

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants: Gregory J. Hannon et al. Confirmation No.: 5718
Application No: 12/152,837 Art Unit: 1635
Filed: May 16,2008 Examiner: K. CHONG
Title: METHODS AND COMPOSITIONS FOR RNA INTERFERENCE

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

AMENDMENT AND RESPONSE TO FINAL OFFICE ACTION

This Amendment is filed in response to the March 18, 2011 Office Action for which a response was due June 18, 2011. Applicants hereby request a three-month extension of time to September 18, 2011. Accordingly, this paper is being timely filed. A Request for Continued Examination accompanies this paper. The Commissioner is authorized to charge any fees due, or to credit any overpayment in fees, to Deposit Account No. 08-0219.

Amendments to the Specification begin on page 2.

Amendments to the Claims begin on page 3.

Amendments to the Drawings begin on page 6.

Remarks begin on page 7.

AMENDMENT

In the Specification

Please amend the paragraph beginning at page 1, line 3, of the specification as filed as follows:

-- This application is a continuation of U.S. Ser. No. 10/055,797, filed on Jan. 22, 2002, the specification of which is a continuation in part of PCT application PCT/US01/08435, filed on Mar. 16, 2001, which claims the benefit of U.S. Provisional applications U.S. Ser. No. 60/189,739, filed on Mar. 16, 2000, and U.S. Ser. No. 60/243,097, filed on Oct. 24, 2000. The specifications of the above-referenced applications are incorporated by reference herein. International Application PCT/US01/08435 was published under PCT Article 21(2) in English.--

In the Claims

Please amend the claims as follows, without prejudice. This listing of the claims will replace all prior versions and listings of claims in the application:

1-47. (Cancelled)

48. (Currently amended) A population of mammalian cells stably transfected or stably transduced with a library of expression constructs, wherein each expression construct encodes a short hairpin RNA, each expression construct comprising:

(i) an RNA polymerase promoter, and

(ii) a sequence encoding a short hairpin RNA molecule comprising a double-stranded region wherein the double-stranded region consists of at least 20 nucleotides but not more than 29 nucleotides,

wherein the short hairpin RNA molecule is a substrate for Dicer-dependent cleavage and does not trigger a protein kinase RNA-activated (PKR) response in the mammalian cells,

wherein the double-stranded region of the short hairpin RNA molecule comprises a sequence that is complementary to a portion of a target gene in the mammalian cells, wherein the target gene is an endogenous gene of the mammalian cells, and

wherein said population of mammalian cells comprises cells in which the short hairpin RNA molecule is stably expressed in an amount sufficient to attenuate expression of the target gene in a sequence specific manner, ~~and is expressed in the cells~~ without use of a PKR inhibitor.

49. (Previously presented) The population of mammalian cells of claim 48, wherein the expression construct further comprises LTR sequences located 5' and 3' of the sequence encoding the short hairpin RNA molecule.

50. (Previously presented) The population of mammalian cells of claim 48, wherein the short hairpin RNA molecule comprises a double-stranded region consisting of at least 21 nucleotides.

51. (Previously presented) The population of mammalian cells of claim 48, wherein the short hairpin RNA molecule comprises a double-stranded region consisting of at least 22 nucleotides.

52. (Previously presented) The population of mammalian cells of claim 48, wherein the short hairpin RNA molecule comprises a double-stranded region consisting of at least 25 nucleotides.

53. (Previously presented) The population of mammalian cells of claim 48, wherein the short hairpin RNA molecule comprises a double-stranded region consisting of 29 nucleotides.

54. (Previously presented) The population of mammalian cells of claim 48, wherein the short hairpin RNA molecule has a total length of about 70 nucleotides.

55. (Previously presented) The population of mammalian cells of claim 48, wherein the RNA polymerase promoter comprises a pol II promoter or a pol III promoter.

56. (Previously presented) The population of mammalian cells of claim 55, wherein the pol III promoter comprises a U6, an H1, or an SRP promoter.

57. (Previously presented) The population of mammalian cells of claim 55, wherein the pol II promoter comprises a U1 or a CMV promoter.

58. (Cancelled)

59. (Cancelled)

60. (Currently amended) A mammalian cell stably transfected or stably transduced with an expression construct encoding a short hairpin RNA molecule, the expression construct comprising:

(i) an RNA polymerase promoter, and

(ii) a sequence encoding a short hairpin RNA molecule comprising a double-stranded region wherein the double-stranded region consists of at least 20 nucleotides but not more than 29 nucleotides,

wherein the short hairpin RNA molecule is a substrate for Dicer-dependent cleavage and does not trigger a protein kinase RNA-activated (PKR) response in the mammalian cell,

wherein the double-stranded region of the short hairpin RNA molecule comprises a sequence that is complementary to a portion of a target gene in the mammalian cell, wherein the target gene is an endogenous gene of the mammalian cell, and

wherein the short hairpin RNA is stably expressed in an amount sufficient to attenuate expression of the target gene in a sequence specific manner, ~~and is expressed in the cell~~ without use of a PKR inhibitor.

61. (Previously presented) The mammalian cell of claim 60, wherein the expression construct further comprises LTR sequences located 5' and 3' of the sequence encoding the short hairpin RNA molecule.

62. (Previously presented) The mammalian cell of claim 60, wherein the short hairpin RNA molecule comprises a double-stranded region consisting of at least 21 nucleotides.

63. (Previously presented) The mammalian cell of claim 60, wherein the short hairpin RNA molecule comprises a double-stranded region consisting of at least 22 nucleotides.

64. (Previously presented) The mammalian cell of claim 60, wherein the short hairpin RNA molecule comprises a double-stranded region consisting of at least 25 nucleotides.

65. (Previously presented) The mammalian cell of claim 60, wherein the short hairpin RNA molecule comprises a double-stranded region consisting of 29 nucleotides.

66. (Previously presented) The mammalian cell of claim 60, wherein the short hairpin RNA molecule has a total length of about 70 nucleotides.

67. (Previously presented) The mammalian cell of claim 60, wherein the RNA polymerase promoter comprises a pol II promoter or a pol III promoter.

68. (Previously presented) The mammalian cell of claim 67, wherein the pol III promoter comprises a U6, an H1, or an SRP promoter.

69. (Previously presented) The mammalian cell of claim 67, wherein the pol II promoter comprises a U1 or a CMV promoter.

70. (Cancelled)

71. (Cancelled)

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