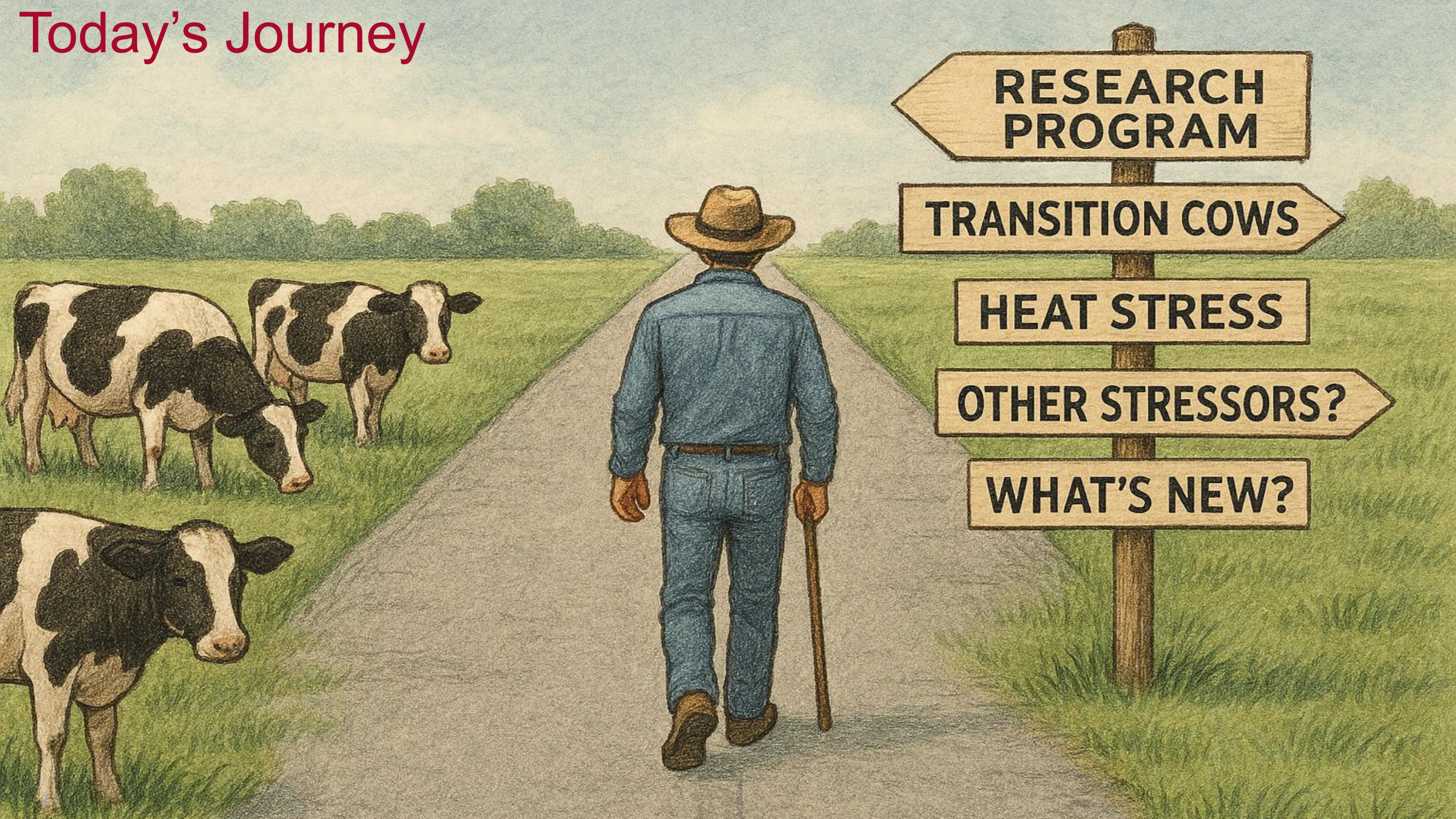
SmartLine™

Nutrition & Health For Lifetime Performance

Danielle Sherlock, PhD
Global Ruminant Technical & Scientific Support Manager

November 6th, 2025
Adisseo NA VIP Seminar
Nashville, TN

Today’s Journey



Adisseo Research Organization

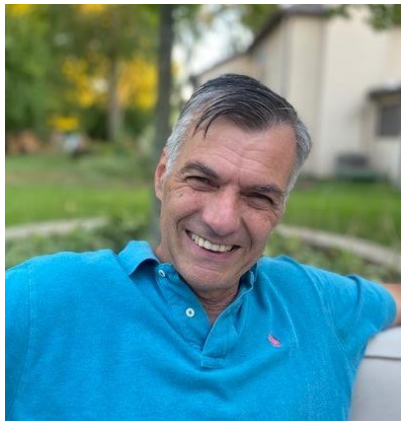
A High Level of Expertise

Adisseo Ruminant Research Program From 2009-2025

- Multiple research trials in 20 Universities from 5 countries:
- 158 abstracts presented at the ADSA/ASAS annual meeting:
- 18 Wine and Cheese** events at the ADSA/ASAS annual meeting
- 5 Amino Acid-University events:
- 3 Transition Illinois + Adisseo Smart Training Events
- 45+ published papers in peer reviewed journals:
- A variety of podcasts on The Dairy Podcast and Blackbelt Nutrition Shows

** First Wine and Cheese at 2008 ADSA

Global Ruminant Technical & Scientific Support Team



DANIEL LUCHINI
Head of Ruminant Tech & Sc Support

Global Ruminant Technical & Scientific Support Managers

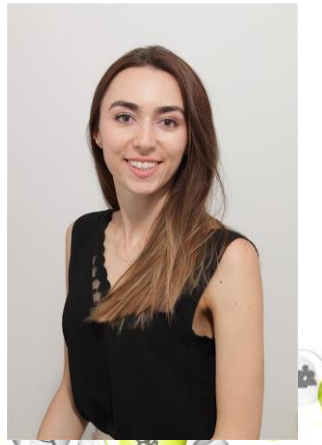
Danielle Sherlock

Mike Shearing

Lahlou Bahloul

Sarper Ozbek

Amine Hachemi



Laura Barrau

NUTRITION & HEALTH FOR LIFETIME PERFORMANCE

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Impacts of Methionine on Lifetime Performance

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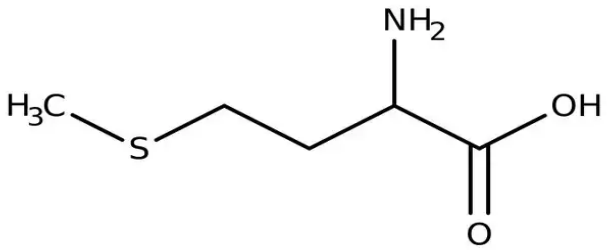
Why Should We Care About Methionine?

- **Methionine** is an amino acid but also an **essential nutrient**, meaning that it cannot be made by the cow, but it is required for important body functions such as production, reproduction, and health; therefore, must be provided by the diet.

- In 2001 and then in 2021, the NRC stated that **typical diets don't provide enough methionine**, limiting overall cow performance.



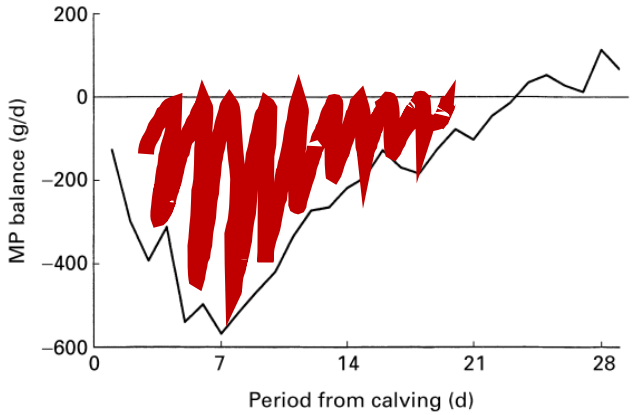
Methionine and the Transition Period

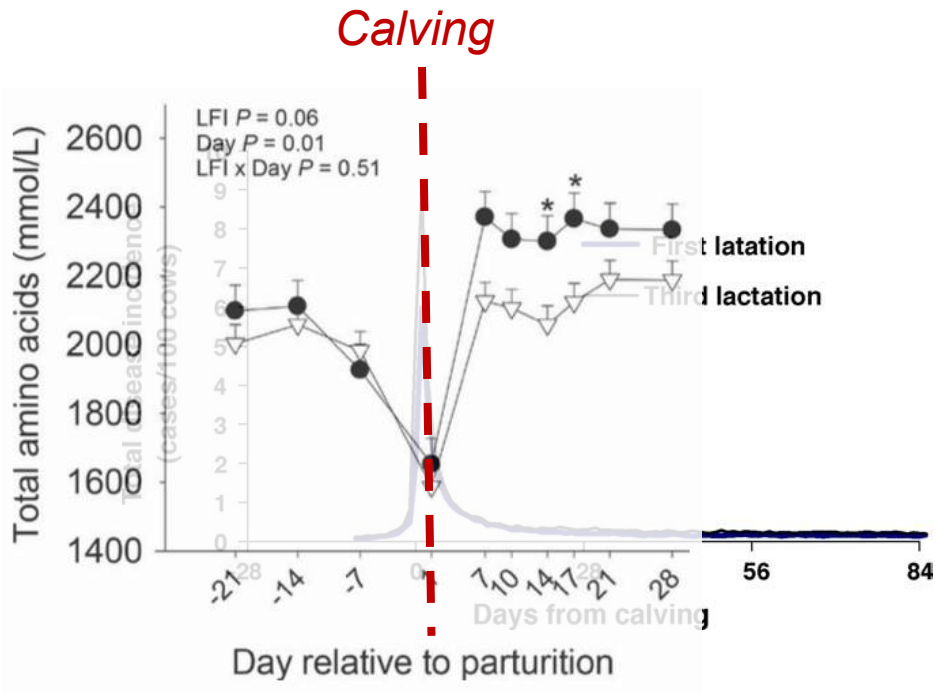
Transition Period Challenges

During the Transition Period:

- ↓ DMI
- Negative energy balance
- Immune dysfunction
- ↓ liver function
- ↑ inflammation
- ↑ oxidative stress

