## UCP1 and leptin expression in human fetal brown adipose tissue

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In mammals, the adipose organ is composed of white adipose tissue (WAT) and brown adipose tissue (BAT). WAT which is the primary site of energy storage also present main site of leptin synthesis. Through uncoupling protein 1 (UCP1) activity, BAT increases energy expenditure in the form of heat. The thermogenic role of BAT is especially relevant in new-born mammals, which are not capable of effective shivering. In a small mammals, such as rodents, BAT persist throughout its lifespan. Until recently it was though that there are no discrete collections of active BAT that can be found in the human adults. In human fetuses and newborns, BAT development begins at the 20th week of pregnancy and it is found in axillary, cervicaly, perirenal and periadrenal regions [1]. A few studies have investigated UCP1 and leptin expression in the adipose organ of small mammals. Until now there are no data about leptin expression in human fetal BAT. Thus, the aim of this study was to examine if UCP1 and leptin are present in human fetal fBAT as well as their localization.

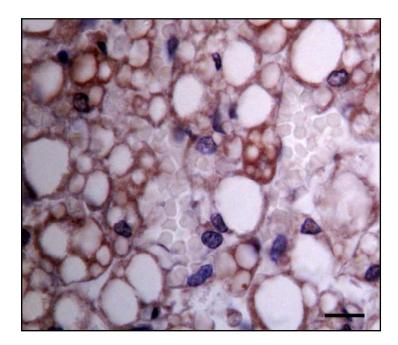
Human fetal BAT was investigated in biopsies from 5 human fetuses at 18-22 week's gestational age and routinely prepared for light microscopy. Immunohistochemistry was carried out on paraffin-embedded tissues with avidin-biotin-peroxidase method by using the UCP1 and leptin primary antibodies.

Light microscopic examination of human fetal BAT showed that majority of adipocytes was multilocular. Strong immunopositive reaction for UCP1 was found in multilocular as well as unilocular adipocyte (Fig. 1). UCP1 was localized mainly in adipocyte cytoplasm, but some nuclei showed immunopositivity. On another hand, both unilocular and multilocular adipocytes were without immunoreaction for leptin. Leptin was found only in BAT circulation, in eritrocytes (Fig. 2). Cinti *et al.* [2] have shown immunohistochemicaly that leptin is produced by the thermogenic inactive, rat's unilocular brown adipocytes. In addition, there are data about reciprocally expression leptin and UCP1 in BAT of small mammals. Our immunohistochemical results suggest that the same relationship between leptin and UCP1 expression exist in human fetal BAT.

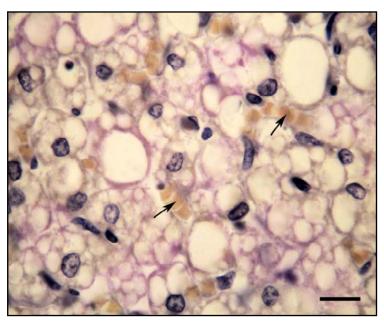
Our study showed that human fBAT appears UCP1 immunopositivity in unilocular and multilocular adipocytes as well their deficiency for leptin expression. Leptin immunopositivity was found only in circulation of human fetal BAT. Besides, we conclude that UCP1 and leptin expression are reciprocally regulated in human fBAT.

Our results additionally support idea that leptin and UCP1 have important role in the in transition from fetus to neonate.

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- 3. This research was supported by Serbian Ministry for Science & Technological development, Grant. #143050.



**Figure 1.** Immunohistochemical staining for UCP1 in human fetal BAT. Both multilocular and unilocular cells show dark brown reaction (mag. x100, original scale bar - 50µm).



**Figure 2.** Immunohistochemical staining for leptin in human fetal BAT. Multilocular as well as unilocular adipocytes are without immunoreaction. In addition, eritrocytes show mild immunoreaction. Eritrocytes – black arrows (mag. x100, original scale bar - 50µm).