CLAIMS

1. A polyinosinic-polycytidylic acid [poly(I:C)] molecule composition comprising double-stranded polyribonucleotides formed by single-stranded poly(I) and poly(C) molecules, respectively, or a salt and/or solvate thereof, wherein

(a) between 5% and 60%, preferably between 10% and 30%, of the double-stranded polyribonucleotides have less than 400 base pairs;

(b) between 20% and 45% or between 15% and 30%, preferably between 20% and 30%, of the double-stranded polyribonucleotides, have between 400 and 850 base pairs;

(c) between 20% and 70%, preferably between 50% and 60%, of the double-stranded polyribonucleotides have between 850 and 5000 base pairs; and

(d) between 0% and 10%, preferably 1% or less, of the double-stranded polyribonucleotides have more than 5000 base pairs.

2. The composition of claim 1, wherein

(a) between 7% and 57% of the double-stranded polyribonucleotides have less than 400 base pairs;

(b) between 20% and 45% of the double-stranded polyribonucleotides have between 400 and 850 base pairs;

(c) between 20% and 70% of the double-stranded polyribonucleotides have between 850 and 5000 base pairs; and

(d) between 0% and 9% of the double-stranded polyribonucleotides have more than 5000 base pairs.

3. The composition of any one of claim 1-2, further comprising glucose or mannitol.

4. The composition of any one of claim 1-2, wherein the respective poly(I) and poly(C) single-stranded molecules are annealed thereby forming double-stranded poly(I:C) molecules, wherein

(a) the poly(I) molecules comprise:

(i) <400 bases consist of 80-95% poly(I) molecules,

(ii) 400-850 bases consist of 5-20% poly(I) molecules,

(iii) 850-5000 bases consist of 0-5% poly(I) molecules, and

(iv) >5000 bases consist of 1% or less poly(I) molecules; and

(b) the poly(C) molecules comprise:

(i) <400 bases consist of 20-82% poly(C) molecules,

(ii) 400-850 bases consist of 15-40% poly(C) molecules,

(iii) 850-5000 bases consist of 3-50% poly(C) molecules, and

(iv) >5000 bases, consist of 1% or less of poly(C) molecules.

5. A polyinosinic-polycytidylic acid [poly(I:C)] molecule composition comprising double-stranded nucleotides formed by single-stranded poly(I) and poly(C) molecules respectively, or a salt and/or solvate thereof, wherein the composition is obtainable by:

(a) dissolving the poly(I) molecules in PBS to form a first aqueous solution;
(b) dissolving the poly(C) molecules in PBS to form a second aqueous solution;
(c) mixing the first aqueous solution and the second aqueous solution at a 1:1 stoichiometry;
(d) applying the resulting solution containing double-stranded poly(I:C) on a GPC (Gel Permeation Chromatography) column.

6. The polyinosinic-polycytidylic acid [poly(I:C)] molecule composition of claim 5, wherein:
(a) between 7% and 57% of the double-stranded polyribonucleotides have less than 400 base pairs;
(b) between 20% and 45% of the double-stranded polyribonucleotides have between 400 and 850 base pairs;
(c) between 20% and 70% of the double-stranded polyribonucleotides have between 850 and 5000 base pairs; and
(d) between 0% and 9% of the double-stranded polyribonucleotides have more than 5000 base pairs.

7. A method for producing the composition of any one of claim 1-4, comprising:
(a) dissolving the poly(I) molecules in PBS to form a first aqueous solution;
(b) separately dissolving the poly(C) molecules in PBS to form a second aqueous solution;(c) filtering each respective solution obtained from step (a) and step (b) using a membrane;
(d) concentrating each respective permeate obtained for each respective filtration step (c) for each respective solution over a membrane to form a respective retentate for each respective solution;
(e) mixing each respective retentate obtained for each respective the first aqueous solution (a) and the second aqueous solution (b) with a PBS solution;
(f) determining the optical density of each respective retentate obtained in step (e) for each respective solution (a) and (b) and adjusting the total volume to a 1:1 stoichiometry;
(g) combining the respective poly(I) solution with the poly(C) solution obtained at step (e) using heat;
(h) cooling the resulting combined solution to room temperature;
(i) filtering the solution obtained from step (h);
(j) applying the solution obtained from step (i) on a gel permeation column (GPC); and
(k) purifying and desalting the resulting solution.

8. A method for producing the composition of claims 5 or 6, comprising:
(a) dissolving the poly(I) molecules in PBS to form a first solution, wherein
(i) 80-95% poly(I) molecules comprises less than 400 bases,
(ii) 5-20% poly(I) molecules comprises 400-850 bases,
(iii) 0-5% poly(I) molecules comprises 850-5000 bases, and
(iv) 1% or less poly(I) molecules comprises at least 5000 bases;
(b) separately dissolving the poly(C) molecules in PBS to form a second solution, wherein
(i) 20-82% poly(C) molecules comprises less than 400 bases,
(ii) 15-40% poly(C) molecules comprises 400-850 bases,

(iii) 3-50% poly(C) molecules comprises 850-5000 bases, and

(iv) 1% or less of poly(C) molecules comprises at least 5000 bases;

(c) filtering each respective solution obtained from step (a) and step (b) using a membrane;

(d) concentrating each respective permeate obtained for each respective filtration step (c) for each respective solution over a membrane to form a respective retentate for each respective solution;

(e) mixing each respective retentate obtained for each respective solution (a) and (b) with a PBS solution;

(f) determining the optical density of each respective retentate obtained in step (e) for each respective solution (a) and (b) and adjusting the total volume to a 1:1 stoichiometry;

(g) combining the respective poly(I) solution with the poly(C) solution obtained at step (e) using heat;

(h) cooling the resulting combined solution to room temperature;

(i) filtering the solution obtained from step (h);

(j) applying the solution obtained from step (i) on a gel permeation column (GPC); and

(k) purifying and desalting the resulting solution.

9. The method of claim 7 or claim 8, wherein at step (c), the filtering membrane comprises a 300 kDa cut-off or a 500 kDa cut-off.

10. The method of any one of claims 7-9, wherein the filtering step (i) is performed using a G3 glass filter, optionally having a pore size of about 15 µm to 40 µm.

11. The method of any one of claims 7-10, wherein the solution in step (j) is lyophilized at room temperature.

12. The method of any one of claims 7-11, wherein

(a) the poly(C) solution of step (b) is heated to a temperature of between 61°C to 66°C prior to mixing with the poly(I) solution of step (a); and

(b) the combining of step (g) is performed at a temperature of 55°C to 58°C, after which the combined mixture is filtered over a 0.2 µm membrane.

13. The composition obtained by the method of any one of claims 7-12, wherein glucose or mannitol is added to the solution before step (i).

14. The composition of any one of claims 1-6, wherein the respective ply(I) and poly(C) single-stranded molecules are annealed thereby forming double-stranded poly(I:C) molecules.