

## INTRODUCTION

- Gastroparesis, or delayed gastric emptying, occurs in 24.2 per 100,000 adults. The prevalence is unknown in the pediatric population.
- Surgeries, infection, malnutrition, and diabetes mellitus are all known triggers of delayed gastric emptying, although the mechanism causing that change is unknown.
- GI dysmotility is reported among a wide range of malnourished groups, including neonates born small-for-gestational-age, children with severe acute malnutrition, and adolescents with anorexia nervosa.
- Few animal model for gastroparesis have been identified, and no laboratory models are available to study malnutrition-induced gastroparesis.
- Animal models are important to both elucidate etiologies and test treatments for gastroparesis.

## OBJECTIVES

To establish and characterize a novel mouse model of gastroparesis induced by early postnatal malnutrition.

To determine whether histologic changes in this model may provide insight into possible mechanisms of malnutrition-induced gastroparesis.

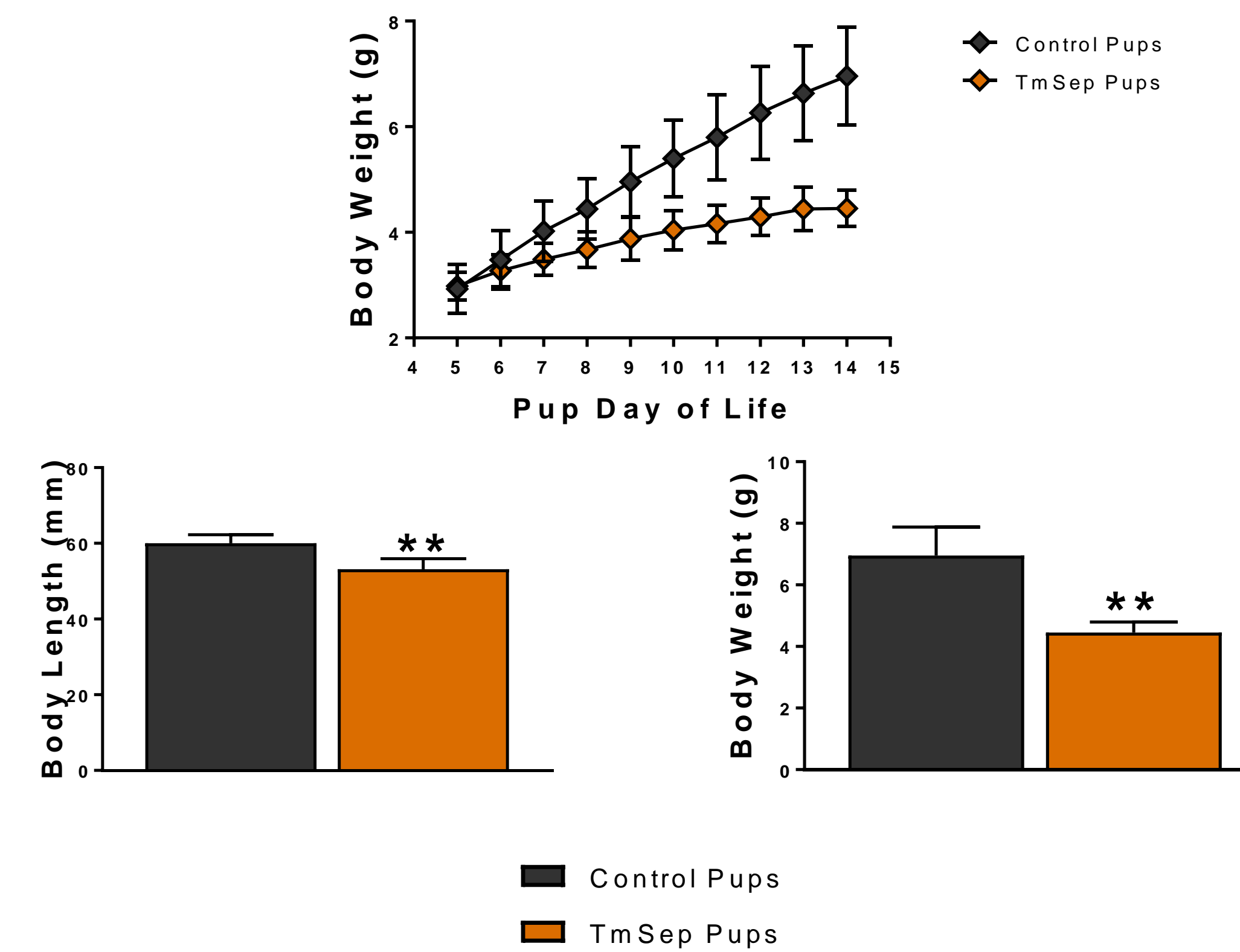
## METHODS

We modeled early-life malnutrition using a separation model and a control in C57BL/6 mice.

