

# Impact of fecal microbiota transfer (FMT) on phenotype of mice fed a standard diet and a western-style diet using a colitis-associated colorectal cancer model

Abbey Horrocks<sup>1</sup>, Daphne Rodriguez<sup>1</sup>, Korry Hintze<sup>2</sup>, and Abby Benninghoff<sup>1</sup>

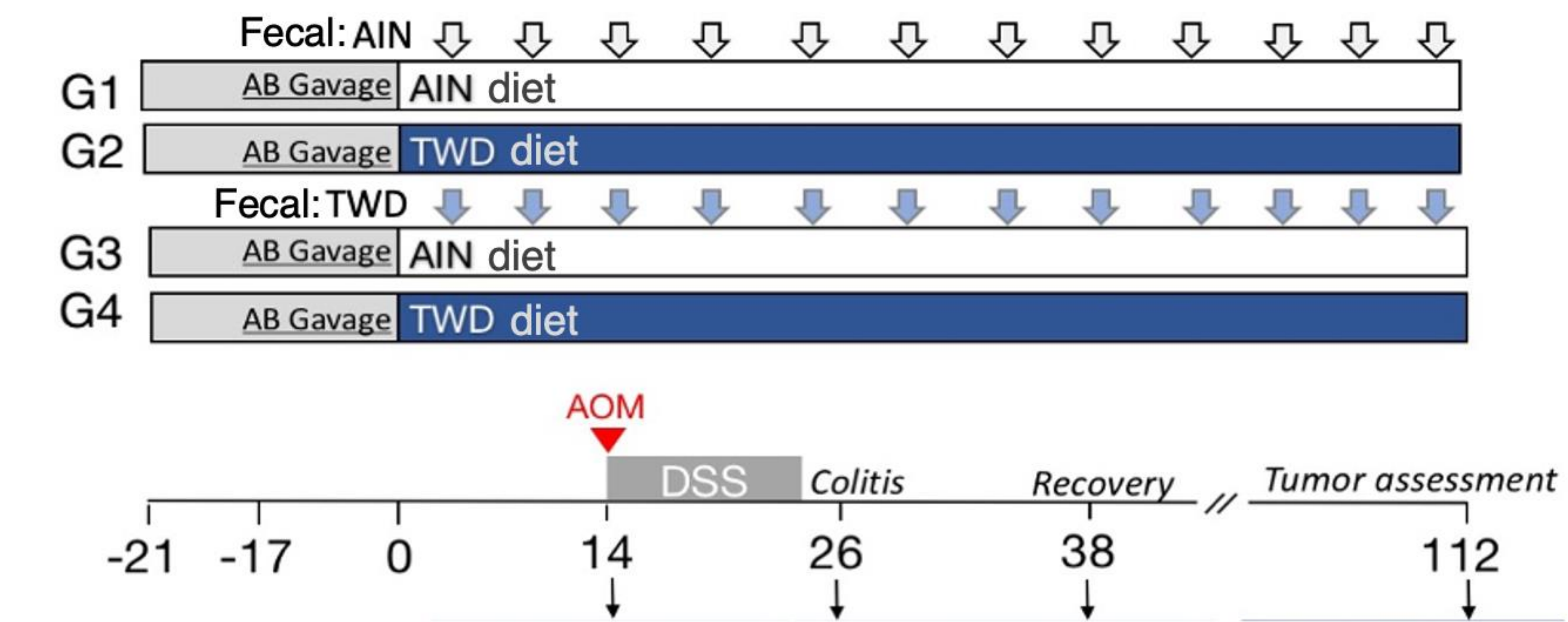
<sup>1</sup> Department of Animal, Dairy and Veterinary Sciences, <sup>2</sup> Department of Nutrition, Dietetics and Food Sciences, Utah State University, Logan, UT



## BACKGROUND

- Approximately 100 trillion bacteria, consisting of 400 to 500 different species inhabit the human gastrointestinal tract.
- A variety of genetic and environmental factors can affect the composition of the human gut microbiota, including a poor diet.
- Western diets are typically associated with dysbiosis and other adverse health outcomes that are expressed phenotypically.
- Animal models are frequently utilized to study the effects of factors such as diet and microbiome on inflammation of the colon and subsequently the development of colorectal cancer.

## STUDY DESIGN



### Mice

- C57BL/6J mice
- 320 Males
- 5 weeks of age

### Experimental Treatments

- Fecal Matter Transplant**
  - FMT from mice fed AIN93G diet
  - FMT from mice fed Total Western Diet

### Experimental diets

- AIN93G**: control diet that promotes rodent health
- Total Western Diet (TWD)**: promotes inflammation-associated colorectal carcinogenesis

### 2x2 Factorial Design

- This study utilized a 2x2 factorial design, where C57BL/6J male mice were fed the standard AIN93G diet or the total Western diet (TWD) for 16 weeks while receiving fecal microbiota transfer (FMT) from donor mice fed either the AIN93G diet or the TWD in a prior study

### Cancer Model

- 10 mg/kg azoxymethane (AOM) to initiate carcinogenesis + 1% (w/v) dextran sodium sulfate to promote colon tumor development

### Body Composition Assessment

- Lean and fat mass of mice were measured using EchoMRI at the terminal time point.

