Effects of supplementation with vitamin E or plant extracts on redox and immune status in early lactating dairy cows

Angélique Corset, Anne Boudon, Aude Remot, Sabrina Philau, Maryline Lemarchand, Colette Mustiere, Laurence Le Normand, Ophelie Dhumez, Jean-François Ricouleau, Benoit Graulet, et al.

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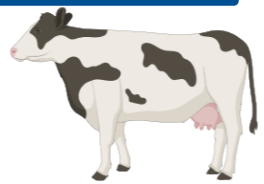
Session 93: Preventive approaches to livestock diseases to reduce drug resistance



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2 Biodevas Laboratoires
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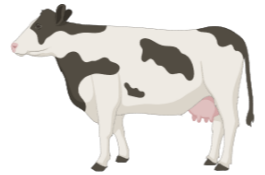
The context of early lactation

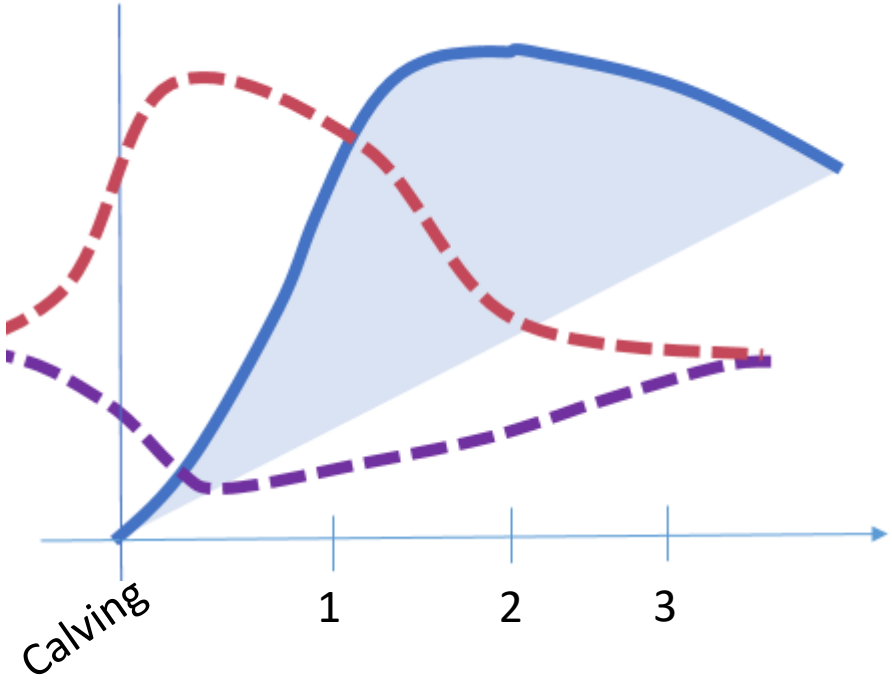


- Early lactation, a critical period — Bradford et al., 2015

  ↗ Milk yield

  ↗ ROS production ↗ Oxidative stress — Castillo et al., 2005

  ↘ Immune capacity — Ingvartsen et Moyes, 2013

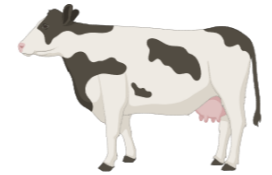


- Risks ↗ Incidence of disease
  ↘ Milk yield

Antioxidant supplementation can be a nutritional strategy to address these issues

ROS: Reactive oxygen species

What nutritional strategy and why ?



