# *Impact of Muscle Depletion & Accretion Across Lactation*


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# *Metabolic Changes Associated with Onset of Lactation – Partial List*

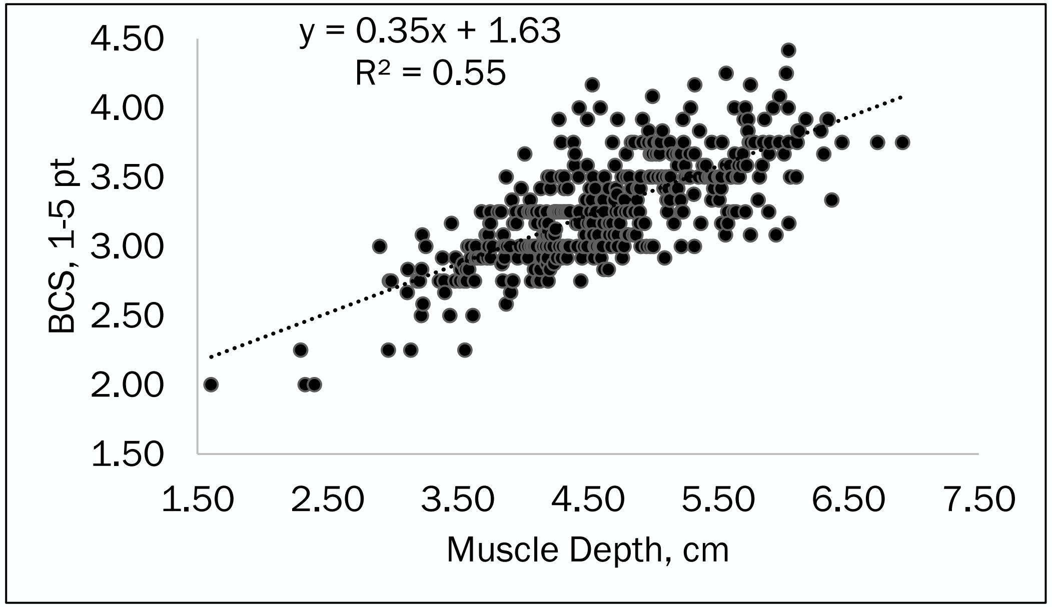
| Biological Function | Metabolic Change | Tissues Involved |
|---|---|---|
| Milk synthesis | Increased use of nutrients | Mammary |
| Lipid metabolism | Increased lipolysis<br>Decreased lipogenesis | Adipose tissue |
| Glucose metabolism | Increased gluconeogenesis<br>Increased glycogenolysis<br>Decreased use of glucose and increased use of lipid as energy source | Liver<br><br>Body tissues in general |
| Protein metabolism | Mobilization of protein reserves | Muscle and other body tissues |
| Mineral metabolism | Increased absorption<br>Increased reserve mobilization | Gut, bone, kidney and liver |
| Intake and digestion | Increased food consumption<br>Hypertrophy of digestive tract<br>Increased nutrient absorption capacity | Central nervous system<br>All segments of the digestive tract |
| Immune function | Increased positive acute phase proteins<br>Decreased negative acute phase proteins | Liver and other tissues |

**Slide adapted from Dr. Dale Bauman**

# How Much Tissue Can Be Utilized

- Body composition
  - Protein – 90 to 125 kg
    - Can mobilize < 25%
    - Variation in amount of protein mobilization
      - Some variation in pattern based on parity?
  - Adipose – < 100 to > 200 kg
    - Dependent on body condition score
    - Can mobilize in excess of 100 kg
  - Subcutaneous fat is highly correlated to body condition score
  - Subcutaneous fat is highly correlated to whole body fat (r = 0.90)
  - Muscle depth and body condition score are moderately correlated (r = 0.50 to 0.60)

Schroder and Staufenbiel, 2006




Data from Gouveia et al., 2024

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# *Protein Balance Post Calving*

- MP balance reaching nadir around 7 DIM
- By about 30 DIM positive protein balance
- Dependent on intake, milk production, and milk protein yield

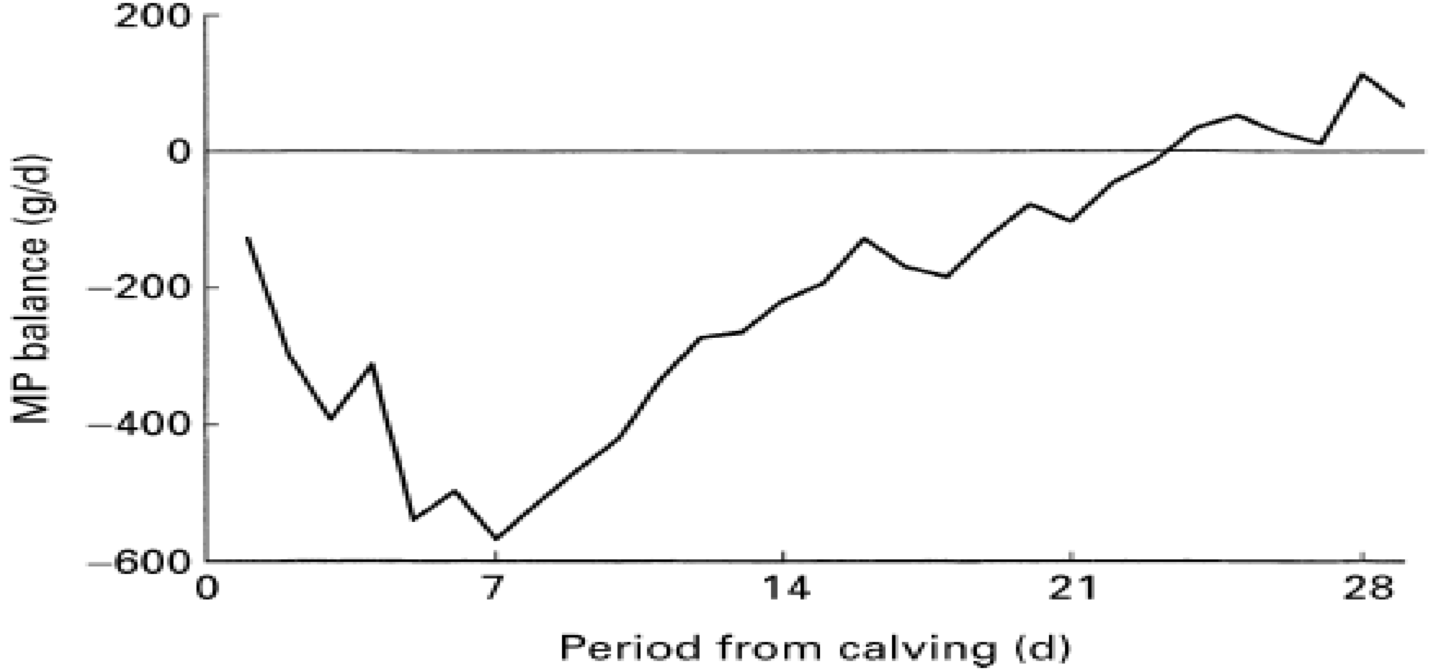


**Fig. 1.** Calculated metabolizable protein (MP) balance in post-parturient cows (*n* 80) fed on a ration containing (/kg DM) 178 g crude protein (nitrogen × 6·25) and 7·0 MJ net energy for lactation. Individual values were calculated from daily individual measurements of crude protein intake and milk yield, and weekly measurements of milk composition.

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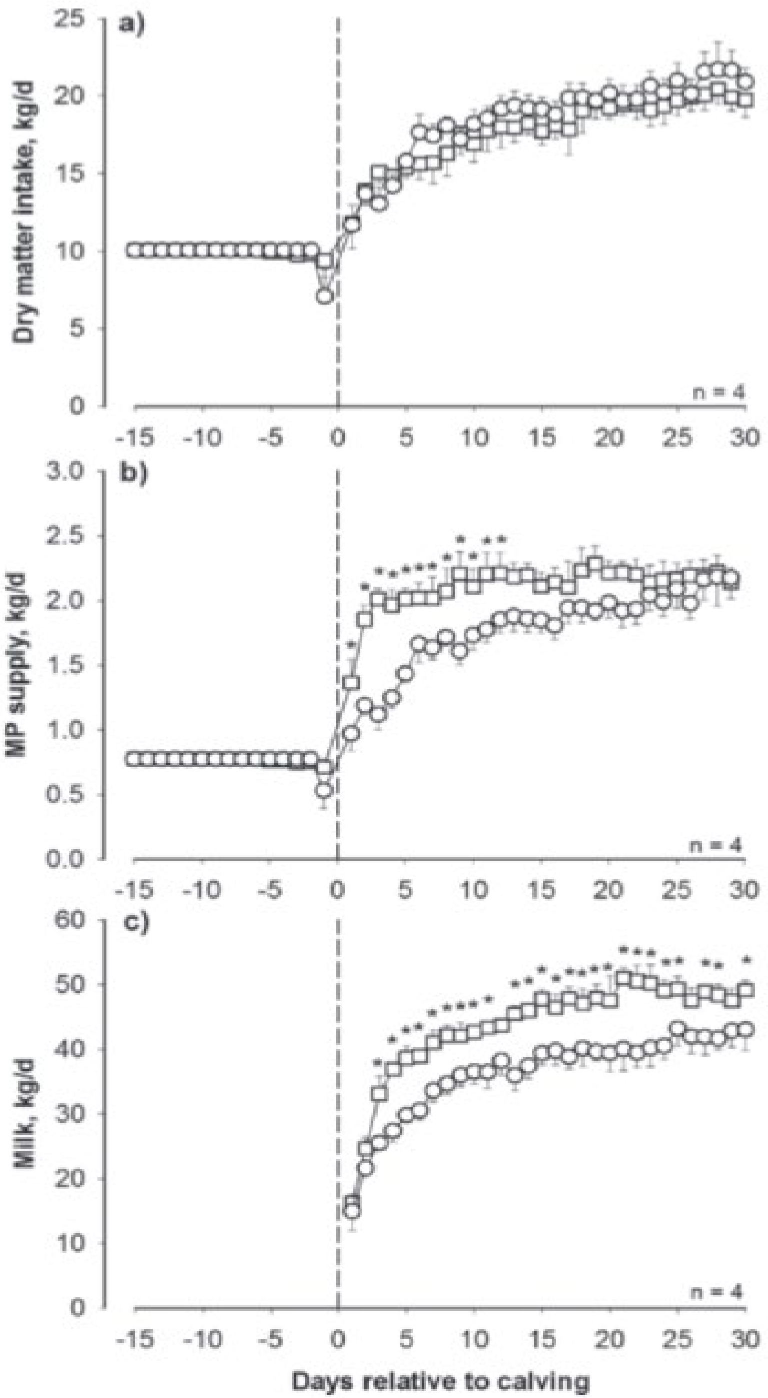
Bell et al., 2000

# *Infusions of Casein Studies*

- Due to the negative MP balance observed in early lactation → abomasal infusions of AA of casein (Larsen et al., 2014) or similar in profile to casein (Larsen et al., 2015)
  - Supply of ~700g/d, ~500 or ~200 g/d at 4, 15, 29 DIM
  - No difference in intake
  - Milk yield was 7.2 kg/d (15.8 lbs/d) greater from through 30 DIM
  - Milk protein yield greater earlier in lactation
- In early lactation → mammary gland is selfish

