Hexokinase Modulates Reactive Oxygen Species Accumulation by Substrate Affinity In Electron Transport System.

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Mitochondrially bound hexokinase (mt-HK) present in plants and mammals recycles ADP trough inner mitochondrial membrane leading to a decrease in membrane potential (?? $_m$) and reactive oxygen species (ROS) production in potato tuber mitochondria (PTM) and rat brain mitochondria (RBM). The mt-HK activity is capable to decrease ?? $_m$ stimulating the oxygen consumption avoiding ROS formation. This effect was demonstrated using succinate. Here we evaluated the antioxidant mechanism of mt-HK in PTM or RBM using other substrates of ETS. In PTM, ROS was measured using succinate, pyruvate/malate (PM) and NADH. Glucose prevents ROS accumulation by 79% with succinate and 48% with NADH as respiratory substrates. Glucose stimulates respiration ten-fold higher using succinate or NADH than using PM as substrate. The concentration dependence for NADH to external NADH dehydrogenase (NADHdh) was increased ten-fold by 0.3 mM ADP and 5 mM glucose decreasing the catalytic efficiency of PTM respiration (V_{max}/K_M) in 26%. In the presence of 1µM FCCP, the apparent K_m increased only two times. For succinate dehydrogenase (SDH) the mt-HK activity increased four times the K_m and the catalytic efficiency was reduced in 32%. In RBM the increase in K_m was the same as that observed for PTM but the catalytic efficiency reduces 60%. The mt-HK activity modulates ROS formation in a process that includes alterations on substrate affinities of NADHdh and SDH either in PTM and RBM. The avoidance of ROS formation by mt-HK activity occurs by selective modulation of substrates affinities for ETS via ?? $_m$, but not exclusively related to a decrease in ?? $_m$ itself.

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