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Published:

- with international search report (Art. 21(3))
- before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments (Rule 48.2(h))
- with sequence listing part of description (Rule 5.2(a))

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25 March 2010



**WO 2009/149191 A3**

(54) Title: METHODS OF TREATING INFLAMMATORY INTESTINAL DISEASE AND MANAGING SYMPTOMS THEREOF

(57) Abstract: Methods and products are disclosed for treating an inflammatory intestinal disease in a mammalian subject in need thereof, or preventing or reducing a symptom of inflammatory intestinal disease. These method include administering to the subject a therapeutically effective dose of (i) an isolated AvrA protein or polypeptide fragment thereof or (ii) a nucleic acid molecule encoding the isolated AvrA protein or polypeptide fragment. Preferred inflammatory intestinal diseases include Inflammatory Bowel Disease, Celiac Disease, and gastroenteritis.

**INTERNATIONAL SEARCH REPORT**

International application No.  
PCT/US 09/46142

**A. CLASSIFICATION OF SUBJECT MATTER**  
 IPC(8) - A61K 38/00 (2010.01)  
 USPC - 514/12  
 According to International Patent Classification (IPC) or to both national classification and IPC

**B. FIELDS SEARCHED**

Minimum documentation searched (classification system followed by classification symbols)  
 IPC(8) - A61K 38/00 (2010.01)  
 USPC - 514/12

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched  
 514/2

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)  
 WEST - DB=PGPB,USPT,USOC,EPAB,JPAB; PLUR=YES; OP=ADJ; Google Scholar  
 Search terms: avra, yopj, yop-j, avrbst, bacterial effector proteins, bacterial effector protein, risk, predispos\$, family history, susepti\$, inflammatory bowel, bowel, gastroent\$, enteritis, intestine, intestinal, celiac, inflamm\$, treat, treatment, treating, treated, symptom,

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X ----- Y	US 2006/0253100 A1 (BURRIGHT et al.) 09 November 2006 (09.11.2006) para [0010]; [0011]; [0013]-[0019]; [[0029]; [0036]; [0044]-[0049].	33, 34 ----- 1, 2, 4-10, 16-21, 28-32, 36
Y	US 2003/0198640 A1 (YU et al.) 23 October 2003 (23.10.2003) para [0026]-[0029]; [0069]-[0071]; [0210]; [0278]; [279]; [0288]; [0396]; [0477]; [0485]; [0501]; [0574]; [0723].	1, 2, 4-10, 16-21, 28-32
Y	(HARDT et al.) A secreted Salmonella protein with homology to an avirulence determinant of plant pathogenic bacteria. Proc. Natl. Acad. Sci. U.S.A. 94:9887-9892 (1997) abstract; p. 9887, footnote; Fig. 2	4, 28, 36

Further documents are listed in the continuation of Box C.

* Special categories of cited documents:	"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"A" document defining the general state of the art which is not considered to be of particular relevance	"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"E" earlier application or patent but published on or after the international filing date	"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"&" document member of the same patent family
"O" document referring to an oral disclosure, use, exhibition or other means	
"P" document published prior to the international filing date but later than the priority date claimed	

Date of the actual completion of the international search 18 January 2010 (18.01.2010)	Date of mailing of the international search report <b>29 JAN 2010</b>
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Name and mailing address of the ISA/US Mail Stop PCT, Attn: ISA/US, Commissioner for Patents P.O. Box 1450, Alexandria, Virginia 22313-1450 Facsimile No. 571-273-3201	Authorized officer: <b>Lee W. Young</b>  PCT Helpdesk: 571-272-4300 PCT OSP: 571-272-7774
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INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 09/46142

Box No. 1 Nucleotide and/or amino acid sequence(s) (Continuation of item 1.c of the first sheet)

1. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international search was carried out on the basis of a sequence listing filed or furnished:

a. (means)

on paper

in electronic form

b. (time)

in the international application as filed

together with the international application in electronic form

subsequently to this Authority for the purposes of search

2.  In addition, in the case that more than one version or copy of a sequence listing has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

3. Additional comments:

**INTERNATIONAL SEARCH REPORT**

International application No.

