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- (81) **Designated States** (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.
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Published:
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[Continued on next page]

(54) **Title:** COMPOSITIONS AND METHODS FOR THE PRODUCTION OF GLUTEN FREE FOOD PRODUCTS

	Gene Design	
	Single clonal copy	
HMW Glutenin	Synthetic gene (concatemer)	Elasticity
	In vitro recombinant	
	Single clonal copy	
Gliadin	Synthetic gene (concatemer)	Viscosity
Gamma-Zein	In vitro recombinant	

(57) **Abstract:** Compositions and methods for the production of baked goods and flour, which do not induce CD are disclosed.

Figure 1A



(88) Date of publication of the international search report:
26 November 2015

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 14/37296

A. CLASSIFICATION OF SUBJECT MATTER
 IPC(8) - C07K 14/415, C12Q 1/02, C12N 15/11 (2014.01)
 CPC - C07K 14/415, G01N 33/505, C12N 15/8257
 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): C07K 14/415, C12Q 1/02, C12N 15/11 (2014.01)
 CPC: C07K 14/415, G01N 33/505, C12N 15/8257

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
 CPC - G01N 33/5008, C12N 15/8241
 (keyword limited; terms below)

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
 PatBase, PubWest, Google Scholar, Google Patents: celiac disease, coeliac disease, celiac sprue, recombinant, glutenin, gliadin, T cell, T lymphocyte, enterocyte cell height, ECH, SI index, stimulation index, wheat, maize, selectable marker, RNAi, RNA interference

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 2008/0175971 A1 (ANDERSON et al.) 24 July 2008 (24.07.2008); para [0004], [0009], [0109], [0127], [0145], [0151], [0155], [0162], [0168], [0169]	5-6, 9/(5-6), 10/(5-6) ----- 1-4, 7-8, 9/(7-8), 10/(7-8)
Y	DEWAR et al., Clinical Features and Diagnosis of Celiac Disease, GASTROENTEROLOGY April 2005, Vol. 128, Pages S19-S24; S20, col 2, para 4-S21, col 1, para 1	1-4
Y	US 2009/0158463 A1 (LUETHY et al.) 18 June 2009 (18.06.2009); Abstract, para [0081]	7, 9/7, 10/7
Y	US 2009/0049573 A1 (DOTSON et al.) 19 February 2009 (19.02.2009); para [0097]	8, 9/8, 10/8

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 04 November 2014 (04.11.2014)	Date of mailing of the international search report 20 NOV 2014
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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 14/37296

Box No. I 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:

The electronic sequence listing submitted on 09 July 2014 in response to the PCT/ISA/225 issued on 1 June 2014 is acknowledged; however, it does not comply with the standard provided for in Annex C of the Administrative Instructions. Therefore, the international search was not carried out on the basis of that non-compliant electronic sequence listing.

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 14/37296

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 1-4, drawn to a method for detecting celiac disease (CD) inducing epitopes in wheat glutenin and gliadin and recombinant wheat proteins produced by said method

Group II: Claims 5-10, drawn to a method for the production of transgenic maize and flour and plants obtained from said method

--please see continuation on extra sheet--

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.:

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.

Continuation of:

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

The inventions listed as Groups I and II 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:

Special Technical Features

Group I requires the steps of a) contacting gluten sensitive T cells with glutenin and gliadin synthetic peptides based on deep sequencing wheat cultivars; b) determining the SI index and/or enterocyte cell height (ECH), of said cells in the presence or absence of said fragments, those fragments which reduce ECH or stimulate sensitive T cell proliferation being associated with the occurrence of CD; steps not required by Group II.

Group II requires the steps of a) introducing DNA constructs comprising sequences encoding one or more wheat glutenin or gliadin proteins, said sequences being altered such that the encoded proteins lack native CD-inducing epitopes, said construct optionally comprising a selectable marker suitable for isolation of transgenic cells; b) propagating said isolated cells to generate a transgenic maize plant; and c) obtaining flour from said plants for use in baking consumable products, said products lacking CD inducing epitopes and thereby being safe to consume by patients exhibiting gluten intolerance; steps not required by Group I.

Common Technical Features

The feature shared by Groups I and II are celiac disease (CD) -inducing epitopes in wheat glutenin and gliadin proteins (shared by claims 1 and 5) as well as wheat glutenin and gliadin proteins lacking CD-inducing epitopes (shared by claims 4 and 5). However, these shared technical feature does not represent a contribution over prior art, because the shared technical feature is taught by US 2008/0175971 A1 to Anderson et al. (hereinafter 'Anderson'). Anderson discloses CD-inducing epitopes in wheat glutenin and gliadin proteins (Table 5 - "T cell epitopes described in coeliac disease" showing epitopes from gliadin and glutenin; para [0114] wild type proteins from genus *Triticum* including wheat). Anderson further teaches wheat gliadin protein lacking CD-inducing epitopes (para [0107]-[0109] - "The mutated gliadin will not cause coeliac disease or will cause decreased symptoms of coeliac disease. Typically the mutation decreases the ability of the epitope to induce a T cell response"; para [0212] gliadin from wheat). Although Anderson does not specifically teach glutenin protein that similarly lacks CD-inducing epitopes, Anderson does teach a method of protein epitope mapping coeliac disease (para [0171]) and using mutation in identified epitopes to produce a protein that does not cause coeliac disease (para [0111]). Since glutenin and gliadin are the two known proteins that bear T cell epitopes in coeliac disease (Table 5), one of ordinary skill in the art would have found it obvious to modify the gliadin epitope mutation method of Anderson for modification of glutenin to obtain glutenin that lacks CD-inducing epitopes. As the technical feature was known in the art at the time of the invention, it cannot be considered a special technical feature that would otherwise unify the groups.

Groups I and II therefore lack unity of invention under PCT Rule 13 because they do not share a same or corresponding special technical feature