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VITAMIN D DEFICIENCY NEGATIVELY IMPACTS GUT MICROBIOTA DURING 5-FLUOROURACIL INDUCED MUCOSITIS

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INTRODUCTION

- Gut microbiota dysbiosis is associated with gastrointestinal mucositis, a common chemotherapy-induced toxicity [2]
- Vitamin D deficiency may correlate with higher cancer incidence and gut inflammation, likely due to vitamin D's anti-inflammatory, immune-regulatory, and microbiome-modulatory properties [1]
- We aimed to investigate the impact of vitamin D deficiency on gut microbiota composition and diversity in mice undergoing chemotherapy treatment

METHODS

- C57Bl/6 male mice (n=6/group) consumed a diet containing 1000 IU/kg or 0 IU/kg of vitamin D, generating vitamin D-replete or deficient mice, respectively, for five weeks pre-chemotherapy
- Five days pre-chemotherapy, mice received daily subcutaneous injections for seven days of 6.25 mg/kg 25-hydroxyvitamin-D (25(OH)D), 500 ng/kg VD1-6 (catabolism inhibitor), 25(OH)D + VD1-6 (vitamin D treatments) or saline (vehicle control)
- After five days, mice received 300 mg/kg of 5-fluorouracil (5-FU) or saline and humanely killed 48 hours later
- Colon contents were aseptically collected, and DNA was extracted
- PacBio Long Read sequencing was conducted (Australian Genomics Research Facility) and analyzed using CLC-Genomics Workbench Software (Version 23.0, Qiagen), assessing microbial relative abundance, alpha diversity [4,5] and beta diversity [3] at the family level

RESULTS

- In vitamin D deficiency alone the relative abundance of Erysipelotrichacea was higher and the relative abundance of Coprobacteraceae, Muribacteria, Bacteriodaceae and Marinifilaceae was lower (Figure 1)
- After 5-FU administration during vitamin D deficiency, the relative abundances of Akkermansiaceae, Coprobacteracaea, Muribaculacaea and Bacteroidaceae were higher, and Lachnospiraceae and Eryslpelotrichaceae relative abundance lowered (Figure 1)
- Vitamin D treatments preserved microbiota composition, the relative abundance of Lachnospiraceae was higher in all vitamin D treatment groups, and Lactobacillaceae relative abundance was higher within the 25(OH)D and 25(OH)D/VD1-6 treatment groups (Figure 1)
- Alpha diversity significantly decreased and beta diversity was affected with vitamin D deficiency ($p < 0.05$) (Figure 2 and Figure 3)
- Vitamin D treatments did not increase alpha diversity compared with vitamin D deficiency, despite a trend with VD1-6 but maintained beta diversity (Figure 2 and Figure 3)

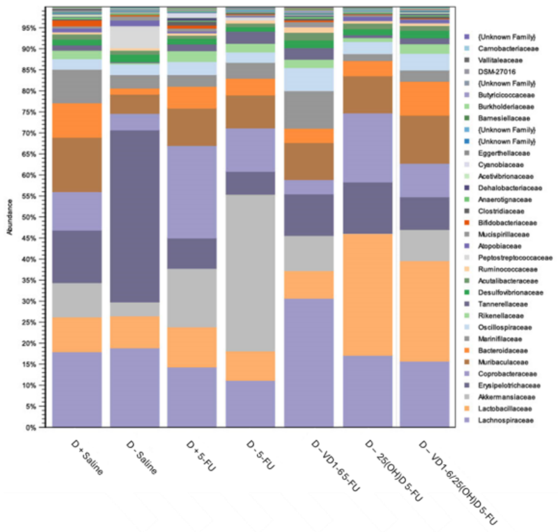

Figure 1. Colon contents microbiota relative abundance (family)

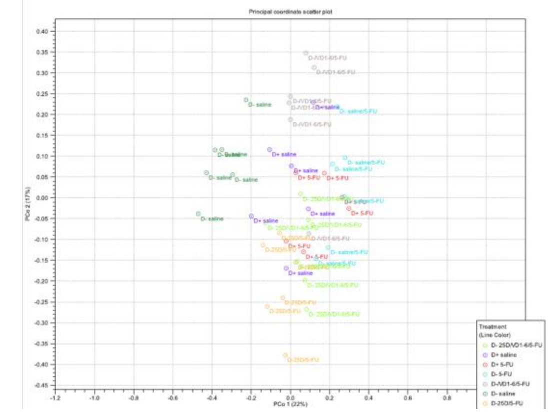

Figure 3. Colon contents Bray-Curtis Dissimilarity (PCOA Plot) beta diversity (family)

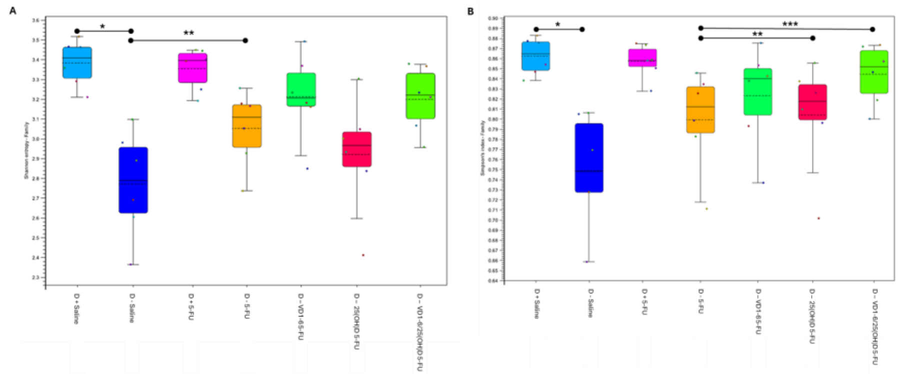

Figure 2. A) Colon contents Shannon's alpha diversity (family), **B)** Colon contents Simpson's alpha diversity (family)

CONCLUSIONS

- 5-FU disrupts gut microbiota composition and diversity, exacerbated by vitamin D deficiency
- Vitamin D treatments can mitigate some microbiota changes caused by 5-FU in vitamin D-deficient mice

REFERENCES

1. *Aggeletopoulou, I, Marangos, M, Assimakopoulos, SF, Mouzaki, A, Thomopoulos, K & Triantos, C 2023, 'Vitamin D and Microbiome: Molecular Interaction in Inflammatory Bowel Disease Pathogenesis', Am J Pathol, Mar 1.*
2. *Al-Qadami, GH, Secombe, KR, Subramaniam, CB, Wardill, HR & Bowen, JM 2022, 'Gut microbiota-derived short-chain fatty acids: Impact on cancer treatment response and toxicities', Microorganisms, vol. 10, no. 10, Oct 17.*
3. *Hardersen, S & La Porta, G 2023, 'Never underestimate biodiversity: How undersampling affects bray–curtis similarity estimates and a possible countermeasure', The European Zoological Journal, vol. 90, no. 2, 2023/12/11, pp. 660-672.*
4. *Herrera, AM, Riera, R & Rodríguez, RA 2023, 'Alpha species diversity measured by shannon's h-index: Some misunderstandings and underexplored traits, and its key role in exploring the trophodynamic stability of dynamic multiscapes', Ecological Indicators, vol. 156, 2023/12/01/, p. 111118.*
5. *Somerfield, P, Clarke, K & Warwick, R 2008, 'Simpson index', pp. 3252-3255.*