ABSTRACT

The Regulation of Pyruvate Dehydrogenase Phosphate Phosphatase in Rat Kidney

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The aim of this work was to investigate the regulation of pyruvate dehydrogenase phosphate phosphatase (PDHP phosphatase) in rat kidney. Primarily, this involved examining the response of pyruvate dehydrogenase (PDC) in intact mitochondria to changes in the nutritional state of rats. On starvation, the rate of activation of PDC was found to undergo a decrease in sensitivity towards the stimulatory ion Mg^{2+} as compared to the sensitivity of the rate of activation in the fed state.

The effect of starvation to decrease the rate of activation of PDC at subsaturating Mg^{2+} persisted through solubilization of PDHP phosphatase. This effect could be reversed in 1h by insulin injection. The effect of insulin was not mimicked by an inhibitor of lipolysis and was not blocked by an inhibitor of protein synthesis. The effect of starvation was abolished by 1µM okadaic

acid or by saturating levels of Mg^{2+}. There was a cation-independent PDHP phosphatase in the solubilized mitochondrial extract which activated PDC to 36% of maximum PDC activity. Okadaic acid caused a 70% diminution in the activity of this phosphatase. The cation-independent PDHP phosphatase may be stimulated by insulin and perhaps plays a regulatory role in the intact animal. This phosphatase may also attack PDHP with a different phosphorylation site preference or priority than that of the cation dependent enzyme.