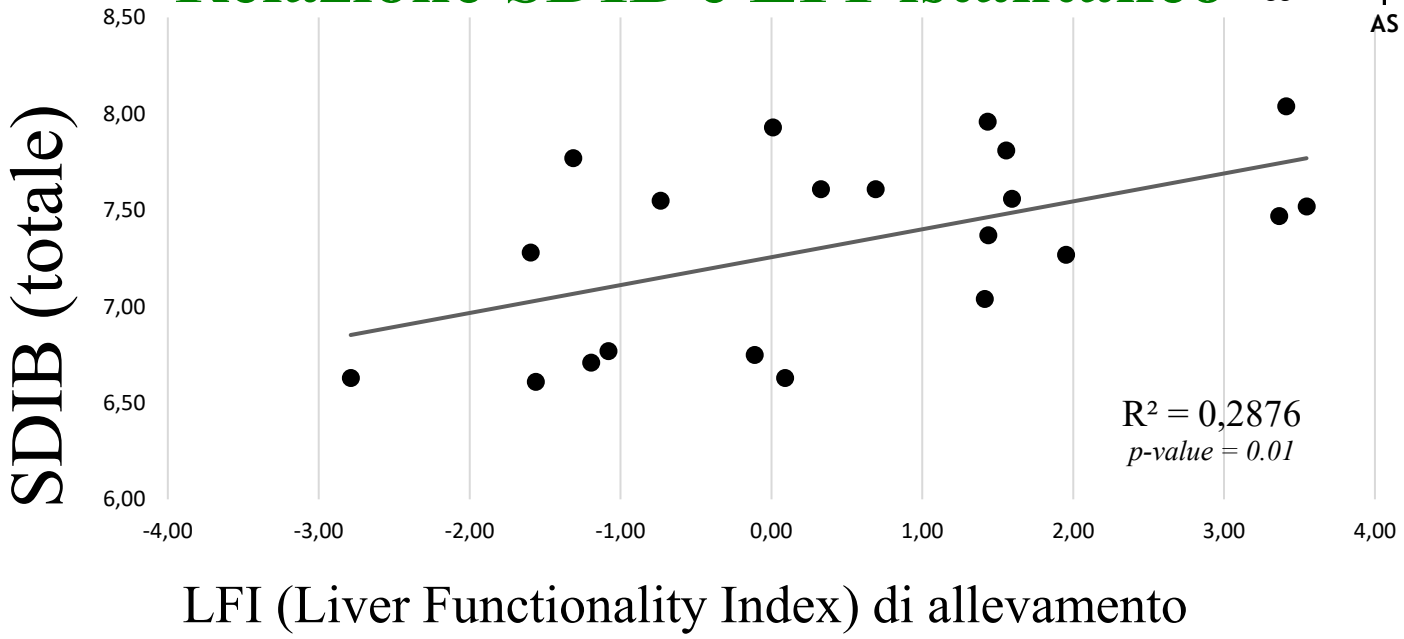
(Bertoni et al., 2008 JDS, 91:3300-3310; Bossaert et al., 2011 Vet.J. 192:222-225)

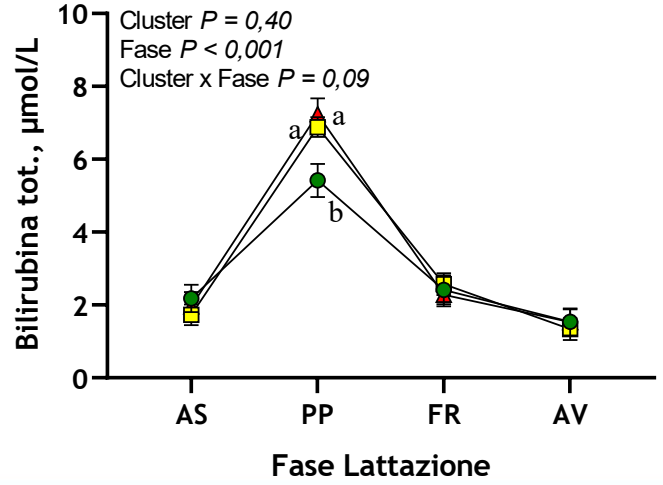
LFI è associato col livello di Benessere (modello SDIB-Ideal - *Premi et al., 2021, Animals 11:1714*)

