



(11)

EP 3 449 255 B1

(12) **EUROPEAN PATENT SPECIFICATION**

(45) Date of publication and mention of the grant of the patent:
21.08.2024 Bulletin 2024/34

(21) Application number: **17790144.4**

(22) Date of filing: **20.04.2017**

(51) International Patent Classification (IPC):
G01N 33/543 ^(2006.01) **G01N 33/564** ^(2006.01)
G01N 33/68 ^(2006.01) **A61B 5/145** ^(2006.01)
A61B 5/00 ^(2006.01)

(52) Cooperative Patent Classification (CPC):
G01N 33/6854; A61B 5/14507; A61B 5/4255;
G01N 2800/065

(86) International application number:
PCT/US2017/028696

(87) International publication number:
WO 2017/189338 (02.11.2017 Gazette 2017/44)

(54) **COMPOSITIONS, DEVICES, AND METHODS OF ULCERATIVE COLITIS SENSITIVITY TESTING**

ZUSAMMENSETZUNGEN, VORRICHTUNGEN UND VERFAHREN FÜR
COLITIS-ULCEROSA-EMPFINDLICHKEITSTESTS

COMPOSITIONS, DISPOSITIFS, ET MÉTHODES D'ANALYSE DE LA SENSIBILITÉ À LA COLITE
ULCÉREUSE

(84) Designated Contracting States:
**AL AT BE BG CH CY CZ DE DK EE ES FI FR GB
GR HR HU IE IS IT LI LT LU LV MC MK MT NL NO
PL PT RO RS SE SI SK SM TR**

(30) Priority: **26.04.2016 US 201662327932 P**

(43) Date of publication of application:
06.03.2019 Bulletin 2019/10

(73) Proprietor: **Biomerica, Inc.
Irvine, California 92614 (US)**

(72) Inventors:
• **IRANI-COHEN, Zackary
Irvine, California 92614 (US)**
• **LADERMAN, Elisabeth
Irvine, California 92614 (US)**

(74) Representative: **Schlich, George
Schlich
9 St Catherine's Road
Littlehampton, West Sussex BN17 5HS (GB)**

(56) References cited:
EP-B1- 1 051 626 EP-B1- 1 051 626
WO-A1-2016/077808 US-A1- 2007 122 840
US-A1- 2007 122 840 US-B2- 7 601 509

US-B2- 7 601 509

- **QIANG ZENG ET AL: "Variable Food-Specific IgG Antibody Levels in Healthy and Symptomatic Chinese Adults", PLOS ONE, vol. 8, no. 1, 1 January 2013 (2013-01-01), pages 1 - 9, XP055367030, DOI: 10.1371/journal.pone.0053612**
- **CHENWEN CAI ET AL: "Serological Investigation of Food Specific Immunoglobulin G Antibodies in Patients with Inflammatory Bowel Diseases", PLOS ONE, vol. 9, no. 11, 13 November 2014 (2014-11-13), pages e112154, XP055459661, DOI: 10.1371/journal.pone.0112154**
- **XINLING MA ET AL: "Food intolerance prevalence in active ulcerative colitis in southwest China", ASIA PACIFIC JOURNAL OF CLINICAL NUTRITION, September 2016 (2016-09-01), Australia, pages 529 - 533, XP055629927, Retrieved from the Internet <URL:https://pdfs.semanticscholar.org/8eb1/be823ce246ed225762d263ee4b7120e9a549.pdf> DOI: 10.6133/apjcn.102015.04**
- **ZENG, QIANG ET AL.: "Variable food-specific IgG antibody levels in healthy and symptomatic Chinese adults", PLOS ONE, vol. 8, no. 1, 3 January 2013 (2013-01-03), pages e53612, XP055367030**

Note: Within nine months of the publication of the mention of the grant of the European patent in the European Patent Bulletin, any person may give notice to the European Patent Office of opposition to that patent, in accordance with the Implementing Regulations. Notice of opposition shall not be deemed to have been filed until the opposition fee has been paid. (Art. 99(1) European Patent Convention).

EP 3 449 255 B1

- CAI, CHENWEN ET AL.: "Serological investigation of food specific immunoglobulin G antibodies in patients with inflammatory bowel diseases", PLOS ONE, vol. 9, no. 11, 13 November 2014 (2014-11-13), pages e112154, XP055459661

Description**Field of the Invention**

5 [0001] The field of the invention is sensitivity testing for food intolerance, and especially as it relates to testing and possible elimination of selected food items as trigger foods for patients diagnosed with or suspected to have Ulcerative Colitis.

Background

10 [0002] The background description includes information that may be useful in understanding the present invention. It is not an admission that any of the information provided herein is prior art or relevant to the presently claimed invention, or that any publication specifically or implicitly referenced is prior art.

15 [0003] Food sensitivity, especially as it relates to Ulcerative Colitis (a type of inflammatory bowel disease), often presents with diarrhea mixed with blood and mucus and underlying causes of Ulcerative Colitis are not well understood in the medical community. Most typically, Ulcerative Colitis is diagnosed by endoscopic and radiological tests, along with blood tests or electrolyte tests to identify inflammatory conditions. Unfortunately, treatment of Ulcerative Colitis is often less than effective and may present new difficulties due to immune suppressive or modulatory effects. Elimination of other one or more food items has also shown promise in at least reducing incidence and/or severity of the symptoms.

20 However, Ulcerative Colitis is often quite diverse with respect to dietary items triggering symptoms, and no standardized test to help identify trigger food items with a reasonable degree of certainty is known, leaving such patients often to trial-and-error.

[0004] While there are some commercially available tests and labs to help identify trigger foods, the quality of the test results from these labs is generally poor as is reported by a consumer advocacy group (e.g., <http://www.which.co.uk/news/2008/08/food-allergy-tests-could-risk-your-health-154711/>). Most notably, problems associated with these tests and labs were high false positive rates, high false negative rates, high intra-patient variability, and inter-laboratory variability, rendering such tests nearly useless. Similarly, further inconclusive and highly variable test results were also reported elsewhere (Alternative Medicine Review, Vol. 9, No. 2, 2004: pp 198-207), and the authors concluded that this may be due to food reactions and food sensitivities occurring via a number of different mechanisms.

30 For example, not all Ulcerative Colitis patients show positive response to food A, and not all Ulcerative Colitis patients show negative response to food B. Thus, even if an Ulcerative Colitis patient shows positive response to food A, removal of food A from the patient's diet may not relieve the patient's Ulcerative Colitis symptoms. In other words, it is not well determined whether food samples used in the currently available tests are properly selected based on the high probabilities to correlate sensitivities to those food samples to Ulcerative Colitis.

35 [0005] Thus, even though various tests for food sensitivities are known in the art, all or almost all of them suffer from one or more disadvantages. Therefore, there is still a need for improved compositions, devices, and methods of food sensitivity testing, especially for identification and possible elimination of trigger foods for patients identified with or suspected of having Ulcerative Colitis.

Summary

40 [0006] The present invention provides a test panel for testing food intolerance in patients diagnosed with or suspected to have ulcerative colitis, comprising:

45 a plurality of distinct food preparations, wherein each food preparation is independently coupled to an individually addressable solid carrier;

wherein the plurality of distinct food preparations consists of green pea, cantaloupe, pinto bean, cucumber, green pepper, grapefruit, carrot, orange, almond, sardine, sweet potato, broccoli, garlic, lima bean, squashes, celery, string bean, tomato, cauliflower, black walnut, sunflower seed, cane sugar, buck wheat, soybean, lemon, barley, oat, oyster, mustard, rye, peach, chili pepper, spinach, peanut, avocado, shrimp, pineapple, cola nut, rice, cabbage, butter, eggplant, apple, egg, wheat, cottage cheese, sole, cashew, olive, parsley, corn, honey, chocolate, cow's milk, potato, onion, tea, and tobacco.

[0007] The plurality of distinct food preparations have an average discriminatory p-value of ≤ 0.07 as determined by raw p-value or an average discriminatory p-value of ≤ 0.10 as determined by FDR multiplicity adjusted p-value.

55 [0008] The present invention also provides an *in vitro* method of testing food intolerance in patients diagnosed with or suspected to have ulcerative colitis, comprising:

contacting green pea, cantaloupe, pinto bean, cucumber, green pepper, grapefruit, carrot, orange, almond, sardine, sweet potato, broccoli, garlic, lima bean, squashes, celery, string bean, tomato, cauliflower, black walnut, sunflower

EP 3 449 255 B1

seed, cane sugar, buck wheat, soybean, lemon, barley, oat, oyster, mustard, rye, peach, chili pepper, spinach, peanut, avocado, shrimp, pineapple, cola nut, rice, cabbage, butter, eggplant, apple, egg, wheat, cottage cheese, sole, cashew, olive, parsley, corn, honey, chocolate, cow's milk, potato, onion, tea, and tobacco with a bodily fluid of a patient that is diagnosed with or suspected to have ulcerative colitis, wherein the bodily fluid is associated with a gender identification, and wherein the step of contacting is performed under conditions that allow IgG from the bodily fluid to bind to at least one component of the food preparation;

measuring IgG bound to the at least one component of the food preparation to obtain a signal;

comparing the signal to a gender-stratified reference value for the food preparation using the gender identification to obtain a result; and

updating or generating a report using the result.

[0009] Various objects, features, aspects and advantages of the embodiments described herein will become more apparent from the following detailed description of preferred embodiments, along with the accompanying drawing figures in which like numerals represent like components.

Brief Description of The Drawings

[0010]

Table 1 shows a list of food items from which food preparations can be prepared.

Table 2 shows statistical data of foods ranked according to 2-tailed FDR multiplicity-adjusted p-values.

Table 3 shows statistical data of ELISA score by food and gender.

Table 4 shows cutoff values of foods for a predetermined percentile rank.

Figure 1A illustrates ELISA signal score of male Ulcerative Colitis patients and control tested with green pea.

Figure 1B illustrates a distribution of percentage of male Ulcerative Colitis subjects exceeding the 90th and 95th percentile tested with green pea.

Figure 1C illustrates a signal distribution in women along with the 95th percentile cutoff as determined from the female control population tested with green pea.

Figure 1D illustrates a distribution of percentage of female Ulcerative Colitis subjects exceeding the 90th and 95th percentile tested with green pea.

Figure 2A illustrates ELISA signal score of male Ulcerative Colitis patients and control tested with cantaloupe.

Figure 2B illustrates a distribution of percentage of male Ulcerative Colitis subjects exceeding the 90th and 95th percentile tested with cantaloupe.

Figure 2C illustrates a signal distribution in women along with the 95th percentile cutoff as determined from the female control population tested with cantaloupe.

Figure 2D illustrates a distribution of percentage of female Ulcerative Colitis subjects exceeding the 90th and 95th percentile tested with cantaloupe.

Figure 3A illustrates ELISA signal score of male Ulcerative Colitis patients and control tested with pinto bean.

Figure 3B illustrates a distribution of percentage of male Ulcerative Colitis subjects exceeding the 90th and 95th percentile tested with pinto bean.

Figure 3C illustrates a signal distribution in women along with the 95th percentile cutoff as determined from the

female control population tested with pinto bean.

Figure 3D illustrates a distribution of percentage of female Ulcerative Colitis subjects exceeding the 90th and 95th percentile tested with pinto bean.

5

Figure 4A illustrates ELISA signal score of male Ulcerative Colitis patients and control tested with cucumber.

Figure 4B illustrates a distribution of percentage of male Ulcerative Colitis subjects exceeding the 90th and 95th percentile tested with cucumber.

10

Figure 4C illustrates a signal distribution in women along with the 95th percentile cutoff as determined from the female control population tested with cucumber.

Figure 4D illustrates a distribution of percentage of female Ulcerative Colitis subjects exceeding the 90th and 95th percentile tested with cucumber.

15

Figure 5A illustrates distributions of Ulcerative Colitis subjects by number of foods that were identified as trigger foods at the 90th percentile.

Figure 5B illustrates distributions of Ulcerative Colitis subjects by number of foods that were identified as trigger foods at the 95th percentile.

20

Table 5A shows raw data of Ulcerative Colitis patients and control with number of positive results based on the 90th percentile.

25

Table 5B shows raw data of Ulcerative Colitis patients and control with number of positive results based on the 95th percentile.

Table 6A shows statistical data summarizing the raw data of Ulcerative Colitis patient populations shown in Table 5A.

30

Table 6B shows statistical data summarizing the raw data of Ulcerative Colitis patient populations shown in Table 5B.

Table 7A shows statistical data summarizing the raw data of control populations shown in Table 5A.

35

Table 7B shows statistical data summarizing the raw data of control populations shown in Table 5B.

Table 8A shows statistical data summarizing the raw data of Ulcerative Colitis patient populations shown in Table 5A transformed by logarithmic transformation.

40

Table 8B shows statistical data summarizing the raw data of Ulcerative Colitis patient populations shown in Table 5B transformed by logarithmic transformation.

Table 9A shows statistical data summarizing the raw data of control populations shown in Table 5A transformed by logarithmic transformation.

45

Table 9B shows statistical data summarizing the raw data of control populations shown in Table 5B transformed by logarithmic transformation.

Table 10A shows statistical data of an independent T-test to compare the geometric mean number of positive foods between the Ulcerative Colitis and non-Ulcerative Colitis samples based on the 90th percentile.

50

Table 10B shows statistical data of an independent T-test to compare the geometric mean number of positive foods between the Ulcerative Colitis and non-Ulcerative Colitis samples based on the 95th percentile.

Table 11A shows statistical data of a Mann-Whitney test to compare the geometric mean number of positive foods between the Ulcerative Colitis and non-Ulcerative Colitis samples based on the 90th percentile.

55

Table 11B shows statistical data of a Mann-Whitney test to compare the geometric mean number of positive foods

between the Ulcerative Colitis and non-Ulcerative Colitis samples based on the 95th percentile.

