

CLAIMS

1. A method of separating a linear polyribonucleotide comprising a target region 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 target region;
 - (b) contacting the sample with an oligonucleotide that hybridizes to the target region; and
 - (c) separating the linear polyribonucleotide comprising the target region that is hybridized to the oligonucleotide from the plurality of polyribonucleotides in the sample.
2. The method of claim 1, wherein the circular polyribonucleotides lack the target region.
3. A method of separating a polyribonucleotide comprising a target region from a plurality of polyribonucleotides, the method comprising:
 - (a) providing a sample comprising the plurality of polyribonucleotides, wherein a subset of the plurality of polyribonucleotides comprise the target region, wherein the target region is not located at a 3' or 5' terminus of the polyribonucleotide comprising the target region;
 - (b) contacting the sample with an oligonucleotide that hybridizes to the target region; and
 - (c) separating the polyribonucleotide comprising the target region that is hybridized to the oligonucleotide from the plurality of polyribonucleotides in the sample.
4. A method of separating a linear polyribonucleotide comprising a target region from a plurality of circular polyribonucleotides comprising the target region, the method comprising:
 - (a) providing a sample comprising the plurality of polyribonucleotides;
 - (b) contacting the sample with an oligonucleotide, wherein the oligonucleotide hybridizes to the target region of the linear polyribonucleotide with a first binding affinity, and wherein the oligonucleotide hybridizes to the target region of the circular polynucleotide with a second binding affinity that is different from the first binding affinity; and
 - (c) separating the linear polyribonucleotide comprising the target region that is hybridized to the oligonucleotide from the plurality of circular polyribonucleotides in the sample.
5. The method of claim 4, wherein the first binding affinity is less than the second binding affinity, and wherein the oligonucleotide preferentially binds the linear polyribonucleotide.
6. A method of separating a polyribonucleotide in a first conformation comprising a target region from a plurality of polyribonucleotides in a second conformation comprising the target region, the method comprising:
 - (a) providing a sample comprising the plurality of polyribonucleotides;
 - (b) contacting the sample with an oligonucleotide, wherein the oligonucleotide hybridizes to the target region of the polynucleotide in the first conformation with a first binding affinity, and wherein the

oligonucleotide hybridizes to the target region of the polynucleotide in the second conformation with a second binding affinity that is different from the first binding affinity; and

(c) separating the polyribonucleotide in the first conformation comprising the target region that is hybridized to the oligonucleotide from the plurality of polyribonucleotides in the second conformation in the sample.

7. The method of claim 6, wherein the first binding affinity is less than the second binding affinity, and wherein the oligonucleotide preferentially binds the polyribonucleotide in the first conformation.

8. The method of any one of claims 1-7, wherein:

(i) step (c) comprises immobilizing the oligonucleotide;

(ii) the target region lacks a polyA sequence; and/or

(iii) the oligonucleotide is conjugated to a particle or a first capture agent, optionally via a linker, wherein, optionally, the linker is triethylene glycol and/or the chemical linker is conjugated to a 3' end or a 5' end of the oligonucleotide.

9. The method of claim 8, wherein the method further comprises providing a second capture agent that binds to the first capture agent, wherein, optionally, the first capture agent comprises an antigen, and the second capture agent comprises an antibody or antigen-binding fragment thereof, wherein optionally, the first capture agent is biotin, and the second capture agent is streptavidin.

10. The method of claim 9, wherein the second capture agent is conjugated to a particle, wherein optionally, the particle is a magnetic particle or a bead.

11. The method of any one of claims 1-10, wherein the polyribonucleotide comprising the target region comprises an intron or portion thereof, wherein, optionally, the target region comprises the intron or portion thereof or wherein the target region is located 5' or 3' to the intron or portion thereof.

12. The method of claim 11, wherein the method comprises separating a spliced polyribonucleotide from a non-spliced or partially spliced polyribonucleotide, wherein, optionally the spliced polyribonucleotide lacks an intron or portion thereof and/or wherein the spliced polyribonucleotide is a circular polyribonucleotide, and the polyribonucleotide comprising the intron or portion thereof is a linear polyribonucleotide.

13. The method of any one of claims 1-12, further comprising washing the captured polyribonucleotide comprising the target region one or more times and/or after step (c), performing a first elution step to release the captured polyribonucleotide comprising the target region.

14. The method of any one of claims 1-13, wherein step (b) comprises collecting a portion of the sample that is not bound by the oligonucleotide.

15. The method of any one of claims 1-14, wherein the method comprises providing a plurality of oligonucleotides, wherein each oligonucleotide hybridizes to a distinct target region.
16. The method of any one of claims 1-15, wherein the oligonucleotide has at least 80%, 85%, 90%, 95%, 97%, 99%, or 100% complementarity to an equal length portion of the target region.
17. A population of polyribonucleotides produced by the method of any one of claims 1-16.
18. A composition comprising a mixture of polyribonucleotides, wherein a first subset of the mixture comprises a circular polyribonucleotide lacking a target region, and a second subset of the plurality of the polyribonucleotides comprises a linear polyribonucleotide comprising the target region, wherein the first subset comprises at least 40% (mol/mol) of the total polyribonucleotides in the composition.
19. A composition comprising a polyribonucleotide comprising a target region and an oligonucleotide configured to hybridize to the target region, wherein the oligonucleotide is conjugated to a first capture agent.
20. The composition of claim 19, further comprising a polyribonucleotide lacking the target region, wherein, optionally, the polyribonucleotide lacking the target region is a circular polyribonucleotide, and/or the target region comprises an intron or portion thereof.