LETTER

The Nuclear Hexokinase 2 Acts as a Glucose Sensor in *Saccharomyces cerevisiae*

This is a response to a letter by Kriegel et al. (1).

In our work (2) we analyze the mechanism by which hexokinase 2 (Hxk2) regulates its incorporation into the repressor complex of the Mig1-dependent gene promoters. Kriegel *et al.* (1) claim that the lack of experimental data on Hxk2 phosphorylation state and conformation questions our conclusions. Nevertheless, it has been described that the shuttling back and forth between the nucleus and the cytoplasm of Hxk2 is regulated by phosphorylation and dephosphorylation of serine 14, mediated by Snf1 kinase and Reg1-dependent Glc7 protein phosphatase, respectively (3). In contrast, Kettner *et al.* (4) suggest that Tda1 protein is the necessary kinase for serine 14 phosphorylation, but in our hands, the Hxk2 nucleocytoplasmic distribution is not affected in Δ*tda1* mutant cells (3). Moreover, *in vitro* experiments, with purified proteins, demonstrate that Snf1 kinase directly phosphorylates Hxk2, and this phosphorylation regulates its binding capacity to the Xpo1 transporter (3).

However, Hxk2 phosphorylation by the Snf1 kinase is not critical to regulate the Hxk2-*SUC2* promoter binding (2). It is well documented that high glucose and low glucose induce a closed and open conformation of *S. cerevisiae* Hxk2, respectively (5, 6). Because in the presence of xylose both *in vivo* and *in vitro* Hxk2-Mig1 interaction is abolished, as happens in low glucose conditions, we conclude that xylose induces a Hxk2 conformation similar to that observed in low glucose conditions (6). Moreover, the conformation of Hxk2 induced by xylose does not require the Hxk2 phosphorylation or an ATP-induced conformation, because it is also observed in the absence of ATP or the non-hydrolyzable analog AMP-PNP (adenosine 5′-(β, γ-imino)triphosphate), respectively (2).

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