- **How does muscle mobilization contribute to production in early lactation?**

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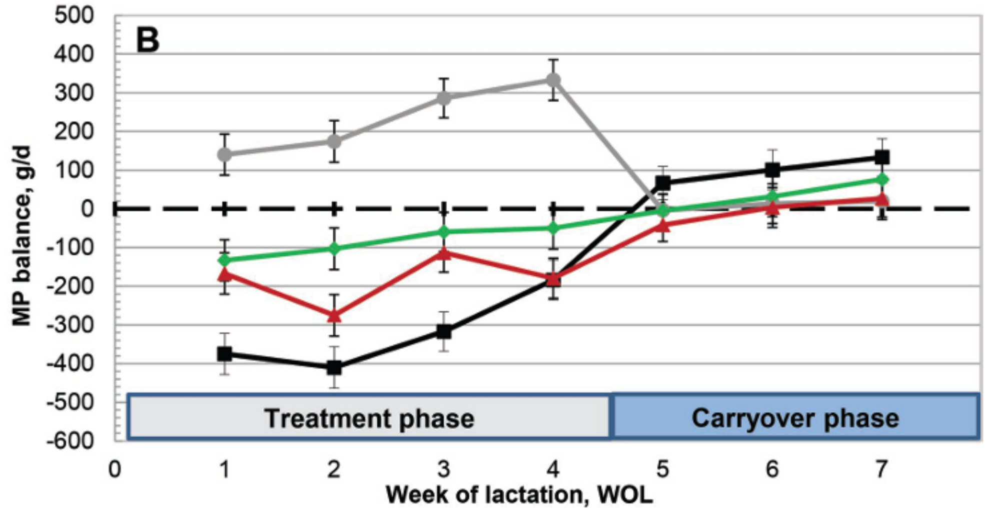
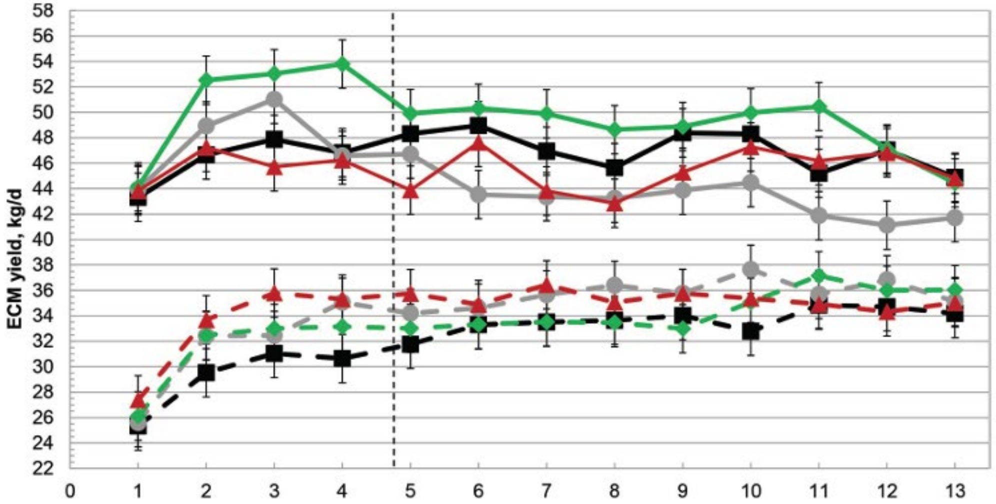
# MP Supplementation Postpartum – Tebbe and Weiss (2021)

- Increasing MP and AA supply may be of greater importance for fresh cows than dietary energy supply because postpartum cows have a greater capacity to mobilize body lipid versus protein (Schei et al., 2005).
- 40 primigravid and 40 multi gravid Holsteins fed common diet prepartum and in the carryover phase.
- After calving to 25 DIM
  - Deficient in MP (DMP; 17% CP; 1,856 g/d MP) BLACK
  - Adequate MP primarily soy (AMP; 20% CP; 2,329 g MP) GRAY
  - Adequate MP primarily R-P AA (Blend; 20% CP; 2,471 g/d MP) RED
  - Blend but less fNDF (Blend-fNDF; 2,482 g/d MP) GREEN

- Different responses in mature vs primiparous cows to MP supplementation in the fresh period.

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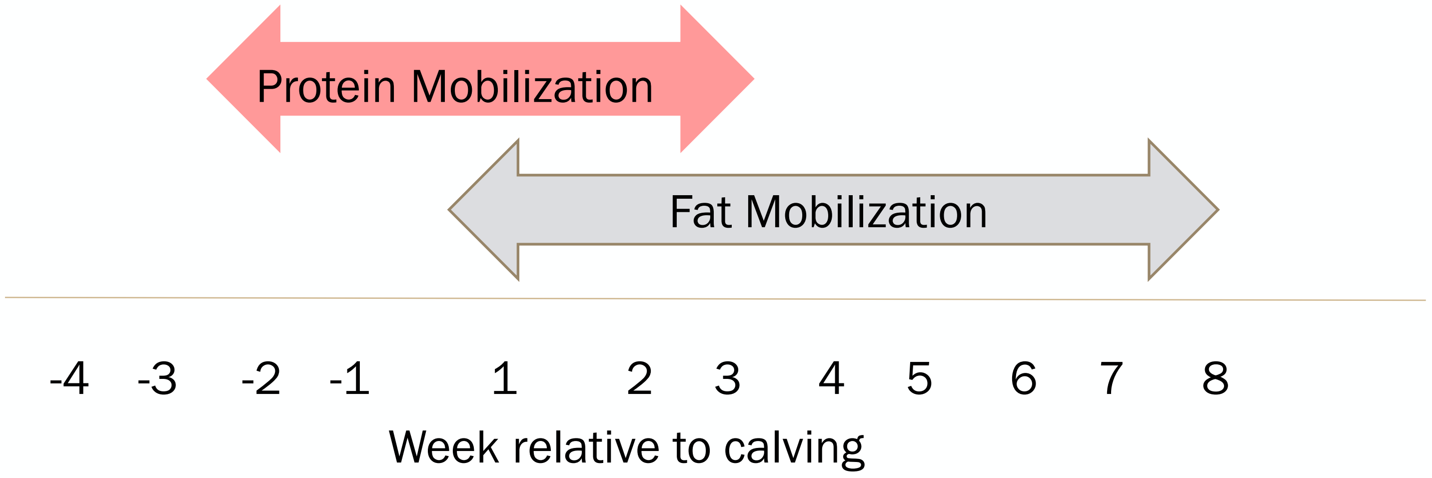
# *Mobilization of Tissue Stores*

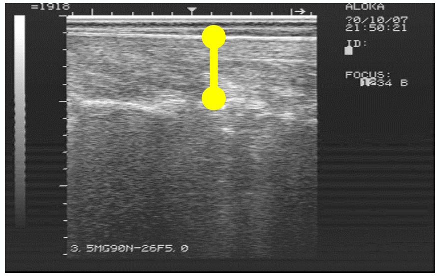
- 3 main stores of tissue to mobilize during the transition period
  - Glycogen – mobilized quickly, not a large reserve
  - Adipose – usually largest pool of tissue unless under-conditioned
  - Protein – mostly skeletal muscle and likely starts prior to calving

    *when it starts is likely dependent on a couple of factors

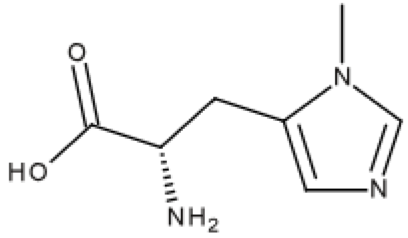



van der Drift et al., 2012

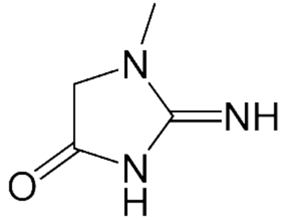
# Measuring Muscle Mobilization



- Serial ultrasound images to measure change in muscle depth



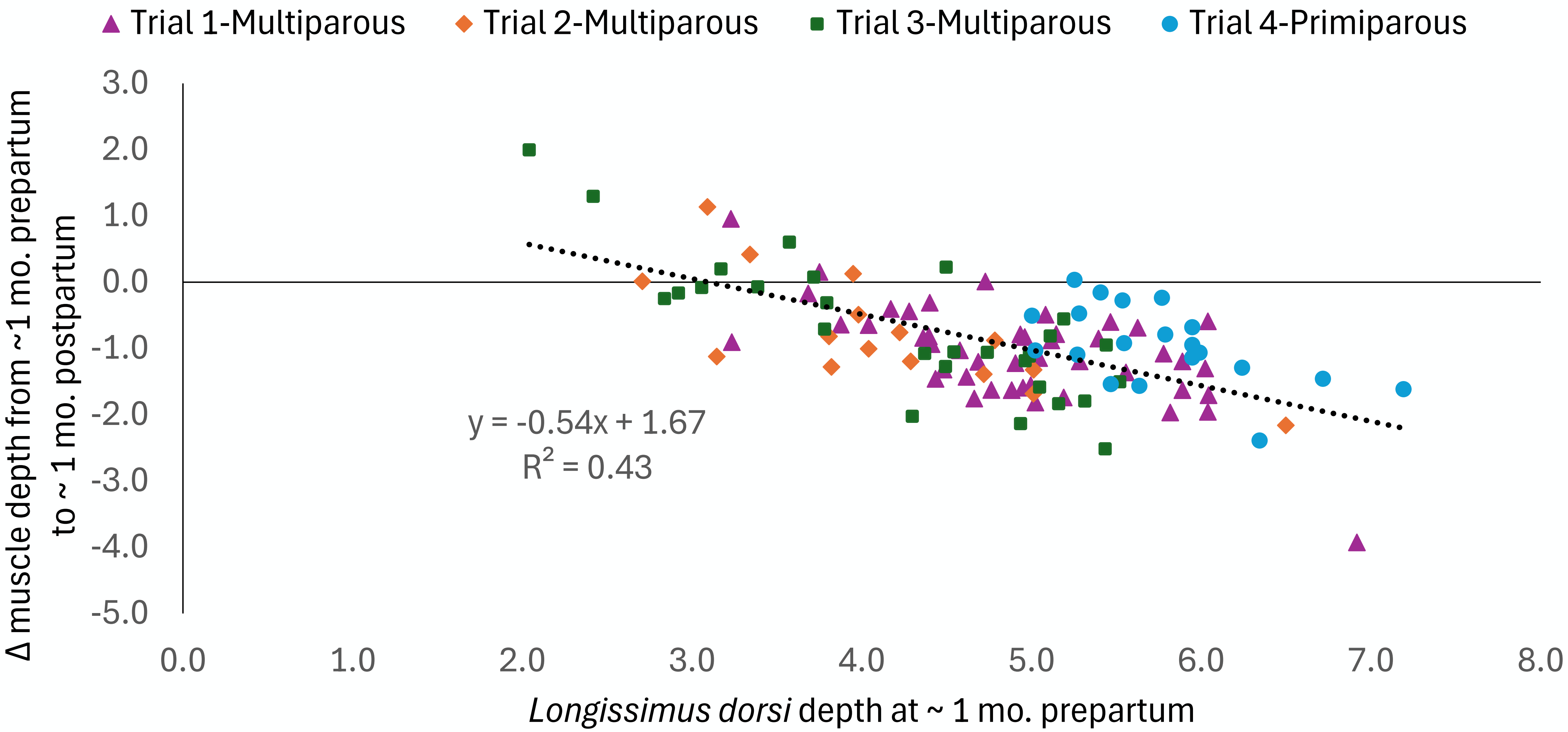
- 3-methylhistidine is released when muscle fiber (actin and myosin) is degraded and is not used for protein synthesis