Metabolizable Protein





Ingvartsen, 2006 & Zhou et al., 2016

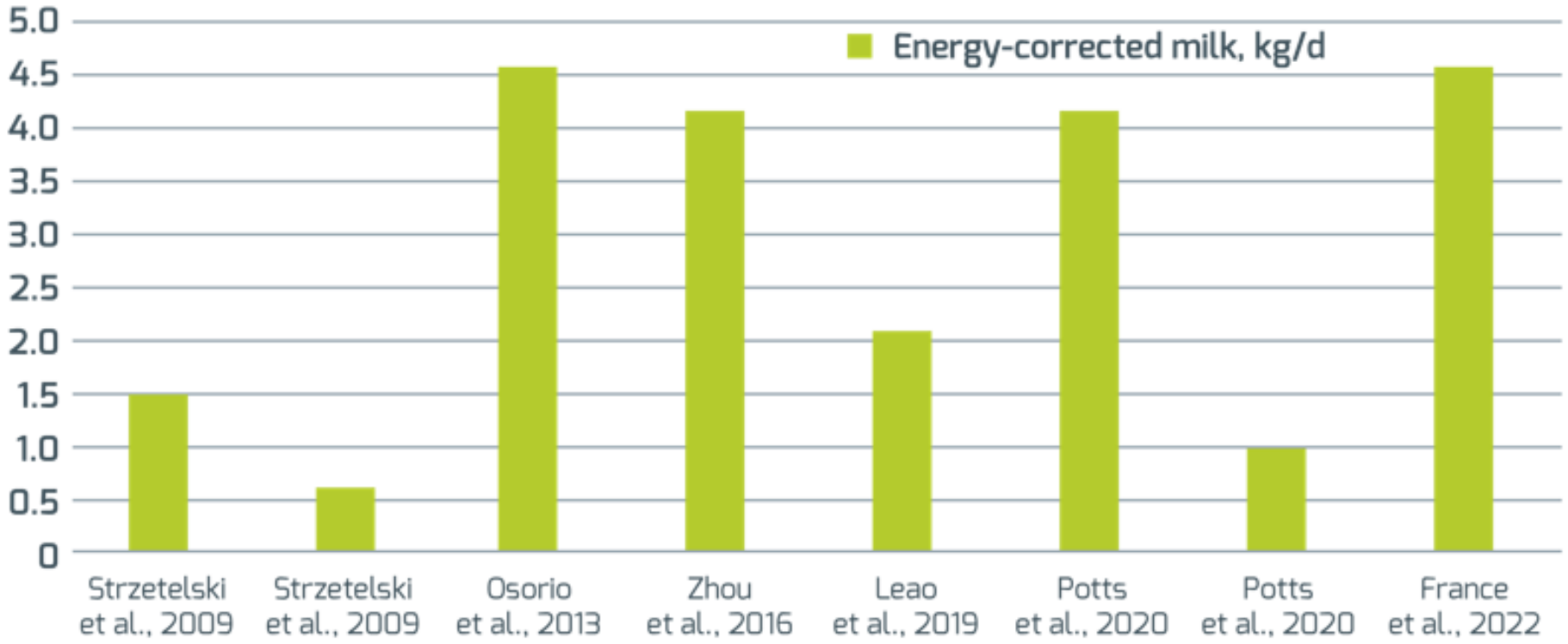
Link between AA and disease incidence.

Increased need for AA.

Methionine Increases Transition Period Production and Components

Smartamine® M and MetaSmart®: 8 transition cow studies

ECM = +2.8 kg/d (fresh cows) DMI = +1.1 kg



+ 89 kg/d Milk Protein

+ 122.5 kg/d Milk Fat

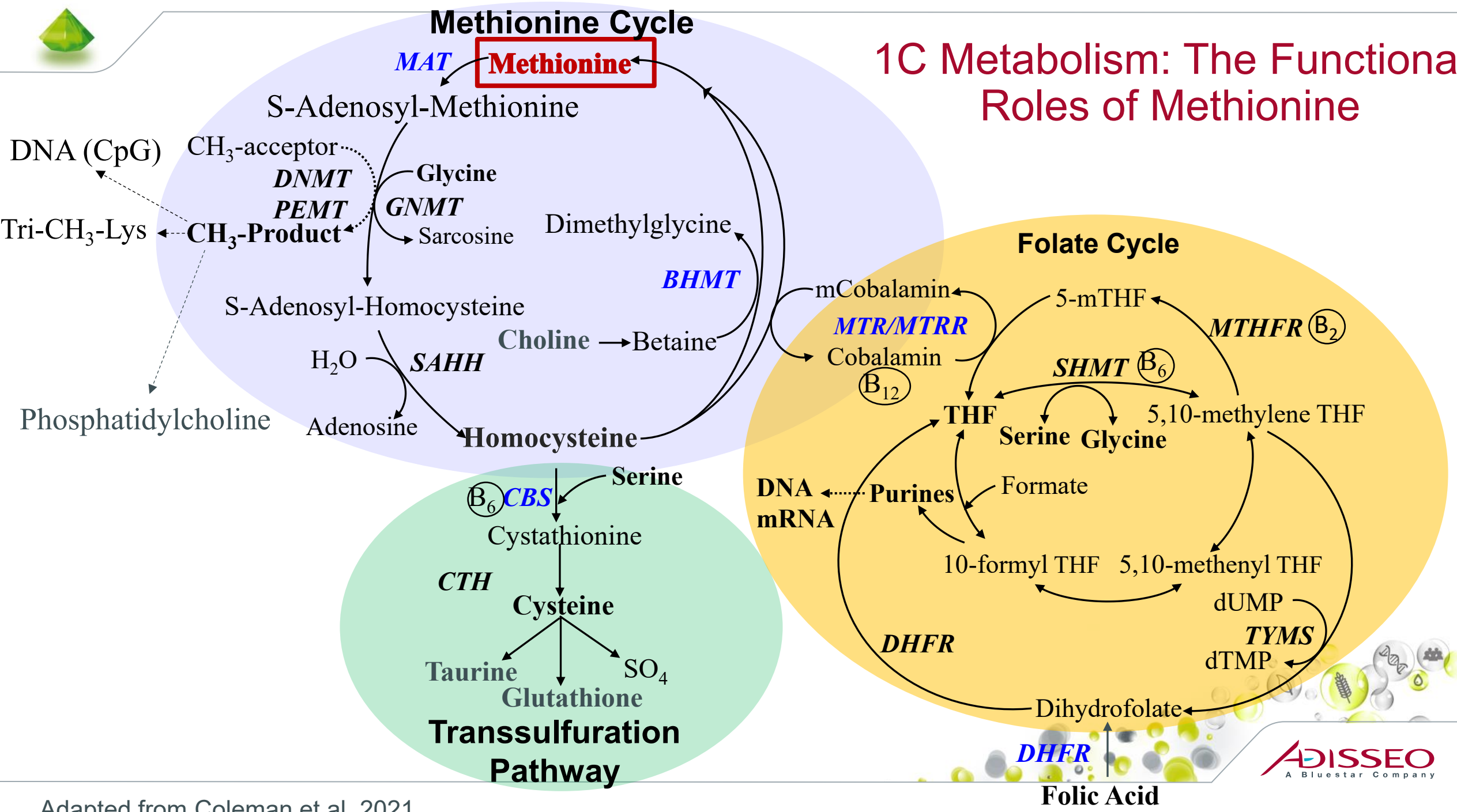
+ 1.8 kg/d Milk Yield

+ 6.4 lb/d ECM
+ 4.0 lb/d Milk Yield
+ 2.4 lb/d DMI
+ 0.20 lb/d Protein
+ 0.27 lb/d Fat

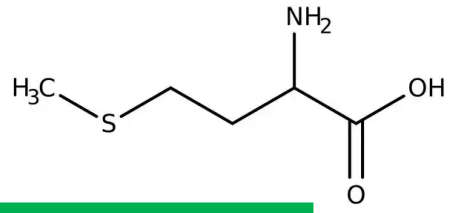
*Average of 6 g increase in metabolizable Met prepartum and 12 g increase in metabolizable Met postpartum. Lys:Met ratio of 2.8 based on NRC.

How Is Methionine Improving Performance?

1C Metabolism: The Functional Roles of Methionine



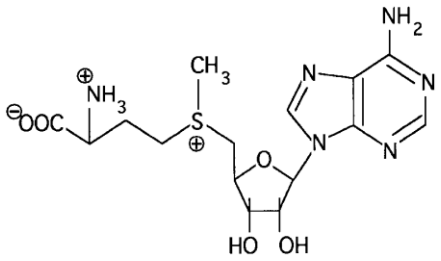
Adapted from Coleman et al. 2021



Methionine

Protein Synthesis

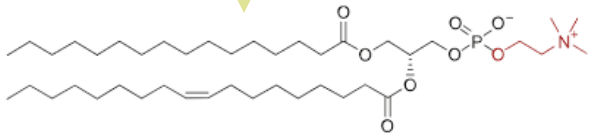
P mTOR



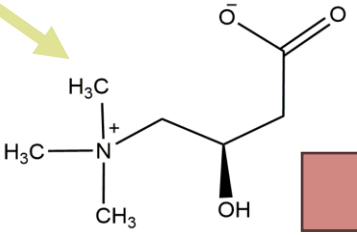
S-adenosylmethionine (SAM)

DNA Methylation

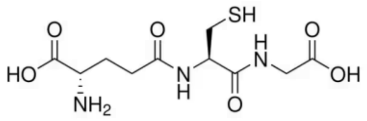
Genes turned on and off



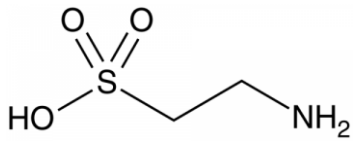
Phosphatidylcholine



Carnitine



Glutathione

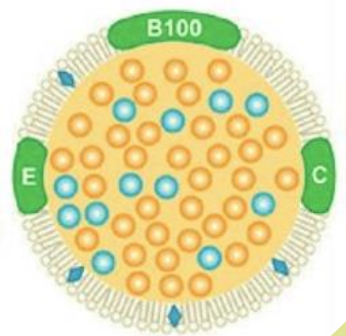


Taurine

Antioxidant Responses

↑ Fatty Acid Synthesis

↑ Protein Synthesis



VLDL

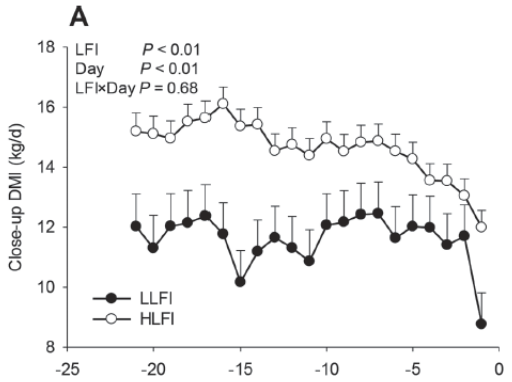
↑ Fatty Acid Export

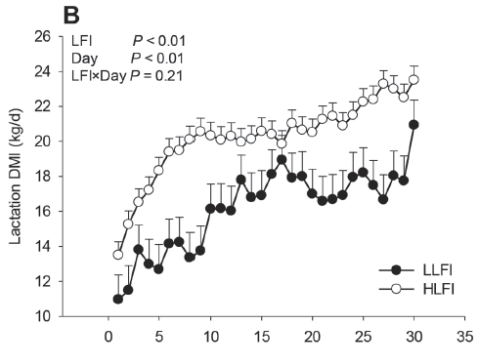
↑ Fatty Acid Oxidation

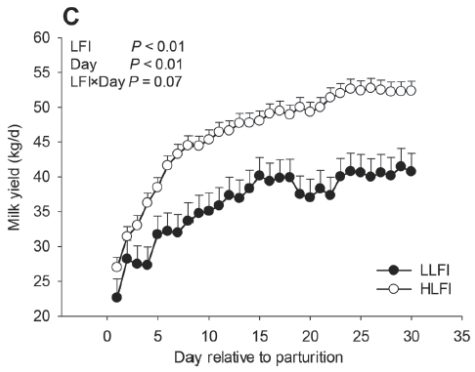
Methionine Improves Liver Function During the Transition Period

- **LFI** (Liver Functionality Index)

Albumin	Indicator of chronic inflammation
Cholesterol	Assessment of lipid export capacity
Bilirubin	Assessment of the liver enzymes and antioxidant status







Methionine supplementation increases the number of high LFI cows.

