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Title: Identifying New Players Involved in Ubiquinone Biosynthesis in Escherichia coli

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Abstract:

Quinones are lipid soluble electron carriers in the electron transport chain (ETC) and help in energy generation. They can be broadly divided into benzoquinones (e.g. ubiquinone) involved in aerobic ETC, and naphthoquinones (e.g. menaquinone and demethylmenaquinone) involved in anaerobic respiration. Our lab conducted a highthroughput genetic screen on a long chain fatty acid (LCFA), oleate, in Escherichia coli and compared the LCFA dataset with published genomewide screens on other carbon sources. This comparative analysis revealed highest requirement of ubiquinone for growth in oleate. In particular, a Δubil strain (Ubil is a hydroxylase involved in ubiquinone biosynthesis), which produces very low level of ubiquinone exhibited growth defect only in oleate. We thus hypothesized that some of the uncharacterized genes (ygenes) in E. coli, deletion of which led to significant growth defect only in oleate, might also be involved in ubiquinone biosynthesis. Detailed studies on one such candidate, yqiC (yqiC encodes a small protein with predicted scaffold function) showed that it is involved in ubiquinone biosynthesis since its deletion resulted in low ubiquinone content. Moreover, the phenotype of ΔyqiC in terms of reduced ubiquinone levels and accumulation of an intermediate was similar to Δubil. Furthermore, a ΔyqiCΔubil double knockout showed a synthetic sick phenotype with no detectable ubiquinone suggesting that the two genes act at the same step in ubiquinone biosynthesis. Introduction of multicopy yqiC clone in Δubil showed slight growth recovery in oleate suggesting that YqiC might promote the function of some other hydroxylase in the absence of Ubil to rescue ubiquinone levels. Since YqiC in Salmonella typhimurium is involved in menaquinone biosynthesis, it is also possible that overexpression of yqiC in Δubil rescues the growth defect of Δubil in oleate by regulating the synthesis of naphthoquinones. In addition to understanding the role of YqiC in ubiquinone biosynthesis, we are also investigating additional y-genes for their involvement in ubiquinone biosynthesis.

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