

***Akkermansia muciniphila*-derived extracellular vesicles ameliorate obesity by impact on tight junction protein, inflammation and energy homeostasis**

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Recent studies show that probiotics bacteria can reinforce the mucosal barrier function, reduce inflammation, and promote homeostasis required for metabolism in obesity by influencing the gut microbiota composition. In this research, we evaluated the anti-obesity and anti-inflammatory effects of *A. muciniphila* and its EVs in HFD-induced-obese (DIO) mice.

Eight-week-old C57BL/6J mice were fed an HFD for three month. After weight gain, treatments with *A. muciniphila* (10⁹ CFU) and its EVs (10 µg) for five weeks along with HFD. Then, we studied body and adipose weight, and also fatty acid oxidation, intestinal barrier integrity, energy homeostasis and inflammatory genes expression in adipose and colon tissue.

Our findings showed that EVs had a better effect on body and adipose weight loss in DIO mice in comparison with *A. muciniphila*. Moreover, administration of *A. muciniphila* and its EVs had significant effects on regulation of gene expression involved in fatty acid oxidation and energy homeostasis e.g. *ppar-α /γ*. Furthermore, EVs induced more reduction in the expression of adipose inflammation genes (e.g. *tnf-α*, *il-6* and *tlr-4*) in DIO mice. In colon, both treatments improved the intestinal barrier integrity, inflammation and energy balance. However, a further increase in the expression of tight junction proteins (e.g. *zo-1*, *ocldn* and *cldn-1*) and a decrease in inflammatory gene (e.g. *tlr-4*) were observed in mice receiving the EVs treatment, compared to *A. muciniphila*. Overall, our data suggested that *A. muciniphila*-derived EVs contain a wide variety of biomolecules, which can have a positive impact on obesity by affecting the obesity-related genes.

In conclusion, EVs derived from *A. muciniphila* can be considered as new tools for treating HFD-induced obesity via impact on various mechanisms.

Keywords: gut microbiota, *Akkermansia muciniphila*, EVs, TLR, tight junction, PPARs, obesity