Figure 6A illustrates a box and whisker plot of data shown in Table 5A.

5 **Figure 6B** illustrates a notched box and whisker plot of data shown in Table 5A.

Figure 6C illustrates a box and whisker plot of data shown in Table 5B.

10 **Figure 6D** illustrates a notched box and whisker plot of data shown in Table 5B.

Table 12A shows statistical data of a Receiver Operating Characteristic (ROC) curve analysis of data shown in Tables 5A-11A.

15 **Table 12B** shows statistical data of a Receiver Operating Characteristic (ROC) curve analysis of data shown in Tables 5B-11B.

Figure 7A illustrates the ROC curve corresponding to the statistical data shown in Table 12A.

20 **Figure 7B** illustrates the ROC curve corresponding to the statistical data shown in Table 12B.

Table 13A shows a statistical data of performance metrics in predicting Ulcerative Colitis status among female patients from number of positive foods based on the 90th percentile.

25 **Table 13B** shows a statistical data of performance metrics in predicting Ulcerative Colitis status among male patients from number of positive foods based on the 90th percentile.

Table 14A shows a statistical data of performance metrics in predicting Ulcerative Colitis status among female patients from number of positive foods based on the 95th percentile.

30 **Table 14B** shows a statistical data of performance metrics in predicting Ulcerative Colitis status among male patients from number of positive foods based on the 95th percentile.

Detailed Description

35 **[0011]** The inventors have discovered that food preparations used in food tests to identify trigger foods in patients diagnosed with or suspected to have Ulcerative Colitis are not equally well predictive and/or associated with Ulcerative Colitis/Ulcerative Colitis symptoms. Indeed, various experiments have revealed that among a wide variety of food items certain food items are highly predictive/associated with Ulcerative Colitis whereas others have no statistically significant association with Ulcerative Colitis.

40 **[0012]** Even more unexpectedly, the inventors discovered that in addition to the high variability of food items, gender variability with respect to response in a test plays a substantial role in the determination of association or a food item with Ulcerative Colitis. Consequently, based on the inventors' findings and further contemplations, test kits and methods are now presented with substantially higher predictive power in the choice of food items that could be eliminated for reduction of Ulcerative Colitis signs and symptoms.

45 **[0013]** The following discussion provides many example embodiments of the inventive subject matter. Although each embodiment represents a single combination of inventive elements, the inventive subject matter is considered to include all possible combinations of the disclosed elements. Thus if one embodiment comprises elements A, B, and C, and a second embodiment comprises elements B and D, then the inventive subject matter is also considered to include other remaining combinations of A, B, C, or D, even if not explicitly disclosed.

50 **[0014]** In some embodiments, the numbers expressing quantities or ranges, used to describe and claim certain embodiments of the invention are to be understood as being modified in some instances by the term "about." Accordingly, in some embodiments, the numerical parameters set forth in the written description and attached claims are approximations that can vary depending upon the desired properties sought to be obtained by a particular embodiment. In some embodiments, the numerical parameters should be construed in light of the number of reported significant digits and by applying ordinary rounding techniques. Notwithstanding that the numerical ranges and parameters setting forth the broad scope of some embodiments of the invention are approximations, the numerical values set forth in the specific examples are reported as precisely as practicable. The numerical values presented in some embodiments of the invention may contain certain errors necessarily resulting from the standard deviation found in their respective testing measurements.

55

Unless the context dictates the contrary, all ranges set forth herein should be interpreted as being inclusive of their endpoints and open-ended ranges should be interpreted to include only commercially practical values. Similarly, all lists of values should be considered as inclusive of intermediate values unless the context indicates the contrary.

5 [0015] As used in the description herein and throughout the claims that follow, the meaning of "a," "an," and "the" includes plural reference unless the context clearly dictates otherwise. Also, as used in the description herein, the meaning of "in" includes "in" and "on" unless the context clearly dictates otherwise.

10 [0016] All methods described herein can be performed in any suitable order unless otherwise indicated herein or otherwise clearly contradicted by context. The use of any and all examples, or exemplary language (e.g., "such as") provided with respect to certain embodiments herein is intended merely to better illuminate the invention and does not pose a limitation on the scope of the invention otherwise claimed. No language in the specification should be construed as indicating any non-claimed element essential to the practice of the invention.

15 [0017] In some embodiments, the numbers expressing quantities of ingredients, properties such as concentration, reaction conditions, and so forth, used to describe and claim certain embodiments of the invention are to be understood as being modified in some instances by the term "about." Accordingly, in some embodiments, the numerical parameters set forth in the written description and attached claims are approximations that can vary depending upon the desired properties sought to be obtained by a particular embodiment. In some embodiments, the numerical parameters should be construed in light of the number of reported significant digits and by applying ordinary rounding techniques. Notwithstanding that the numerical ranges and parameters setting forth the broad scope of some embodiments of the invention are approximations, the numerical values set forth in the specific examples are reported as precisely as practicable. The
20 numerical values presented in some embodiments of the invention may contain certain errors necessarily resulting from the standard deviation found in their respective testing measurements. Moreover, and unless the context dictates the contrary, all ranges set forth herein should be interpreted as being inclusive of their endpoints and open-ended ranges should be interpreted to include only commercially practical values. Similarly, all lists of values should be considered as inclusive of intermediate values unless the context indicates the contrary.

25 [0018] While not limiting to the inventive subject matter, food preparations will typically be drawn from foods generally known or suspected to trigger signs or symptoms of Ulcerative Colitis. Particularly suitable food preparations may be identified by the experimental procedures outlined below.

[0019] Therefore, exemplary food preparations include foods 1-58 of Table 2. Still further especially contemplated food items and food additives from which food preparations can be prepared are listed in Table 1.

30 [0020] The recitation of ranges of values herein is merely intended to serve as a shorthand method of referring individually to each separate value falling within the range. Unless otherwise indicated herein, each individual value is incorporated into the specification as if it were individually recited herein. All methods described herein can be performed in any suitable order unless otherwise indicated herein or otherwise clearly contradicted by context. The use of any and all examples, or exemplary language (e.g., "such as") provided with respect to certain embodiments herein is intended
35 merely to better illuminate the invention and does not pose a limitation on the scope of the invention otherwise claimed. No language in the specification should be construed as indicating any non-claimed element essential to the practice of the invention.

40 [0021] Of course, it should be noted that the particular format of the test kit or panel may vary considerably and contemplated formats include micro well plates, dip sticks, membrane-bound arrays, etc. Consequently, the solid carrier to which the food preparations are coupled may include wells of a multiwell plate, a bead (e.g., color-coded or magnetic), or an adsorptive film (e.g., nitrocellulose or micro/nanoporous polymeric film), or an electrical sensor (e.g., a printed copper sensor or microchip).

[0022] Consequently, the inventors also contemplate a method of testing food intolerance in patients that are diagnosed with or suspected to have Ulcerative Colitis.

45 [0023] As also noted above, all of the different food preparations have an average discriminatory p-value of ≤ 0.07 as determined by raw p-value, and/or or an average discriminatory p-value of ≤ 0.10 as determined by FDR multiplicity adjusted p-value.

50 [0024] While in certain embodiments food preparations are prepared from single food items as crude extracts, or crude filtered extracts, it is contemplated that food preparations can be prepared from mixtures of a plurality of food items (e.g., a mixture of citrus comprising lemon, orange, and a grapefruit, a mixture of yeast comprising baker's yeast and brewer's yeast, a mixture of rice comprising a brown rice and white rice, a mixture of sugars comprising honey, malt, and cane sugar. In some embodiments, it is also contemplated that food preparations can be prepared from purified food antigens or recombinant food antigens.

55 [0025] As it is generally preferred that the food preparation is immobilized on a solid surface (typically in an addressable manner), it is contemplated that the step of measuring the IgG bound to the component of the food preparation is performed via an ELISA test. Exemplary solid surfaces include, but are not limited to, wells in a multiwell plate, such that each food preparation may be isolated to a separate microwell. In certain embodiments, the food preparation will be coupled to, or immobilized on, the solid surface. In other embodiments, the food preparation(s) will be coupled to a

molecular tag that allows for binding to human immunoglobulins (e.g., IgG) in solution.

[0026] Thus, it should be appreciated that by having a high-confidence test system as described herein, the rate of false-positive and false negatives can be significantly reduced, and especially where the test systems and methods are gender stratified or adjusted for gender differences as shown below. Such advantages have heretofore not been realized and it is expected that the systems and methods presented herein will substantially increase the predictive power of food sensitivity tests for patients diagnosed with or suspected to have Ulcerative Colitis.

Experiments

[0027] General Protocol for food preparation generation: Commercially available food extracts (available from Biomerica Inc., 17571 Von Karman Ave, Irvine, CA 92614) prepared from the edible portion of the respective raw foods were used to prepare ELISA plates following the manufacturer's instructions.

[0028] For some food extracts, the inventors expect that food extracts prepared with specific procedures to generate food extracts provides more superior results in detecting elevated IgG reactivity in Ulcerative Colitis patients compared to commercially available food extracts. For example, for grains and nuts, a three-step procedure of generating food extracts is preferred. The first step is a defatting step. In this step, lipids from grains and nuts are extracted by contacting the flour of grains and nuts with a non-polar solvent and collecting residue. Then, the defatted grain or nut flour are extracted by contacting the flour with elevated pH to obtain a mixture and removing the solid from the mixture to obtain the liquid extract. Once the liquid extract is generated, the liquid extract is stabilized by adding an aqueous formulation. In a preferred embodiment, the aqueous formulation includes a sugar alcohol, a metal chelating agent, protease inhibitor, mineral salt, and buffer component 20-50 mM of buffer from 4-9 pH. This formulation allowed for long term storage at -70 °C and multiple freeze-thaws without a loss of activity.

[0029] For another example, for meats and fish, a two step procedure of generating food extract is preferred. The first step is an extraction step. In this step, extracts from raw, uncooked meats or fish are generated by emulsifying the raw, uncooked meats or fish in an aqueous buffer formulation in a high impact pressure processor. Then, solid materials are removed to obtain liquid extract. Once the liquid extract is generated, the liquid extract is stabilized by adding an aqueous formulation. In a preferred embodiment, the aqueous formulation includes a sugar alcohol, a metal chelating agent, protease inhibitor, mineral salt, and buffer component 20-50 mM of buffer from 4-9 pH. This formulation allowed for long term storage at -70 °C and multiple freeze-thaws without a loss of activity.

[0030] For still another example, for fruits and vegetables, a two step procedure of generating food extract is preferred. The first step is an extraction step. In this step, liquid extracts from fruits or vegetables are generated using an extractor (e.g., masticating juicer, etc) to pulverize foods and extract juice. Then, solid materials are removed to obtain liquid extract. Once the liquid extract is generated, the liquid extract is stabilized by adding an aqueous formulation. In a preferred embodiment, the aqueous formulation includes a sugar alcohol, a metal chelating agent, protease inhibitor, mineral salt, and buffer component 20-50 mM of buffer from 4-9 pH. This formulation allowed for long term storage at -70 °C and multiple freeze-thaws without a loss of activity.

[0031] Blocking of ELISA plates: To optimize signal to noise, plates will be blocked with a proprietary blocking buffer. In a preferred embodiment, the blocking buffer includes 20-50 mM of buffer from 4-9 pH, a protein of animal origin and a short chain alcohol. Other blocking buffers, including several commercial preparations, can be attempted but may not provide adequate signal to noise and low assay variability required.

[0032] ELISA preparation and sample testing: Food antigen preparations were immobilized onto respective microtiter wells following the manufacturer's instructions. For the assays, the food antigens were allowed to react with antibodies present in the patients' serum, and excess serum proteins were removed by a wash step. For detection of IgG antibody binding, enzyme labeled anti-IgG antibody conjugate was allowed to react with antigen-antibody complex. A color was developed by the addition of a substrate that reacts with the coupled enzyme. The color intensity was measured and is directly proportional to the concentration of IgG antibody specific to a particular food antigen.

[0033] Methodology to determine ranked food list in order of ability of ELISA signals to distinguish Ulcerative Colitis from control subjects: Out of an initial selection (e.g., 100 food items, or 150 food items, or even more), samples can be eliminated prior to analysis due to low consumption in an intended population. In addition, specific food items can be used as being representative of a larger generic food group, especially where prior testing has established a correlation among different species within a generic group (most preferably in both genders, but also suitable for correlation for a single gender). For example, green pepper could be dropped in favor of chili pepper as representative of the "pepper" food group, or sweet potato could be dropped in favor of potato as representative of the "potato" food group. In further preferred aspects, the final list foods will be shorter than 50 food items, and more preferably equal or less than of 40 food items.

[0034] Since the foods ultimately selected for the food intolerance panel will not be specific for a particular gender, a gender-neutral food list is necessary. Since the observed sample will be at least initially imbalanced by gender (e.g., Controls: 40% female, Ulcerative Colitis: 55% female), differences in ELISA signal magnitude strictly due to gender will

be removed by modeling signal scores against gender using a two-sample t-test and storing the residuals for further analysis. For each of the tested foods, residual signal scores will be compared between Ulcerative Colitis and controls using a permutation test on a two-sample t-test with a relative high number of resamplings (e.g., >1,000, more preferably >10,000, even more preferably >50,000). The Satterthwaite approximation can then be used for the denominator degrees

of freedom to account for lack of homogeneity of variances, and the 2-tailed permuted p-value will represent the raw p-value for each food. False Discovery Rates (FDR) among the comparisons, will be adjusted by any acceptable statistical procedures (e.g., Benjamini-Hochberg, Family-wise Error Rate (FWER), Per Comparison Error Rate (PCER), etc.).

