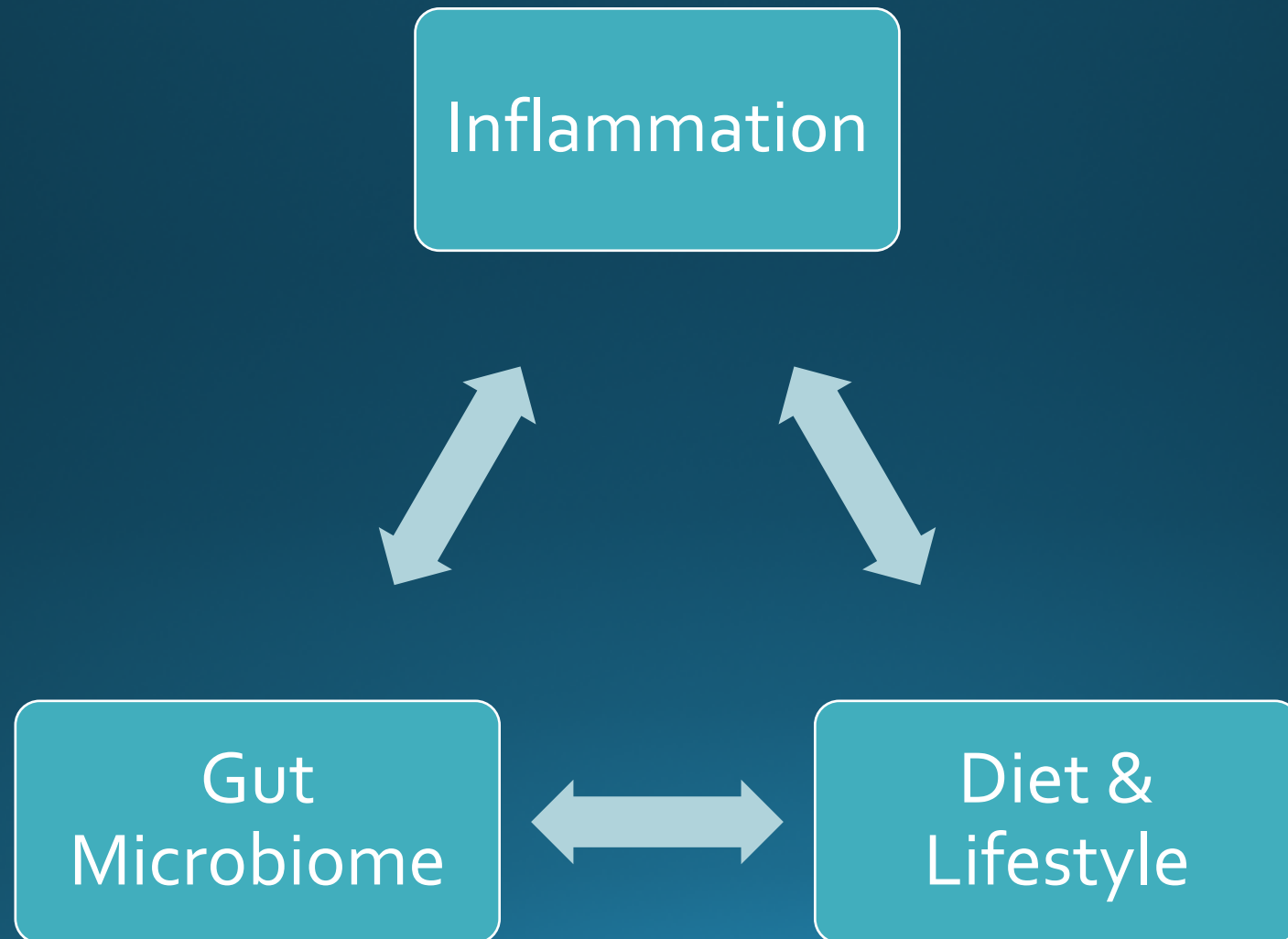


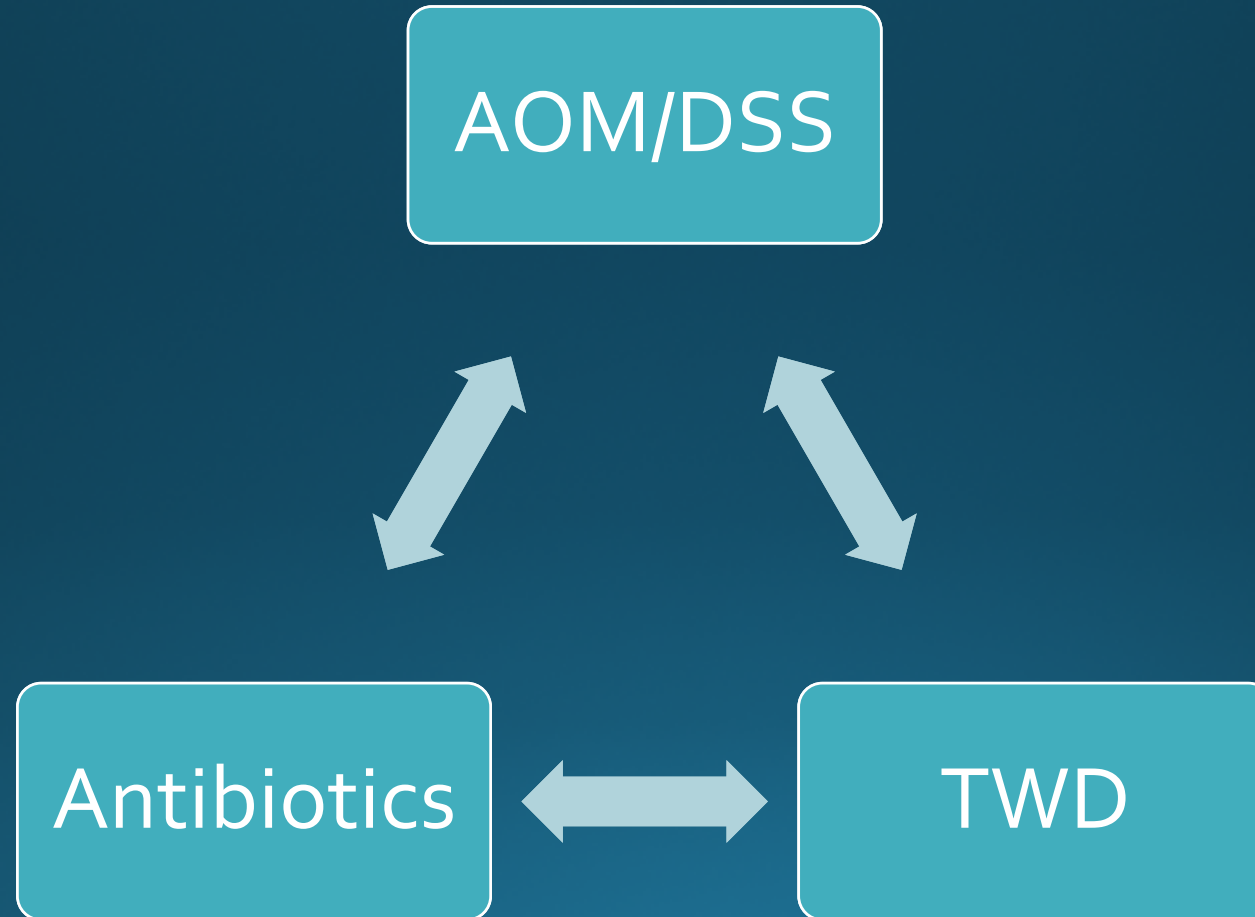
The Total Western Diet and Vancomycin Increase Inflammation Mediated Colorectal Cancer

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Factors



Pre-clinical studies (i.e. Animal Models)



The Question

What is the effect of the total Western diet, vancomycin-induced changes to the gut microbiome, and the combination of the two on colorectal cancer in the presence of DSS-induced inflammation?

