

Engineered tail sequences for enhanced protein expression of synthetic mRNA

BECKI YI KUANG 旷怡

RNA ENGINEERING AND SOFT MATERIALS LAB

ASSISTANT PROFESSOR

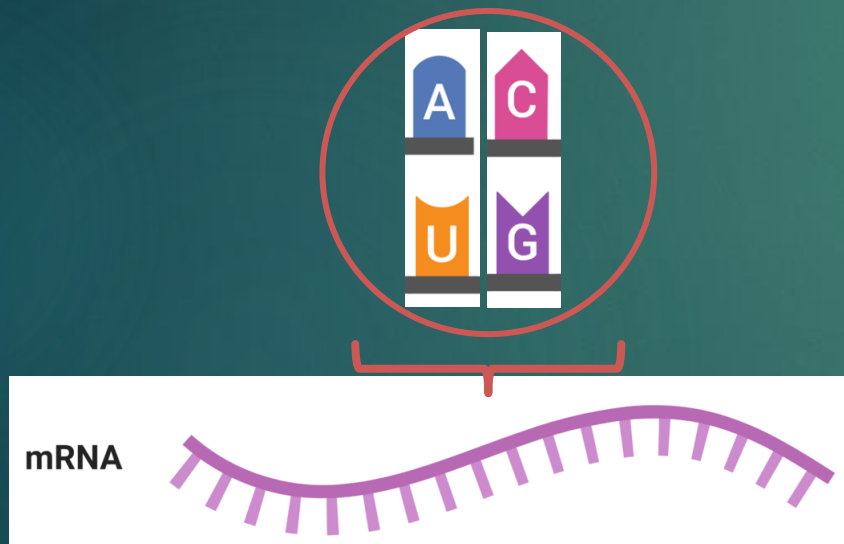
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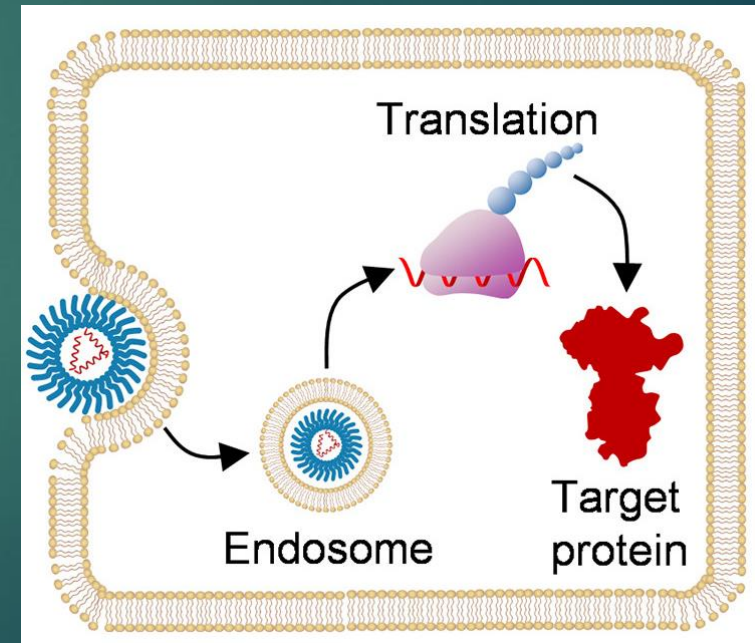
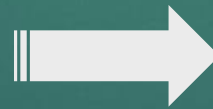


Synthetic mRNA

- ▶ Synthetic mRNAs are mRNAs made in the test tube.
- ▶ After being delivered to cells, synthetic mRNAs act as natural mRNAs to produce protein.



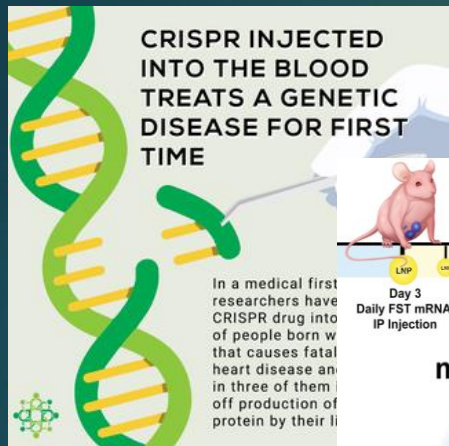
Can produce any protein!



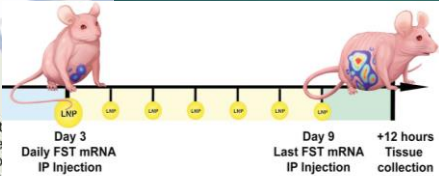
Era of synthetic mRNA-based therapeutics

- ▶ The global mRNA therapeutics market size is expected to continue expanding.

