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Regulatory network of the allosteric ATP inhibition of *E. coli* phosphofructokinase-2 studied by hybrid dimers

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12 Abstract

We have proposed an allosteric ATP inhibition mechanism of Pfk-2 determining the structure 13 14 of different forms of the enzyme together with a kinetic enzyme analysis. Here we complement the mechanism by using hybrid oligomers of the homodimeric enzyme to get 15 insights about the allosteric communication pathways between the same sites or different ones 16 located in different subunits. Kinetic analysis of the hybrid enzymes indicate that homotropic 17 interactions between allosteric sites for ATP or between substrate sites for fructose-6-P have a 18 19 minor effect on the enzymatic inhibition induced by ATP. In fact, the sigmoid response for 20 fructose-6-P observed at elevated ATP concentrations can be eliminated even though the enzymatic inhibition is still operative. Nevertheless, leverage coupling analysis supports 21 heterotropic interactions between the allosteric ATP and fructose-6-P binding occurring 22 between and within each subunit. 23

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