# Prolong Cellular Half-life of Synthetic mRNA Using Modified Poly(A) Tail


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**Abstract**

mRNA, having the ability of directly producing functional protein inside living cell, holds enormous potential to revolutionize vaccination, protein replacement therapies, and the treatment of genetic diseases. Since the first pre-clinical studies of mRNA therapeutics in the 1990s, significant process has been made through deigning high performance mRNA and improving their delivery methods. To enhance the translatability and stability and to reduce the immunostimulatory activity of mRNAs, various type of natural and artificial modifications were explored. For example, the use of synthetic ARCA cap enhances mRNA translatability and the use of 5mC reduces innate immune response caused by mRNA transfection. While cap analogues and modified based are extensively studied, little research explored poly(A) tail modification. Poly(A) tail is essential for the stability and translation initiation of mRNAs. Sequencing data also revealed that several kinds of modifications existing on natural mRNAs, suggesting the modifications might interfere with poly(A) tail function. Through screening of natural poly(A) tail modifications, we discovered one particular modification that can significantly prolong the half-life of synthetic mRNA. After sequence optimization, we obtained modified poly(A) tail sequence that enables high protein expression of mRNA for over 48 hours. Such effect is cell-type independent and can be administrated together with other mRNA modifications to achieve synergic effect. We believe the modified poly(A) tail can greatly impact mRNA therapeutics for reducing the number of mRNA administration per treatment and for minimizing the dosage of mRNA.

**Biography**

Becki Yi Kuang received her bachelor degree from Sun Yat-Sen University in 2006, her Master degree in bioengineering from Hong Kong University of Science and Technology in 2008, and her PhD degree in Chemistry from Brandeis University in 2013. She worked at the Center for iPS Cell Research and Application at Kyoto University, first as a HFSP Research Fellow and then as a JSPS Research Fellow. She is currently Assistant professor at Chemical and Biological Engineering Department in Hong Kong University of Science and Technology. Her recent research are focused on developing cell fate controlling RNA machinery and high-performance mRNA drugs.