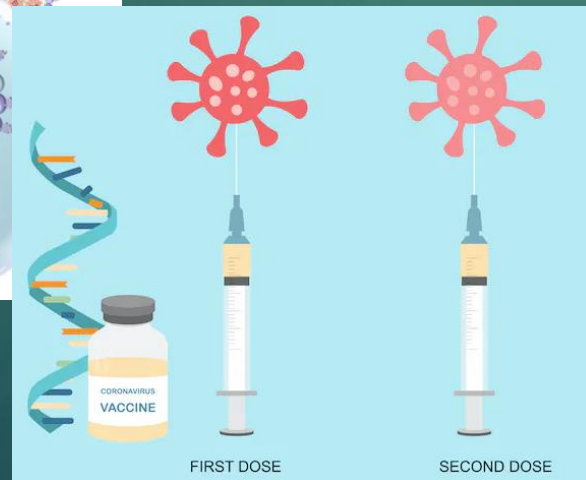
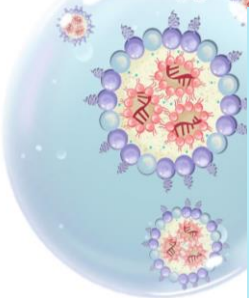
CRISPR INJECTED INTO THE BLOOD TREATS A GENETIC DISEASE FOR FIRST TIME



In a medical first researchers have CRISPR drug into of people born w that causes fatal heart disease an in three of them off production of protein by their li

