Dipeptidyl Peptidase-4 (DPP4) inhibition: role in obesity-induced inflammation and tissue injury

E. DOZIO ; M. M. CORSI ROMANELLI

Obesity and diabetes are risk factors for cardio-vascular, kidney and liver disorders. Dipeptidyl peptidase 4 (DPP4) is a membrane-bound aminopeptidase implicated in the regulation of metabolic homeostasis and inflammatory processes. DPP4 represents the enzyme most involved in the catabolism of the incretin hormones, therefor, its activity impacts on appetite, energy balance and the fine regulation of glucose homeostasis. Besides the membrane-bound form, DPP4 exists also as a secreted molecule and its plasma activity has been shown to increase with obesity and to contribute to reduced incretin activity in the setting of obesity and insulin resistance. Obesity can also stimulate DPP4 expression in many organs, like the kidney, liver, adipose tissue, and immune cells. DPP4 inhibitors (DPP4i) are antidiabetic drugs that can exert additional protective effects regardless their glucose lowering action. Although the role of DPP4 as enhancer of tissue inflammation has been previously described, it is unknown how DPP4 inhibition can prevent obesity-induced inflammation and activation of pathways leading to tissue damages, such as fibrosis and steatosis. The aim of the present study is to explore the effects of the DPP4i, Linagliptin (L), on transcriptome and proteome for identifying potential protective mechanisms against obesity-induced tissue damages. A murine model of high fat (HF) diet-induced obesity (DIO) and an in vitro model of murine macrophages will be used. Our study deals with the possibility to identify mechanisms protecting against obesity-related complications and explain additional beneficial effects associated to the use of DPP4i. This could open to further studies about the use of these molecules in different inflammatory disorders and dentification of molecules that could be further validated as biomarkers of risk and organ damages in obesity.