[0035] Foods were then ranked according to their 2-tailed FDR multiplicity-adjusted p-values. Foods with adjusted p-values equal to or lower than the desired FDR threshold are deemed to have significantly higher signal scores among Ulcerative Colitis than control subjects and therefore deemed candidates for inclusion into a food intolerance panel. A typical result that is representative of the outcome of the statistical procedure is provided in **Table 2**. Here the ranking of foods is according to 2-tailed permutation T-test p-values with FDR adjustment.

[0036] Based on earlier experiments (data not shown here, see US 62/327932), the inventors contemplate that even for the same food preparation tested, the ELISA score for at least several food items will vary dramatically, and exemplary raw data are provided in **Table 3**. As should be readily appreciated, data unstratified by gender will therefore lose significant explanatory power where the same cutoff value is applied to raw data for male and female data. To overcome such disadvantage, the inventors therefore contemplate stratification of the data by gender as described below.

[0037] Statistical Method for Cutpoint Selection for each Food: The determination of what ELISA signal scores would constitute a "positive" response can be made by summarizing the distribution of signal scores among the Control subjects. For each food, Ulcerative Colitis subjects who have observed scores greater than or equal to selected quantiles of the Control subject distribution will be deemed "positive". To attenuate the influence of any one subject on cutpoint determination, each food-specific and gender-specific dataset will be bootstrap resampled 1000 times. Within each bootstrap replicate, the 90th and 95th percentiles of the Control signal scores will be determined. Each Ulcerative Colitis subject in the bootstrap sample will be compared to the 90th and 95% percentiles to determine whether he/she had a "positive" response. The final 90th and 95th percentile-based cutpoints for each food and gender will be computed as the average 90th and 95th percentiles across the 1000 samples. The number of foods for which each Ulcerative Colitis subject will be rated as "positive" was computed by pooling data across foods. Using such method, the inventors will be now able to identify cutoff values for a predetermined percentile rank that in most cases was substantially different as can be taken from **Table 4**.

[0038] Typical examples for the gender difference in IgG response in blood with respect to green pea is shown in **Figures 1A-1D**, where Figure 1A shows the signal distribution in men along with the 95th percentile cutoff as determined from the male control population. Figure 1B shows the distribution of percentage of male Ulcerative Colitis subjects exceeding the 90th and 95th percentile, while Figure 1C shows the signal distribution in women along with the 95th percentile cutoff as determined from the female control population. Figure 1D shows the distribution of percentage of female Ulcerative Colitis subjects exceeding the 90th and 95th percentile. In the same fashion, **Figures 2A-2D** exemplarily depict the differential response to cantaloupe, **Figures 3A-3D** exemplarily depict the differential response to pinto bean, and **Figures 4A-4D** exemplarily depict the differential response to cucumber. **Figures 5A-5B** show the distribution of Ulcerative Colitis subjects by number of foods that were identified as trigger foods at the 90th percentile (5A) and 95th percentile (5B). Inventors contemplate that regardless of the particular food items, male and female responses will be notably distinct.

[0039] It should be noted that nothing in the art have provided any predictable food groups related to Ulcerative Colitis that is gender-stratified. Thus, a discovery of food items that show distinct responses by gender is a surprising result, which could not be obviously expected in view of all previously available arts. In other words, selection of food items based on gender stratification provides an unexpected technical effect such that statistical significances for particular food items as triggering food among male or female Ulcerative Colitis patients have been significantly improved.

[0040] Normalization of IgG Response Data: While the raw data of the patient's IgG response results can be used to compare strength of response among given foods, it is also contemplated that the IgG response results of a patient are normalized and indexed to generate unit-less numbers for comparison of relative strength of response to a given food. For example, one or more of a patient's food specific IgG results (e.g., IgG specific to orange and IgG specific to malt) can be normalized to the patient's total IgG. The normalized value of the patient's IgG specific to orange can be 0.1 and the normalized value of the patient's IgG specific to malt can be 0.3. In this scenario, the relative strength of the patient's response to malt is three times higher compared to orange. Then, the patient's sensitivity to malt and orange can be indexed as such.

[0041] In other examples, one or more of a patient's food specific IgG results (e.g., IgG specific to shrimp and IgG specific to pork) can be normalized to the global mean of that patient's food specific IgG results. The global means of the patient's food specific IgG can be measured by total amount of the patient's food specific IgG. In this scenario, the patient's specific IgG to shrimp can be normalized to the mean of patient's total food specific IgG (e.g., mean of IgG levels to shrimp, pork, Dungeness crab, chicken, peas, etc.). However, it is also contemplated that the global means of

the patient's food specific IgG can be measured by the patient's IgG levels to a specific type of food via multiple tests. If the patient have been tested for his sensitivity to shrimp five times and to pork seven times previously, the patient's new IgG values to shrimp or to pork are normalized to the mean of five-times test results to shrimp or the mean of seven-times test results to pork. The normalized value of the patient's IgG specific to shrimp can be 6.0 and the normalized value of the patient's IgG specific to pork can be 1.0. In this scenario, the patient has six times higher sensitivity to shrimp at this time compared to his average sensitivity to shrimp, but substantially similar sensitivity to pork. Then, the patient's sensitivity to shrimp and pork can be indexed based on such comparison.

[0042] Methodology to determine the subset of Ulcerative Colitis patients with food sensitivities that underlie Ulcerative Colitis: While it is suspected that food sensitivities plays a substantial role in signs and symptoms of Ulcerative Colitis, some Ulcerative Colitis patients may not have food sensitivities that underlie Ulcerative Colitis. Those patients would not be benefit from dietary intervention to treat signs and symptoms of Ulcerative Colitis. To determine the subset of such patients, body fluid samples of Ulcerative Colitis patients and non-Ulcerative Colitis patients can be tested with ELISA test using test devices with up to 58 food samples.

[0043] **Table 5A** and **Table 5B** provide exemplary raw data. As should be readily appreciated, the data indicate number of positive results out of 58 sample foods based on 90th percentile value (**Table 5A**) or 95th percentile value (**Table 5B**). The first column is Ulcerative Colitis (n=103); second column is non-Ulcerative Colitis (n=163) by ICD-10 code. Average and median number of positive foods was computed for Ulcerative Colitis and non-Ulcerative Colitis patients. From the raw data shown in **Table 5A** and **Table 5B**, average and standard deviation of the number of positive foods was computed for Ulcerative Colitis and non-Ulcerative Colitis patients. Additionally, the number and percentage of patients with zero positive foods was calculated for both Ulcerative Colitis and non-Ulcerative Colitis. The number and percentage of patients with zero positive foods in the Ulcerative Colitis population is more than 6-fold lower than the percentage of patients with zero positive foods in the non-Ulcerative Colitis population (3% vs. 19%, respectively) based on 90th percentile value (**Table 5A**), and the percentage of patients in the Ulcerative Colitis population with zero positive foods is also less than half of that seen in the non-Ulcerative Colitis population (12 % vs. 31%, respectively) based on 95th percentile value (**Table 5B**). Thus, it can be easily appreciated that the Ulcerative Colitis patient having sensitivity to zero positive foods is unlikely to have food sensitivities underlying their signs and symptoms of Ulcerative Colitis.

[0044] **Table 6A** and **Table 7A** show exemplary statistical data summarizing the raw data of two patient populations shown in Table 5A. The statistical data includes normality, arithmetic mean, median, percentiles and 95% confidence interval (CI) for the mean and median representing number of positive foods in the Ulcerative Colitis population and the non-Ulcerative Colitis population. **Table 6B** and **Table 7B** show exemplary statistical data summarizing the raw data of two patient populations shown in Table 5B. The statistical data includes normality, arithmetic mean, median, percentiles and 95% confidence interval (CI) for the mean and median representing number of positive foods in the Ulcerative Colitis population and the non-Ulcerative Colitis population.

[0045] **Table 8A** and **Table 9A** show exemplary statistical data summarizing the raw data of two patient populations shown in Table 5A. In Tables 8A and 9A, the raw data was transformed by logarithmic transformation to improve the data interpretation. **Table 8B** and **Table 9B** show another exemplary statistical data summarizing the raw data of two patient populations shown in Table 5B. In Tables 8B and 9B, the raw data was transformed by logarithmic transformation to improve the data interpretation.

[0046] **Table 10A** and **Table 11A** show exemplary statistical data of an independent T-test (Table 10A, logarithmically transformed data) and a Mann-Whitney test (Table 11A) to compare the geometric mean number of positive foods between the Ulcerative Colitis and non-Ulcerative Colitis samples. The data shown in Table 10A and Table 11A indicate statistically significant differences in the geometric mean of positive number of foods between the Ulcerative Colitis population and the non-Ulcerative Colitis population. In both statistical tests, it is shown that the number of positive responses with 58 food samples is significantly higher in the Ulcerative Colitis population than in the non-Ulcerative Colitis population with an average discriminatory p-value of ≤ 0.0001 . These statistical data is also illustrated as a box and whisker plot in **Figure 6A**, and a notched box and whisker plot in **Figure 6B**.

[0047] **Table 10B** and **Table 11B** show exemplary statistical data of an independent T-test (Table 10A, logarithmically transformed data) and a Mann-Whitney test (Table 11B) to compare the geometric mean number of positive foods between the Ulcerative Colitis and non-Ulcerative Colitis samples. The data shown in Table 10B and Table 11B indicate statistically significant differences in the geometric mean of positive number of foods between the Ulcerative Colitis population and the non-Ulcerative Colitis population. In both statistical tests, it is shown that the number of positive responses with 58 food samples is significantly higher in the Ulcerative Colitis population than in the non-Ulcerative Colitis population with an average discriminatory p-value of ≤ 0.0001 . These statistical data is also illustrated as a box and whisker plot in **Figure 6C**, and a notched box and whisker plot in **Figure 6D**.

[0048] **Table 12A** shows exemplary statistical data of a Receiver Operating Characteristic (ROC) curve analysis of data shown in Tables 5A-11A to determine the diagnostic power of the test used in Table 5 at discriminating Ulcerative Colitis from non-Ulcerative Colitis subjects. When a cutoff criterion of more than 5 positive foods is used, the test yields a data with 66% sensitivity and 68% specificity, with an area under the curve (AUROC) of 0.720. The p-value for the

ROC is significant at a p-value of <0.0001 . **Figure 7A** illustrates the ROC curve corresponding to the statistical data shown in Table 12A. Because the statistical difference between the Ulcerative Colitis population and the non-Ulcerative Colitis population is significant when the test results are cut off to a positive number of 5, the number of foods for which a patient tests positive could be used as a confirmation of the primary clinical diagnosis of Ulcerative Colitis, and whether it is likely that food sensitivities underlies on the patient's signs and symptoms of Ulcerative Colitis. Therefore, the above test can be used as another 'rule in' test to add to currently available clinical criteria for diagnosis for Ulcerative Colitis.

[0049] As shown in Tables 5A-12A, and Figure 7A, based on 90th percentile data, the number of positive foods seen in Ulcerative Colitis vs. non-Ulcerative Colitis subjects is significantly different whether the geometric mean or median of the data is compared. The number of positive foods that a person has is indicative of the presence of Ulcerative Colitis in subjects. The test has discriminatory power to detect Ulcerative Colitis with -66% sensitivity and -68% specificity. Additionally, the absolute number and percentage of subjects with 0 positive foods is also very different in Ulcerative Colitis vs. non-Ulcerative Colitis subjects, with a far lower percentage of Ulcerative Colitis subjects (3%) having 0 positive foods than non-Ulcerative Colitis subjects (19%). The data suggests a subset of Ulcerative Colitis patients may have Ulcerative Colitis due to other factors than diet, and may not benefit from dietary restriction.

[0050] **Table 12B** shows exemplary statistical data of a Receiver Operating Characteristic (ROC) curve analysis of data shown in Tables 5B-1 1B to determine the diagnostic power of the test used in Table 5 at discriminating Ulcerative Colitis from non-Ulcerative Colitis subjects. When a cutoff criterion of more than 3 positive foods is used, the test yields a data with 60.2% sensitivity and 75.5% specificity, with an area under the curve (AUROC) of 0.719. The p-value for the ROC is significant at a p-value of <0.0001 . **Figure 7B** illustrates the ROC curve corresponding to the statistical data shown in Table 12B. Because the statistical difference between the Ulcerative Colitis population and the non-Ulcerative Colitis population is significant when the test results are cut off to positive number of >3 , the number of foods that a patient tests positive could be used as a confirmation of the primary clinical diagnosis of Ulcerative Colitis, and whether it is likely that food sensitivities underlies on the patient's signs and symptoms of Ulcerative Colitis. Therefore, the above test can be used as another 'rule in' test to add to currently available clinical criteria for diagnosis for Ulcerative Colitis.

[0051] As shown in Tables 5B-12B, and Figure 7B, based on 95th percentile data, the number of positive foods seen in Ulcerative Colitis vs. non-Ulcerative Colitis subjects is significantly different whether the geometric mean or median of the data is compared. The number of positive foods that a person has is indicative of the presence of Ulcerative Colitis in subjects. The test has discriminatory power to detect Ulcerative Colitis with ~60% sensitivity and -76% specificity. Additionally, the absolute number and percentage of subjects with 0 positive foods is also very different in Ulcerative Colitis vs. non-Ulcerative Colitis subjects, with a far lower percentage of Ulcerative Colitis subjects (-19%) having 0 positive foods than non-Ulcerative Colitis subjects (-31%). The data suggests a subset of Ulcerative Colitis patients may have Ulcerative Colitis due to other factors than diet, and may not benefit from dietary restriction.

