Amendments to the Claims

What is claimed is:

1. (Original) A method for determining efficacy of a cyclodextrin therapy in a subject afflicted with a disorder involving the accumulation of one or more oxysterols, comprising:

(a) obtaining at least one first body fluid sample from the subject prior to administering a cyclodextrin to the subject;

(b) administering the cyclodextrin to the subject;

(c) obtaining at least one second body fluid sample from the subject after the administering the cyclodextrin;

(d) subjecting the at least one first body fluid sample to a first chromatography-mass spectroscopy analysis to determine concentration of 24-hydroxycholesterol;

(e) subjecting the at least one second body fluid sample to a second chromatography-mass spectroscopy analysis to determine concentration of 24-hydroxycholesterol; and

(f) determining magnitude of difference between the 24-hydroxycholesterol concentration of the at least one first body fluid sample and the at least one second body fluid sample, whereby an increase or stabilization of 24-hydroxycholesterol concentration in the second sample compared to the first sample indicates efficacy of the cyclodextrin therapy.

2. (Original) A method in accordance with claim 1, wherein each of the first chromatography-mass spectroscopy analysis and the second chromatography-mass spectroscopy analysis comprises:

(a) adding to the body fluid sample a known amount of an internal standard comprising an oxysterol other than 24(S)-hydroxycholesterol;

(b) isolating 24(S)-hydroxycholesterol from the biological sample; and

(c) quantifying the isolated 24(S)-hydroxycholesterol.

3. (Currently amended) A method in accordance with claim 2, wherein the quantifying 24(S)-hydroxycholesterol comprises determining the relative concentration of 24(S)-hydroxycholesterol and the known amount of internal standard in the body fluid sample by correlating the area under the curve obtained for the 24(S)-hydroxycholesterol with the area under the curve obtained for the internal standard.

4. (Original) A method in accordance with claim 1, wherein the first biological sample and the second biological are each selected from the group consisting of plasma, serum, blood, sputum and amniotic fluid.

5. (Original) A method in accordance with claim 1, wherein the body fluid sample is selected from the group consisting of plasma, serum and blood.

6. (Original) A method in accordance with claim 1, wherein each of the first chromatography-mass spectroscopy analysis and the second chromatography-mass spectroscopy analysis is a liquid chromatography-mass spectroscopy analysis.

7. (Original) A method in accordance with claim 1, wherein the disorder involving the accumulation of an oxysterol is selected from the group consisting of a lysosomal storage disease, a cholesterol trafficking disease, a neurodegenerative disease and a combination thereof.

8. (Original) A method in accordance with claim 1, wherein the disorder involving the accumulation of an oxysterol is selected from the group consisting of Niemann-Pick C (NPC) disease, infantile neuronal ceroid lipofuscinosis, GM1 gangliosidosis ("GM-1"), GM-2 gangliosidosis ("GM-2"), Gaucher's disease and hepatosplenomegaly.

9. (Original) A method in accordance with claim 8, wherein the GM-2 gangliosidosis ("GM-2") is Tay-Sachs disease.

10. (Original) A method in accordance with claim 1, wherein the disorder involving the accumulation of an oxysterol is Niemann-Pick C (NPC) disease.

11. (Withdrawn) A method for determining efficacy of a cyclodextrin therapy in a subject afflicted with a disorder involving the accumulation of one or more oxysterols, comprising:

(a) obtaining at least one first body fluid sample from the subject prior to administering a cyclodextrin to the subject;

(b) administering the cyclodextrin to the subject;

(c) obtaining at least one second body fluid sample from the subject after the administering the cyclodextrin;

(d) subjecting the at least one first body fluid sample to a first chromatography-mass spectroscopy analysis to determine concentration of cholestane-3β,5α,6β-triol.

(e) subjecting the at least one second body fluid sample to a second chromatography-mass spectroscopy analysis to determine concentration of cholestane-3β.5α,6β-triol; and

(f) determining magnitude of difference between the cholestane-3β,5α,6β-triol concentration of the at least one first body fluid sample and the at least one second body fluid sample, whereby a reduction in cholestane-3β.5α,6β-triol concentration in the second sample compared to the first sample indicates efficacy of the cyclodextrin therapy.

12. (Withdrawn) A method in accordance with claim 11, wherein each of the first chromatography-mass spectroscopy analysis and the second chromatography-mass spectroscopy analysis comprises:

(a) adding to the body fluid sample a known amount of an internal standard comprising an oxysterol other than cholestane-3β,5α,6β-triol;

(b) isolating cholestane-3β.5α,6β-triol from the biological sample; and

(c) quantifying the isolated cholestane-3β,5α,6β-triol.

13. (Withdrawn) A method in accordance with claim 12, wherein the quantifying cholestane-3β,5α,6β-triol comprises determining the relative concentration of cholestane-3β,5α,6β-triol and the known amount of internal standard in the body fluid sample by correlating the area under the curve obtained for the cholestane-3β.5α,6β-triol with the area under the curve obtained for the internal standard

14. (Withdrawn) A method in accordance with claim 11, wherein the first biological sample and the second biological are each selected from the group consisting of plasma, serum, blood, sputum and amniotic fluid.

15. (Withdrawn) A method in accordance with claim 11, wherein the body fluid sample is selected from the group consisting of plasma, serum and blood.

16. (Withdrawn) A method in accordance with claim 11, wherein each of the first chromatography-mass spectroscopy analysis and the second chromatography-mass spectroscopy analysis is a liquid chromatography-mass spectroscopy analysis.

17. (Withdrawn) A method in accordance with claim 11, wherein the disorder involving the accumulation of an oxysterol is selected from the group consisting of a lysosomal storage

disease, a cholesterol trafficking disease, a neurodegenerative disease and a combination thereof.

18. (Withdrawn) A method in accordance with claim 11, wherein the disorder involving the accumulation of an oxysterol is selected from the group consisting of Niemann-Pick C (NPC) disease, infantile neuronal ceroid lipofuscinosis, GM1 gangliosidosis ("GM-1"), GM-2 gangliosidosis ("GM-2"), Gaucher's disease and hepatosplenomegaly.

19. (Withdrawn) A method in accordance with claim 18, wherein the GM-2 gangliosidosis ("GM-2") is Tay-Sachs disease.

20. (Withdrawn) A method in accordance with claim 11, wherein the disorder involving the accumulation of an oxysterol is Niemann-Pick C (NPC) disease.

