MANIPULATING THE GENETIC CODE IN BACTERIA

The genetic code is degenerate, meaning multiple codons can encode the same amino acid. For example, CCU, CCC, CCA, and CCG all code for proline. This redundancy has inspired researchers to systematically reassign codons in bacterial genomes, a process that opens new possibilities in synthetic biology and biotechnology.

Imagine modifying a bacterium by replacing all CCU codons with CCC. Since both encode proline, this change has no effect on bacterial function. Then, the gene encoding the CCU-specific tRNA is deleted, again without consequences for the bacterium. However, when a phage infects the bacterium, it encounters CCU codons in its genes but finds no corresponding tRNA. As a result, its proteins cannot be synthesized, rendering the phage harmless [1].

This concept of genetic firewalling is a promising strategy to protect industrially valuable bacterial strains from viral infections. For example, a bacterial culture producing human insulin could be immune to phage attacks, ensuring stable and uninterrupted production.

The study by Grome et al.[2] in Nature takes this approach further by constructing a genomically recoded organism (GRO) named “Ochre”, which compresses all stop codons into a single functional stop codon (UAA) while liberating and manipulating other codons for synthetic amino acid incorporation. Additionally, Release Factor 2 was manipulated so that it exclusively recognized UAA stop codons while losing affinity for UGA. In this way they prevented efficient translation termination at UGA, rendering viral transcripts containing UGA non-functional.

1. https://www.science.org/doi/10.1126/science.abg3029?url_ver=Z39.88-2003&rfr_id=ori:rid:crossref.org&rfr_dat=cr_pub%20%200pubmed

2. https://www.nature.com/articles/s41586-024-08501-x