SUMMARY

Skeletal muscle plays an important role in the maintenance of whole-body metabolic homeostasis. Metabolic alterations of skeletal muscle contribute to the pathogenesis of a wide range of human diseases, such as obesity, type 2 diabetes and hypertension. Relative excess and suboptimal composition of nutrients negatively affect skeletal muscle metabolism and a better understanding of mechanisms involved in these changes is of central importance. The aim of the work presented in this thesis was to explore cell viability and mitochondrial respiratory parameters following experimentally induced changes in the availability or composition of selected nutrients (fatty acids and glutamine). We attempted to elucidate the mechanisms responsible for the observed changes, such as mitochondrial DNA (mtDNA) damage, or nuclear receptors activation. The studies were performed *in vitro* on skeletal muscle cell culture models. In addition, we examined mitochondrial function and fat accumulation in skeletal muscle of vegans, i.e. subjects consuming a strict plant-based diet.

Using C2C12 skeletal muscle cells we studied the effects of free fatty acids (FFA). We found that relatively low doses of saturated palmitic acid increased hydrogen peroxide production and induced mtDNA damage, mitochondrial respiratory dysfunction and cell death in myoblasts. Differentiated myotubes were more resistant to this lipotoxic effect and despite observed mtDNA damage mitochondrial respiration and cell viability were not compromised. Mitochondria-targeted antioxidants MitoQ and MitoTEMPOL did not prevent palmitic acid-induced damage. In the same model we also showed that unsaturated FFA effectively protect cells against the lipotoxic action of palmitic acid but this effect is not mediated by an activation of peroxisome proliferator-activated receptors δ (PPARδ). In addition to FFA, we also studied the effect of different doses of the amino acid glutamine in primary human skeletal muscle cells. We found that levels consistent with moderate clinical hypoglutaminemia are well tolerated and are optimal for the proliferation of myoblasts and efficient oxidative phosphorylation of both myoblasts and myotubes. High levels of glutamine then uncoupled mitochondrial respiration.

In addition, we showed that metabolic benefits of a diet strictly avoiding animal products, particularly higher insulin sensitivity, are not associated with changes in mitochondrial density or fat accumulation in skeletal muscle.

We believe that our results contribute to the understanding of the effects of selected nutrients (i.e. saturated and unsaturated fatty acids and glutamine) on skeletal muscle energy metabolism. A better understanding of the cellular biology and pathophysiology associated with changes in the availability of these nutrients can provide a framework for evidence-based prevention and treatment of many pathological states.