### Terminal endpoints

- Energy and Food Intake
- Body weight gain
- Body composition
- Colitis Assessment
- Tumor Outcome
- Organ Weights
- Histopathological Scores
- Gene Expression
- Inflammation Biomarkers
- Gut microbiome composition

## OBJECTIVE & HYPOTHESIS

### Objective

- The primary objective of this study is to determine the contribution of gut microbiota from mice donors who have previously consumed one of two basal diets: 1) the standard AIN93G diet, which is designed to promote rodent health; and 2) the total Western diet (TWD), which promotes inflammation-associated colorectal tumorigenesis.

### Hypothesis

- Fecal microbiota transplants (FMT) from donor mice which were fed the total Western diet (TWD) will lead to more serious health outcomes than mice who receive transplants from AIN93G donors. Additionally, mice fed the TWD directly that receive FMT from other mice fed TWD FMT will have the most severe health outcomes.

## ACKNOWLEDGMENTS

- USTAR Applied Nutrition Research, Utah State University
- USDA NIFA AFRI grant no. 2018-67017-27516 and 2014-67017-21755



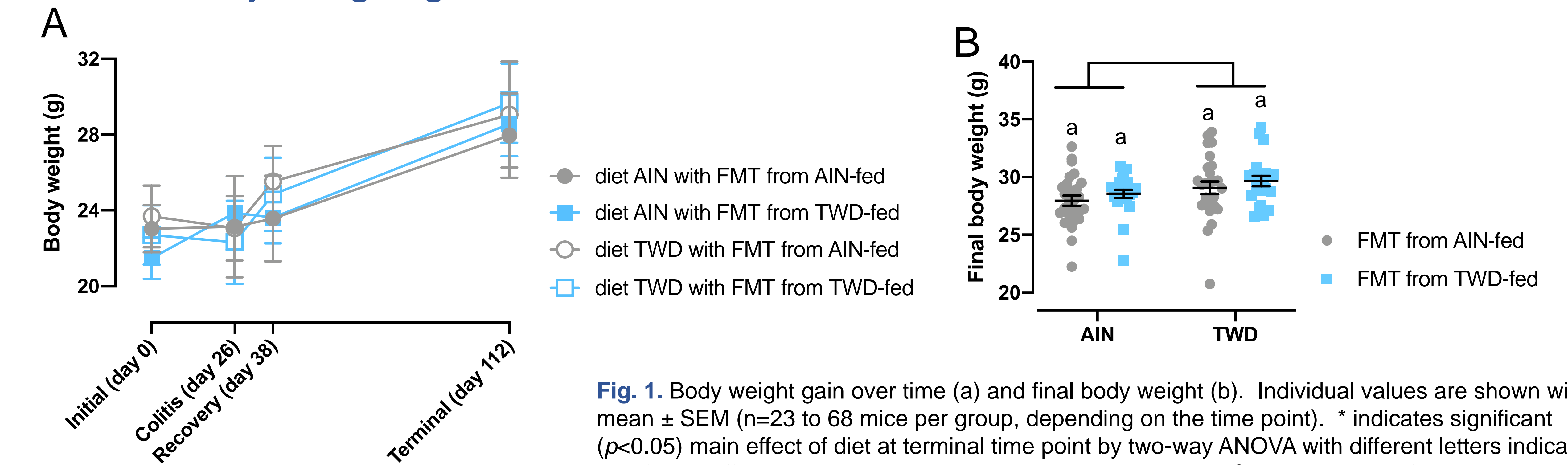
## CONTACT

Project Director  
Abby Benninghoff  
abby.benninghoff@usu.edu

Graduate Student  
Daphne Rodriguez  
daphne.rodriguez@aggiemail.usu.edu

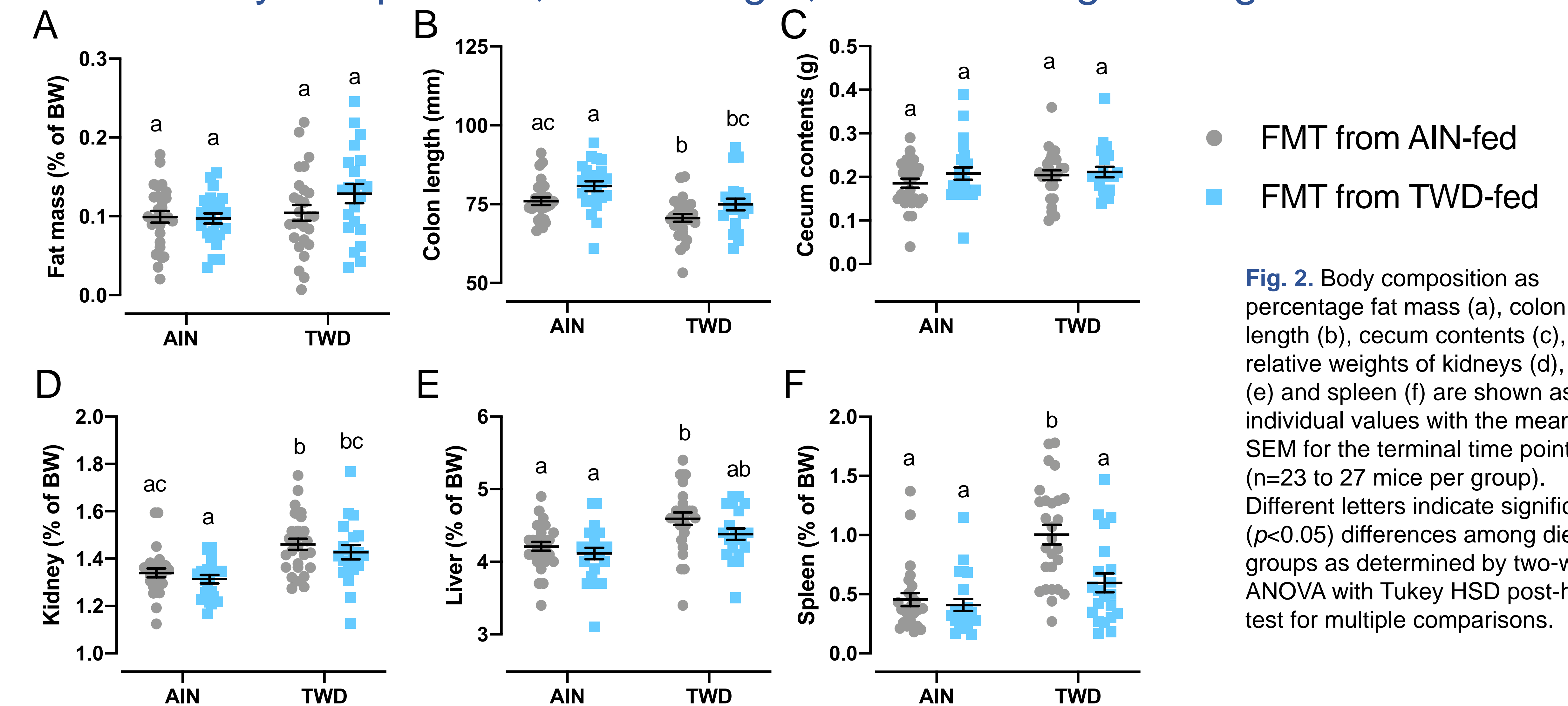
## PRELIMINARY RESULTS

### FIG. 1. Body weight gain



**Fig. 1.** Body weight gain over time (a) and final body weight (b). Individual values are shown with mean  $\pm$  SEM (n=23 to 68 mice per group, depending on the time point). \* indicates significant ( $p < 0.05$ ) main effect of diet at terminal time point by two-way ANOVA with different letters indicating significant differences among experimental groups by Tukey HSD post-hoc test for multiple comparisons. Energy intake among experimental groups was not statistically different (not shown).