High LFI

↑ DMI

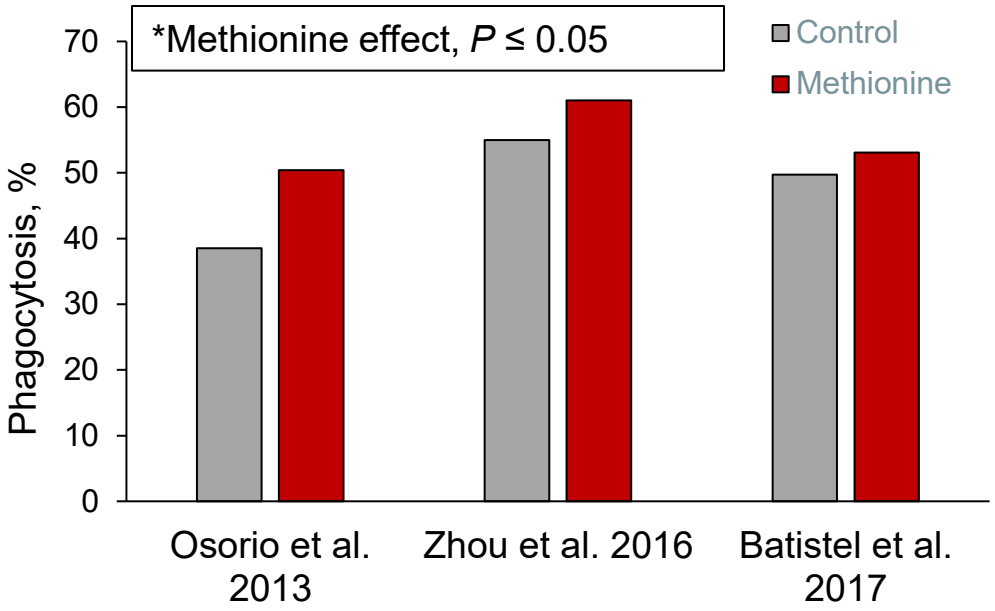
↑ Milk yields

Zhou et al., 2017

Methionine Improves Immune Responses and Decreases Oxidative Stress

Biomarker	Response to Met[1]	Biological function
Metabolism		
Carnitine	↑ (liver)	β-oxidation of Fatty Acids
Cholesterol	↑↑ (plasma)	Lipoprotein metabolism
Inflammation		
IL-1beta	↓ (plasma)	Pro-inflammatory cytokine
Haptoglobin	↓↓ (plasma)	Inflammation signal
Albumin	↑↑ (plasma)	Acute-phase response
Oxidative stress		
Reactive oxygen metabolites (ROM)	↔/↓ (plasma)	Peroxides, superoxide, OH-radicals
Glutathione	↑↑ (liver, blood)	Antioxidant
Taurine	↔/↑ (plasma)	Antioxidant
Antioxidant capacity	↔/↑ (plasma)	Total antioxidants in blood
Paraoxonase	↑↑ (plasma)	Antioxidant enzyme

[1]Relative to a control or rumen-protected choline supplemented diet (Osorio et al., 2013a; Zhou et al., 2017; Sun et al., 2016; Batistel et al., 2018).

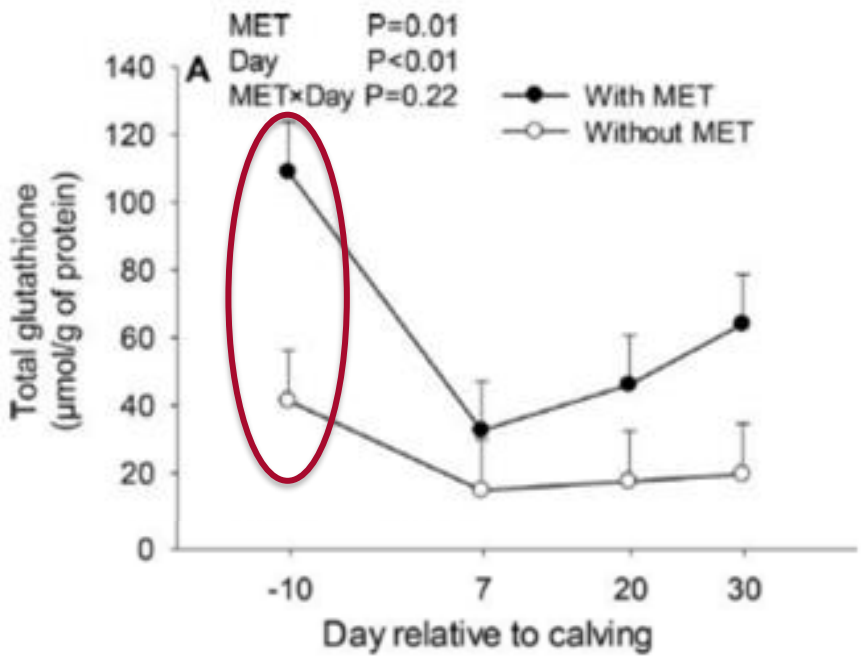


Adapted from Coleman et al., 2020

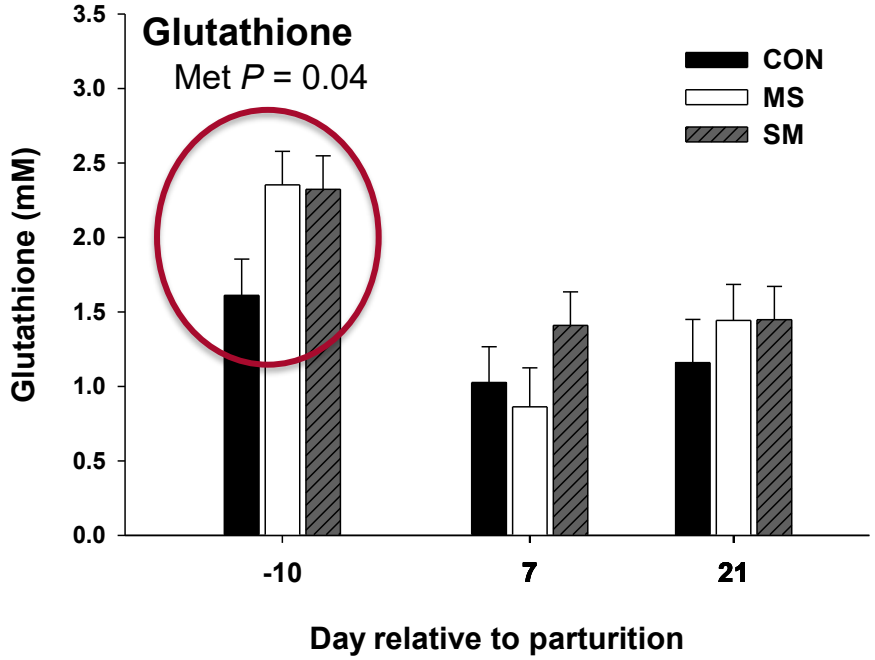
Glutathione Priming Effect of Methionine

Methionine increases glutathione synthesis

Primes the cow to handle oxidative stress!



Zhou et al., 2016



Osorio et. al., 2014

Slide adapted from Osorio et al., 2023

Glutathione Priming Effect is Increases DMI and Milk Yield

J. Dairy Sci. 96:1–16
http://dx.doi.org/10.3168/jds.2012-5790

Supplemental Smartamine M or MetaSmart during the transition period benefit postpartal cow performance and blood neutrophil function

J. S. Osorio,*† P. Ji,*†[1] J. K. Drackley,† D. Luchini,‡ and J. J. Loor*†[2]
*Mammalian NutriPhysioGenomics, and
†Department of Animal Sciences and Division of Nutritional Sciences, University of Illinois, 1207 West Gregory Drive, Urbana 61801
‡Adisseo, Alpharetta, GA 30022

J. Dairy Sci. 99:8956–8969
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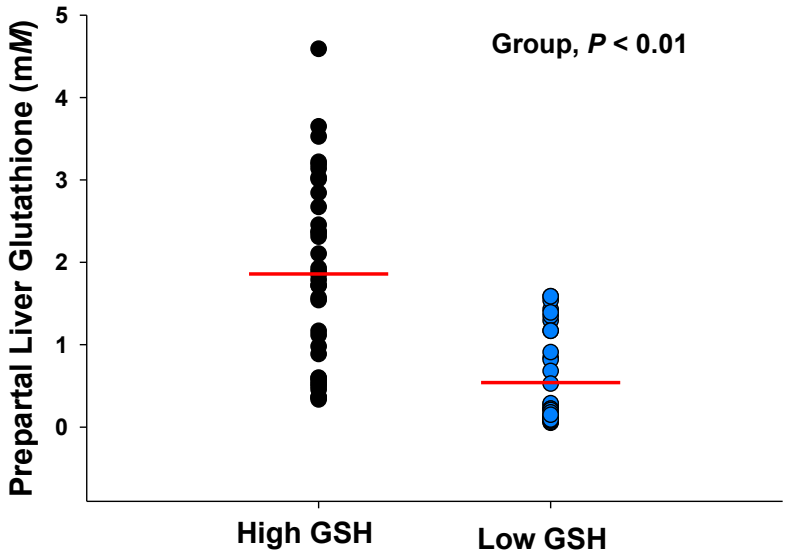
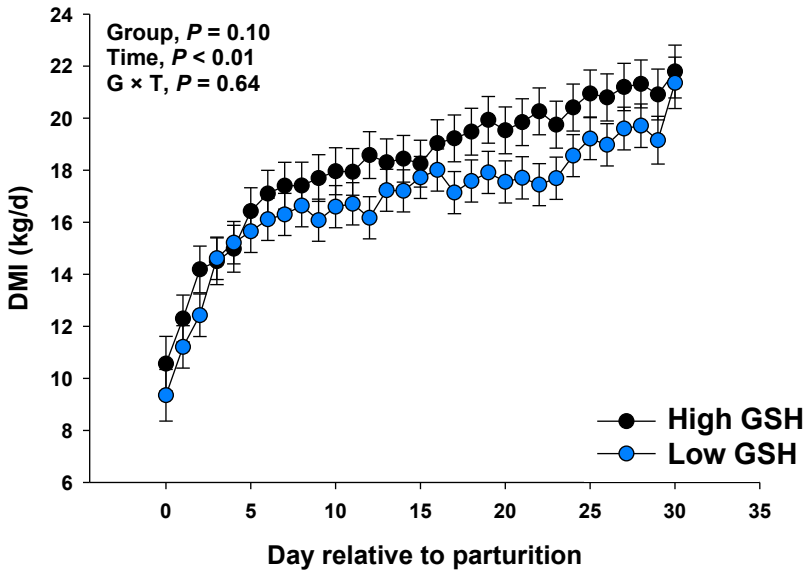
Rumen-protected methionine compared with rumen-protected choline improves immunometabolic status in dairy cows during the peripartal period

