

## BACKGROUND

- Extruterine growth restriction is a common adverse outcome in preterm infants
  - Associated with reduced lean growth and long-term morbidities
- Our previous work showed continuous feeding blunts muscle protein synthesis compared to intermittent bolus feeding in neonatal pigs **born at term**
  - The neonatal pig is a highly translatable model for the human neonate
- Continuous feeding is still indicated in some infants due to feeding intolerance
- We have previously found that intermittent parenteral leucine (Leu) pulses during continuous feeding increases skeletal muscle mTORC1 signaling and protein synthesis in neonatal pigs born at term

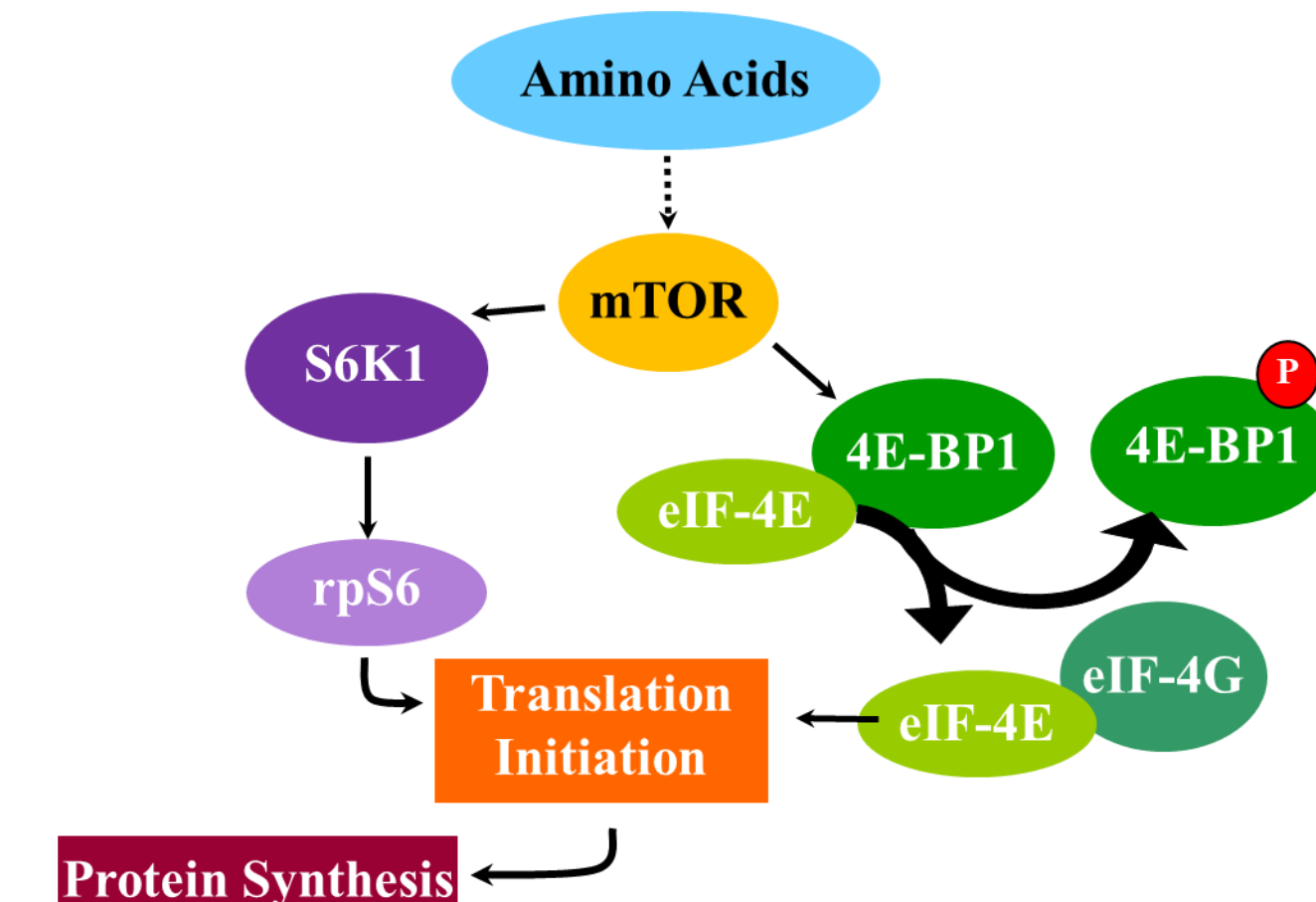
## METHODS

- **Animals**
  - Piglets delivered via cesarian section at d 105 of gestation (equivalent to ~ 32 weeks preterm in human infants)
  - **Surgeries:**
    - Orogastric tube (small diameter) and umbilical catheter (Day 1)
    - Orogastric tube (large diameter) and jugular and carotid catheters (Day 7)
  - **Diet:** Milk-replacer at 150mL·kg BW<sup>-1</sup>·d<sup>-1</sup>
