Brown adipose tissue in deep cervical fat of adult ENT patients

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Introduction:
Brown adipose tissue (BAT) is a thermogenic tissue, found in small mammals. In humans it was until recently only described in newborns. Discovery of metabolically active BAT in adult humans attracted many scientists to join the quest for finding the safe and effective physiological tool to battle obesity epidemic. Most of the available knowledge was generated in cell culture and animal models. However, imaging data, clearly indicated the presence of metabolically active brown fat in the neck of adult humans. The aim of our pilot study was to detect and characterize the BAT in the cervical region of adult ENT patients undergoing elective surgery.

Subjects and Methods:
Twenty adult patients (M:F=18:2, 39.4±13.02 years) were recruited. In all subjects, subcutaneous and deep cervical fat samples (~1 g) were taken during the surgery under general anesthesia. Spectrum of surgical procedures during which the adipose tissue samples were harvested involved hemi-thyroidectomy or total thyroidectomy (14 cases), branchial cleft cyst surgery (4), and parathyroidectomy (2). Diagnoses of these patients are shown in figure 1.

The deep cervical fat was taken mostly from peritracheal soft connective tissue. Tissue samples were immediately cleaned up from blood & connective tissue and (i) frozen in liquid nitrogen for RNA isolation and qPCR analyses or (ii) fixed in Bouins fixative for histological examination. Samples were examined histologically for the presence of brown adipose tissue typical multilocular adipocyte morphology. Expression of brown (CIDEA, EVA1, UCP1), beige (TMEM26, TBX1, CD137/TNFRSF9) and white (FABP4) adipocyte markers was determined by the qPCR using ABI-7900HT & the TaqMan Gene Expression Assays (Applied Biosystems, USA). Markers of metabolic and endocrine state were determined preoperatively for each subject, by measuring body mass index, fat mass and muscle mass by bioimpedance, levels of thyroid hormones, and serum biochemistry. Physical activity of the patients was evaluated by questionnaire. Study was approved by Ethics Committee of the University Hospital in Bratislava and all participants signed written informed consent prior entering the study.

Results and Discussion:
Brown adipose tissue was detected in fat samples of 9 patients (45%). It was visually identified using light microscopy in 3 patients (fig. 2), while genetic markers were positive in 9 cases (fig. 3). The presence of BAT was not dependent on age or sex, but it negatively correlated with the subjects’ body mass index and serum TSH level. We did not detect the BAT in subjects with BMI exceeding 26 (mean 25.11, SD 3.34). In these patients, BAT is probably masked by higher proportion of adjacent white adipose tissue. Similarly, it was not observed in participants with TSH levels > 2 mIU/L. This may correspond to the published data on increased activation of brown fat in thyroid hyperfunction.

Conclusions:
Brown adipose tissue (BAT) is rather unknown tissue to ENT specialists. Here we provide direct evidence of its presence in the deep soft tissue of the neck in adults. Its unique physiological role in energy metabolism is being intensively studied to develop new prevention/treatment strategies for metabolic diseases. As the neck is one of the major sources of BAT in adult human body, it should also raise awareness in our clinical field. Our ongoing research is focused on detailed molecular-genetic characterization of this tissue with the aim to detect factors modulating its physiological activity and function. From ENT perspective, future goals in the research may be also focused on the role of BAT and metabolic changes in head and neck patients e.g. after neck dissections or radiotherapy.

Figure 1: Preoperative diagnoses in examined subjects.

Figure 2: A - Human white adipose tissue containing large unilocular adipocytes, B - Human brown adipose tissue containing many small lipid droplets in multilocular adipocytes with cytoplasm rich in mitochondria. Haematoxylin and eosin staining, magnification 200x, Axio Scope. A1 microscope (Zeiss, Germany).

Figure 3: Relative changes in beige/white adipocyte markers in 9 patients with identified BAT (fold ratio).