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Title: A genome-wide screen in Escherichia coli reveals that ubiquinone is a key antioxidant for

metabolism of long chain fatty acids

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Abstract:

Long chain fatty acids (LCFAs) are used as a rich source of metabolic energy by several bacteria including important pathogens. Since LCFAs also induce oxidative stress, which may be detrimental to bacterial growth, it is imperative to understand the strategies employed by bacteria to counteract such stresses. Here, we performed a genetic screen in Escherichia coli on the LCFA, oleate, and compared our results with published genome-wide screens of multiple nonfermentable carbon sources. This large-scale analysis revealed that amongst components of the aerobic electron transport chain (ETC), only genes involved in the biosynthesis of ubiquinone, an electron carrier in the ETC, are highly required for growth in LCFAs when compared to other carbon sources. Using genetic and biochemical approaches, we show that this increased requirement of ubiquinone is to mitigate elevated levels of reactive oxygen species (ROS) generated by LCFA degradation. Intriguingly, we find that unlike other ETC components whose requirement for growth is inversely correlated with the energy yield of non-fermentable carbon sources, the requirement of ubiquinone correlates with oxidative stress. Our results therefore suggest that a mechanism in addition to the known electron carrier function of ubiquinone is required to explain its antioxidant role in LCFA metabolism. Importantly, among the various oxidative stress combat players in E. coli, ubiquinone acts as the cell's first line of defense against LCFA-induced oxidative stress. Taken together, our results emphasize that ubiquinone is a key antioxidant during LCFA metabolism and therefore provides a rationale for investigating its role in LCFA-utilizing pathogenic bacteria.

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