

# Diet-induced peripheral tissue changes associated with risk factors for Alzheimer's disease

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Growing evidence shows that what we eat can influence the risk and progression of Alzheimer's disease. This study compared a Mediterranean diet with a typical American diet in mice. The American diet led to fat buildup in the liver and larger fat cells, signs of metabolic stress. In contrast, the Mediterranean diet increased the number of goblet cells in the colon, which may enhance gut protection. Overall, these findings suggest that diet can impact key organs and potentially influence neurodegenerative risk.

## Introduction

- In the U.S, 10.8% of the population aged 65+ is impacted by AD (Rajan et al., 2021).
- Systemic metabolic dysfunction contributes significantly to the acceleration of AD onset and progression (Giuffrè et al., 2024).
- Macronutrient composition plays a decisive role in shaping biological processes such as systemic inflammation and adipose tissue (Sun et al., 2011)
- To evaluate the systemic pathways linking diet to AD risk, structural changes in peripheral tissues such as the liver, small intestine, and white adipose tissue (WAT) are particularly informative, they are sensitive to metabolic alterations and can be affected by TAD-induced oxidative stress or protected by MED-associated mechanisms (Cheon & Song, 2022; Estrada et al., 2019).

## Conclusions

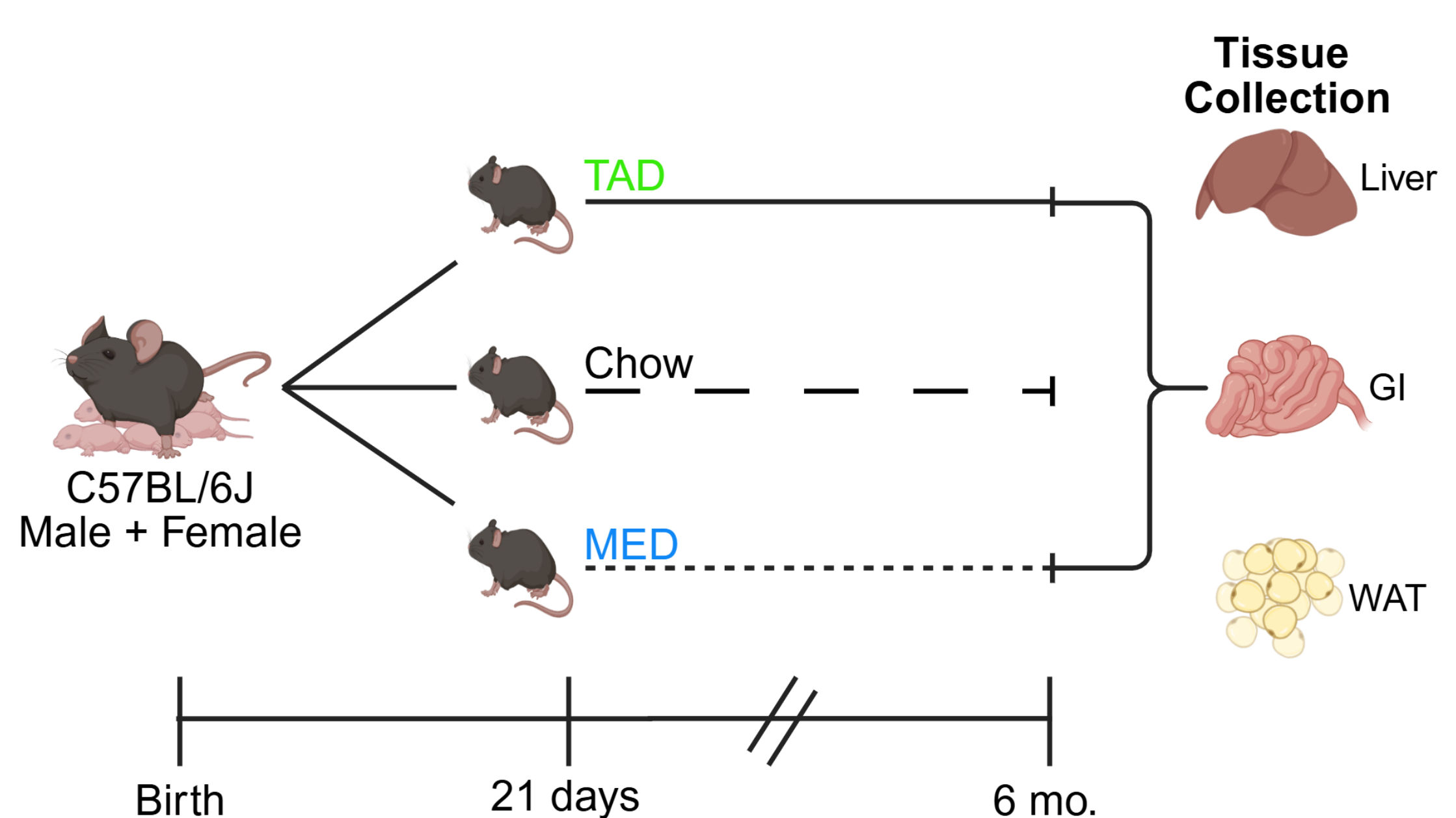
- TAD exposure leads to increased lipid droplet deposition within hepatocytes, signaling significant alterations in lipid metabolism and metabolic regulation.
  - Significant increases in adipocyte size WAT suggest chronic metabolic stress and systemic energy imbalance induced by poor nutritional quality.
  - The Mediterranean diet enhances gut protection by increasing mucin production, while neither diet significantly alters small intestine structure or induces detectable inflammation.
  - Dietary-induced structural remodeling in peripheral tissues serves as an early indicator of metabolic and gastrointestinal dysfunction, potentially creating a systemic environment that accelerates Alzheimer's Disease risk via the gut-brain axis.
- Future Directions:**
- Can switching from a TAD to a MED later in life reverse the detrimental effects of TAD.

