CLAIMS

1. A method of separating a linear polyribonucleotide comprising an aptamer from a plurality of polyribonucleotides comprising a mixture of linear polyribonucleotides and circular polyribonucleotides, the method comprising:

(a) providing a sample comprising the plurality of polyribonucleotides, wherein a subset of the plurality of polyribonucleotides comprise the linear polyribonucleotide comprising the aptamer;

(b) contacting the sample with a reagent that binds to the aptamer; and

(c) separating the linear polyribonucleotide comprising the aptamer bound to the reagent from the plurality of polyribonucleotides.

2. The method of claim 1, wherein the linear polyribonucleotide comprising the aptamer is transcribed from a deoxyribonucleotide encoding the linear polyribonucleotide comprising the aptamer.

3. The method of claim 1, further comprising the step of producing the linear polyribonucleotide comprising the aptamer by attaching the aptamer to the linear polyribonucleotide.

4. A method of separating a linear polyribonucleotide from a plurality of polyribonucleotides comprising a mixture of linear polyribonucleotides and circular polyribonucleotides, the method comprising:

(a) providing a sample comprising the plurality of polyribonucleotides, wherein a subset of the plurality of polyribonucleotides comprise the linear polyribonucleotide;

(b) attaching an aptamer to the linear polyribonucleotide;

(c) contacting the sample with a reagent that binds to the aptamer; and

(d) separating the linear polyribonucleotide comprising the aptamer bound to the reagent from the plurality of polyribonucleotides.

5. The method of claim 3 or 4, wherein attaching the aptamer to the linear polyribonucleotide comprises covalently attaching the aptamer to a 3' or 5' terminus of the linear polyribonucleotide.

6. The method of claim 3 or 4, wherein attaching the aptamer to the linear polyribonucleotide comprises hybridizing the aptamer to a region of the linear polyribonucleotide.

7. The method of any one of claims 1-6, wherein the circular polyribonucleotides lack the aptamer.

8. The method of any one of claims 1-7, wherein the step of separating comprises collecting a portion of the sample that is not bound by the reagent.

9. The method of claim 7 or 8, wherein the portion of the sample that is not bound by the reagent comprises the circular polyribonucleotide.

10. The method of any one of claims 1-9, wherein the reagent is a polypeptide, a small molecule, a lipid, a carbohydrate, an RNA, or a metal.

11. The method of claim 10, wherein:

(a) the reagent is a polypeptide selected from Table 1 or is Protein A, streptavidin, lambda peptide, or MS2 bacteriophage coat protein, and/or the aptamer comprises a nucleic acid sequence selected from any one of SEQ ID NOs: 1-66;
(b) the reagent is a small molecule selected from Table 2 or is biotin or tetracycline, and/or the aptamer comprises a nucleic acid sequence selected from any one of SEQ ID NOs: 67-119;
(c) the reagent is an RNA selected from Table 3, and/or the aptamer comprises a nucleic acid sequence selected from SEQ ID NO: 120 or 121; or
(d) the reagent is a metal selected from Table 4, and/or the aptamer comprises a nucleic acid sequence selected from any one of SEQ ID NOs: 122-124.

12. The method of any one of claims 1-9, wherein the step of separating comprises immobilizing the reagent.

13. The method of claim 10, wherein the reagent is conjugated to a particle, wherein, optionally, the particle comprises a magnetic bead; or wherein the reagent is conjugated to a resin comprising a plurality of the particles.

14. The method of claim 13, wherein a column comprises the resin, and the method comprises contacting the sample with the column and collecting an eluate comprising a portion of the sample that is not bound to the reagent from the plurality of polyribonucleotides in the sample.

15. The method of any one of claims 1-14, wherein the method further comprises, prior to step (a), providing a linear precursor polyribonucleotide and circularizing the linear precursor to produce the circular polyribonucleotide.

16. The method of claim 15, wherein:

(a) the linear precursor comprises a 5' self-splicing intron fragment and a 3' self-splicing intron fragment, and wherein the circular polyribonucleotide is produced by self-splicing of the linear precursor, wherein, optionally the 5' self-splicing intron fragment and the 3' self-splicing intron fragment are each a Group I or Group II self-splicing intron fragment; or
(b) circularizing the circular polyribonucleotide is produced by splint-ligation of the linear precursor.

17. The method of any one of claims 1-16, wherein the step of separating further comprises washing the polyribonucleotide comprising the aptamer that is bound to the reagent one or more times and/or eluting the polyribonucleotide comprising the aptamer from the reagent.

18. The method of any one of claims 1-17, wherein the method comprises providing a plurality of reagents, wherein each reagent binds to a distinct aptamer region.

19. A population of polyribonucleotides produced by the method of any one of claims 1-18.

20. The population of polyribonucleotides of claim 19, wherein the population comprises a circular polyribonucleotide lacking the aptamer and the circular polyribonucleotide comprises at least 40% (mol/mol) of the total polyribonucleotides in the composition; and/or the population comprises less than 40% (mol/mol) linear polyribonucleotides of the total polyribonucleotides in the composition.