- Creatinine is an indicator of muscle mass

- Ratio of 3-methylhistidine to creatinine would indicate muscle mobilization per unit of muscle mass
  - Higher → more muscle mobilization

# *If Cows Have More Muscle They Mobilize More Muscle In The Transition Period*

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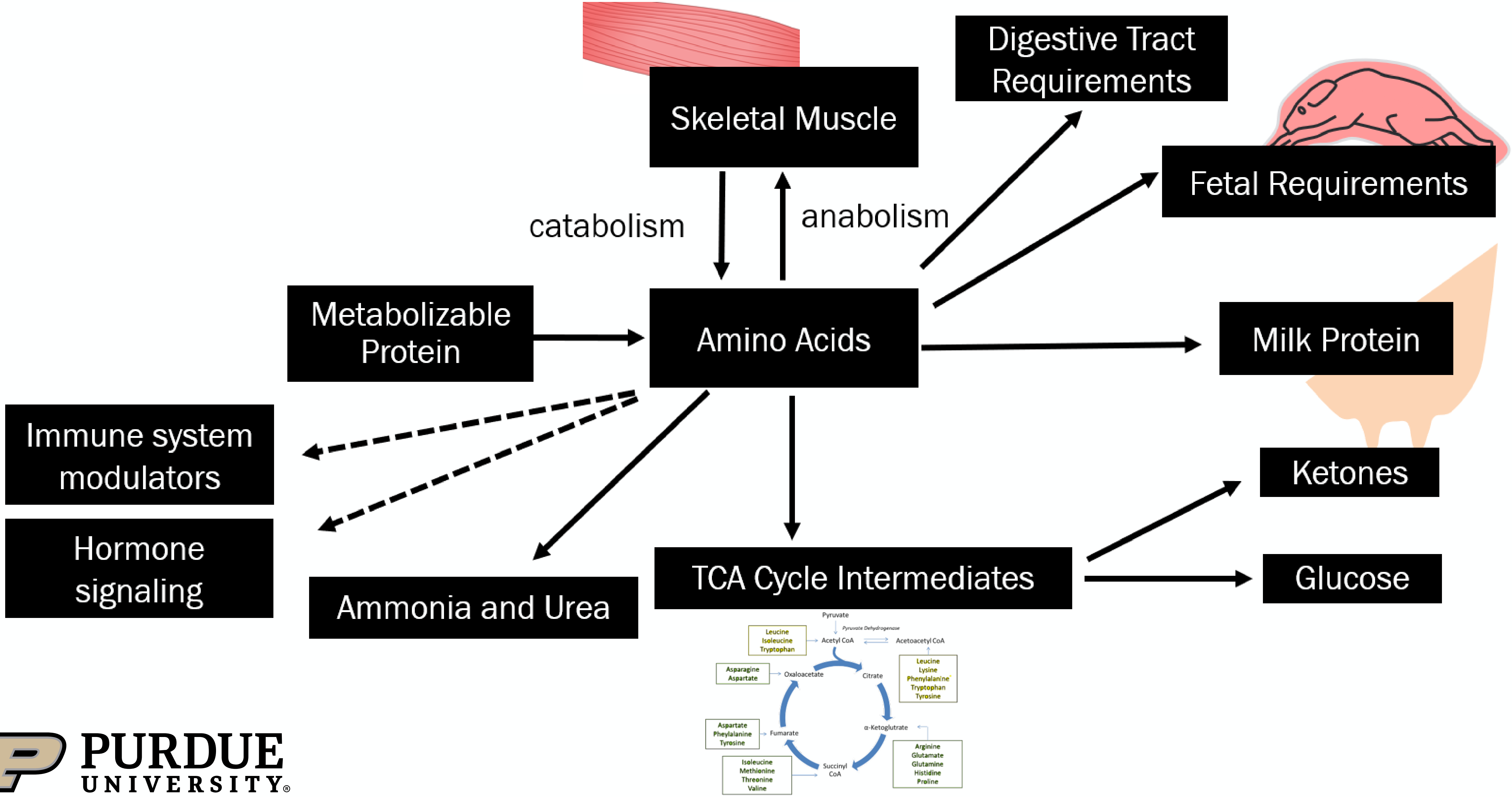
# *Uses for Skeletal Muscle*

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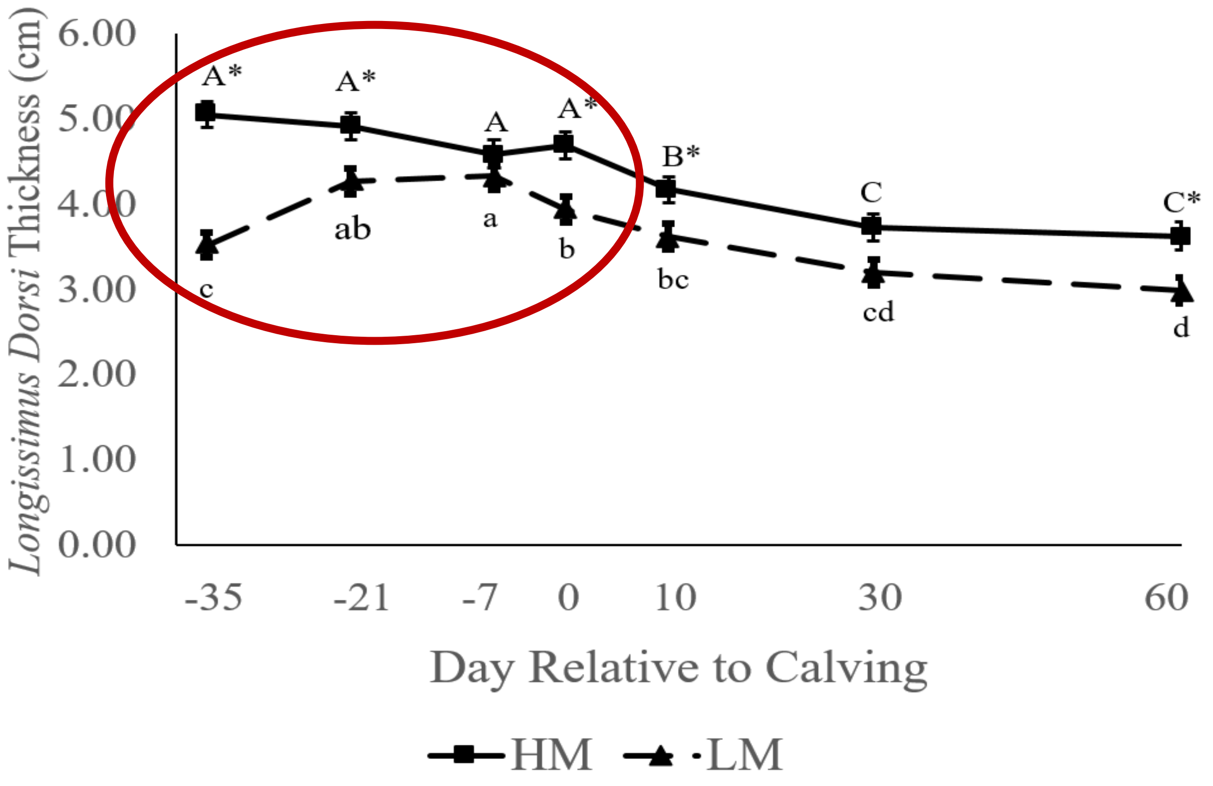
# *How Dynamic is Muscle Amount in the Transition Period?*

- Separated animals into low muscle and high muscle from 35 d before calving to 60 DIM based on *longissmus dorsi* thickness

- High muscle (HM) "mobilized" average of 1.54 cm (n=20)
- Low muscle (LM) "mobilized" average of 0.52 cm (n=21)
  - Because gained muscle during prepartum period




Differences in uppercase letters indicate a difference between time points within HM, lowercase letters indicate a difference between days within LM, and an asterisk indicates a difference between groups within a day at *P*<0.05.

McCabe et al., 2021

# *High Muscle Cows Have Higher 3-MH and 3-MH:CRE → More Muscle Mobilization*

| Item | 2 DIM | | 7 DIM | | 14 DIM | | 21 DIM | | | *P*- Value |
|---|---|---|---|---|---|---|---|---|---|---|
| | HM | LM | HM | LM | HM | LM | HM | LM | SEM | Group |
| Insulin (ng/mL) | 0.21 | 0.37 | 0.18 | 0.41 | 0.15 | 0.31 | 0.31 | 0.24 | 0.10 | 0.26 |
| Glucose (mg/dL) | 68.1 | 69.8 | 70.8 | 64.6 | 66.3 | 64.8 | 69.6 | 68.8 | 2.2 | 0.32 |
| BHB (mmol/L) | 0.97 | 1.04 | 1.15 | 1.11 | 1.08 | 0.99 | 0.95 | 0.87 | 0.17 | 0.80 |
| NEFA (mmol/L) | 0.64 | 0.54 | 0.72 | 0.62 | 0.63 | 0.63 | 0.75 | 0.51 | 0.09 | 0.15 |
| CRE (ng/mL) | 3,588 | 3,477 | 3,398 | 3,407 | 3,173 | 3,178 | 3,196 | 2,994 | 125 | 0.57 |
| 3-MH (ng/mL) | 493[abc] | 437[cd] | 538[a] | 414[d] | 581[a] | 471[c] | 520[ab] | 428[cd] | 34 | 0.02 |
| 3-MH:CRE | 0.137[c] | 0.122[c] | 0.163[b] | 0.118[c] | 0.188[a] | 0.143[bc] | 0.167[b] | 0.141[bc] | 0.010 | <0.01 |

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*McCabe et al., 2021*

# *High Muscle Multiparous Cows Produce Heavier Calves*

7.5 lbs. larger calves
No significant difference in ECM

| Item | HM | LM | SEM | Group *P*-value |
|---|---|---|---|---|
| Calf Birthweight (kg) | 45.2 | 41.8 | 0.7 | <0.01 |
| Milk Yield (kg/d) | 38.8 | 41.6 | 0.8 | 0.02 |
| Fat % | 4.33 | 4.05 | 0.12 | 0.09 |
| Protein % | 2.83 | 2.88 | 0.03 | 0.28 |
| Lactose % | 4.75 | 4.71 | 0.04 | 0.42 |
| Fat Yield (g) | 1703 | 1612 | 66 | 0.32 |
| Protein Yield (g) | 1102 | 1160 | 34 | 0.21 |
| Lactose Yield (g) | 1843 | 1918 | 57 | 0.35 |
| Milk Urea Nitrogen (mg/dL) | 7.44 | 8.08 | 0.30 | 0.12 |

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*McCabe et al., 2021*

# *Prepartum Muscle Depth Results*

48 multiparous cows
High Muscle (HM) > 4.6 cm
Low Muscle (LM) ≤ 4.6 cm

| | High Muscle | Low Muscle | SEM | *P*-values |
|---|---|---|---|---|
| DMI, kg/d | 13.7 | 13.3 | 0.47 | 0.52 |
| BW, kg | 789 | 762 | 22.3 | 0.38 |
| BCS, 1-5 scale | 3.61 | 3.29 | 0.06 | **<0.01** |
| Glucose, mg/dL | 78.6 | 76.8 | 0.89 | 0.16 |
| BHB, mmol/L | 0.61 | 0.60 | 0.02 | 0.76 |
| Insulin, ng/mL | 0.54 | 0.66 | 0.11 | 0.26 |

