BRC Science Highlight
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Near-Equilibrium Glycolysis Supports Metabolic Homeostasis and Energy Yield

Background/objective

While the steps of glycolysis are well-known, its control is still incompletely understood. Energetics are a key aspect of any metabolic pathway, as each step must have a negative ΔG in order to proceed and irreversible steps with large negative ΔG values are good points for pathway control. Therefore, a better understanding of glycolytic thermodynamics could improve metabolic engineering. Existing methods of determining ΔG based on substrate and product concentrations are hampered by analytical limitations. Here, researchers present an improved method of measuring ΔG, GibbsIT (Gibbs energy from isotope tracing), based solely on isotope-labeling data.

Approach

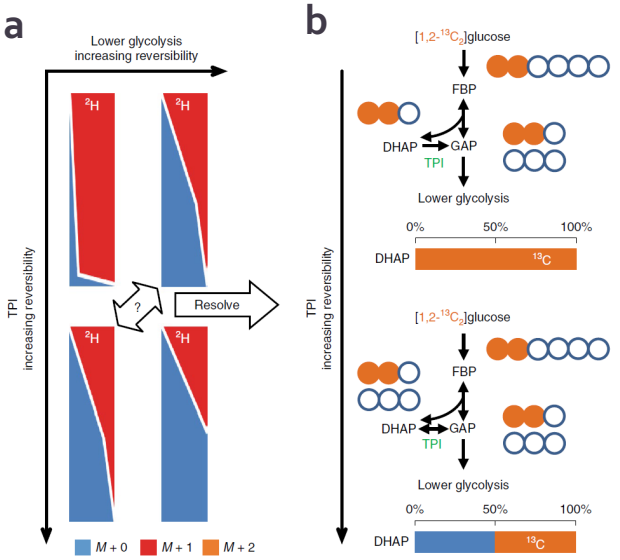
- Selected isotope-labeled substrate ([5-$^{2}H_1$] and [1,2-$^{13}C_2$] glucose) such that strongly forward-driven reactions would retain the isotope-labeling pattern through sequential steps, while, in near-equilibrium steps, unlabeled intermediates would travel metabolically upstream.
- Tested initially in model microorganisms across diverse environments of bioenergy relevance (N-limited, P-limited, anoxic) and then in DOE-relevant cellulose-degrading microbe.

Results

- The method was used to successfully determine ΔG under different metabolic conditions.
- Near-equilibrium steps provided (i) flexibility to enable rapid environmental adaptation and (ii) energy efficiency.

Significance

A new measurement tool (GibbsIT) for metabolic engineering will help drive energy-efficient and robust transformations.



[5-$^{2}H_1$] labeling alone provides inadequate information (a), but, in combination with [1,2-$^{13}C_2$] labeling (b), allows for determination of ΔG of the glycolysis reaction.

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