- Timed Separation (TmSep) pups:** Starting at day of life 5, pups were isolated from lactating dams for 12 h/d - sampled at 2 wk in the fed state.
- Control pups:** pups nursed uninterrupted and were sampled at 2 weeks. With these 2 groups we measured:
  - Gastric emptying and mean geometric center of gavaged fluorescein isothiocyanate (FITC) conjugated to 70 kDa dextran were calculated 30 minutes after gavage.
  - H&E-stained sections were imaged on an Eclipse 90i microscope using 4x, 10x, and 20x magnification.
  - Thickness of muscularis propria and mucosa was measured by a blinded observer using NIS Elements (Nikon).
  - 6 regions of tissue were reviewed for each blinded specimen. Measurements were obtained using Image J software (NIH).
  - Measurements of mucosa and muscularis were averaged to one data point per histologic layer per pup.

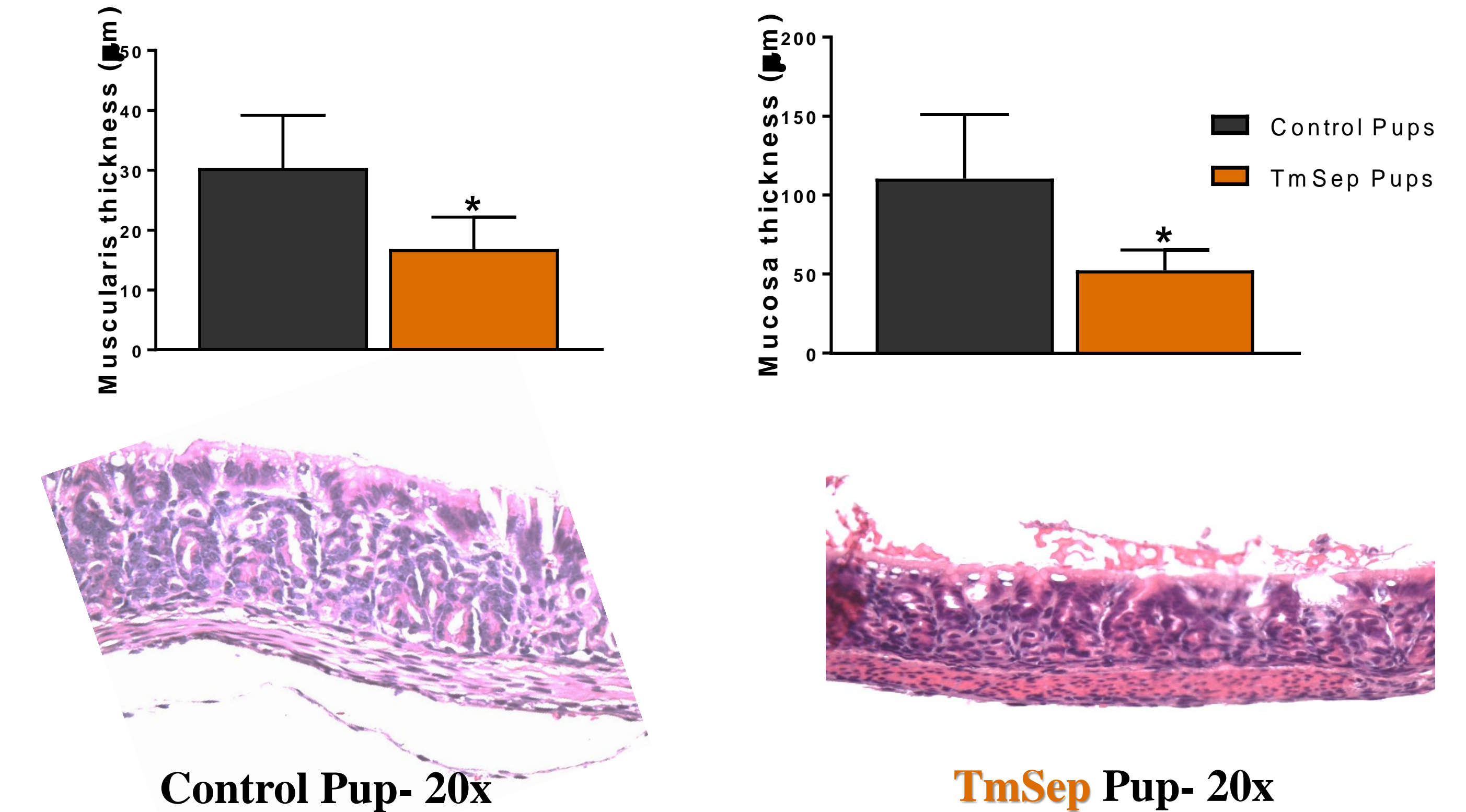
## RESULTS

1. The **TmSep** protocol produced stunted and underweight mouse pups at 14 days of life.



## RESULTS

5. Blinded measurements showed that the **TmSep** mouse pups had significantly decreased thickness in both mucosa and muscularis.

