Title:	To investigate the regulation on ubiquinone during long-chain fatty acid metabolism in Escherichia coli
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Abstract:	All organisms, including bacteria, require energy for performing different cellular activities which they acquire by metabolism. During metabolism, nutrients undergo breakdown via several catabolic reactions producing reduced cofactors and various growth intermediates. The reduced cofactors are oxidized by the electron transport chain (ETC) ultimately resulting in ATP (adenosine triphosphate) production by oxidative phosphorylation. Our lab works on the metabolism of long-chain fatty acid (LCFA), a rich nutrient source for several bacteria including Escherichia coli. LCFAs are carboxylic acids containing long unbranched aliphatic chains of 12-20 carbon atoms. Previously our lab showed that LCFA metabolism produces high levels of reduced cofactors, the oxidation of which creates an increased electron flow in the ETC. Ubiquinone, a lipid-soluble electron carrier in the ETC, plays a critical role in metabolism by rapidly transferring electrons from respiratory dehydrogenases to terminal oxidases. Additionally, ubiquinone plays a vital role in the uptake of electrons from the disulfide bond forming machinery, that catalyses disulfide bond formation in several extracytoplasmic proteins in the bacterial cell envelope. Work from our lab showed that as electrons from both carbon metabolism and disulfide bond formation converge at the level of ubiquinone, LCFA metabolism which generates large number of electrons, renders ubiquinone limiting for its electron transfer function, resulting in redox stress in E. coli. Moreover, our lab showed that E. coli counteracts the LCFA-induced stress by upregulating ubiquinone levels ~1.8 fold. However, the mechanism behind the upregulation of ubiquinone during LCFA metabolism is unknown. My project aims to investigate whether there is a transcriptional regulation of the genes involved in ubiquinone biosynthesis (ubi genes) during LCFA metabolism. Previous studies have identified a ubiquinone biosynthesis multi-protein complex comprising of at least 12 proteins in E. coli. To check for transcriptional regulation, transcriptional reporter constructs for all 12 ubi genes were created and β-galactosidase activity assays were performed. We found that several ubi genes are upregulated during stationary phase in the LCFA-utilising cells. We further investigated the role of FadR, a well-known transcriptional regulator during fatty acid metabolism, for the transcriptional regulation on ubi genes, however, we did not observe any FadR regulation on the ubi genes. Future studies aimed at investigating the role of other transcriptional regulators for induction of ubi genes is required to unravel the mechanistic details for ubiquinone upregulation during LCFA metabolism.
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