AMENDMENTS TO THE CLAIMS

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

Listing of Claims

1. (**Currently Amended**) An isolated polypeptide selected from the group consisting of:

an isolated polypeptide consisting of the NTS-DBL1x-Id1-DBL2x region of ~~the~~ VAR2CSA, the erythrocyte membrane protein 1 of *Plasmodium falciparum*; and [[;]]

an isolated polypeptide consisting of [[~~or~~]] a biologically active fragment ~~thereof~~ of the NTS-DBL1x-Id1-DBL2x region of VAR2CSA, the erythrocyte membrane protein 1 of *Plasmodium falciparum*, wherein the biologically active fragment comprises the Id1-DBL2x region of the VAR2CSA protein.

2. (**Currently Amended**) The isolated polypeptide according to claim 1, wherein the ~~isolated polypeptide~~ biologically active fragment consists of the Id1-DBL2x region of the VAR2CSA protein.

3. (**Previously Presented**) The isolated polypeptide according to claim 1, wherein the Id1-DBL2x region of the VAR2CSA protein has the sequence set forth in SEQ ID NO: 2.

4. (**Previously Presented**) The isolated polypeptide according to claim 1, wherein the NTS-DBL1x-Id1-DBL2x region of the VAR2CSA protein has the sequence set forth in SEQ ID NO: 1.

5. (**Currently Amended**) A fusion protein consisting of ~~at least one~~ the polypeptide according to claim 1 fused to at least one fusion partner ~~for use in the treatment or prevention of pregnancy associated malaria~~, wherein the fusion partner is selected from the group consisting of maltose binding protein, signal sequence of the maltose binding protein, poly-histidine tag, S-Tag, glutathione-S-transferase, thioredoxin, β-galactosidase, streptavidin, dihydrofolate reductase, pelB signal sequence, ompA signal sequence, signal sequence of

alkaline phosphatase, green fluorescent protein (GFP), toxins, human growth hormone, interleukin-2 (IL-2), granulocyte macrophage colony stimulating factor (GM-CSF), granulocyte colony stimulating factor (G-CSF), calcitonin, interferon-beta, interferon-alpha, glucagon like peptide 1 (GLP-1), glucagon like peptide 2 (GLP-2), PA toxin, parathyroid hormone (PTH(1-34) and PTH(1-84)), butyrylcholinesterase, glucocerebrosidase (GBA), and exendin-4.

6. (**Withdrawn**) An isolated polynucleotide consisting of a sequence encoding a polypeptide according to claim 1 and elements necessary to the *in vitro* or *in vivo* expression of said polypeptide.

7. (**Withdrawn**) A cloning or expression vector comprising at least one polynucleotide according to claim 6.

8. (**Withdrawn**) A host cell comprising at least one polypeptide according to claim 6.

9. (**Currently Amended**) An immunogenic composition comprising ~~at least one~~ a pharmaceutically acceptable carrier or excipient and ~~at least one~~ the polypeptide according to claim 1.

10. (**Withdrawn**) A DNA vaccine against pregnancy-associated malaria comprising a naked DNA comprising a nucleotide sequence encoding a polypeptide according to claim 1 and elements necessary to the *in vivo* expression of said polypeptide.

11. (**Currently Amended**) A protein vaccine against pregnancy-associated malaria comprising [[~~a~~]] the polypeptide according to claim 1.

12. (**Withdrawn**) The DNA vaccine according to claim 10 further comprising at least one adjuvant.

13. (**Withdrawn**) A method of preventing or treating pregnancy-associated malaria in a female subject comprising a step of administering a therapeutically effective amount of an immunogenic composition of claim 9 to the subject.

14. (**Withdrawn**) The method according to claim 13, wherein the female subject is a prepubertal girl, a postpupertal girl or a primigravidae woman.

15. (**Withdrawn**) A host cell comprising at least one vector according to claim 7.

16. (**Previously Presented**) The protein vaccine according to claim 11 further comprising at least one adjuvant.

17. (**Currently Amended**) An immunogenic composition comprising ~~at least one~~ a pharmaceutically acceptable carrier or excipient and [[a]] the fusion protein according to claim 5.

18. (**Withdrawn**) An immunogenic composition comprising at least one pharmaceutically acceptable carrier or excipient and a polynucleotide according to claim 6.