    - ME = 195 kcal·kg body weight (BW)<sup>-1</sup>·d<sup>-1</sup>
    - Protein = 13.5 g·kg BW<sup>-1</sup>·d<sup>-1</sup>
- **Two Treatment Groups**
  - Leucine (LEU)
    - Received IV infusion ("pulse") of 1.6 mmol·kg BW<sup>-1</sup>·4 h<sup>-1</sup>
    - n = 4
  - Alanine (ALA) – *Isonitrogenous Control*
    - Received IV pulse of 1.6 mmol/kg BW/4 hours
    - n = 4
- **Analysis**
  - Average daily gain by weighing pigs every two days
  - Body composition using dual X-ray absorptiometry (DXA) on Day 22
  - Intracellular protein signaling activation by Western blots (postprandially, 60 min after initiation of last pulse on Day 24)

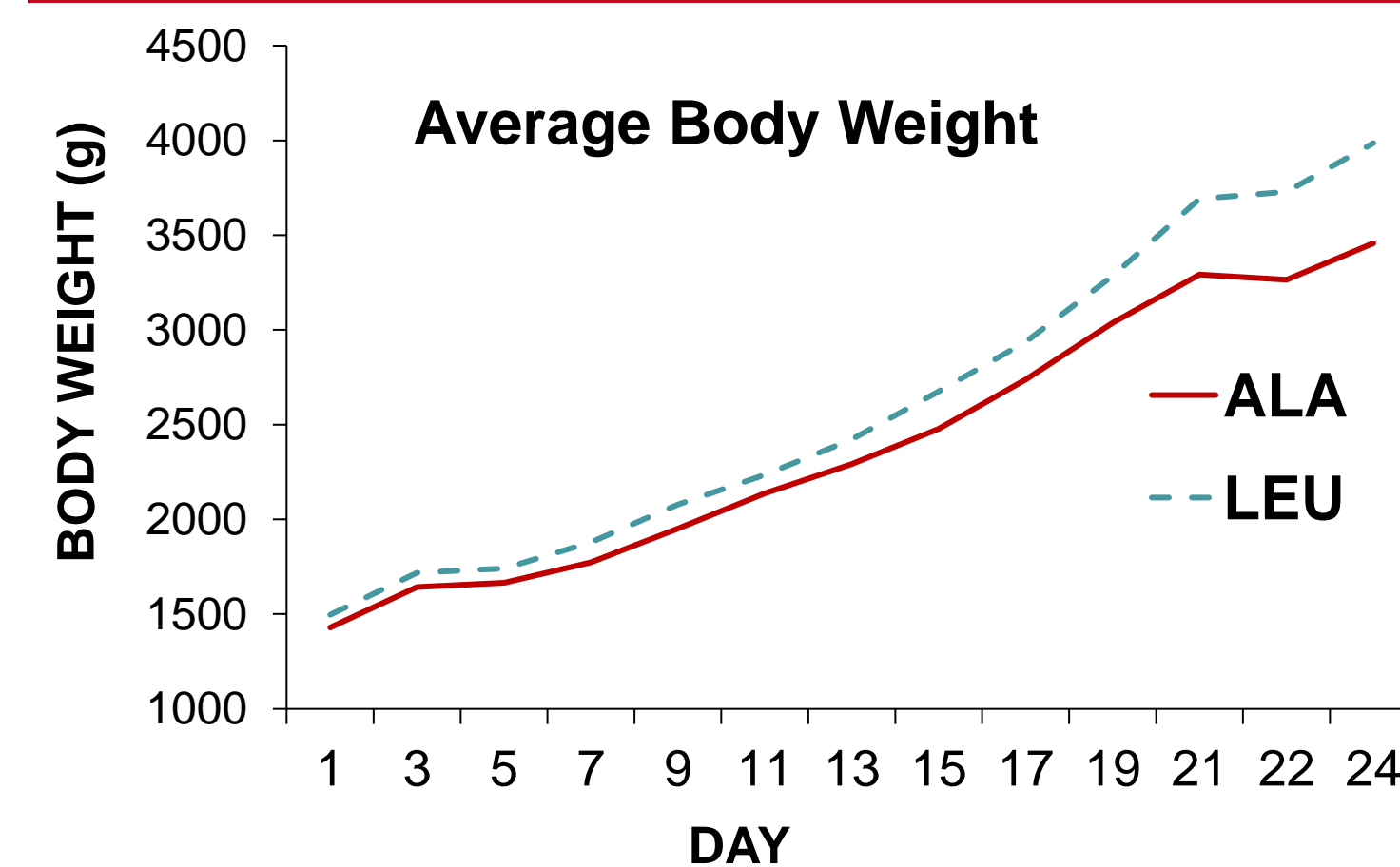
## HYPOTHESES

- Administration of leucine pulsing during continuous orogastric feeding will enhance protein synthesis in preterm piglet model.
- Leucine pulses during continuous orogastric feeding will activate mTORC1 signaling pathway and increase protein synthesis in preterm piglet model.
- Leucine pulses during continuous feeding will improve lean growth in a preterm piglet model.