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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
[redacted]	01/06/2013	[redacted]	[redacted]	6469

95830 7590 08/01/2014

[redacted]

EXAMINER	
SHEN, BIN	
ART UNIT	**PAPER NUMBER**
1653	
MAIL DATE	**DELIVERY MODE**
08/01/2014	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. [redacted]	Applicant(s) [redacted]	
	Examiner BIN SHEN	Art Unit 1653	AIA (First Inventor to File) Status No

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTHS FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on 6/24/2014.

☐ A declaration(s)/affidavit(s) under **37 CFR 1.130(b)** was/were filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ An election was made by the applicant in response to a restriction requirement set forth during the interview on _____; the restriction requirement and election have been incorporated into this action.

4)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims*

5)☒ Claim(s) 1-20 is/are pending in the application.

5a) Of the above claim(s) 11-20 is/are withdrawn from consideration.

6)☐ Claim(s) _____ is/are allowed.

7)☒ Claim(s) 1-10 is/are rejected.

8)☐ Claim(s) _____ is/are objected to.

9)☐ Claim(s) _____ are subject to restriction and/or election requirement.

* If any claims have been determined allowable, you may be eligible to benefit from the **Patent Prosecution Highway** program at a participating intellectual property office for the corresponding application. For more information, please see http://www.uspto.gov/patents/init_events/pph/index.jsp or send an inquiry to PPHfeedback@uspto.gov.

Application Papers

10)☐ The specification is objected to by the Examiner.

11)☒ The drawing(s) filed on 3/6/3013 is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

Certified copies:

a)☐ All b)☐ Some** c)☐ None of the:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

** See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)

2) ☐ Information Disclosure Statement(s) (PTO/SB/08a and/or PTO/SB/08b) Paper No(s)/Mail Date _____.

3) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.

4) ☐ Other: _____.

The present application is being examined under the pre-AIA first to invent provisions.

DETAILED ACTION

Status of Claims

Applicant's election **with traverse** of Group I, claims 1-10 in the reply filed on 6/24/2014 is acknowledged. The traversal is based upon the fact that there is no search burden for the Examiner to consider all claims. It is considered not persuasive because the two methods are measuring different/distinct compound which needs different search. Furthermore, a search for publications pertinent to claims of group I is not the same as a search for publications pertinent to claims of group II (see Umetani 2007 who measures 24S-hydroxycholesterol without measuring cholestane-3β, 5α, 6β-triol even though they are both oxysterols).

The restriction requirement is maintained, and is therefore made **FINAL**.

Claims 11-20 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 6/24/2014.

Only claims 1-10 are presented for examination on the merits.

Priority

This application is a CON of 12/385,529 (filed 4/10/2009) PAT 8497122 which claims benefit of 61/071,074 (filed 4/11/2008).

Specification

The continuation data on page 1 of the specification needs to be updated.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-10 are rejected under 35 U.S.C. 101 because the claimed invention is not directed to patent eligible subject matter. Based upon an analysis with respect to the claim as a whole, claims 1-10 are determined to be directed to a law of nature/natural principle. The rationale for this determination is explained below:

In the last few years, the Supreme Court has addressed abstract ideas (*Bilski v. Kappos*, 2010); laws of nature (*Mayo v. Prometheus*, 2012); natural products (*AMP v. Myriad*, 2013). The courts have interpreted the four statutory categories (process; machine; manufacture; composition of matter) to exclude certain subject matter (called "judicial exceptions"): abstract ideas; laws of nature/natural principles; natural phenomena; natural products. "Laws of nature" and "natural phenomena" include natural principles, naturally occurring relations or correlations, etc. Focus is on whether the claim as a whole recites something significantly different than a judicial exception. The following factors are used to weighing evidence toward eligibility (factors a)-f)) or against eligibility (factors g)-k)), wherein factors a) and g) only applicable to product claims while factors b)-f) and h)-k) applicable to all claims:

a) Claim is a product claim reciting something that initially appears to be a natural product, but after analysis is determined to be non-naturally occurring and markedly different in structure from naturally occurring products.

b) Claim recites element(s)/steps in addition to the judicial exception(s) that impose meaningful limits on claim scope, i.e. the element(s)/steps narrow the scope of the claim so that others are not substantially foreclosed from using the judicial exception(s).

c) Claim recites element(s)/steps in addition to the judicial exception(s) that relate to the judicial exception in a significant way, i.e., the element(s)/steps are more than nominally, insignificantly, or tangentially related to the judicial exception(s).

d) Claim recites element(s)/steps in addition to the judicial exception(s) that do more than describe the judicial exception(s) with general instructions to apply or use the judicial exception(s).

e) Claim recites element(s)/steps in addition to the judicial exception(s) that include a particular machine or transformation of a particular article, where the particular machine/transformation implements one or more judicial exception(s) or integrates the judicial exception(s) into a particular practical application. (see MPEP 2106(II)(B)(1)) for an explanation of the machine or transformation factors).

f) Claim recites one or more element(s)/steps in addition to the judicial exception(s) that add a feature that is more than well-understood, purely conventional or routine in the relevant field.

g) Claim is a product claim reciting something that appears to be a natural product that is not markedly different in structure from naturally occurring products.

h) Claim recites element(s)/steps in addition to the judicial exception(s) at a high level of generality such that substantially all practical applications of the judicial exception(s) are covered.

i) Claim recites element(s)/steps in addition to the judicial exception(s) that must be used/taken by others to apply the judicial exception(s).

j) Claim recites element(s)/steps in addition to the judicial exception(s) that are well-understood purely conventional or routine in the relevant field.

k) Claim recites element(s)/steps in addition to the judicial exception(s) that are insignificant extra-solution activity, e.g., are merely appended to the judicial exception(s).

i) Claim recites elements/steps in addition to the judicial exception(s) that amount to nothing more than a mere field of use.

In the instant case, for claim 1, the judicial exception (JE) is the correlation between the measured concentration of 24-hydroxycholesterol and the efficacy of the cyclodextrin therapy. All the steps in claim 1 are data gathering steps that must be taken in order to apply JE itself because no correlation can be made without measuring the concentration of 24-hydroxycholesterol in the sample. These steps (including other steps in the independent claims) are highly general that cover essentially any chromatography-mass spectroscopy method of measuring concentration of 24-hydroxycholesterol (see Umetani, Nature Medicine, 2007, 13(10):1185-1192, page 1191, right column, 1st full paragraph, also page 1186, left column, line 2++). Furthermore, both cyclodextrin (Loftsson, Expert Opin. Drug Deliv., 2005, 2:335-351, page 335, para 2., line 1++) and 24-hydroxycholesterol (as oxidized derivatives of cholesterol as supported by the instant specification, page 5, pare [0025], line 4++) are products of nature that is not markedly different in structure from naturally occurring products. Thus the claim amount to a monopoly on the correlation (in general) itself and therefore is not eligible under 101 [satisfies the above listed factors h-l against eligibility] and the correlation (including data collection) between the measured concentration of 24-hydroxycholesterol and the efficacy of the cyclodextrin therapy is considered reflection of law of nature/natural principle.

