Abstract

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

Fatemeh Ashrafian1,2*, Farzam Vaziri1,2, Sara Ahmadi Badi1,2, Arfa Moshiri3,4, Abolfazl Fateh1,2, Shohreh Khatami5 and Seyed Davar Siadat1,2

1 Department of Mycobacteriology and Pulmonary Research, Pasteur Institute of Iran, Tehran, Iran
2 Microbiology Research Center (MRC), Pasteur Institute of Iran, Tehran, Iran
3 Laboratory of Experimental Therapies in Oncology, IRCCS Istituto Giannina Gaslini, Genova, Italy
4 Gastroenterology and Liver Diseases Research Center, Research Institute for Gastroenterology and Liver Diseases, Shahid Beheshti University of Medical Sciences, Tehran, Iran
5 Department of Biochemistry, Pasteur Institute of Iran, Tehran, Iran

*Fatemeh.ashrafian24@gmail.com

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 (10^9 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