Strain optimization for enhanced robustness in stringent response modulated E.coli platform

Escherichia coli (E. coli) is a widely used microbial chassis in biotechnology to produce diverse range of proteins efficiently. Industrial microbial fermentations are often characterized by spatial and temporal gradients, resulting in starvation zones. These conditions can cause unpredictable loss in productivity and robustness in conventional production strains such as E. coli. Hence, engineering strains with lower maintenance energy requirements and improved performance under heterogeneous, industrially relevant conditions are key to improving robustness. E. coli SR strain is engineered to avoid global stress regulation system called stringent response by modulating the ppGpp (guanosine pentaphosphate) to basal level, which is the key controller of this mechanism. The strain exhibits increased tolerance to industrial-scale stresses positioning it as a potential robust chassis for large scale bio-manufacturing. This thesis seeks to engineer and validate an E. coli SR strain through rational genomic deletions & modifications that reduce the organism's maintenance energy requirements. By streamlining the genome using application of genetic engineering tools like CRISPR-Cas9, the project aims to enhance the robustness and productivity of E. coli SR strain.

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