Metabolic pathway deficiencies are compensated by higher energy dissipation to maintain microbiological growth rate in Saccharomyces cerevisiae

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The development of experimental methods for earlier detection of diseases is a crucial step for improving treatment efficiency. In this work, the energy dissipation rate during cellular growth was tested as an early biomarker for metabolic perturbations. This was achieved by using calorimetry to follow the heat dissipated throughout the growth cycle of *Saccharomyces cerevisiae* (*Sc*), in media with different levels of complexity and nutrient content. By supplementing the calorimetric measurements with the determination of key cellular parameters (e.g. cell count), fundamental insights into the speed, accuracy and energy cost trade-offs associated with cell adaption to growth media were obtained.

Medium of higher complexity was observed to decrease the rate of cell adaptation to growth media (measured by the duration of the lag phase). In other words, *Sc* cells adjust their internal molecular machinery to achieve a better fitting to the environmental conditions faster if the medium components are smaller and more accessible molecules. Surprisingly, decreasing the non-carbon nutrient abundancy led to a 60% higher energy dissipation rate, but the microbiological growth was not affected with the accuracy of cell adaptation to growth media (measured by the maximal proliferative rate) remaining similar in all conditions. Thus, a higher energy dissipation rate compensates for partial nutritive limitations allowing *Sc* cells to maintain their microbiological growth rate. Supporting these observations, *Sc* cells under nutrient limitations spent a larger amount of resources in order to fully adapt to the growth medium, e.g. glucose consumption and funneling of glycolytic metabolites into other metabolic pathways increased.

In conclusion, the rate of energy dissipation is largely affected long before nutrient limitations impact the growth curve in terms of traditional microbiological measurements. Detection of this enhanced energy waste, therefore, provides a potential biomarker for metabolic deficiencies, either inborn or age-related, or triggered by pharmaceuticals or environmental xenobiotics.