Z. Zhou,* O. Bulgari,*† M. Vailati-Riboni,* E. Trevisi,‡ M. A. Ballou,§ F. C. Cardoso,* D. N. Luchini,# and J. J. Loor*[1]
*Mammalian NutriPhysioGenomics, Department of Animal Sciences and Division of Nutritional Sciences, University of Illinois, Urbana 61801
†Dipartimento di Medicina Molecolare e Traslazionale, Università degli Studi di Brescia, 25121 Brescia, Italy
‡Istituto di Zootecnica Facoltà di Scienze Agrarie, Alimentari e Ambientali, Università Cattolica del Sacro Cuore, 29122, Piacenza, Italy
§Department of Animal Sciences, Texas Tech University, Lubbock 79409
#Adisseo, Alpharetta, GA 30022

Prepartal liver Glutathione at -10 d



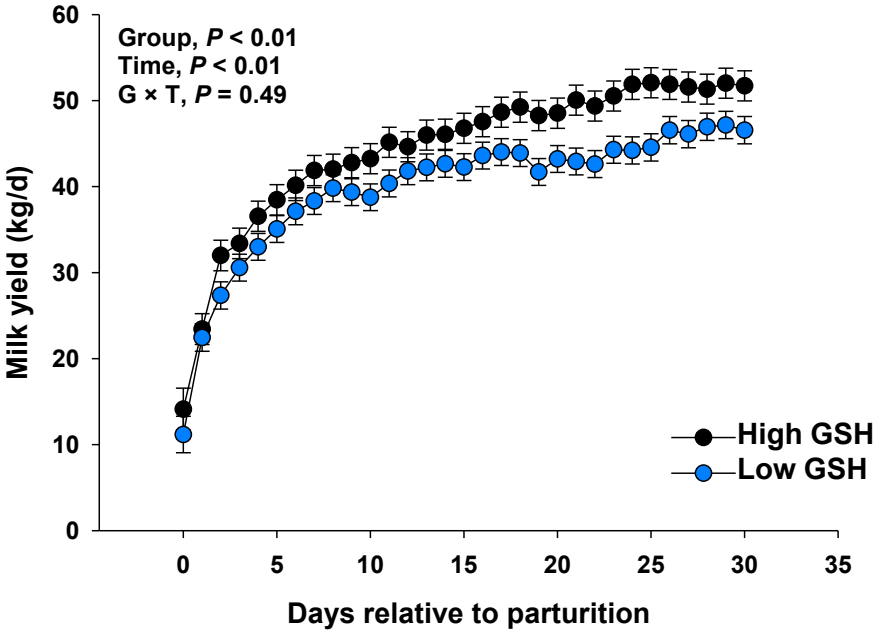


1.4 kg/d increased Dry matter intake

3.1 lb/d increased Dry matter intake

4.5 kg/d increased milk yield

9.9 lb/d increased milk yield



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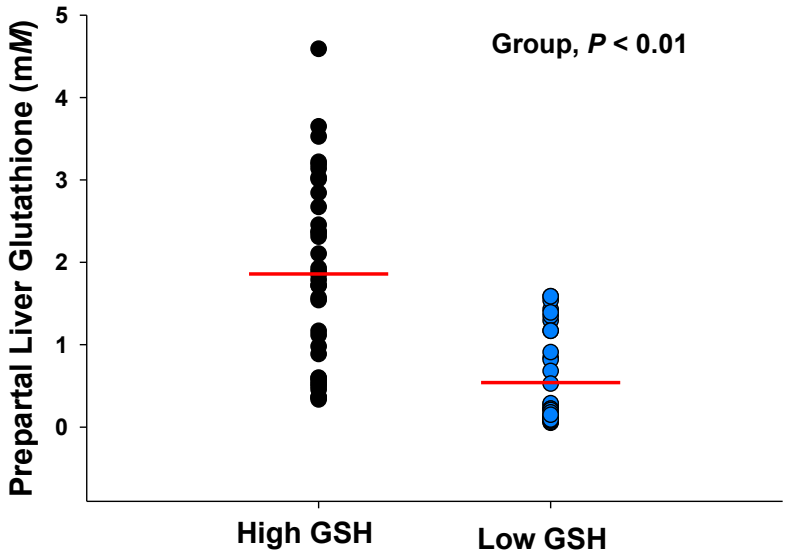
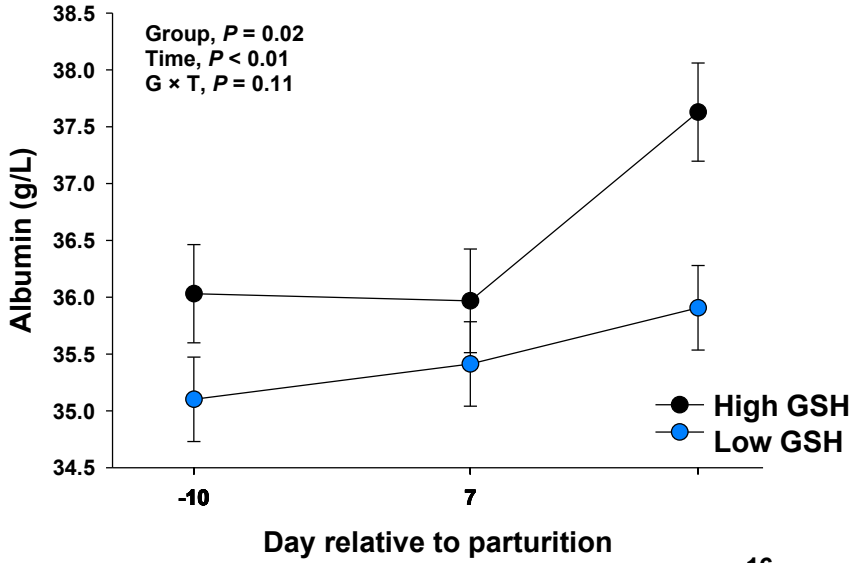
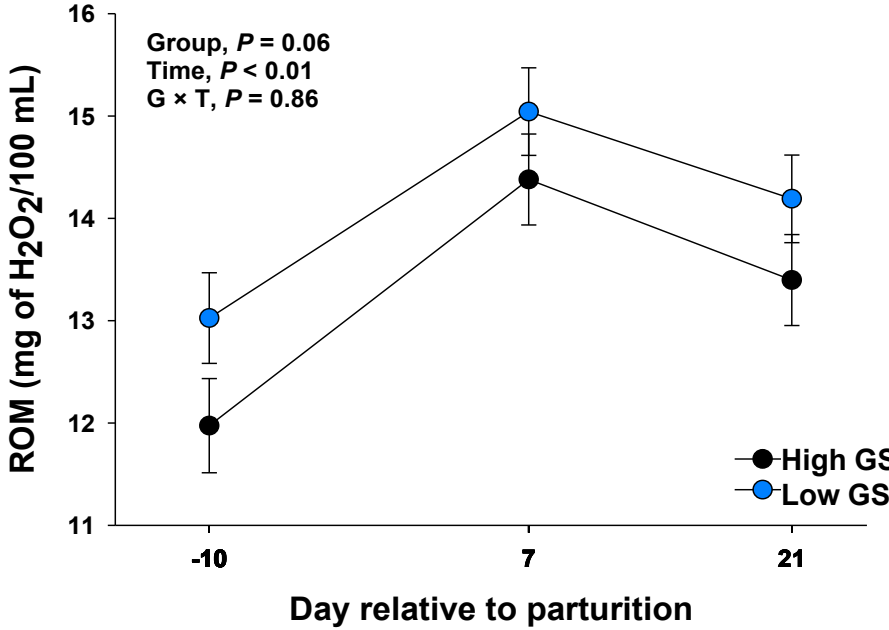




Albumin

Reactive Oxygen Metabolites

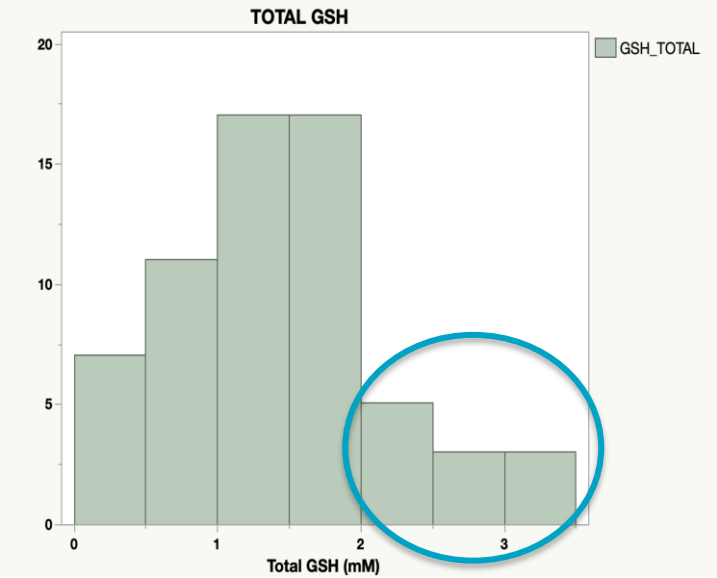


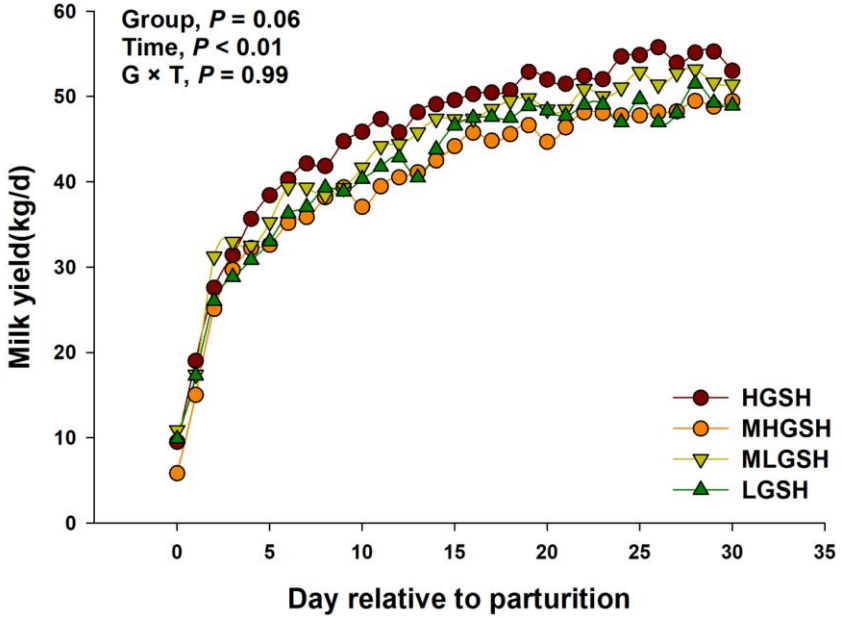
Slide adapted from Osorio et al., 2023

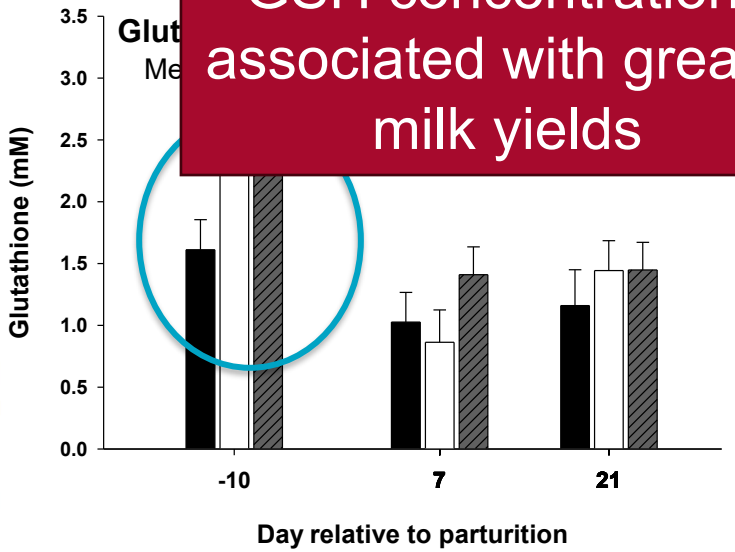
Latest Glutathione Research at Virginia Tech

