Abstract

Isolated deficiency of F_1F_O-ATPsynthase is a soubgroup of mitochondrial diseases caused by mutations in nuclear and mitochondrial-encoded structural subunits, or nuclear-encoded assembly factors of F_1F_O-ATPsynthase. The most often mutations are found in a *MTATP6* gene localized in the mitochondrial DNA and a *TMEM70* gene, localized in the nuclear DNA. A *MTATP6* gene encodes subunit a of F_1F_O-ATPsynthase and its mutation usually leads to reduced phosphorylation activity of F_1F_O-ATPsynthase. A *TMEM70* gene encodes a 21 kDa mitochondrial protein of the inner mitochondrial membrane of not completely explained function and its mutation results in the decrease in a content of fully assembled F_1F_O-ATPsynthase. The aim of this thesis was to investigate the impact of isolated F_1F_O-ATPsynthase deficiency on the oxidative phosphorylation system (complex I-IV), other selected mitochondrial proteins, and mitochondrial network in two cell lines of primary human skin fibroblasts with an isolated deficiency of F_1F_O-ATPsynthase (mutation m.8851T>C in *MTATP6* and mutation c.317-2A>G in *TMEM70*) during the first days of their cultivation in media containing galactose or glucose as a carbohydrate source with a presence or absence of L-glutamine.

The control cell line was found to have higher amounts of respiratory chain complexes including F_1F_O-ATPsynthase except complex III in a DMEM medium containing galactose as carbohydrate source compared to cultivation in a DMEM medium containing glucose as a carbohydrate source. However in the cell lines with the isolated F_1F_O-ATPsynthase deficiency, only higher amounts of complex IV of the respiratory chain were found. L-glutamine increased the viability and growth of cell lines with isolated deficiency of F_1F_O-ATPsynthase in media containing galactose as a carbohydrate source.

The impact of isolated deficiency of F_1F_O-ATPsynthase on other respiratory chain complexes depended on the type of cultivation media containing galactose as a carbohydrate source. It was further supported by similar observations in the control line in these media. In cell lines with isolated F_1F_O-ATPsynthase deficiency higher amounts of respiratory chain subunits were found compared to a control cell line in Leibovitz medium. On the contrary, lower amounts of respiratory chain subunits (except of complex III subunit) were found in DMEM medium.

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