[0052] Method for determining distribution of per-person number of foods declared "positive": To determine the distribution of number of "positive" foods per person and measure the diagnostic performance, the analysis will be performed with 58 food items from Table 2, which shows most positive responses to Ulcerative Colitis patients. To attenuate the influence of any one subject on this analysis, each food-specific and gender-specific dataset will be bootstrap resampled 1000 times. Then, for each food item in the bootstrap sample, sex-specific cutpoint will be determined using the 90th and 95th percentiles of the control population. Once the sex-specific cutpoints are determined, the sex-specific cutpoints will be compared with the observed ELISA signal scores for both control and Ulcerative Colitis subjects. In this comparison, if the observed signal is equal or more than the cutpoint value, then it will be determined "positive" food, and if the observed signal is less than the cutpoint value, then it will be determined "negative" food.

[0053] Once all food items were determined either positive or negative, the results of the 116 (58 foods x 2 cutpoints) calls for each subject will be saved within each bootstrap replicate. Then, for each subject, 58 calls will be summed using 90th percentile as cutpoint to get "Number of Positive Foods (90th)," and the rest of 58 calls will be summed using 95th percentile to get "Number of Positive Foods (95th)." Then, within each replicate, "Number of Positive Foods (90th)" and "Number of Positive Foods (95th)" will be summarized across subjects to get descriptive statistics for each replicate as follows: 1) overall means equals to the mean of means, 2) overall standard deviation equals to the mean of standard deviations, 3) overall medial equals to the mean of medians, 4) overall minimum equals to the minimum of minimums, and 5) overall maximum equals to maximum of maximum. In this analysis, to avoid non-integer "Number of Positive Foods" when computing frequency distribution and histogram, the authors will pretend that the 1000 repetitions of the same original dataset were actually 999 sets of new subjects of the same size added to the original sample. Once the summarization of data is done, frequency distributions and histograms will be generated for both "Number of Positive Foods (90th)" and "Number of Positive Foods (95th)" for both genders and for both Ulcerative Colitis subjects and control subjects using programs "a_pos_foods.sas, a_pos_foods_by_dx.sas".

[0054] Method for measuring diagnostic performance: To measure diagnostic performance for each food items for each subject, we will use data of "Number of Positive Foods (90th)" and "Number of Positive Foods (95th)" for each subject within each bootstrap replicate described above. In this analysis, the cutpoint was set to 1. Thus, if a subject has one or more "Number of Positive Foods (90th)", then the subject will be called "Has Ulcerative Colitis." If a subject

EP 3 449 255 B1

has less than one "Number of Positive Foods (90th)", then the subject will be called "Does Not Have Ulcerative Colitis." When all calls were made, the calls were compared with actual diagnosis to determine whether a call was a True Positive (TP), True Negative (TN), False Positive (FP), or False Negative (FN). The comparisons will be summarized across subjects to get the performance metrics of sensitivity, specificity, positive predictive value, and negative predictive value for both "Number of Positive Foods (90th)" and "Number of Positive Foods(95th)" when the cutpoint is set to 1 for each method. Each (sensitivity, 1-specificity) pair becomes a point on the ROC curve for this replicate.

[0055] To increase the accuracy, the analysis above will be repeated by incrementing cutpoint from 2 up to 58, and repeated for each of the 1000 bootstrap replicates. Then the performance metrics across the 1000 bootstrap replicates will be summarized by calculating averages using a program "t_pos_foods_by_dx.sas". The results of diagnostic performance for female and male are shown in **Tables 13A and 13B** (90th percentile) and **Tables 14A and 14B** (95th percentile).

Table 1

Abalone	Cured Cheese	Onion	Walnut, black
Adlay	Cuttlefish	Orange	Watermelon
Almond	Duck	Oyster	Welch Onion
American Cheese	Durian	Papaya	Wheat
Apple	Eel	Paprika	Wheat bran
Artichoke	Egg White (separate)	Parsley	Yeast (<i>S. cerevisiae</i>)
Asparagus	Egg Yolk (separate)	Peach	Yogurt
Avocado	Egg, white/yolk (comb.)	Peanut	
Baby Bok Choy	Eggplant	Pear	FOOD ADDITIVES
Bamboo shoots	Garlic	Pepper, Black	Arabic Gum
Banana	Ginger	Pineapple	Carboxymethyl Cellulose
Barley, whole grain	Gluten - Gliadin	Pinto bean	Carrageenan
Beef	Goat's milk	Plum	FD&C Blue #1
Beets	Grape, white/concord	Pork	FD&C Red #3
Beta-lactoglobulin	Grapefruit	Potato	FD&C Red #40
Blueberry	Grass Carp	Rabbit	FD&C Yellow #5
Broccoli	Green Onion	Rice	FD&C Yellow #6
Buckwheat	Green pea	Roquefort Cheese	Gelatin
Butter	Green pepper	Rye	Guar Gum
Cabbage	Guava	Saccharine	Maltodextrin
Cane sugar	Hair Tail	Safflower seed	Pectin
Cantaloupe	Hake	Salmon	Whey
Caraway	Halibut	Sardine	Xanthan Gum
Carrot	Hazelnut	Scallop	
Casein	Honey	Sesame	
Cashew	Kelp	Shark fin	
Cauliflower	Kidney bean	Sheep's milk	
Celery	Kiwi Fruit	Shrimp	
Chard	Lamb	Sole	
Cheddar Cheese	Leek	Soybean	
Chick Peas	Lemon	Spinach	
Chicken	Lentils	Squashes	
Chili pepper	Lettuce, Iceberg	Squid	
Chocolate	Lima bean	Strawberry	
Cinnamon	Lobster	String bean	
Clam	Longan	Sunflower seed	
Cocoa Bean	Mackerel	Sweet potato	
Coconut	Malt	Swiss cheese	
Codfish	Mango	Taro	
Coffee	Marjoram	Tea, black	

EP 3 449 255 B1

(continued)

	Cola nut	Millet	Tobacco
	Corn	Mung bean	Tomato
5	Cottage cheese	Mushroom	Trout
	Cow's milk	Mustard seed	Tuna
	Crab	Oat	Turkey
	Cucumber	Olive	Vanilla

10 **Ranking of Foods according to 2-tailed Permutation T-test p-values with FDR adjustment**

[0056]

Table 2

	Rank	Food	Raw p-value	FOR Multiplicity-adj p-value
	1	Green_Pea	0.0000	0.0000
	2	Cantaloupe	0.0000	0.0009
20	3	Pinto_Bean	0.0001	0.0021
	4	Cucumber	0.0001	0.0021
	5	Green_Pepper	0.0001	0.0021
	6	Grapefruit	0.0002	0.0021
	7	Carrot	0.0002	0.0021
25	8	Orange	0.0002	0.0021
	9	Almond	0.0002	0.0021
	10	Sardine	0.0003	0.0021
	11	Sweet_Pot_	0.0003	0.0021
30	12	Broccoli	0.0003	0.0021
	13	Garlic	0.0003	0.0021
	14	Lima_Bean	0.0003	0.0021
	15	Squashes	0.0004	0.0024
	16	Celery	0.0004	0.0025
35	17	String_Bean	0.0006	0.0030
	18	Tomato	0.0008	0.0040
	19	Cauliflower	0.0009	0.0041
	20	Walnut_BlK	0.0010	0.0046
40	21	Sunflower_Sd	0.0012	0.0051
	22	Cane_Sugar	0.0012	0.0051
	23	Buck_Wheat	0.0028	0.0106
	24	Soybean	0.0028	0.0106
	25	Lemon	0.0030	0.0108
45	26	Barley	0.0047	0.0163
	27	Oat	0.0051	0.0170
	28	Oyster	0.0055	0.0173
	29	Mustard	0.0056	0.0173
50	30	Rye	0.0058	0.0173
	31	Peach	0.0068	0.0196
	32	Chili_Pepper	0.0072	0.0201
	33	Spinach	0.0082	0.0222
	34	Peanut	0.0084	0.0222
55	35	Avocado	0.0088	0.0226
	36	Shrimp	0.0094	0.0236
	37	Pineapple	0.0098	0.0239

EP 3 449 255 B1

(continued)

	<i>Rank</i>	<i>Food</i>	<i>Raw p-value</i>	<i>FOR Multiplicity-adj p-value</i>
5	38	Cola_Nut	0.0118	0.0275
	39	Rice	0.0119	0.0275
	40	Cabbage	0.0131	0.0294
	41	Butter	0.0150	0.0330
	42	Eggplant	0.0156	0.0330
10	43	Apple	0.0158	0.0330
	44	Egg	0.0176	0.0359
	45	Wheat	0.0215	0.0419
	46	Cottage_Ch_	0.0219	0.0419
	47	Sole	0.0219	0.0419
15	48	Cashew	0.0238	0.0446
	49	Olive	0.0259	0.0476
	50	Parsley	0.0276	0.0496
	51	Corn	0.0340	0.0578
20	52	Honey	0.0340	0.0578
	53	Chocolate	0.0345	0.0578
	54	Cow_Milk	0.0347	0.0578
	55	Potato	0.0359	0.0587
	56	Onion	0.0467	0.0750
25	57	Tea	0.0506	0.0799
	58	Tobacco	0.0625	0.0970
	59	Banana	0.0706	0.1078
	60	Strawberry	0.0751	0.1127
30	61	Coffee	0.0771	0.1138
	62	Malt	0.0823	0.1195
	63	Scallop	0.0887	0.1268
	64	Chicken	0.0987	0.1388
	65	Yeast_Baker	0.1152	0.1595
35	66	Millet	0.1171	0.1597
	67	Swiss_Ch_	0.1770	0.2378
	68	Turkey	0.1806	0.2381
	69	Cheddar_Ch_	0.1826	0.2381
40	70	Yeast_Brewer	0.2178	0.2801
	71	Yogurt	0.2255	0.2859
	72	Cinnamon	0.2600	0.3250
	73	Clam	0.2998	0.3696
	74	Tuna	0.3102	0.3762
45	75	Beef	0.3135	0.3762
	76	Lettuce	0.3266	0.3868
	77	Trout	0.3672	0.4292
	78	Safflower	0.4487	0.5178
	79	Codfish	0.4712	0.5368
50	80	Salmon	0.5076	0.5711
	81	Mushroom	0.5634	0.6260
	82	Grape	0.5825	0.6389
	83	Blueberry	0.5892	0.6389
55	84	Pork	0.7160	0.7667
	85	Sesame	0.7241	0.7667
	86	Amer_Cheese	0.7739	0.8099

EP 3 449 255 B1

(continued)

Rank	Food	Raw p-value	FOR Multiplicity-adj p-value
87	Lobster	0.7946	0.8220
88	Halibut	0.8497	0.8690
89	Goat_Milk	0.9112	0.9215
90	Crab	0.9888	0.9888

Basic Descriptive Statistics of ELISA Score by Food and Gender Comparing Ulcerative Colitis to Control

[0057]

Table 3

Sex	Food	Diagnosis	N	Mean	ELISA Score		
					SD	Min	Max
FEMALE	Almond	Ulcerative_Colitis	57	10.079	25.036	0.439	158.47
		Control	66	4.034	2.187	0.100	13.068
		Diff (1-2)	—	6.045	17.107	—	—
	Amer_Cheese	Ulcerative_Colitis	57	21.630	31.036	1.602	140.07
		Control	66	23.434	52.616	0.100	400.00
		Diff (1-2)	—	-1.804	43.965	—	—
	Apple	Ulcerative_Colitis	57	5.340	4.304	0.493	28.693
		Control	66	4.432	3.291	0.100	15.890
		Diff (1-2)	—	0.908	3.793	—	—
	Avocado	Ulcerative_Colitis	57	3.858	3.507	0.100	21.077
		Control	66	2.930	2.339	0.100	14.256
		Diff (1-2)	—	0.927	2.938	—	—
	Banana	Ulcerative_Colitis	57	19.827	46.868	0.100	256.94
		Control	66	8.063	14.962	0.100	83.654
		Diff (1-2)	—	11.765	33.717	—	—
	Barley	Ulcerative_Colitis	57	25.942	30.538	1.974	165.95
		Control	66	19.090	12.984	3.026	64.831
		Diff (1-2)	—	6.851	22.851	—	—
	Beef	Ulcerative_Colitis	57	11.027	14.479	1.479	83.266
		Control	66	10.288	13.960	3.026	104.76
		Diff (1-2)	—	0.739	14.202	—	—
	Blueberry	Ulcerative_Colitis	57	5.142	3.166	1.206	17.780
		Control	66	5.440	3.773	0.100	26.772
		Diff (1-2)	—	-0.298	3.505	—	—
Broccoli	Ulcerative_Colitis	57	11.435	15.944	1.355	99.132	
	Control	66	6.280	5.292	0.100	36.378	
	Diff (1-2)	—	5.154	11.520	—	—	
Buck_Wheat	Ulcerative_Colitis	57	12.377	18.040	1.848	104.34	
	Control	66	8.034	4.990	1.316	29.397	
	Diff (1-2)	—	4.342	12.806	—	—	
Butter	Ulcerative_Colitis	57	25.891	26.436	3.865	154.85	
	Control	66	21.874	29.162	0.100	204.33	
	Diff (1-2)	—	4.017	27.933	—	—	
Cabbage	Ulcerative_Colitis	57	13.302	23.916	0.123	135.74	
	Control	66	7.362	10.123	0.100	56.932	
	Diff (1-2)	—	5.940	17.882	—	—	
Cane_Sugar	Ulcerative_Colitis	57	32.174	30.535	8.009	178.78	

EP 3 449 255 B1

(continued)