Hypothesis

- We hypothesize that *vancomycin treatment will decrease the overall tumor burden, as measured by total tumor volume/colon, in mice fed the total Western diet in the presence of DSS-induced inflammation, and that this attenuation will be supported by a significant diet x treatment interaction.*

Study Design

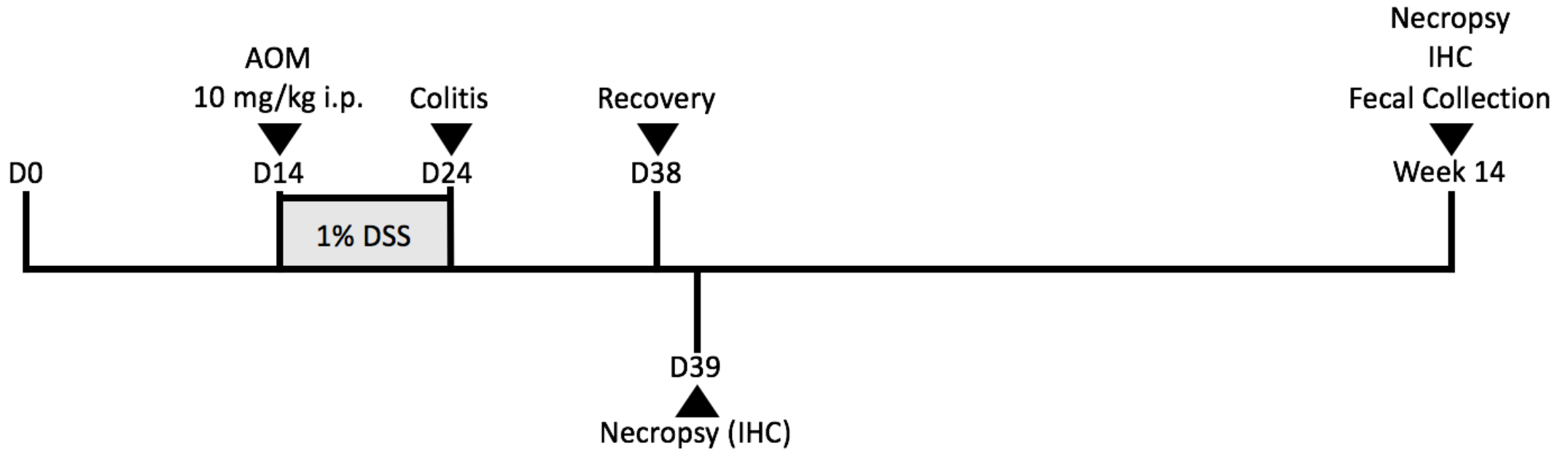


144 mice; 9 cages per group x 4 mice per cage (n=36)

Endpoints

- Tumor Burden (total tumor volume/colon)
- Tumor Multiplicity (number of tumors/colon)
- Tumor Size (mm³)
- Mucosal Injury and Inflammation
- Visual Colitis Assessment
- Microbiome
 - Taxonomic Summaries
 - Species Richness
 - Community Similarity

Timeline

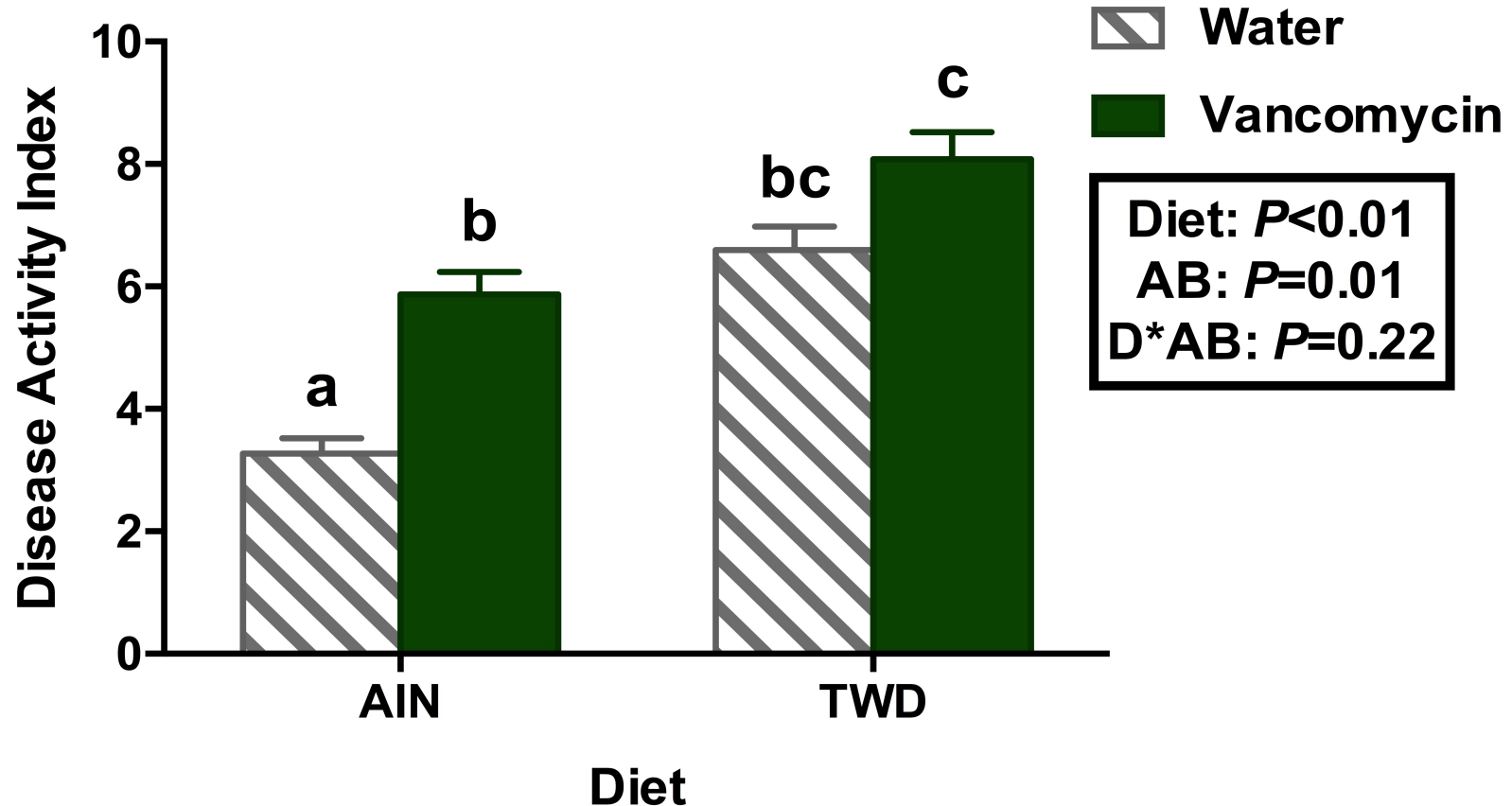


Statistical Analysis

- All data were analyzed using SAS On Demand.
- Data were tested for the main effects of diet, vancomycin treatment, and the diet x treatment interaction.
- Cage effect was taken into account when performing statistical analysis.
- Group mean analysis was performed using the Ryan-Einot-Gabriel-Welsh (REGWQ) test.

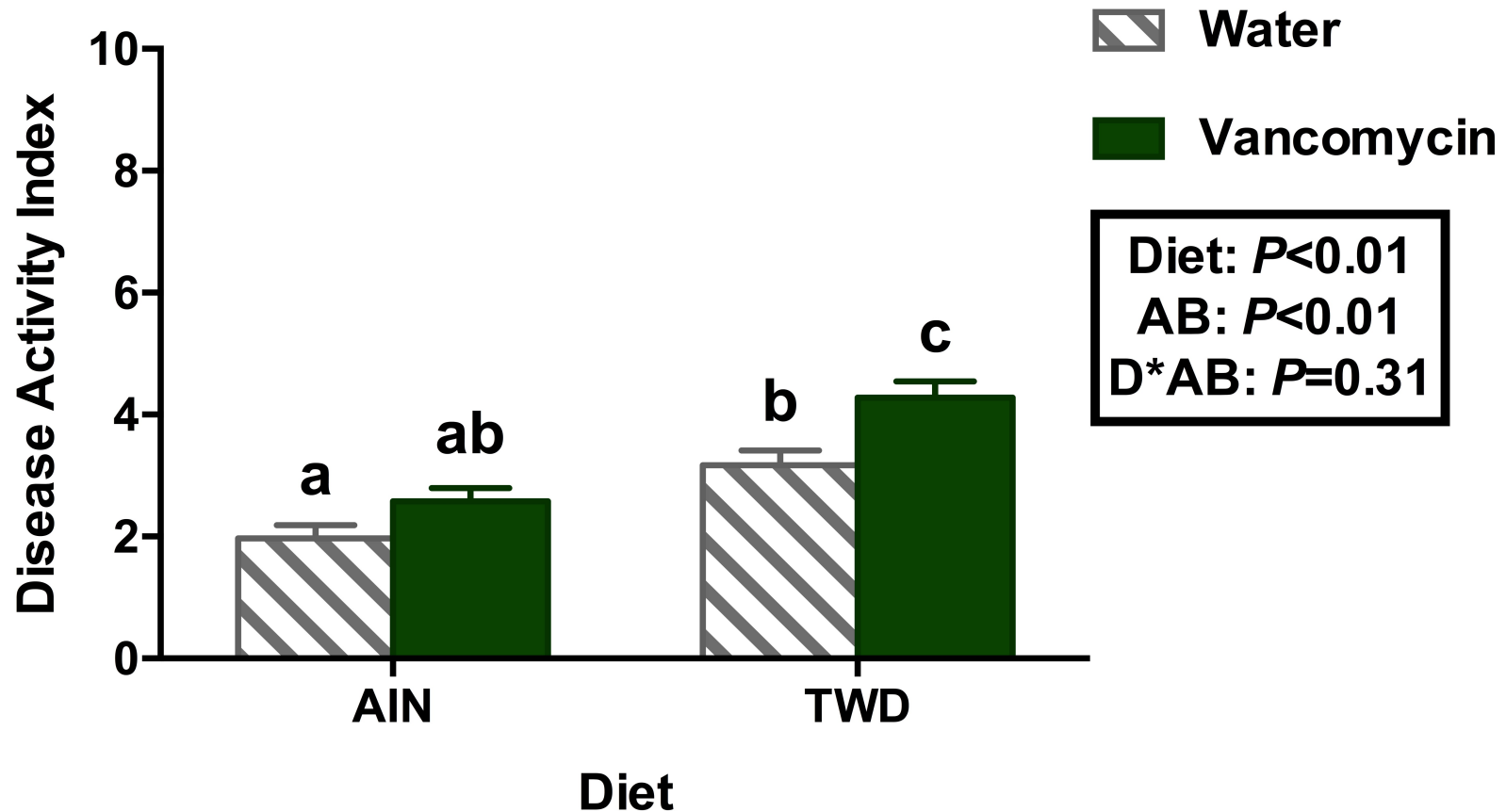
Results

Colitis Assessment 1 (1 day post-DSS)

