

# Post-sleeve gastrectomy microbiome enriches bacterially produced 3-hydroxy fatty acids that reduce adiposity

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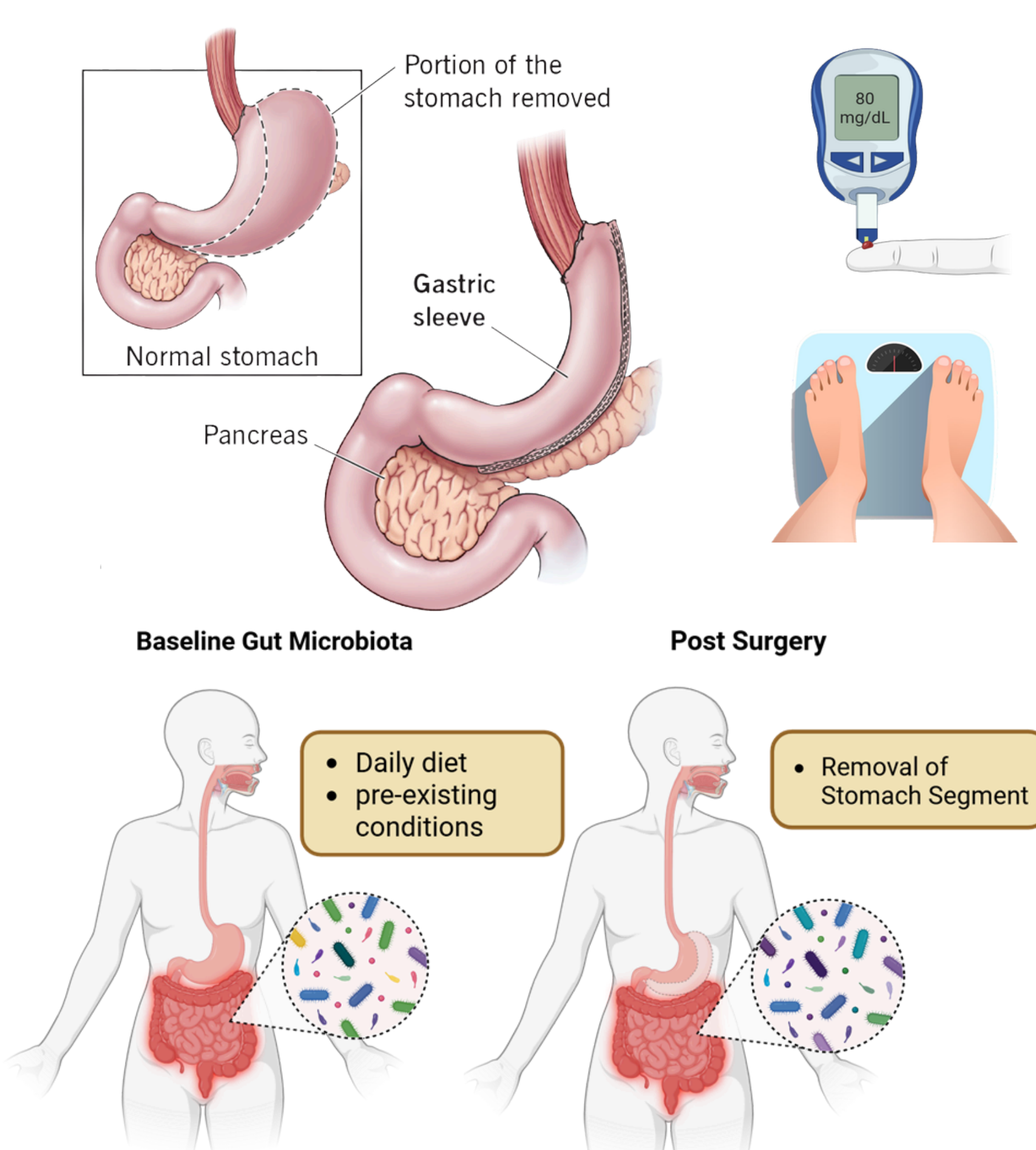
## INTRODUCTION

Sleeve gastrectomy (SG) is the one of the most effective treatments for obesity and type II diabetes (T2D).

