# Abstract

Aim of this thesis was to observe changes in oxidative metabolism and expression of important neuroenergetic proteins in human neuroblastoma cell line SH-SY5Y due to inhibition of FTO. FTO is a RNA demethylase that uses N6-methyladenosine as substrate. Differences in enzyme expression are connected to broad area of effects involving energy homeostasis.

Mitochondria are cellular powerhouses, a key elements in production of energy and metabolic substrates, yet a source of potentially dangerous reactive oxygen species (ROS) and analogous reactive molecules. In order to better understand FTO purpose in neuronal energetic metabolism, we examined mitochondrial respiratory chain. Using high-resolution respirometry we were capable of observing impairment in mitochondrial respiration after FTO inhibition. There was considerable decline in endogenous respiration, maximal respiration rate and reserve capacity. In order to obtain more detailed view into mitochondrial respiration, expression levels of electron-transport complexes were quantified by Western blot technique. Slight reduction was identified in subunits of complex I and IV. However, the most prominent alteration was seen in complex II subunit. There were no differences in expression of complex III and ATP synthase subunits. Beside disrupted activity of electron-transport system, ROS production can reflect mitochondrial dysfunction. By using fluorescence probes, we managed to observe increased ROS production in cells treated with FTO inhibitor.

Furthermore, we studied how FTO inhibition affects insulin signaling. Expression of selected proteins involved in insulin signaling was detected by Western blot. Increased levels of insulin receptor and insulin degrading enzyme accompanied FTO inhibition. Additionally, decreased ratio of p-Akt/Akt and p-p38/p38 together with elevated ratio of p-ERK/ERK was observed. Minimal difference was sighted in PI3K p110 expression or p-GSK3β/GSK3β ratio.

Taken together, these results suggest considerable link between FTO activity and neuronal signaling and metabolic actions. Further research could undoubtedly prove to be beneficial in gaining knowledge about bioenergetics processes in the nervous system.