

Hepatic mitochondrial function in dairy cows with different levels of pasture inclusion during lactation

M. García-Roche¹ and M. Carriquiry¹

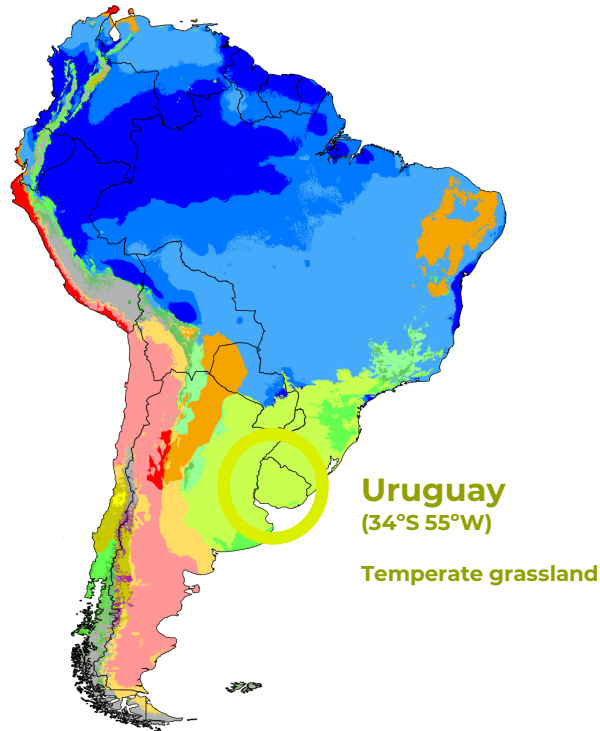
¹Departamento de Producción Animal y Pasturas, Facultad de Agronomía, Universidad de la República, Uruguay.

Presenter: M. García-Roche, PhD
Adjunct Professor

Departamento de Producción Animal y Pasturas
mercedesg@fagro.edu.uy



INTRODUCTION

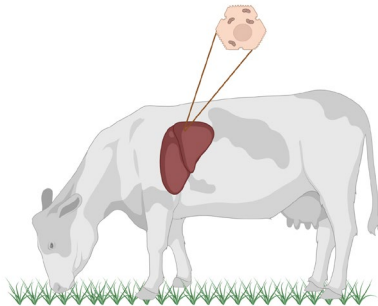


- Exports >70% of milk production (INALE, 2024)
- 9th exporter (INALE, 2024)
- Maximizing harvested pasture and minimizing reliance on supplementary feed are key to profitable pasture-based systems (Neal and Roche, 2019)
- Dependence on environmental conditions and management (Wales et al., 2013; Chilbroste et al., 2015; Chilbroste et al., 2005)
- Insufficient DMI and unstable nutrient availability (Chilbroste et al., 2012, Kolver and Muller, 1998)

INTRODUCTION

Cows in grazing systems show a poorer metabolic status ($\uparrow$ BHB, $\uparrow$ NEFA $\downarrow$ Ins., $\downarrow$ IGF-I) and lower performance when compared to cows in confined systems (Meikle et al., 2013; Astessiano et al., 2015)

Cows in a TMR+Grazing systems vs. cows in a Grazing+Concentrate system have $\uparrow$ DMI, $\uparrow$ milk yield, $\uparrow$ %fat, $\uparrow$ %protein, $\downarrow$ BCS loss (Wales et al., 2013).

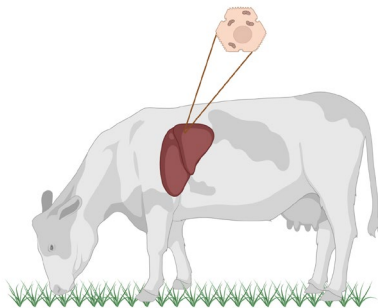


Liver plays a key role coordinating nutrient fluxes to support lactation and is central to the adaptation of metabolic pathways (Drackley et al., 2001).

INTRODUCTION

The mitochondrion is the organelle responsible for most of the ATP produced in the cell and although it is dynamic, it is highly prone to damage (Nicholls and Ferguson, 2011).

Liver mitochondria are related to metabolic adaptations of lactation as higher mitochondrial function is associated with increased milk yield (Favorit et al., 2021).



Impaired hepatic mitochondrial function has been observed in dairy cows in pasture-based systems during early lactation (García-Roche et al., 2019, 2023).

Nutrient utilization for metabolic processes in the hepatocyte differs among feeding strategies and Holstein strains (García-Roche et al., 2021, 2022).

HYPOTHESIS

Hepatic ATP-synthesis will be decreased in feeding systems with higher levels of pasture inclusion during early lactation

OBJECTIVE

Study the association between stage of lactation and proportion of pasture on hepatic mitochondrial function.