Vitamin E

all-rac-alpha-acetate de tocopherol

- reduces oxidative stress in dairy cows
- improved dairy cows immunity
- reduces the number of clinical mastitis cases

Bouwstra et al., 2008
Politis et al., 2004
Weiss et al., 1997

biodevas LABORATOIRES

Plant extracts

- several 100% natural plant extracts

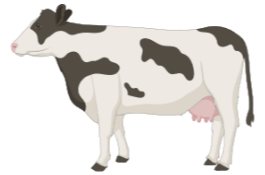
Sambucus nigra, Salix alba, Laurus nobilis, Haragophytum procumbens, Silybum marianum, Arctium lappa

- gene expression activators
- *in vitro*: stimulated antioxidant enzyme synthesis in cell culture

Vitamin E according to NASEM recommendations
before calving **100 g/d** or **3000 IU/d**
after calving **35 g/d** or **1000 IU/d**

Plant extracts according to company recommendation
after calving **10 g/d**

Material and Methods



3 groups of 45 dairy cows

1- control n = 15

8 multiparous & 7 primiparous

2- vitamin E n = 16

+ Vitamin E

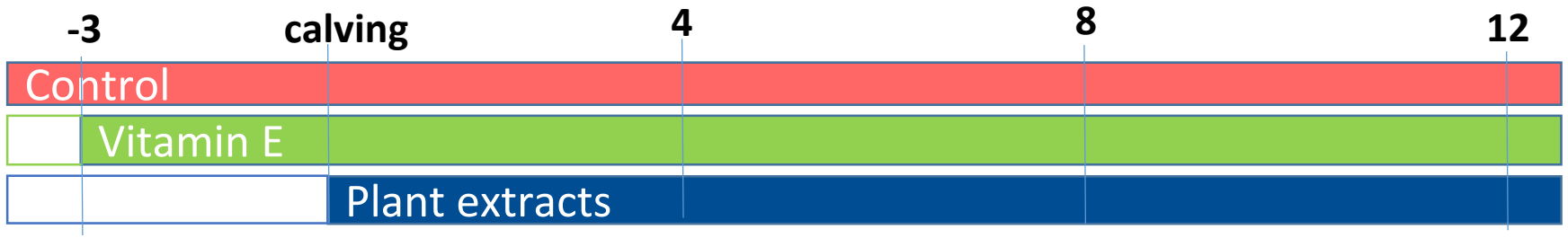
8 multiparous & 8 primiparous

3- plant extracts n = 14

+ Plant extracts

8 multiparous & 6 primiparous

Nutritional supplementation according to lactation weeks:



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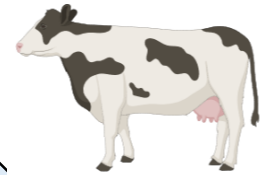
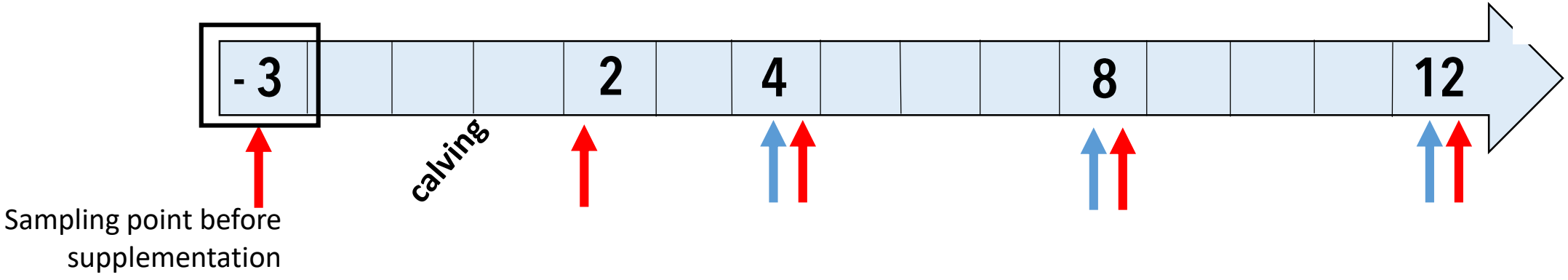
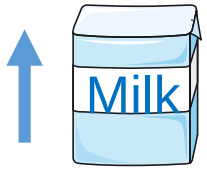




Anti and pro-oxidant indicators
Inflammation
Immune response (*ex vivo* tests)