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Gouveia et al., 2024

# *Prepartum Dam Muscle Depth - Calf Results*

~8 lbs. larger calves from HM dams

| | High Muscle | Low Muscle | SEM | *P*-values |
|---|---|---|---|---|
| Birthweight, kg | 48.8 | 45.2 | 1.04 | 0.01 |
| Muscle metabolic activity, fluor g-1 h-1/1000 | 2,846 | 2,253 | 187 | 0.02 |
| Creatinine, ng/µL | 10.2 | 8.81 | 0.59 | 0.10 |
| 3-methylhistinine, ng/µL | 3.78 | 3.13 | 0.38 | 0.21 |

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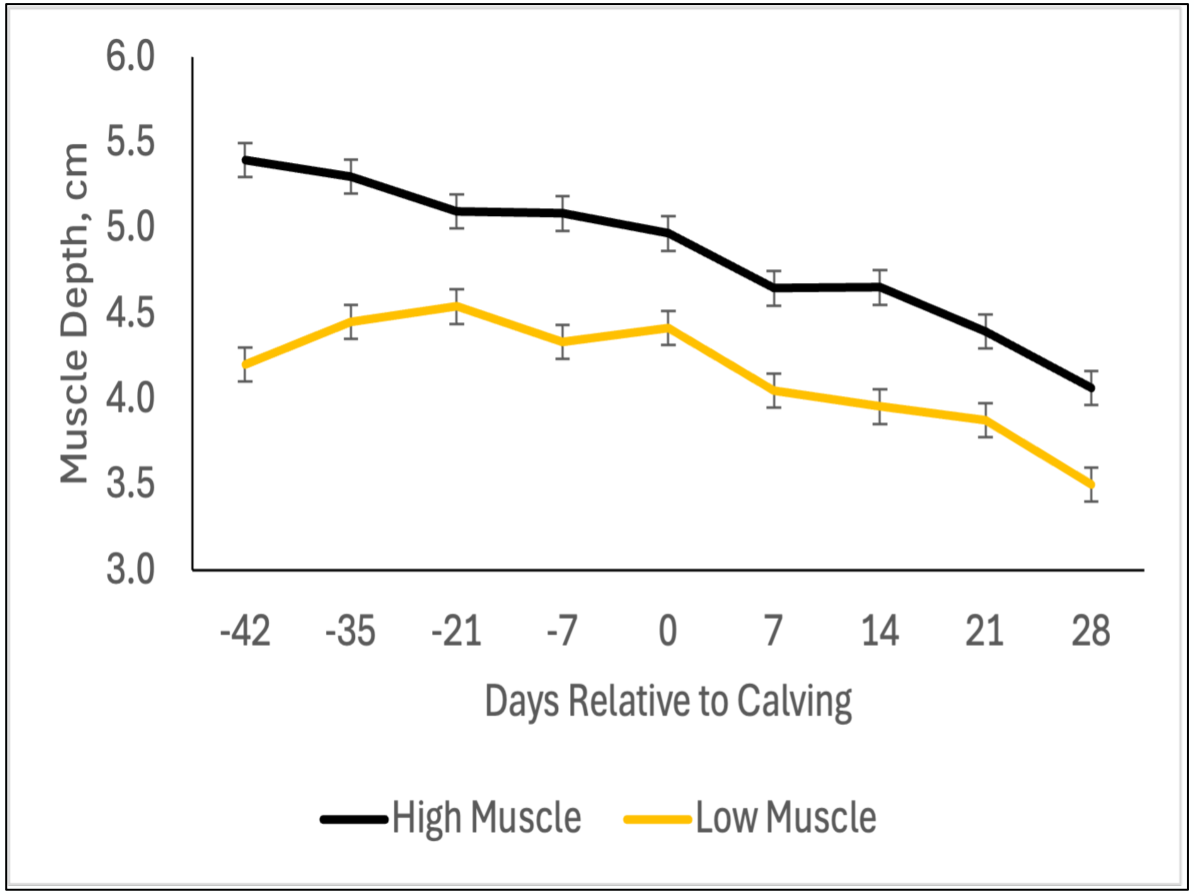
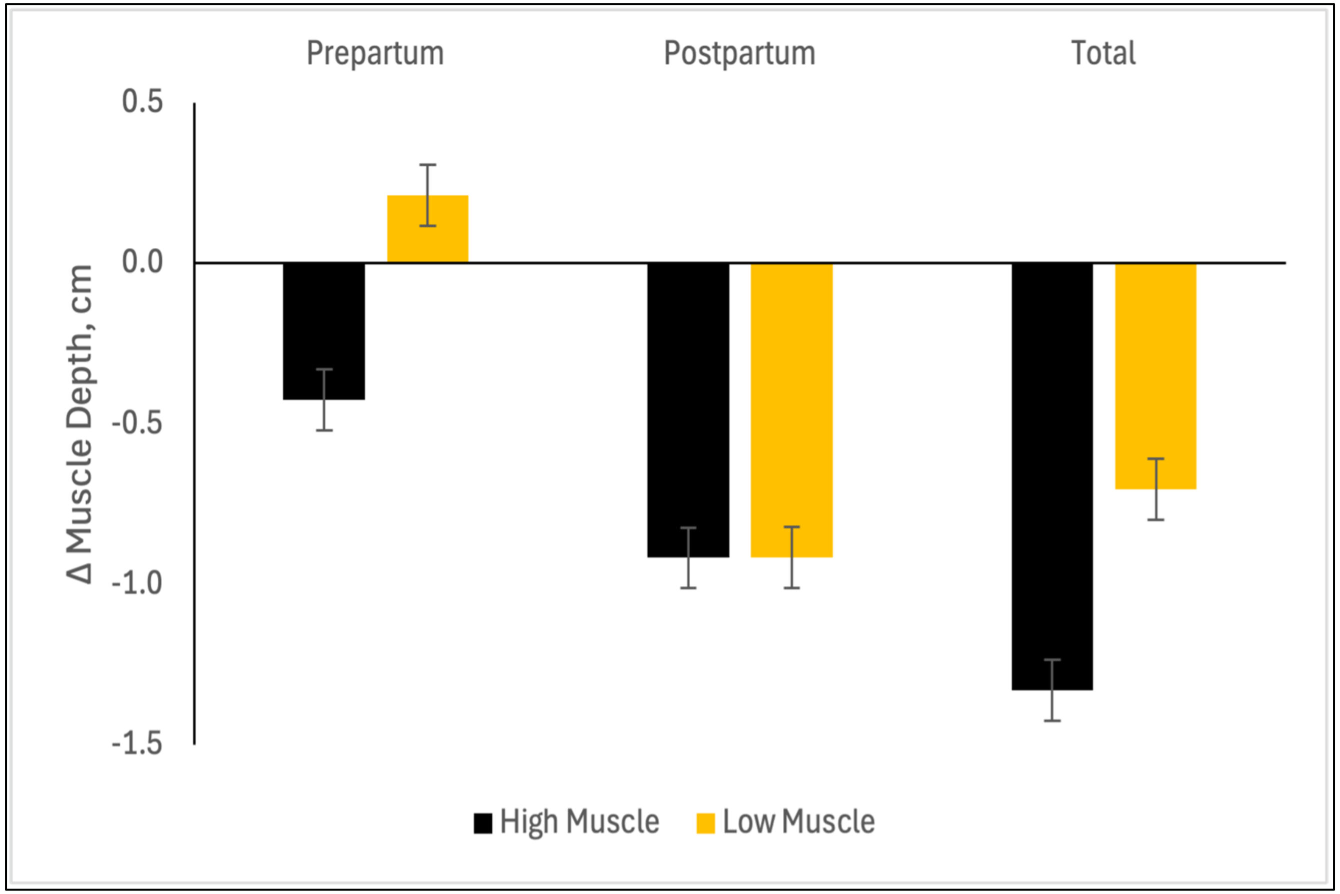
Beckett et al., 2025

# *High Muscle Cows Mobilize Muscle ~5 Weeks Before Calving*




Gouveia et al., 2024

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# *High Muscle Cows Make More Milk*

14 lbs. of ECM based on muscle reserves

| | High Muscle | Low Muscle | SEM | *P*-value |
|---|---|---|---|---|
| Postpartum DMI, kg/d | 20.1 | 19.4 | 0.21 | 0.02 |
| ECM, kg/d | 47.8 | 41.4 | 1.06 | <0.01 |
| Milk fat, kg/d | 1.90 | 1.63 | 0.05 | <0.0001 |
| Milk protein, kg/d | 1.32 | 1.18 | 0.03 | 0.0001 |
| Milk lactose, kg/d | 2.04 | 1.76 | 0.05 | <0.0001 |
| Glucose, mg/dL | 78.4 | 76.4 | 0.96 | 0.10 |
| BHB, mmol/L | 0.90 | 0.90 | 0.04 | 0.96 |

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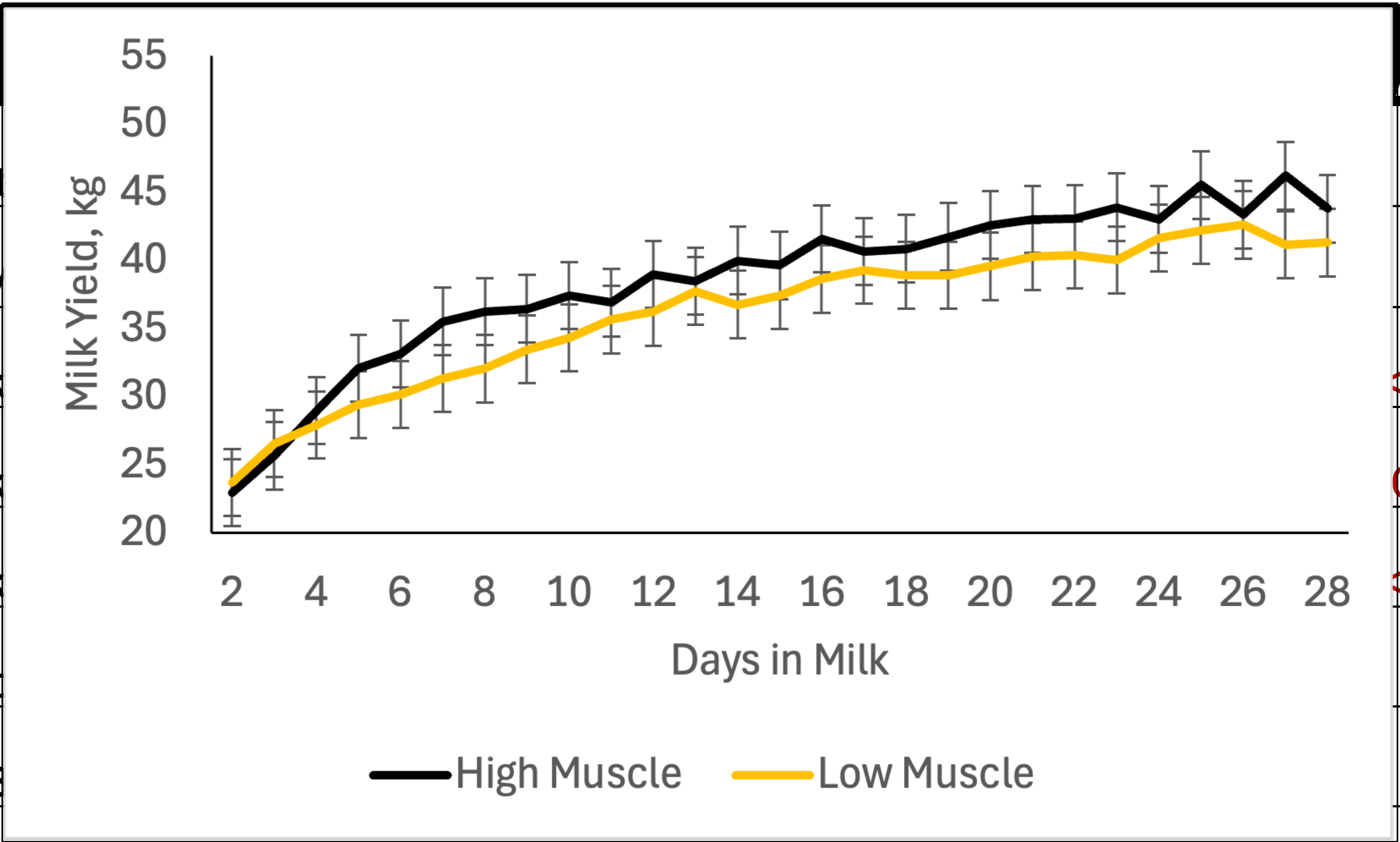
Adapted from Gouveia et al., 2024