19. (**Withdrawn**) An immunogenic composition comprising at least one pharmaceutically acceptable carrier or excipient and a polynucleotide according to claim 7.

20. (**Withdrawn**) An isolated polynucleotide consisting of a sequence encoding a fusion protein according to claim 5 and elements necessary to the in vitro or in vivo expression of said fusion protein.

21. (**Withdrawn**) A DNA vaccine against pregnancy-associated malaria comprising a naked DNA comprising a nucleotide sequence encoding a fusion protein according to claim 5 and elements necessary to the in vivo expression of said fusion protein.

22. (**Currently Amended**) A protein vaccine against pregnancy-associated malaria comprising [[a]] the fusion protein according to claim 5.

23. (**Withdrawn**) A method of preventing or treating pregnancy-associated malaria in a female subject comprising a step of administering a therapeutically effective amount of a DNA vaccine according to claim 10 to the subject.

24. (**Withdrawn**) A method of preventing or treating pregnancy-associated malaria in a female subject comprising a step of administering a therapeutically effective amount of a protein vaccine according to claim 11 to the subject.

25. (**New**) The isolated polypeptide according to claim 1 consisting of the amino acid sequence set forth in SEQ ID NO: 2.

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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
13/812,197	01/25/2013	Nicaise Tuikue Ndam	28944/47428	5419

4743 7590 07/28/2014

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EXAMINER	
DEVI, SARVAMANGALA J N	
ART UNIT	**PAPER NUMBER**
1645	

NOTIFICATION DATE	DELIVERY MODE
07/28/2014	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):

mgbdocket@marshallip.com

Office Action Summary	Application No. 13/812,197	Applicant(s) TUIKUE NDAM ET AL.	
	Examiner S. DEVI, Ph.D	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 _____.

☐ 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) 1-25 is/are pending in the application.

5a) Of the above claim(s) 6-8, 10, 12-15, 18-21, 23 and 24 is/are withdrawn from consideration.

6)☐ Claim(s) _____ is/are allowed.

7)☒ Claim(s) 1-5,9,11,16,17,22 and 25 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: _____.

Applicants cite case law and contend that Miller fails to disclose each and every element of the amended claims. Applicants assert that the biologically active fragment of an isolated polypeptide consisting of the NTS-DBL1x-Id1-DBL2x region of the erythrocyte protein 1, VAR2CSA, of *Plasmodium falciparum*, in claim 1 comprises the Id1-DBL2x region of the VAR2CSA protein. Applicants submit that Miller's SEQ ID NO: 13 is a fragment of SEQ ID NO: 2 recited in instant claim 3, i.e., a fragment of the minimal antigenic region of VAR2CSA identified by the present inventors, and therefore is not encompassed in amended claim 1.

Applicants' arguments have been carefully considered, but are not persuasive. Miller's SEQ ID NO: 13 is not encompassed within the scope of claims 3 and 4. However, claims 1 and 2, as amended, the biologically active fragment *comprising* the Id1-DBL2x region as recited in the amended claims 1 and 2 lacks a structure (SEQ ID number), length or size limit. The biologically active fragment comprising the Id1-DBL2x region as generically recited in the amended claims 1 and 2 is not required to be SEQ ID NO: 2 or is not even required to be associated with SEQ ID NO: 2. The fragment can have any generic biological activity such as intrinsic antigenicity or immunogenicity. Therefore, Miller's teachings anticipate the instant claims. The rejection stands.

Rejection(s) under 35 U.S.C § 101

12) 35 U.S.C § 101 states:

> 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.

13) Claim 1 and the dependent claims 2-4, 9, 11, 16 and 25 are rejected under 35 U.S.C § 101 because the claimed invention is directed to patent eligible subject

matter. Based upon an analysis with respect to the claims as a whole, claims are determined to be directed to a law of natural/natural principle. The rationale for this determination is explained below.

