

OVEREXPRESSION OF THE MITOCHONDRIAL PYRUVATE CARRIER INCREASES CHO CELL AND RECOMBINANT PROTEIN PRODUCTIVITY AND REDUCES LACTATE PRODUCTION

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The metabolism of CHO cells is characterized by a low efficiency of glucose metabolism, resulting in lactate production. We hypothesized that the cause of such low efficiency is a slow transportation of pyruvate into the mitochondria. The mitochondrial pyruvate carrier (mpc), responsible of introducing pyruvate into the mitochondria, is formed of two subunits, mpc1 and mpc2. We constructed stable CHO cell lines overexpressing both genes in order to facilitate the entry of pyruvate into the mitochondria and its incorporation into oxidative pathways. Overexpression of both genes was verified by qPCR and Western Blot, showing a significant increase compared to the basal level on the control cells. Kinetic evaluation of the CHO-mpc cells showed a 50% reduction of the lactate concentration respect to the control. Cell growth rate and maximum concentration were also increased, and an increase of 40% on the production of recombinant secreted placental alkaline phosphatase was observed. We show that transport of pyruvate into the mitochondria limits the efficiency of oxidation of glucose, which can be overcome by a cell engineering approach.

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