- Title: ***The impact of prepartal liver glutathione on milk performance parameters and welfare of peripartal dairy cows***

Retrospective analysis based on liver glutathione (GSH) concentrations at -10 DIM







Higher prepartum liver GSH concentrations associated with greater milk yields

Few cows classified as HGSH

Still see association with greater milk

Methionine increases proportion of cows classified as HGSH

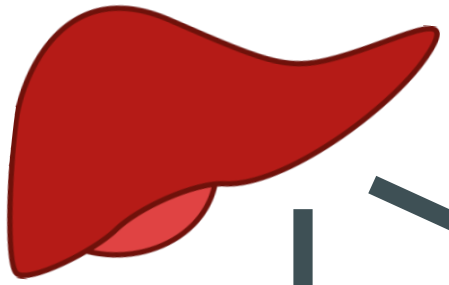
*No Met added to the diet

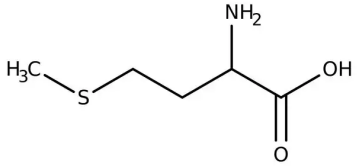
Methionine has a big impact on GSH prepartum. Helps handle stress and drive production!

HGSH = High glutathione; **MHGS** = Medium high glutathione; **MLGSH** = Medium low glutathione; **LGSH**= Low glutathione

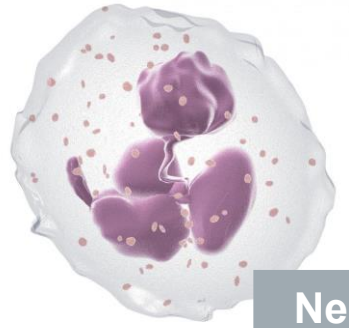
Slide adapted from Osorio et al., 2023

Methionine Prepares the Cow to Handle the Challenges of the Transition Period





Methionine



Neutrophil

↑ Liver Functionality Index (LFI)

Indicator of metabolism and inflammation

Cows with high LFI have greater DMI and milk yields

↑ Glutathione Concentrations

Potent antioxidant

Prepares the cow to handle oxidative stress

↑ mTOR activation

Regulates cellular processes

Increases protein and fat synthesis

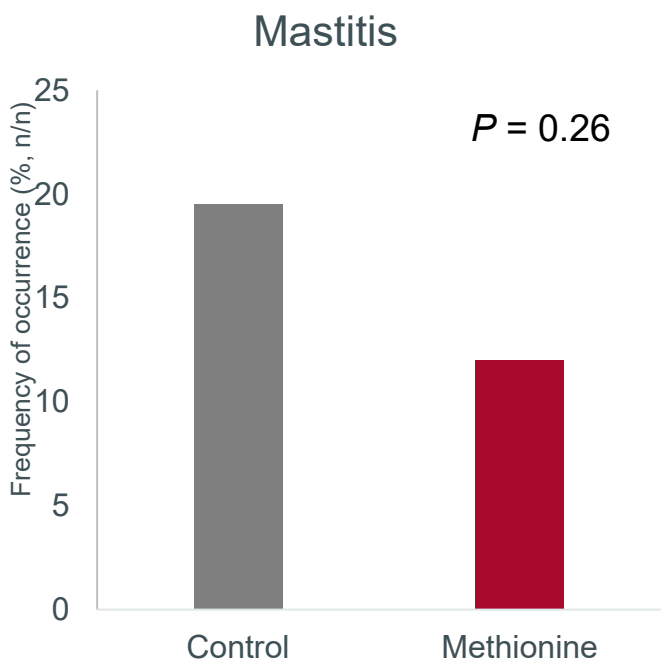
↑ Phagocytosis

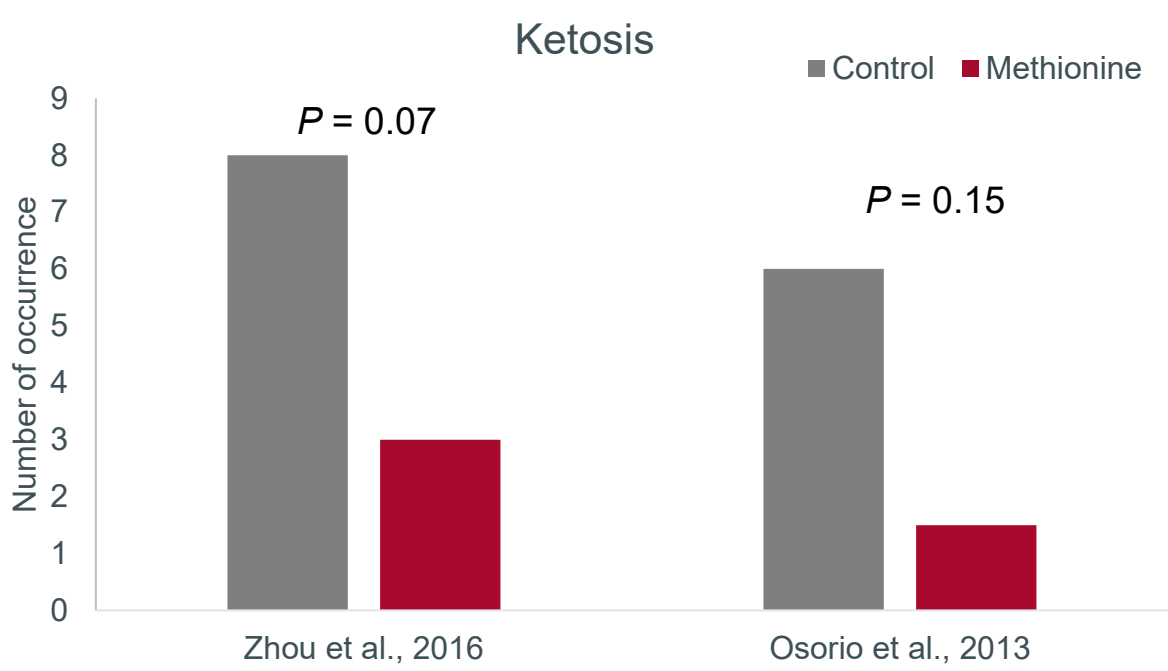
Killing of pathogens

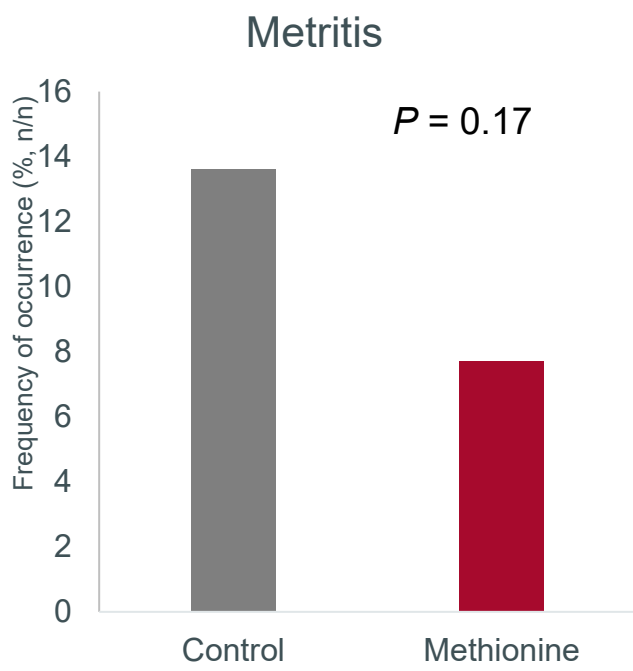
Better able to handle an immune challenge

↑ Milk production and health

Enhanced Methionine Supply Decreases Post-Calving Disorders







Osorio et al., 2013, Zhou et al., 2016, Stangaferro et al., 2017

Methionine Supports Better Reproduction

- Follicle quality: more estradiol and better size
- Better uterine environment: less PMN/inflammation, more lipids/energy as nutrient for the embryo
- Embryo composition: more lipid, bigger size
- Pregnancy recognition: increase concentration of interferon tau (embryo size)
- Reduced the Culling Rate: better health and better reproduction performance

- Decreased embryo mortality (- 4%) and pregnancy loss (-13%)
- Improve heard longevity

Acosta et al., 2016, Toledo et al., 2017, Guadagnin et al., 2021, Toledo et al., 2023, Leao et al., 2024, Stella et al., 2024

