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Towards Discovering Inhibitors of Cytochrome c Biogenesis

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Cytochrome *c* (cyt *c*) is a heme protein found in most organisms (including human pathogens) that plays an essential role as an electron carrier in the electron transport chain and a signal for apoptosis. The biosynthesis of *c*-type cytochromes occurs by three different systems (Systems I and II in bacteria and System III in humans). Besides requiring different protein systems, their site of synthesis also differs. Systems I and II function in the bacterial periplasmic space while System III functions in the mitochondrial intermembrane space. These differences may allow for selective targeting of bacterial systems using antimicrobial compounds which could be beneficial in combating infectious bacterial diseases. My first project focuses on 1) the development, and 2) utilization of a robust assay to monitor cyt *c* synthesis in the presence of potential inhibitors. The Kranz Lab has engineered all three systems to function in recombinant *E. coli*, where Systems I and II produce cyt *c* in the periplasm while System III makes cyt *c* in the cytoplasm. My findings suggest that the luminescence assay developed by the Kranz Lab which detects the presence of matured cyt *c* in the periplasm does not detect cyt *c* production in the cytoplasm, most likely due to limited luminol access. I optimized a separate screen to quantitatively detect cyt *c* maturation by all three systems and analyzed cyt *c* maturation in the presence and absence of known and potential inhibitors.