# *High Muscle Cows Make More Milk*

14 lbs. of ECM based on muscle reserves

| | *P*-value |
|---|---|
| Post | 0.02 |
| ECM | <0.01 |
| Milk | <0.0001 |
| Milk | 0.0001 |
| Milk | <0.0001 |
| Gluc | 0.10 |
| BHB | 0.96 |

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Adapted from Gouveia et al., 2024

# Springing Heifers with Greater Muscle Reserves Are A Bit Different

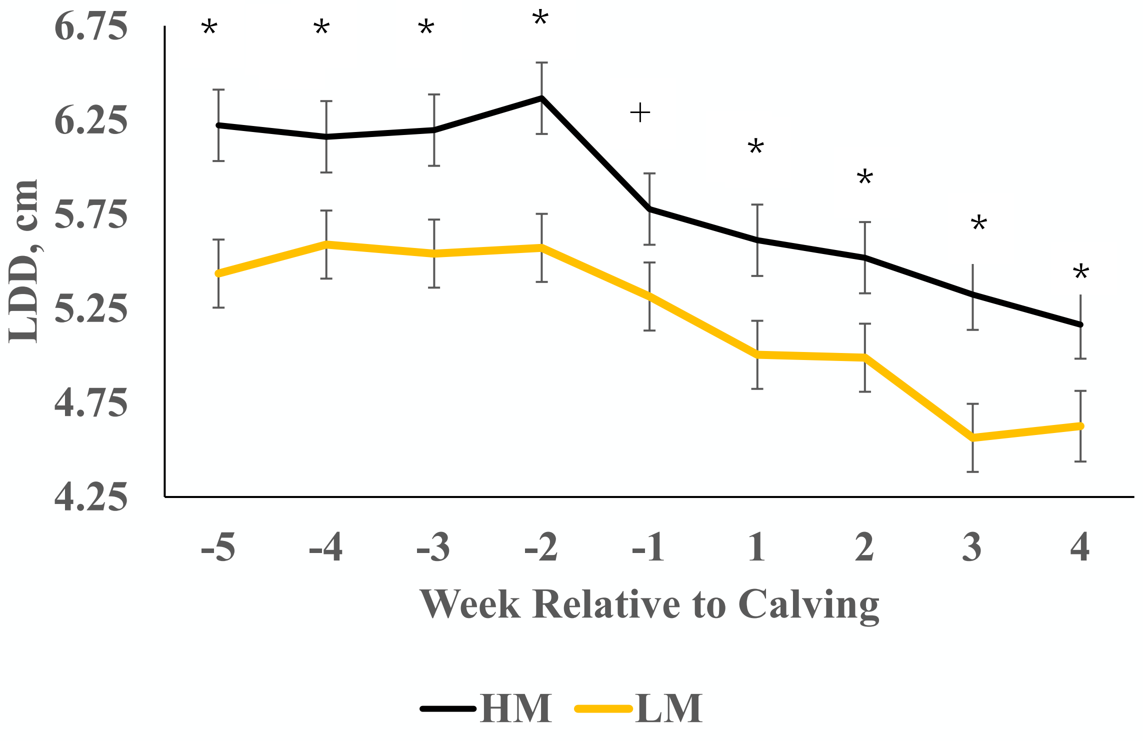
- They don't appear to give birth to larger calves and they don't lose muscle reserves until right before calving

- They start with more muscle → no difference in ECM between muscle groups

- Heifers have competing processes → they are still growing, myofibers increase in size as they age while they go through the transition period they should be reducing in size
  - Heifers have higher insulin concentrations → which may limit some mobilization

- Measured muscle at 280 DIM, similar to muscle depth at 4 wk of lactation

| | Muscle Group | |
|---|---|---|
| Variable | HM | LM |
| Calf wt., kg | 41.6 ± 3.73 | 41.9 ± 4.14 |
| Colostrum wt., kg | 6.80 ± 3.02 | 8.25 ± 4.05 |
| Brix, % | 31.0 ± 2.64 | 28.4 ± 4.70 |




Coombe et al., accepted JDS

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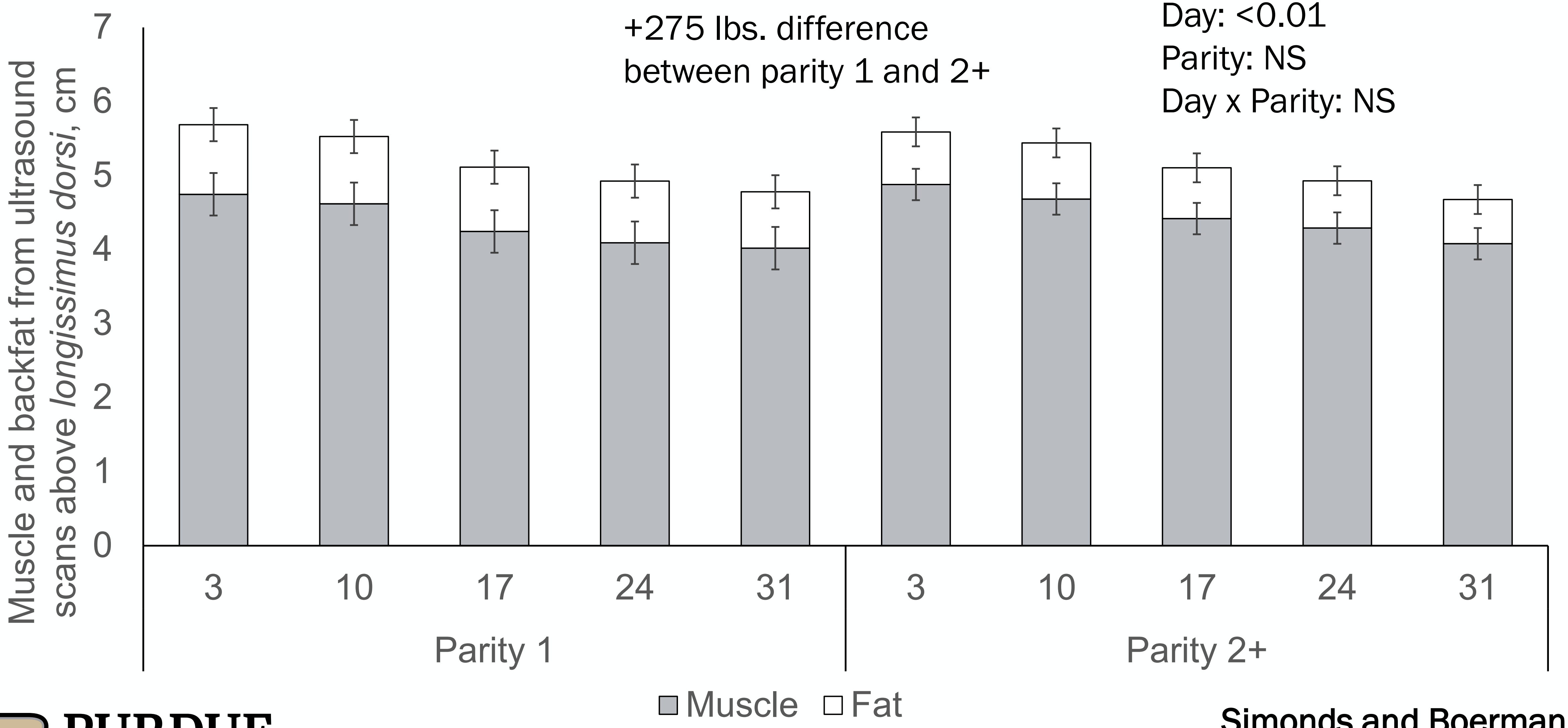
# *Parity Effects of Tissue Reserves After Calving*

*Muscle and Backfat Depth*
***P*-values**
Day: <0.01
Parity: NS
Day x Parity: NS

+275 lbs. difference between parity 1 and 2+

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Simonds and Boerman, preliminary data

# *Production and Body Composition Changes Across Lactation*

| | 0-60 DIM | | 60-240 DIM | | 240-300 DIM | | | *P*-values | | |
|---|---|---|---|---|---|---|---|---|---|---|
| Variable | HM | LM | HM | LM | HM | LM | SEM | Muscle Group | Time | Muscle Group×Time |
| Milk Production | | | | | | | | | | |
| Milk Yield (kg/d) | 43.5 | 41.0 | 39.1 | 37.7 | 28.8 | 30.6 | 1.75 | <0.01 | <0.01 | <0.01 |
| Milk Fat (%) | 4.15 | 3.84 | 4.21 | 4.00 | 4.04 | 4.11 | 0.11 | 0.05 | 0.50 | 0.12 |
| Milk Protein (%) | 3.03 | 3.09 | 3.29 | 3.31 | 3.48 | 3.52 | 0.05 | 0.23 | <0.01 | 0.89 |
| Absolute Change | | | | | | | | | | |
| Δ Body Weight (kg) | -71.4 | -45.8 | 65.1 | 61.5 | 26.3 | 29.5 | 8.70 | 0.20 | <0.01 | 0.18 |
| Δ Muscle Depth (cm) | -2.12 | -1.42 | 0.01 | 0.41 | 1.04 | 0.54 | 0.16 | 0.09 | <0.01 | <0.01 |
| Δ Backfat Depth (cm) | -0.15 | -0.10 | 0.15 | 0.12 | 0.05 | 0.04 | 0.03 | 0.97 | <0.01 | 0.17 |
| Percent Change | | | | | | | | | | |
| Δ Body Weight (%) | -9.0 | -6.5 | 9.5 | 9.8 | 3.4 | 4.2 | 1.21 | 0.20 | <0.01 | 0.60 |
| Δ Muscle Depth (%) | -35.1 | -30.8 | 2.8 | 13.9 | 26.7 | 15.2 | 3.85 | 0.65 | <0.01 | 0.01 |
| Δ Backfat Depth (%) | -28.4 | -21.3 | 45.3 | 35.6 | 12.8 | 9.0 | 5.58 | 0.61 | <0.01 | 0.27 |