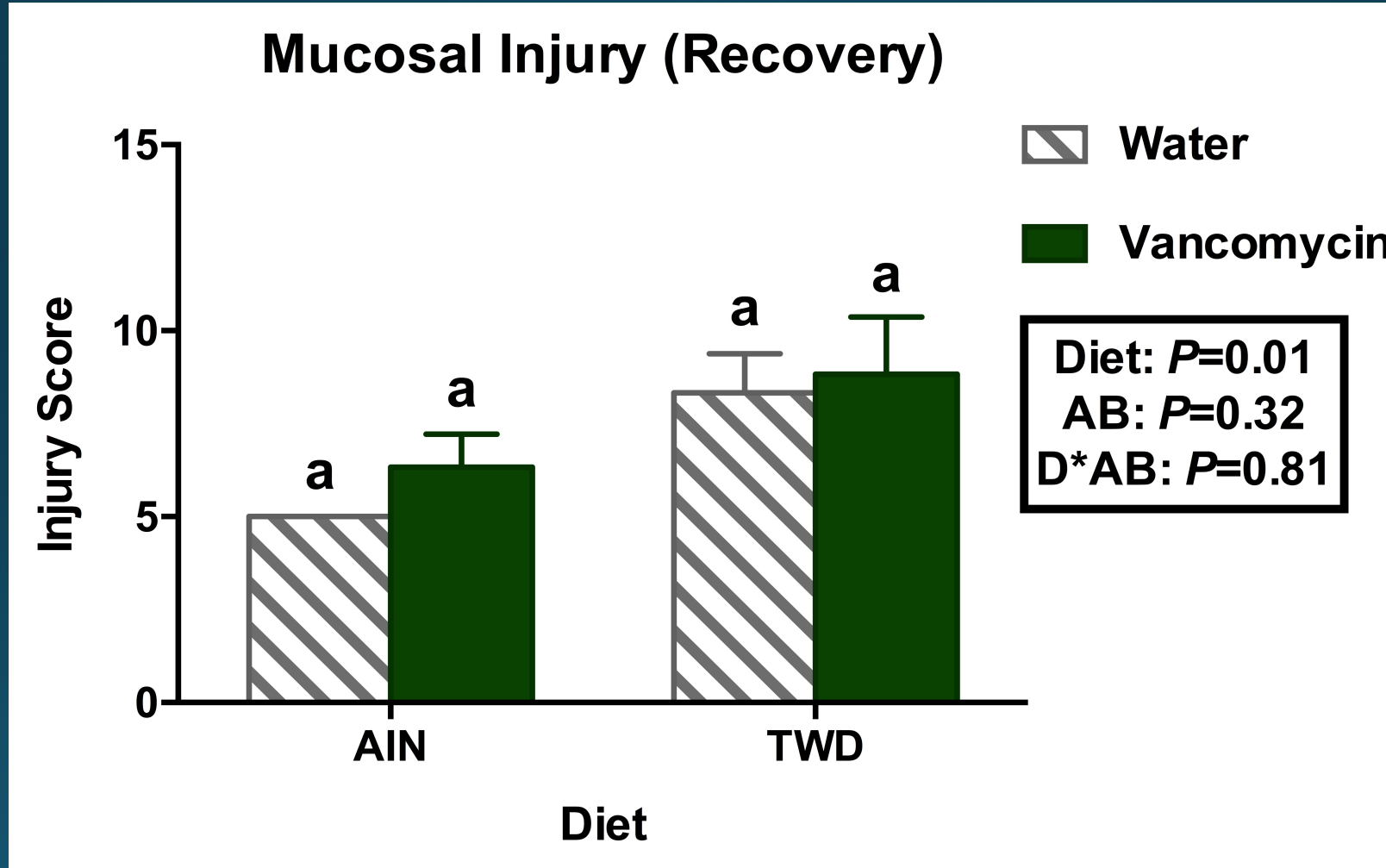


Results

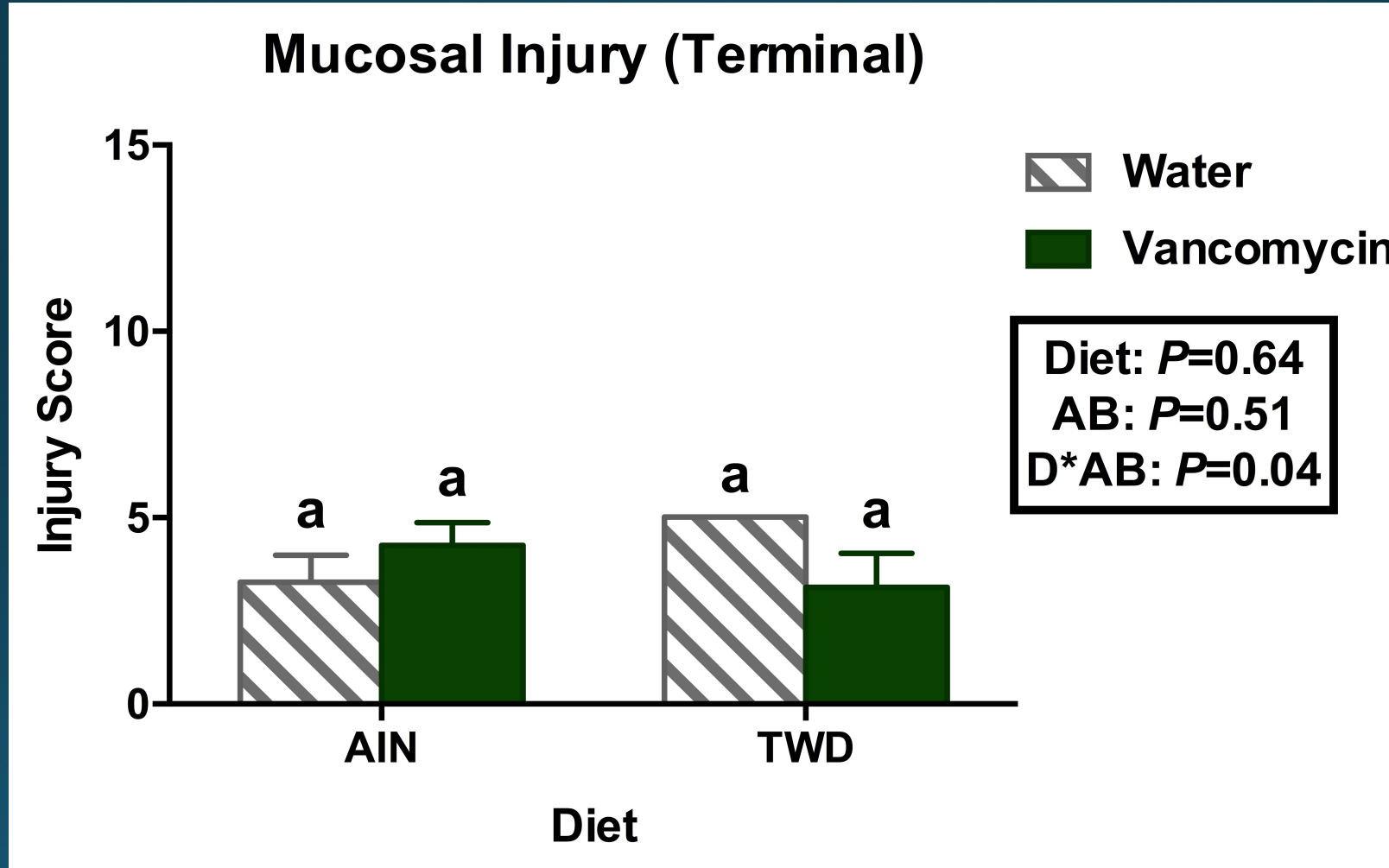
Colitis Assessment 2 (14 days post-DSS)