24 Allevamenti
LFI istantaneo (prelievo stesso momento a soggetti a 3 e 28 DIM)



Relazione SDIB e LFI-istantaneo





LFI can predict the success of TP

Trevisi et al., 2011 (ISBN 979-953-307-033-8)

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MEASURED DATA

Cows with high (vs low) values of LFI

- ↑DMI (+13%) ↑ rumination
- ↓ reserves mobilization (~30% less)
- ↑ milk production +10%
- Better immune response [lower liver APR; fewer clinical diseases (-85%), lower rectal T°]
- less severe NEB: -21%; less sever N balance: -13%
- ↓ Maintenance energy (less energy & AA for immune system)
- ↑ efficiency: +15% en. & MP
- ↑ welfare
- ↑ fertility
- ↓ GHG
- ↑ longevity

Utilizzo dell'LFI in allevamento

- **SCOPO: indice di adattamento/resilienza delle bovine durante il TP. Identifica soggetti con problemi subclinici e prevede prossime patologie** (entro prime settimane lattazione)
- **All'interno della mandria identifica soggetti:**
  - **con problemi subclinici (a 30 DIM) che:**
  - **che necessitano ancora di attenzione e cure**
  - **a maggior rischio di infertilità**
- **Tra allevamenti consente di:**
  - **classificare "buoni" vs "scarsi" nel TP**
  - **monitorare stato di salute e livello di benessere nel periparto**

Si può anticipare diagnosi rispetto a LFI?

✓Allevatori e tecnici desiderano strumenti più tempestivi: indici che segnalano soggetti (clinici e subclinici) a rischio entro 7 DIM

✓Es. PIRI (**Post-calving Inflammatory Response Index)**

- strumento diagnostico veloce
- considera vari aspetti coinvolti nella risposta
- sorprende casi subclinici a 3-7 DIM
- *sfuggono patologie che sviluppano successivamente*

✓PIRI va approfondita sua efficacia valutando:

- costo/benefici (prime applicazioni promettenti)
- indicazioni in combinazione con strumenti "in line"

PIRI Post-calving Inflammatory Response Index

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bovine

56 bovine, frequentemente controllate nel periparto (tra -28 e +28 DIM) per stato salute, prod. latte, BCS, ampio profilo metabolico

selezione

- Analisi delle COMPONENTI PRINCIPALI: scelti 4 parametri che al 7° DIM spiegavano meglio performance entro 28 DIM: aptoglobina (HP), reactive oxygen metabolites (ROM), colesterolo (CHOL) e paraoxonasi (PON)

score

- Ad ogni parametro attribuito score tra: 10 (migliore) e 0 (peggiore), su base bibliografica