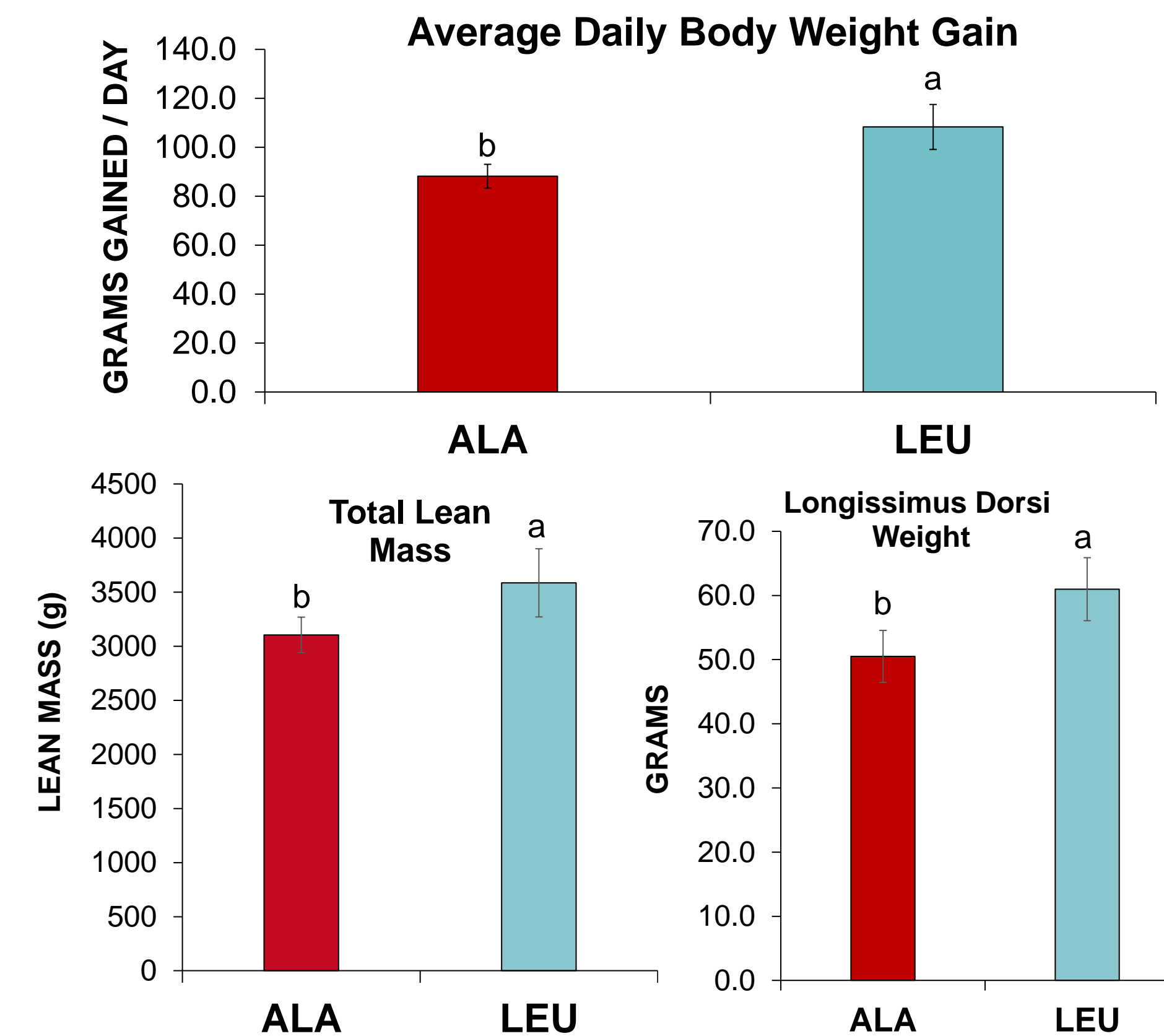
## Figure 1. Amino Acid Signaling Pathway



