Filed Amendment

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1. Isolated double-stranded RNA molecule, wherein each RNA strand has a length from 19-23 nucleotides and at least one strand has a 3' overhang from 1-3 nucleotides, wherein said RNA molecule is capable of target-specific RNA interference and one strand of the RNA molecule excluding 3' overhang consists of a sequence with an identity of 100% to the predetermined mRNA target molecule, and wherein the mRNA target molecule is present in a cell or an organism.

2. The RNA molecule of claim 1, wherein each strand has a length from 20-22 nucleotides.

3. The RNA molecule of claim 1 or 2, wherein the 3'-overhang is stabilized against degradation.

4. The RNA molecule of any one of claims 1-3, which contains at least one modified ribonucleotide.

5. The RNA molecule of claim 4, wherein the modified ribonucleotide is selected from sugar-, backbone-, or nucleobase-modified ribonucleotides.

6. The RNA molecule according to claim 4 or 5, wherein the modified ribonucleotide is a sugar-modified ribonucleotide, wherein the 2'-OH group is replaced by a group selected from H, OR, R, halo, SH, SR^1, NH_2, NHR, NR_2 or CN, wherein R is C_1-C_6 alkyl, alkenyl or alkynyl and halo is F, Cl, Br or I.

7. The RNA molecule of claim 4 or 5, wherein the modified ribonucleotide is a backbone-modified ribonucleotide containing a phosphothioate group.

8. A method of preparing a double-stranded RNA molecule of any one of claims 1-7 comprising the steps:

(a) synthesizing two RNA strands each having a length from 19-23 nucleotides, wherein said RNA strands are capable of forming a double-stranded RNA molecule,

(b) combining the synthesized RNA strands under conditions, wherein a double-stranded RNA molecule is formed, which is capable of target specific RNA interference.

9. The method of claim 8, wherein the RNA strands are chemically synthesized.

10. The method of claim 8, wherein the RNA strands are enzymatically synthesized.

11. A method of mediating target-specific RNA interference in an animal cell [~~or an organism (except a human)~~] comprising the steps:

(a) contacting said cell [~~or organism~~] with the double-stranded RNA molecule of any one of claims 1-7 under conditions wherein target-specific RNA interference can occur, and

(b) mediating a target-specific RNA interference effected by the double-stranded RNA towards a target nucleic acid having a sequence portion identical [~~substantially corresponding~~] to the double-stranded RNA.

12. The method of claim 11, wherein said contacting comprises introducing said double-stranded RNA molecule into a target cell in which the target-specific RNA interference can occur.

13. The method of claim 12, wherein the introducing comprises a carrier mediated delivery or injection.

14. Use of the method of any one of claims 11-13 for determining the function of a gene in an animal cell [~~or an organism (except a human)~~].

15. Use of the method of any one of claims 11-13 for inhibiting [~~modulating~~] the function of a gene in an animal cell [~~or an organism (except a human)~~].

16. The use of claim 14 or 15, wherein the gene is associated with a pathological condition.

17. The use of claim 16, wherein the gene is a pathogen-associated gene.

18. The use of claim 17, wherein the gene is a viral gene.

19. The use of claim 16, wherein the gene is a tumor-associated gene.

20. The use of claim 16, wherein the gene is an autoimmune disease associated gene.

21. An animal cell [~~A eukaryotic cell or a eukaryotic non-human organism~~] exhibiting a target gene-specific knockout phenotype wherein said cell [~~or organism~~] is transfected with at least one double-stranded RNA molecule capable of inhibiting the expression of an endogeneous target gene or with a DNA encoding at least one double-stranded RNA

molecule capable of inhibiting the expression of at least one endogeneous target gene, wherein each RNA strand of the double-stranded RNA molecule has a length from 19-23 nucleotides and at least one strand has a 3' overhang from 1-3 nucleotides, and wherein one strand of the RNA molecule excluding 3' overhang consists of a sequence with an identity of 100% to the predetermined mRNA target molecule.

22. The cell [~~or organism~~] of claim 21 which is a mammalian cell.

23. The cell [~~or organism~~] of claim 22 which is a human cell.

24. The cell [~~or organism~~] of any one of claims 21-23 which is further transfected with at least one exogeneous target nucleic acid coding for the target protein or a variant or mutated form of the target protein, wherein said exogeneous target nucleic acid differs from the endogeneous target gene on the nucleic acid level such that the expression of the exogeneous target nucleic acid is [~~substantially~~] less inhibited by the double stranded RNA molecule than the expression of the endogeneous target gene.

25. The cell [~~or organism~~] of claim 24 wherein the exogeneous target nucleic acid is fused to a further nucleic acid sequence encoding a detectable peptide or polypeptide.

26. Use of the cell [~~or organism~~] of any of claims 21-25 for analytic procedures.

27. The use of claim 26 for the analysis of gene expression profiles.

28. The use of claim 26 for a proteome analysis.

29. The use of any one of claims 26-28, wherein an analysis of a variant or mutant form of the target protein encoded by an exogeneous target nucleic acid is carried out.

30. The use of claim 29 for identifying functional domains of the target protein.

31. The use of any one of claims 26-30, wherein a comparison of at least two <u>animal</u> cells [~~or organisms (except a human)~~] is carried out selected from:

(i) a control cell [~~or control organism~~] without target gene inhibition,

(ii) a cell [~~or organism~~] with target gene inhibition and

(iii) a cell [~~or organism~~] with target gene inhibition plus target gene complementation by an exogeneous target nucleic acid.

32. The use of any one of claims 26-31, wherein the analysis comprises a functional and/or phenotypic analysis.

33. Use of the cell [~~or organism~~] of any one of claims 21-25 for preparative procedures.

34. The use of claim 33 for the isolation of proteins or protein complexes from eukaryotic cells.

35. The use of claim 34 for the isolation of high molecular weight protein complexes.

36. The use of claim 35, wherein the high molecular weight protein complexes contain nucleic acids.

37. The use of any one of claims 26-36 in a procedure for identifying and/or characterizing pharmacological agents.

38. A system for identifying and/or characterizing a pharmacological agent acting on at least one target protein comprising:

(a) an animal cell [~~a eukaryotic cell or a eukaryotic non-human organism~~] capable of expressing at least one target gene coding for said at least one target protein,

(b) at least one double-stranded RNA molecule capable of inhibiting the expression of said at least one endogeneous target gene, wherein each RNA strand of the double-stranded RNA molecule has a length from 19-23 nucleotides and at least one strand has a 3' overhang from 1-3 nucleotides, and wherein one strand of the RNA molecule excluding 3' overhang consists of a sequence with an identity of 100% to the predetermined mRNA target molecule, and

(c) a test substance or a collection of test substances wherein pharmacological properties of said test substance or said collection are to be identified and/or characterized.

39. The system of claim 38 further comprising:

(d) at least one exogeneous target nucleic acid coding for the target protein or a variant or mutated from of the target protein wherein said exogeneous target nucleic acid differs from the endogeneous target gene on the nucleic acid level such that the expression of the exogeneous target nucleic acid is [~~substantially~~] less inhibited by the double stranded RNA molecule than the expression of the endogeneous target gene.