FEATURES

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Intracellular Glucose Signaling

Kaisa Karhumaa, Boqian Wu, and Morten C. Kielland-Brandt

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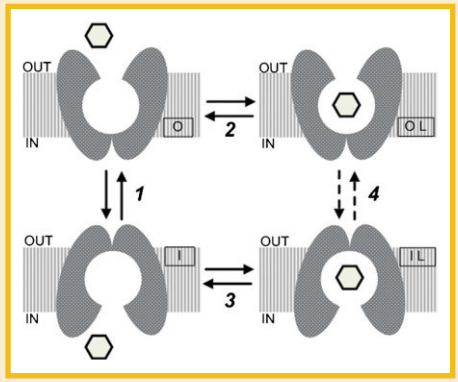
The importance of glucose homeostasis in human blood is well known and well studied. Intracellular glucose homeostasis is less studied because of technical challenges in measuring concentrations of nutrients and metabolites that have high turnover rates. The yeast *Saccharomyces cerevisiae* possesses a non-transporting, transporter-like glucose sensor, Snf3, known to mediate a response to extracellular glucose consisting in signaling for synthesis of glucose transporters, resulting in increased glucose uptake. Using intracellular cleavage of maltose into glucose in a mutant lacking glucose transporters, Karhumaa et al. have now found that intracellular glucose inhibits the Snf3-mediated signaling triggered by extracellular glucose, a phenomenon that is likely to contribute significantly to intracellular glucose homeostasis. This discovery of a new regulatory interaction in central carbon metabolism may help engineering of glycolytic flux for optimization of yields and/or productivities of fermentations. The authors propose that an inward-facing, non-signaling conformation of Snf3 binds intracellular glucose, which thereby disfavors an outward-facing or occluded signaling conformation of Snf3. Such a mechanism would conform to models for transporter-like sensors previously proposed on the basis of the behavior of non-transporting (Ssy1) and transporting (Gap1) amino acid sensors.



ILK and Bone Resorption

Tanya Dossa, Alice Arabian, Jolene J. Windle, Shoukat Dedhar, Steven L. Teitelbaum, F. Patrick Ross, G. David Roodman, and René St-Arnaud

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Osteoclastic bone resorption requires matrix recognition and attachment of the osteoclast through the $\alpha_v\beta_3$ integrin, which induces the assembly of multiprotein complexes that transduce downstream signals. A component of these complexes is the multifunctional protein Integrin-Linked Kinase (ILK), which interacts with the cytoplasmic β_3 integrin domain. The contribution of ILK-mediated signaling to resorptive activity is unknown and was addressed by Dossa et al. using tissue-specific inactivation of *Ilk*. Osteoclast-specific *Ilk* mutant mice had increased bone volume and an augmented number of osteoclasts that had decreased resorption activity. Compound heterozygous mice in which one allele of *Ilk* and one allele of the β_3 integrin gene were inactivated showed a partial phenocopy, confirming that β_3 integrin and *Ilk* form part of the same genetic cascade. Dossa et al. results thus show that ILK is important for the function, but not the differentiation, of osteoclasts and identify a novel target that could be pharmacologically manipulated to modulate bone resorption.