Milk sample for isolation of mammary epithelial cells (MEC)

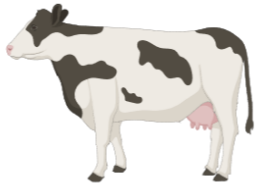
Statistical test: ANOVA to take into account **parity**, **treatment**, lactation **week**, their interactions, and cow random

$$Y(ijkl) = \mu + \text{covariate} + \text{treatment}_i + \text{week}_j + (\text{treatment x week})_{ij} + \text{parity}\ k + (\text{parity x week})_{kj} + (\text{treatment x parity})_{ik} + (\text{treatment x week x parity})_{ijk} + 1\,|\,\text{cow}_l + \text{calving date}_m + \varepsilon$$

group

Objective

Demonstrate the effects of nutritional supplementation with vitamin E or plant extracts on redox and immune status

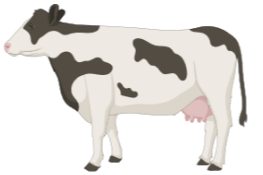


Hypotheses

Part 1 – Redox status → Reduce oxidative stress?

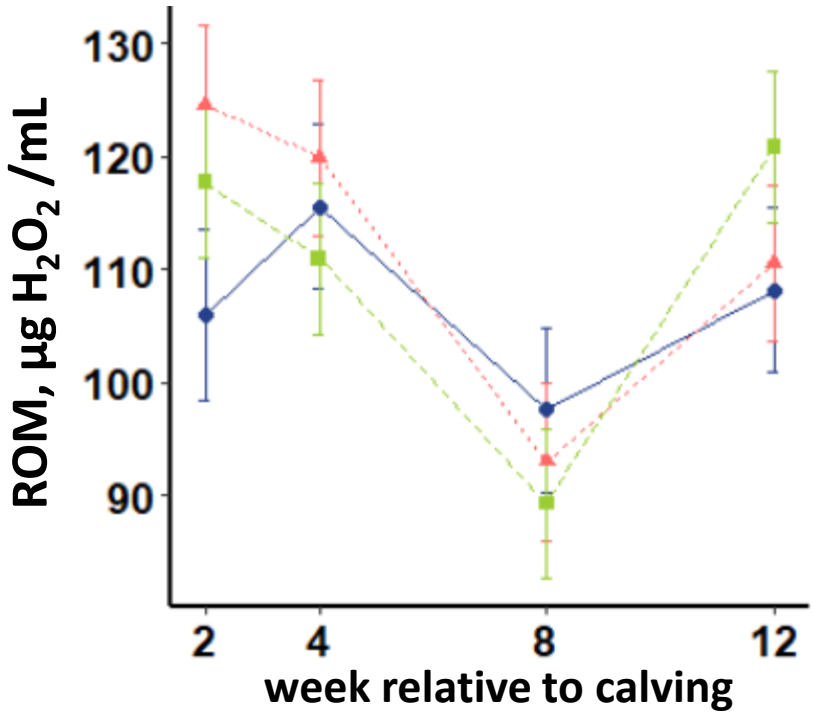
Part 2 – Immune status→ Reduce pro-inflammation?

Redox status: oxidative stress was present in first week of lactation



control
vitamin E
plant extracts

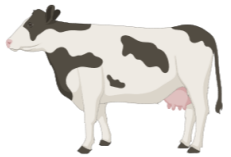
Treat: *P* = 0.78 **Wk: *P* < 0.001**
Treat *x* Wk**:** *P* = 0.20