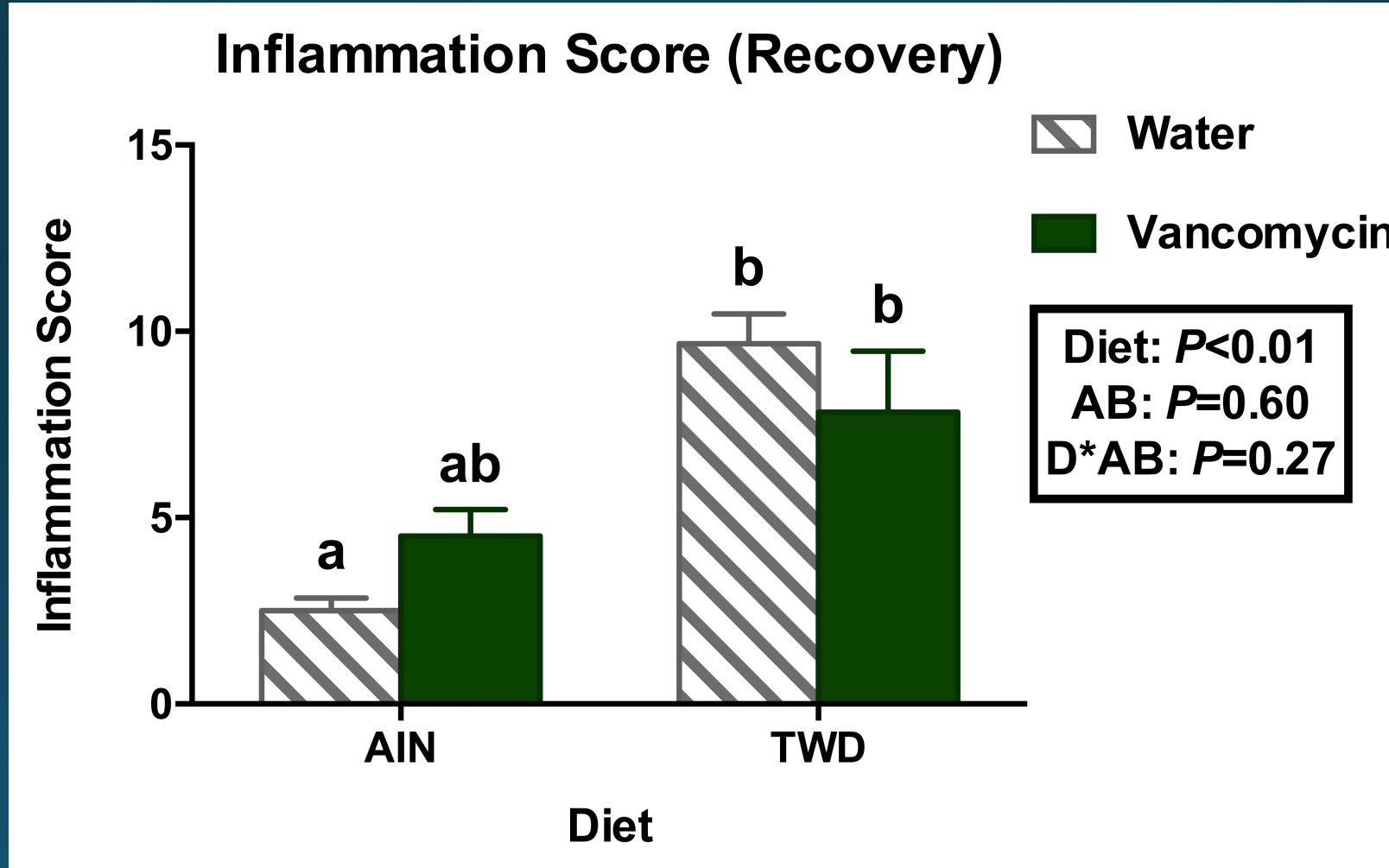
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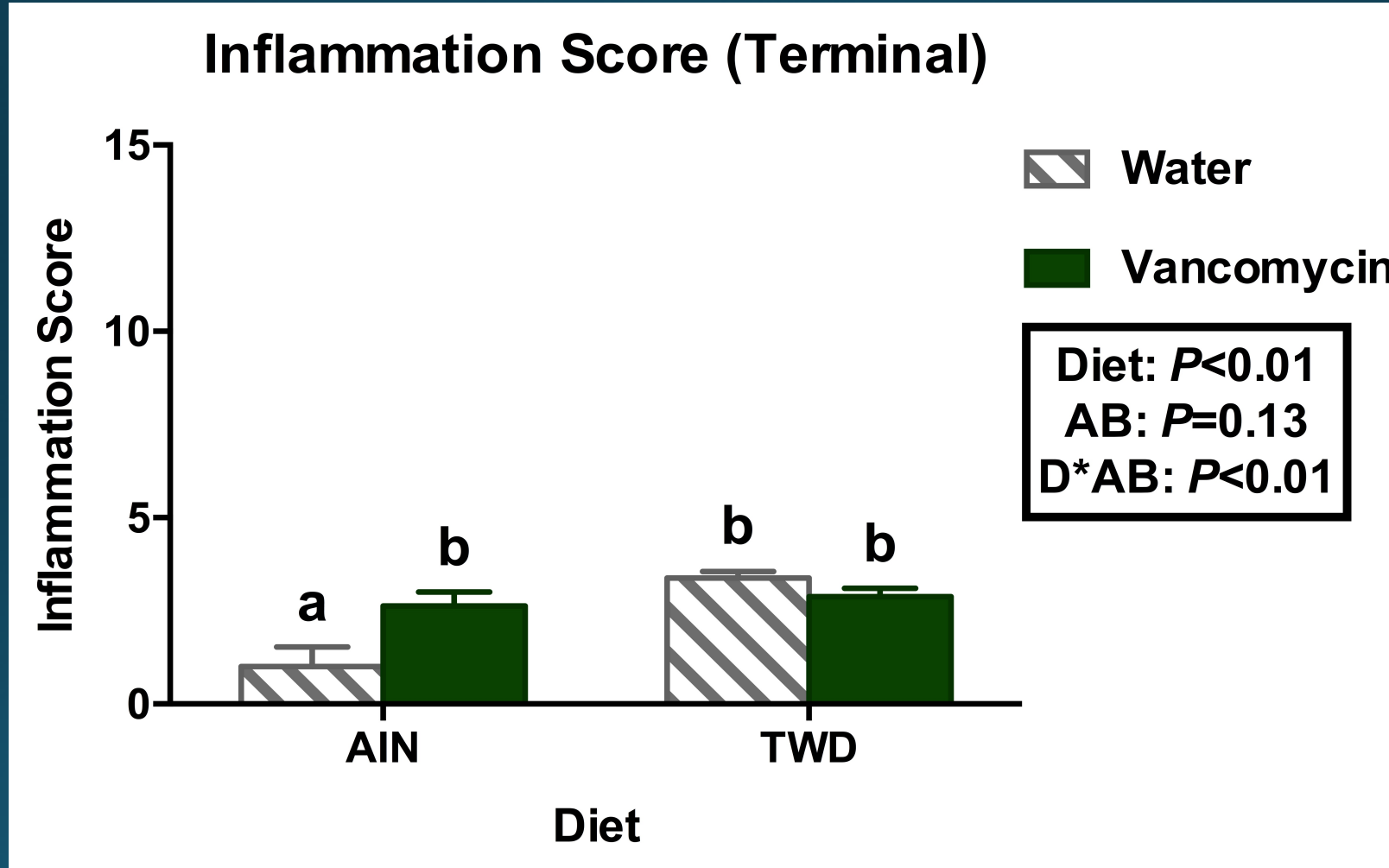
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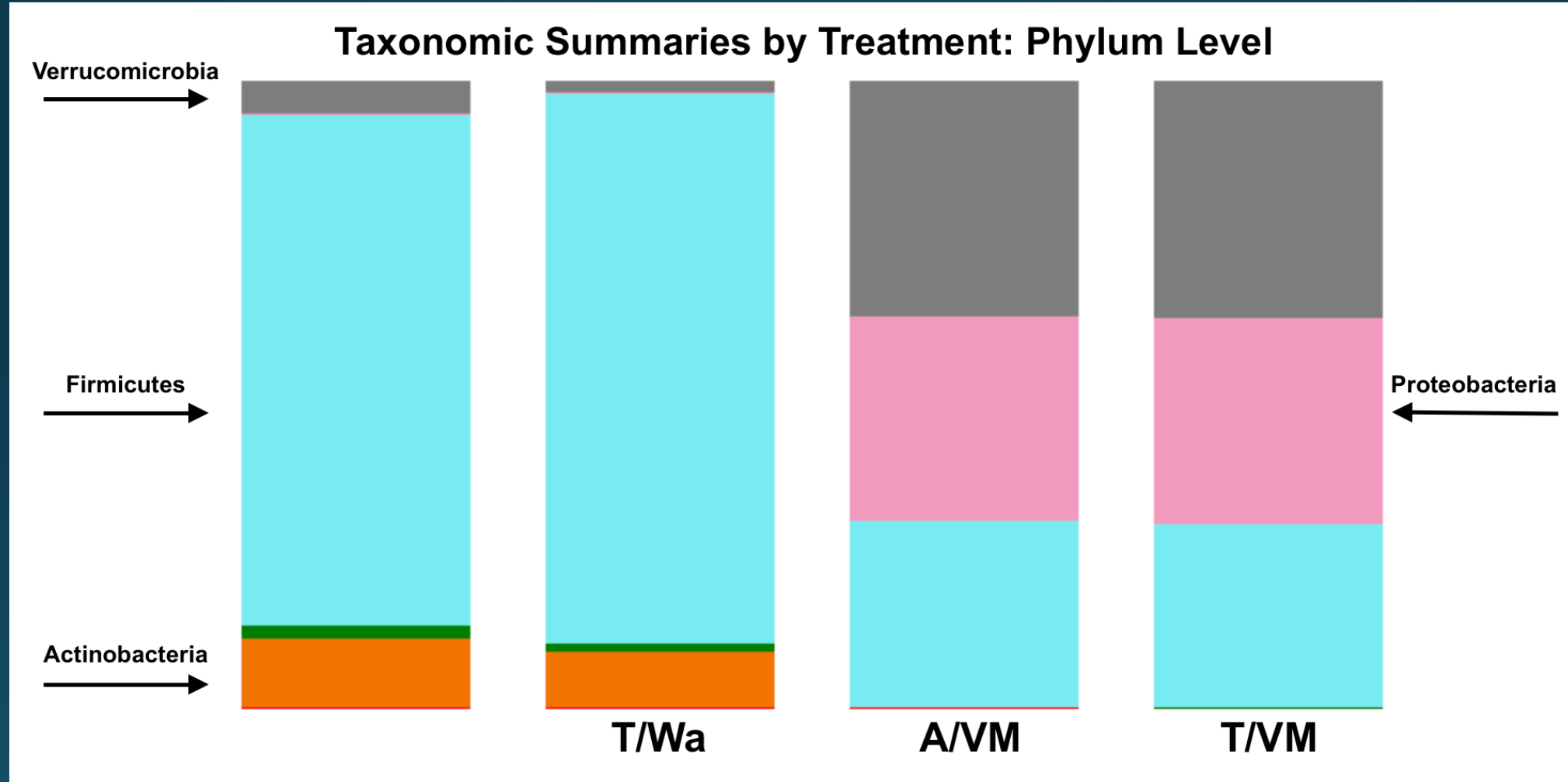
Results