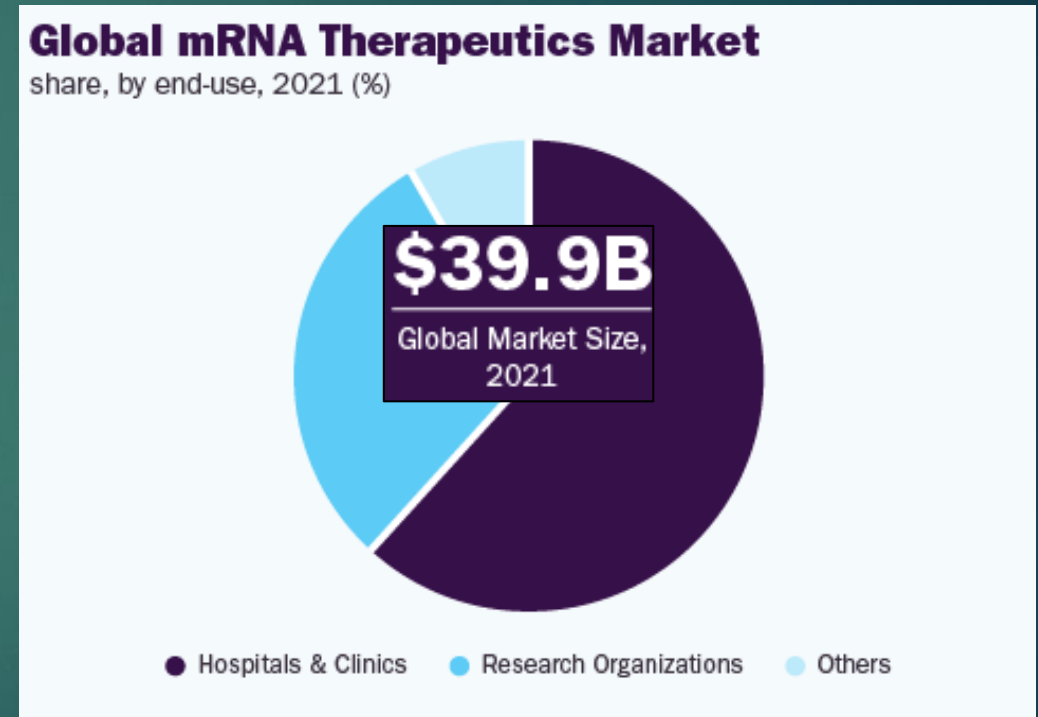


mRNA therapy



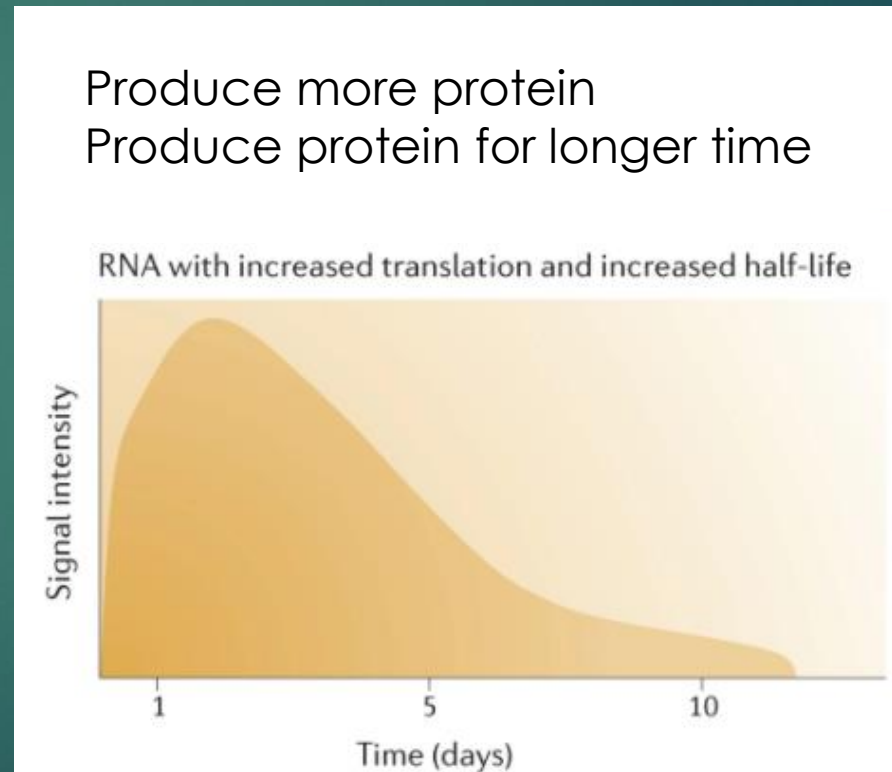
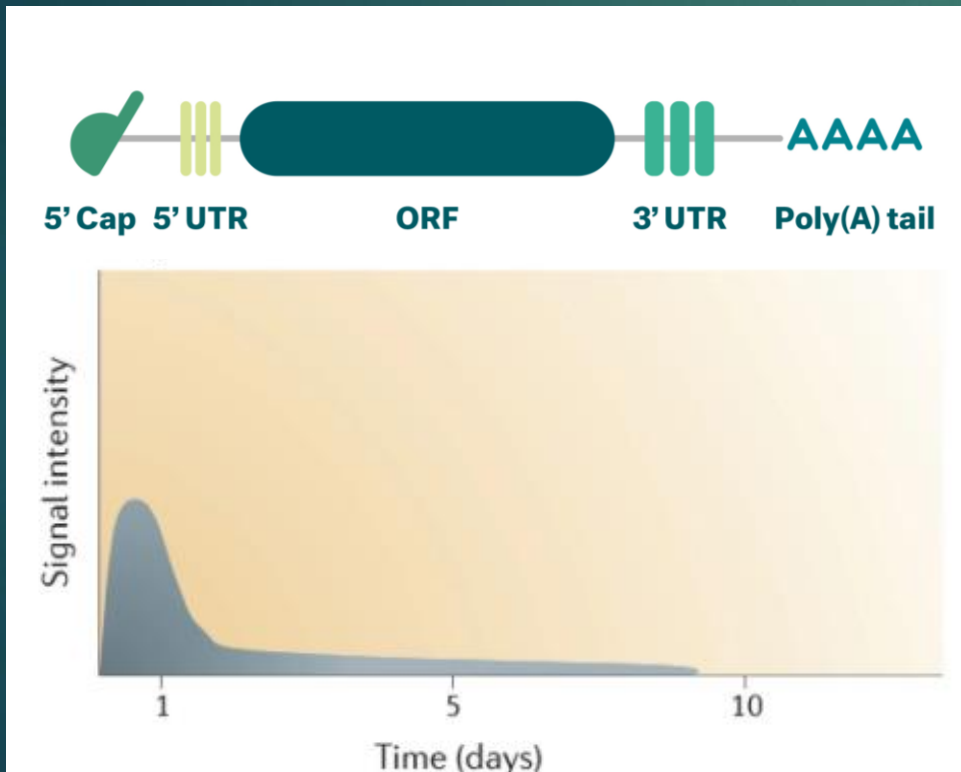
CORONAVIRUS VACCINE

