LETTER

Regulatory Function of Hexokinase 2 in Glucose Signaling in *Saccharomyces cerevisiae*

Vega *et al.* (1) analyze the mechanism by which hexokinase 2 (Hxk2) contributes to glucose-dependent signal transduction in *Saccharomyces cerevisiae*. Considering the absence of experimental data on Hxk2 conformation, phosphorylation state, and structural integrity, the authors' interpretation of underlying molecular events deserves comment.

First, the possibility is highlighted that Hxk2 constitutes an intracellular glucose sensor, which operates in response to glucose levels via the conformational change that is associated with the open/close induced fit domain movement of the enzyme to control its recruitment to the *SUC2* repressor complex. The authors do not, however, provide direct evidence proving such a mode of action. In particular, the hypothesis that xylose could induce an open conformation mimicking low glucose conditions is presented without support by structural data. By contrast, it seems rather likely that due to similar binding modes xylose and glucose may stabilize a closed hexokinase conformation (2).

Second, the authors conclude from the analysis of the Hxk2-*SUC2* promoter interaction in a Δ*snf1* background that Hxk2-S15 phosphorylation is not essential for regulation of complex formation. This conclusion ignores the finding that protein kinase Ymr291w/Tda1 rather than Snf1 is indispensable for the above modification (3). Therefore, the involvement of Hxk2-S15 phosphorylation in *SUC2* promoter binding cannot be excluded.

Finally, the authors do not consider the existence of multiple molecular forms of hexokinases in yeast that differ in their oligomeric state, conformation, and state of phosphorylation (4). In consequence, the molecular form of Hxk2 that is a constituent of the *SUC2* repressor complex remains to be identified.

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