FUNCTIONAL ELECTRON TRANSPORT CHAIN IS NECESSARY FOR STRESS RESISTANCE IN QUIESCENT CELLS

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Mitochondria are organelles central to energy metabolism and cell death. In the present work we investigated the role of functional electron transfer chain (ETC) in cell's adaptation to the quiescent state, using ETC-deficient (ρ^0 cells) endothelial cell line EA.hy926 as a model. Preliminary results showed an increase in glucose consumption and lactate production in ETC-deficient quiescent cells compared to their proliferative counterparts. Unlike control cells, quiescent cells lacking the ETC were highly susceptible to reactive oxygen species (ROS) inducers such as phenethyl isothicyanate (PEITC). This was surprising, as the ETC-deficient quiescent cells, similar to ETC-functional counterparts, showed elevated activity of mitochondrial antioxidant defense. Interestingly, we observed a reduced autophagic flux in quiescent ρ^0 cells. Moreover, pharmacological interference with autophagy or the knock down of ATG5, a protein essential for autophagy, not only reduced autophagic flux but also increased sensitivity to ROS and the ROS-induced cell death in quiescent cells with functional ETC, recapitulating the ETC-deficient phenotype. This suggest that quiescent ETC-deficient cells are metabolically stressed, leading to compromised autophagic flux and limited protection from ROS.