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PHOSPHORYLATION IS SWITCH BETWEEN NON-ALLOSTERIC AND ALLOSTERIC FORMS OF L-TYPE PYRUVATE KINASE

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There are four pyruvate kinase isoenzymes M1, M2, R and L, whereas only M1 is considered as a non-allosteric enzyme. In our work we have shown that not only M1 is non-allosteric enzyme, but also non-phosphorylated L-type pyruvate kinase (L-PK) shows hyperbolic kinetics toward its substrate phosphoenolpyruvate (PEP) and can be characterized by hyperbolic Michaelis-Menten plot and K_{PEP} = 0.11 mM. The L-type PK is the only one isoenzyme which activity can be regulated by phosphorylation. It takes place at Ser(12) residue, flanked by peptide sequence Arg(9)-Arg(10)-Ala(11)-Ser(12)-Val(13). Phosphorylation of L-PK by cAMP-dependent protein kinase changes the catalytic properties of pyruvate kinase. We have discovered that the non-phosphorylated enzyme is not allosterically regulated and through phophorylation the enzyme obtaines cooperativity. This means that phosphorylation is a molecular switch between non-allosteric and allosteric forms of the enzyme. The phosphorylated allosteric enzyme was characterized by K_{ADP} = 0.1 mM, K_{PEP} = 2.2 mM, and the Hill coefficient n = 2.5. Also it was observed that phosphorylation of the first subunit of the tetrameric enzyme switches on the allosteric mechanism, while further phosphorylation only modulates this effect. The discovery that phosphorylation is a switch between allosteric and non-allosteric states of L-PK seems to be important for understanding the interrelationship between allostery and the regulatory phosphorylation in general [1].

1. I. Faustova, A. Kuznetsov, E. Juronen, M. Loog, J. Järv, *CEJB.*, in press