↗ Oxidative stress in blood at early lactation without any treatment effect

ROM: Reactive Oxygen Metabolites

Redox status: Vitamin E and plant extracts had different antioxidant response



control
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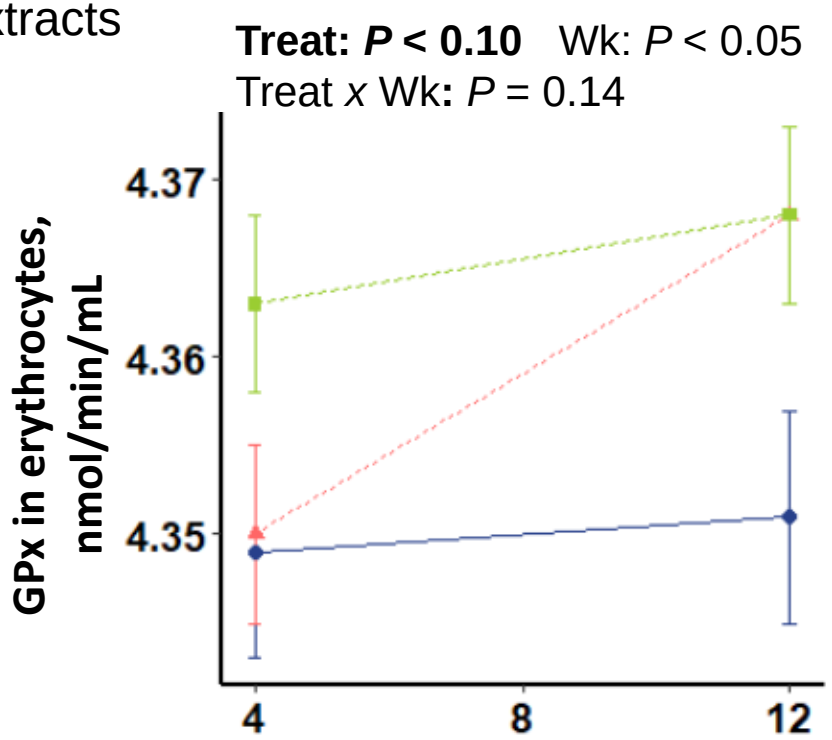
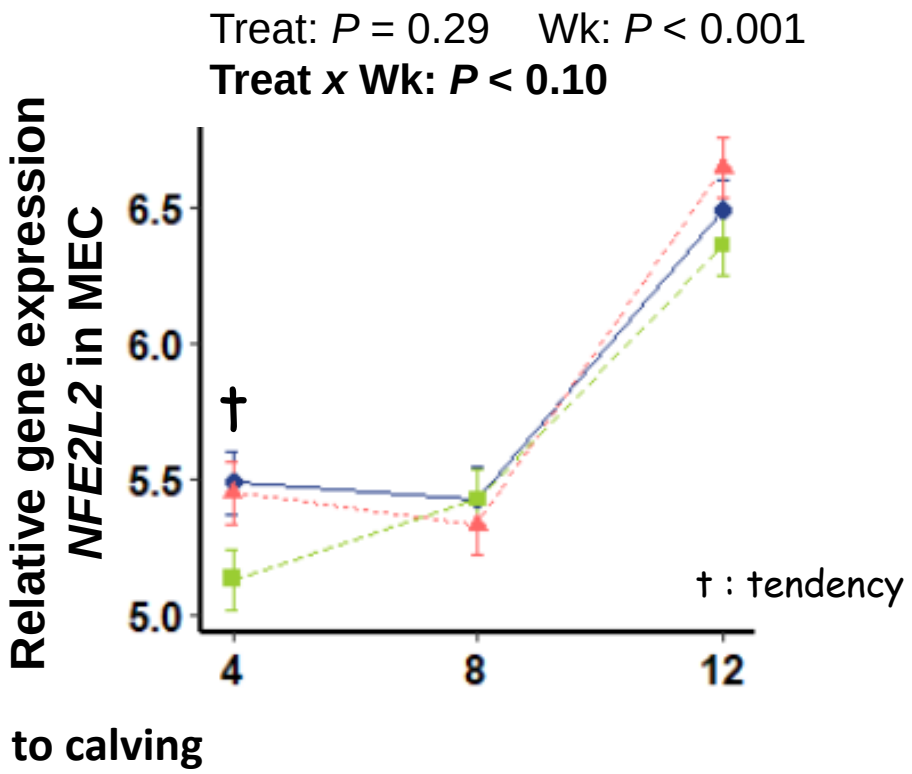




