153c Defining Gene Knockout Search Trajectories: Many Genotypes for the Same Phenotype?

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Systematic and combinatorial tools for the identification of gene knockout and overexpression targets have been effectively employed in the improvement of cellular phenotype. Previously, we have showed how these tools can be combined to identify strains of interest spanning the metabolic landscape. However, it is unknown how the overall search trajectory biases the exploration of the metabolic landscape. In particular, nonlinearities in the metabolic landscape and the instance of recurrence in metabolic phenotypes confound the search for global maxima. Here, we present results of an iterative application of combinatorial gene knockout searches in *Escherichia coli* to search for lycopene overproducing strains. In particular, these combinatorial tools are employed in the background of eight different genotypes spanning various regions of the originally explored metabolic landscape. Several interesting observations arise from this exploration of different gene knockout search trajectories. Initial examination of clusters and recurrence of gene knockout targets suggests key areas of metabolism correlating with lycopene productions. However, divergent genotypes indicate the potential of multiple, distinct paths to obtain comparable metabolic phenotypes. These targets and search trajectories are analyzed for their production potential and underlying mechanism.