Hanno et al., 2025

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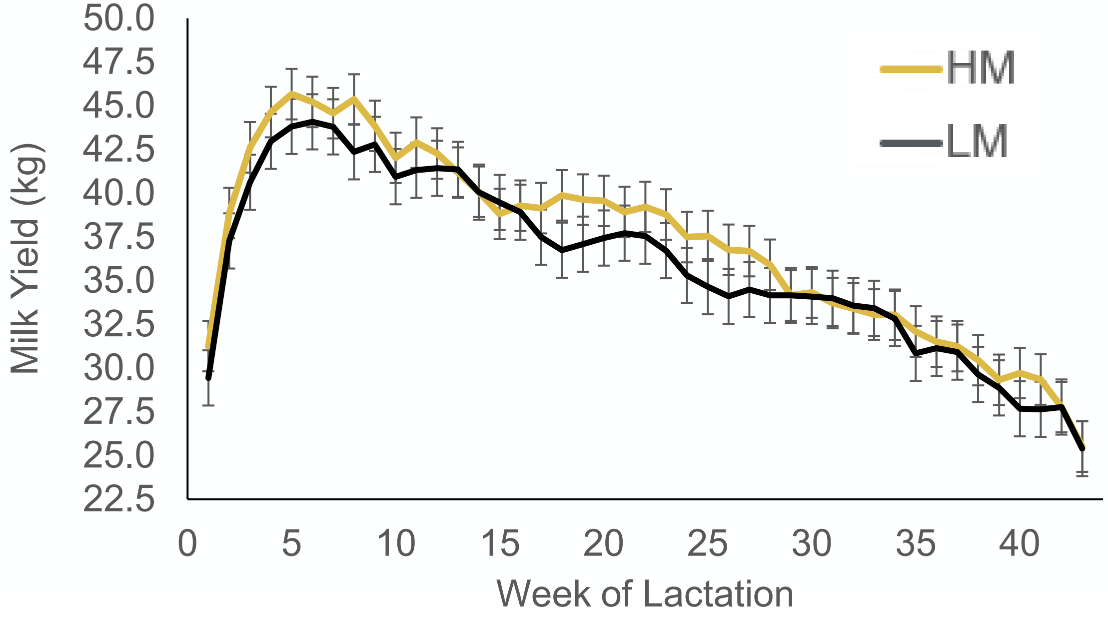
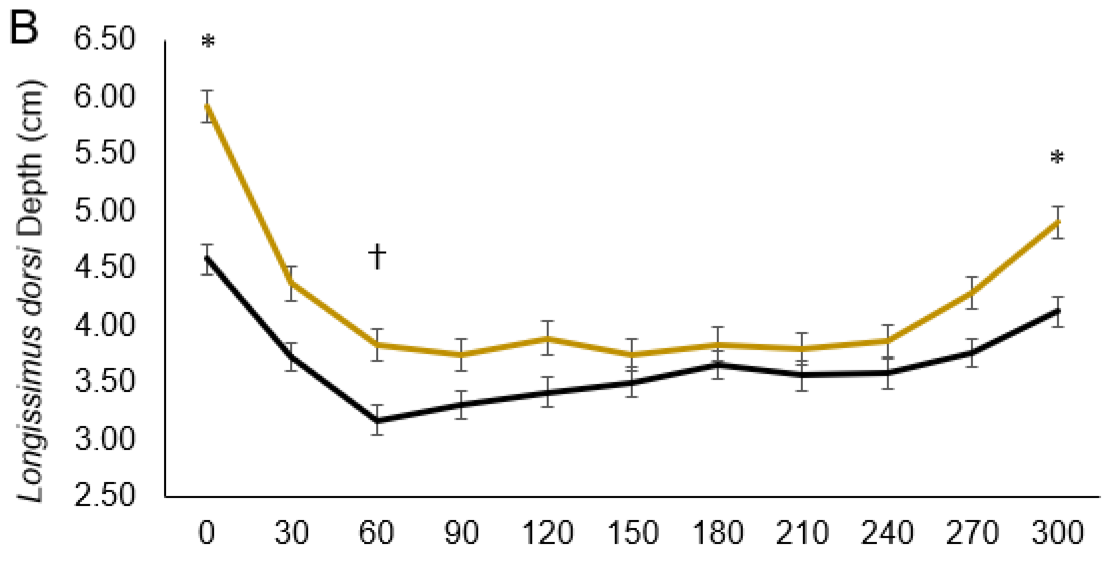
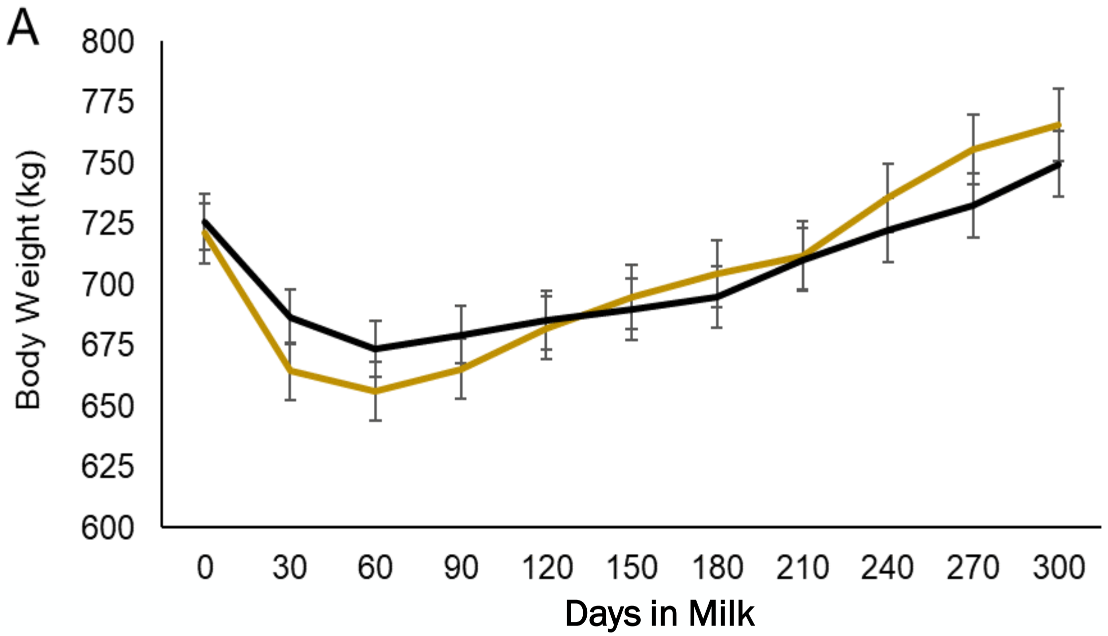
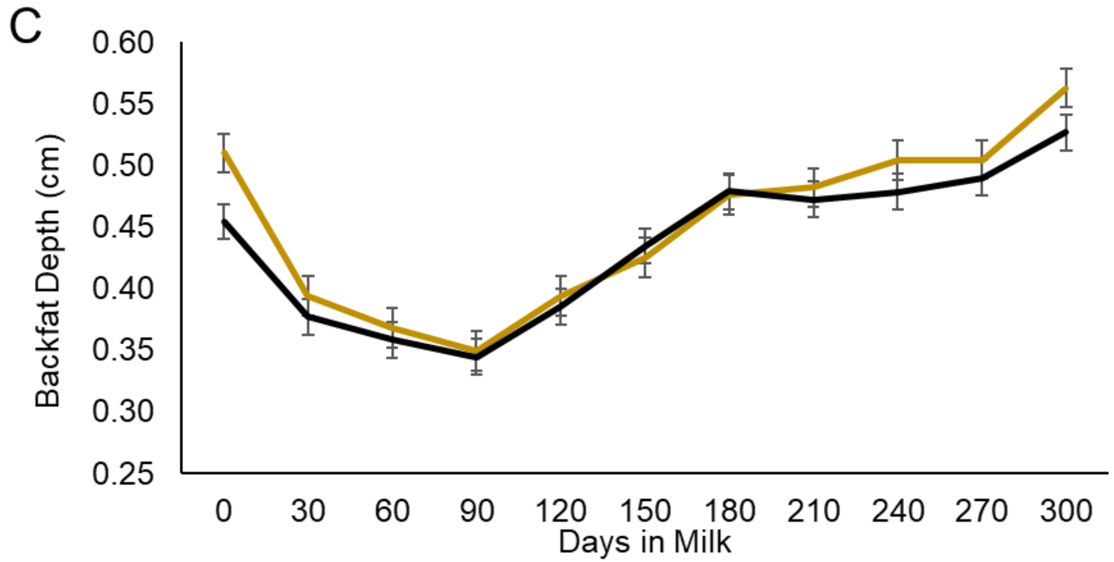
# Milk Yield and Body Composition