Tab. 1 – Extreme score for each parameters

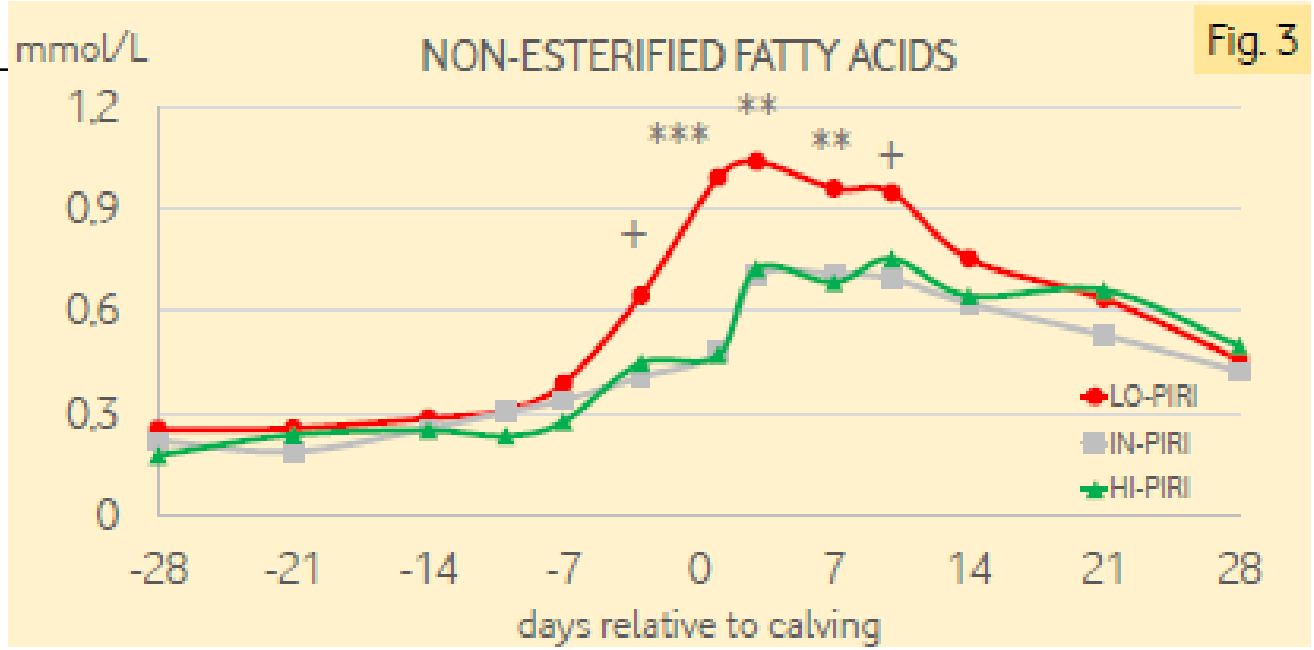
Parameter	Max score = 10	Min score = 0
Haptoglobin [g/L]	≤ 0.3	≥ 1.5
ROM [mg H_2O_2/100 mL]	≤ 11	≥ 18
Cholesterol [mmol/L]	≥ 3	≤ 2
PON [U/mL]	≥ 120	≤ 60

Grossi et al., 2013. XX ASPA Congress , BO, June 11-13 2013

PIRI Post-calving Inflammatory Response Index

- ✓ Sulla base degli estremi dell'intervallo di riferimento è stata definita per ciascun parametro una regressione lineare, al fine di attribuire un punteggio a ciascun soggetto
- ✓ PIRI = HP score + ROM score + CHOL score + PON score
- ✓ **Alto PIRI** = modesta infiammazione e stress ossidativo post-parto, meno patologie cliniche, migliori performance

Tertile of PIRI	PIRI score	% on cows with clinical diseases
LO-PIRI	13.76 ±4.29	53
IN-PIRI	23.33 ±1.49	26
HI-PIRI	31.17 ±3.59	16



Grossi et al., 2013. XX ASPA Congress , BO, June 11-13

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Dipartimento di Scienze animali, della nutrizione e degli alimenti
29122 PIACENZA - VIA EMILIA PARMENSE , 84 - TEL. (0523) 599281 - TELEFAX 599275

Prelevatore	XXXXXXX	**Data prelievo**	27/09/2018
Azienda agricola	XXXXXXX	**Data di analisi**	05/10/2018
Specie	Bovina	**Ora prelievo**	09:00
Razza	Frisona	**Ora arrivo**	10:30
Categoria	Vacche fresche		
Campioni	Plasma		

NOTE: Interpretazione indice PIRI *(Post-calving Inflammatory Response Index)*

- conseguenze su salute e performance molto severe dopo il parto
- conseguenze su salute e performance severe dopo il parto
- adattamento al periparto adeguato, ma con qualche difficoltà
- buon adattamento al periparto e rapido recupero

SIGLA DI STALLA	3573	3609	3943	3959							media	ds	
Ora prelievo	09:00	09:00	09:00	09:00									
Note			P	P									
Giorni dal parto	3	2	6	6									
SIGLA DI LABORATORIO	**HB298**	**HB301**	**HB296**	**HB300**									
PIRI	**11.3**	**14.2**	**11.5**	**26.5**							**15.88**	7.22	

SIGLA DI LABORATORIO	**HB283**	**HB284**	**HB285**	**HB286**									
PIRI	**28.9**	**4.2**	**4.9**	**4.8**							**10.67**	12.12	

PIRI	**2.9**	**15.9**	**8.2**	**0.0**							**6.74**	6.97	

Infiammazione predetta con spettro latte

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Giannuzzi et al., 2023. J. Dairy Sci. 106:3321–3344
https://doi.org/10.3168/jds.2022-22454

Good prediction accuracy was achieved for glucose, albumin, ROM, thiol groups, globulins, haptoglobin

Milk Fourier-transform mid-infrared (FTIR) spectra and various machine learning (ML) algorithms to develop prediction equations for a panel of 29 blood metabolites, including those related to energy metabolism, liver function/hepatic damage, oxidative stress, inflammation/innate immunity, and minerals.

