Abstract

Adipose tissue plays a crucial role in nutrient and energy homeostasis. At the time of worldwide pandemy of obesity and consequent metabolic syndrome, a great effort is made to find new treatments with potential to preserve insulin sensitivity, or even counteract development of obesity and type 2 diabetes. There are three principal possibilities how the adipose tissue biology can contribute to this goal: 1) induction of UCP1-dependent energy dissipation in brown adipose tissue; 2) conversion of white adipose depots to brown-like tissue (i.e. "browning"); and 3) stimulation of UCP1-independent thermogenesis in white adipose tissue.

This thesis is based on two published works and one article under preparation. Generaly, it is focused on three different approaches targeting the above mentioned processes in adipose tissue of laboratory mouse: 1) diet supplementation with bile acids; 2) combination treatment of ω-3 polyunsaturated fatty acids and calorie restriction; and 3) cold exposure.

In the experiments with administration of bile (specifically chenodeoxycholic) acid to mice, we confirm specific induction of UCP1 in both brown and subcutaneous white adipose tissue, as well as reversion of obesity in the response to the treatment. Nevertheless, most of the acute beneficial effects are mediated by transiently decreased food intake, while elevated thermogenesis in brown fat may play role rather in long term.

Combination of calorie restriction and feeding by ω-3 polyunsaturated fatty acids proves to counteract deleterious effects of high fat feeding due to UCP1-independent stimulation of lipid catabolism in epididymal white adipose tissue without consequent recruitment of brown adipose tissue. The excessive energy is probably consumed by consequently stimulated synthesis of triglycerides and/or fatty acids.

The phenomenon of inducible futile cycling was confirmed also in epididymal adipose tissue of mice exposed to cold for 7 days. The rate of triglyceride synthesis was especially high in animals of AJ strain (in comparison to B6 strain), which are known for their resistance to dietary obesity. Flexible futile cycling thus may contribute to protection of AJ metabolism in conditions of high-fat feeding.

Despite the fact that both white adipose tissue browning and UCP1-independent induction of futile cycling probably fail to influence whole body energy expenditure, but they can exert beneficial effects in buffering plasma and tissue fatty acids levels, and thus preventing impairment of glucose tolerance.