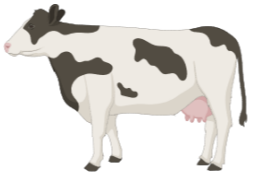
Tendency ↗ GPx antioxidant enzyme activity in erythrocytes in **VitE** than in **PE**

GPx: Glutathione peroxidase

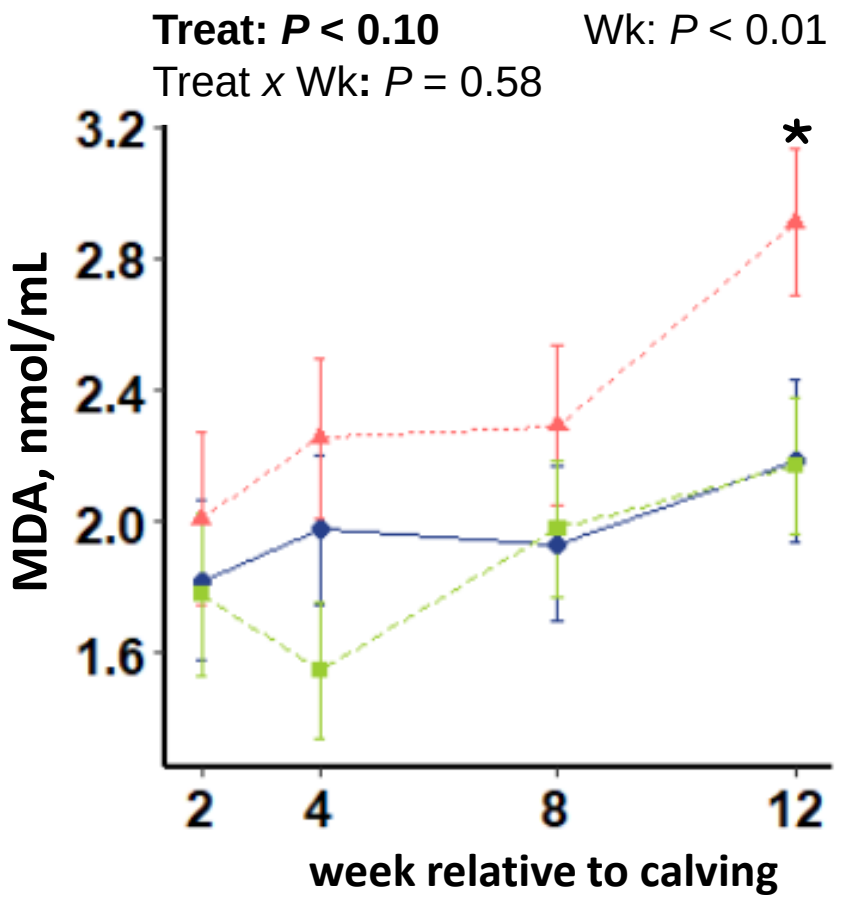
Tendency ↗ expression of the antioxidant pathway transcription factor in mammary epithelial cells in **PE** than in **VitE**

NFE2L2: Nuclear factor (erythroid-derived 2)-like 2
MEC: Mammary epithelial cells