Data set comprised observations from 1,204 Holstein-Friesian dairy cows belonging to 5 herds.

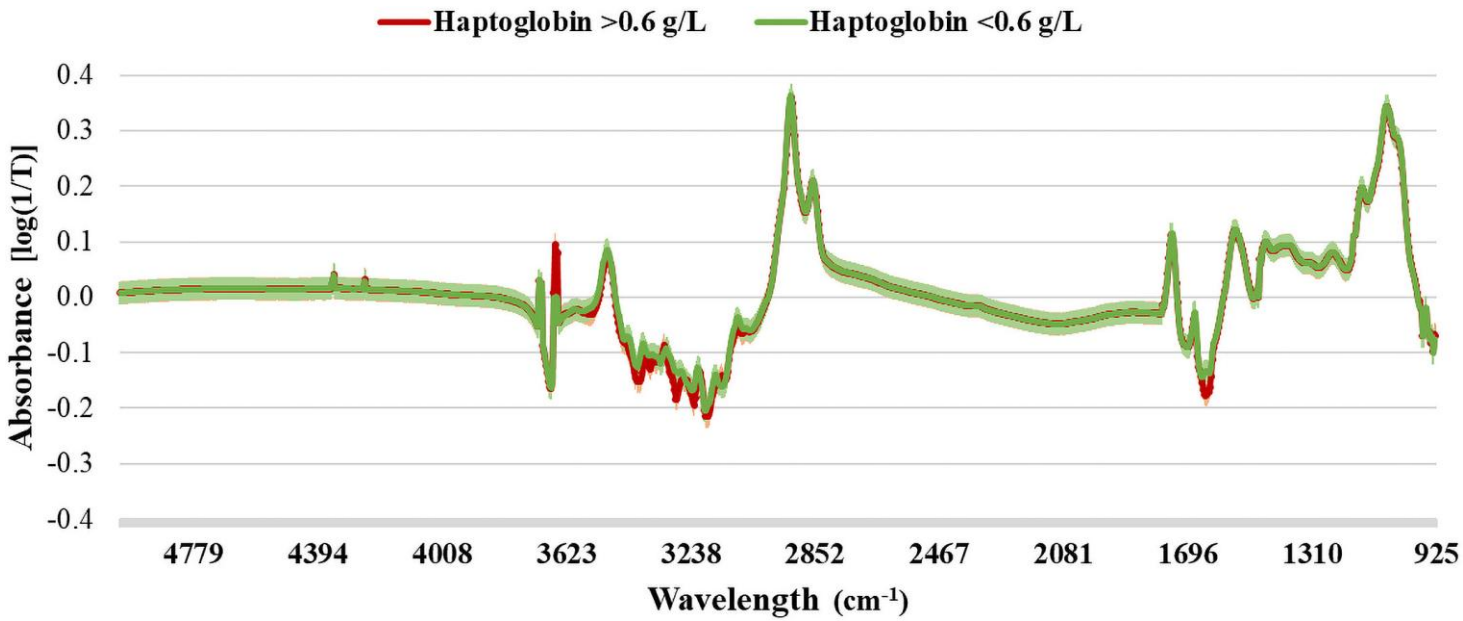


Figure 6. *Comparison of the entire Fourier-transform mid-infrared spectrum (1,060 wavelengths) between cows with high serum levels of haptoglobin (red line) and the rest of the population (green line). Light-green and orange halos show the SD.*