DPAP

MATERIALS AND METHODS: Animal trials

2015-2016

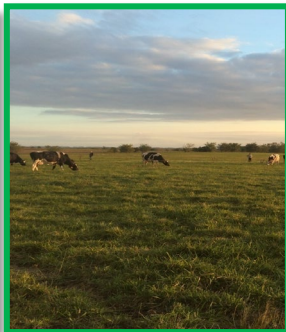
Estación experimental
"Dr. Mario A. Cassinoni".
Facultad de Agronomía

Universidad de la República.



- N = 24
- Multiparous NA Holstein
- Spring calving
- 664 ± 65 kgBW
- 3.0 ± 0.4 BCS
- Blocked according to BW, BCS, calving date, parity and previous annual milk yield

TMR (0)
100% TMR (60:40,
DM ratio)



Grazing (100)
85% Pasture^{1,2}
15% Commercial
concentrate
(offered basis)

2017-2018-2019

Estación experimental
"Dr. Alberto Boerger"
INIA La Estanzuela
Semillero, Colonia



- N = 48
- Multiparous NA and NZ Holstein
- Fall calving



538 ± 63 kgBW 582 ± 59 kgBW
 3.23 ± 0.19 BCS 3.03 ± 0.28 BCS



PMR (30)
31-33% Pasture¹
67-69% TMR
(55:45, DM ratio)



Grazing (100)
75-80% Pasture¹ +
Forrage reserves²
(40-50% grazed)
20-25% Commercial
concentrate



DIM = -21, 35, 60, 110, 180, 250
Daily milk yield
Milk composition, BW, BCS - fortnightly



DIM = -45, 21, 100, 180
Daily milk yield
Milk composition, BW, BCS - fortnightly

¹*Festuca arundinacea* + *Medicago sativa*.

²Diet change due to <<ITH (113-180 DPP) cows
grazed *Festuca arundinacea* (20
kgDM/cow/day) + TMR (15 kgDM/cow/day)

¹*Festuca arundinacea*, *Dactylis glomerata* +
Medicago sativa.

².. Corn silage + pasture haylage 75:25 (DM)



DPAP

MATERIALS AND METHODS:

1



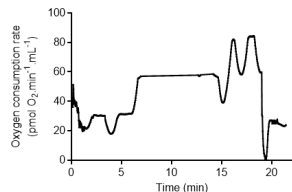
Levels of plasma and liver metabolites were determined with commercial kits



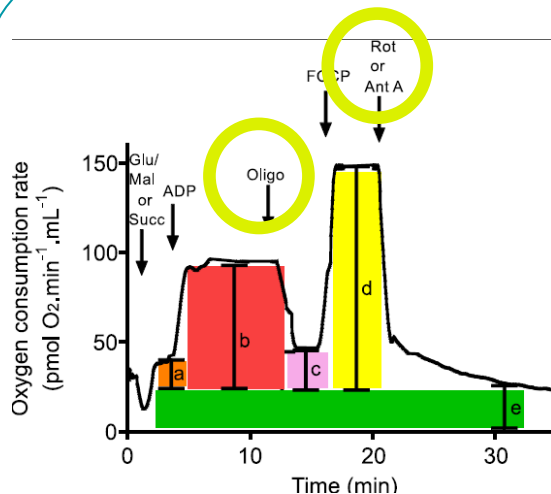
2



O2k-High Resolution respirometry using mitochondrial substrates and inhibitors



3



García-Roche et al., 2018

- Respiration destined to ATP-synthesis
- Proton leak
- Non-mitochondrial respiration

4



Variables were grouped:

1. Mitochondrial parameters related to ATP synthesis (n = 10)
2. Mitochondrial parameters not related to ATP synthesis (n = 8)
3. Energy balance markers (n = 5)

PROC FACTOR – Principal component analysis
Previously confirmed with Bartlett's Sphericity Tests on the three groups ($P < 0.001$)