- removes about 80% of the stomach
- restrict food intake and reduce hunger hormones
- T2D improvement or remission
- produces metabolic improvements in weight, glucose tolerance, and adiposity

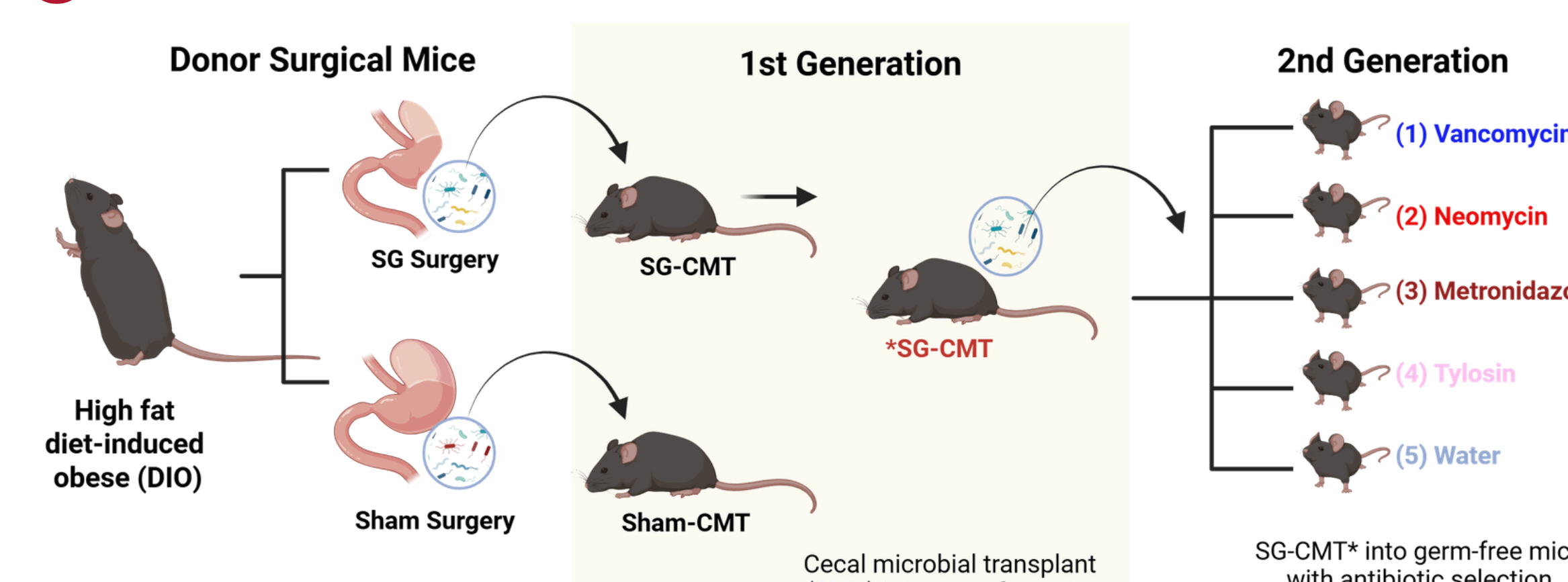
Cecal microbiota transfer experiments confirm that the post-SG microbiome is sufficient to confer these benefits in germ-free recipients, yet the specific microbial metabolites responsible remain largely uncharacterized.

We hypothesize that the post-sleeve gastrectomy gut microbiome produces bioactive small molecules impact adipocyte lipid accumulation and promote adipose tissue metabolic remodeling.

