ABSTRACT

Adipose tissue and its hormones have an irreplaceable role in the physiology of mammals. The imbalance between energy intake and energy expenditure leads to the expansion of adipose tissue and changes in its secretion profile. With obesity are associated diseases including cardiovascular diseases, dyslipidemia, hypertension and insulin resistance, one of the major public health issues.

Long-chain n-3 polyunsaturated fatty acids (LC n-3 PUFAs) from marine origin, mainly eicosapentaenoic (EPA) and docosahexaenoic (DHA) acids exert numerous beneficial effects, such as improvements of lipid metabolism and prevention of obesity and diabetes. Studies with obesity-prone model mice (C57BL/6) provide us important knowledge regarding their effect on mammalian tissues and to test potential therapeutic interventions.

The thesis is based on five published studies (A-E). Three studies are focused on white adipose tissue. In these works we proved that adipose tissue is a flexible organ and LC n-3 PUFAs are potent regulators of adipose tissue biology. Our results document that LC n-3 PUFAs affect adipose tissue mass by a mechanism, which depends on counteraction of both, differentiation and proliferation of adipose cell (publication A). The anti-obesity effect of EPA and DHA could be magnified by mild calorie restriction (10%). Our results demonstrate activation of lipid catabolism and synergistic induction of anti-inflammatory lipid markers in white adipose tissue (publication B). LC n-3 PUFAs are also involved in improvement of whole-body insulin sensitivity. We showed for the first time that EPA and DHA stimulate expression and secretion of insulin-senziting hormone adiponectin from mature adipocytes (publication C). In the study focused on muscle insulin sensitivity we described the beneficial effect of combination treatment using EPA and DHA and the anti-diabetic drug rosiglitazone. EPA, DHA and rosiglitazone exerted an additive effect on muscle glycogen synthesis and its sensitivity to insulin (publication D). The last study was focused on the liver and the role of AMP–activated protein kinase (AMPK) in improvement of hepatic insulin sensitivity mediated by LC n-3 PUFAs. In this study mice were used with a whole-body deletion of the α2 catalytic subunit of AMPK. We demonstrated that LC n-3 PUFAs prevent hepatic insulin resistance in AMPKα2-dependent manner (publication E).

In conclusion, this PhD thesis shows that marine lipids, mainly EPA and DHA, play an important role in lipid and glucose homeostasis. Diet supplementation of LC n-3 PUFAs, especially in combination with rosiglitazone or calorie restriction, could become an important part in the prevention and in the treatment of metabolic disorders associated with obesity.