	Sex	Food	Diagnosis	N	Mean	ELISA Score		
						SD	Min	Max
5			Control	66	18.288	9.172	2.632	43.466
			Diff (1-2)	—	13.885	21.833	—	—
		Cantaloupe	Ulcerative_Colitis	57	12.200	20.373	0.751	149.18
			Control	66	6.154	6.160	0.100	48.752
10			Diff (1-2)	—	6.046	14.576	—	—
		Carrot	Ulcerative_Colitis	57	6.467	6.804	0.987	47.767
			Control	66	4.813	3.705	0.100	24.141
			Diff (1-2)	—	1.654	5.367	—	—
		Cashew	Ulcerative_Colitis	57	12.920	21.204	0.966	98.745
15			Control	66	9.924	16.382	0.100	94.907
			Diff (1-2)	—	2.996	18.768	—	—
		Cauliflower	Ulcerative_Colitis	57	9.756	18.230	0.100	131.25
			Control	66	5.977	8.336	0.100	58.808
20			Diff (1-2)	—	3.778	13.825	—	—
		Celery	Ulcerative_Colitis	57	12.601	15.076	3.080	107.65
			Control	66	9.634	5.975	0.395	32.141
			Diff (1-2)	—	2.967	11.152	—	—
		Cheddar_Ch_	Ulcerative_Colitis	57	32.153	50.450	1.833	266.75
25			Control	66	26.852	55.697	0.100	400.00
			Diff (1-2)	—	5.302	53.333	—	—
		Chicken	Ulcerative_Colitis	57	21.024	19.326	3.865	106.76
			Control	66	18.303	10.514	4.743	61.887
			Diff (1-2)	—	2.721	15.240	—	—
30		Chili_Pepper	Ulcerative_Colitis	57	9.931	9.801	1.517	56.432
			Control	66	8.577	7.784	0.100	42.583
			Diff (1-2)	—	1.355	8.775	—	—
		Chocolate	Ulcerative_Colitis	57	18.043	15.319	3.510	71.901
35			Control	66	14.350	6.578	3.006	35.317
			Diff (1-2)	—	3.693	11.483	—	—
		Cinnamon	Ulcerative_Colitis	57	34.013	22.107	5.090	119.22
			Control	66	32.170	24.180	5.374	132.49
			Diff (1-2)	—	1.843	23.244	—	—
40		Clam	Ulcerative_Colitis	57	39.841	37.147	9.968	197.01
			Control	66	52.166	58.253	7.819	400.00
			Diff (1-2)	—	-12.324	49.614	—	—
		Codfish	Ulcerative_Colitis	57	17.321	10.395	3.450	50.000
45			Control	66	29.652	31.720	6.200	168.28
			Diff (1-2)	—	-12.330	24.300	—	—
		Coffee	Ulcerative_Colitis	57	38.327	69.479	2.523	400.00
			Control	66	29.631	46.880	5.215	346.81
			Diff (1-2)	—	8.696	58.436	—	—
50		Cola_Nut	Ulcerative_Colitis	57	35.111	16.941	14.321	94.417
			Control	66	29.138	12.588	8.723	58.129
			Diff (1-2)	—	5.972	14.763	—	—
		Corn	Ulcerative_Colitis	57	21.320	39.276	1.426	231.14
55			Control	66	11.407	23.137	0.100	187.68
			Diff (1-2)	—	9.913	31.646	—	—
		Cottage_Ch_	Ulcerative_Colitis	57	93.700	117.494	2.594	400.00

EP 3 449 255 B1

(continued)

	Sex	Food	Diagnosis	N	Mean	ELISA Score		
						SD	Min	Max
5			Control	66	76.158	92.333	0.100	400.00
			Diff (1-2)	—	17.543	104.732	—	—
		Cow_Milk	Ulcerative_Colitis	57	85.720	104.244	0.682	400.00
			Control	66	75.882	86.959	0.100	400.00
10			Diff (1-2)	—	9.838	95.349	—	—
		Crab	Ulcerative_Colitis	57	19.921	13.939	4.440	70.735
			Control	66	23.583	17.654	3.803	93.236
			Diff (1-2)	—	-3.661	16.042	—	—
		Cucumber	Ulcerative_Colitis	57	16.195	18.948	1.232	120.91
15			Control	66	8.461	8.149	0.100	38.939
			Diff (1-2)	—	7.735	14.207	—	—
		Egg	Ulcerative_Colitis	57	85.576	122.235	2.451	400.00
			Control	66	55.102	89.966	0.100	400.00
20			Diff (1-2)	—	30.475	106.127	—	—
		Eggplant	Ulcerative_Colitis	57	9.361	12.488	0.100	69.989
			Control	66	5.732	5.993	0.100	31.330
			Diff (1-2)	—	3.628	9.564	—	—
		Garlic	Ulcerative_Colitis	57	20.485	17.805	2.413	90.456
25			Control	66	11.174	5.779	3.380	28.482
			Diff (1-2)	—	9.310	12.832	—	—
		Goat_Milk	Ulcerative_Colitis	57	13.970	15.091	1.146	78.345
			Control	66	15.413	28.452	0.100	180.08
			Diff (1-2)	—	-1.443	23.243	—	—
30		Grape	Ulcerative_Colitis	57	20.135	11.537	4.169	78.950
			Control	66	20.276	6.827	10.650	47.817
			Diff (1-2)	—	-0.141	9.308	—	—
		Grapefruit	Ulcerative_Colitis	57	5.675	9.301	0.100	68.905
35			Control	66	3.278	2.446	0.100	14.364
			Diff (1-2)	—	2.397	6.576	—	—
		Green_Pea	Ulcerative_Colitis	57	15.251	15.940	0.658	79.774
			Control	66	8.631	7.160	0.496	32.502
			Diff (1-2)	—	6.620	12.047	—	—
40		Green_Pepper	Ulcerative_Colitis	57	7.641	14.196	0.100	107.26
			Control	66	4.149	2.875	0.100	14.364
			Diff (1-2)	—	3.492	9.885	—	—
		Halibut	Ulcerative_Colitis	57	10.765	5.076	2.587	27.746
45			Control	66	11.119	7.129	2.729	44.884
			Diff (1-2)	—	-0.354	6.263	—	—
		Honey	Ulcerative_Colitis	57	12.330	7.625	2.742	37.290
			Control	66	10.185	4.203	4.227	19.876
			Diff (1-2)	—	2.145	6.033	—	—
50		Lemon	Ulcerative_Colitis	57	3.296	3.105	0.100	22.003
			Control	66	2.482	2.159	0.100	14.688
			Diff (1-2)	—	0.814	2.639	—	—
		Lettuce	Ulcerative_Colitis	57	11.835	9.147	2.711	59.964
55			Control	66	11.368	6.472	0.921	29.851
			Diff (1-2)	—	0.467	7.825	—	—
		Lima_Bean	Ulcerative_Colitis	57	10.268	8.919	0.329	39.575

EP 3 449 255 B1

(continued)

	Sex	Food	Diagnosis	N	Mean	ELISA Score		
						SD	Min	Max
5			Control	66	6.624	8.761	0.100	65.634
			Diff (1-2)	—	3.643	8.835	—	—
		Lobster	Ulcerative_Colitis	57	12.931	10.997	1.181	62.481
			Control	66	13.398	8.359	3.938	46.560
10			Diff (1-2)	—	-0.468	9.670	—	—
		Malt	Ulcerative_Colitis	57	23.676	17.406	5.814	105.68
			Control	66	21.743	11.326	3.684	57.151
			Diff (1-2)	—	1.933	14.461	—	—
		Millet	Ulcerative_Colitis	57	5.424	5.233	0.487	27.187
15			Control	66	4.889	7.091	0.100	46.663
			Diff (1-2)	—	0.535	6.299	—	—
		Mushroom	Ulcerative_Colitis	57	9.754	12.339	0.100	69.107
			Control	66	13.174	12.549	1.117	49.656
20			Diff (1-2)	—	-3.419	12.452	—	—
		Mustard	Ulcerative_Colitis	57	11.854	15.378	2.545	98.146
			Control	66	8.842	5.224	0.100	23.452
			Diff (1-2)	—	3.011	11.140	—	—
		Oat	Ulcerative_Colitis	57	40.965	76.954	0.768	400.00
25			Control	66	16.237	14.506	0.100	76.165
			Diff (1-2)	—	24.727	53.421	—	—
		Olive	Ulcerative_Colitis	57	31.615	30.330	3.573	180.11
			Control	66	23.704	14.281	5.272	59.488
			Diff (1-2)	—	7.911	23.137	—	—
30		Onion	Ulcerative_Colitis	57	17.905	24.231	0.438	119.13
			Control	66	11.329	16.935	1.184	114.37
			Diff (1-2)	—	6.576	20.635	—	—
		Orange	Ulcerative_Colitis	57	26.028	25.192	1.206	112.32
35			Control	66	15.289	11.608	1.489	47.125
			Diff (1-2)	—	10.738	19.134	—	—
		Oyster	Ulcerative_Colitis	57	63.062	63.526	4.608	372.89
			Control	66	42.674	33.485	5.656	168.59
			Diff (1-2)	—	20.388	49.699	—	—
40		Parsley	Ulcerative_Colitis	57	6.938	11.992	0.100	70.169
			Control	66	5.005	6.541	0.100	34.932
			Diff (1-2)	—	1.933	9.462	—	—
		Peach	Ulcerative_Colitis	57	13.457	20.732	0.123	124.35
45			Control	66	7.145	7.742	0.100	33.820
			Diff (1-2)	—	6.312	15.203	—	—
		Peanut	Ulcerative_Colitis	57	14.262	48.433	0.219	349.73
			Control	66	5.563	4.941	0.100	26.567
			Diff (1-2)	—	8.699	33.147	—	—
50		Pineapple	Ulcerative_Colitis	57	53.335	86.808	0.329	400.00
			Control	66	23.710	46.114	0.100	278.44
			Diff (1-2)	—	29.626	68.044	—	—
		Pinto_Bean	Ulcerative_Colitis	57	16.597	22.820	2.254	152.98
55			Control	66	10.138	8.167	0.100	48.623
			Diff (1-2)	—	6.459	16.639	—	—
		Pork	Ulcerative_Colitis	57	15.004	15.800	2.962	80.448

EP 3 449 255 B1

(continued)

	Sex	Food	Diagnosis	N	Mean	ELISA Score		
						SD	Min	Max
5			Control	66	15.347	10.345	4.339	65.759
			Diff (1-2)	—	-0.343	13.154	—	—
		Potato	Ulcerative_Colitis	57	17.934	24.208	4.278	183.78
			Control	66	13.615	6.063	6.200	40.802
10			Diff (1-2)	—	4.318	17.058	—	—
		Rice	Ulcerative_Colitis	57	31.549	49.019	6.184	362.21
			Control	66	21.551	16.950	3.350	92.642
			Diff (1-2)	—	9.998	35.587	—	—
		Rye	Ulcerative_Colitis	57	6.931	12.152	1.338	92.310
15			Control	66	5.237	3.633	0.100	22.824
			Diff (1-2)	—	1.694	8.685	—	—
		Safflower	Ulcerative_Colitis	57	8.917	6.880	2.531	41.242
			Control	66	8.776	8.189	1.722	48.833
20			Diff (1-2)	—	0.140	7.611	—	—
		Salmon	Ulcerative_Colitis	57	9.369	6.906	2.413	44.560
			Control	66	9.377	7.261	2.862	56.530
			Diff (1-2)	—	-0.008	7.099	—	—
		Sardine	Ulcerative_Colitis	57	44.148	20.802	12.069	102.96
25			Control	66	37.084	16.695	7.190	88.964
			Diff (1-2)	—	7.064	18.708	—	—
		Scallop	Ulcerative_Colitis	57	61.726	39.681	14.451	165.26
			Control	66	64.291	29.551	18.605	148.58
			Diff (1-2)	—	-2.565	34.610	—	—
30		Sesame	Ulcerative_Colitis	57	73.122	118.220	0.100	400.00
			Control	66	80.704	93.902	5.984	400.00
			Diff (1-2)	—	-7.582	105.854	—	—
		Shrimp	Ulcerative_Colitis	57	21.492	22.231	1.717	137.49
35			Control	66	33.150	27.875	6.607	113.66
			Diff (1-2)	—	-11.658	25.419	—	—
		Sole	Ulcerative_Colitis	57	6.020	3.293	1.316	20.885
			Control	66	6.440	6.960	0.100	54.883
			Diff (1-2)	—	-0.419	5.571	—	—
40		Soybean	Ulcerative_Colitis	57	21.445	26.605	4.187	187.77
			Control	66	15.294	9.373	2.481	49.071
			Diff (1-2)	—	6.151	19.360	—	—
		Spinach	Ulcerative_Colitis	57	26.961	49.539	6.802	367.99
45			Control	66	20.485	13.172	6.051	66.626
			Diff (1-2)	—	6.476	35.057	—	—
		Squashes	Ulcerative_Colitis	57	17.555	11.532	4.059	53.553
			Control	66	13.415	11.597	1.842	74.279
			Diff (1-2)	—	4.140	11.567	—	—
50		Strawberry	Ulcerative_Colitis	57	6.064	5.341	0.100	28.233
			Control	66	5.563	5.305	0.100	35.745
			Diff (1-2)	—	0.501	5.321	—	—
		String_Bean	Ulcerative_Colitis	57	54.019	30.799	7.680	149.68
55			Control	66	41.957	22.678	9.539	125.69
			Diff (1-2)	—	12.063	26.744	—	—
		Sunflower_Sd	Ulcerative_Colitis	57	15.717	21.185	2.084	103.84

EP 3 449 255 B1

(continued)