Redox status: vitamin E and plant extracts reduced lipid peroxidation



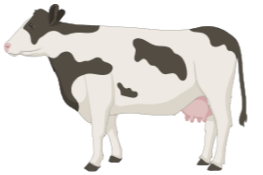
control
vitamin E
plant extracts

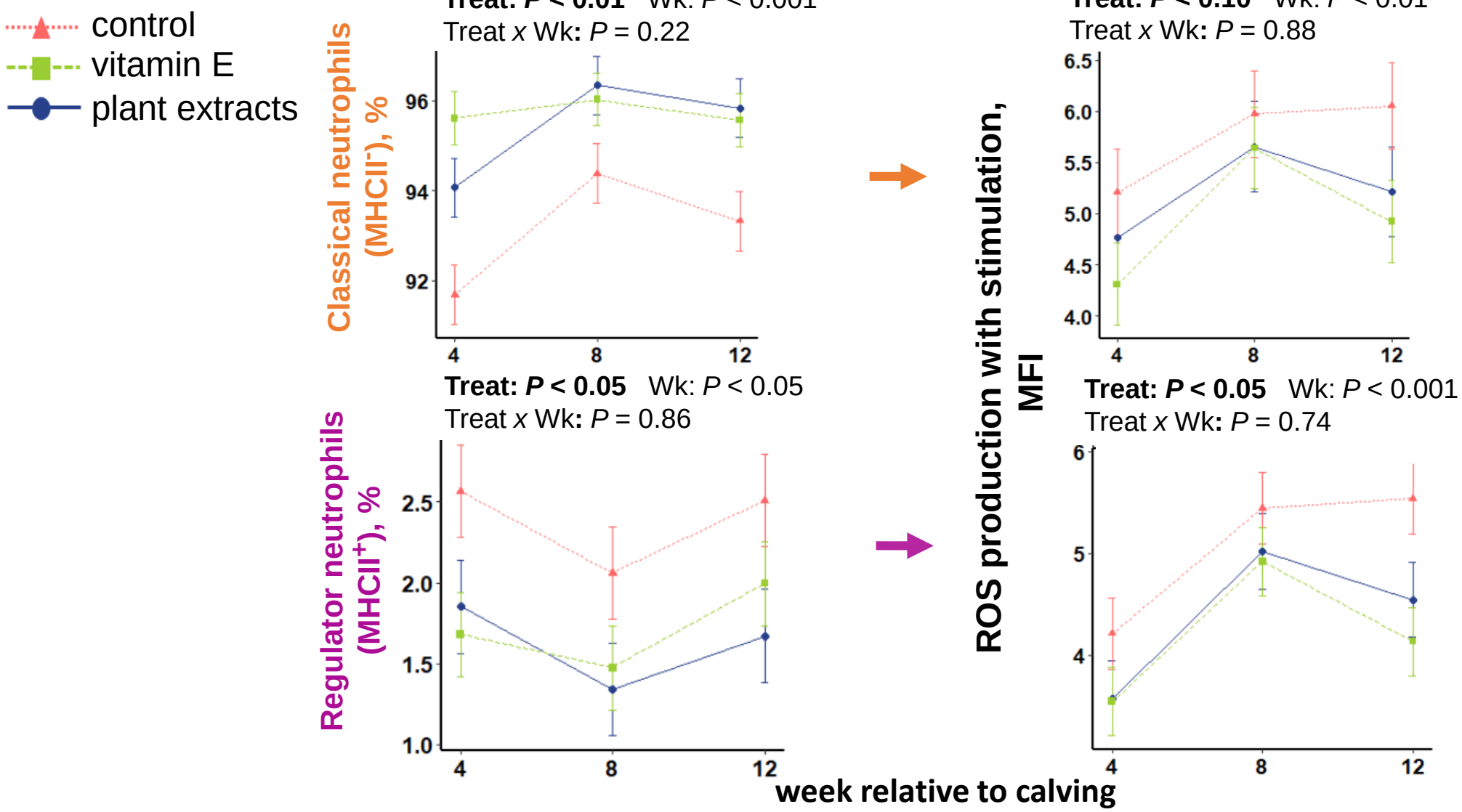


After 12 week, ↘ lipid peroxidation in VitE and PE than in control

MDA: Malondialdehyde

Immune status: blood neutrophils and their ROS production



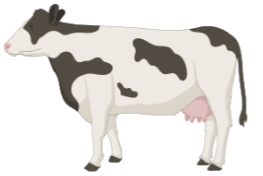


vitE and **PE** induced a change in neutrophil subpopulation

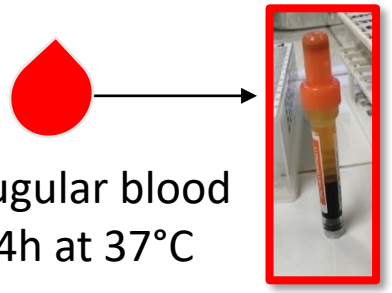
With *ex vivo* stimulation, **vitE** and **PE** ↘ ROS production in both types of neutrophils