PROC CORR – Spearman's correlations, heatmap

PROC MIXED – Mixed models with repeated measures

Fixed effects: STAGE of lactation, PROP – proportion of pasture, STAGE x PROP

Random effect: Holstein strain

Covariate: Trial

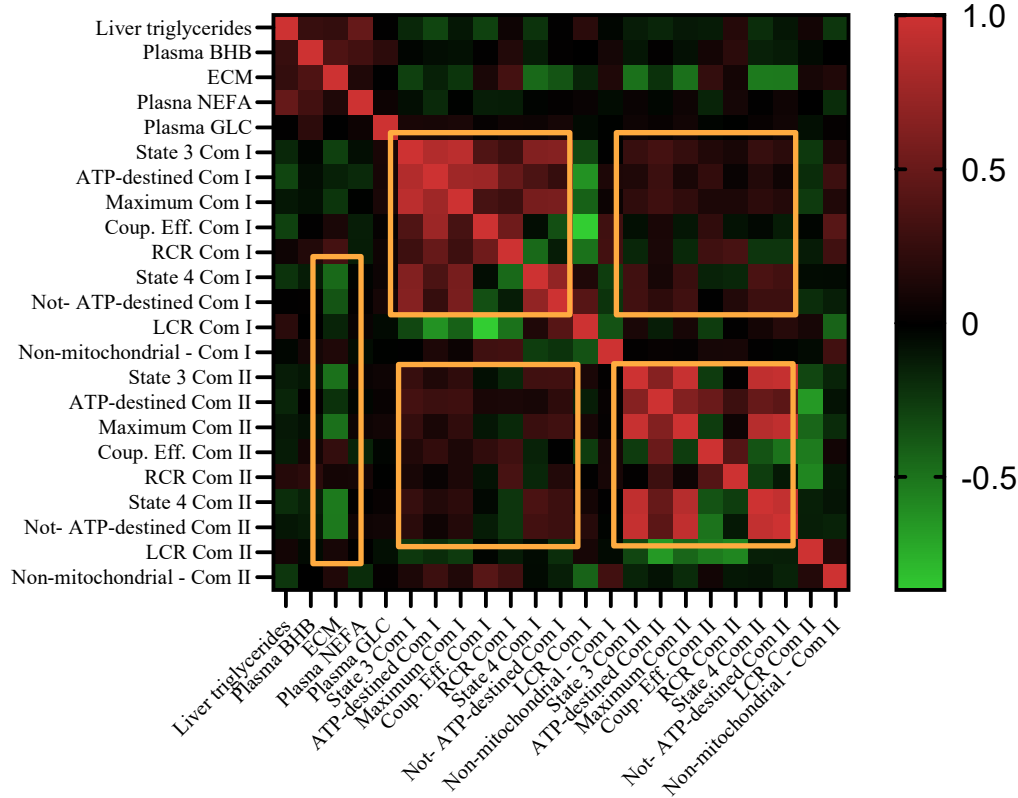
Least square means for mean separation
Means were considered to differ when $P \leq 0.05$ and tendencies when $0.05 < P \leq 0.10$

PROC UNIVARIATE, REG – check normality and t student residuals



DPAP

RESULTS



Mitochondrial parameters when the same mitochondrial substrate was used correlated positively ($\rho = 0.20 - 0.90$, $P < 0.01$)

Did not correlate between complexes

Differences among mitochondrial substrates -different pathways that direct their reducing equivalents to either Complex I (TCA) or II (AA and fatty acids).

Weak to moderate negative correlations were observed between ECM and mitochondrial parameters ($\rho = -0.20$ to -0.52 , $P < 0.0001$).



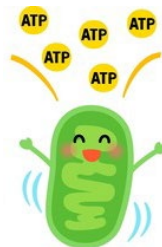
DPAP



PC1 and 2 explain 58% of the variance

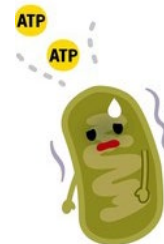
Factor Pattern	
	Factor1
Plasma BHB	0.81231
ECM	0.63578
Liver TAG	0.62209
Plasma NEFA	0.59463
Plasma GLC	0.20657

