CLAIMS

We claim:

1. A method of purifying messenger RNA (mRNA), comprising

(a) subjecting an impure preparation comprising *in vitro* synthesized mRNA to a denaturing condition; and

(b) purifying the mRNA from the impure preparation from step (a) by tangential flow filtration;

wherein the mRNA purified from step (b) is substantially free of prematurely aborted RNA sequences and/or enzyme reagents used in *in vitro* synthesis.

2. The method of claim 1, wherein step (a) comprises adding a protein denaturing agent to the impure preparation.

2a. The method of claim 2, wherein step (a) comprises incubating the impure preparation with the protein denaturing agent added at room temperature for ~~about~~ 5 minutes.

3. The method of claim 2 or 2a, wherein the protein denaturing agent is selected from the group consisting of urea, guanidinium thiocyanate, KCl, sodium dodecyl sulfate, sarcosyl, and combination thereof.

4. The method of any one of the preceding claims, wherein step (a) comprises adding urea to the impure preparation to achieve a resulting urea concentration of ~~about~~ 1 M or greater.

5. The method of claim 4, wherein the resulting urea concentration is ~~about~~ 2 M or greater, 3 M or greater, 4 M or greater, 5 M or greater, 6 M or greater, 7 M or greater, 8 M or greater, 9 M or greater, or 10 M or greater.

6. The method of any one of the preceding claims, wherein step (a) comprises adding guanidinium thiocyanate to the impure preparation to achieve a resulting guanidinium thiocyanate concentration of ~~about~~ 4 M or greater.

7. The method of claim 6, wherein the resulting guanidinium thiocyanate concentration is ~~about~~ 4 M or greater, 5 M or greater, 6 M or greater, 7 M or greater, 8 M or greater, 9 M or greater, or 10 M or greater.

8. The method of any one of the preceding claims, wherein step (a) comprises adding KCl to the impure preparation to achieve a resulting KCl concentration of ~~about~~ 1 M or greater.

9. The method of claim 8, wherein the resulting KCl concentration is ~~about~~ 2 M or greater, 3 M or greater, 4 M or greater, or 5 M or greater.

10. The method of any one of the preceding claims, wherein the tangential flow filtration is performed using only aqueous solvents.

11. The method of claim 10, wherein the tangential flow filtration is performed using water as solvent.

12. The method of any one of the preceding claims, wherein the mRNA purified from step (b) contains less than 1% of prematurely aborted RNA sequences and/or enzyme reagents used in *in vitro* synthesis.

13. The method of any one of the preceding claims, wherein the mRNA purified from step (b) contains less than 0.5% of prematurely aborted RNA sequences and/or enzyme reagents used in *in vitro* synthesis.

14. The method of any one of the preceding claims, wherein the mRNA purified from step (b) contains less than 0.1% of prematurely aborted RNA sequences and/or enzyme reagents used in *in vitro* synthesis.

15. The method of any one of the preceding claims, wherein the mRNA purified from step (b) contains undetectable prematurely aborted RNA sequences and/or enzyme reagents used in *in vitro* synthesis as determined by agarose gel electrophoresis or chromatographic methods.

16. The method of any one of the preceding claims, wherein the prematurely aborted RNA sequences comprise less than 15 bases.

17. The method of any one of the preceding claims, wherein the prematurely aborted RNA sequences comprise ~~about~~ 8-12 bases.

18. The method of any one of the preceding claims, wherein the enzyme reagents used in *in vitro* synthesis comprise T7 RNA polymerase, DNAse I, pyrophosphatase, and/or RNAse inhibitor.

19. The method of any one of the preceding claims, wherein the enzyme reagents used in *in vitro* synthesis comprise T7 RNA polymerase.

20. The method of any one of the preceding claims, wherein the tangential flow filtration is performed before a cap and poly-A tail are added to the *in vitro* synthesized mRNA.

21. The method of any one of claims 1-19, wherein the tangential flow filtration is performed after a cap and poly-A tail are added to the *in vitro* synthesized mRNA.

22. The method of any one of claims 1-19, wherein the tangential flow filtration is performed both before and after a cap and poly-A tail are added to the *in vitro* synthesized mRNA.

23. The method of any one of the preceding claims, wherein the *in vitro* synthesized mRNA is greater than ~~about~~ 1 kb, 1.5 kb, 2 kb, 2.5 kb, 3 kb, 3.5 kb, 4 kb, 4.5 kb, or 5 kb in length.

24. The method of any one of the preceding claims, wherein the *in vitro* synthesized mRNA comprises one or more modifications to enhance stability.

25. The method of claim 24, wherein the one or more modifications are selected from modified nucleotide, modified sugar phosphate backbones, 5' and/or 3' untranslated region.

26. The method of any one of claims 1-23, wherein the *in vitro* synthesized mRNA is unmodified.

27. The method of any one of the preceding claims, wherein the mRNA purified from step (b) has an integrity greater than 95%.

28. The method of any one of the preceding claims, wherein the mRNA purified from step (b) has an integrity greater than 98%.

29. The method of any one of the preceding claims, wherein the mRNA purified from step (b) has an integrity greater than 99%.

30. A method for manufacturing messenger RNA (mRNA) comprising:

synthesizing mRNA *in vitro*; and

purifying the *in vitro* synthesized mRNA using a method according to any one of the preceding claims.

~~31. A messenger RNA (mRNA) purified using a method according to any one of the preceding claims.~~