FIRST DOSE SECOND DOSE



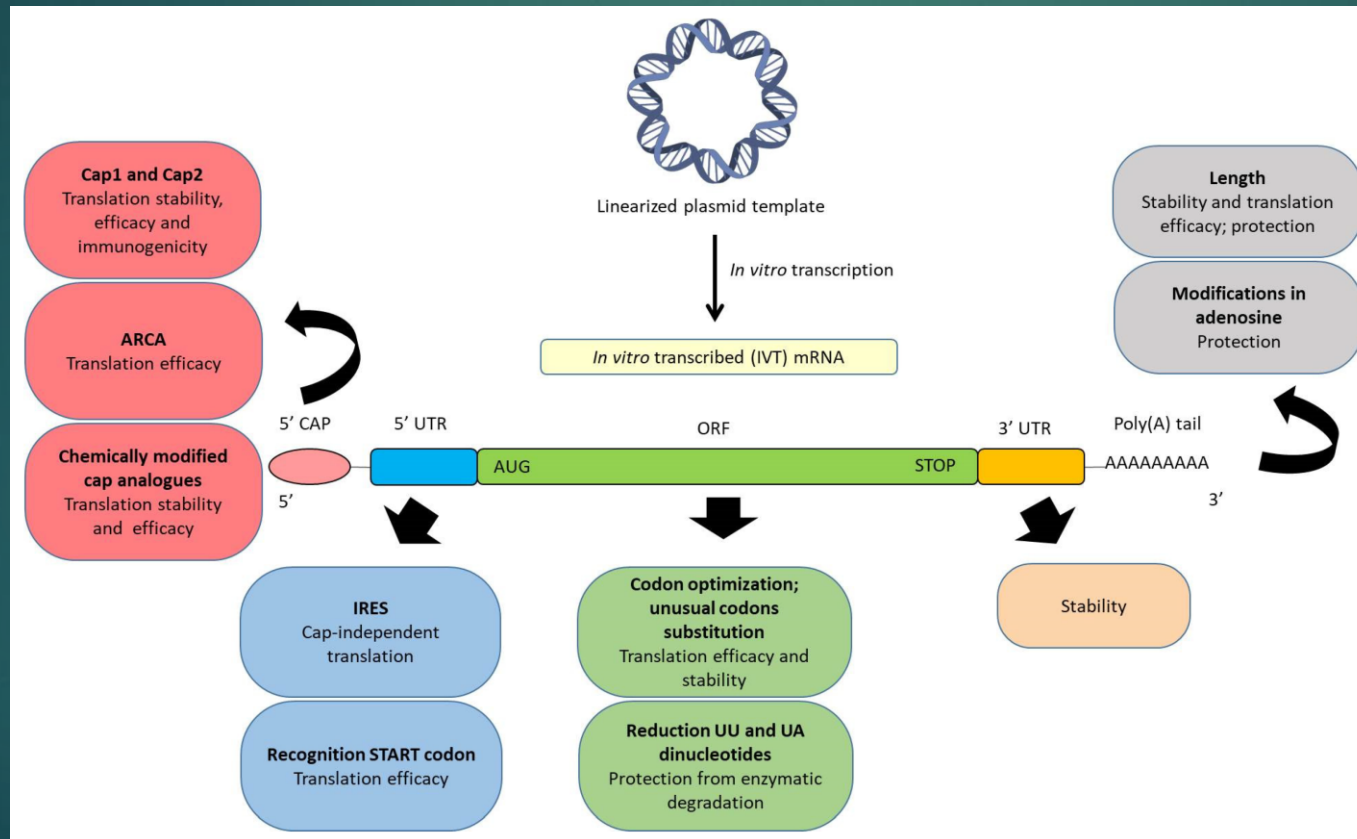
Engineering of synthetic mRNA

- ▶ Goal: optimized the mRNA design to increase and prolong protein production



Engineering of synthetic mRNA: overlooked part

- ▶ Tail gives mRNA its identity: translation cannot happen without the tail.
- ▶ Removal of the tail leads to a degradation of the RNA.