RESULTS



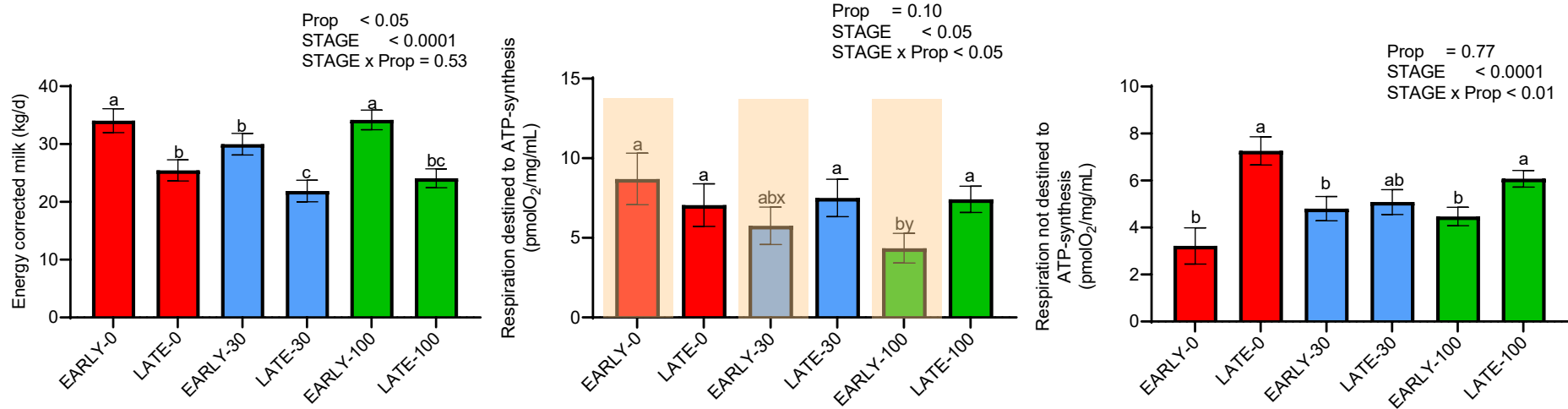
PC1 and 2 explain 60% of the variance

	Factor Pattern		
	Factor1	Factor2	Factor3
ATP-destined Com I	0.8955	-0.29247	-0.26165
State 3 Com I	0.88441	-0.12381	-0.27316
Maximum Com I	0.84251	-0.10784	-0.24736
ATP-destined Com II	0.62715	0.45808	0.52388
Coup. Eff. Com I	0.56942	-0.4043	-0.1677
State 3 Com II	0.38995	0.89202	0.0436
Maximum ComII	0.3873	0.88952	0.09494
Coup. Eff. Com II	0.33183	-0.44197	0.68432
RCR Com I	0.26643	-0.379	0.22889
RCR Com II	0.15545	-0.25426	0.70378



PC1 and 2 explain 54% of the variance

	Factor Pattern	
	Factor1	Factor2
Not - destined ATP Com I	0.75877	-0.25411
Not - destined ATP Com II	0.74006	0.55841
State 4 Com I	0.72403	-0.14845
State 4 Com II	0.71724	0.58275
LCR Com I	0.48163	-0.50561
LCR Com II	-0.13119	0.07384
Non-mitochondrial Com I	-0.19076	0.6317
Non-mitochondrial Com II	-0.24114	0.65202



Liver mitochondria are related to metabolic adaptations of lactation as higher mitochondrial function is associated with increased milk yield (Favorit et al., 2021).

Uncoupling proteins (UCPs) 1, 2 and 3 and adenine nucleotide translocase induce proton leak in response to high fatty acid levels, superoxide or lipid peroxidation products (Toime and Brand, 2010).

UCPs may play a central role in the adaptation to increased fatty acid supply by enhanced fatty acid oxidation (Cortez-Pinto and Machado, 2009)

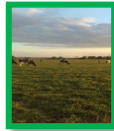
UCPs regulate oxidative phosphorylation efficiency protecting against oxidative damage (Brand, 2005).

CONCLUSION



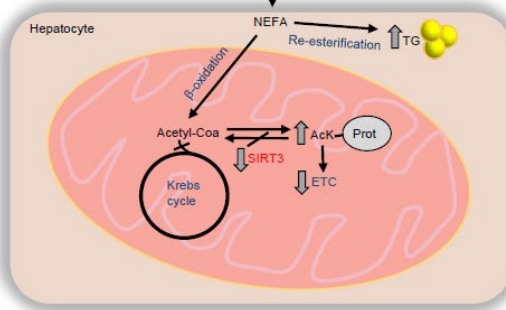
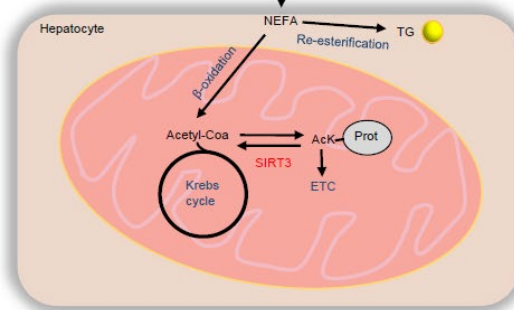
Adipose tissue

NEFA



Adipose tissue

NEFA



García-Roche et al., 2019

- Greater mobilization leads to **greater esterification of liver TAGs** during **early lactation**
- Hepatocytes of dairy cows with different levels of pasture inclusion show different **adaptive strategies during lactation**
- Highlight the **plasticity** of hepatic **mitochondria** to adapt to different energy demands and nutrients

We thank all the staff of the Experimental Stations of INIA and EEMAC and acknowledge funding from CSIC I+D, MIA and CAP



Thank you