Therefore, claims 1-10 do not include steps that are sufficient to ensure that the claims amount to significantly more than the natural principle itself. Additional steps/limitations are needed to integrates the law of nature and transform the claims to a patent-eligible practical application.

Conclusion

No claim is allowed.

Any inquiry concerning rejections or objections in this communication or earlier communications from the examiner should be directed to Bin Shen, whose telephone number is (571) 272-9040. The examiner can normally be reached on Monday through Friday, 9am-5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's

supervisor, Sharmila Landau can be reached at (571) 272-0614.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Bin Shen/

Primary Examiner, Art Unit 1653

AMENDMENTS TO THE CLAIMS

Listing of the Claims:

The listing of claims will replace all prior versions, and listings, of claims in the application:

1. (Currently amended) A composition for interfering with replication of cancer comprising at least one sequence of SEQ ID NO(s): 6-14 ~~SEQ ID NO(s): 1-203~~.

2. (Currently amended) The composition of claim 1 comprising at least one peptide consisting essentially of at least one of SEQ ID NO(s): 6-14 SEQ ID NO(s): 1-203.

3. (Currently amended) The composition of claim 1 comprising a mixture of at least two peptides of SEQ ID NO(s): 6-14 ~~SEQ ID NO(s): 1-27, SEQ ID NO(s): 28-52, SEQ ID NO(s): 53-103, SEQ ID NO(s): 104-148, SEQ ID NO(s): 149-165, and SEQ ID NO(s): 166-203~~.

4. (Currently amended) The composition of claim 1 comprising a protein comprising at least one sequence of SEQ ID NO(s): 6-14 ~~SEQ ID NO(s): 1-203~~.

5. (Original) The composition of claim 1, wherein said composition is for direct or indirect interference with replication of cancer.

6. (Original) The composition of claim 5, wherein said composition is for indirect interference with cancer where the indirect interference is mediated by an immune response.

7. (Currently amended) An isolated or synthesized protein fragment or peptide comprising at least one of SEQ ID NO(s): 6-14 ~~SEQ ID NO(s): 1-203~~ or a sequence sharing at least 70% identity with at least one of SEQ ID NO(s): 6-14 ~~SEQ ID NO(s): 1-203~~.

8. (Currently amended) The isolated or synthesized protein fragment or peptide of claim 7 consisting essentially of a peptide of at least one of SEQ ID NO(s): 6-14 ~~SEQ ID NO(s): 1-203~~.

9. (Currently amended) The isolated or synthesized protein fragment or peptide of claim 7 consisting of at least one of SEQ ID NO(s): 6-14 ~~SEQ ID NO(s): 1-203~~.

10. (Currently amended) A vaccine comprising at least one of SEQ ID NO(s): 6-14 ~~SEQ ID NO(s): 1-27, SEQ ID NO(s): 28-52, SEQ ID NO(s): 53-103, SEQ ID NO(s): 104-148, SEQ ID NO(s): 149-165, and SEQ ID NO(s): 166-203~~ or a sequence sharing at least 70% identity with at

least one of SEQ ID NO(s): 6-14 ~~SEQ ID NO(s): 1-27, SEQ ID NO(s): 28-52, SEQ ID NO(s): 53-103, SEQ ID NO(s): 104-148, SEQ ID NO(s): 149-165, and SEQ ID NO(s): 166-203~~.

11. (Currently amended) A vaccine of claim 10 comprising a mixture of at least two of a sequence of SEQ ID NO(s): 6-14 ~~SEQ ID NO(s): 1-203~~ or a sequence sharing at least 70% identity with a sequence of SEQ ID NO(s): 6-14 ~~SEQ ID NO(s): 1-203~~.

12. (Currently amended) A vaccine of claim 10 directed against cancer in a patient suffering from HIV ~~comprising at least one sequence of SEQ ID NO(s): 104-148 or a sequence sharing at least 70% identity with a sequence of SEQ ID NO(s): 104-148~~.

13. (Currently amended) A vaccine of claim 10 directed against one or more of glioblastoma multiforme, ~~pancreatic cancer,~~ lung cancer, and leukemia~~, colon cancer, colorectal cancer, cervical cancer, and breast cancer~~.

14. (Currently amended) A vaccine of claim 13 directed at least against glioblastoma multiforme cancer ~~comprising a sequence of SEQ ID NO(s): 1-27 or a sequence sharing at least 70% identity with a sequence of SEQ ID NO(s): 1-27~~.

15. (Cancel).

16. (Currently amended) A vaccine of claim 13 directed at least against lung cancer ~~comprising a sequence of SEQ ID NO(s): 53-103 or a sequence sharing at least 70% identity with a sequence of SEQ ID NO(s): 53-103~~.

17. (Currently amended) A vaccine of claim 13 directed at least against leukemia comprising a sequence of SEQ ID NO: 7 ~~SEQ ID NO(s): 149-165~~ or a sequence sharing at least 70% identity with a sequence of SEQ ID NO: 7 ~~SEQ ID NO(s): 149-165~~.

18-19. (Cancel).

20. (Currently amended) A vaccine of claim 10 comprising at least one protein comprising at least one of SEQ ID NO(s): 6-14 ~~SEQ ID NO(s): 1-203~~ or at least one protein fragment comprising at least one of SEQ ID NO(s): 6-14 ~~SEQ ID NO(s): 1-203~~.

21-22. (Cancel).

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APPLICATION NO	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO
[redacted]	07/19/2012	[redacted]	[redacted]	6345

75582 7590 06/17/2014

[redacted]

EXAMINER	
HOLSEN, AGNIESZKA	
ART UNIT	PAPER NUMBER
1648	

NOTIFICATION DATE	DELIVERY MODE
06/17/2014	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

[redacted]

Office Action Summary	Application No. [redacted]	Applicant(s) [redacted]	
	Examiner AGNIESZKA BOESEN	Art Unit 1648	AIA (First Inventor to File) Status No

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTHS FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *May 27, 2014*.

