Drug efflux pumps are well studied for their role in extruding antibiotics from the bacterial cell; however, in addition to their role in the antibiotic resistance crisis, they have also been implicated in essential physiological functions such as pH homeostasis and the efflux of toxic metabolites. The association of efflux pumps with physiological functions suggests their deletion would negatively impact fitness. However, to our current knowledge, there are only two described instances of the deletion of efflux-encoding or efflux-associated genes decreasing the fitness of *Escherichia coli*. The Cox lab has newly identified a further contextually essential role of efflux pumps in *E. coli*; the cumulative deletion of nine efflux-encoding genes (Δ9) significantly impacts bacterial fitness and cellular morphology in nutrient-limited conditions. Single copy genomic integration of each efflux pump-encoding gene in the deficient strain revealed that AcrD, MdtF, MdtL and Bcr efflux pumps can individually restore fitness. I hypothesize loss of the AcrD, MdtF, MdtL, and Bcr efflux pumps causes severe growth defects and changes in cellular morphology due to their previously undescribed role in *E. coli* physiology. The molecular basis underlying this phenotype will be assessed via (1) investigating the impact of AcrD, MdtF, MdtL, and Bcr on the fitness and morphology of *E. coli*, (2) pairwise analysis of the proteomic and metabolomic cellular responses to efflux impairment in the Δ9 mutant strain, and (3) ascertaining the physiological role(s) of AcrD, MdtF, MdtL and Bcr in nutrient limitation.