# ABSTRACT

Mitochondria are found in virtually all eukaryotic cells where their main function is the production of ATP in the oxidative phosphorylation system (OxPhos). OxPhos is build-up of both nuclear and mitochondrial encoded protein subunits. Due to the potential function threatening defects, the quality of these protein subunits is constantly under tight control by specialized proteins. The recognition and selective removal of defective mitochondrial proteins is carried out by specific mitochondrial ATP-dependent proteases. So far, four such proteolytic complexes active within distinct mitochondrial subcompartments were identified. Both i- and m-AAA protease complexes are found in the inner mitochondrial membrane. Whereas the i-AAA protease is active in the intermembrane space, the homologous m-AAA protease functions on the matrix side of the inner membrane. The aim of the present work was to characterize cellular function of the human orthologue YME1L of the yeast i-AAA protease subunit YME1 using human HEK293 cell model. We found that human YME1L is an integral membrane protein with molecular weight of approx. 600-1100 kDa, exposing the carboxy-terminal domain to intermembrane space. The HEK293 cell line with shRNA silenced expression of YME1L showed accumulation of Ndufb6 and ND1 subunits of complex I and increased stability of subunit Cox4 of complex IV. The YME1L deficient cells were further found to exhibit reduced growth rate, increased apoptosis and carbonylation of mitochondrial membrane proteins. Our results thus demonstrate that human YME1L protease is required for the maintenance of mitochondrial protein homeostasis and further emphasize its importance for mitochondrial and cellular function and integrity. (In Czech).