☐ A declaration(s)/affidavit(s) under **37 CFR 1.130(b)** was/were filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ An election was made by the applicant in response to a restriction requirement set forth during the interview on _____; the restriction requirement and election have been incorporated into this action.

4)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims*

5)☒ Claim(s) *1-14,16,17 and 20* is/are pending in the application.

5a) Of the above claim(s) _____ is/are withdrawn from consideration.

6)☐ Claim(s) _____ is/are allowed.

7)☒ Claim(s) *1-14,16,17 and 20* is/are rejected.

8)☐ Claim(s) _____ is/are objected to.

9)☐ Claim(s) _____ are subject to restriction and/or election requirement.

* If any claims have been determined allowable, you may be eligible to benefit from the **Patent Prosecution Highway** program at a participating intellectual property office for the corresponding application. For more information, please see http://www.uspto.gov/patents/init_events/pph/index.jsp or send an inquiry to PPHfeedback@uspto.gov.

Application Papers

10)☐ The specification is objected to by the Examiner.

11)☒ The drawing(s) filed on *12/6/2012* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

Certified copies:

a)☐ All b)☐ Some** c)☐ None of the:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

** See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)

2) ☒ Information Disclosure Statement(s) (PTO/SB/08a and/or PTO/SB/08b) Paper No(s)/Mail Date *8/13/2013*.

3) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date _____.

4) ☐ Other: _____.

The present application is being examined under the pre-AIA first to invent provisions.

DETAILED ACTION

This Office action is in response to Applicant's election on 5/27/2014.

Election/Restrictions

Applicant's election of group I, claims 1-20 and SEQ ID NO: 6-11 is acknowledged. Applicant canceled claims 15, 18-19, 21 and 22. Claims 1-14, 16-17 and 20 are under examination in this Office action.

Information Disclosure Statement

The information disclosure statement (IDS) submitted on 8/13/2013 are in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-14, 16-17 and 20 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

The claims are directed to naturally occurring peptides derived from Brown Norway Rat. Those peptides even when isolated from their natural state are identical to the peptides or proteins found in nature. Gibbs et al. (Nature, 2004, Vol. 428. p. 493-521) and accession number F1MAT1_RAT disclose rat sequence comprising present SEQ ID NO: 6 and SEQ ID NO: 7 (see sequence alignment below. It is noted that fragments consisting of SEQ ID NO: 6 are also

considered non-statutory subject matter because they are identical with the naturally occurring fragments. Also "mixture of two or more peptides" is considered naturally occurring because the peptides in the mixture are naturally occurring. See Association for Molecular Pathology v. Myriad Genetics Inc., 133 SCt 2107, 106 USPQ2d 1972 (U.S. 2013).

Present SEQ ID NO: 6 also comprising SEQ ID NO: 7 and Accession number FIMAT1_RAT

```
Query Match             100.0%;  Score 47;  DB 64;  Length 48;
  Best Local Similarity   100.0%;
  Matches    8;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps
0;

Qy           1 HKEHKKDK 8
               ||||||||
Db          18 HKEHKKDK 25
```

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112(a):

> (a) IN GENERAL.—The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same, and shall set forth the best mode contemplated by the inventor or joint inventor of carrying out the invention.

The following is a quotation of the first paragraph of pre-AIA 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same, and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-14, 16-17 and 20 are rejected under 35 U.S.C. 112(a) or 35 U.S.C. 112 (pre-AIA), first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable

IN THE CLAIMS:

This listing of claims will replace all prior versions and listings of claims in the application:

1. Cancelled.

2. (Withdrawn) An isolated nucleic acid sequence coding for a polypeptide which comprises an amino acid sequence identified as SEQ ID NO: 4, or an amino acid sequence wherein one or two amino acid residues have been removed, substituted or added to the sequence identified as SEQ ID NO: 4, and wherein property of inducing an immune response against ectoparasites in fish is maintained.

3. (Original) An isolated polypeptide which comprises the amino acid sequence identified as SEQ ID NO: 4.

4. (Currently Amended) A composition comprising SEQ ID NO: 4, or a polypeptide with an amino acid sequence at least ~~70%~~ 80% identical to the full length sequence identified as SEQ ID NO: 4.

5. (Cancelled)

6. (Withdrawn) A method for inducing an immune response in fish against different ectoparasite species, and/or reducing the number of said parasites in the fish, said method comprising administering an effective amount of a composition comprising SEQ ID NO: 4 to the fish.

7. (Withdrawn) The method according the claim 6, wherein the composition is administered by injection at doses ranging between 0.1-10 μg/g of body weight of the fish.

8. (Withdrawn) The method according to claim 6, wherein the composition is administered in feed formulations at doses ranging between 0.1-300 µg/g of feed.

9. (Withdrawn) The method according to claim 6, wherein the vaccine composition is administered by immersion baths at doses ranging between 0.01-1 mg/l of water.

10. (Cancelled)

11. (Currently Amended) A fusion polypeptide comprising an isolated polypeptide consisting of the amino acid sequence identified as SEQ ID NO: 4, or an amino acid sequence at least ~~70%~~ 80% identical to the full length sequence identified as SEQ ID NO: 4, and a peptide that enhances the antigenic properties of said sequence in a composition for the induction of immune response in fish against different ectoparasite species, and/or reduction of the number of parasites in the fish, wherein the peptide that enhances the antigenic properties comprises a promiscuous T cell epitope.

12. (Cancelled)

13. (Withdrawn) The method according to claim 6, wherein said fish is a salmonid.

14-15. (Cancelled)

16. (Withdrawn) A vector comprising the isolated nucleic acid sequence according to claim 2.

17-32. Cancelled.

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APPLICATION NO	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
[redacted]	04/09/2013	[redacted]	[redacted]	7325

23869 7590 07/08/2014

[redacted]

EXAMINER
TONGUE, LAKIA J

ART UNIT	PAPER NUMBER
1645	

MAIL DATE	DELIVERY MODE
07/08/2014	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. [redacted]	Applicant(s) [redacted]	
	Examiner LaKia Tongue	Art Unit 1645	AIA (First Inventor to File) Status No

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTHS FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *3/24/14*.

☐ A declaration(s)/affidavit(s) under **37 CFR 1.130(b)** was/were filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ An election was made by the applicant in response to a restriction requirement set forth during the interview on _____; the restriction requirement and election have been incorporated into this action.

