Abstract:

Mitochondria are some of the most complex organelles of eukaryotic cell. They have their own genome and transcriptional apparatus and maintain several key cellular functions. A substantial part of cellular energetic metabolism happens in the mitochondria, as well as formation of iron-sulfur complexes, synthesis of several key molecules and they are also the essential organelles for the apoptotic pathway. In order to maintain the quality of proteins in their oxidative environment, mitochondria have developed a complex system of proteases that reaches all the mitochondrial compartments that degrade damaged proteins and thus promote mitochondrial turnover. The aim of this work was to characterise function of ClpP subunit of ClpXP matrix protease, which role was not yet extensively investigated in human cells. Therefore, we used RNA-interference to silence expression of ClpP in HEK 293 cells and then we performed rescue experiment during which we reintroduced ClpP in cells. Our results show that the ClpP subunit does not actively participate in apoptotic pathway, nevertheless it is essential for correct assembly of all the respiratory complexes as well as the quality of mitochondria itself. We have also shown that the system of mitochondrial proteases is highly functional and that a lack of ClpP proteolytic function causes its disbalance when proteases of inner mitochondrial membrane copy the level of active ClpP by their own levels. We found out that absence of ClpX has even more drastic effect on cells then absence of ClpP. Overall these results confirm that ClpXP complex is an important mitochondrial quality control protease that ensures the maintenance of healthy mitochondrial status in human cells.