Adisseo Methionine for Dairy Cow Lifetime Performance

HEALTH STATUS

- + Glutathione synthesis
- + LFI
- ↓ Inflammation
- ↓ Health Disorders

PRODUCTION

- + Milk protein
- + Milk fat
- + Milk yield
- + DMI

REPRODUCTIVE SUCCESS

- ↑ Embryo size
- ↓ Pregnancy Loss
- ↓ Culling Rate

How Methionine Helps During Heat Stress

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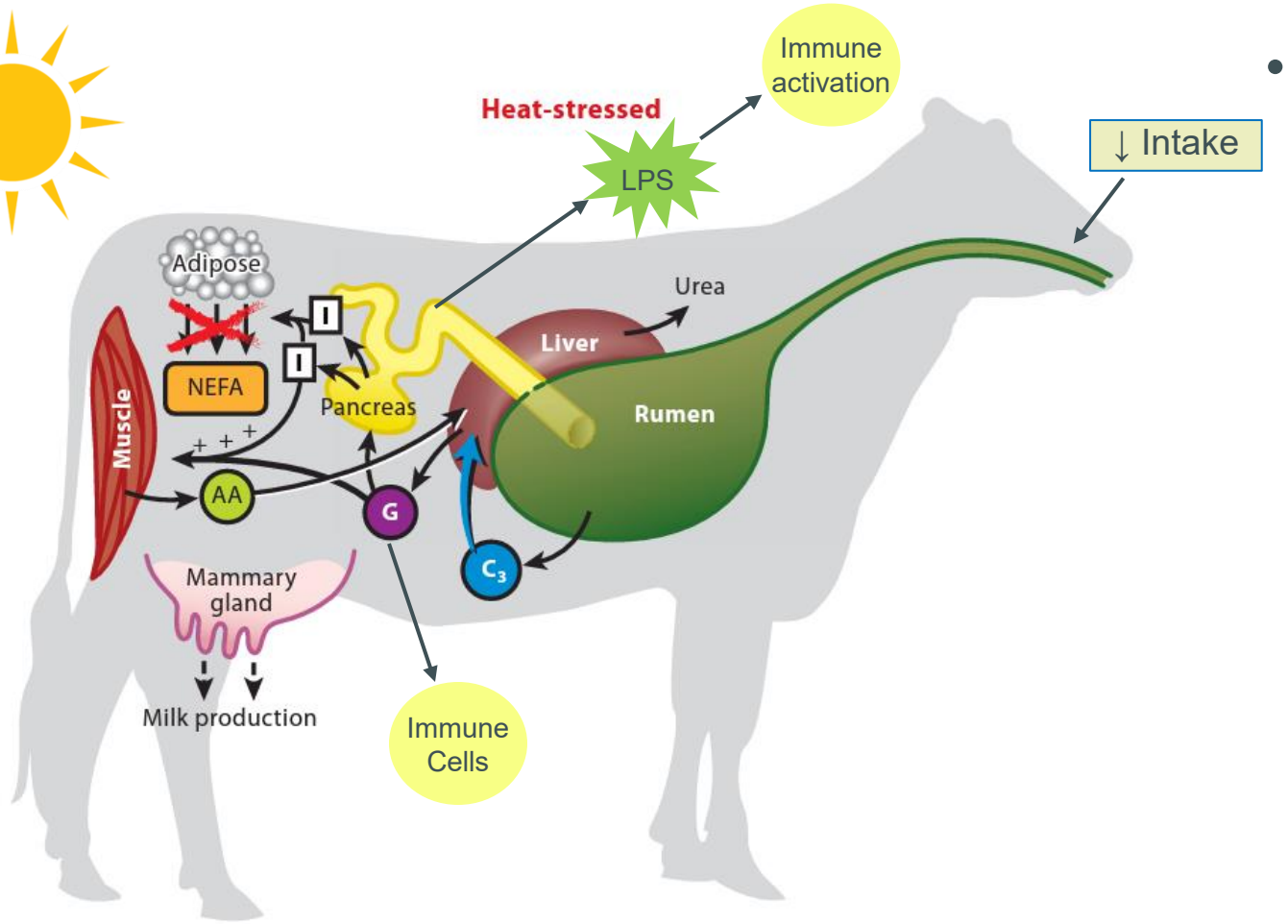
Negative Effects of Heat Stress on Immunometabolism and Production



- Summary of heat stress effects:
  - ↓ DMI
  - ↓ Milk yield
  - ↓ Milk fat and protein
  - ↑ Intestinal barrier dysfunction, aka "leaky gut"
  - ↑ Oxidative stress
  - ↑ Immune responses
  - ↑ Inflammation
  - ↓ Reproductive efficiency
  - ↓ Offspring growth and production

Adapted from Baumgard et al., 2013

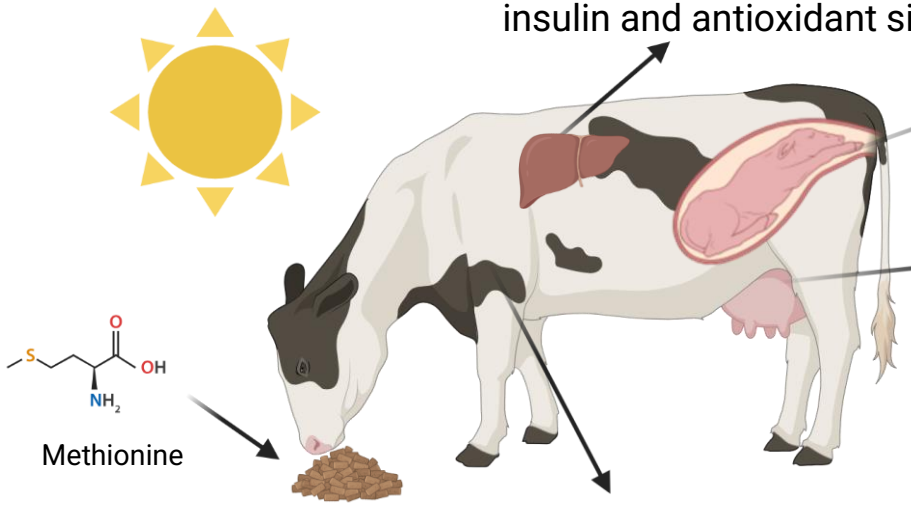
Can focusing on essential nutrient requirements ameliorate negative effects of heat stress?

Supplementary Methionine Helps Counteract Heat Stress

Better liver metabolism

- ↑ mTOR activation
- ↑ Enzyme activity for antioxidant synthesis

Maintained homeostasis in insulin and antioxidant signaling



Offspring growth and development

- ↑ Withers height at birth
- ↑ Placenta weight
- ↑ Placenta AA transporters
- ↓ Calf thermoregulation

Improved milk production and mammary metabolism

- ↑ Milk protein and fat
- ↑ mTOR activation

Fewer apoptotic (dying) cells

Better immune responses

- ↑ Mammary alveoli and epithelial cells

Improved immunometabolic biomarkers

- ↓ Cellular damage
- ↑ Antioxidant responses
- ↓ Inflammation
- ↑ LFI

Methionine is essential for overcoming negative effects of heat stress in both the cow and calf!

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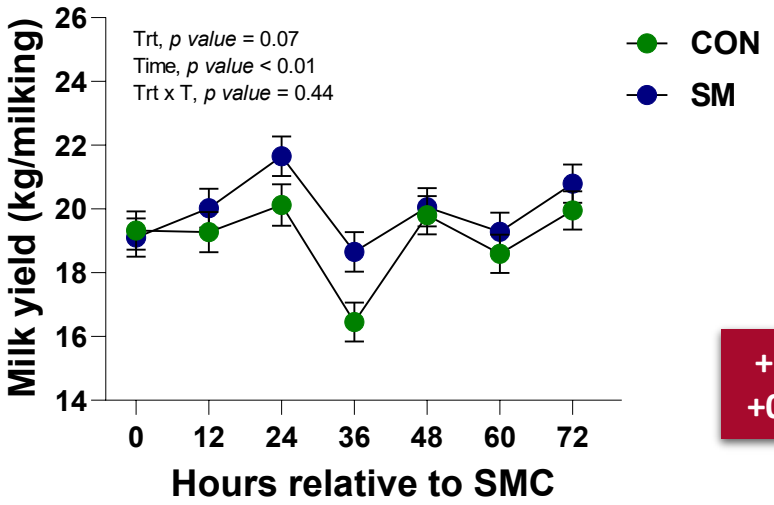
Han et al., 2009; Pate et al., 2020 and 2021; Coleman et al., 2022a,b; Davidson et al., 2024; ADSA Abstracts Guadagnin et al., 2023; Larsen et al., 2024 Davidson et al., 2025

Does Methionine Help Mitigate the Effects of Other Stressors?

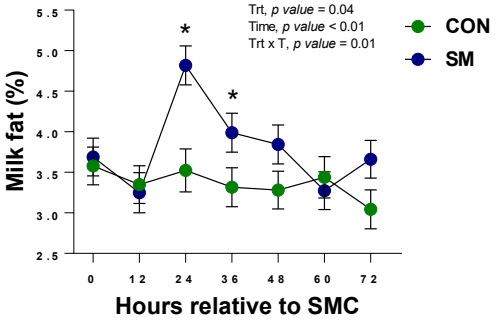
Methionine Improves Response to Stressors: Better Production After Mastitis Challenge

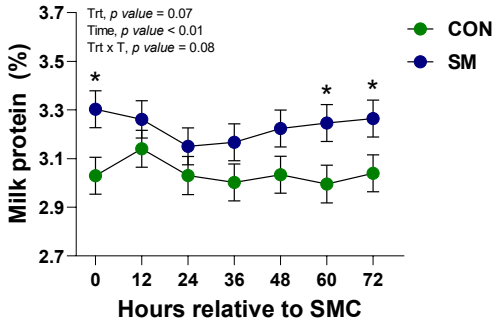
- Supplemented Smartamine (0.09% DMI) and induced subclincal mastitis using *S. uberis* (145 ± 51 DIM).
- Better milk yield, milk fat and protein post-challenge.



+ 0.87 kg/milking
+ 1.94 lb/milking

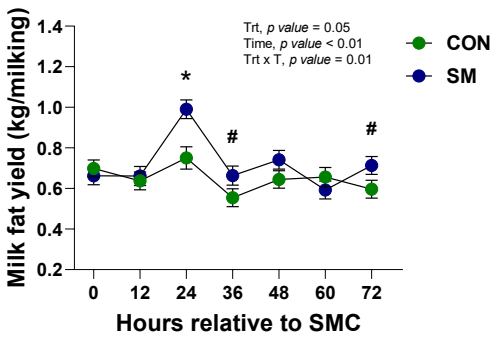
+ 0.43% milk fat

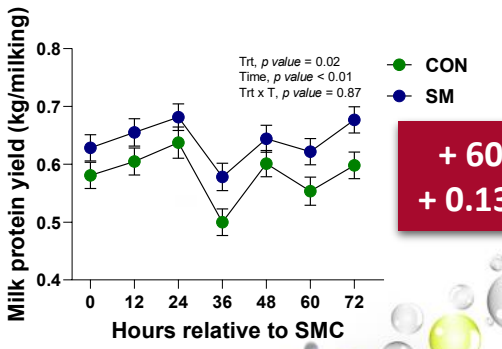




+ 0.19% milk protein

+ 70 g fat/milking
+0.15 lb fat/milling





+ 60 g protein/milking
+ 0.13 lb protein/milking

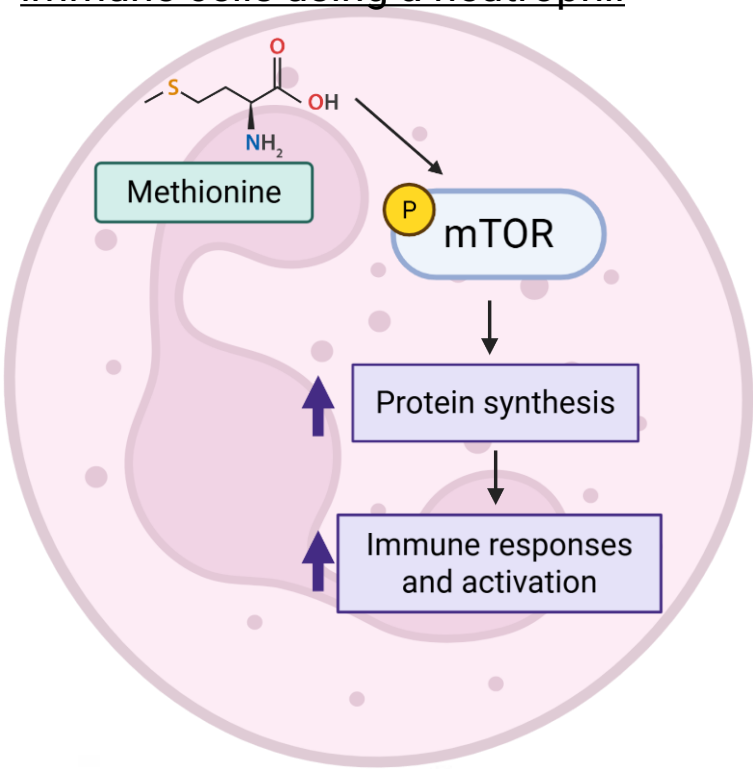
+13.4 g Metabolizable Met; Lys:Met 2.53 for RPM and 3.23 for CON

Paz et al., 2024

Methionine Improves Response to Stressors: Less Oxidative Stress and Inflammation and Better Immune Response During Mastitis Challenge

Biomarker	Change with RPM vs Control	What biomarker is and conclusion drawn
Liver glutathione	↑	Antioxidant. Better antioxidant capacity.
Reactive oxygen species	↓	Marker of oxidative stress. Better oxidative status.
Ceruloplasmin	↓	Acute phase protein. Lower systemic inflammatory status.
Leukocyte phosphorylation of mTOR proteins	↑	Greater mTOR signaling = better immune responses.