Results



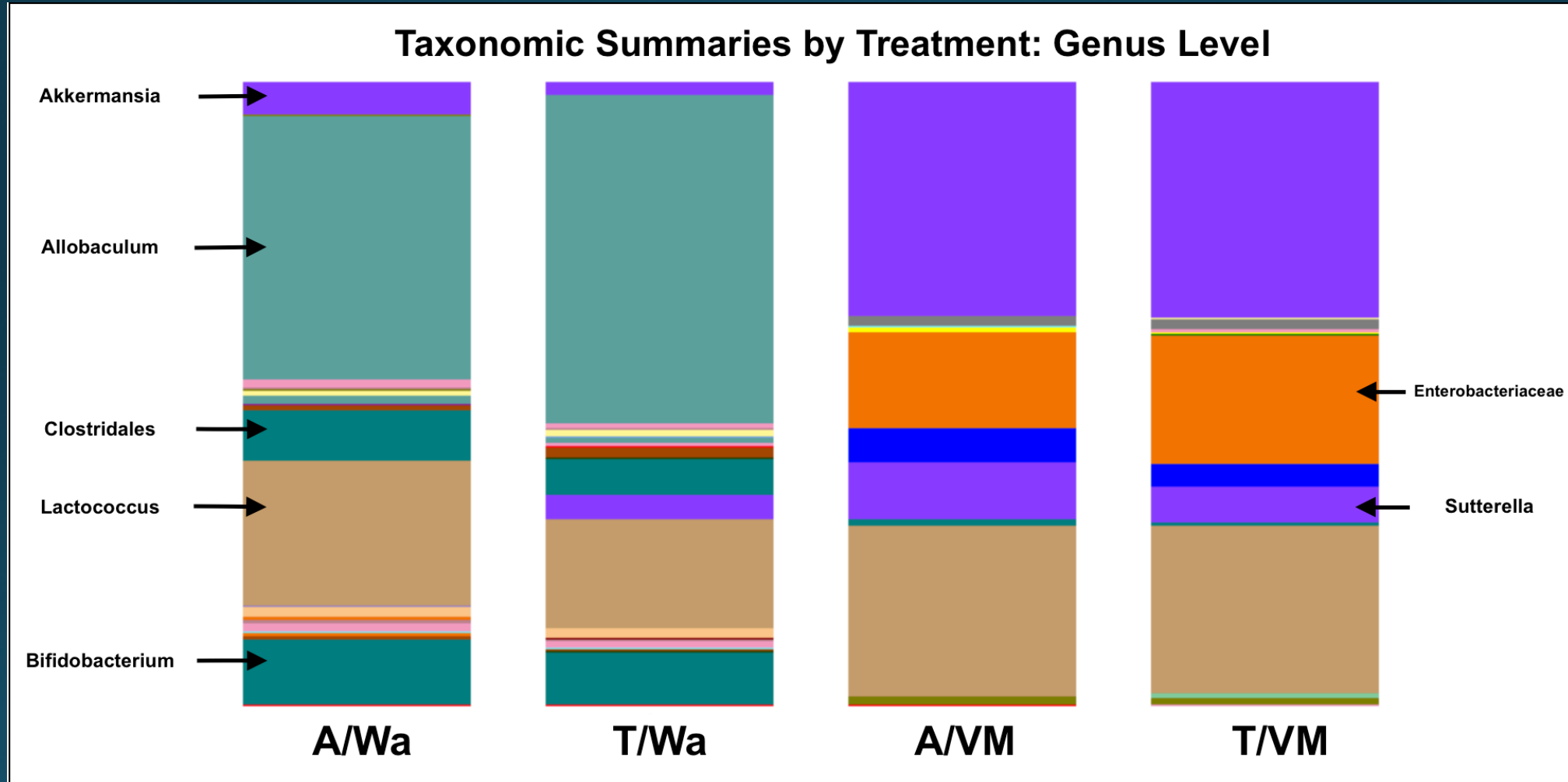
Results



Results

Taxa with largest differences					
Type	A/Wa	T/Wa	A/VM	T/VM	P-value
Verrucomicrobia	5.2%	1.9%	37.5%	37.9%	<0.0001
Firmicutes	81.4%	87.7%	29.8%	29.3%	<0.0001
Actinobacteria	11.2%	8.9%	0.0%	0.0%	<0.0001
Proteobacteria	0.1%	0.0%	32.5%	32.7%	<0.0001
Bacteroidetes	1.9%	1.3%	0.0%	0.0%	<0.0001

