

Phosphorylation of Muscle Glycogen Synthase Maintains Metabolic Homeostasis

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ABSTRACT

Experimental studies of mammalian muscle glycogen synthesis using metabolic control analysis concluded that glycogen synthase (GSase) does not control the glycogenic flux but rather adapts to the flux which is controlled by the activity of the proximal glucose transporter(1). Here we show that the phosphorylation of GSase is a mechanism for controlling the concentration of G6P instead of controlling the flux. The increase in GSase fractional activity by dephosphorylation has been quantitatively established, by proportional activation analysis, to maintain G6P homeostasis. This role for covalent phosphorylation is a novel solution to the Kacser and Acarenza paradigm which required coordinated activity changes of the enzymes proximal and distal to a shared intermediate, to avoid unwanted flux changes. The maintenance of homeostasis by enzymatic phosphorylation is an alternative to its traditional role of controlling flux.

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[1] Shulman, R.G. and Rothman, D.L. Enzymatic phosphorylation of muscle glycogen synthase: A mechanism for maintenance of metabolic homeostasis. Proc. Natl. Acad. Sci. USA, 93: 7491-7495 (1996).