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Title:	Uncovering The Mechanism By Which De Novo Designed Proteins Rescue Auxotrophic E. Coli Cells
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Abstract:	One subfield of synthetic biology is protein design. The study of protein design is motivated to impart proteins with non-natural functions and to learn how proteins developed throughout evolutionary time to possess life-sustaining functions. By using large combinatorial protein libraries, we can search for novel functional proteins and probe how they function. This knowledge of novel protein function can guide future protein design in an iterative fashion, similar to how evolution works on naturally occurring protein sequences. To this end, we have utilized large combinatorial libraries of four-helix bundle proteins to search for proteins that sustain life in auxotrophic E. coli, which contain single gene deletions that prohibit the cells from thriving on minimal medium. Previously, it was found that numerous novel proteins sustain life, or rescue, the ΔserB, ΔgltA, Δfes, and ΔilvA strains, but it was not known how the proteins rescue these strains. The results presented in this thesis describe how de novo proteins rescue auxotrophic strains by altering gene regulation. Chapter 2 describes how SynSerB3 rescues ΔserB cells by upregulating an endogenous enzyme HisB. This protein HisB has a weak promiscuous function that when overexpressed, can rescue the deletion of SerB. Not only does SynSerB3 rescue an auxotroph by altering gene regulation, but SynGltA and SynFes5 also function by upregulating endogenous genes. Together, these studies illuminate the life-sustaining functions of de novo designed proteins.
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