4)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims*

5)☒ Claim(s) *2-4,6-9,11,13 and 16* is/are pending in the application.

5a) Of the above claim(s) *2,6-9,13 and 16* is/are withdrawn from consideration.

6)☐ Claim(s) _____ is/are allowed.

7)☒ Claim(s) *3,4 and 11* is/are rejected.

8)☐ Claim(s) _____ is/are objected to.

9)☐ Claim(s) _____ are subject to restriction and/or election requirement.

* If any claims have been determined allowable, you may be eligible to benefit from the **Patent Prosecution Highway** program at a participating intellectual property office for the corresponding application. For more information, please see http://www.uspto.gov/patents/init_events/pph/index.jsp or send an inquiry to PPHfeedback@uspto.gov.

Application Papers

10)☒ The specification is objected to by the Examiner.

11)☒ The drawing(s) filed on *4-9/13* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

Certified copies:

a)☒ All b)☐ Some** c)☐ None of the:

1.☐ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. 12/601,974.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

** See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)

2) ☐ Information Disclosure Statement(s) (PTO/SB/08a and/or PTO/SB/08b) Paper No(s)/Mail Date _____.

3) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.

4) ☐ Other: _____.

thereof, the skilled artisan could not immediately recognize or distinguish members of the claimed genus. Therefore, because the art is unpredictable, in accordance with the Guidelines, the description of a particular derivative is not deemed representative of the genus of immunogenic compositions to which the claims refer and hence do not meet the written description requirements

New Grounds of Rejection

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

7. Claims 3 and 4 are rejected under 35 U.S.C. 101 because the claimed invention is not directed to patent eligible subject matter. Based upon an analysis with respect to the claim as a whole, claim(s) 3 and 4 do not recite something significantly different than a judicial exception. The rationale for this determination is explained below:
Claim 3 is drawn to an isolated polypeptide which comprises the amino acid sequence identified as SEQ ID NO: 4. Claim 4 is drawn to a composition comprising SEQ ID NO: 4, or a polypeptide with an amino acid sequence at least 80% identical to the full length sequence identified as SEQ ID NO: 4. The claims are drawn to an isolated polypeptide which appear to be a naturally-occurring polypeptide or fragment thereof, whether isolated or not, said polypeptide is not patent-eligible pursuant to the Supreme Court decision in *Association for Molecular Pathology v. Myriad Genetics, Inc.*, --U.S.--(June 13, 2013).

AMENDMENTS TO THE CLAIMS:

Claims 126-141 are canceled without prejudice or disclaimer. Claims 142-161 are added. The following is the status of the claims of the above-captioned application, as amended.

Claims 1-141 (Canceled).

Claim 142 (New). A method of providing color clarification of laundry, comprising treating the laundry with a soaking, washing or rinsing liquor comprising a polypeptide having cellulase activity selected from the group consisting of:

(a) a polypeptide encoded by a nucleic acid sequence with hybridizes with SEQ ID NO: 7, 9, 13, 15, 21, or 25 carried out in 2 x SSC, 5 x Denhardt's solution, 0.5% (w/v) SDS, 100 micrograms/ml denatured salmon sperm DNA for 20 h at 65°C followed by washes in 5 x SSC at 25°C (2 x 15 minutes), 2 x SSC, 0.5% SDS at 65°C (30 minutes), 0.2 x SSC, 0.5% SDS at 65°C (30 minutes) and finally in 5 x SSC (2 x 15 minutes) at 25°C;

(b) a polypeptide having an amino acid sequence which has a degree of identity of at least 90% with SEQ ID NO: 8, 10, 14, 16, 22, or 26, wherein the degree of identity is determined by means of GAP provided in the GCG program package using settings of a GAP creation penalty of 3.0 and GAP extension penalty of 0.1; and

(c) a fragment of SEQ ID NO: 12.

Claim 143 (New). The method of claim 142, wherein the polypeptide has endoglucanase activity.

Claim 144 (New). The method of claim 143, wherein the polypeptide has a degree of identity of at least 90% with SEQ ID NO: 8.

Claim 145 (New). The method of claim 143, wherein the polypeptide comprises the amino acid sequence of SEQ ID NO: 8.

Claim 146 (New). The method of claim 143, wherein the polypeptide has a degree of identity of at least 90% with SEQ ID NO: 10.

Claim 147 (New). The method of claim 143, wherein the polypeptide comprises the amino acid sequence of SEQ ID NO: 10.

Claim 148 (New). The method of claim 143, wherein the polypeptide has a degree of identity of at least 90% with SEQ ID NO: 14.

Claim 149 (New). The method of claim 143, wherein the polypeptide comprises the amino acid sequence of SEQ ID NO: 14.

Claim 150 (New). The method of claim 143, whereln the polypeptide has a degree of identity of at least 90% with SEQ ID NO: 16.

Claim 151 (New). The method of claim 143, wherein the polypeptide comprises the amino acid sequence of SEQ ID NO: 16.

Claim 152 (New). The method of claim 143, wherein the polypeptide has a degree of identity of at least 90% with SEQ ID NO: 22.

Claim 153 (New). The method of claim 143, wherein the polypeptide comprises the amino acid sequence of SEQ ID NO: 22.

Claim 154 (New). The method of claim 143, wherein the polypeptide has a degree of identity of at least 90% with SEQ ID NO: 26.

Claim 155 (New). The method of claim 143, wherein the polypeptide comprises the amino acid sequence of SEQ ID NO: 26.

Claim 156 (New). The method of claim 143, wherein the polypeptide is a fragment of SEQ ID NO: 12.

Claim 157 (New). The method of claim 142, wherein the laundry is treated in a washing machine.

Claim 158 (New). The method of claim 142, wherein the polypeptide is present in the soaking, washing, or rinsing liquor in an amount of between 1 and 1000 S-CEVU per liter of liquor during machine cycle use conditions.

Claim 159 (New). The method of claim 142, wherein the pH of the soaking, washing, or rinsing liquor is between 6 and 10.5.

Claim 160 (New). The method of claim 142, wherein the temperature is between 15°C and 60°C.

Claim 161 (New). The method of claim 142, wherein the soaking, washing or rinsing liquor further comprises one or more enzymes selected from the group consisting of proteases, cellulases, xylanases, amylases, lipases, peroxidases and laccases.

