Design of Advanced Synthetic mRNA Devices for Biomedical Purposes

by

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Abstract

Synthetic biological devices, harboring the ability to sense biomolecules and to perform versatile biological outputs, have broad potentials in biomedical fields, including disease treatment, drug discovery and biomedical study. Recently, synthetic mRNA devices are on the rise in treatment of various diseases, ranging from cancers to infectious diseases, for their ability to specifically express functional proteins in the patients. At present, synthetic mRNA devices suffer from several drawbacks. Their short half-lives in biological environment limit their efficiency. As a result, large amount of synthetic mRNA is generally required to generate a transient effect in the patient. Therefore, a generally applicable method, which prolongs the half-lives of synthetic mRNA devices, is expected to greatly widen the applications of synthetic mRNA devices.

We first examined how different factors influence the half-life of natural mRNAs. One of the mRNA degradation mechanisms is the manipulation of the poly(A) tail. Recent sequencing studies have revealed that many of the human mRNAs exhibit post-transcriptional modifications on their poly(A) tails. Bioinformatic studies have found that these modifications are relevant to the varied half-lives of natural human mRNAs. Based on these findings, we explored the use of poly(A) tail post-transcriptional modifications and their combinations to prolong the half-lives of synthetic mRNA devices. Our research was performed on a non-biased platform on various types of cells, with both their functional and physical features examined. Based on the data revealed from these systematic studies, we designed an artificial poly(A) tail sequence with multiple non-canonical nucleotides, which not only substantially prolongs the half-life of synthetic mRNA, but also enhances protein expression of synthetic mRNAs. In addition, the performance of this artificial poly(A) tail has been validated in several types of synthetic mRNA devices using a range of cell lines.

Date: 30 Jul 2020 (Thursday)
Time: 2:00 pm
Venue: Online via Zoom

Examination Committee:
Prof. Henry Lam (Chair)
Prof. Becki Y Kuang (Supervisor)
Prof. Terence Wong

All are welcome!

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