Example of mTOR signaling in immune cells using a neutrophil

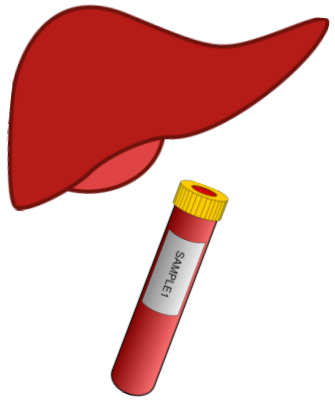


Paz et al., 2024

Methionine Supplementation is Essential to Handle the Immunometabolic Effects of Stressors

Overall take away message

- During periods of stress, Met helps to counteract negative effects by:
  - –Supporting milk protein and fat synthesis
  - –Promoting antioxidant synthesis to maintain homeostasis in immunometabolism



Immunometabolism

Risk of metabolic disorders, disease and negative effects of stress

Milk production, reproduction and healthier cows

- These effects are observed during transition period, heat stress, mastitis and other stressors.

What Else Is Adisseo Researching?

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Adisseo-UW Madison R&I Agreement: A Unique Collaboration

A research agreement between Adisso and the University of Wisconsin-Madison was established in 2020.

Objective: To create a platform in the US, acting as a hub for our global ruminant research to collaborate on research projects.

12 research orders have been funded in the last 5 years.

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Projects at UW-Madison

Investigating the role of energy source on essential AA stimulation of milk solids production

- Objective: investigate the potential interaction between energy source and AA on milk fat and protein production.

- Treatments: 2 x 2 factorial
  1. glucogenic energy vs. ketogenic energy
  2. balanced for Lys, Met and Leu

- Results:
  - Balanced AA supplementation stimulated milk components independently of energy source (no interaction).
  - Mammary uptake of essential AA increased when diet was balanced for AA.
  - Cows used N more efficiently when consuming glucogenic diet.

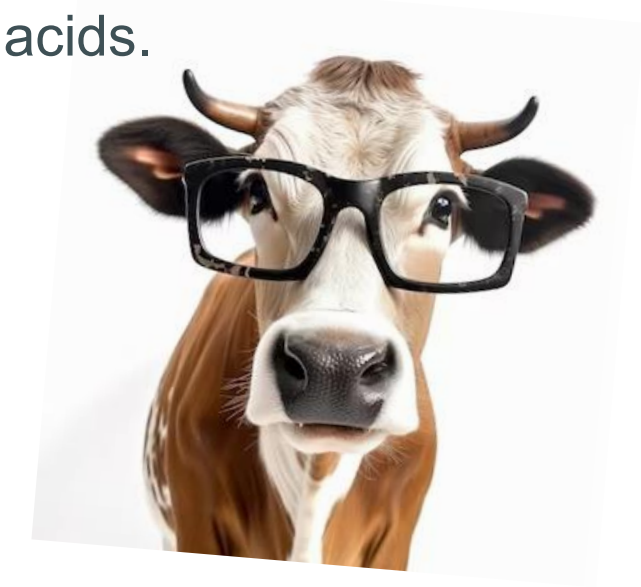
- Takeaway: Amino acid balancing drives milk synthesis by increasing mammary AA uptake, regardless of energy source.

ADSA Abstracts Ruh et al., 2022 and 2023

Projects at UW-Madison

Amino acid supplementation as a potential strategy to mitigate milk fat depression (MFD)

- Objective: determine the effects of increasing metabolizable Met and Leu supply on milk fat production during MFD induced by dietary polyunsaturated fatty acids.



- Treatments: 2 x 2 factorial
  1. with or without unsaturated fatty acids to induce MFD
  2. balanced or not balanced for Met and Leu

- Results:
  - Supplying soybean oil induced MFD: decreased milk fat % and yield.
  - AA had an overall positive effect on fat yield.
  - Soybean oil altered adipose tissue genes, while AA altered metabolic genes in the mammary gland.

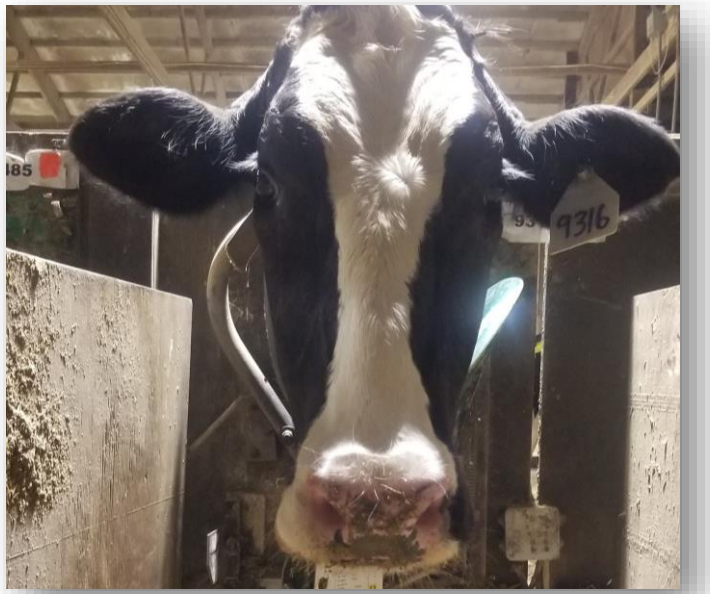
- Takeaway: amino acid supplementation did not overcome the induced MFD but results further underscore the beneficial effects of AA supplementation on increasing milk fat production.

ADSA Abstracts Ruh et al., 2023 and 2024

Projects at UW-Madison

Strategies to maximize histidine effect on production and nutrient efficiency

Objective: determine if balancing lactating dairy cow diets for the TOR-AA Met and Leu alters the response to His when supplemented as a rumen undegradable protein source.



Treatments: 2 x 2 factorial

1. low or high TOR-AA (Met and Leu)
2. low or high His

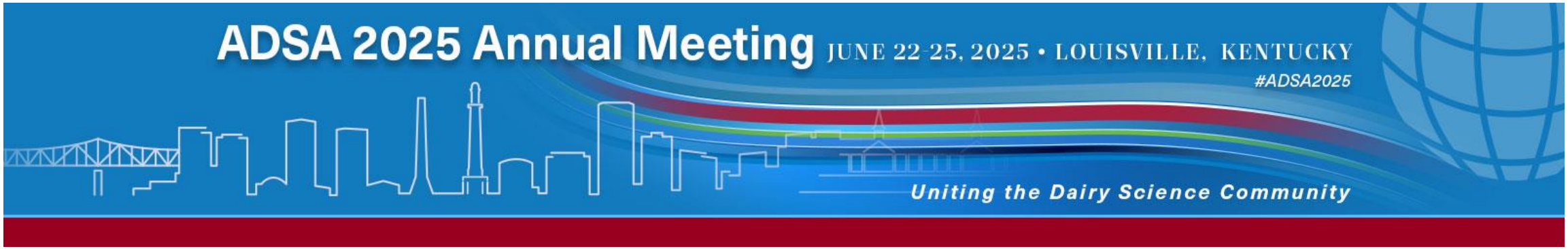
Results:

- Histidine increased DMI, milk yield, protein % and yield and fat yield (preformed and de novo fatty acids).
- TOR-AA increased DMI, milk yield, protein % and yield, and fat yield (de novo and mixed fatty acids).
- Additive effect of His and TOR-AA on ECM, protein and de novo fatty acids.
- TOR-AA decreased N use efficiency (NUE).

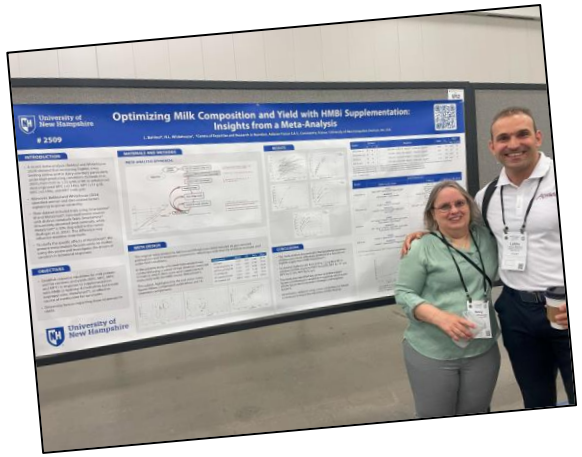
Takeaway: Balancing lactation diets for His, in addition to TOR-AA, increased milk components yield without negatively affecting NUE.

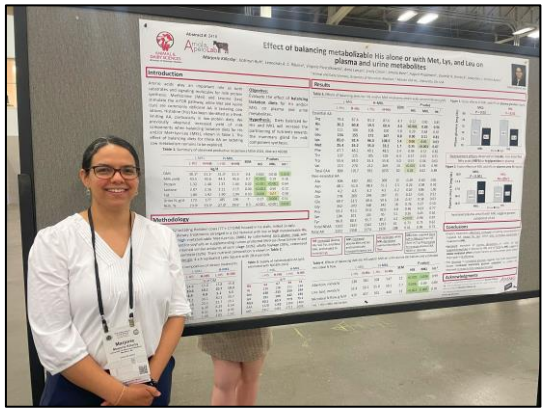
ADSA Abstract Killerby et al., 2024, 2025

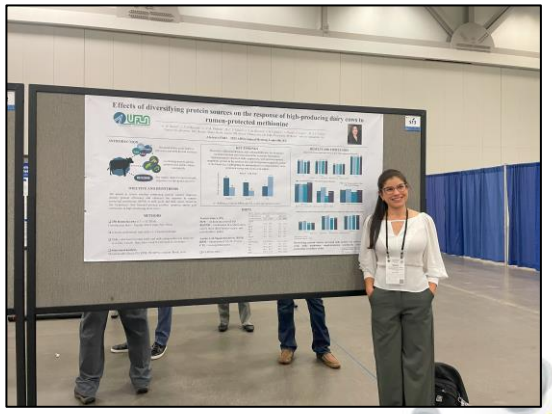
Other ADSA Abstract Highlights

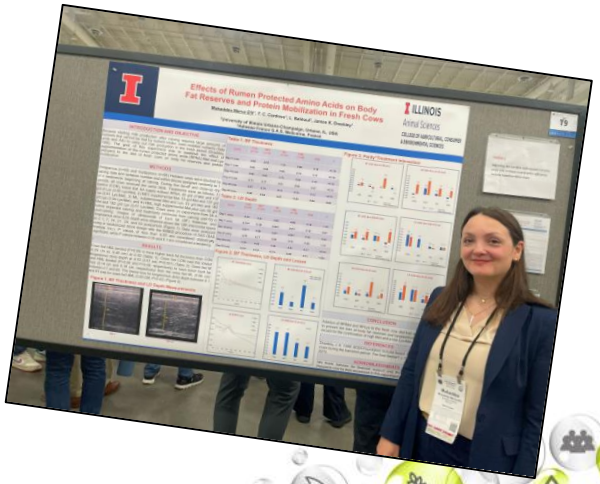


- 6 Abstracts total this year from Adisseo funded research.