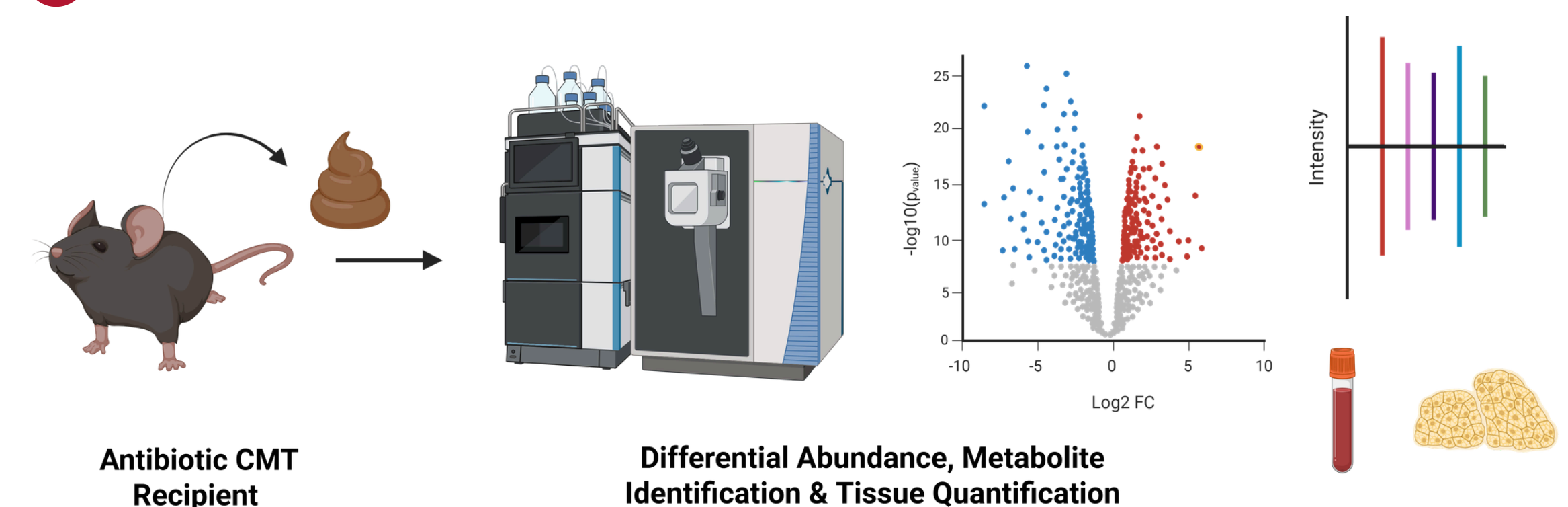


## METHODS

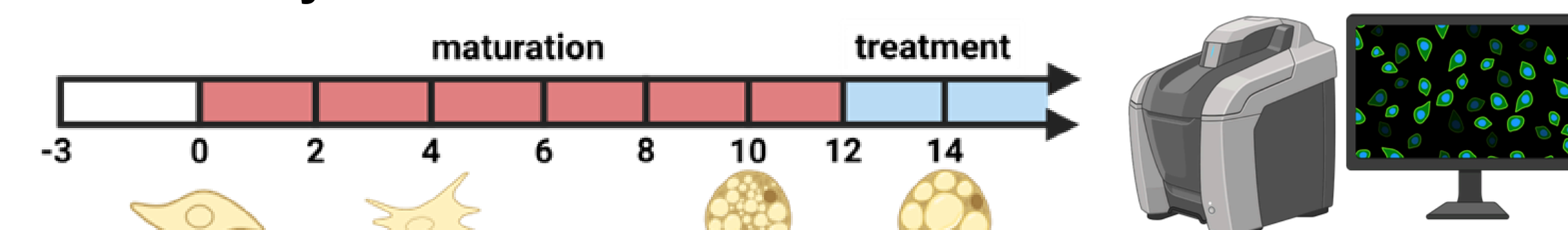
### 1 Phenotype Analysis of SG CMT