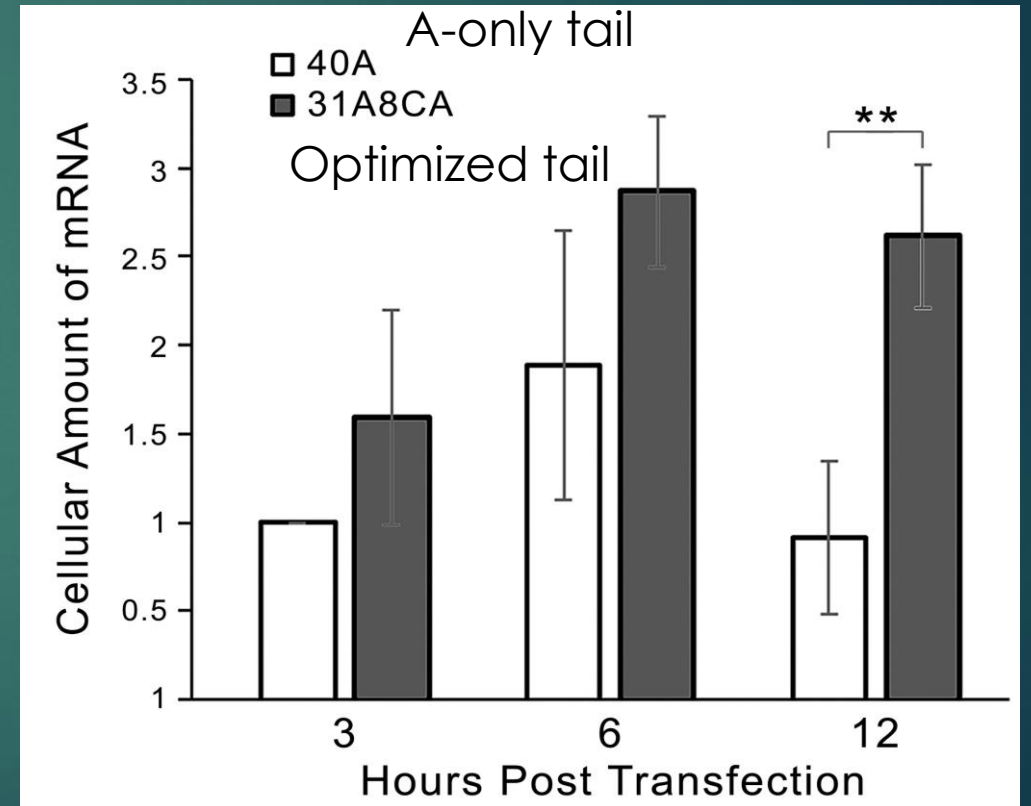
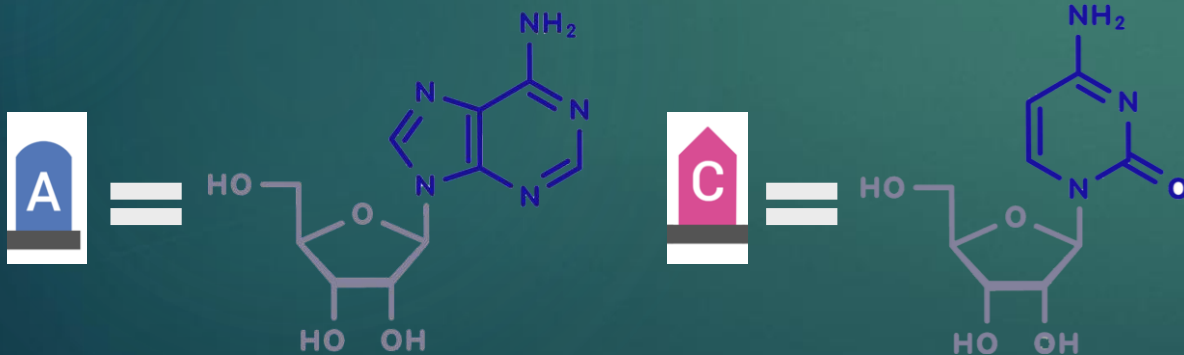


Many natural mRNAs have UGC in their tails.

So why don't we optimize the tail sequence?

Optimized tails slows down mRNA degradation

- ▶ Some enzymes degrade mRNA with optimized tails slower.