## Method

### Diets:

**Macronutrient distribution** and key ingredients across diets. TAD and MED share similar macros (50% carbs, 15% protein, 35% fat) but differ in sources: TAD relies on corn starch, casein, and mixed animal fats, while MED uses whole grains, fish/egg protein, and plant-based oils. Chow is higher in carbs (65%), moderate in protein (21%), and lower in fat (14%).

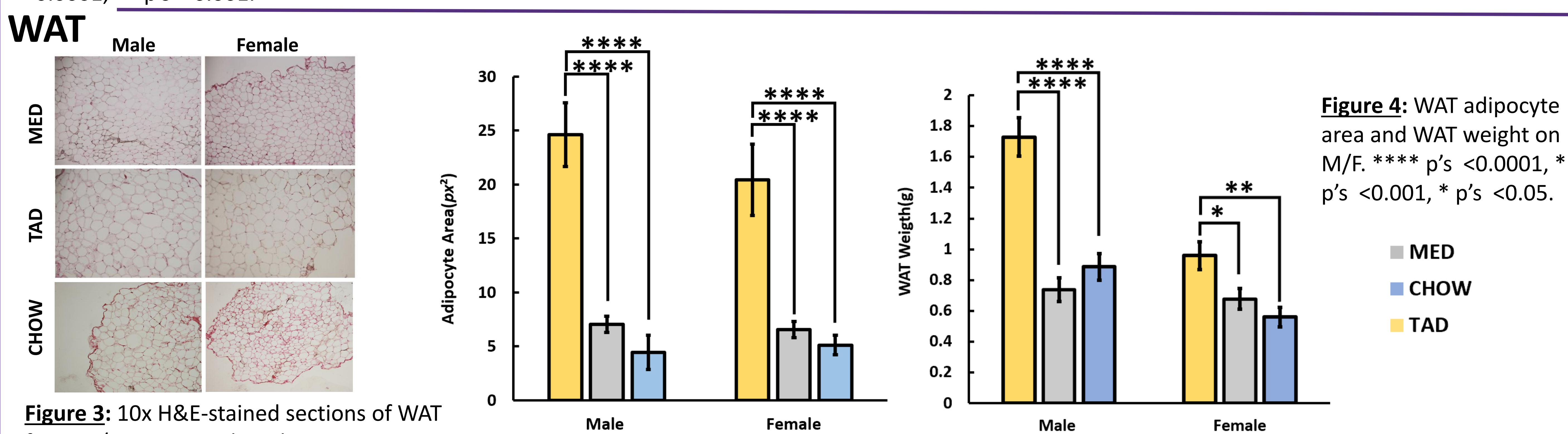
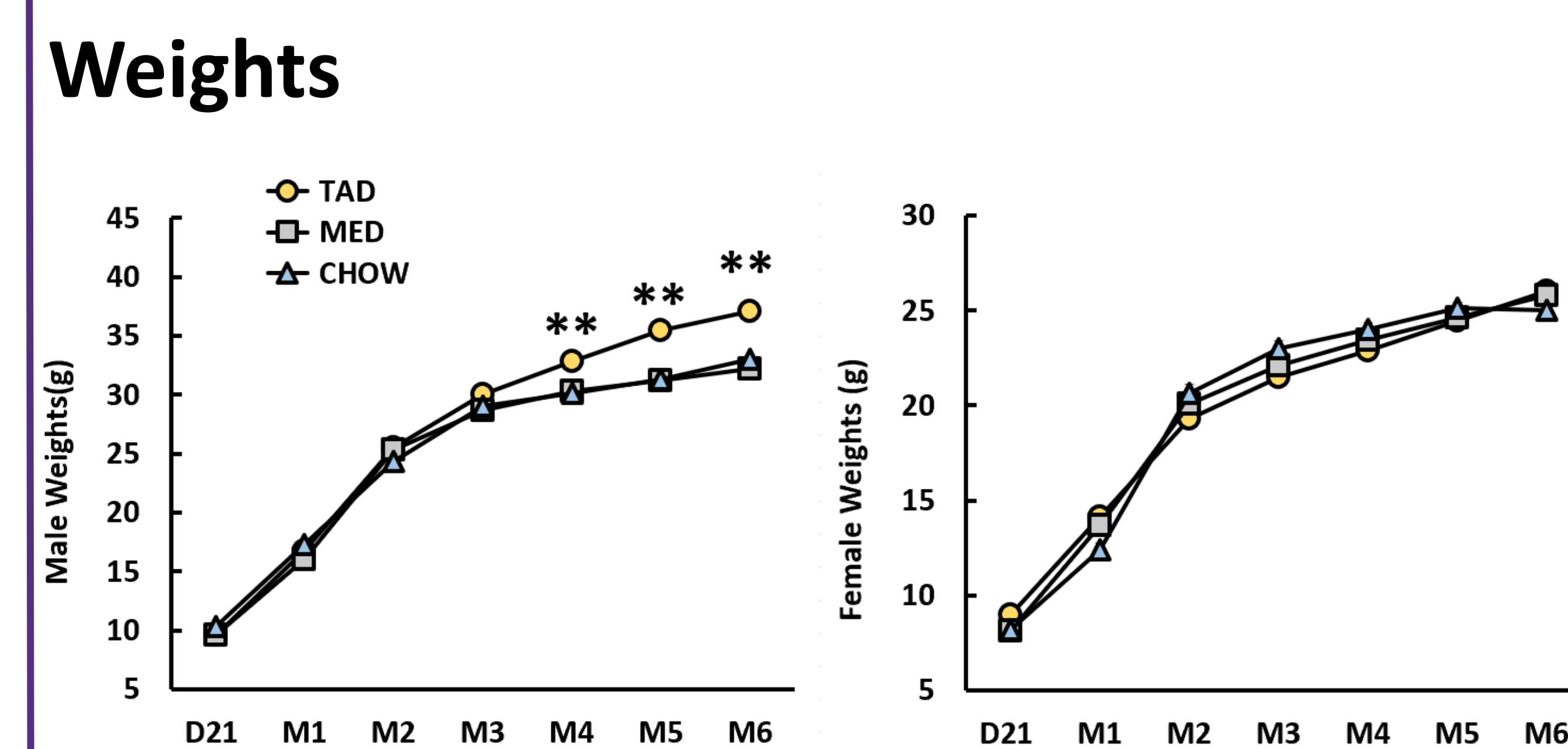
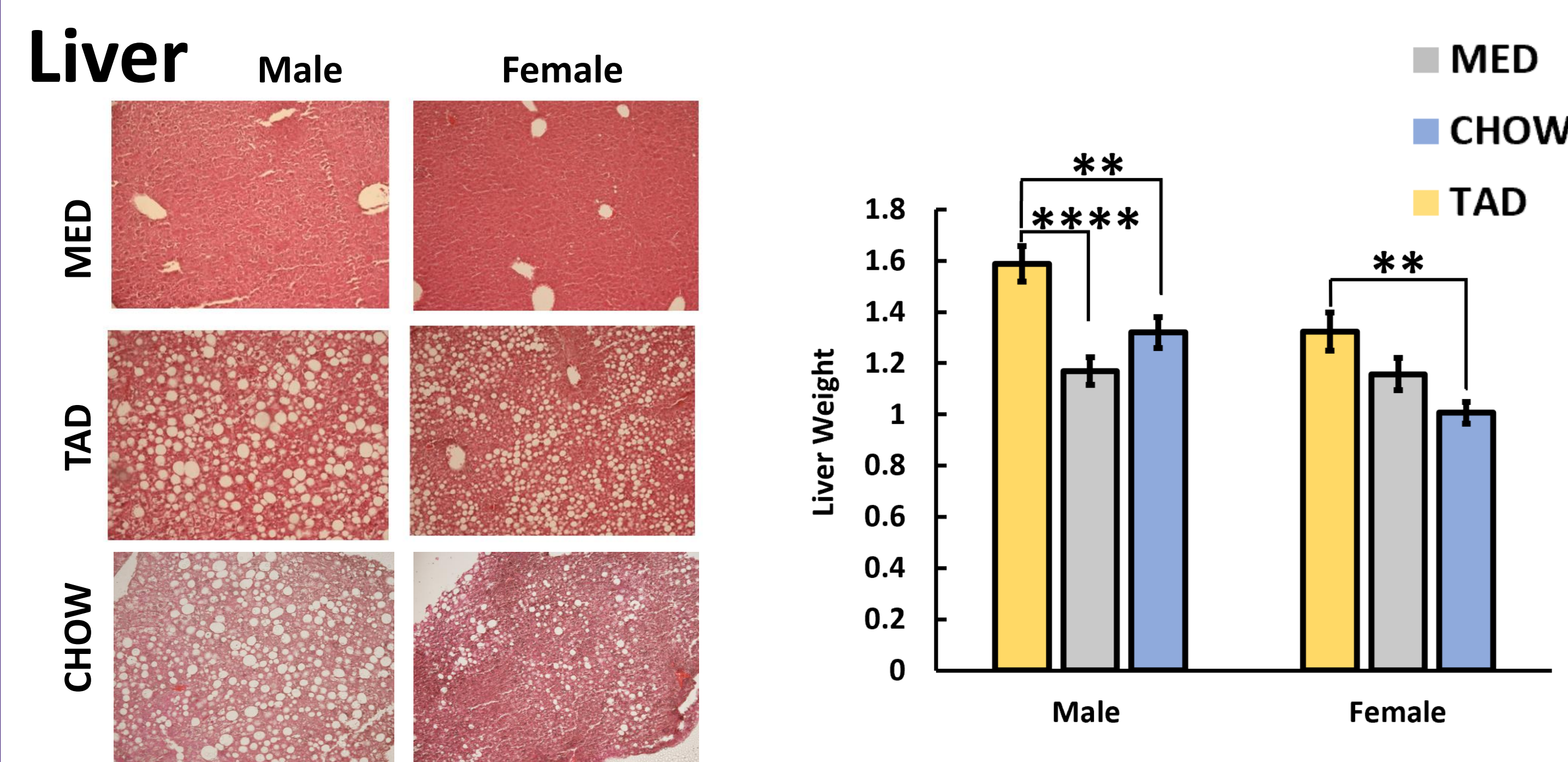
	TAD		MED		Chow	
	kcal%	Key components	kcal%	Key Components	kcal%	Key Components
<b>Carbohydrates</b>	50.0	Corn starch	50.0	Brown rice, wheat starch	65.0	Corn, wheat, oats
<b>Protein</b>	15.0	Casein	15.0	Egg whites, fish, soy	21.0	Soybean meal, fish meal, porcine meal
<b>Fat (Total)</b>	35.0	Safflower oil, beef fat, butter	35.0	Olive, fish, and flaxseed oil	14.0	Porcine animal fat, soybean oil