PCT/US 09/46142

**Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)**

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1.  Claims Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:
  
2.  Claims Nos.: 3, 14, 25, 27, 35 and 39; Partially unsearchable: 4, 15, 26, 28, 36, and 40  
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:  
Claims 3, 14, 25, 27, 35, and 39 have been held unsearchable because they are limited to SEQ ID NO: 19; however, the CRF submitted on 10 September 2009 only contained SEQ ID NOS: 1-18. Accordingly, the USPTO cannot supply a search for SEQ ID NO: 19. Further, claims 4, 15, 26, 28, 36, and 40 have been held partially unsearchable as they are limited, in the alternative, to SEQ ID NO: 19. Accordingly, claims 4, 15, 26, 28, 36, and 40 are searchable to the extent that they are limited to SEQ ID NOS: 1-18.
  
3.  Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

**Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)**

This International Searching Authority found multiple inventions in this international application, as follows:  
This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional examination fees must be paid.

Group I+: Claims 1-2, 4-10, 16-21, 28-34, and 36 are drawn to a method for treating inflammatory intestinal disease or disorder in a mammalian subject in need thereof, of a pharmaceutical composition, wherein claims 1 and 16 are limited to the administration of an avra peptide, where the first named invention will be searched and includes Group I, wherein claims 4, 28, and 36 are limited SEQ ID NO: 1. Applicant may have additional sequences searched for an additional search fee per sequence.

(continued on first blank sheet attached)

1.  As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
  
2.  As all searchable claims could be searched without effort justifying additional fees, this Authority did not invite payment of additional fees.
  
3.  As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
  
4.  No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:  
1-2, 4-10, 16-21, 28-34 and 36 limited to SEQ ID NO: 1

- Remark on Protest**
- The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.
  - The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.
  - No protest accompanied the payment of additional search fees.

## INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 09/46142

(continuation of Box No. III: Observations where unity of invention is lacking)

Group II+: Claims 1-2, 4-5, 11-13, 15-18, 22-24, 26, 28, 29, 37, 38, 40, and 41 are drawn to a method for treating inflammatory intestinal disease or disorder in a mammalian subject in need thereof, or a vector, wherein claims 1 and 16 are limited to the administration of an avra nucleic acid. Each sequence (SEQ ID NO:) represents a distinct invention. Applicant may have additional sequences searched for an additional search fee per sequence.

The inventions of the listed groups do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

The distinguishing technical feature of Group I is the administration of an avra peptide to treat an inflammatory intestinal disease or disorder, including, for example claims limited by specific amounts of protein or route of administration (e.g. claims 7 and 8).

The distinguishing technical feature of Group II is the administration of an avra nucleic acid to treat an inflammatory intestinal disease or disorder, including, for example, claims limited by a specific promoter (e.g. claim 13).

The technical feature that links Groups I and II is a method for treating inflammatory intestinal disease comprising administering Avra ; however, this is not an improvement over the prior art of Sun et al. ("Methods of Treating Inflammatory Bowel Disease or Celiac Disease and Managing Systems Thereof"; 25 Mar 2008; University of Rochester Medical Center [online]; retrieved from the internet URL: <http://www.urmc.rochester.edu/technology-transfer/find-technologies/index.cfm?TechnolID=466061>) who teach a method utilizing Avra as a treatment to treat inflammatory bowel disease or celiac disease (pg 2, "applications" section).

In addition, each group (i.e. Group I drawn to administratin of an avra peptide and Group II drawn to an avra nucleic acid) contains several inventions, each drawn to a distinct peptide sequence. The sequences have different structure and function. Although sequence identity may exist between the peptide sequences, this shared feature does not represent an improvement over the prior art UniProt entry O30621\_SALTY (1 Jan 1998: UniProtKB [online] retrieved from the internet URL: <http://www.uniprot.org/uniprot/O30621>) which teaches SEQ ID NO: 1.

Accordingly, unity of invention is lacking.