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APPLICATION NO	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO	CONFIRMATION NO
[redacted]	11/21/2012	[redacted]	[redacted]	9432

25908 7590 06/30/2014

[redacted]

EXAMINER	
ROBINSON, HOPE A	

ART UNIT	PAPER NUMBER
1652	

NOTIFICATION DATE	DELIVERY MODE
06/30/2014	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

[redacted]

Office Action Summary	Application No. [redacted]	Applicant(s) [redacted]	
	Examiner HOPE ROBINSON	Art Unit 1652	AIA (First Inventor to File) Status No

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTHS FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *3/26/14*.

☐ A declaration(s)/affidavit(s) under **37 CFR 1.130(b)** was/were filed on _____.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ An election was made by the applicant in response to a restriction requirement set forth during the interview on _____; the restriction requirement and election have been incorporated into this action.

4)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims*

5)☒ Claim(s) *142-161* is/are pending in the application.

5a) Of the above claim(s) _____ is/are withdrawn from consideration.

6)☐ Claim(s) _____ is/are allowed.

7)☒ Claim(s) *142-156 and 159-161* is/are rejected.

8)☒ Claim(s) *157-158* is/are objected to.

9)☐ Claim(s) _____ are subject to restriction and/or election requirement.

* If any claims have been determined allowable, you may be eligible to benefit from the **Patent Prosecution Highway** program at a participating intellectual property office for the corresponding application. For more information, please see http://www.uspto.gov/patents/init_events/pph/index.jsp or send an inquiry to PPHfeedback@uspto.gov.

Application Papers

10)☐ The specification is objected to by the Examiner.

11)☒ The drawing(s) filed on *11/21/12* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

Certified copies:

a)☐ All b)☐ Some** c)☐ None of the:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

** See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)

2) ☐ Information Disclosure Statement(s) (PTO/SB/08a and/or PTO/SB/08b) Paper No(s)/Mail Date _____.

3) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.

4) ☐ Other: _____.

DETAILED ACTION

Application Status

1. Applicant's response filed on March 26, 2014, is acknowledged. The terminal disclaimers filed have been approved by the Office.

Claim Disposition

2. Claims 1-141 have been canceled. Claims 142-161 have been added and are pending. Claims 142-161 are under examination.

Claim Objection

3. Claims 142,144, 146, 148, 150, 152, 154 and 157-158 are objected to because of the following informalities:

For clarity and precision of claim language it is suggested that claims 142,144,

146, 148, 150, 152 and 154 are amended to read, "...the polypeptide has [[a degree of identity of]] at least 90% sequence identity [[with]] to SEQ ID NO: ...".

Claims 157-158 are objected to as depending from a rejected base claim.

Correction is required.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

4. Claims 142-156 and 159-161 are rejected under 35 U.S.C. 101 because the claimed invention is not directed to patent eligible subject matter.

Based upon the guidance put forth in the *2014 Procedure for Subject Matter Eligibility Analysis of Claims Reciting Or Involving Laws of Nature/Natural Principles, Natural Phenomena, And/Or Natural products* ("Procedure") with respect to the claim as a whole, claims 142-161 do not recite something significantly different than a judicial exception. The rationale for this determination is explained below.

The claimed invention is directed to "a method of providing color clarification of laundry, comprising **treating the laundry with a soaking, washing or rinsing liquor comprising a polypeptide having cellulase activity** selected from the group consisting of:

(a) a polypeptide encoded by a nucleic acid sequence with hybridizes with SEQ ID NO:

7, 9, 13, 15, 21, or 25 carried out in 2 x SSC, 5 x Denhardt's solution, 0.5% (w/v) SDS, 100 micrograms/ml denatured salmon sperm DNA for 20 h at 65°C followed by washes in 5 x SSC at 25°C (2 x 15 minutes), 2 x SSC, 0.5% SDS at 65°C (30 minutes), 0.2 x SSC, 0.5% SDS at 65°C (30 minutes) and finally in 5 x SSC (2 x 15 minutes) at 25°C; (b) a polypeptide having an amino acid sequence which has a degree of identity of at least 90% with SEQ ID NO: 8, 10, 14, 16, 22, or 26, wherein the degree of identity is determined by means of GAP provided in the GCG program package using settings of a GAP creation penalty of 3.0 and GAP extension penalty of 0.1; and
(c) a fragment of SEQ ID NO: 12. The claimed invention encompasses products that appear to be naturally occurring and there are no indicia in the claims representing a product that markedly differs from the naturally occurring product.

There are several Factors to consider that weigh against eligibility, however, only the pertinent ones are provided herein:

Factor (c) is not met, and is directed to whether the claims recite elements/steps in addition with the judicial exception(s) that relate to the judicial exception in a significant way such that the elements/steps are more than nominally, insignificantly or tangentially related to the judicial exception. The instant method recites one step, 'treating' and the single step of treating does not impact the judicial exception. In claim 142 the method recites treating the laundry with a soaking, washing or rinsing liquor comprising a polypeptide, there is no change to the structure of the polypeptide, no requirement of direct contact of the polypeptide with the laundry and no indication of the

polypeptide being mixed or combined in such a way to alter the naturally occurring polypeptide. The specification identifies the polypeptide as being obtained from natural microorganisms (see page 83 for example). Factor (g) pertains to a product that appears to be a natural product that is not markedly different in structure from the naturally occurring product, however, Factor "g" is not relevant because the claims are directed to processes. Factor (h) addresses the fact that the claim recites elements/steps in addition to the judicial exception(s) at a high level of generality such that substantially all practical applications of the judicial exception(s) are covered. Factor "h" is not informative because while the claims are limited to the use of an enzyme in a method that treats laundry with a liquor comprising the enzyme, the claimed technique is recited at a very high level of generality in that it broadly encompasses the use of any protein encoded by a DNA that hybridizes with the recited structures in the claim and the treating step involves soaking, washing or a rinsing liquor which does not appear to alter the structure of the product in any way. For example, the instant specification discloses the following at page 58,

The DNA sequence of the cDNA encoding the endoglucanase from *Myceliophthora thermophila* is SEQ ID NO: 1 and the corresponding amino acid sequence is SEQ ID NO: 2. The cDNA is obtainable from the plasmid in DSM 9770. The DNA sequence of the cDNA encoding the endoglucanase from *Acremonium sp.* is SEQ ID NO: 7 and the corresponding amino acid sequence is SEQ ID NO: 8. The cDNA is obtainable from the plasmid in DSM 10082. The DNA sequence of the cDNA encoding the endoglucanase from *Thielavia terrestris* is SEQ ID NO: 11 and the corresponding amino acid sequence is SEQ ID NO: 12. The cDNA is obtainable from the plasmid in DSM 10081. The DNA sequence of the cDNA encoding the endoglucanase from *Volutella colletotrichoides* is SEQ ID NO. 21

and the corresponding amino acid sequence is SEQ ID NO: 22. The cDNA is obtainable from the plasmid in DSM 10571', thus the products are from natural organisms. The recited percent language in the claims reads on the natural product since "at least 90%" encompasses a 100%. The claims are given their broadest reasonable interpretation and the pH and temperature recited in some claims are also ineligible because water naturally had a neutral pH of 7 and ambient temperature is 32 degrees is encompassed in the recited range. Further, the limitation of additional enzymes in the composition does not rectify the issues raised because these are also naturally occurring, having no evidence of an altered structure in the claims.

