



AP Bio

FRQ Fridays

2022 #6
Post-Transcriptional Modification
& mRNA Half Life



FRQ Friday #18

2022 #6

Researchers are studying the use of RNA vaccines to protect individuals against certain diseases. To develop the vaccines, particular cells are first removed from an individual. Then mRNAs coding for specific proteins from a pathogen are introduced into the cells. The altered cells are injected back into the individual, where the cells make the proteins encoded by the introduced mRNAs. The individual then produces an immune response to the proteins that will help to protect the individual from developing a disease if exposed to the pathogen in the future.

When introduced into cells, the mRNAs used for vaccines must be stable so that they are not degraded before the encoded proteins are produced. Researchers developed several modified caps that they hypothesized might make the introduced mRNAs more stable than mRNAs with the normal GTP cap. To test the effect of the modified caps, the researchers produced mRNAs that differed only in their cap structure (no cap, the normal cap, or modified caps I, II, or III). They introduced the same amount of each mRNA to different groups of cells and measured the amount of time required for half of the mRNAs to degrade (mRNA half-life) and the total amount of protein translated from the mRNAs (Table 1).



TABLE 1. EFFECT OF mRNA CAP STRUCTURE ON mRNA HALF-LIFE AND PROTEIN TRANSLATED FROM THE INTRODUCED mRNA

5' Cap Structure	mRNA Half-Life $\pm 2SE_{\bar{x}}$ (hours after introduction into cells)	Total Amount of Protein Translated from mRNA $\pm 2SE_{\bar{x}}$ (relative to amount in normal cap)
No cap	1.41 ± 0.02	0.011 ± 0.000
Normal GTP cap	16.10 ± 1.83	1.000 ± 0.007
Modified cap I	15.50 ± 1.57	4.777 ± 0.042
Modified cap II	27.00 ± 2.85	13.094 ± 0.307
Modified cap III	18.09 ± 0.81	6.570 ± 0.075



(a) Based on the data, **identify** which cap structure is most likely to protect the end of the mRNAs from degradation.

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● Modified cap II



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(a) Based on the data, **identify** which cap structure is most likely to protect the end of the mRNAs from degradation.

- Modified cap II

Begin your response to question 6 on this page. Do not skip lines.

a) Modified cap II increased the mRNA half life the most and protected the end of the mRNAs from degradation.



(b) Based on the data for the mRNAs with modified caps, describe the relationship between the mRNA half-life and the total amount of protein produced.

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Accept one of the following:

- A longer mRNA half-life is associated with more protein.
- There is a positive correlation/relationship.



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(b) Based on the data for the mRNAs with modified caps, describe the relationship between the mRNA half-life and the total amount of protein produced.

Accept one of the following:

- A longer mRNA half-life is associated with more protein.
- There is a positive correlation/relationship.

b) The greater the mRNA half life, the more protein was translated from the mRNA. Modified cap 1 is a curious outlier, producing almost 5x as much protein despite degrading in a similar (statistically identical) period of time as the normal GTP cap.



(c) After examining the data on mRNA half-lives and the amount of protein produced, the researchers hypothesized that each mRNA molecule with modified cap I was translated more frequently than was each mRNA molecule with the normal GTP cap. Evaluate their hypothesis by comparing the data in Table 1.

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- The data support their hypothesis because the half-lives of the two mRNAs are the same, but the amount of protein produced from the mRNA with modified cap I is more than (four times as much as) that produced from the mRNA with the normal cap.



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- The data support their hypothesis because the half-lives of the two mRNAs are the same, but the amount of protein produced from the mRNA with modified cap I is more than (four times as much as) that produced from the mRNA with the normal cap.

d) The mRNA molecules with the modified cap I degraded in a statistically identical period of time as the mRNA molecules with the normal cap. However, the amount of protein translated from the modified cap I mRNA molecules was greater than that translated from the normal GTP cap molecules. Given that the same amount of mRNA was added to each cell, this suggests that the researchers' hypothesis was correct.



(d) Introduction of mRNAs into cells allows the cells to produce foreign proteins that they might not normally produce. **Explain** why the production of a foreign protein may be more likely from the introduction of mRNA than DNA into cells.

Accept one of the following:

- Protein production from the DNA requires (transcription) factors to initiate transcription.
- Protein production from the mRNA does not depend on (correct posttranscriptional) processing of the pre-mRNA.
- The cells may be unable to transcribe the DNA (while mRNA can be directly translated).



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d) Proteins are produced directly from mRNA. If DNA coding for a specific protein was introduced to a cell, for the protein to be produced, first mRNA must be created. Not only does introducing mRNA reduce the complexity of the operation, but also controls during the transcription and translation process increase the ~~chance~~ likelihood that this gene is not expressed. For instance, the mRNA ~~might be spliced~~ resulting from transcribing the DNA might be spliced, preventing the protein from being produced.