### FIG. 2. Body composition, colon length, & relative organ weights



**Fig. 2.** Body composition as percentage fat mass (a), colon length (b), cecum contents (c), and relative weights of kidneys (d), liver (e) and spleen (f) are shown as individual values with the mean  $\pm$  SEM for the terminal time point (n=23 to 27 mice per group). Different letters indicate significant ( $p < 0.05$ ) differences among diet groups as determined by two-way ANOVA with Tukey HSD post-hoc test for multiple comparisons.

## PRELIMINARY CONCLUSIONS

- Preliminary analyses suggest that body weight and body composition were similar among experimental groups regardless of diet fed to the experimental mice or FMT from mice previously fed AIN or TWD diets, though a significant main effect of TWD for higher body weight was noted.
- Also, the relative kidney weight was overall greater in mice fed TWD, though again without an effect of FMT. Alternatively, spleen weight was greater in mice fed TWD that received FMT from previously AIN-fed mice, though not for those that received FMT from TWD-fed mice.
- Interestingly, a significant effect of experimental diet was noted for colon length, with mice fed TWD having shorter colons than their AIN-fed counterparts, though without an effect of FMT.
- Overall these preliminary analyses suggest that most effects appeared driven by the diet consumed by the experimental mice, with a few differential effects of FMT from TWD-fed mice noted, which appeared to improve outcomes rather than worsen them (as for the spleen weight).