	Sex	Food	Diagnosis	N	Mean	ELISA Score		
						SD	Min	Max
5			Control	66	9.948	6.094	2.632	33.347
			Diff (1-2)	—	5.769	15.089	—	—
		Sweet_Pot_	Ulcerative_Colitis	57	13.118	18.306	2.218	138.11
			Control	66	8.592	4.479	0.395	25.009
10			Diff (1-2)	—	4.525	12.879	—	—
		Swiss_Ch_	Ulcerative_Colitis	57	49.090	77.461	2.316	400.00
			Control	66	39.219	73.725	0.100	400.00
			Diff (1-2)	—	9.871	75.477	—	—
		Tea	Ulcerative_Colitis	57	35.381	24.818	12.508	160.22
15			Control	66	29.771	12.014	11.634	64.535
			Diff (1-2)	—	5.610	19.042	—	—
		Tobacco	Ulcerative_Colitis	57	39.527	26.849	10.906	135.98
			Control	66	33.566	16.789	7.809	82.097
20			Diff (1-2)	—	5.961	22.024	—	—
		Tomato	Ulcerative_Colitis	57	15.238	16.813	2.218	107.39
			Control	66	9.066	7.694	0.100	42.078
			Diff (1-2)	—	6.172	12.753	—	—
		Trout	Ulcerative_Colitis	57	13.805	8.087	3.749	47.896
25			Control	66	16.138	10.667	5.596	76.221
			Diff (1-2)	—	-2.333	9.560	—	—
		Tuna	Ulcerative_Colitis	57	15.838	10.358	2.254	56.001
			Control	66	18.092	12.707	3.873	64.090
			Diff (1-2)	—	-2.253	11.679	—	—
30		Turkey	Ulcerative_Colitis	57	16.023	14.275	3.006	95.919
			Control	66	14.461	6.976	4.094	32.151
			Diff (1-2)	—	1.561	10.975	—	—
		Walnut_BlK	Ulcerative_Colitis	57	40.389	58.256	8.009	400.00
35			Control	66	25.386	17.254	6.943	117.46
			Diff (1-2)	—	15.003	41.601	—	—
		Wheat	Ulcerative_Colitis	57	25.837	67.552	2.304	400.00
			Control	66	18.402	29.364	0.790	209.95
			Diff (1-2)	—	7.435	50.746	—	—
40		Yeast_Baker	Ulcerative_Colitis	57	12.519	30.904	1.316	223.99
			Control	66	5.545	3.349	0.526	18.811
			Diff (1-2)	—	6.974	21.167	—	—
		Yeast_Brewer	Ulcerative_Colitis	57	25.350	61.479	2.194	400.00
45			Control	66	10.847	7.818	0.100	43.887
			Diff (1-2)	—	14.503	42.215	—	—
		Yogurt	Ulcerative_Colitis	57	21.430	20.338	4.240	101.82
			Control	66	22.930	30.973	0.100	215.73
			Diff (1-2)	—	-1.500	26.585	—	—
50	MALE	Almond	Ulcerative_Colitis	46	9.713	10.631	0.100	48.413
			Control	97	4.049	2.231	0.100	12.591
			Diff (1-2)	—	5.664	6.282	—	—
		Amer_Cheese	Ulcerative_Colitis	46	27.588	27.243	0.100	105.40
55			Control	97	22.619	34.069	0.468	197.38
			Diff (1-2)	—	4.969	32.049	—	—
		Apple	Ulcerative_Colitis	46	5.840	4.036	0.100	20.284

EP 3 449 255 B1

(continued)

	Sex	Food	Diagnosis	N	Mean	ELISA Score		
						SD	Min	Max
5			Control	97	4.383	2.900	0.100	13.795
			Diff (1-2)	—	1.457	3.305	—	—
		Avocado	Ulcerative_Colitis	46	3.569	2.010	0.100	11.275
			Control	97	2.720	2.992	0.100	28.693
10			Diff (1-2)	—	0.849	2.717	—	—
		Banana	Ulcerative_Colitis	46	11.987	18.952	0.100	96.512
			Control	97	8.576	36.151	0.100	350.69
			Diff (1-2)	—	3.411	31.693	—	—
		Barley	Ulcerative_Colitis	46	37.135	58.378	0.100	400.00
15			Control	97	19.214	11.923	4.612	58.865
			Diff (1-2)	—	17.921	34.416	—	—
		Beef	Ulcerative_Colitis	46	12.163	15.192	0.100	89.210
			Control	97	9.327	11.981	2.059	93.494
20			Diff (1-2)	—	2.836	13.092	—	—
		Blueberry	Ulcerative_Colitis	46	6.305	4.453	0.100	26.859
			Control	97	5.393	2.868	0.100	19.410
			Diff (1-2)	—	0.911	3.454	—	—
		Broccoli	Ulcerative_Colitis	46	10.771	6.468	0.100	29.342
25			Control	97	6.790	8.012	0.131	72.543
			Diff (1-2)	—	3.981	7.554	—	—
		Buck_Wheat	Ulcerative_Colitis	46	9.904	5.030	0.100	23.189
			Control	97	6.978	3.384	2.656	24.338
			Diff (1-2)	—	2.926	3.984	—	—
30		Butter	Ulcerative_Colitis	46	28.310	23.146	2.104	87.745
			Control	97	17.846	20.091	1.490	131.60
			Diff (1-2)	—	10.464	21.114	—	—
		Cabbage	Ulcerative_Colitis	46	11.079	9.922	0.100	41.324
35			Control	97	6.540	18.133	0.100	174.96
			Diff (1-2)	—	4.539	15.977	—	—
		Cane_Sugar	Ulcerative_Colitis	46	28.481	24.975	2.955	147.61
			Control	97	22.356	18.718	2.789	100.82
			Diff (1-2)	—	6.125	20.919	—	—
40		Cantaloupe	Ulcerative_Colitis	46	12.177	10.882	0.100	60.013
			Control	97	6.052	5.569	0.468	38.706
			Diff (1-2)	—	6.126	7.675	—	—
		Carrot	Ulcerative_Colitis	46	9.182	8.539	0.100	50.970
45			Control	97	4.684	3.636	0.468	28.593
			Diff (1-2)	—	4.498	5.681	—	—
		Cashew	Ulcerative_Colitis	46	17.599	28.317	0.100	167.72
			Control	97	8.362	10.271	0.100	55.749
			Diff (1-2)	—	9.237	18.103	—	—
50		Cauliflower	Ulcerative_Colitis	46	9.803	9.337	0.100	42.378
			Control	97	4.385	4.396	0.100	36.593
			Diff (1-2)	—	5.418	6.402	—	—
		Celery	Ulcerative_Colitis	46	16.290	11.968	0.100	52.534
55			Control	97	8.930	4.985	2.394	26.982
			Diff (1-2)	—	7.360	7.914	—	—
		Cheddar_Ch_	Ulcerative_Colitis	46	41.438	45.998	0.100	208.47

EP 3 449 255 B1

(continued)

	Sex	Food	Diagnosis	N	Mean	ELISA Score		
						SD	Min	Max
5			Control	97	28.479	49.022	1.169	298.91
			Diff (1-2)	—	12.959	48.077	—	—
		Chicken	Ulcerative_Colitis	46	21.425	15.312	0.100	71.379
			Control	97	17.778	11.456	5.137	69.503
10			Diff (1-2)	—	3.646	12.813	—	—
		Chili_Pepper	Ulcerative_Colitis	46	13.087	11.692	0.100	61.496
			Control	97	7.802	5.945	1.591	31.070
			Diff (1-2)	—	5.286	8.227	—	—
		Chocolate	Ulcerative_Colitis	46	20.511	13.811	0.100	69.232
15			Control	97	16.536	11.276	1.726	63.673
			Diff (1-2)	—	3.975	12.143	—	—
		Cinnamon	Ulcerative_Colitis	46	43.331	30.200	7.718	117.58
			Control	97	35.928	28.520	3.136	146.95
			Diff (1-2)	—	7.403	29.067	—	—
20		Clam	Ulcerative_Colitis	46	38.009	28.872	3.421	121.47
			Control	97	38.293	21.598	6.370	103.47
			Diff (1-2)	—	-0.284	24.159	—	—
		Codfish	Ulcerative_Colitis	46	26.039	20.205	0.100	86.059
25			Control	97	22.538	29.644	4.176	269.16
			Diff (1-2)	—	3.501	26.992	—	—
		Coffee	Ulcerative_Colitis	46	34.715	62.443	3.884	400.00
			Control	97	20.037	24.002	2.705	192.24
			Diff (1-2)	—	14.679	40.455	—	—
30		Cola_Nut	Ulcerative_Colitis	46	38.888	16.023	11.891	84.315
			Control	97	32.919	20.025	3.851	112.10
			Diff (1-2)	—	5.969	18.840	—	—
		Corn	Ulcerative_Colitis	46	13.329	9.353	0.100	53.955
35			Control	97	10.126	15.048	1.520	117.90
			Diff (1-2)	—	3.203	13.494	—	—
		Cottage_Ch_	Ulcerative_Colitis	46	127.105	127.624	1.867	400.00
			Control	97	74.814	101.386	1.446	400.00
			Diff (1-2)	—	52.292	110.439	—	—
40		Cow_Milk	Ulcerative_Colitis	46	115.427	111.909	2.595	400.00
			Control	97	68.606	94.032	1.343	400.00
			Diff (1-2)	—	46.821	100.085	—	—
		Crab	Ulcerative_Colitis	46	29.571	61.851	2.104	400.00
45			Control	97	24.550	29.311	3.108	252.41
			Diff (1-2)	—	5.021	42.496	—	—
		Cucumber	Ulcerative_Colitis	46	13.314	9.189	0.100	39.378
			Control	97	8.320	9.298	0.234	69.188
			Diff (1-2)	—	4.994	9.263	—	—
50		Egg	Ulcerative_Colitis	46	71.044	98.867	0.935	400.00
			Control	97	44.335	66.828	0.100	400.00
			Diff (1-2)	—	26.709	78.487	—	—
		Eggplant	Ulcerative_Colitis	46	8.891	11.349	0.100	74.721
55			Control	97	5.856	10.455	0.100	92.376
			Diff (1-2)	—	3.035	10.749	—	—
		Garlic	Ulcerative_Colitis	46	17.749	14.628	0.100	72.515

EP 3 449 255 B1

(continued)

	Sex	Food	Diagnosis	N	Mean	ELISA Score		
						SD	Min	Max
5			Control	97	13.476	12.122	3.097	70.591
			Diff (1-2)	—	4.274	12.975	—	—
		Goat_Milk	Ulcerative_Colitis	46	21.482	21.250	0.100	81.830
			Control	97	17.999	36.202	0.100	275.19
10			Diff (1-2)	—	3.483	32.194	—	—
		Grape	Ulcerative_Colitis	46	22.888	11.749	0.100	71.188
			Control	97	23.308	7.422	11.900	41.654
			Diff (1-2)	—	-0.420	9.031	—	—
		Grapefruit	Ulcerative_Colitis	46	5.464	4.181	0.100	20.502
15			Control	97	3.049	2.306	0.100	14.648
			Diff (1-2)	—	2.415	3.033	—	—
		Green_Pea	Ulcerative_Colitis	46	19.698	18.404	0.100	78.678
			Control	97	9.229	11.366	0.100	71.765
			Diff (1-2)	—	10.469	14.002	—	—
20		Green_Pepper	Ulcerative_Colitis	46	7.397	6.122	0.100	27.348
			Control	97	3.972	2.664	0.100	15.744
			Diff (1-2)	—	3.425	4.098	—	—
		Halibut	Ulcerative_Colitis	46	14.268	13.472	0.100	81.343
25			Control	97	12.657	15.451	0.818	142.09
			Diff (1-2)	—	1.611	14.848	—	—
		Honey	Ulcerative_Colitis	46	12.703	6.605	0.100	33.490
			Control	97	11.082	6.215	2.434	31.202
			Diff (1-2)	—	1.620	6.343	—	—
30		Lemon	Ulcerative_Colitis	46	3.113	1.709	0.100	7.749
			Control	97	2.310	1.436	0.100	8.383
			Diff (1-2)	—	0.803	1.528	—	—
		Lettuce	Ulcerative_Colitis	46	12.892	7.188	0.100	29.846
35			Control	97	11.271	8.295	2.871	52.209
			Diff (1-2)	—	1.621	7.958	—	—
		Lima_Bean	Ulcerative_Colitis	46	8.928	5.835	0.100	29.759
			Control	97	5.994	5.650	0.100	37.640
			Diff (1-2)	—	2.934	5.710	—	—
40		Lobster	Ulcerative_Colitis	46	11.944	7.361	0.117	37.739
			Control	97	15.678	11.555	0.468	61.064
			Diff (1-2)	—	-3.734	10.402	—	—
		Malt	Ulcerative_Colitis	46	26.092	17.394	0.100	105.54
45			Control	97	21.137	12.373	3.182	58.638
			Diff (1-2)	—	4.955	14.170	—	—
		Millet	Ulcerative_Colitis	46	5.919	7.006	0.100	42.933
			Control	97	4.006	6.783	0.100	67.831
			Diff (1-2)	—	1.913	6.855	—	—
50		Mushroom	Ulcerative_Colitis	46	14.755	16.831	0.100	68.603
			Control	97	12.883	12.397	1.350	59.949
			Diff (1-2)	—	1.873	13.966	—	—
		Mustard	Ulcerative_Colitis	46	17.526	26.970	1.089	183.13
55			Control	97	9.168	5.413	1.044	28.538
			Diff (1-2)	—	8.358	15.878	—	—
		Oat	Ulcerative_Colitis	46	29.789	33.374	0.100	193.73

EP 3 449 255 B1

(continued)

