Adaptive Evolution of Phosphorus Metabolism in Prochlorococcus

Inorganic phosphorus is scarce in the eastern Mediterranean Sea, where the high-light-adapted ecotype HLI of the marine picocyanobacterium *Prochlorococcus marinus* thrives. Physiological and regulatory control of phosphorus acquisition and partitioning has been observed in HLI both in culture and in the field; however, the optimization of phosphorus metabolism and associated gains for its phosphorus-limited-growth (PLG) phenotype have not been studied. Here, we reconstructed a genome-scale metabolic network of the HLI axenic strain MED4 (iJC568), consisting of 568 metabolic genes in relation to 794 reactions involving 680 metabolites distributed in 6 subcellular locations. iJC568 was used to quantify metabolic fluxes under PLG conditions, and we observed a close correspondence between experimental and computed fluxes. We found that MED4 has minimized its dependence on intracellular phosphate, not only through drastic depletion of phosphorus-containing biomass components but also through network-wide reductions in phosphate-reaction participation and the loss of a key enzyme, succinate dehydrogenase. These alterations occur despite the stringency of having relatively few pathway redundancies and an extremely high proportion of essential metabolic genes (47%; defined as the percentage of lethal *in silico* gene knockouts). These strategies are examples of nutrient-controlled adaptive evolution and confer a dramatic growth rate advantage to MED4 in phosphorus-limited regions.