GORDON AND BETTY MOORE FOUNDATION

Team Karl Highlight

Global optimization of phosphorus metabolism in *Prochlorococcus*

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Inorganic phosphorus is scarce in the Eastern Mediterranean Sea, where the high-light adapted strain MED4 of the oligotrophic marine picocyanobacterium *Prochlorococcus marinus* thrives. Physiological and regulatory control of phosphorus acquisition and partitioning has been observed in MED4 both in culture and in the field, however the optimization of phosphorus metabolism and associated growth rate gains for its phosphorus limited growth (PLG) phenotype has not been studied. Constraint-based modeling of a genome-scale metabolic network reconstruction of axenic strain MED4 (*i*JC568), consisting of 568 metabolic genes encoding 794 reactions with 680 metabolites distributed in 5 sub-cellular locations, was used to quantify metabolic fluxes under PLG conditions. The *i*JC568 stoichiometric model is mass and charge balanced, with close correspondence between experimental and computed fluxes. In keeping with the stringency of having few pathway redundancies and an extremely high proportion of essential metabolic genes (47%; defined as the percentage of lethal textitin silico gene knockouts), we identified three strategies which evolved in MED4 to cope with low phosphorus avialability: (1) network-wide reductions in phosphate-reaction participation, (2) drastic depletion of phosphorus-containing biomass components, and (3) loss of succinate dehydrogenase. These strategies are examples of nutrient-driven adaptive evolution and confer a dramatic growth rate advantage to MED4 in phosphorus-deplete regions.