with Antibiotic Selection



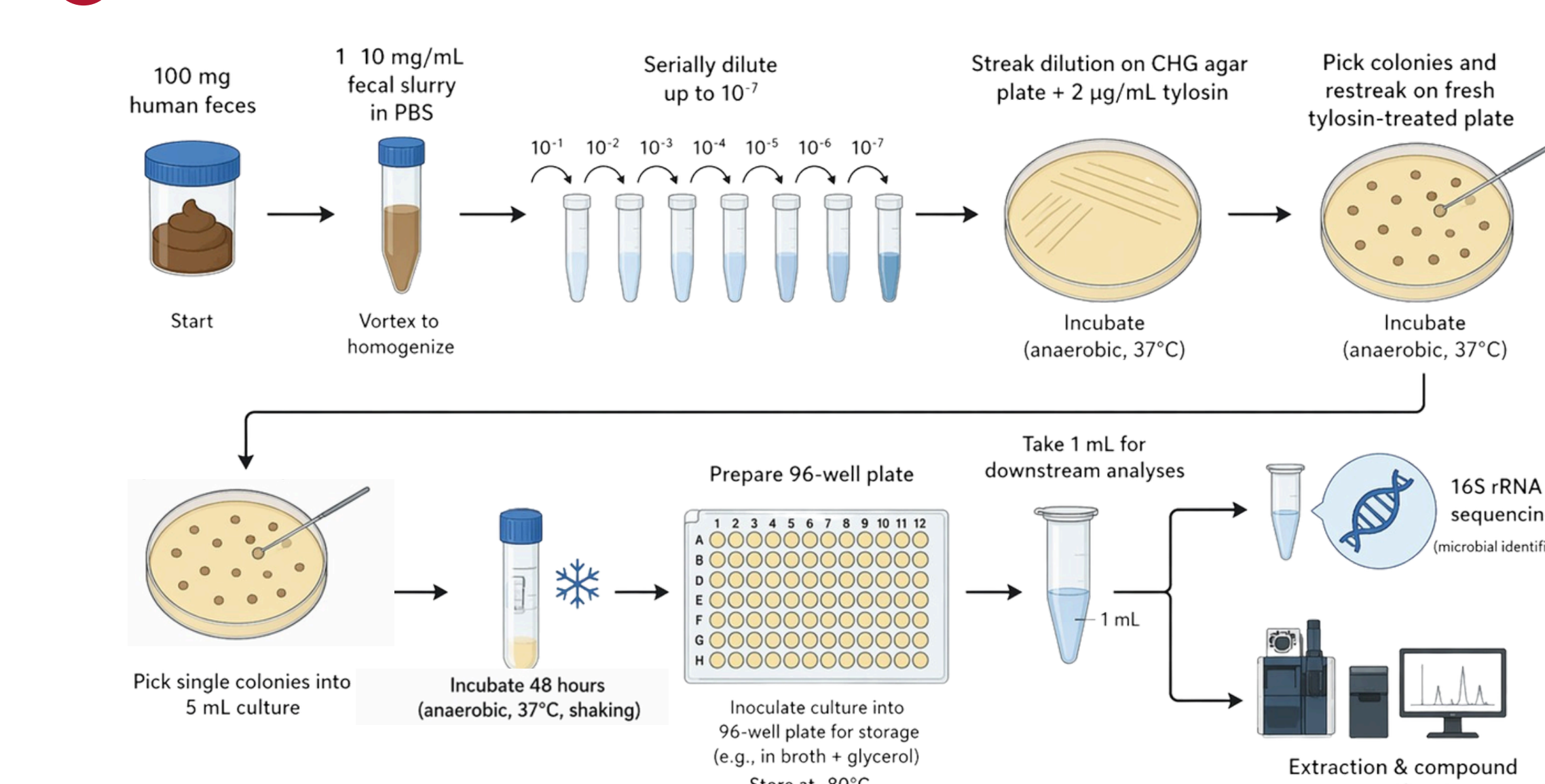
### 2 Differential Abundance & Metabolite Identification