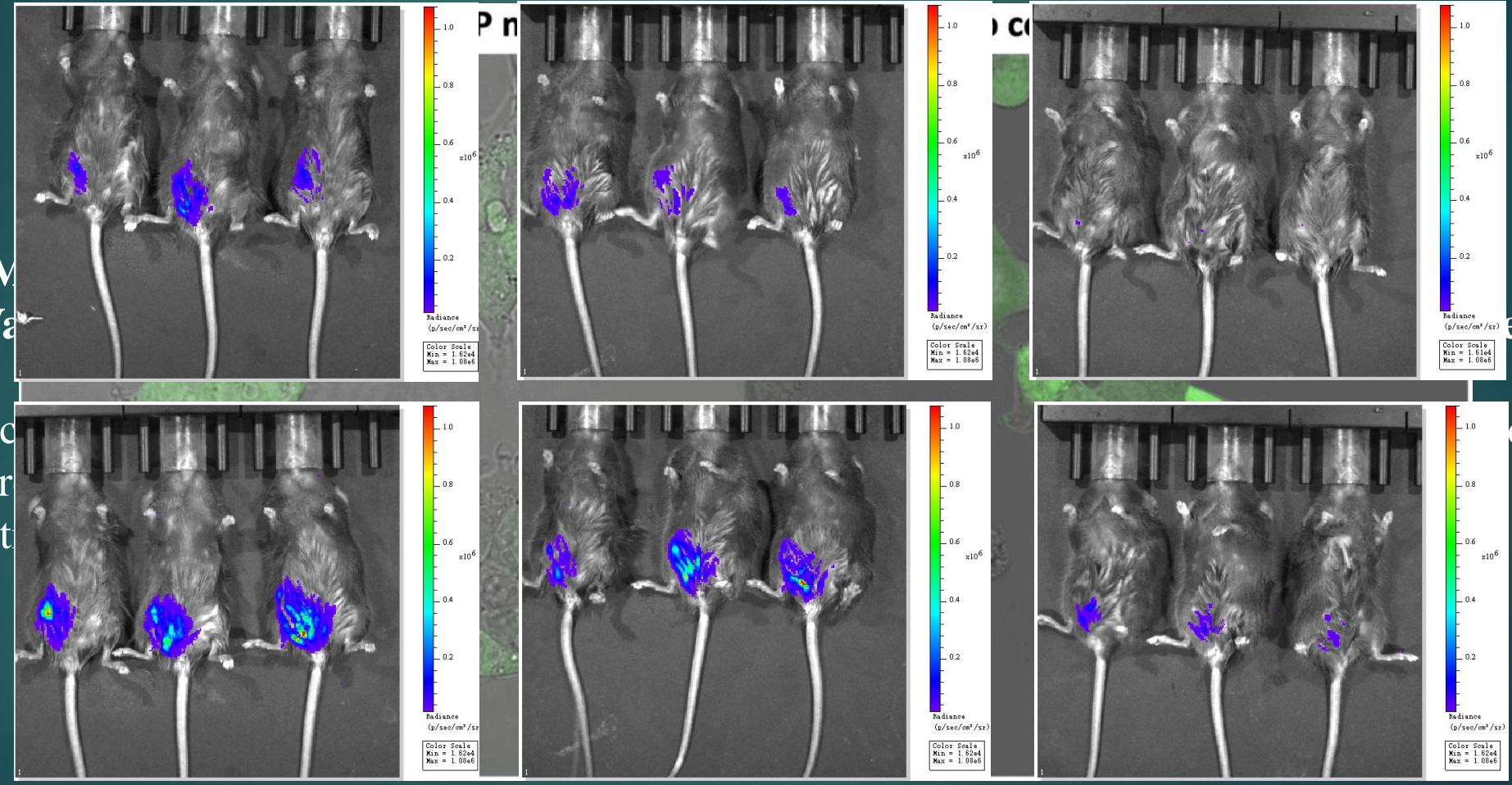
C-tails enable high and stable protein production

