Docket #: S21-056

"mRNA hotfix" rapidly re-code a stabilized mRNA to code for a protein mutant

mRNA_hotfix is heuristic approach to adapt a stabilized mRNA to code for a protein mutation variant substitutes mutated codons with codons that maintain low predicted degradation. It can modify highly stable Superfolders, mRNA coded for the SARS-CoV-2 Spike protein 2P mutation, designed with Eterna. It can be used to code for mutations of UK, South Africa, and Manaus strains. These mutant strain mRNAs are twice as stable as conventionally-designed mRNAs. mRNA_hotfix usesna novel version of Computing Average Unpaired Probability, to evaluate and return mRNA solution with maximal stability and links the average unpaired probability of an mRNA, or AUP, to its overall rate of hydrolysis.

Applications

- The “hotfix” has been used in our lab to modify highly-stable “Superfolder” mRNAs that originally coded for the SARS-CoV-2 Spike protein 2P mutation, designed on the RNA design platform Eterna. The hotfix was used to create mRNAs that code for spike protein mutations in the SARS-CoV-2 U.K. strain (B.1.1.7), the South Africa strain (B.1.351), and the Manaus strain (P.1). This invention would be broadly useful for any company designing mRNA vaccines.

Advantages

- The designed mRNAs encoding mutant strains have been computationally demonstrated to maintain 2-fold increased stability over conventionally-designed messenger RNAs.

Patents

- Published Application: WO2022177597
- Published Application: 20240131196

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