### 3 Adipocyte Differentiation Assay to Evaluate Metabolite Activity

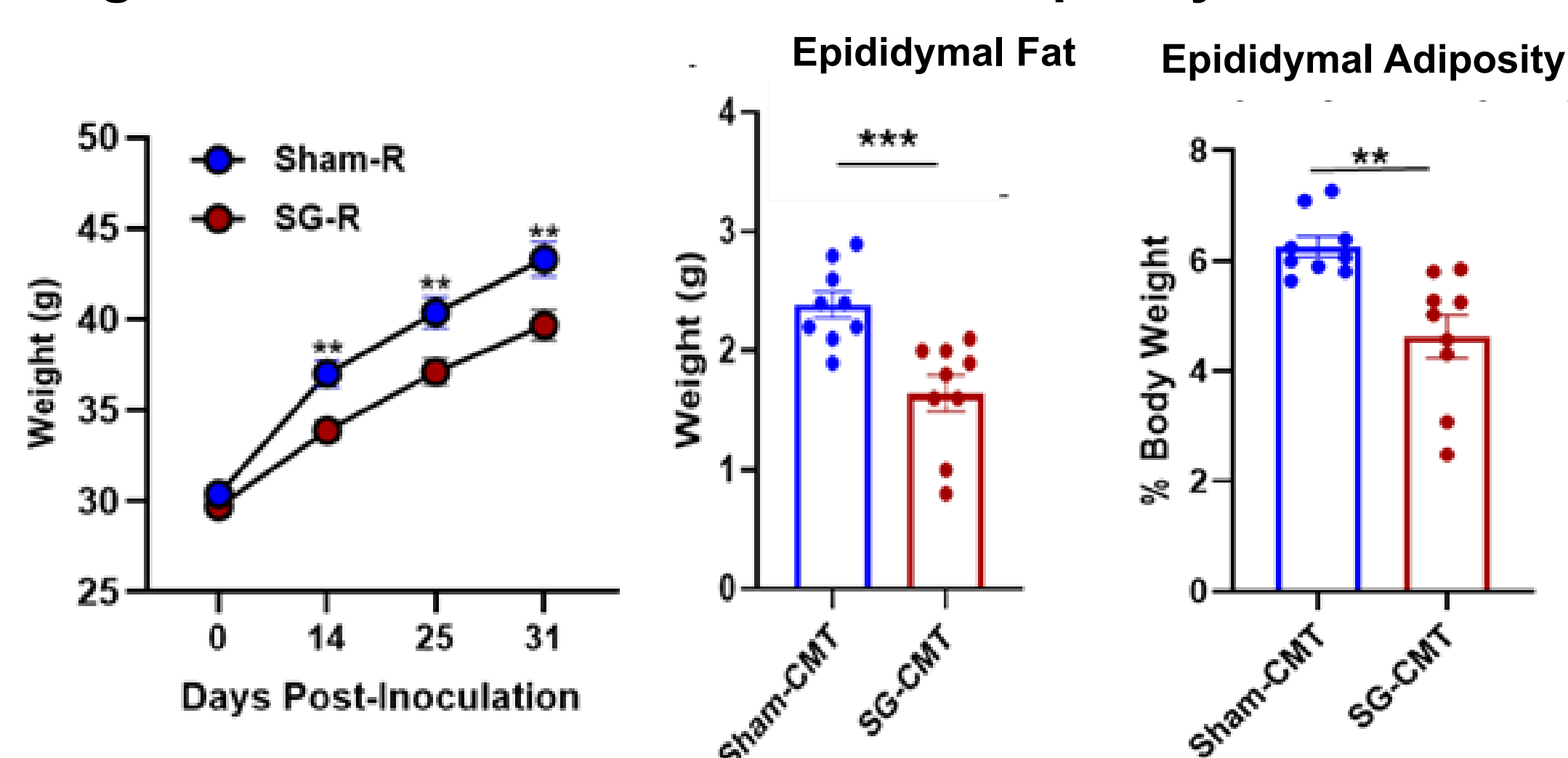