↘ pro-inflammatory response

Immune status: vitamin E and plant extracts reduced pro-inflammatory cytokines after an *ex vivo* stimulation of blood cells



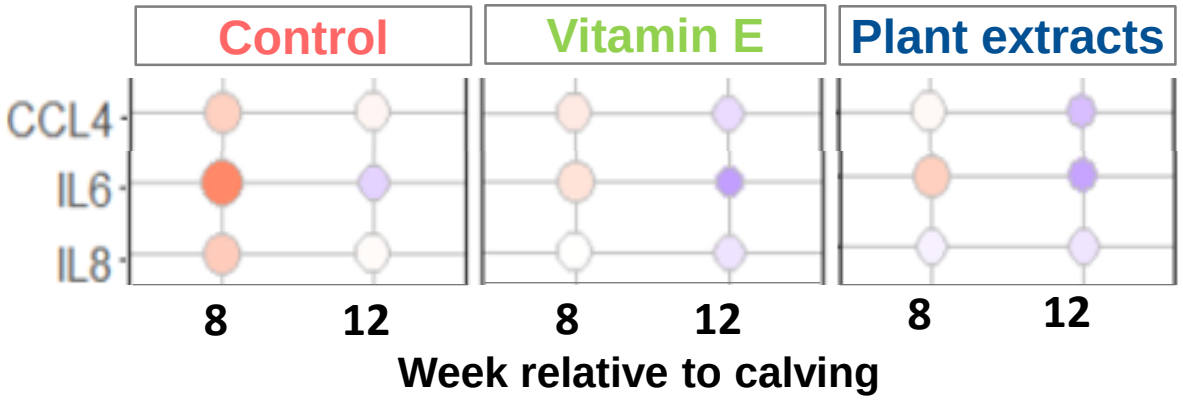
Heat killed bacteria *E. coli*



Jugular blood
24h at 37°C

Cytokine production measured by bead-based multiplex assay

Lesueur *et al.*, 2022

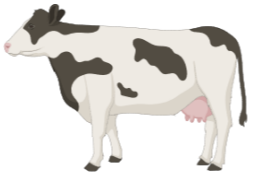


	P-value		
	Treat	Wk	Treat x Wk
CCL4	< 0.05	< 0.001	0.57
IL6	< 0.10	< 0.001	0.56
IL8	< 0.05	< 0.01	0.29

↘ CCL4 with **plant extracts**
↘ IL6 with **vitamin E**
↘ IL8 with **vitamin E** and **plant extracts**

↘ reduced pro-inflammatory response

Immune status: vitamin E and plant extracts had a specific immune response after an *ex vivo* stimulation of blood cells



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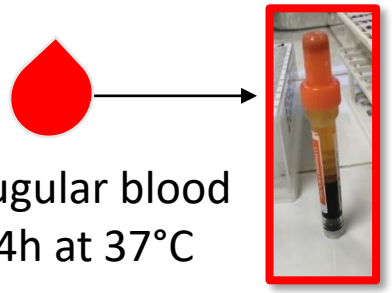

