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Chasing down the role of conserved GTPase LepA (EF4)

Professor Kurt Fredrick
Department of Microbiology
Ohio State University, Columbus, OH 43210-1292, USA

LepA is a paralog of EF-G found in all bacteria. Deletion of lepA confers no obvious growth defect in E. coli, and the physiological role of LepA has remained unclear. It has been proposed that the LepA (also known as EF4) promotes reverse translocation, but we have been unable to confirm this activity. To gain clues about LepA function, we identified nine strains (ΔdksA, ΔmolR1, ΔrsgA, ΔtatB, ΔtonB, ΔtolR, ΔubiF, ΔubiG, or ΔubiH) in which ΔlepA confers a synthetic growth phenotype. These strains are compromised for gene regulation, ribosome assembly, transport and/or respiration, indicating that LepA contributes to these functions in some way. We then used ribosome profiling to deduce the effects of LepA on translation in log-phase E. coli cells. We found that loss of LepA alters the average ribosome density (ARD) for hundreds of mRNA coding regions in the cell, substantially reducing ARD in many cases. By contrast, only subtle and codon-specific changes in ribosome distribution along mRNA were seen. These data suggest that LepA contributes mainly to the initiation phase of translation. Consistent with this interpretation, the effect of LepA on ARD is related to the sequence of the Shine-Dalgarno region. More recent findings that explain the molecular basis of these effects will also be presented.