### 4 Human & Mouse Feces Cultureomic Screening

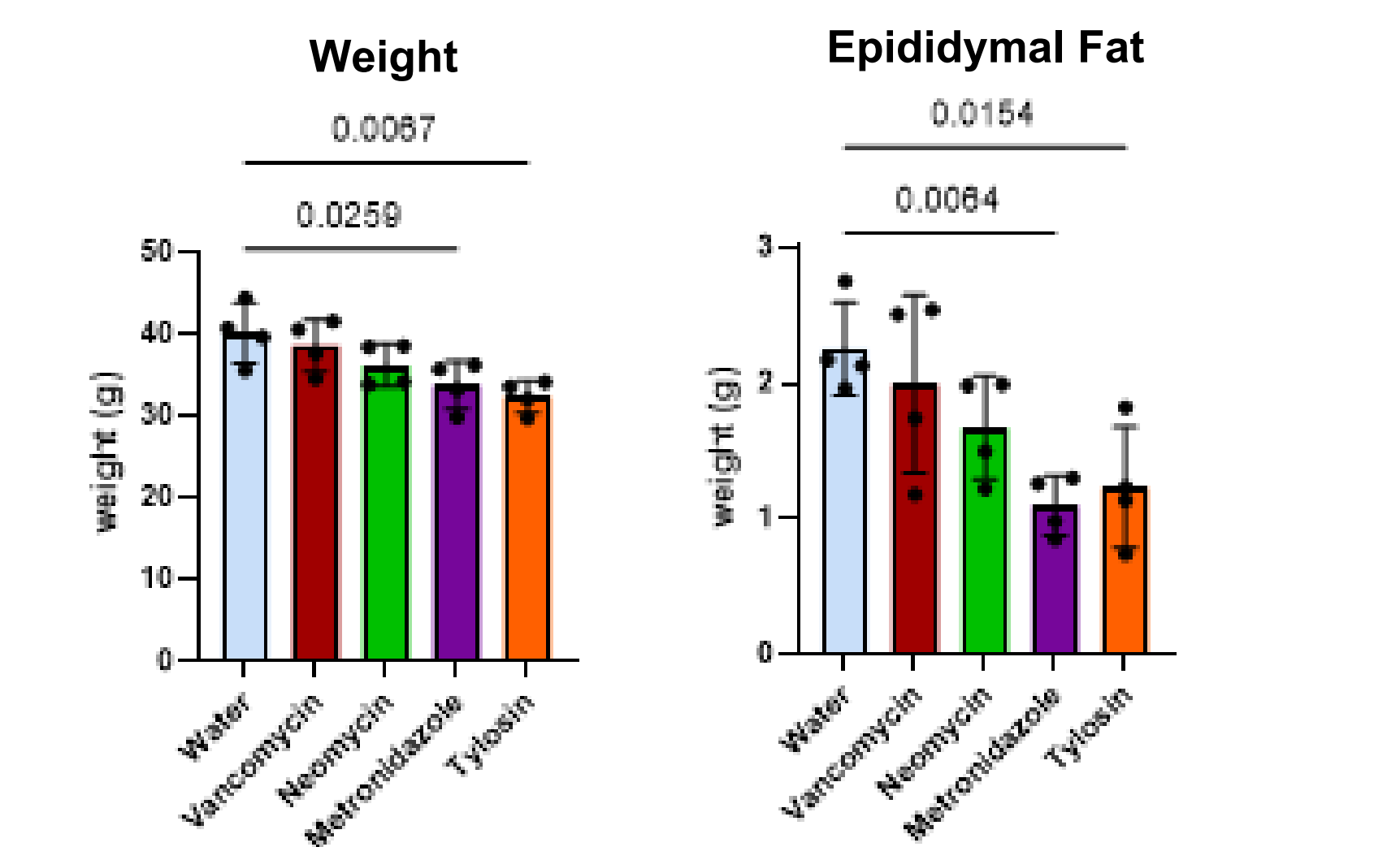


## RESULTS

### SG-CMT recipient mice show conserved improvement