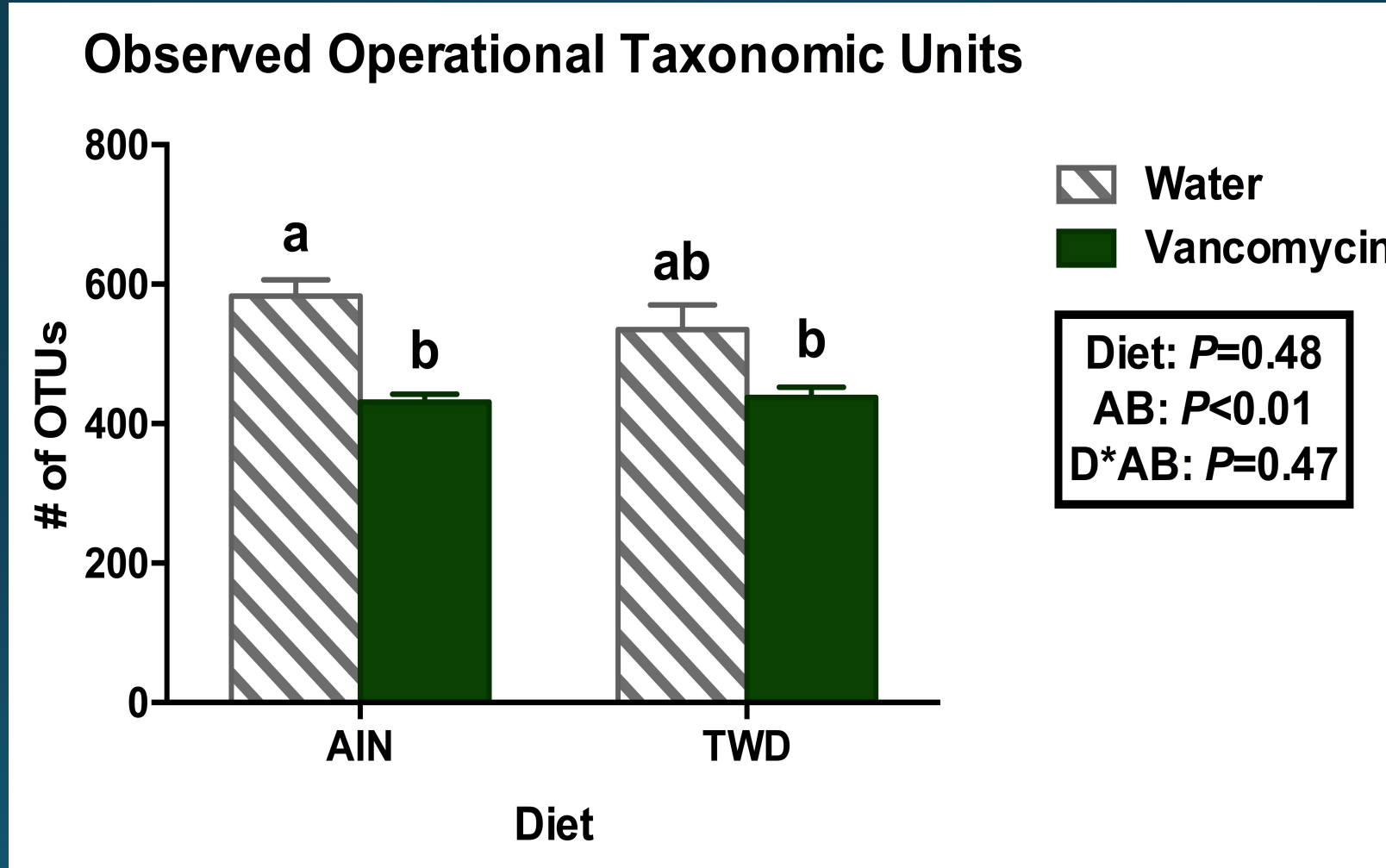
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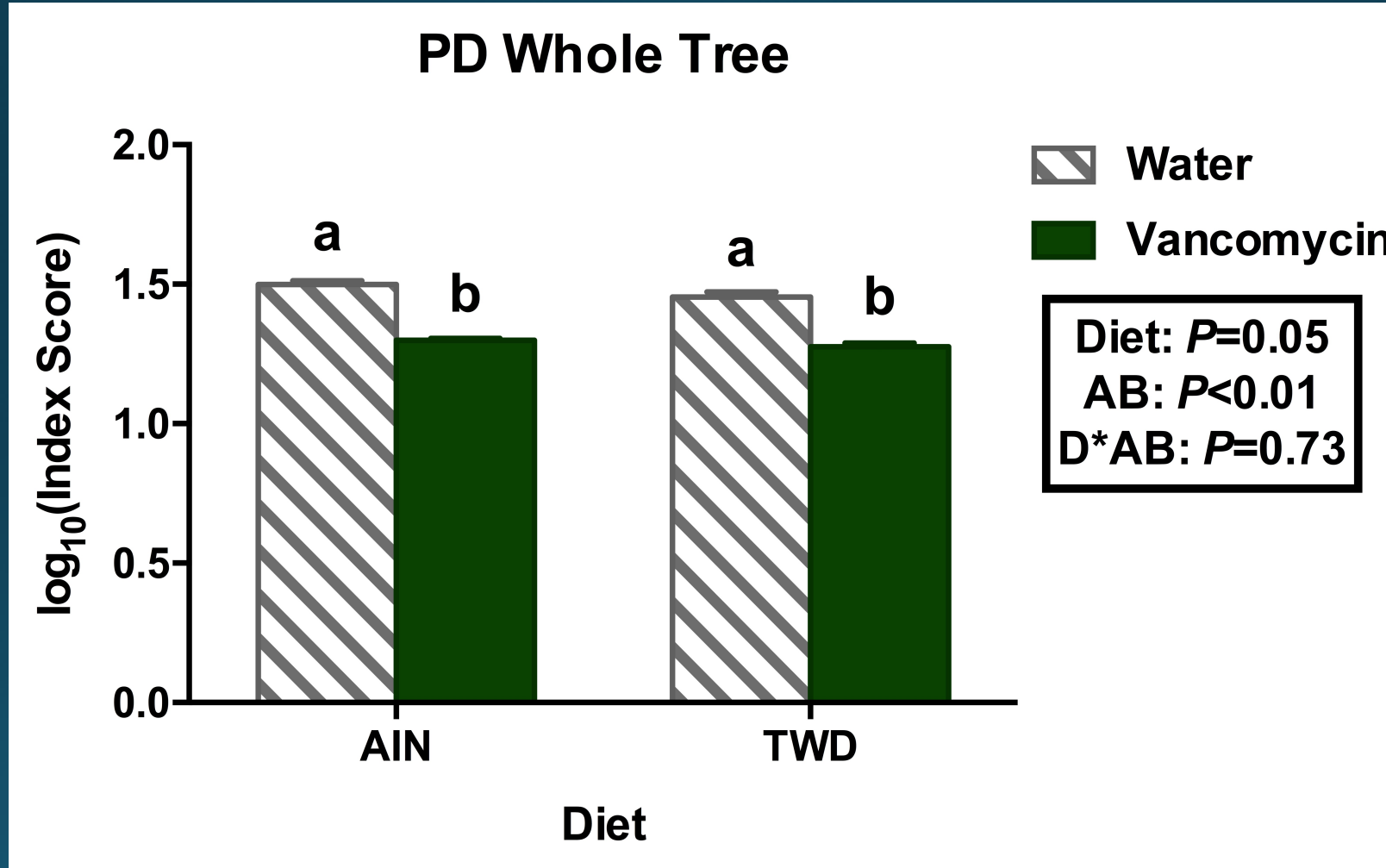
Results

Taxa with largest differences					
Type	A/Wa	T/Wa	A/VM	T/VM	P-value
p_Verrucomicrobia: g_Akkermansia	5.1%	1.9%	37.6%	37.9%	<0.0001
p_Firmicutes: g_Allobaculum	42.7%	52.7%	0.0%	0.0%	<0.0001
p_Firmicutes: o_Clostridiales	7.7%	5.8%	0.9%	0.4%	0.05
p_Firmicutes: g_Lactococcus	23.1%	17.4%	27.3%	26.8%	<0.0001
p_Actinobacteria: g_Bifidobacterium	10.6%	8.5%	0.0%	0.0%	<0.0001
p_Proteobacteria: f_Enterobacteriaceae	0.0%	0.0%	15.3%	20.5%	<0.0001
p_Proteobacteria: g_Sutterella	0.0%	0.0%	8.9%	5.7%	<0.0001

