Abstract

In their bioenergetic metabolism mammalian cells are primarily dependent on ATP production through the oxidative phosphorylation system (OXPHOS). Defects of OXPHOS function can lead to occurrence of mitochondrial disorders with different severity and diverse symptoms. Most severely affected are usually tissues with high energy demand which are also difficult to access for biochemical and other examinations. The aim of this thesis was mainly to characterize the effects of mutations in seven different genes (*OPA1*, *DARS2*, *NDUFS8*, *NR2F1*, *HTRA2*, *MGME1*, *POLG*) on bioenergetic metabolism and mitochondrial network structure of skin fibroblasts from eight different patients diagnosed with mitochondrial disorders. The main method used was measurement of oxygen uptake by permeabilized cells using highly sensitive polarography. Significant changes in fibroblast respiration of four patients were found. Changes in mitochondrial network morphology were found in two of those and two other patient cell lines compared to controls using fluorescent microscopy and different cultivating conditions. Skin fibroblasts are relatively easy to obtain and offer a number of benefits for both diagnostic and study purposes. The results of this work illustrate the possibilities of their use for validation of potential causal mutations of mitochondrial diseases and other purposes, especially in combination with other methods and tissues.