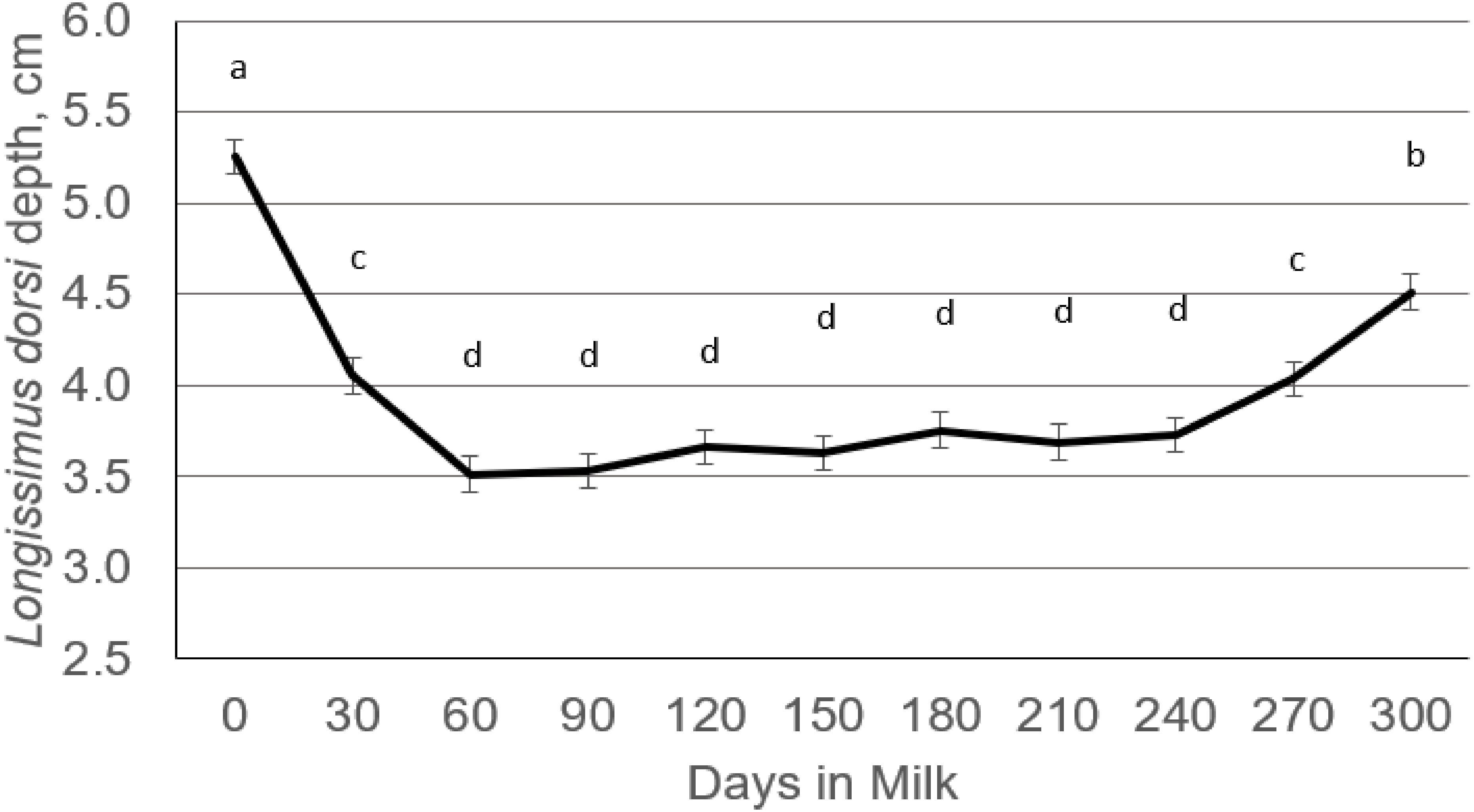




Hanno et al., 2025

# *Timing of Muscle Depletion and Accretion Throughout Lactation*




Adapted from Hanno et al., 2025

# Tissue Accretion/Depletion Related Metabolites Across Lactation

| | 7 DIM | | 150 DIM | | 300 DIM | | | *P*-values | | |
|---|---|---|---|---|---|---|---|---|---|---|
| Variable | HM | LM | HM | LM | HM | LM | SEM | Muscle Group | Time | Muscle Group×Time |
| 3-MH (ng/µL) | 2.09 | 1.86 | 2.16 | 1.78 | 0.99 | 0.97 | 0.18 | 0.19 | <0.01 | 0.54 |
| Creatinine (ng/µL) | 5.95 | 5.75 | 4.43 | 4.43 | 5.97 | 5.80 | 0.27 | 0.60 | <0.01 | 0.91 |
| 3-MH: Creatinine | 0.35 | 0.33 | 0.49 | 0.46 | 0.17 | 0.17 | 0.04 | 0.60 | <0.01 | 0.89 |
| NEFA (mmol/L) | 0.54 | 0.54 | 0.13 | 0.12 | 0.11 | 0.12 | 0.04 | 0.97 | <0.01 | 0.99 |
| Insulin (µIU/mL) | 0.39 | 0.37 | 0.40 | 0.35 | 0.64 | 0.62 | 0.08 | 0.52 | <0.01 | 0.97 |

Higher mobilization in early and mid-lactation.
Lowest muscle mass in mid-lactation.
Highest NEFA in early lactation.
Highest insulin in late lactation.

Hanno et al., 2025

# *Parity Differences Between Heifers and Cows*

- Meta-analysis of 27 studies suggests that heifers benefit more from additional MP prepartum compared with cows where only milk protein was impacted with additional MP prepartum (Husnain and Santos, 2019). INTAKE DIFFERENCES, GROWTH REQUIREMENTS

- Tebbe and Weiss (2021), more of a response in multiparous cows with addition MP supplementation postpartum and best response with less fNDF compared with other treatments, not the same for primiparous cows.

- What we have observed from ultrasounding and measuring metabolites of both groups
  - Heifers/primiparous cows → have more muscle, don't lose muscle until right before calving, if they transition ok they may lose a smaller % of muscle compared to multiparous cows. Primiparous cows have higher insulin/glucose concentrations → which may reduce the need for muscle mobilization.
  - Multiparous cows → if they are higher muscle one lactation, the next lactation they will also be high muscle. They end their lactation with less muscle than when they calved. The reduction in muscle depth is related to a reduction in myofiber cross sectional area (primarily Type IIA).

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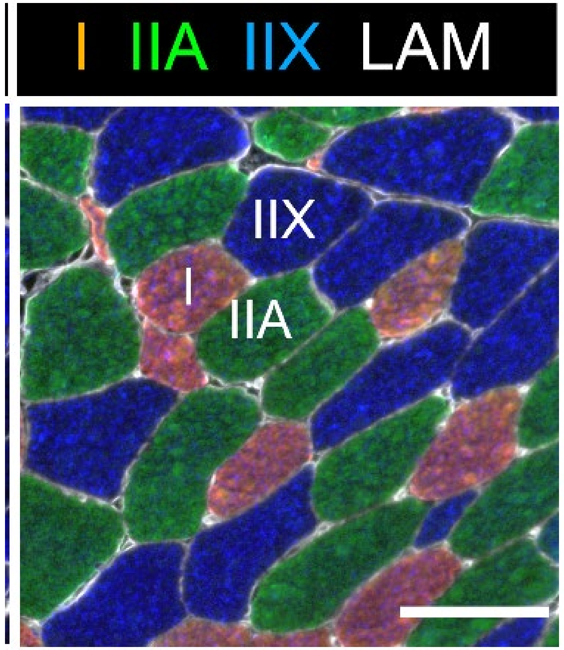
# *A Little More Background on Muscle*

- Skeletal muscle tissue is comprised of many, multinucleated muscle cells (myofibers)
- Bovine myofibers differ by myosin chain isoforms and can be distinguished by staining
  - Type IIX – primarily relies on anaerobic respiration, more glycogen storage, increased use of glucose (fast twitch)
  - Type IIA – intermediate between Type IIX and Type I
  - Type I – primarily relies on aerobic respiration, utilizes glucose more efficiently (slow twitch, endurance)
- Skeletal muscle is responsible for greater than 75% of the insulin-mediated glucose dispersal throughout the body (Feraco et al. 2021)
- We believe myofiber switching occurs between the pre and postpartum period, towards I which can be seen in the relative proportion of the type II myofibers changing between pre and postpartum



Coombe et al., accepted JDS.

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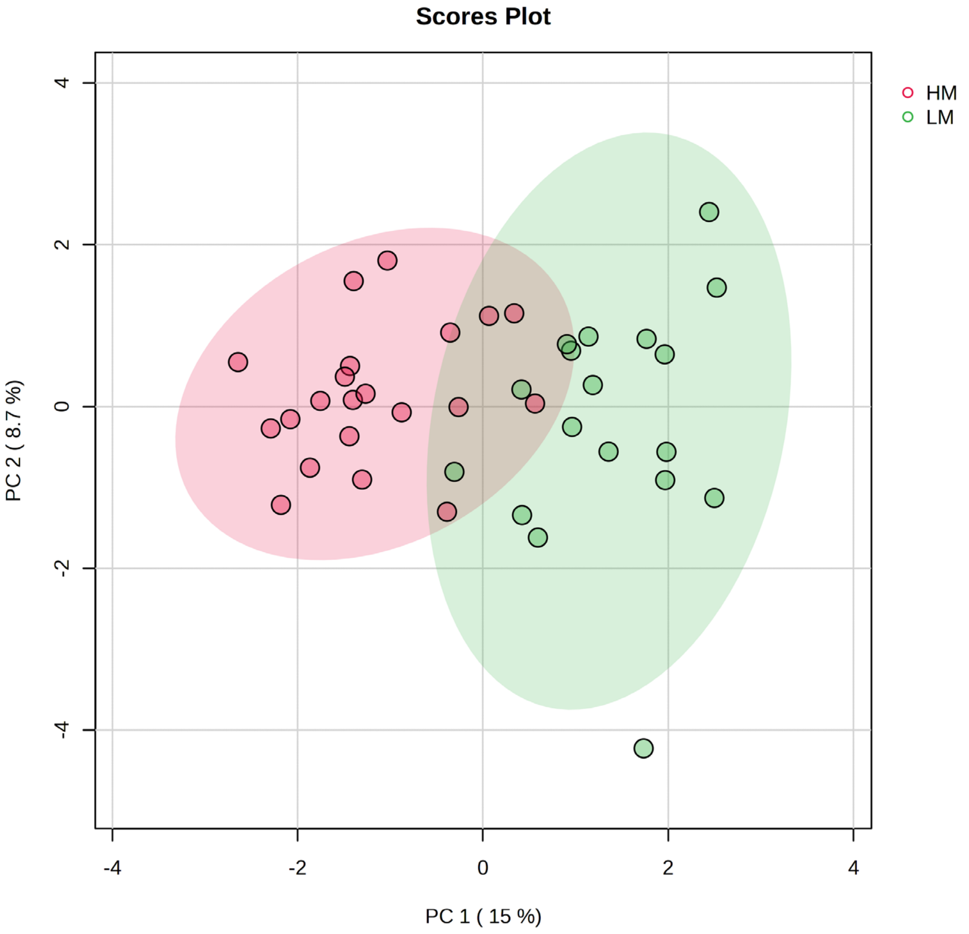
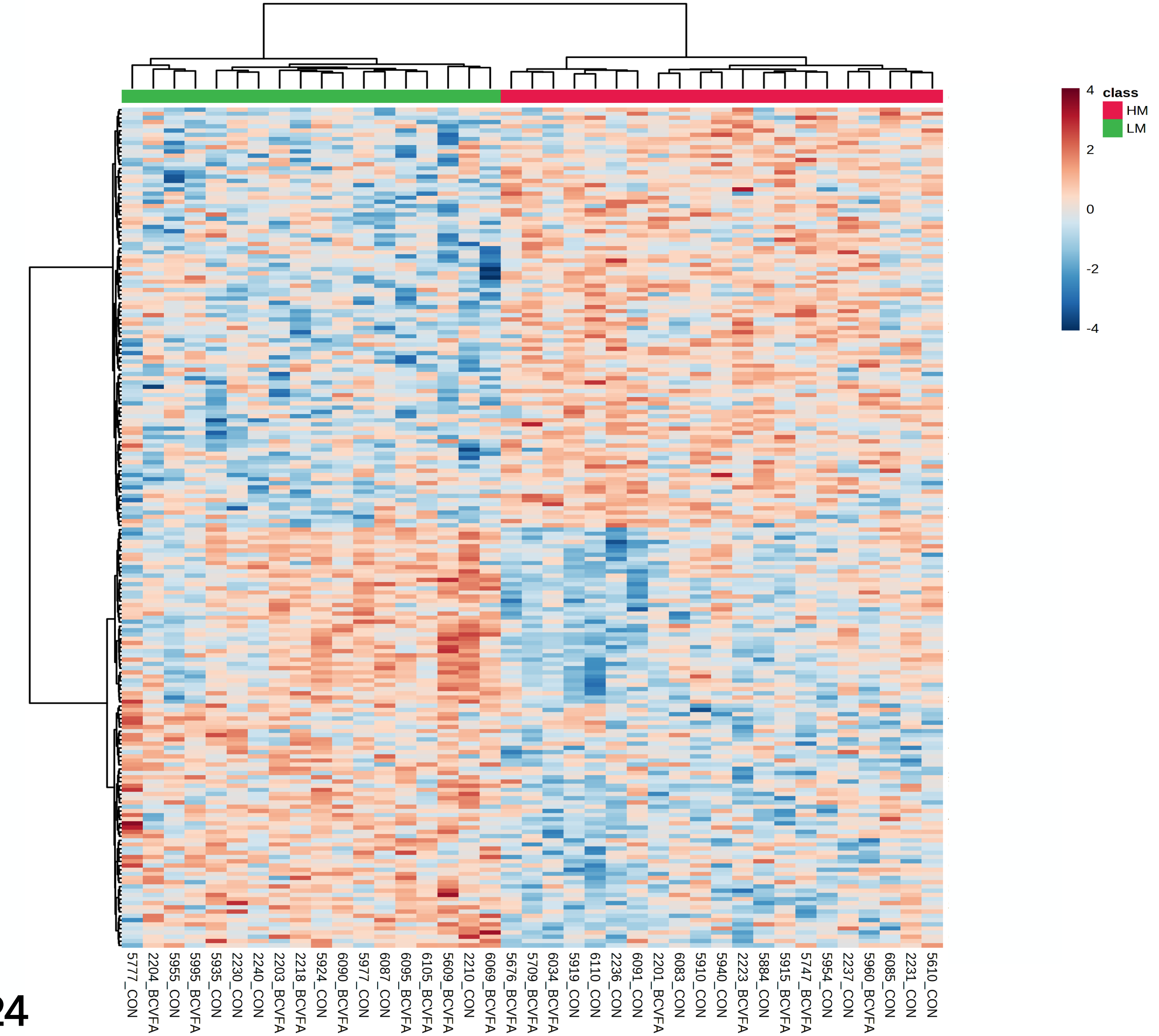
# *Differentiation Between High and Low Muscle Cows (Prepartum)*