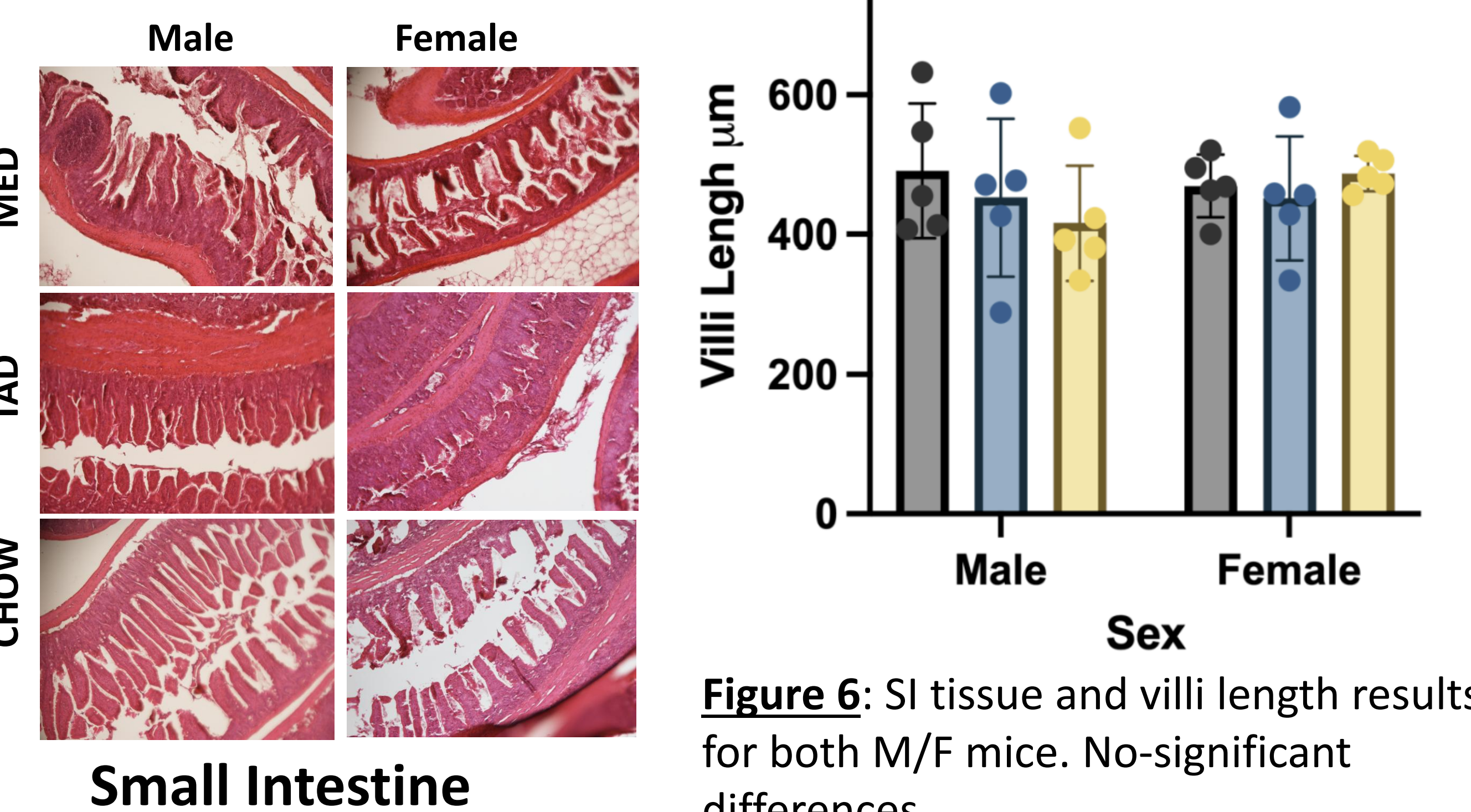
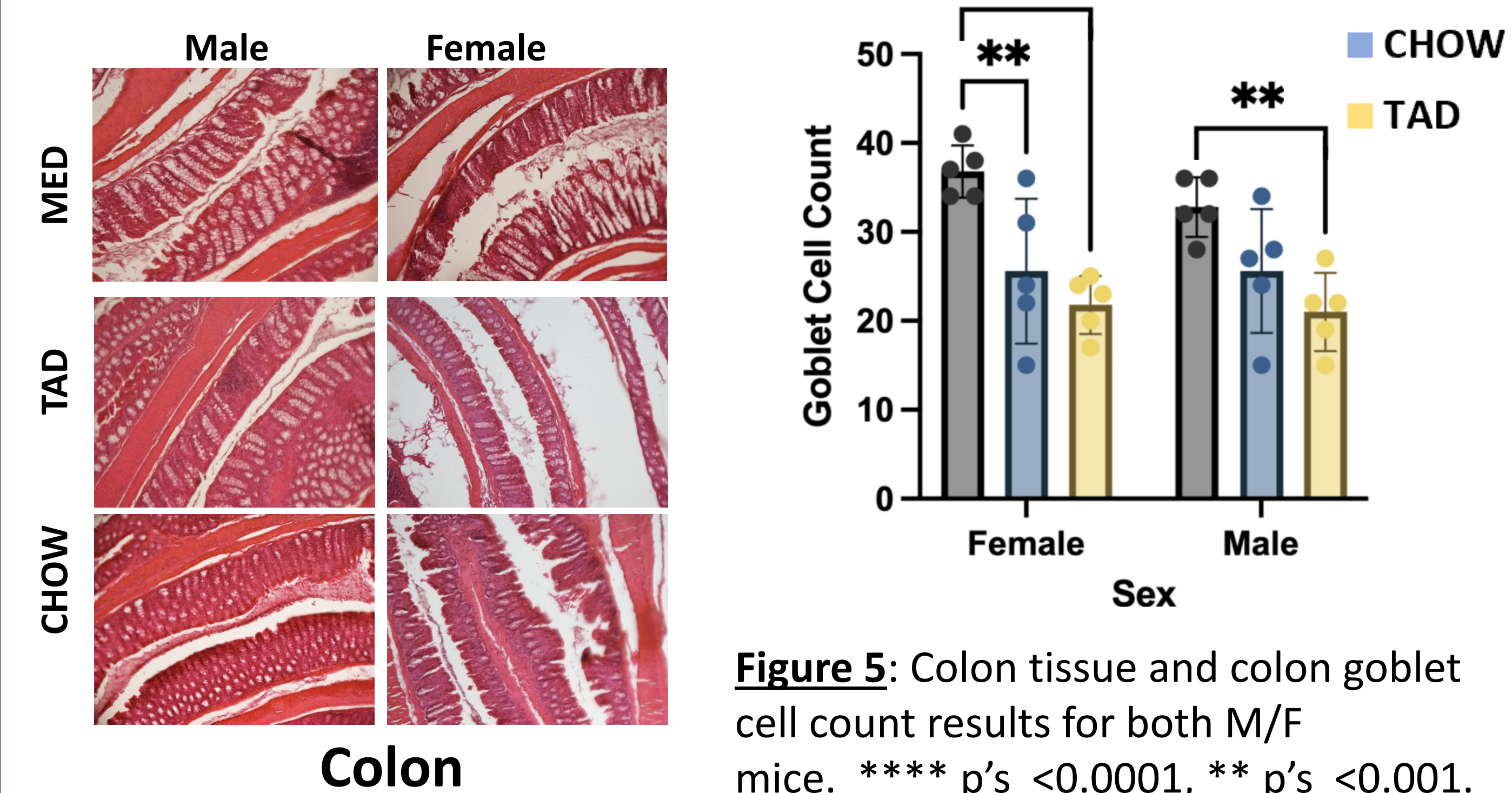
### Staining:

- **Histological Staining:** Standard Hematoxylin and Eosin (H&E) staining protocols were employed to assess tissue morphology.
- Tissue was processed through a series of graded alcohols and staining buffers (Leica Biosystems) and mounted with DPX.

## Results



## Colon and Small Intestine



## References

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