in glucose tolerance and reduced adiposity

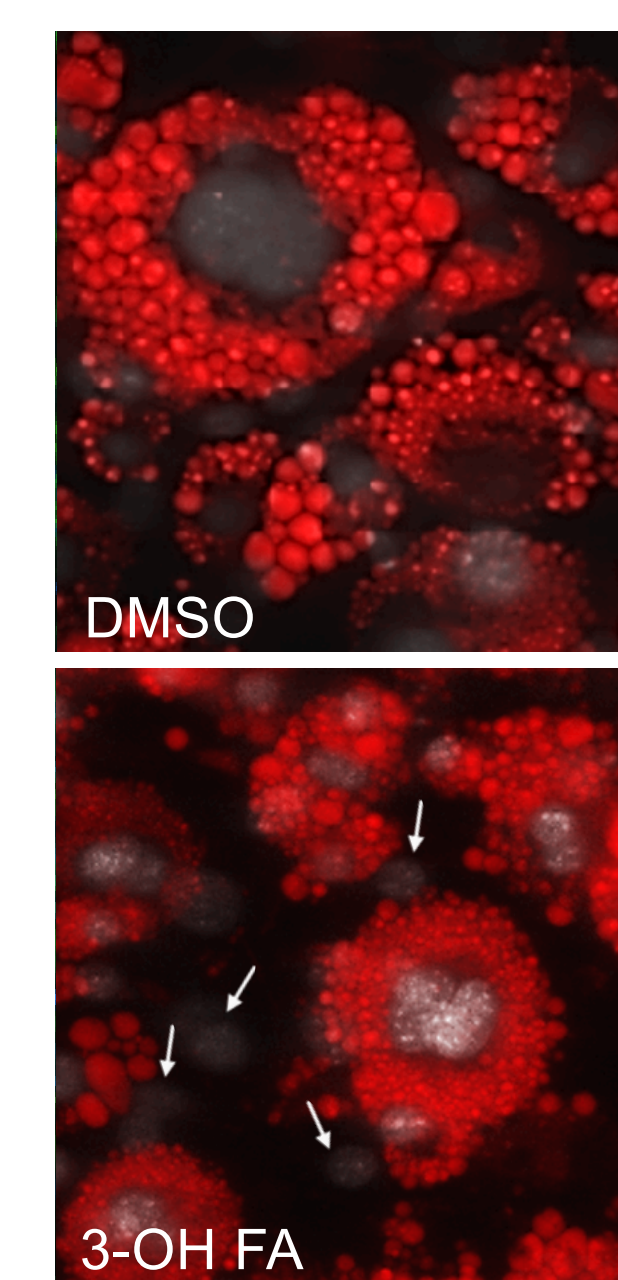
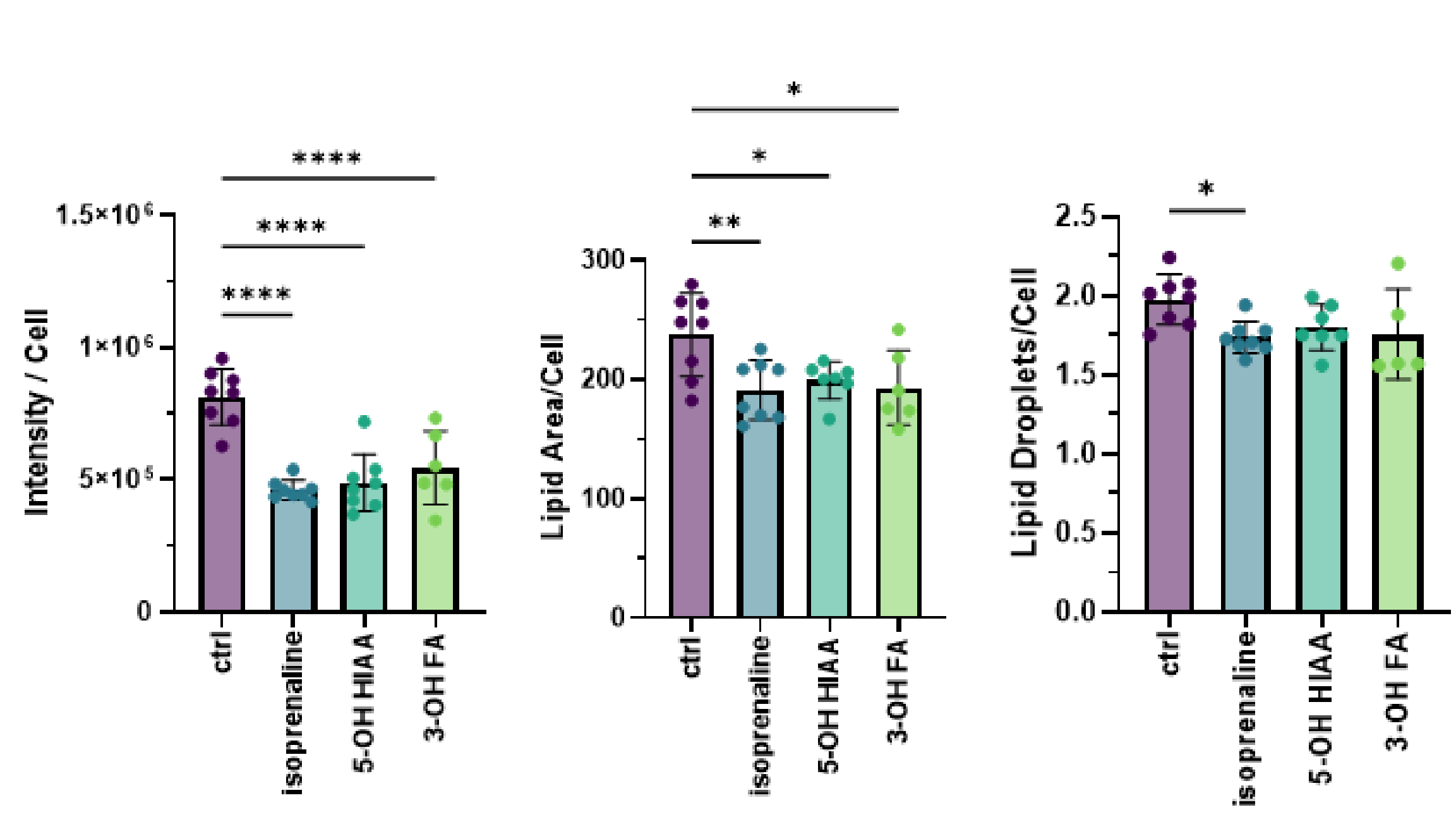


