Institute of Nutrition and Translational Research in Metabolism

Disruption to Recovery: Antibiotics, Dietary Fiber, and the Fate of Bacterial Membrane Vesicles in Human Metabolic health

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Background

The microbiome plays a crucial role in human health and substrate-metabolism. Gut-bacteria produce factors that leave the intestine and signal to host organs such as the liver, adipose tissue, and skeletal muscle [1]. Disruptions of the microbiota caused by antibiotics can lead to abnormal vesicle populations, which may be modulated/restored through prebiotic supplementation.

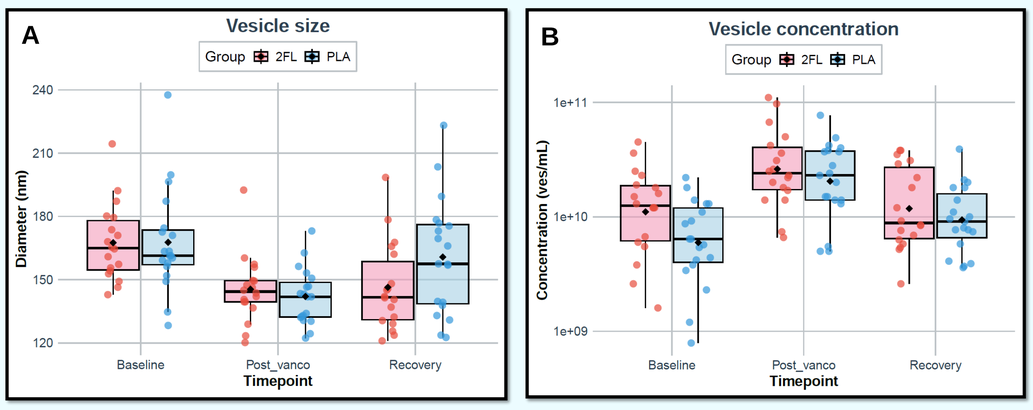
Objective

To investigate how the gut-bacterial membrane vesicle repertoire changes in response to vancomycin-induced dysbiosis and subsequent recovery under 2'fucosyllactose (2FL) supplementation

Results

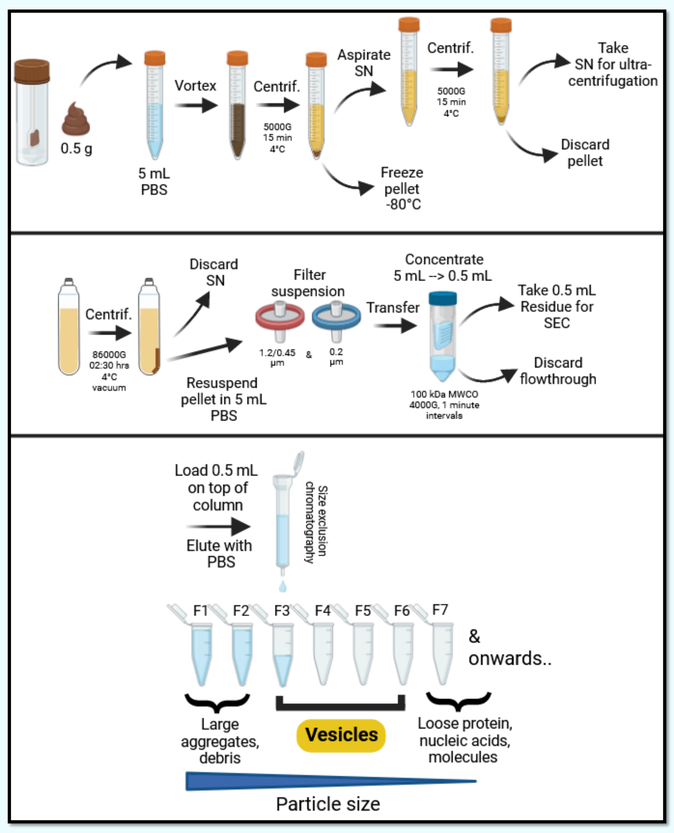
Following vancomycin intake, the mean bMV diameter decreased (from 168±21 nm to 144±14 nm, p<0.0001) **(A)**, while the mean concentration increased (1.1x10^10 bMVs/mL to 3.0x10^10 bMVs/mL, p<0.0001) **(B)**. Strikingly, for size, only in the placebo group (161±27 nm) and not in the 2FL group (146±21 nm) mean vesicle diameters returned to baseline following 8 weeks of supplementation. For concentration, no significant differences between the groups were found post recovery.

The activation of Toll-like receptor 4 (TLR4) increased post vancomycin (OD655 0.48 to 1.31, p = <0.0001) indicating an increased presence of bacterial endotoxin (LPS) **(C)**. Post recovery, no differences in vesicle endotoxin were detected although TLR4 activation had not fully returned to baseline in either group (mean OD655 0.55 for 2FL, 0.72 for PLA).

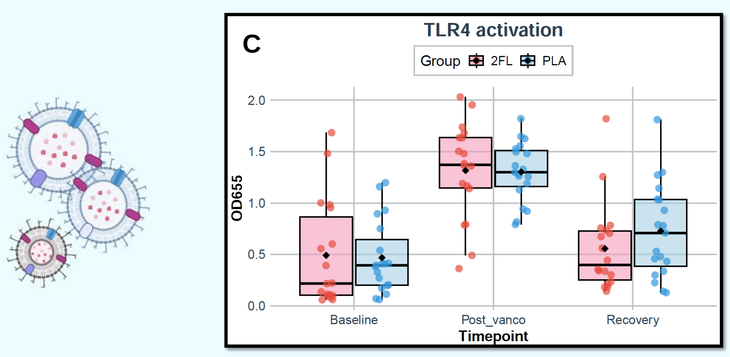


Methods

Fecal samples were obtained from 37 participants with overweight/obesity (BMI 25-40 kg/m^2) and normal glucose tolerance. (i) From baseline samples, (ii) after a seven-day course of vancomycin, and (iii) after 8 weeks of 2FL or placebo supplementation.



Vesicles were isolated using (ultra)centrifugation and size exclusion chromatography. Nanoparticle tracking analysis (NTA) was employed to determine bMV size and concentration. Functional characterization of vesicles is performed using HEK-blue reporter cells detecting bacterial endotoxin.



Conclusion

We demonstrate that vancomycin alters the human gut microbial bMV profile. Predominantly Gram-negative surviving bacteria produce smaller and more bMVs that are richer in endotoxin (LPS). The full nature of these vesicles post recovery requires elucidation using complementary techniques (metagenomics, metaproteomics) to understand of bMV production in the context of dysbiosis and metabolic disease.

References

1. Verbunt, J., Jocken, J., Blaak, E., Savelkoul, P., & Stassen, F. (2024). Gut-bacteria derived membrane vesicles and host metabolic health: a narrative review. *Gut Microbes*, *16*(1), 2359515.
2. Biorender.com is acknowledged as tool for creating figures.

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