	Sex	Food	Diagnosis	N	Mean	ELISA Score		
						SD	Min	Max
5			Control	97	20.964	22.946	1.461	107.25
			Diff (1-2)	—	8.825	26.720	—	—
		Olive	Ulcerative_Colitis	46	30.506	20.247	0.139	118.07
			Control	97	24.794	22.708	5.137	160.63
10			Diff (1-2)	—	5.711	21.952	—	—
		Onion	Ulcerative_Colitis	46	14.182	12.107	0.100	50.545
			Control	97	11.600	17.551	1.175	158.57
			Diff (1-2)	—	2.583	16.016	—	—
		Orange	Ulcerative_Colitis	46	28.800	21.379	0.100	110.43
15			Control	97	17.767	16.361	2.146	79.419
			Diff (1-2)	—	11.034	18.114	—	—
		Oyster	Ulcerative_Colitis	46	63.323	74.746	6.369	357.39
			Control	97	43.016	35.689	5.069	216.58
			Diff (1-2)	—	20.306	51.481	—	—
20		Parsley	Ulcerative_Colitis	46	9.862	16.304	0.100	74.199
			Control	97	4.867	7.352	0.100	58.674
			Diff (1-2)	—	4.995	11.029	—	—
		Peach	Ulcerative_Colitis	46	16.604	35.101	0.100	236.47
25			Control	97	8.390	8.373	0.100	50.444
			Diff (1-2)	—	8.214	20.999	—	—
		Peanut	Ulcerative_Colitis	46	8.452	9.914	0.100	51.491
			Control	97	4.241	4.514	0.855	41.070
			Diff (1-2)	—	4.211	6.726	—	—
30		Pineapple	Ulcerative_Colitis	46	34.321	47.506	0.100	207.41
			Control	97	23.259	48.769	0.100	400.00
			Diff (1-2)	—	11.061	48.370	—	—
		Pinto_Bean	Ulcerative_Colitis	46	14.680	10.767	0.100	49.004
35			Control	97	8.132	5.524	0.664	28.288
			Diff (1-2)	—	6.548	7.601	—	—
		Pork	Ulcerative_Colitis	46	14.508	12.409	0.100	73.385
			Control	97	13.403	10.218	1.637	57.274
			Diff (1-2)	—	1.106	10.965	—	—
40		Potato	Ulcerative_Colitis	46	18.153	11.266	0.100	55.737
			Control	97	14.555	5.951	5.259	49.002
			Diff (1-2)	—	3.598	8.039	—	—
		Rice	Ulcerative_Colitis	46	43.673	60.315	1.867	400.00
45			Control	97	25.220	18.948	5.149	118.12
			Diff (1-2)	—	18.453	37.490	—	—
		Rye	Ulcerative_Colitis	46	11.156	18.678	0.100	113.72
			Control	97	4.801	2.690	0.653	15.288
			Diff (1-2)	—	6.355	10.783	—	—
50		Safflower	Ulcerative_Colitis	46	9.950	6.790	0.100	33.143
			Control	97	8.672	6.177	1.958	38.914
			Diff (1-2)	—	1.278	6.379	—	—
		Salmon	Ulcerative_Colitis	46	9.627	5.825	0.100	28.441
55			Control	97	10.920	13.350	0.100	125.74
			Diff (1-2)	—	-1.293	11.496	—	—
		Sardine	Ulcerative_Colitis	46	48.386	21.967	10.375	121.32

EP 3 449 255 B1

(continued)

	Sex	Food	Diagnosis	N	Mean	ELISA Score		
						SD	Min	Max
5			Control	97	37.035	15.979	7.037	90.406
			Diff (1-2)	—	11.351	18.106	—	—
		Scallop	Ulcerative_Colitis	46	81.379	44.060	12.717	186.86
			Control	97	60.721	32.618	8.942	167.75
10			Diff (1-2)	—	20.658	36.660	—	—
		Sesame	Ulcerative_Colitis	46	72.997	95.118	0.100	400.00
			Control	97	60.406	79.861	2.115	400.00
			Diff (1-2)	—	12.592	85.028	—	—
		Shrimp	Ulcerative_Colitis	46	22.090	14.510	2.955	63.471
15			Control	97	34.490	42.689	2.663	342.67
			Diff (1-2)	—	-12.400	36.165	—	—
		Sole	Ulcerative_Colitis	46	7.515	4.149	0.100	20.953
			Control	97	4.912	2.238	0.100	14.303
			Diff (1-2)	—	2.603	2.984	—	—
20		Soybean	Ulcerative_Colitis	46	26.364	27.186	0.778	141.84
			Control	97	15.880	9.273	4.912	71.264
			Diff (1-2)	—	10.484	17.159	—	—
		Spinach	Ulcerative_Colitis	46	24.393	17.724	2.770	95.908
25			Control	97	14.656	7.304	3.054	39.867
			Diff (1-2)	—	9.737	11.687	—	—
		Squashes	Ulcerative_Colitis	46	18.247	11.663	0.100	50.213
			Control	97	12.688	7.539	1.637	49.775
			Diff (1-2)	—	5.558	9.062	—	—
30		Strawberry	Ulcerative_Colitis	46	6.490	5.578	0.100	34.770
			Control	97	4.767	4.446	0.100	30.664
			Diff (1-2)	—	1.724	4.836	—	—
		String_Bean	Ulcerative_Colitis	46	59.790	51.398	4.432	325.08
35			Control	97	40.720	22.088	5.609	141.76
			Diff (1-2)	—	19.070	34.283	—	—
		Sunflower_Sd	Ulcerative_Colitis	46	21.265	47.116	0.100	326.78
			Control	97	9.071	5.842	2.523	46.948
			Diff (1-2)	—	12.193	27.050	—	—
40		Sweet_Pot_	Ulcerative_Colitis	46	13.540	9.152	0.100	38.861
			Control	97	8.456	4.878	0.100	30.052
			Diff (1-2)	—	5.084	6.552	—	—
		Swiss_Ch_	Ulcerative_Colitis	46	62.321	76.987	0.100	353.99
45			Control	97	43.413	79.791	0.100	400.00
			Diff (1-2)	—	18.908	78.907	—	—
		Tea	Ulcerative_Colitis	46	34.993	14.697	8.857	76.433
			Control	97	31.353	13.716	8.890	70.271
			Diff (1-2)	—	3.640	14.036	—	—
50		Tobacco	Ulcerative_Colitis	46	52.669	54.079	10.677	354.77
			Control	97	39.354	26.787	6.106	134.30
			Diff (1-2)	—	13.315	37.708	—	—
		Tomato	Ulcerative_Colitis	46	19.627	43.625	0.100	301.96
55			Control	97	9.088	7.957	0.100	48.338
			Diff (1-2)	—	10.539	25.504	—	—
		Trout	Ulcerative_Colitis	46	17.035	10.017	0.100	57.313

EP 3 449 255 B1

(continued)

	Sex	Food	Diagnosis	N	Mean	ELISA Score		
						SD	Min	Max
5			Control	97	16.891	15.673	0.100	144.46
			Diff (1-2)	—	0.144	14.116	—	—
		Tuna	Ulcerative_Colitis	46	17.635	11.232	0.100	48.815
			Control	97	18.392	16.755	3.156	110.69
10			Diff (1-2)	—	-0.757	15.211	—	—
		Turkey	Ulcerative_Colitis	46	17.700	13.152	0.100	60.557
			Control	97	14.840	10.829	2.789	69.572
			Diff (1-2)	—	2.860	11.621	—	—
		Walnut_BlK	Ulcerative_Colitis	46	41.473	31.581	2.178	146.59
15			Control	97	25.520	14.492	4.249	71.927
			Diff (1-2)	—	15.952	21.478	—	—
		Wheat	Ulcerative_Colitis	46	46.983	93.083	0.100	400.00
			Control	97	14.494	12.413	2.741	90.037
			Diff (1-2)	—	32.489	53.574	—	—
20		Yeast_Baker	Ulcerative_Colitis	46	11.891	14.388	0.100	81.470
			Control	97	9.617	17.250	1.305	116.43
			Diff (1-2)	—	2.273	16.391	—	—
		Yeast_Brewer	Ulcerative_Colitis	46	25.256	36.449	0.100	190.55
25			Control	97	22.646	47.630	1.931	308.34
			Diff (1-2)	—	2.611	44.369	—	—
		Yogurt	Ulcerative_Colitis	46	27.628	20.117	0.100	77.470
			Control	97	19.210	20.751	0.234	120.51
30			Diff (1-2)	—	8.418	20.551	—	—

Upper Quantiles of ELISA Signal Scores among Control Subjects as Candidates for Test Cutpoints in Determining "Positive" or "Negative" Top 58 Foods Ranked by Descending order of Discriminatory Ability using Permutation Test Ulcerative_Colitis Subjects vs. Controls

[0058]

Table 4

	Food Ranking	Food	Sex	Cutpoint	
				90th percentile	95th percentile
40	1	Green_Pea	FEMALE	20.814	23.684
			MALE	19.788	32.100
	2	Cantaloupe	FEMALE	9.672	13.552
45			MALE	11.337	16.219
	3	Pinto_Bean	FEMALE	18.863	27.923
			MALE	16.119	20.774
	4	Cucumber	FEMALE	20.944	26.779
			MALE	17.891	23.472
50	5	Green_Pepper	FEMALE	8.275	10.402
			MALE	7.054	9.712
	6	Grapefruit	FEMALE	6.215	7.611
			MALE	5.330	7.738
55	7	Carrot	FEMALE	9.212	11.448
			MALE	7.807	10.836

EP 3 449 255 B1

(continued)

	<i>Food Ranking</i>	<i>Food</i>	<i>Sex</i>	<i>Cutpoint</i>	
				<i>90th percentile</i>	<i>95th percentile</i>
5	8	Orange	FEMALE	33.707	40.739
			MALE	37.082	56.031
	9	Almond	FEMALE	6.751	8.235
			MALE	7.259	8.824
10	10	Sardine	FEMALE	58.683	73.442
			MALE	57.359	64.811
	11	Sweet_Pot_	FEMALE	14.644	17.301
			MALE	13.894	18.378
15	12	Broccoli	FEMALE	11.826	14.843
			MALE	13.203	15.982
	13	Garlic	FEMALE	19.323	22.695
			MALE	27.228	41.008
	14	Lima_Bean	FEMALE	12.667	18.798
			MALE	10.738	14.912
20	15	Squashes	FEMALE	22.217	32.815
			MALE	22.931	26.147
	16	Celery	FEMALE	17.085	22.342
			MALE	15.101	19.687
25	17	String_Bean	FEMALE	68.618	84.869
			MALE	65.384	83.179
	18	Tomato	FEMALE	17.721	23.905
			MALE	18.818	26.329
30	19	Cauliflower	FEMALE	11.527	17.829
			MALE	8.004	11.222
	20	Walnut_Blk	FEMALE	45.008	56.778
			MALE	45.356	56.848
35	21	Sunflower_Sd	FEMALE	16.611	22.529
			MALE	14.239	18.733
	22	Cane_Sugar	FEMALE	29.824	36.249
			MALE	45.468	64.941
	23	Buck_Wheat	FEMALE	14.739	18.482
			MALE	11.356	12.773
40	24	Soybean	FEMALE	30.770	34.674
			MALE	26.301	31.395
	25	Lemon	FEMALE	4.556	5.959
			MALE	4.179	5.210
45	26	Barley	FEMALE	35.136	46.859
			MALE	36.197	45.928
	27	Oat	FEMALE	33.278	44.414
			MALE	55.311	72.680
50	28	Oyster	FEMALE	86.278	114.96
			MALE	82.294	119.88
	29	Mustard	FEMALE	17.479	19.400
			MALE	16.227	20.884
	30	Rye	FEMALE	8.475	12.141
			MALE	8.360	10.635
55	31	Peach	FEMALE	17.987	26.936
			MALE	17.616	26.755

EP 3 449 255 B1

(continued)

	<i>Food Ranking</i>	<i>Food</i>	<i>Sex</i>	<i>Cutpoint</i>	
				<i>90th percentile</i>	<i>95th percentile</i>
5	32	Chili_Pepper	FEMALE	16.296	25.191
			MALE	14.040	21.503
	33	Spinach	FEMALE	37.895	48.052
			MALE	24.957	28.650
10	34	Peanut	FEMALE	11.190	16.279
			MALE	6.920	9.159
	35	Avocado	FEMALE	5.397	7.247
			MALE	4.483	5.566
15	36	Shrimp	FEMALE	81.870	98.743
			MALE	69.799	101.18
	37	Pineapple	FEMALE	65.230	122.14
			MALE	65.661	106.68
20	38	Cola_Nut	FEMALE	48.288	53.448
			MALE	59.969	72.288
	39	Rice	FEMALE	40.837	58.139
			MALE	52.100	63.388
25	40	Cabbage	FEMALE	18.343	28.722
			MALE	9.730	18.345
	41	Butter	FEMALE	47.381	71.040
			MALE	44.178	58.044
30	42	Eggplant	FEMALE	12.557	18.816
			MALE	9.359	14.446
	43	Apple	FEMALE	9.017	11.837
			MALE	8.631	10.597
35	44	Egg	FEMALE	144.38	280.18
			MALE	106.91	197.02
	45	Wheat	FEMALE	30.663	56.824
			MALE	27.355	37.901
40	46	Cottage_Ch_	FEMALE	200.80	287.02
			MALE	220.78	348.31
	47	Sole	FEMALE	9.355	14.730
			MALE	7.466	9.176
45	48	Cashew	FEMALE	23.551	44.896
			MALE	17.371	32.259
	49	Olive	FEMALE	48.012	55.113
			MALE	42.612	61.277
50	50	Parsley	FEMALE	11.123	19.965
			MALE	8.545	17.265
	51	Corn	FEMALE	20.036	31.057
			MALE	19.953	30.126
55	52	Honey	FEMALE	16.276	17.419
			MALE	19.199	24.877
	53	Chocolate	FEMALE	23.555	25.869
			MALE	32.644	37.625
50	54	Cow_Milk	FEMALE	199.39	248.98
			MALE	181.23	316.72
	55	Potato	FEMALE	20.155	25.293
			MALE	21.203	24.281

EP 3 449 255 B1

(continued)