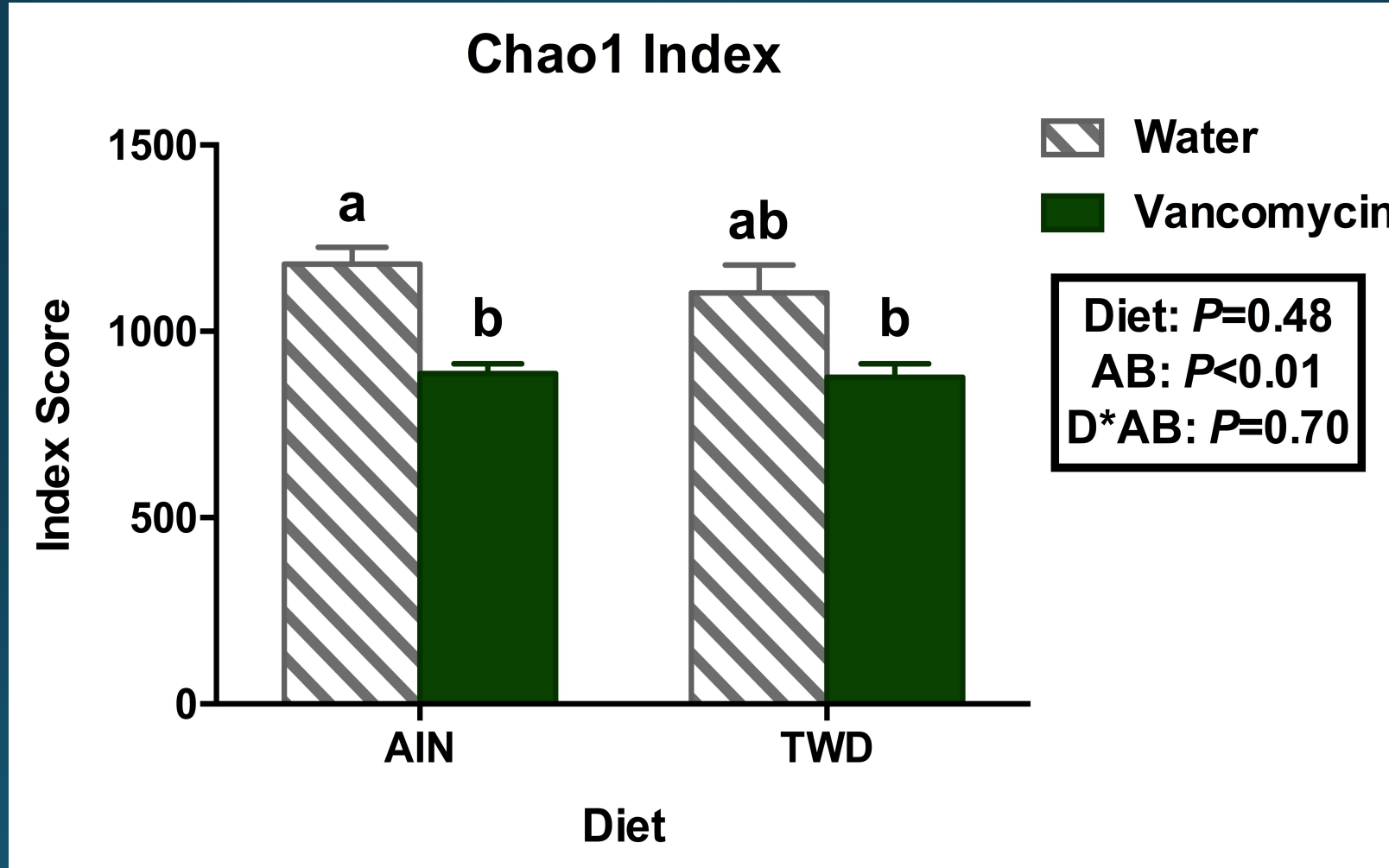
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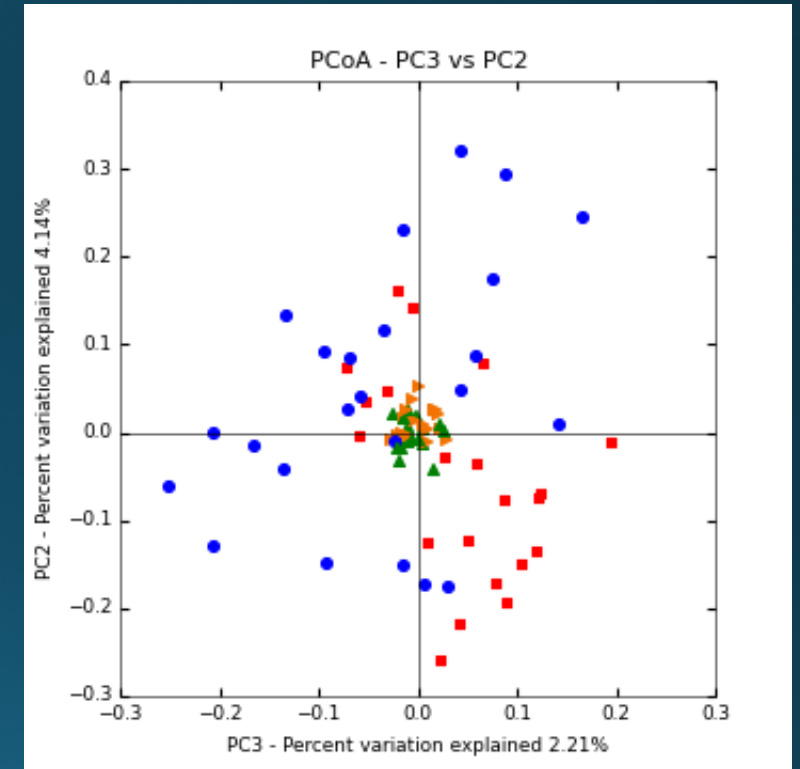
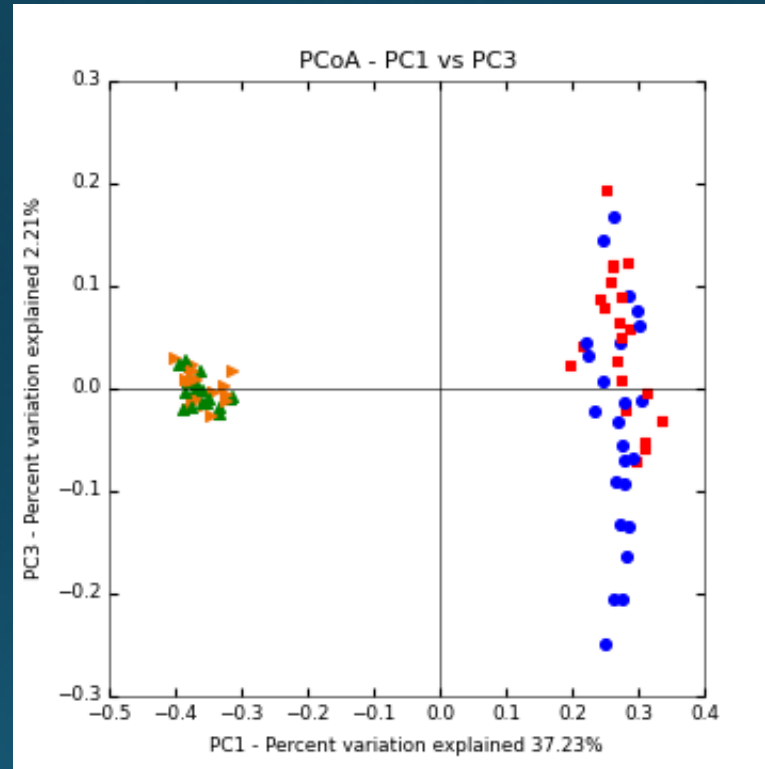
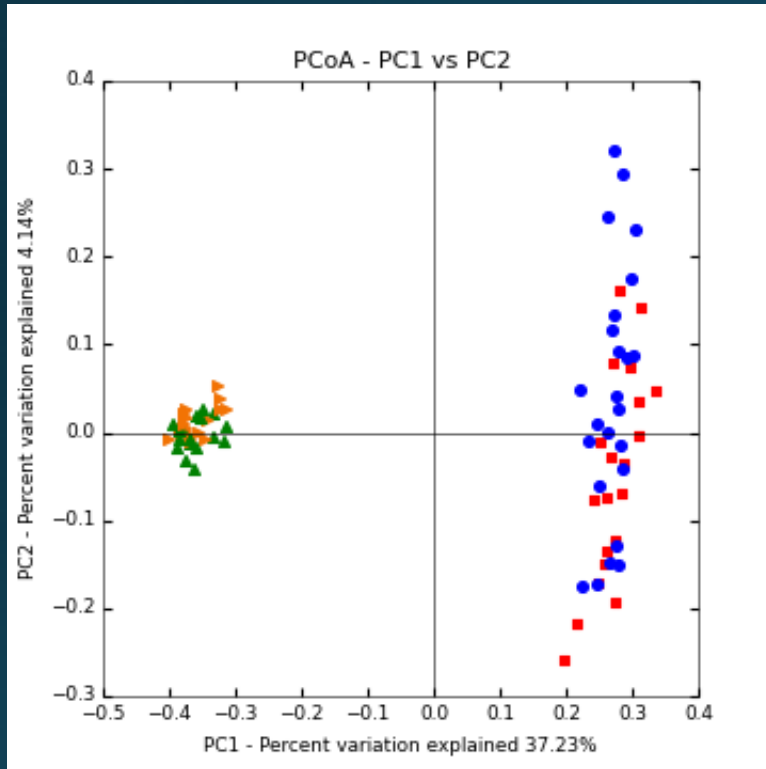
Results