Instant claims are drawn to an ineligible subject matter because the claims do not include any elements in addition to the natural product. A naturally-occurring product, whether isolated or not, is not patent-eligible pursuant to the Supreme Court decision in *Association for Molecular Pathology v. Myriad Genetics, Inc.*, 569 U. S. (June 13, 2013). See the March 4, 2014 *Guidance for Determining Subject Matter Eligibility of Claims Reciting or Involving Laws of Nature, Natural Phenomena, & Natural Products* (the Guidance). The instantly claimed polypeptide consisting of the NTS-DBL1x-Id1-DBL2x region of VAR2CSA, or the Id1-DBL2x fragment are not markedly different from naturally occurring *Plasmodium falciparum* polypeptides. The claimed polypeptide reads on naturally occurring NTS-DBL1x-Id1-DBL2x region of VAR2CSA, or the Id1-DBL2x fragment, SEQ ID NO: 1 and SEQ ID NO: 2 of a naturally occurring strain of *Plasmodium falciparum* intrinsically containing therein or expressing said polypeptide or said fragment. See for example the sequence from Singh *et al.* below and its sequence alignment with Applicants' SEQ ID NO: 2. The naturally occurring polypeptide composition of claims 9 and 16 is present with another judicial exception, because a pharmaceutically acceptable carrier or adjuvant such as heat shock protein adjuvant is also naturally present in naturally occurring *Plasmodium falciparum* cells, and therefore such a polypeptide is not markedly different from a naturally occurring polypeptide of *Plasmodium falciparum* that occur in nature along with its heat shock protein. Furthermore, claims 11 and 16 recite a vaccine in addition to the natural product(s) that amounts to nothing more

