# ABSTRACT

Type 2 diabetes mellitus represents a metabolic disease reaching epidemic dimensions in the 21st century. Fatty acid-induced apoptosis of pancreatic β-cells significantly contributes to its pathogenesis. Saturated fatty acids (FAs) are strongly cytotoxic for β-cells, whereas unsaturated FAs are well tolerable by β-cells, they are even able to inhibit proapoptotic effects of saturated FAs when co-incubated. According to recent studies, FAs-induced apoptosis in pancreatic β-cells is partly regulated by autophagy, a catabolic process involved in the degradation and recyclation of cell components in lysosomes.

The aim of this diploma thesis was to contribute to the clarification of the role of autophagy in FAs-induced apoptosis regulation. We induced apoptosis in human pancreatic β-cell line NES2Y by 1 mM stearic acid (SA) and inhibited it with 0.2 mM oleic acid (OA) co-incubated with SA.

We revealed, that the saturated SA used in apoptosis-inducing concentration simultaneously inhibits the autophagic flux in pancreatic NES2Y cell line. When SA is co-incubated with unsaturated OA in concentration sufficient for inhibition of proapoptotic effect of SA, OA is also able to inhibit the block of autophagy induced by the effect of SA. Application of unsaturated OA alone in this concentration did not exhibit any effect on the basal levels of autophagy. The results also suggested that in pancreatic β-cell line NES2Y neither the basal activity, nor the FAs-induced autophagy is regulated by signaling pathway of mTOR1 kinase. Silencing of Atg7, which is an essential autophagy-specific protein, using siRNA showed, that autophagy is not involved in FAs-induced apoptosis regulation in human pancreatic NES2Y cell line.

**Key words:** apoptosis, autophagy, bafilomycin A1, caspases, fatty acids (FAs), pancreatic β-cells, rapamycin