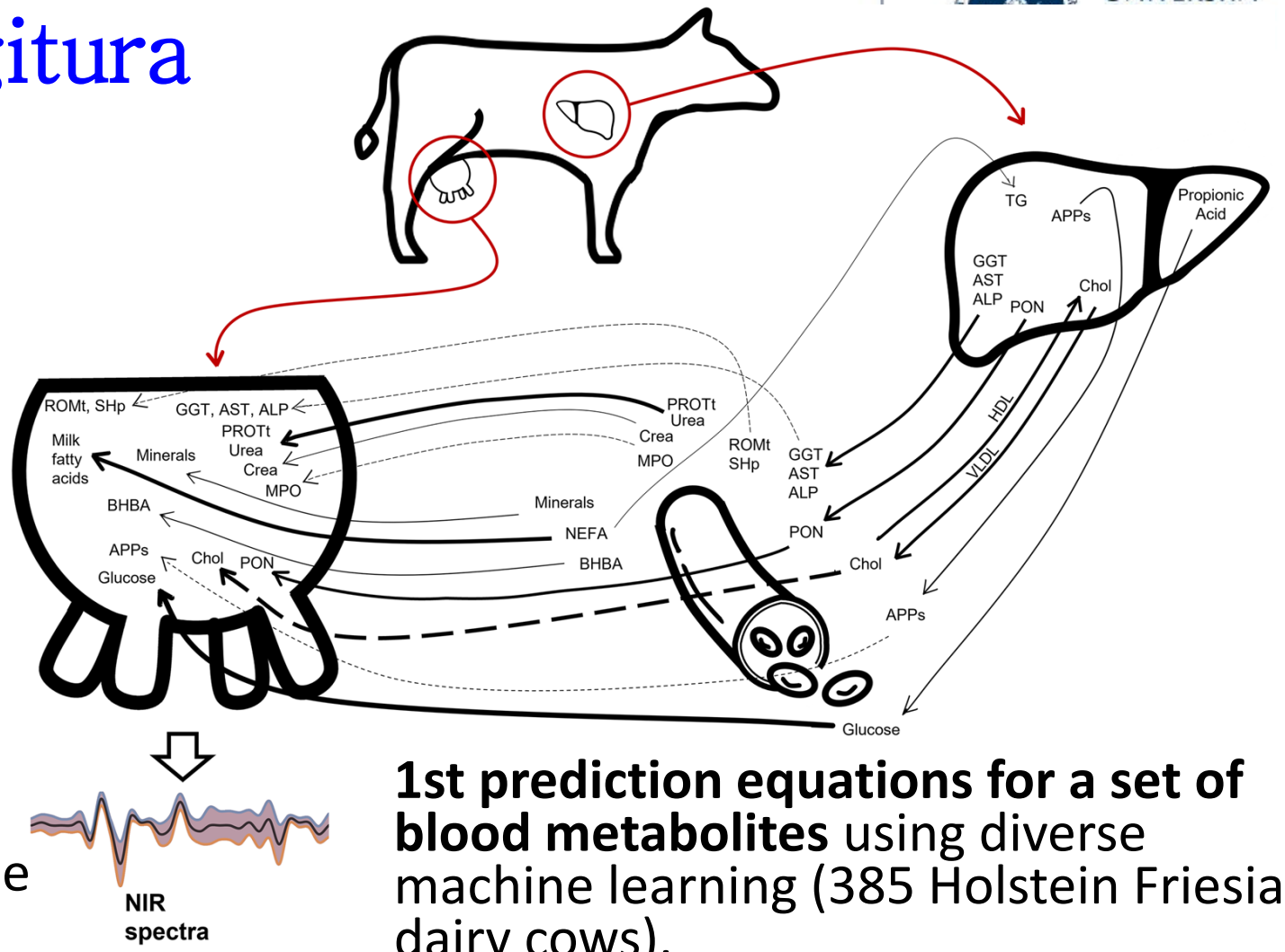
Infiammazione predetta con spettro latte alla mungitura

scientific reports
(2022) 12:8058 | https://doi.org/10.1038/s41598-022-11799-0

OPEN

In-line near-infrared analysis of milk coupled with machine learning methods for the daily prediction of blood metabolic profile in dairy cattle

Diana Giannuzzi[✉], Lucio Flavio Macedo Mota[1], Sara Pegolo[1], Luigi Gallo[1], Stefano Schiavon[1], Franco Tagliapietra[1], Gil Katz[2], David Fainboym[2], Andrea Minuti[3], Erminio Trevisi[3] & Alessio Cecchinato[1]



Aim: **to predict blood metabolites from milk samples**. This might allow a continuous monitoring of animal health and welfare parameters in order to optimize nutrition and productivity in the whole lactation.

