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**A mechanism by which gut microbiota elevates permeability and inflammation in obese/diabetic mice and human gut - Mishra S, Wang B, Jain S, et al.**

Mishra S, Wang B, Jain S, et al. [*A mechanism by which gut microbiota elevates permeability and inflammation in obese/diabetic mice and human gut.*](https://gut.bmj.com/content/72/10/1848) Gut 2023; 72: 1848-1865. doi: 10.1136/gutjnl-2022-327365.

Western indulgent lifestyles have led to the rising prevalence of obesity and type 2 diabetes. The sequelae of end-organ dysfunction have large morbidity and mortality implications. Misha et al., builds on our increased understanding of the interaction of gut microbiota contributing to these conditions and posits a novel treatment option.

Gut permeability is limited by healthy and abundant tight junctions. These are made from zona occludens-1 (Zo1) or occludins and claudins. Cells lacking these complexes show higher permeability and flux of large (40kDa) solutes. Zo1 expression is reduced in the intestines of obese and diabetic gut mice. There is a bidirectional relationship between host and gut microbiota. Host-produced micro (mi)-RNAs influence gene expression of tight junctions. Conversely, gut microbiota and their metabolites, influence expression of miRNAs. By analysing metabolomic signatures, ethanolamine was implicated in elevating the promoter activity of miRNA-101a-3p via transcription factor ARID3a (AT-Rich Interaction Domain 3A) binding in gut epithelial cells, thereby inducing gut permeability by reducing Zo-1 expression. Obese microbiota was shown to induce inflammatory pathways allowing gut permeability and impairment in glucose metabolism. Mishra et al., observed that there was decreased abundance of ethanolamine metabolising bacteria in the stools of obese mice versus controls. Screening of commensal gut bacteria identified Lactobacillus (L.) rhamnosus HL-200 exhibited the highest activity in metabolising ethanolamine. HL-200 suppressed an increase in gut permeability, endotoxaemia and dysfunction in glucose metabolism by suppressing upstream gene expression of miRNA-101a-3p.

This study shines a light on potential novel strategies in using human-origin probiotic therapy with possible translational potential.