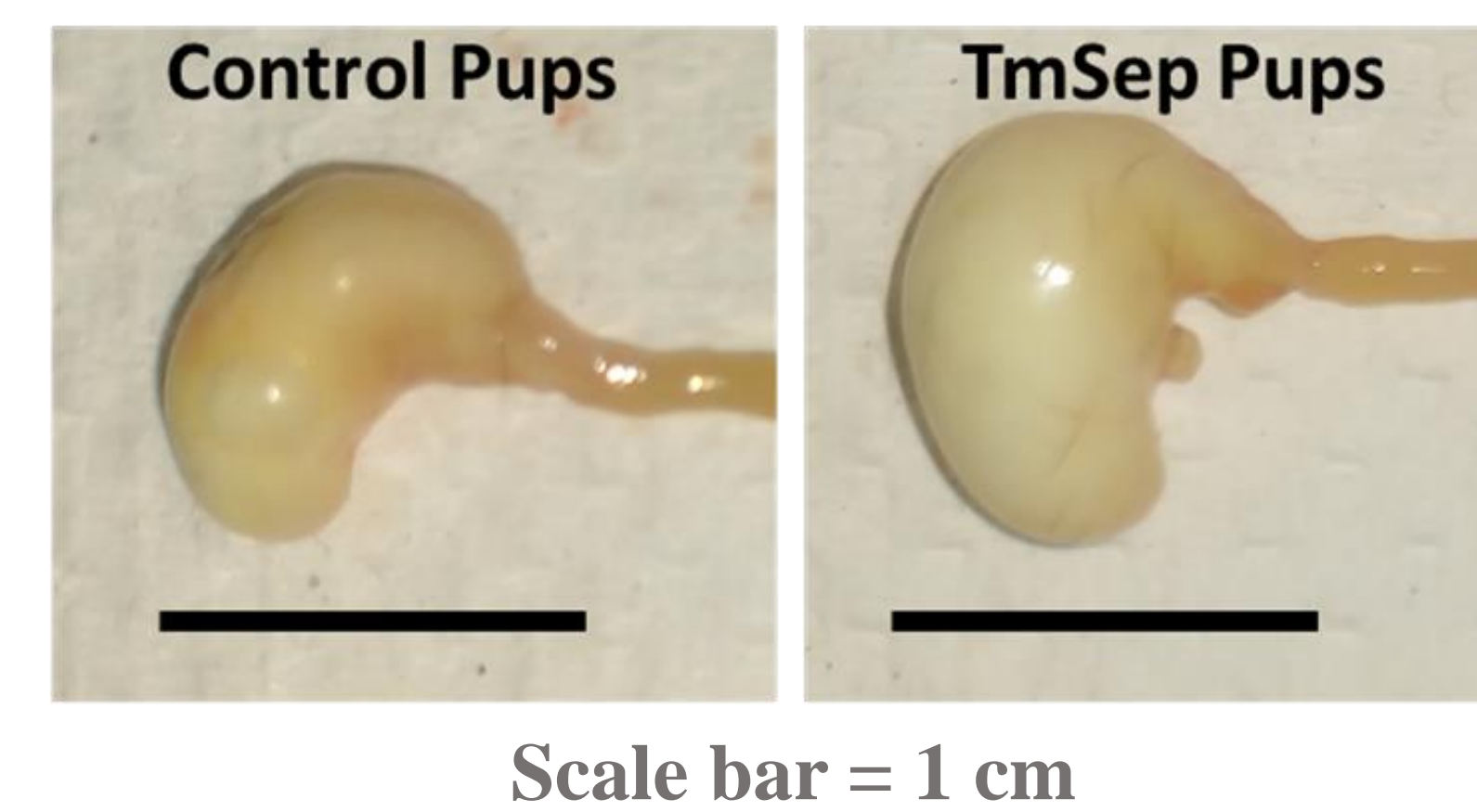


## DISCUSSION

- We present a novel model of gastroparesis induced by timed separation of mouse pups from lactating dams.
- The muscle layer in the **TmSep** mice was significantly more atrophic. These changes to the muscle layer may contribute to decreased emptying of stomach.
- Other contributors to gastroparesis in this model may include altered enteric nervous system, gut microbiota, or neuro-hormonal signaling pathways.
- Further investigation into this model can better describe the microscopic and macroscopic changes that may contribute to smooth muscle atrophy and delayed emptying of stomach.
- My future study into this model will investigate changes to enteric nervous system in this model as well as influence of the gastrointestinal microbiome.

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2. The **TmSep** mouse pups had notably distended stomachs when compared with controls.



3. The **TmSep** mouse pups had decreased clearance of FITC, indicating delayed gastric emptying.