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6 hours

24 hours

48 hours

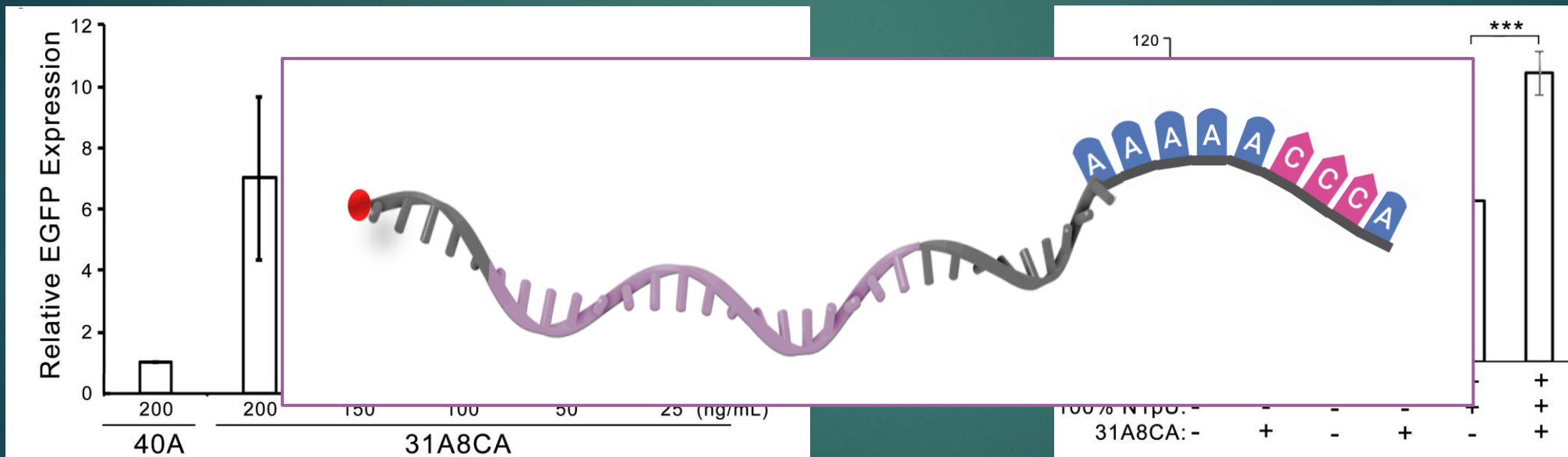


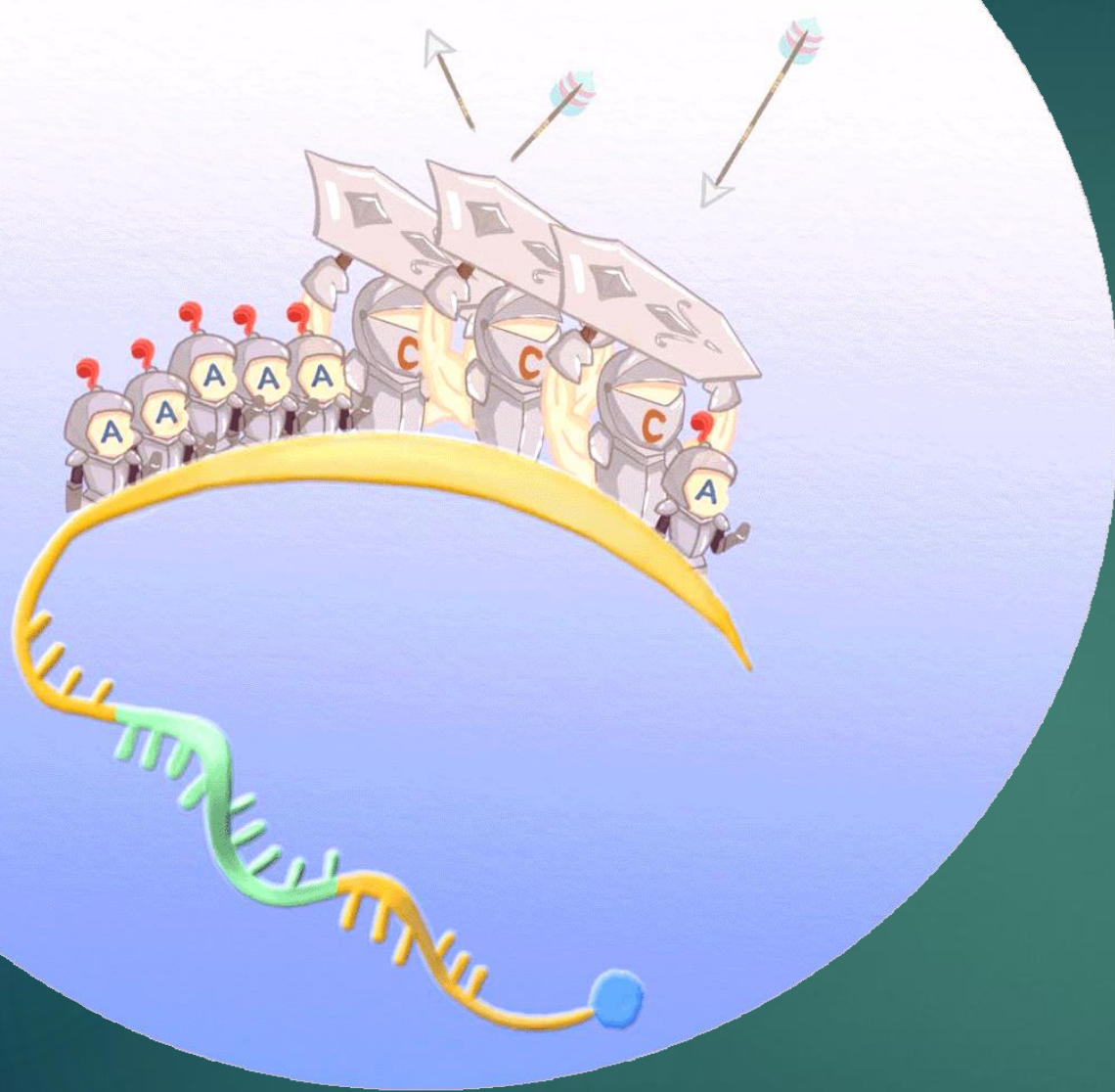
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C-tails can enhance mRNA drugs and vaccines

- ▶ Doesn't no increase synthesis cost.
- ▶ Reduce the dosage of synthetic mRNAs.
- ▶ Can be combined with existing technologies.