PLF Tool: Milk near-infrared spectra collected by the **AfiLab instrument**

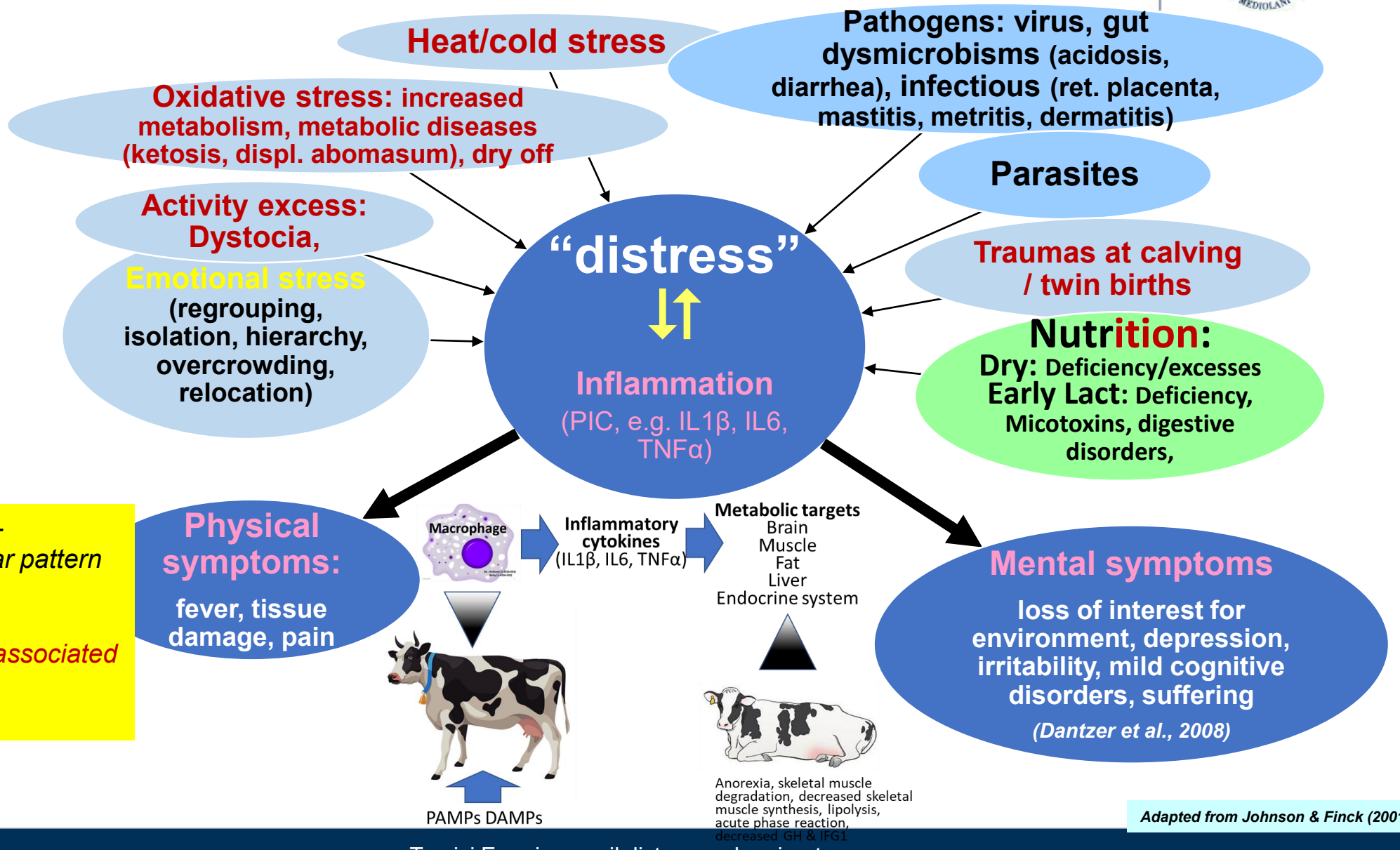
1st prediction equations for a set of blood metabolites using diverse machine learning (385 Holstein Friesian dairy cows).

