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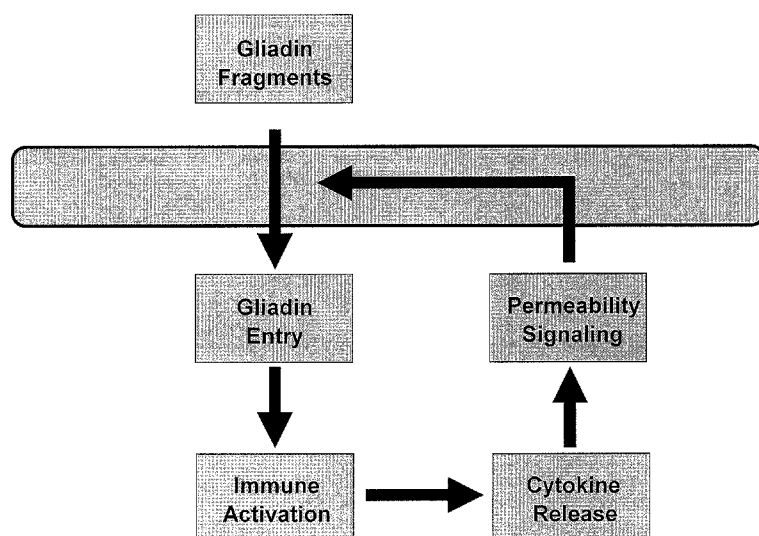
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[Continued on next page]

(54) **Title:** INHIBITION OF GLIADIN PEPTIDES

Figure 1



(57) **Abstract:** Novel compounds and methods for the inhibition of biological barrier permeability and for the inhibition of peptide translocation across biological barriers are identified. Assays for determining modulators of biological barrier permeability and for peptide translocation across biological barriers are provided. Methods for treating diseases relating to aberrant biological barrier permeability and peptide translocation across biological barriers are provided. Such diseases include celiac disease, necrotizing enterocolitis, diabetes, cancer, inflammatory bowel diseases, asthma, COPD, excessive or undesirable immune response, gluten sensitivity, gluten allergy, food allergy, rheumatoid arthritis, multiple sclerosis, immune-mediated or type 1 diabetes mellitus, systemic lupus erythematosus, psoriasis, scleroderma and autoimmune thyroid diseases.

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Published:

- *with international search report (Art. 21(3))*
- *with sequence listing part of description (Rule 5.2(a))*

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INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 09/42973

A. CLASSIFICATION OF SUBJECT MATTER
 IPC(8) - A61K 38/04; A61K 38/00 (2009.01)
 USPC - 530/328; 514/16
 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 38/04; A61K 38/00 (2009.01)
 USPC - 530/328; 514/16

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
 USPC - 530/328; 514/16
 (Text Search)

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
 PubWEST (PGPB, USPT, USOC, EPAB, JPAB); DialogPRO (Engineering); PubMed and Google Scholar: peptide, antagonist, zonulin, permeab\$, inhibi\$, gliadin, dermatitis herpetiformis, diabet\$, dermatitis, herpetiformis, combin\$, conjunction, coadminist\$, agent, therapeut\$, medication, medicine, drug, tight junction, tj, suppres\$, reduc\$. GenCore 6.3: SEQ I

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 2008/0103100 A1 (FASANO et al.) 01 May 2008 (01.05.2008) SEQ ID NO: 15; para [0002]-[0005], [0005], [0025], [0030]-[0032], [0038], [0065], [0073]-[0075], [0089], [0098]-[0099], [0110]-[0117], [0212]-[0215], [0228]	1, 3-4, 6-7, 9-14, 16, 18-19, 21-22, 24-29, 31-32, 34, 36-37 and 39 ----- 15, 30, 35, 40-42, 44-45
Y	US 2007/0196501 A1 (PATERSON et al.) 23 August 2007 (23.08.2007) SEQ ID NO: 1; para [0017], [0021]-[0022], [0044], [0066], [0076], [0078]-[0079], [0084], [0086], [0088]-[0089]	15, 30, 35, 40 and 45
Y	ARRIETA, et al. Alterations in Intestinal Permeability. Gut October 2006, 55(10):1512-1520; pg 1517, right col, para 7 to pg 1518, left col, para 1, 2	41-42 and 44-45

Further documents are listed in the continuation of Box C.

- * Special categories of cited documents:
- "A" document defining the general state of the art which is not considered to be of particular relevance
 - "E" earlier application or patent but published on or after the international filing date
 - "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)
 - "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
 - "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
 - "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
 - "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
 - "&" document member of the same patent family

Date of the actual completion of the international search 09 December 2009 (09.12.2009)	Date of mailing of the international search report 15 DEC 2009
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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: Lee W. Young PCT Helpdesk: 571-272-4300 PCT OSP: 571-272-7774
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INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 09/42973

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.: 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:
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 1-45, drawn to a peptide permeability inhibitor and a method of using said inhibitor. The first invention encompasses a peptide inhibitor of SEQ ID NO: 1. Should an additional fee(s) be paid, Applicant is invited to elect an additional SEQ ID NO(s) to be searched. The exact claims searched will depend on the specifically elected SEQ ID NO(s).

[NOTE: Claims 2, 5, 8, 17, 20, 23, 33, 38, 43 are drawn to a non-elected subject matter and therefore were not searched.]

*****Continued in Supplemental Box*****

- 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. [X] 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, 3-4, 6-7, 9-16, 18-19, 21-22, 24-32, 34-37, 39-42 and 44-45, restricted 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
Information on patent family members

International application No.
PCT/US 09/42973

***** Supplemental Box *****

Continuation of: Box No. III - Observations where unity of invention is lacking:

The inventions listed as Groups I+ 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 inventions of Group I+ share the technical feature of a peptide permeability inhibitor. However, this shared technical feature does not represent a contribution over prior art. Specifically, US 2006/0276399 A1 (Fasano) discloses peptide antagonists of Zonulin, a protein that participates in tight junctions between cells of the wall of the digestive tract. In addition, Fasano discloses a zonulin antagonist identical to the claimed peptide of SEQ ID NO: 1 (Fasano, SEQ ID NO 15). As said peptide permeability inhibitor agent was known at the time of the invention, this cannot be considered a special technical feature that would otherwise unify the groups.

Group I+ therefore lack unity under PCT Rule 13 because they do not share a same or corresponding special technical feature.