Abstract

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Regulation of mammalian pyruvate dehydrogenase.

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BACKGROUND: In mammalian tissues, two types of regulation of the pyruvate dehydrogenase complex have been described: end product inhibition by acetyl CoA and NADH: and the interconversion of an inactive phosphorylated form and an active nonphosphorylated form by an ATP requiring kinase and a specific phosphatase.

FINDINGS: This article is largely concerned with the latter type of regulation of the complex in adipose tissue by insulin (and other hormones) and in heart muscle by lipid fuels. Effectors of the two interconverting enzymes include pyruvate and ADP which inhibit the kinase, acetoin which activates the kinase and Ca2+ and Mg2+ which both activate the phosphatase and inhibit the kinase. Evidence is presented that all components of the pyruvate dehydrogenase complex including the phosphatase and kinase are located within the inner mitochondrial membrane. Direct measurements of the matrix concentration of substrates and effectors is not possible by techniques presently available. This is the key problem in the identification of the mechansims involved in the alterations in pyruvate dehydrogenase activity observed in adipose tissue and muscle.

SUMMARY: A number of indirect approaches have been used and these are reviewed. Most hopeful is the recent finding in this laboratory that in both adipose tissue and heart muscle, differences in activity of pyruvate dehydrogenase in the intact tissue persist during preparation and subsequent incubation of mitochondria.

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