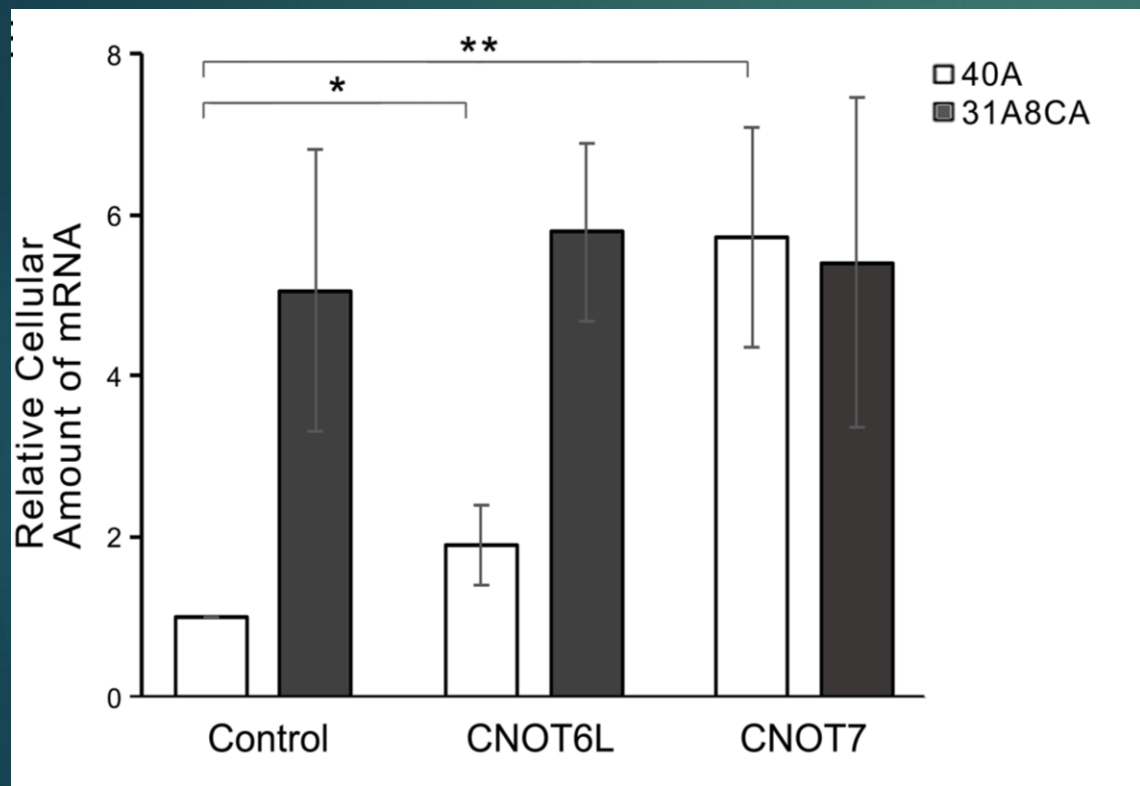
Conclusion

Optimized tail sequence with Cytidine near the end elevate and prolong protein production of synthetic mRNA.

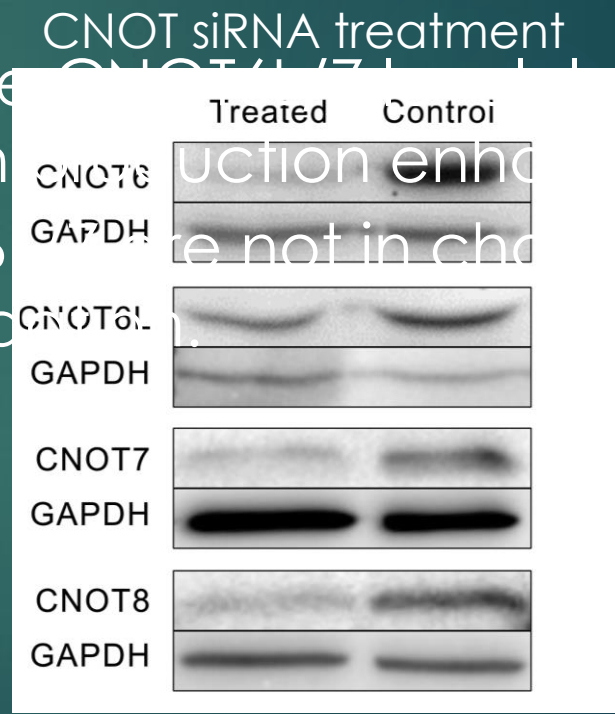
mRNA therapeutics are expected to have stronger and better efficacy.

We envision this technology can reduce the dosage and injection number of mRNA therapeutics.

C-tails slow down mRNA degradation



- ▶ Reduce CNOT6/7 protein levels lower the mRNA stability.
- ▶ CNOT6/7 knockdown is not in charge of C-tail degradation.



What about G?

- ▶ G in the tail triggers immune response during transfection.