Results

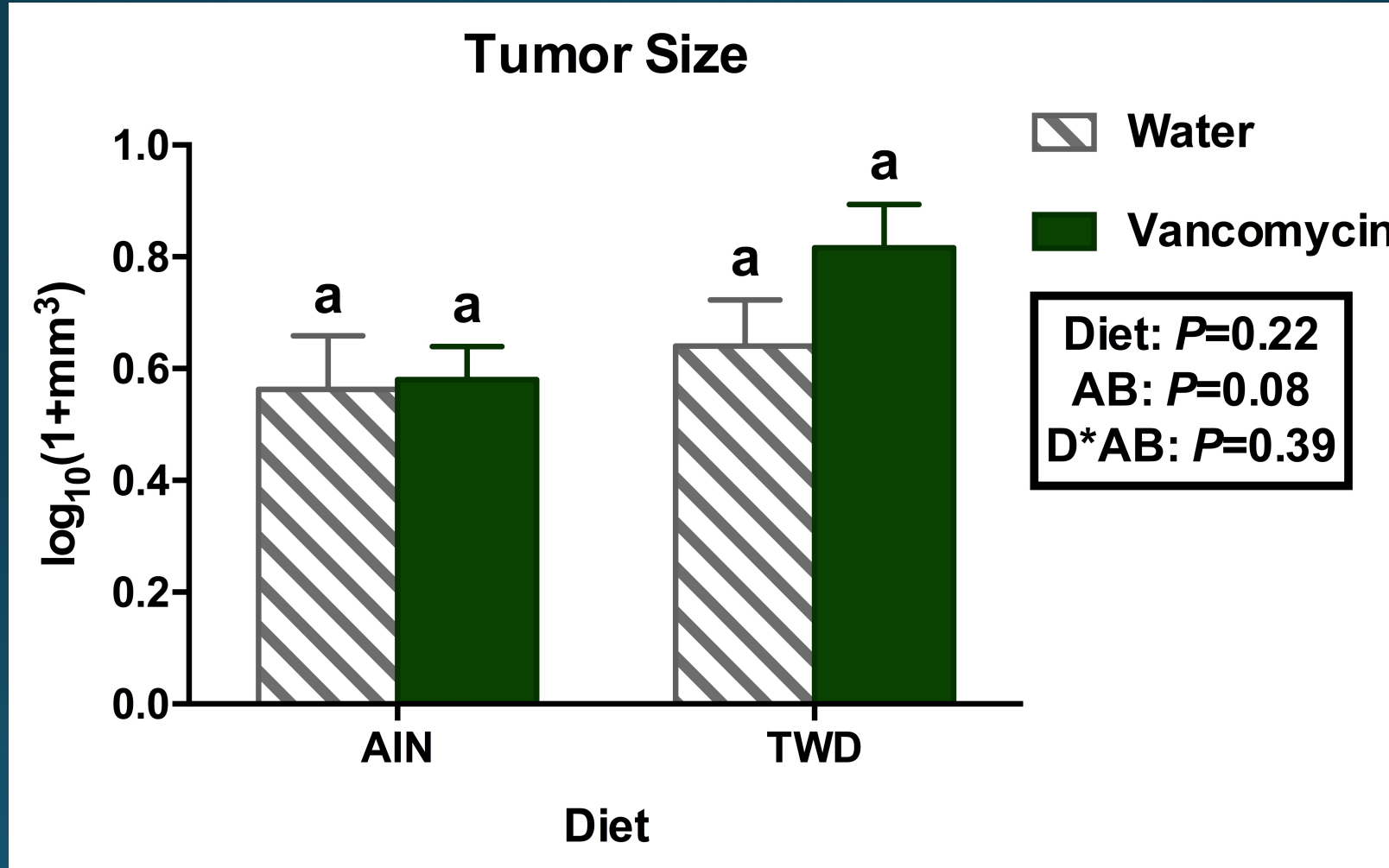


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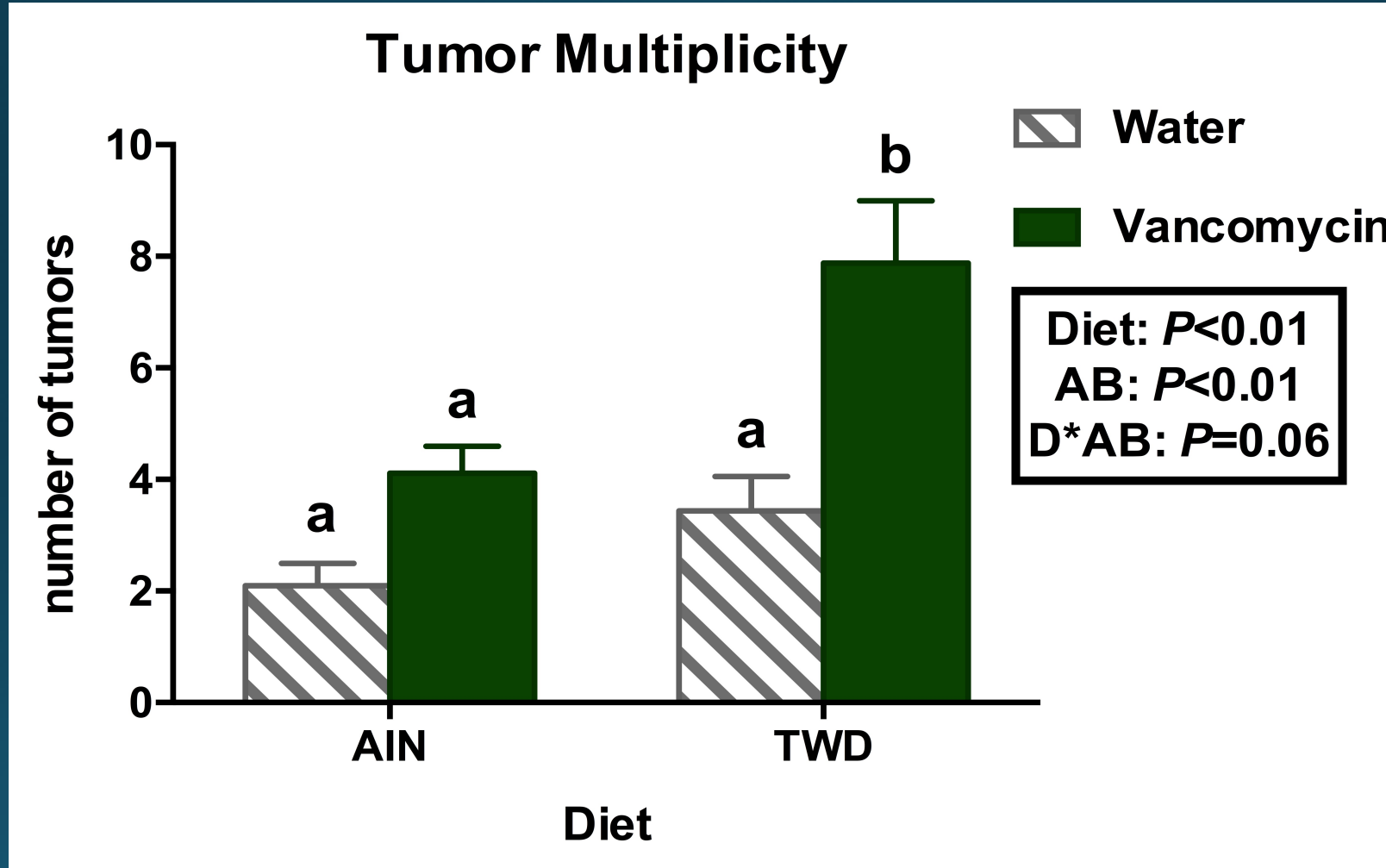


	A/VM		A/Wa
	T/VM		T/Wa

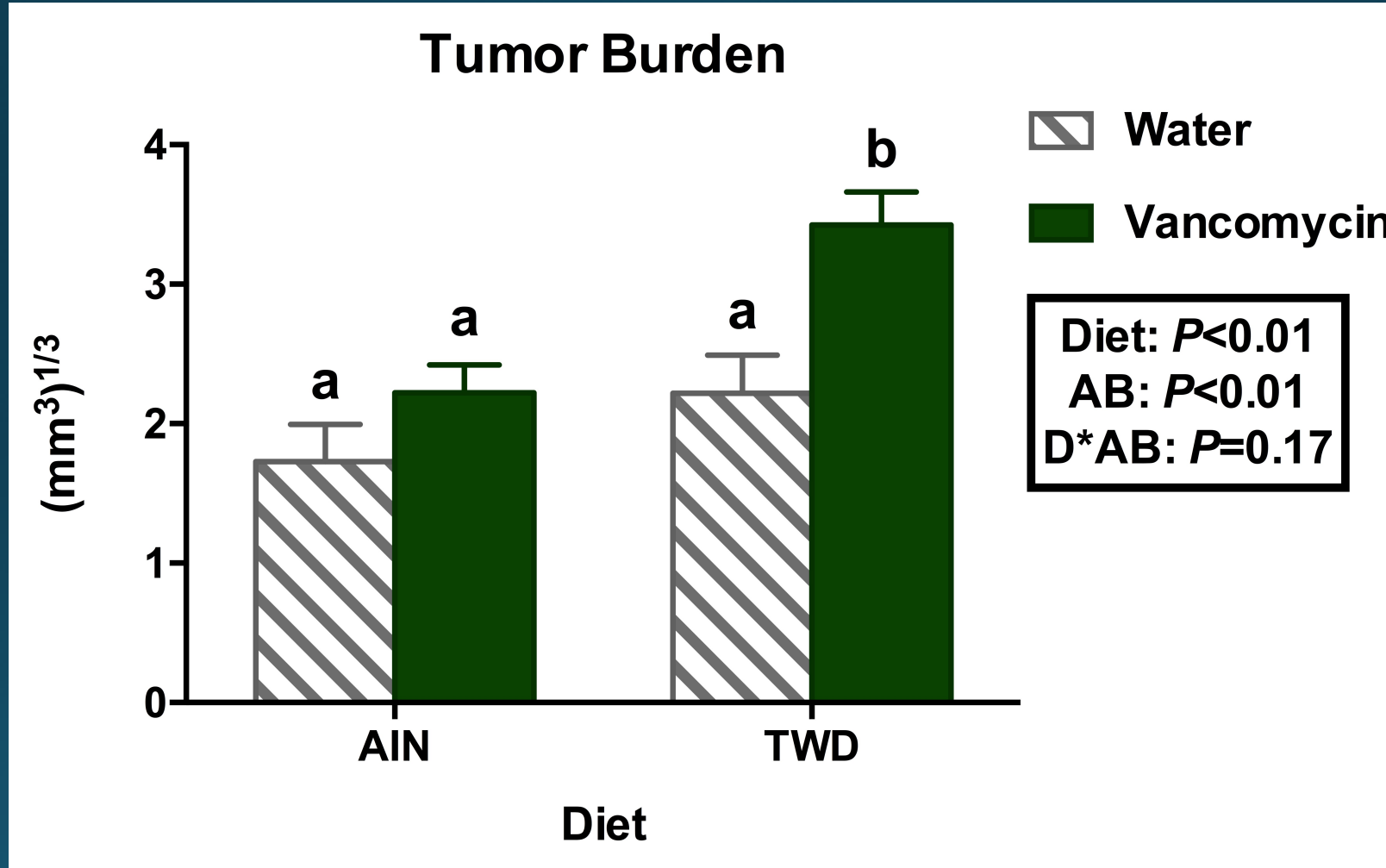
Results



Results



Results



Summary

- TWD and VM increase DSS-induced colitis.
- TWD increases gut inflammation long-term.
- TWD increases colonic mucosal injury immediately following DSS treatment.
- VM alters gut microbial composition.
 - Relative taxonomic abundance
 - Species Richness
 - Community Similarity
- VM and TWD significantly increase colon tumorigenesis.
 - Tumor burden and multiplicity

Conclusion

The total Western diet and vancomycin-induced changes to the gut microbiome increase inflammation-induced colitis as measured by total tumor volume.