

Abstract

Pheochromocytoma and functional paraganglioma (PPGL) are rare neuroendocrine tumors characterized by catecholamines overproduction, which give a rise to disorders of glucose, lipid, and energy metabolism. The role of adipose tissue in these processes remains unclear. Our aim was to determine the gene expression profile in subcutaneous and visceral adipose tissue of patients with PPGL focusing on endocrine functions of adipose tissue, occurrence of brown (BAT) and beige adipose tissue (BeAT), all in connection with other measured metabolic and energy parameters and levels of circulating adipokines.

We demonstrate signs of UCP1-dependent norepinephrine induced thermogenesis connected with overexpression of *DIO2* in retroperitoneal VAT of PPGL and higher expression of key transcriptional factors of brown/beige adipogenesis, namely *PPARGC1 α* , *CEBPB* and *PRDM16*. However, classic murine BAT or BeAT gene signature in VAT of PPGL was not detected. In subcutaneous adipose tissue (SAT) of PPGL we found signs of possible BeAT transformation, however without simultaneously undergoing UCP1-dependent thermogenesis.

We also demonstrate that patients with PPGL have higher serum levels of FGF21 compared to healthy controls and these levels do not differ from obese patients. Furthermore, successful tumor removal decreased significantly FGF21 levels. Elevated FGF21 levels were more evident in patients with secondary diabetes mellitus and were related positively to fasting glucose levels and BMI in PPGL. The consequences of the elevation of FGF21 in PPGL are unclear. We cannot identify from our work whether the elevation of FGF21 is the result of a controversial FGF21 resistance or whether FGF21 has some biological effect. We assume, that elevated levels of FGF21 in patients with PPGL are biologically significant and reflect metabolic abnormalities associated with diabetes mellitus and obesity. We did not find a relationship between FGF21 or UCP1 expression and hypermetabolic state in PPGL.

We also extend possible endocrine functions of BAT/BeAT of hormone adiponectin and visfatin. We did not find difference in circulating levels of resistin, lipocalin 2, PAI-1 and adiponectin in patients with PPGL.