Based upon consideration of claims **142-156 and 159-161** as a whole and the above relevant factors, it is concluded that the claims are not patent eligible, because the claims do not recite something significantly different than the judicial exception since general instructions are provided, no machine or transformation is recited in the claims that integrates the judicial exception, claims simply recite, "treat" via soaking, rinsing or washing which is routine in the art or purely conventional and very general. Therefore claims **142-156 and 159-161** are rejected as ineligible subject matter under 35 U.S.C. 101.

Response to Arguments

5. Applicant's comments have been considered in full, withdrawn objections/rejections will not be discussed herein as applicant's comments are moot.

Note that a new ground of rejection has been instituted under 35 USC 101 based on the amendments made to the claims for the reasons set forth above.

Conclusion

6. No claims are allowable.

7. Applicant's amendment necessitated the new/modified ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Hope A. Robinson whose telephone number is 571-272-0957. The examiner can normally be reached on Monday-Friday from 9:00 a.m. to 5:30 p.m. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Robert Mondesi, can be reached at (571) 272-0956.

The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Hope A. Robinson/

Primary Examiner, Art Unit 1652

AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions, and listings, of claims in the application.

Claims 1-100 (Cancelled).

Claim 101 (Previously Presented): An isolated or recombinant polypeptide fragment comprising at least 50 consecutive amino acids of any of SEQ ID NOs: 3-18, wherein the fragment comprising at least 50 consecutive amino acids is immunogenic and the immunogenic polypeptide fragment comprises less than 1100 amino acids of the applicable polypeptide of SEQ ID NOs: 3-18.

Claim 102 (**Currently amended**): The ~~isolated or recombinant~~ polypeptide fragment of claim 101 wherein the fragment comprising at least 50 consecutive amino acids includes an amino acid sequence selected from the group consisting of SEQ ID NOs: 219-307 or comprises at least amino acids 595-1008 of SEQ ID NOs: 3-18.

Claims 103-104 (Cancelled).

Claim 105 (Previously Presented): A composition comprising the isolated or recombinant immunogenic polypeptide of claim 101 in admixture with an adjuvant.

Claims 106-108 (Cancelled).

Claim 109 (**Currently amended**): The ~~immunogenic~~ polypeptide fragment of claim 101 comprising a deletion relative to the applicable polypeptide of SEQ ID NOs: 3-18, which increases solubility of the fragment as compared to the applicable full length polypeptide of SEQ ID NOs: 3-18 and wherein the fragment ~~raises a substantially similar immune response in a subject as~~ provides at least 70% of protection in a subject provided by the applicable full length polypeptide of SEQ ID NOs: 3-18.

Claim 110 (**Currently amended**): The ~~immunogenic~~ polypeptide fragment of claim 109, wherein the deletion comprises a putative amino-terminal translocator domain and/or the fragment of at least 50 consecutive amino acids includes the amino acid sequence of SEQ ID NO: 642.

Claim 111 (**Currently amended**): A[[n]] ~~immunogenic~~ composition comprising the polypeptide fragment of claim 109 in admixture with an adjuvant.

Claims 112-113 (Cancelled).

Claim 114 (New): A method for raising an immune response in a mammal comprising the step of administering to the mammal an effective amount of the immunogenic composition of claim 105.

Claim 115 (New): A method for raising an immune response in a mammal comprising the step of administering to the mammal an effective amount of the immunogenic composition of claim 111.

Office Action Summary	Application No. [redacted]	Applicant(s) [redacted]
	Examiner Patricia A. Duffy	Art Unit 1645
		AIA (First Inventor to File) Status No

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTHS FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *6-13-2014*.

☐ A declaration(s)/affidavit(s) under **37 CFR 1.130(b)** was/were filed on _____.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ An election was made by the applicant in response to a restriction requirement set forth during the interview on _____; the restriction requirement and election have been incorporated into this action.

4)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims*

5)☒ Claim(s) *101, 102, 105, 109, 110, 111, 114 and 115* is/are pending in the application.

5a) Of the above claim(s) *114 and 115* is/are withdrawn from consideration.

6)☐ Claim(s) _____ is/are allowed.

7)☒ Claim(s) *101,102,105 and 109-111* is/are rejected.

8)☐ Claim(s) _____ is/are objected to.

9)☐ Claim(s) _____ are subject to restriction and/or election requirement.

* If any claims have been determined allowable, you may be eligible to benefit from the **Patent Prosecution Highway** program at a participating intellectual property office for the corresponding application. For more information, please see http://www.uspto.gov/patents/init_events/pph/index.jsp or send an inquiry to PPHfeedback@uspto.gov.

Application Papers

10)☐ The specification is objected to by the Examiner.

11)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

Certified copies:

a)☐ All b)☐ Some** c)☐ None of the:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

** See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)

2) ☐ Information Disclosure Statement(s) (PTO/SB/08a and/or PTO/SB/08b) Paper No(s)/Mail Date _____.

3) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.

4) ☐ Other: _____.

RESPONSE TO AMENDMENT

The amendment filed 6-13-2014 has been entered into the record. Claims 1-100, 103-104, 106-108 and 112-113 have been cancelled. Claims 101, 102, 105, 109, 110, 111, 114 and 115 are pending. Claims 101, 102, 105, 109, 110 and 111 are under examination.

The text of Title 35 of the U.S. Code not reiterated herein can be found in the previous office action.

Election/Restrictions

Newly submitted claims 114 and 115 are directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: the claims are drawn to a method of use of the product under examination.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 114 and 115 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

Rejections Withdrawn

The rejection of claims 109, 110 and 111 under 35 U.S.C. 112(b) or 35 U.S.C. 112 (pre-AIA), second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which the inventor or a joint inventor, or for pre-AIA the applicant regards as the invention is withdrawn based upon the amendment to the claims.