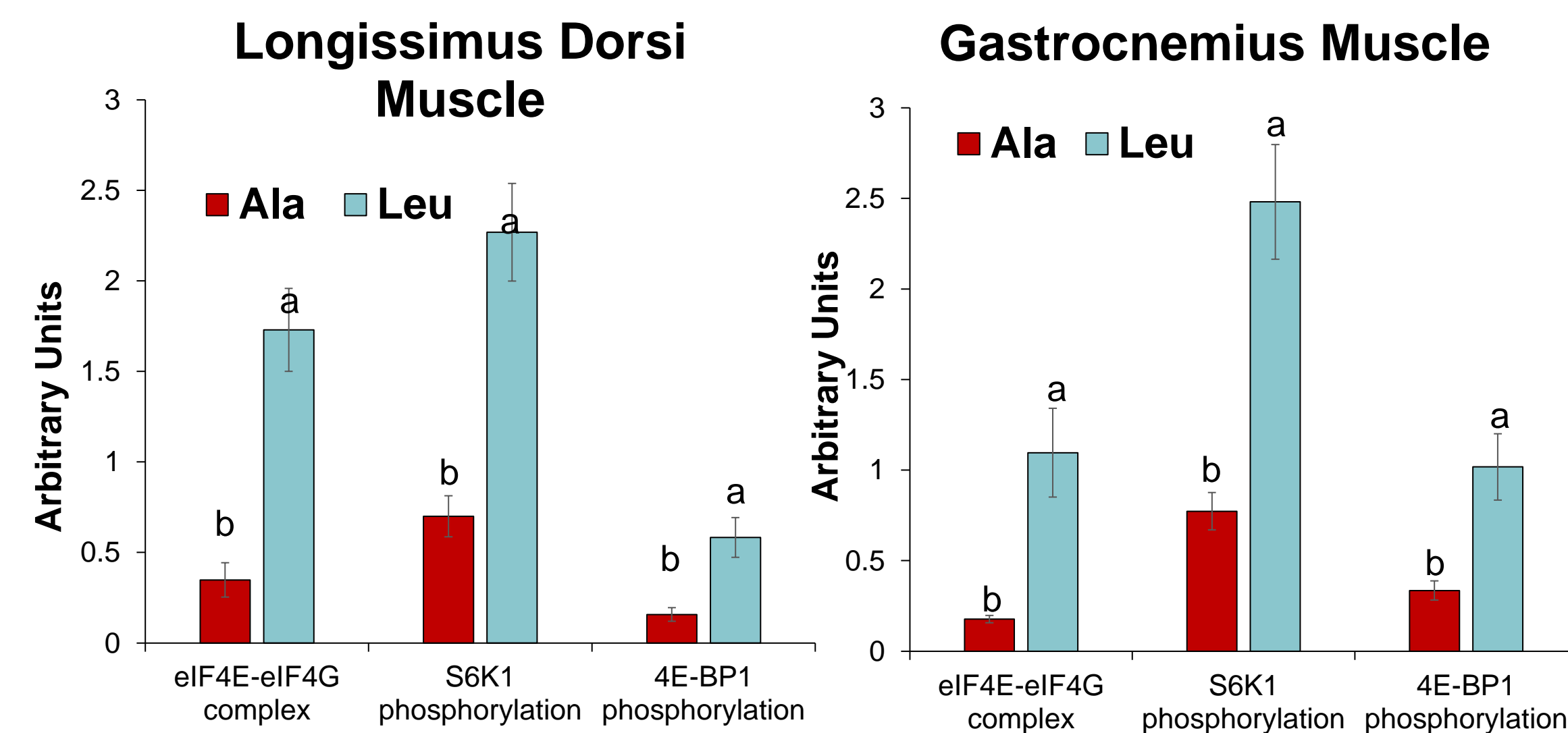
## Figure 2. Final body weight is increased in LEU pigs



## Figure 3. LEU pigs had a higher average daily gain than ALA pigs and increased lean gain



## Figure 4. Translation initiation is enhanced by LEU pulse during continuous feeding



## RESULTS

- Leu-treated pigs had a higher average daily gain (ADG) (P < 0.05)
- LEU pigs had 13% higher final body weight than ALA pigs (P < 0.05).
- Total lean mass tended to be higher (+13%; P < 0.06) in LEU pigs compared to ALA pigs
- Longissimus dorsi (LD) muscle weight was heavier in LEU pigs compared to ALA pigs (P = 0.01).
- Indices of mTORC1 activation increased in the LD and gastrocnemius muscles of LEU pigs compared to ALA pigs
  - Phosphorylation of S6K1
  - Phosphorylation of 4EBP1
  - Abundance of the eIF4E-eIF4G complex

## CONCLUSIONS

- Administration of leucine pulses during continuous orogastric feeding enhances mTORC1-activated translation initiation in preterm piglet skeletal muscle.
- Leucine pulsing during continuous orogastric feeding increases weight gain by increasing lean growth in a preterm piglet model.

## REFERENCES

1. Boutry et al. Am J Physiol Endocrinol Metab. 2016
2. El-Kadi et al. Am J Clin Nutr. 2018
3. Gazzaneo et al. J Nutr. 2011