Many moderate correlations (*r*) between plasma parameters and peaks of milk spectra.

Summary

- **Dal Profilo Metabolico al profile Immuno-metabolico**
- **Indici utili a classificare la severità dei processi infiammatori nel periparto**
  - **LAI (Liver Activity Index)**
  - **LFI (Liver Functionality Index) & come usarlo?**
  - **Indici più rapidi di distress immunometabolico**
- **Prospettive e implicazioni**

LFI è associato a sollecitazioni del periparto



PAMPs *= pathogen-associated molecular pattern (EXOGENOUS);*

DAMPs *= damage-associated molecular pattern (ENDOGENOUS)*

Adapted from Johnson & Finck (2001)

Take home messages

- Risposta del Sistema immunitario innato si può misurare nel TP con la risposta di fase acuta
- Le conseguenze della risposta infiammatoria distinguono livello di resilienza nel TP ed individuano casi subclinici
- Le negAPP & parametri correlate sono gli indicatori più sensibili per valutare la risposta delle bovine

- LFI è strumento efficace, poco costoso e semplice per valutare le condizioni delle bovine e degli allevamenti
- LFI aiuta a valutare efficacia di trattamenti (nutrizionali, gestionali, terapeutici)
- LFI indice di benessere
- Necessità di sviluppare un indicatore istantaneo (per ora disponibile LFI di Gruppo)

Many thanks for the attention

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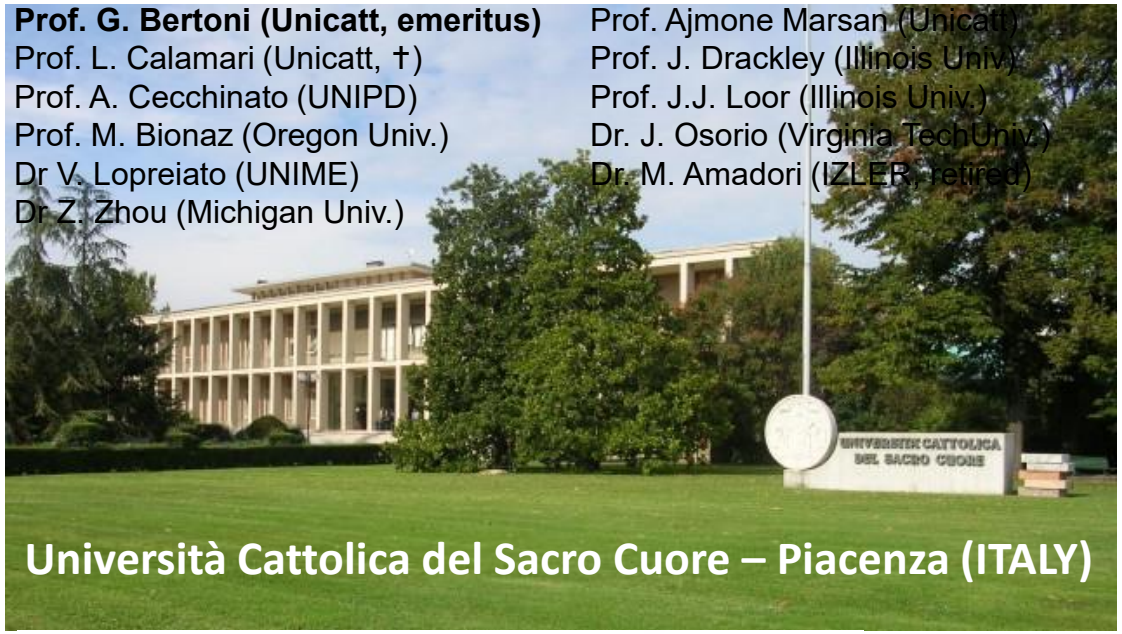

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Prof. Luigi Calamari

DOMANDE?

Dr Luca Cattaneo

Dr Matteo Mezzetti

Prof. Andrea Minuti

Dott. Fiorenzo Piccioli- Cappelli

La STALLA per la RICERCA