Rejections Maintained

Claims 101, 102, 105, 109, 110 and 111 stand rejected under 35 U.S.C. 101 because the claimed invention is not directed to patent eligible subject matter. Based upon an

analysis with respect to the claim as a whole, claim(s) 101, 102, 105, 109, 110 and 111 are determined to be directed to a law of nature/natural principle.

Applicant's arguments have been considered but are not persuasive. Applicants argue that the polypeptides fragments are not naturally occurring and are markedly different in structure.

Applicant argues that the isolation of the protein fragment confers a marked difference from the naturally existing protein by imparting a significant function on the protein that it would not otherwise exhibit in nature and that by virtue of isolation the claimed protein fragment may function as a vaccine antigen where it previously could not in its full length form. That is the act of isolation of the fragment imparts a new function on the protein as solubility; that is the ability to function as a vaccine. This is not persuasive because in order to be patent eligible, the product or composition must be **both** non-naturally occurring and markedly different from the naturally occurring product. While "isolation" of a protein fragment indicates the hand of man, it is insufficient in this case to confer a marked difference in structure. The structure of a protein fragment is determined by the sequences of amino acids along with any post-translational modifications of the primary amino acid sequence (e.g. prenylation, glycosylation). In the instant case, the method of production or isolation does not on its face provide a difference in the primary amino acid sequence of the fragment as compared to the naturally occurring protein. In contrast to Applicant's assertions, protein fragments do occur in nature as proteins are routinely digested and broken down by proteases. Furthermore, the proteins are built one amino acid at a time and as such every protein at some point exists as a two amino acid fragment, a three amino acid fragment and so forth. The arguments with respect the function of generating a vaccine/immune response that it would not otherwise have in its full length insoluble form, it is noted that an immune response is a property/function of the host and not the protein *per se*. Additionally, denatured and insoluble antigens can generate and immune response and there is no

evidence in the specification that the full-length insoluble fragment is incapable of generating an immune response. The art has long found that insoluble antigens presented in gel fragments or powders are capable of generating an immune response and the art teaches that particulate antigens make excellent immunogens (see Harlow et al, Antibodies A Laboratory Manual, Cold Spring Harbor 1988, Chapter 5, pages 67-71 and page 91). Therefore, the arguments of counsel cannot take the place of evidence in the record. *In re Schulze*, 346 F.2d 600, 602, 145 USPQ 716, 718 (CCPA 1965); *In re Geisler*, 116 F.3d 1465, 43 USPQ2d 1362 (Fed. Cir. 1997) ("An assertion of what seems to follow from common experience is just attorney argument and not the kind of factual evidence that is required to rebut a *prima facie* case of obviousness.") There is no evidence in the specification as filed regarding the lack of an immune response toward the full length antigen. Additionally, the argument is directly contrary to the claims which state that the fragments provide "at least 70% of protection in a subject provided by the applicable full length polypeptide". As such, the full length protein was expected by Applicants to provide for a protective response. If the full length protein is incapable of generating a protective immune response then Applicants argument is not understood as 70% of zero is still zero and the claim limitation would therefore have no meaning. The assertion of vaccines is not relevant to the claims as the claims are not drawn to vaccines. Additionally, the specification does not demonstrate protection from infection as asserted by Applicant's, merely an increased survival from a lethal challenge. No apparent full-length protein was injected or examined as such Applicants assertion of any difference as compared to the full-length protein lacks evidentiary support in the specification as filed. The mere fragmentation of a protein is similar to the 101 guidance for DNA primers, the primers are more soluble and have the function of being able to bind to the nucleic acid and provide for amplification because they are fragments. However, the structure is not markedly different. Similarly, the fragments of the protein likewise do not meet the

statute because they are a fragment of a naturally occurring protein and are not markedly different.

The specification does not describe any manipulation of the actual sequence structure of the protein to produces a marked difference in primary amino acid sequence as compared to the naturally occurring protein product. There is no change to the sequence or structure of the protein fragment *per se*. It does not change the chemical nature of the amino acids in the fragment. As such, the response fails satisfy the markedly different requirement as the protein fragment is derived from a naturally occurring protein found in nature and fails to demonstrate a structural difference from the naturally occurring protein as the fragment does not change its primary structure from that which is found in the full-length protein. The markedly different inquiry focuses on the structural characteristics of the product and not the function of solubility in water. The claims do not state solubility in water and such a comparison cannot apparently be found in the text of the specification. As such, the protein fragment is not markedly different as fragments would be expected to be more soluble in a variety of solvents such as (e.g. urea, acetonitrile, phosphate buffered saline) and the claims merely state any increase and no particular solvent. The specification does not disclose the parameters for solubility of the full-length protein in water as compared to the solubility of the fragments in water as argued. The combination of the fragment with the adjuvant does not change the structure of either the protein fragment or the adjuvant as the mere combination does not change the individual elements from what the individually exists in nature. In this case it is found that the primary amino acid sequence of the structure of the protein fragment *per se* is not changed in a manner and as such, it is not markedly different. The addition of the adjuvant adds a feature that is well-understood, purely conventional and routine in the art in order to use the judicial exception. The combination is a product of two naturally occurring substances that are both naturally occurring or non-naturally occurring and not markedly different in structure with another naturally

occurring adjuvant substance and the mere combination does not provide for a change in structure.

The rejection is maintained.

New Rejections Based on Amendment

Claims 109, 110 and 111 are rejected under 35 U.S.C. 112(b) or 35 U.S.C. 112 (pre-AIA), second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which the inventor or a joint inventor, or for pre-AIA the applicant regards as the invention.

The claims now recites "at least 70% protection" but does not state protection from what. As such it unclear what precise condition that 70% protection relates to infection/sepsis/death ?

Claims 109, 110 and 111 are rejected under 35 U.S.C. 112(a) or 35 U.S.C. 112 (pre-AIA), first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor or a joint inventor, or for pre-AIA the inventor(s), at the time the application was filed, had possession of the claimed invention. *This is a new matter rejection.*

The claims now recite that the polypeptide fragment "provides at least 70% of protection in a subject provided by the applicable full length polypeptide". The specification at page 65, line 24 indicates that it is protection against lethal challenge. The term protection can also be applicable to protection from infection, protection from disease, protection from sepsis. As such, the contemplation of protection against lethal challenge does not support the genus of protection now claimed.