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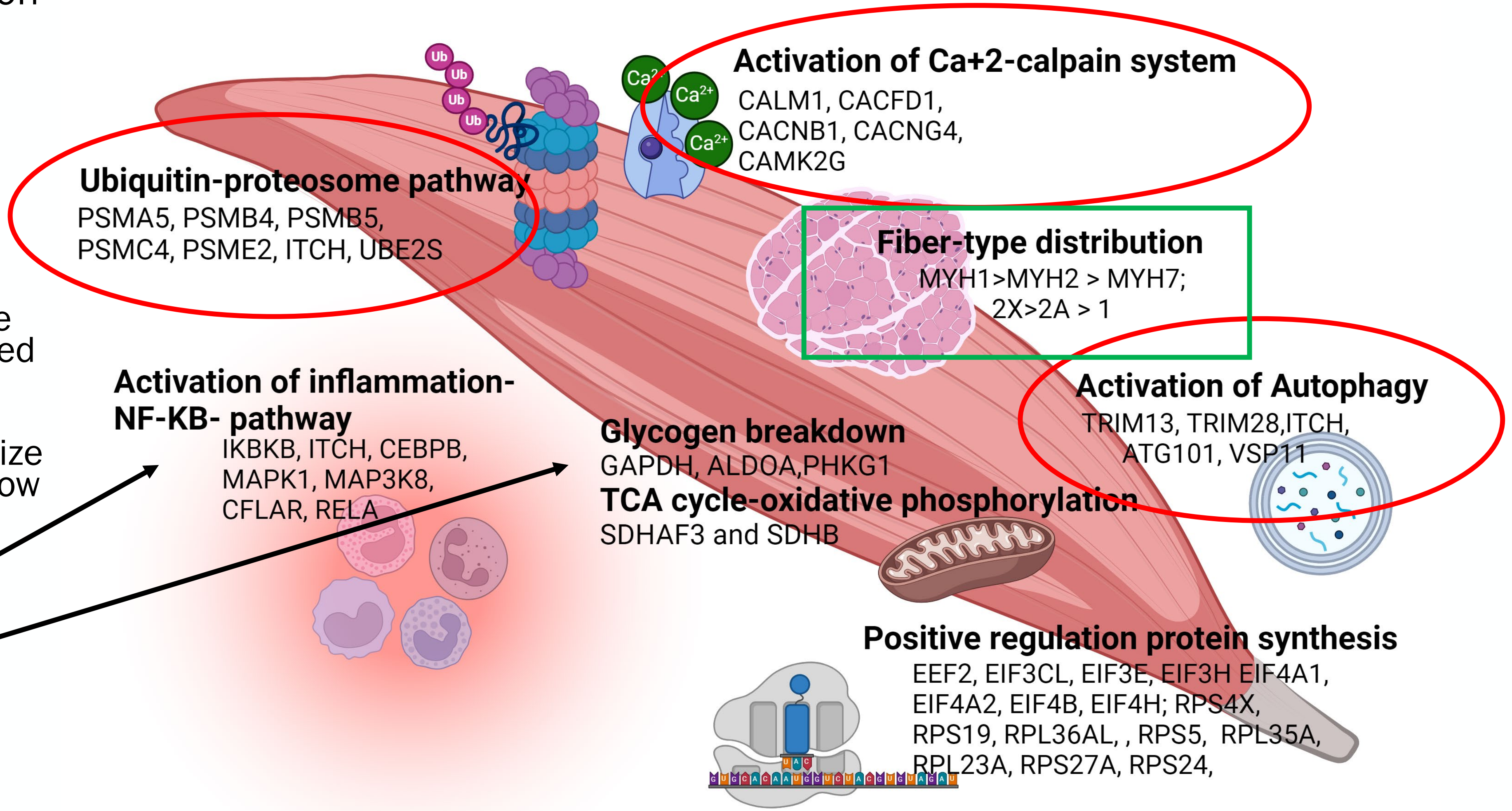
Casey et al., 2024

# *Distinct Molecular Signatures Based on Prepartum Muscle*

- Increased in all 3 pathways related to protein degradation
  - Ubiquitin-proteosome pathway
  - Ca+2-calpain system
  - Autophagy – lysosomal
- Myofiber Type IIx > IIa > I
  - Type IIx – primarily rely on anaerobic respiration, more glycogen storage – increased use of glucose (fast twitch)
  - Type I – primarily rely on aerobic respiration and utilize glucose more efficiently (slow twitch, endurance)
- Increased inflammation pathways
- Increased glycogen breakdown

## Transcriptional signature of low muscle cattle in late gestation




Casey et al., 2024

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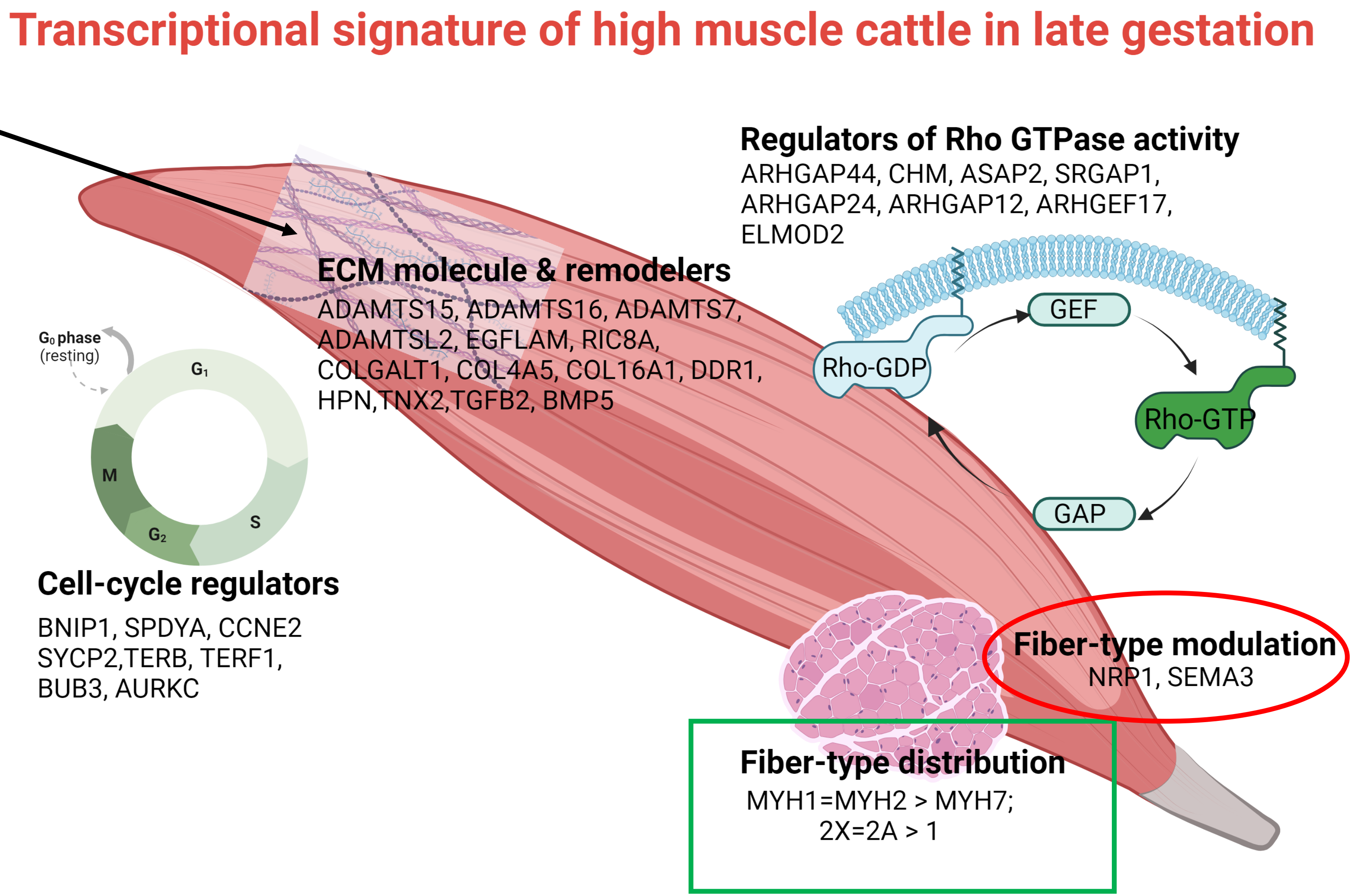
# *Distinct Molecular Signatures Based on Prepartum Muscle*

- Changes in extracellular matrix
- Different muscle fiber type distribution IIx = IIa > I
  - More Type IIa – more efficient use of glucose and more mitochondria compared to IIx
- Fiber type modulation potentially impacting myofiber switching
- Why could this matter → can be a metabolic adaptation to conserve more efficient muscle fibers

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# Summary

- Cows lose skeletal muscle postpartum but also can lose muscle prepartum, amount dependent on muscle reserves
  - On average mobilize 30-35% of their muscle depth (not all protein)

- Cows can accrete skeletal muscle at the end of lactation (during the dry period)
  - Ended lactation with less muscle than at calving

- High muscle reserves → higher calf birthweights and more milk yield (most of the time in multiparous cows)
  - Primiparous cows and LM cows don't mobilize muscle until right before calving → therefore no extra AA for calf and no extra AA for mammary gland development

- Prepartum there are parity effects, heifers are not depleting muscle until right before parturition but after calving they deplete muscle similar to cows
  - Primiparous cows have higher insulin concentrations which may limit some muscle depletion

# *Take Away Messages*

- Considerable variation exists between cows for tissue mobilization, extent of mobilization is dependent on amount of tissue → cows are also depleting muscle when they have mastitis or lameness events, we can see it in ultrasounds

- Muscle mobilization occurs prior to fat mobilization, need for AA at the end of gestation

- We are not accounting for muscle gain during the dry period in transition cows when it comes to MP requirements
  - Cows with little muscle reserves can gain muscle during this time and can draw on it in early lactation
  - Cows with higher muscle reserves use this muscle in late gestation and early lactation → fetus or mammary gland

- We are starting to do work on commercial farms to have larger numbers of cows to look at impacts of muscle mobilization on reproduction, health events, and the role of genetics on muscle amount and extent of muscle mobilization.

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