Inverse Metabolic Engineering of *Synechocystis* PCC 6803 for Improved Growth Rate and Poly-3-hydroxybutyrate Production

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***Abstract* – *Synechocystis* PCC 6803 is a photosynthetic bacterium that has the potential to make bioproducts from carbon dioxide and light. Biochemical production from photosynthetic organisms is attractive because it replaces the typical bioprocessing steps of crop growth, milling, and fermentation, with a one-step photosynthetic process. However, low yields and slow growth rates limit the economic potential of such endeavors. Rational metabolic engineering methods are hindered by limited cellular knowledge and inadequate models of *Synechocystis*. Instead, *inverse metabolic engineering*, a scheme based on combinatorial gene searches which does not require detailed cellular models, but can exploit sequence data and existing molecular biological techniques, was used to find genes that (1) improve the production of the biopolymer poly-3-hydroxybutyrate (PHB) and (2) increase the growth rate. A fluorescence activated cell sorting assay was developed to screen for high PHB producing clones. Separately, serial sub-culturing was used to select clones that improve growth rate. Novel gene knock-outs were identified that increase PHB production and others that increase the specific growth rate. These improvements make this system more attractive for industrial use and demonstrate the power of inverse metabolic engineering to identify novel phenotype-associated genes in poorly understood systems.**