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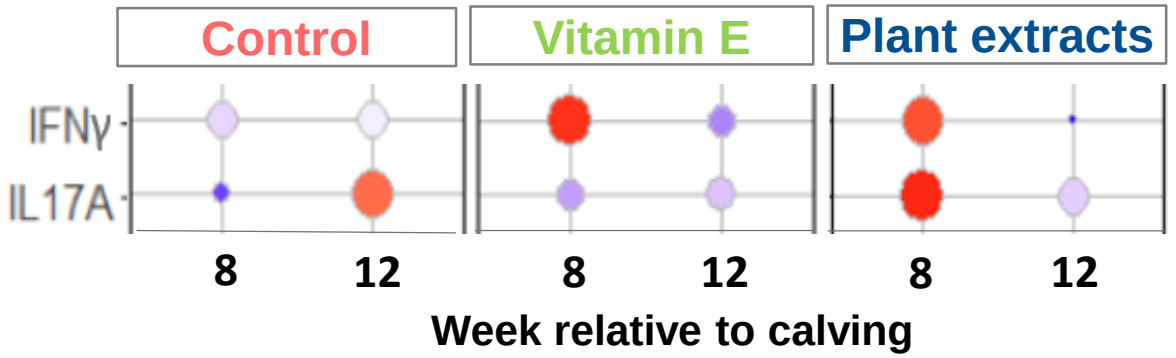
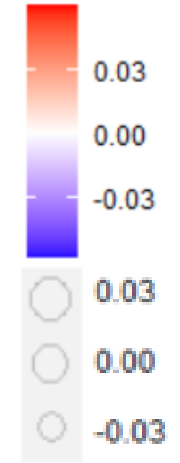


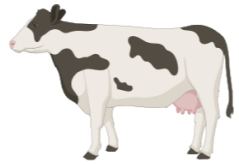
	P-value		
	Treat	Wk	Treat x Wk
IFNγ	0.87	**< 0.05**	**< 0.10**
IL17A	0.65	0.62	**< 0.05**



↗ IFNγ with **vitamin E** and **plant extracts**
↗ IL17A with **plant extracts**

Specific immune response against bacteria

Conclusion Effects of nutritional supplementation with vitamin E or plant extracts:



Part 1 – Redox status

VitE + systemic antioxidant response

PE + antioxidant capacity local to the mammary gland

Bouwstra et al., 2009

💡A different mode of action? Localisation in the organism ?

Part 2 – Immune status

vitE PE - regulator neutrophils

💡Regulator neutrophils suppress T-cell proliferation → **VitE** and **PE** avoid immune suppression

Rambault et al., 2021

vitE PE - inflammatory response in stimulated *ex vivo* test conditions: avoid hyperinflammation

Hidiroglou et al., 1997

vitE PE + IL17A and IFNγ

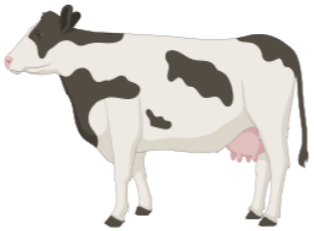
💡Specific immune response against bacteria as suggested in literature to fight mastitis

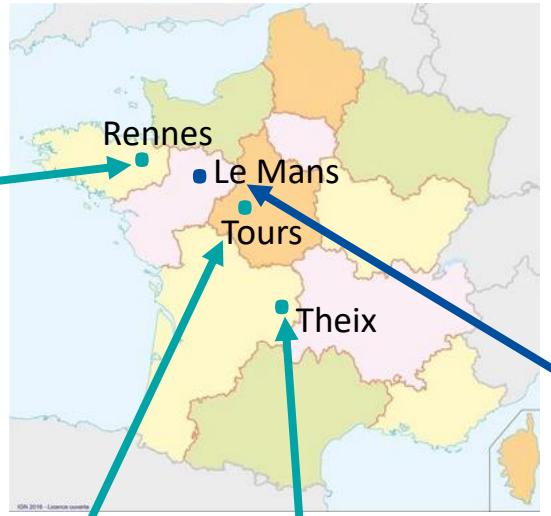
Rainard et al., 2020

Opening

VitE or **PE** modulated immune response, but this study was conducted in healthy cows.
Coming soon: Results of a second experiment with an inflammation test after intramammary lipopolysaccharide challenge (Poster number 49.26).

Thank you for your attention





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Post doctoral research related to my thesis