### Antibiotic selected microbiomes show enhanced beneficial phenotypes

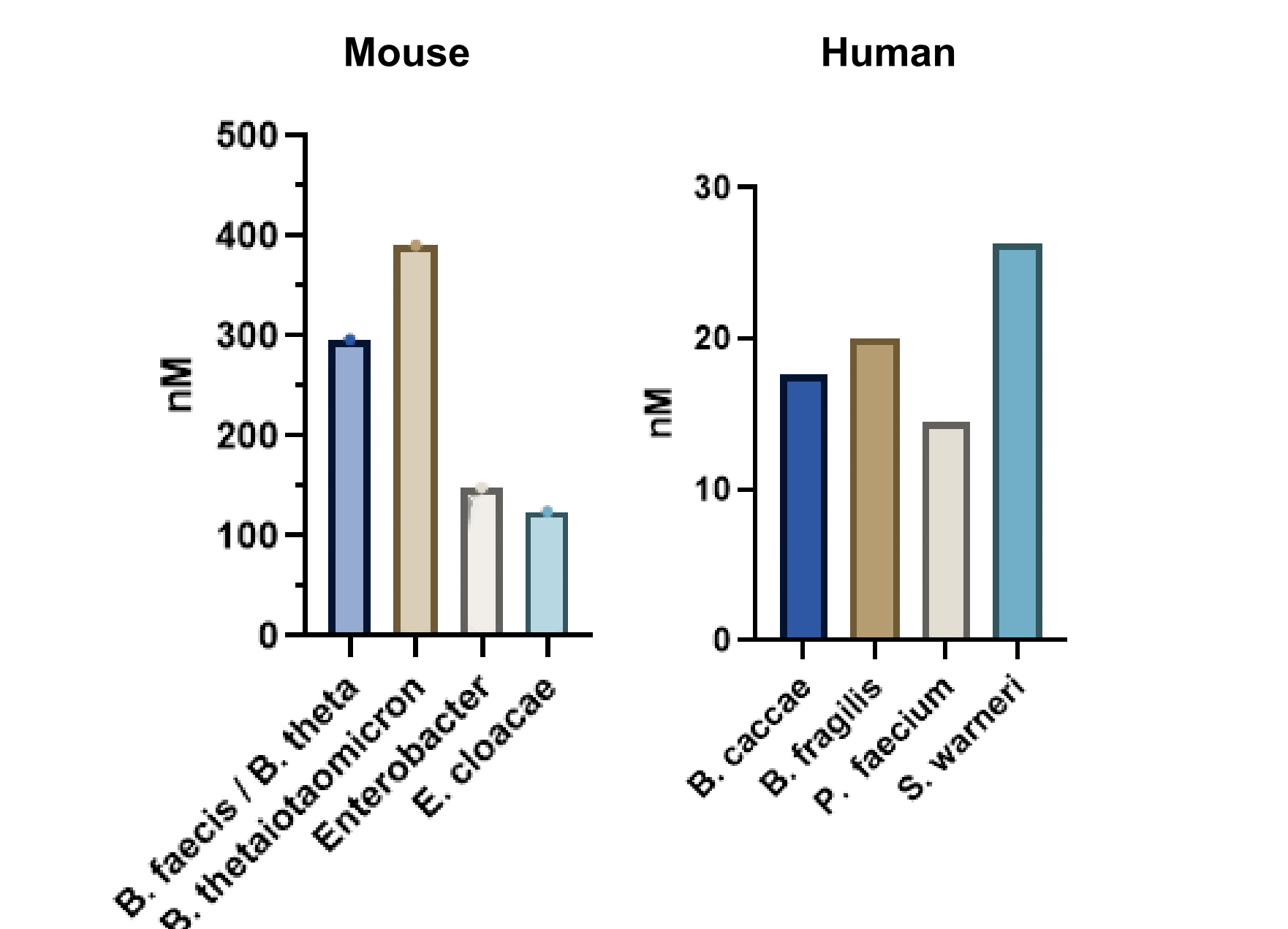


## RESULTS

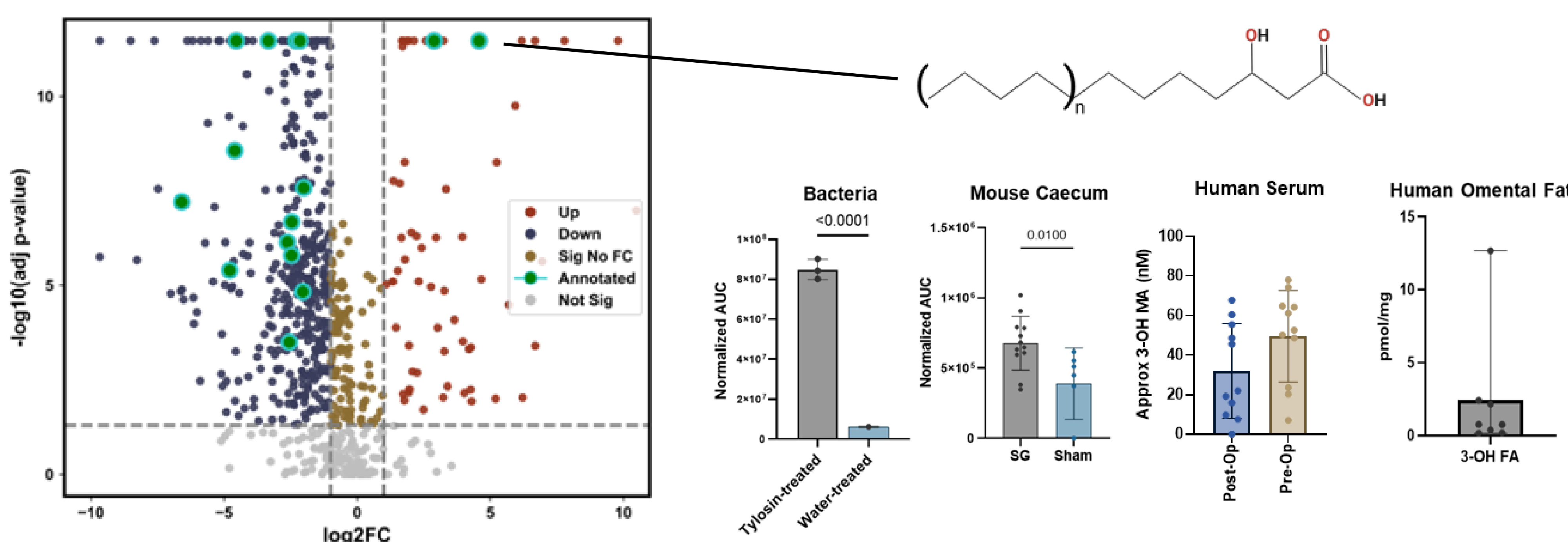
### 3-OH FA reduces lipid droplet accumulation/fusion in vitro



### Mouse and human fecal isoaltes shown to produce 3-OH FA nanomolar concentrations



### Differentially abundant hydroxy fatty acid (3 OH FA) detected in mouse cecum, human feces, blood, and omental fat.



## CONCLUSION

- Antibiotic selection of the post-SG microbiome narrows the transplanted community while amplifying metabolic benefit, indicating a subset of taxa is sufficient to confer reduced adiposity and improved glucose tolerance.
- Untargeted metabolomics identifies a 3-OH fatty acid as differentially abundant across mouse cecum, human serum, and omental fat, establishing its relevance beyond the gut lumen.
- 3-OH FA reduces lipid droplet accumulation and fusion in differentiating adipocytes, demonstrating a functional microbiome-to-adipose signaling axis.
- Bacteroides isolates from both mouse and human feces produce 3-OH fatty acids, though human-derived isolates produce at lower concentrations, suggesting species-level or community-level differences in biosynthetic capacity between host contexts.