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ADSA Abstracts – UNH/Adisseo

University of New Hampshire

- Optimizing milk composition and yield with HMBi supplementation: Insights from at meta-analysis
  - Objective: to establish response equations for milk protein and fat contents and yields (MPC, MFC, MPY, and MFY) in response to supplementation with HMBi, and to identify factors influencing those responses.
  - Results:
    - The models indicated that increasing mMet by 0.29 g/Mcal ME resulted in increases of 0.16% and 82 g/d for MPC and MPY, respectively, with additional increases of 0.06% and 10.0 g/d during early lactation (0-60DIM).
    - Similarly, MFC and MFY increased by 0.20% and 107 g/d, respectively, with an additional rise of 0.39% and 126 g/d in early lactation.
  - Takeaway: The meta-analysis provides accurate predictive models to help nutritionists precisely formulate Met supply using HMBi.

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Bahloul and Whitehouse, 2025

ADSA Abstracts – University of Illinois

- Effects of rumen protected amino acids on body fat reserves and protein mobilization in fresh cows

**At 2024 ADSA they reported that supplying both methionine and lysine from calving until 63 DIM improved milk fat, protein and energy-corrected milk yields.*

  - Objective: to establish the effect of rumen protected methionine and lysine supplementation in the diet of fresh cows on body fat reserves and protein mobilization.
  - Results:
    - Ultrasonography used to measure back fat thickness and *longissimus dorsi* muscle depth at d 1, 7, 14, 21, 28 and 63 d postpartum.
    - Supplementation of methionine and lysine prevented the loss of body fat reserves and *longissimus dorsi* muscle depth compared to control cows.
  - Takeaway: Amino acid balancing in early lactation supports better adipose and muscle metabolism, allowing the cow to have greater milk production without compromising body reserves.

ADSA Abstracts – UFLA

- Effects of diversifying protein sources on the response of high-producing dairy cows to rumen-protected methionine (RPM)

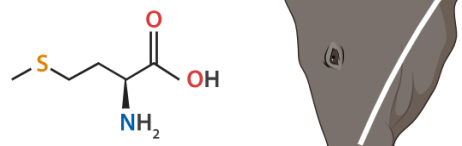
  - Objective: Evaluate if combining protein sources (blend of soybean meal, canola and DDGS vs. soybean meal) enhances dietary protein utilization and improves the response to RPM.

  - Results:
    - No interaction between protein source and RPM.
    - However, BLEND increased milk protein yield but reduced fat production vs. SOY.
    - Supplementation of RPM increased both milk protein, fat and energy-corrected milk.
    - Milk urea nitrogen was lower in BLEND than SOY but increased with RPM.
    - De novo fatty acids lower in BLEND than SOY but increased with RPM.

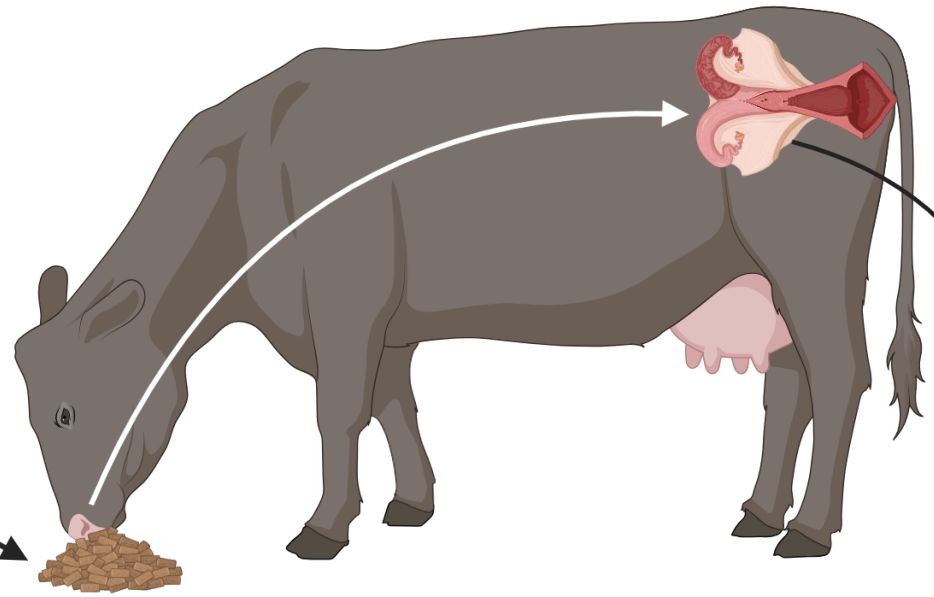
  - Takeaway: The improvements in milk components with RPM is consistent with previous work and reiterates the importance of methionine for both protein and fat. Further analyses will provide information on how AA balancing and lowering dietary N load can improve nitrogen use efficiency.

Souza et al., 2025

New Beef Research: Periconceptional Methionine

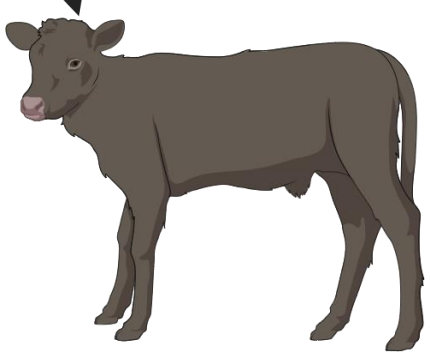


Methionine

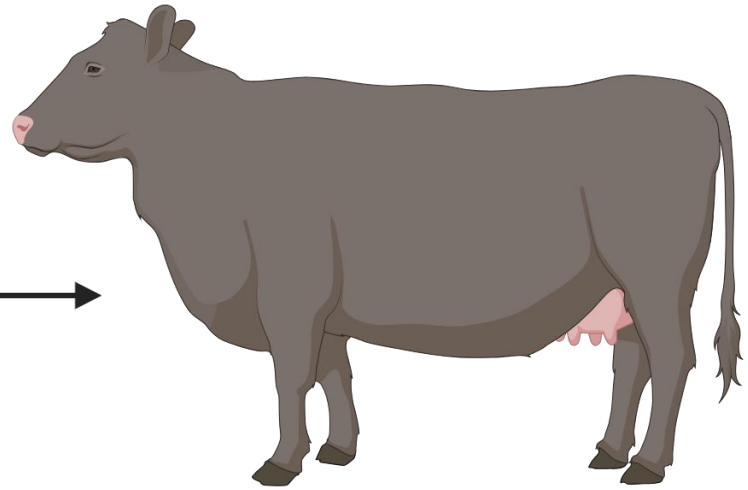


Fed 7 d before and after conception

Altered postnatal and postweaning growth



Withers height through weaning



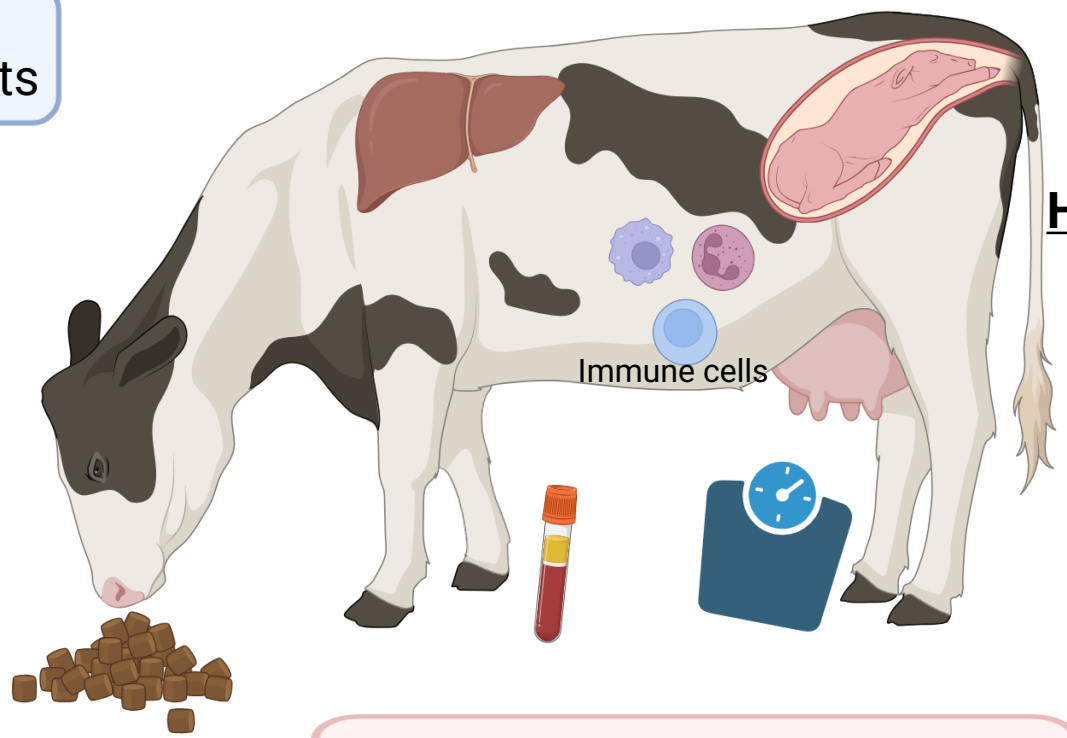
Altered hepatic and muscle gene expression

Heredia et al. 2025

Nutrition & Health For Lifetime Performance

Transition and Production Benefits

- ↑ Fat
- ↑ Protein
- ↑ Milk yield
- ↑ ECM
- ↑ DMI
- ↑ mTOR
- ↓ Post calving disorders



Health Support and Stress Mitigation

Heat stress, transition period, mastitis

- ↑ LFI
- ↑ Glutathione synthesis
- ↓ Oxidative stress
- ↓ Inflammation
- ↑ Immune function
- ↑ mTOR

New Research and Future Focus

- Amino acid balancing optimization and interactions
- Effects of nutrients on immunometabolism
- Periconceptional AA supplementation
- Impacts of AA on offspring performance

Final Stop

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Questions?

Save the Date for Our Next Webinar on November 13th

Featuring Dr. Johan Osorio

Topic: Optimizing Cow Health and Performance via Amino Acid-Driven Cellular Pathways

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