than a mere field of use. Depicted below is the sequence match for instantly recited SEQ ID NO: 2.

```
Q6UDW7_PLAFA
ID   Q6UDW7_PLAFA
AC   Q6UDW7;
DT   05-JUL-2004, integrated into UniProtKB/TrEMBL.
DT   05-JUL-2004, sequence version 1.
DT   18-SEP-2013, entry version 30.
DE   SubName: Full=Erythrocyte membrane protein 1;
OS   Plasmodium falciparum.
OC   Eukaryota; Alveolata; Apicomplexa; Aconoidasida; Haemosporida;
OC   Plasmodium; Plasmodium (Laverania).
OX   NCBI_TaxID=5833;
RN   [1]
RP   NUCLEOTIDE SEQUENCE.
RC   STRAIN=IT4/25/5;
RX   PubMed=14651636; DOI=10.1046/j.1365-2958.2003.03814.x;
RA   Kraemer S.M., Smith J.D.;
RT   "Evidence for the importance of genetic structuring to the structural
RT   and functional specialization of the Plasmodium falciparum var gene
RT   family.";
RL   Mol. Microbiol. 50:1527-1538(2003).
RN   [2]
RP   X-RAY CRYSTALLOGRAPHY (1.80 ANGSTROMS) OF 1218-1577 IN COMPLEX WITH
RP   SULFATE.
RX   PubMed=18550531; DOI=10.1074/jbc.C800086200;
RA   Higgins M.K.;
RT   "The structure of a chondroitin sulfate-binding domain important in
RT   placental malaria.";
RL   J. Biol. Chem. 283:21842-21846(2008).
RN   [3]
RP   X-RAY CRYSTALLOGRAPHY (1.90 ANGSTROMS) OF 1220-1580.
RX   PubMed=19172746; DOI=10.1038/nsmb.1479;
RA   Singh K., Gittis A.G., Nguyen P., Gowda D.C., Miller L.H., Garboczi D.N.
RT   "Structure of the DBL3x domain of pregnancy-associated malaria protein
RT   VAR2CSA complexed with chondroitin sulfate A.";
RL   Nat. Struct. Mol. Biol. 15:932-938(2008).
RN   [4]
RP   X-RAY CRYSTALLOGRAPHY (1.84 ANGSTROMS) OF 2326-2631.
RX   PubMed=23429057;
RA   Gangnard S., Badaut C., Ramboarina S., Baron B., Ramdani T.,
RA   Gamain B., Deloron P., Lewit-Bentley A., Bentley G.A.;
RT   "Structural and immunological correlations between the variable blocks
RT   of the VAR2CSA domain DBL6? from two Plasmodium falciparum parasite
RT   lines.";
RL   J. Mol. Biol. 425:1697-1711(2013).
DR   EMBL; AY372123; AAQ73926.1; Genomic_DNA.
DR   PDB; 2Y8D; X-ray; 1.84 A; A=2326-2631.
DR   PDB; 3BQI; X-ray; 2.20 A; A=1218-1577.
DR   PDB; 3BQK; X-ray; 1.80 A; A=1218-1577.
DR   PDB; 3BQL; X-ray; 2.00 A; A=1218-1577.
DR   PDB; 3CML; X-ray; 1.90 A; A=1220-1580.
```

```
DR   PDB; 3CPZ; X-ray; 2.80 A; A=1220-1580.
DR   ProteinModelPortal; Q6UDW7
DR   PRIDE; Q6UDW7
DR   EvolutionaryTrace; Q6UDW7
DR   GO; GO:0016021; C:integral to membrane; IEA:InterPro.
DR   GO; GO:0004872; F:receptor activity; IEA:InterPro.
DR   GO; GO:0009405; P:pathogenesis; IEA:InterPro.
DR   InterPro; IPR008602; Duffy-antigen_binding.
DR   Pfam; PF05424; Duffy_binding; 6.
PE   1: Evidence at protein level;
SQ   SEQUENCE   3064 AA;  355237 MW;  0AB574E4C1ABC9FE CRC64

Query Match 100%; Score 2591; DB 9; Length 3064; Best Local Similarity 100%;
Matches  475; Conservative 0; Mismatches 0; Indels 0; Gaps 0.

Qy          1 PYFAEYATKLSFILNPSDANNPSGETANHNDEACNCNESGISSVGQAQTSGPSSNKTCIT 60
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        392 PYFAEYATKLSFILNPSDANNPSGETANHNDEACNCNESGISSVGQAQTSGPSSNKTCIT 451

Qy         61 HSSIKTNKKKECKDVKLGVRENDKDLKICVIEDTSLSGVDNCCCQDLLGILQENCSDNKR 120
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        452 HSSIKTNKKKECKDVKLGVRENDKDLKICVIEDTSLSGVDNCCCQDLLGILQENCSDNKR 511

Qy        121 GSSSNDSCDNKNQDECQKKLEKVFASLTNGYKCDKCKSGTSRSKKKWIWKKSSGNEEGLQ 180
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        512 GSSSNDSCDNKNQDECQKKLEKVFASLTNGYKCDKCKSGTSRSKKKWIWKKSSGNEEGLQ 571

Qy        181 EEYANTIGLPPRTQSLYLGNLPKLENVCEDVKDINFDTKEKFLAGCLIVSFHEGKNLKKR 240
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        572 EEYANTIGLPPRTQSLYLGNLPKLENVCEDVKDINFDTKEKFLAGCLIVSFHEGKNLKKR 631

Qy        241 YPQNKNSGNKENLCKALEYSFADYGDLIKGTSIWDNEYTKDLELNLQNNFGKLFGKYIKK 300
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        632 YPQNKNSGNKENLCKALEYSFADYGDLIKGTSIWDNEYTKDLELNLQNNFGKLFGKYIKK 691

Qy        301 NNTAEQDTSYSSLDELRESWWNTNKKYIWTAMKHGAEMNITTCNADGSVTGSGSSCDDIP 360
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        692 NNTAEQDTSYSSLDELRESWWNTNKKYIWTAMKHGAEMNITTCNADGSVTGSGSSCDDIP 751

Qy        361 TIDLIPQYLRFLQEWVENFCEQRQAKVKDVITNCKSCKESGNKCKTECKTKCKDECEKYK 420
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        752 TIDLIPQYLRFLQEWVENFCEQRQAKVKDVITNCKSCKESGNKCKTECKTKCKDECEKYK 811

Qy        421 KFIEACGTAGGGIGTAGSPWSKRWDQIYKRYSKHIEDAKRNRKAGTKNCGTSSTT 475
              |||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        812 KFIEACGTAGGGIGTAGSPWSKRWDQIYKRYSKHIEDAKRNRKAGTKNCGTSSTT 866
```

Conclusion

14) Claims 1-5, 9, 11, 16, 17, 22 and 25 stand rejected.

Correspondence

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.
13/553,137	07/19/2012	Samuel Bogoch	13794/48102	6345

75582 7590 06/17/2014

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EXAMINER	
BOESEN, AGNIESZKA	
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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):

dnicholson@replikins.com

Office Action Summary	Application No. 13/553,137	Applicant(s) BOGOCH ET AL.	
	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

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- 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 F1MAT1_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.
13/859,314	04/09/2013	Yamila Carpio Gonzalez	976-70 PCT/US/CIP	7325

23869 7590 07/08/2014

Hoffmann & Baron LLP
6900 Jericho Turnpike
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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. 13/859,314	Applicant(s) CARPIO GONZALEZ ET AL.	
	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)).

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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).