	<i>Food Ranking</i>	<i>Food</i>	<i>Sex</i>	<i>Cutpoint</i>	
				<i>90th percentile</i>	<i>95th percentile</i>
5	56	Onion	FEMALE	20.204	37.487
			MALE	25.719	33.230
	57	Tea	FEMALE	46.116	53.257
			MALE	49.893	56.701
10	58	Tobacco	FEMALE	57.943	64.379
			MALE	73.610	101.38

15

20

25

30

35

40

45

50

55

EP 3 449 255 B1

5
10
15
20
25
30
35
40
45
50
55

ULCERATIVE COLITIS POPULATION	
Sample ID	# of Positive Results Based on 90th Percentile
160905AAC0012	13
160905AAC0013	14
160905AAC0008	37
160905AAC0001	26
160905AAC0003	15
BRH1274374	4
BRH1274378	9
BRH1274380	10
BRH1272208	4
BRH1272209	36
BRH1272210	6
BRH1272213	43
BRH1272218	7
BRH1272220	28
BRH1272223	25
BRH1272224	7
BRH1272225	7
BRH1272226	40
BRH1272227	5
BRH1265975	33
BRH1265977	7
BRH1265978	9
BRH1265979	33
BRH1265980	3
BRH1265982	23
BRH1265983	11
BRH1265985	8
BRH1265987	22
BRH1265988	0
BRH1265992	1
BRH1265995	26
BRH1269735	29
BRH1269736	13
BRH1269737	18
BRH1269739	18
BRH1269741	25
BRH1269746	4
BRH1269747	19
BRH1269748	2
BRH1269752	1
BRH1269753	2

NON-ULCERATIVE COLITIS POPULATION	
Sample ID	# of Positive Results Based on 90th Percentile
BRH1244900	3
BRH1244901	14
BRH1244902	2
BRH1244903	1
BRH1244904	1
BRH1244905	1
BRH1244906	15
BRH1244907	0
BRH1244908	5
BRH1244909	7
BRH1244910	6
BRH1244911	2
BRH1244912	4
BRH1244913	1
BRH1244914	11
BRH1244915	1
BRH1244916	8
BRH1244917	24
BRH1244918	4
BRH1244919	0
BRH1244920	5
BRH1244921	4
BRH1244922	33
BRH1244923	3
BRH1244924	1
BRH1244925	5
BRH1244926	19
BRH1244927	3
BRH1244928	9
BRH1244929	6
BRH1244930	1
BRH1244931	0
BRH1244932	15
BRH1244933	8
BRH1244934	13
BRH1244935	21
BRH1244936	5
BRH1244937	7
BRH1244938	14
BRH1244939	6
BRH1244940	2

EP 3 449 255 B1

5
10
15
20
25
30
35
40
45
50
55

ULCERATIVE COLITIS POPULATION	
Sample ID	# of Positive Results Based on 90th Percentile
BRH1269755	19
BRH1269756	6
BRH1269758	24
DLS16-69619	1
DLS16-32252	13
160905AAC0014	37
160905AAC0015	9
160905AAC0016	5
160905AAC0005	8
160905AAC0006	4
160905AAC0007	53
160905AAC0009	24
160905AAC0010	2
160905AAC0011	1
160905AAC0002	5
160905AAC0004	2
BRH1274375	4
BRH1274376	6
BRH1274377	6
BRH1274379	2
BRH1274381	15
BRH1274382	2
BRH1274383	14
BRH1272211	6
BRH1272212	3
BRH1272214	11
BRH1272215	8
BRH1272216	2
BRH1272217	8
BRH1272219	26
BRH1272221	0
BRH1272222	50
BRH1272228	6
BRH1265976	1
BRH1265981	1
BRH1265984	10
BRH1265986	16
BRH1265989	37
BRH1265990	1
BRH1265991	8
BRH1265993	4

NON-ULCERATIVE COLITIS POPULATION	
Sample ID	# of Positive Results Based on 90th Percentile
BRH1244941	1
BRH1244942	10
BRH1244943	2
BRH1244944	38
BRH1244945	0
BRH1244946	12
BRH1244947	8
BRH1244948	6
BRH1244949	4
BRH1244950	2
BRH1244951	0
BRH1244952	2
BRH1244953	5
BRH1244954	0
BRH1244955	0
BRH1244956	43
BRH1244957	4
BRH1244958	4
BRH1244959	1
BRH1244960	1
BRH1244961	1
BRH1244962	2
BRH1244963	4
BRH1244964	8
BRH1244965	5
BRH1244966	2
BRH1244967	3
BRH1244968	0
BRH1244969	2
BRH1244970	9
BRH1244971	11
BRH1244972	1
BRH1244973	7
BRH1244974	1
BRH1244975	0
BRH1244976	4
BRH1244977	0
BRH1244978	0
BRH1244979	0
BRH1244980	0
BRH1244981	2

EP 3 449 255 B1

ULCERATIVE COLITIS POPULATION	
Sample ID	# of Positive Results Based on 90th Percentile
BRH1265994	8
BRH1265996	20
BRH1265997	14
BRH1265998	3
BRH1265999	9
BRH1266000	12
BRH1269734	3
BRH1269738	2
BRH1269740	27
BRH1269742	13
BRH1269743	11
BRH1269744	4
BRH1269745	19
BRH1269749	0
BRH1269750	23
BRH1269751	8
BRH1269754	5
BRH1269757	3
DLS16-32288	8
DLS16-68885	13
DLS16-69258	3

No of Observations	103
Average Number	12.7
Median Number	8

# of Patients w/ 0 Pos Results	3
% Subjects w/ 0 pos results	2.9

NON-ULCERATIVE COLITIS POPULATION	
Sample ID	# of Positive Results Based on 90th Percentile
BRH1244982	0
BRH1244983	2
BRH1244984	3
BRH1244985	5
BRH1244986	0
BRH1244987	1
BRH1244988	11
BRH1244989	3
BRH1244990	2
BRH1244991	0
BRH1244992	1
BRH1267320	0
BRH1267321	15
BRH1267322	9
BRH1267323	0
BRH1244993	0
BRH1244994	0
BRH1244995	0
BRH1244996	2
BRH1244997	2
BRH1244998	5
BRH1244999	2
BRH1245000	8
BRH1245001	3
BRH1245002	4
BRH1245003	5
BRH1245004	1
BRH1245005	1
BRH1245006	0
BRH1245007	0
BRH1245008	16
BRH1245009	4
BRH1245010	11
BRH1245011	14
BRH1245012	1
BRH1245013	26
BRH1245014	0
BRH1245015	2
BRH1245016	17

EP 3 449 255 B1

5
10
15
20
25
30
35
40
45
50
55

ULCERATIVE COLITIS POPULATION	
Sample ID	# of Positive Results Based on 90th Percentile

NON-ULCERATIVE COLITIS POPULATION	
Sample ID	# of Positive Results Based on 90th Percentile
BRH1245017	0
BRH1245018	0
BRH1245019	6
BRH1245020	19
BRH1245021	1
BRH1245022	26
BRH1245023	3
BRH1245024	2
BRH1245025	11
BRH1245026	8
BRH1245027	20
BRH1245029	2
BRH1245030	5
BRH1245031	3
BRH1245032	0
BRH1245033	4
BRH1245034	6
BRH1245035	1
BRH1245036	17
BRH1245037	0
BRH1245038	4
BRH1245039	9
BRH1245040	4
BRH1245041	2
BRH1267327	5
BRH1267329	3
BRH1267330	2
BRH1267331	2
BRH1267333	2
BRH1267334	26
BRH1267335	11
BRH1267337	6
BRH1267338	0
BRH1267339	10
BRH1267340	18
BRH1267341	0
BRH1267342	2
BRH1267343	9
BRH1267345	0
BRH1267346	1
BRH1267347	1
BRH1267349	2

EP 3 449 255 B1

ULCERATIVE COLITIS POPULATION	
Sample ID	# of Positive Results Based on 90th Percentile

NON-ULCERATIVE COLITIS POPULATION	
Sample ID	# of Positive Results Based on 90th Percentile

No of Observations	163
Average Number	5.7
Median Number	3

# of Patients w/ 0 Pos Results	31
% Subjects w/ 0 pos results	19.0

Table 5A

5
10
15
20
25
30
35
40
45
50
55

EP 3 449 255 B1

5
10
15
20
25
30
35
40
45
50
55

ULCERATIVE COLITIS POPULATION	
Sample ID	# of Positive Results Based on 95th Percentile
160905AAC0012	7
160905AAC0013	4
160905AAC0008	31
160905AAC0001	22
160905AAC0003	6
BRH1274374	4
BRH1274378	7
BRH1274380	2
BRH1272208	1
BRH1272209	23
BRH1272210	3
BRH1272213	28
BRH1272218	3
BRH1272220	17
BRH1272223	17
BRH1272224	5
BRH1272225	4
BRH1272226	26
BRH1272227	4
BRH1265975	25
BRH1265977	3
BRH1265978	4
BRH1265979	16
BRH1265980	0
BRH1265982	9
BRH1265983	5
BRH1265985	6
BRH1265987	6
BRH1265988	0
BRH1265992	0
BRH1265995	22
BRH1269735	19
BRH1269736	11
BRH1269737	8
BRH1269739	10
BRH1269741	16
BRH1269746	1
BRH1269747	8
BRH1269748	0
BRH1269752	0
BRH1269753	1

NON-ULCERATIVE COLITIS POPULATION	
Sample ID	# of Positive Results Based on 95th Percentile
BRH1244900	2
BRH1244901	5
BRH1244902	2
BRH1244903	0
BRH1244904	1
BRH1244905	0
BRH1244906	5
BRH1244907	0
BRH1244908	2
BRH1244909	5
BRH1244910	2
BRH1244911	0
BRH1244912	1
BRH1244913	0
BRH1244914	7
BRH1244915	0
BRH1244916	4
BRH1244917	16
BRH1244918	1
BRH1244919	0
BRH1244920	4
BRH1244921	2
BRH1244922	17
BRH1244923	2
BRH1244924	1
BRH1244925	1
BRH1244926	13
BRH1244927	2
BRH1244928	3
BRH1244929	2
BRH1244930	1
BRH1244931	0
BRH1244932	7
BRH1244933	2
BRH1244934	5
BRH1244935	11
BRH1244936	3
BRH1244937	3
BRH1244938	5
BRH1244939	2
BRH1244940	1

EP 3 449 255 B1

5
10
15
20
25
30
35
40
45
50
55

ULCERATIVE COLITIS POPULATION	
Sample ID	# of Positive Results Based on 95th Percentile
BRH1269755	15
BRH1269756	3
BRH1269758	11
DLS16-69619	1
DLS16-32252	9
160905AAC0014	30
160905AAC0015	6
160905AAC0016	4
160905AAC0005	5
160905AAC0006	2
160905AAC0007	47
160905AAC0009	15
160905AAC0010	1
160905AAC0011	0
160905AAC0002	2
160905AAC0004	0
BRH1274375	2
BRH1274376	4
BRH1274377	3
BRH1274379	1
BRH1274381	8
BRH1274382	1
BRH1274383	9
BRH1272211	4
BRH1272212	1
BRH1272214	7
BRH1272215	6
BRH1272216	1
BRH1272217	6
BRH1272219	17
BRH1272221	0
BRH1272222	46
BRH1272228	1
BRH1265976	1
BRH1265981	1
BRH1265984	5
BRH1265986	9
BRH1265989	23
BRH1265990	0
BRH1265991	5
BRH1265993	1

NON-ULCERATIVE COLITIS POPULATION	
Sample ID	# of Positive Results Based on 95th Percentile
BRH1244941	1
BRH1244942	5
BRH1244943	1
BRH1244944	14
BRH1244945	0
BRH1244946	4
BRH1244947	3
BRH1244948	0
BRH1244949	3
BRH1244950	1
BRH1244951	0
BRH1244952	0
BRH1244953	1
BRH1244954	0
BRH1244955	0
BRH1244956	31
BRH1244957	3
BRH1244958	1
BRH1244959	0
BRH1244960	0
BRH1244961	1
BRH1244962	1
BRH1244963	1
BRH1244964	5
BRH1244965	2
BRH1244966	1
BRH1244967	1
BRH1244968	0
BRH1244969	1
BRH1244970	3
BRH1244971	4
BRH1244972	1
BRH1244973	3
BRH1244974	1
BRH1244975	0
BRH1244976	2
BRH1244977	0
BRH1244978	0
BRH1244979	0
BRH1244980	0
BRH1244981	1

EP 3 449 255 B1

ULCERATIVE COLITIS POPULATION	
Sample ID	# of Positive Results Based on 95th Percentile
BRH1265994	3
BRH1265996	15
BRH1265997	11
BRH1265998	0
BRH1265999	7
BRH1266000	7
BRH1269734	0
BRH1269738	2
BRH1269740	19
BRH1269742	7
BRH1269743	8
BRH1269744	1
BRH1269745	15
BRH1269749	0
BRH1269750	18
BRH1269751	6
BRH1269754	1
BRH1269757	3
DLS16-32288	2
DLS16-68885	11
DLS16-69258	3

No of Observations	103
Average Number	8.1
Median Number	5

# of Patients w/ 0 Pos Results	12
% Subjects w/ 0 pos results	11.7

NON-ULCERATIVE COLITIS POPULATION	
Sample ID	# of Positive Results Based on 95th Percentile
BRH1244982	0
BRH1244983	2
BRH1244984	1
BRH1244985	2
BRH1244986	0
BRH1244987	0
BRH1244988	8
BRH1244989	1
BRH1244990	1
BRH1244991	1
BRH1244992	0
BRH1267320	0
BRH1267321	12
BRH1267322	3
BRH1267323	0
BRH1244993	0
BRH1244994	0
BRH1244995	0
BRH1244996	1
BRH1244997	1
BRH1244998	4
BRH1244999	1
BRH1245000	3
BRH1245001	0
BRH1245002	1
BRH1245003	1
BRH1245004	0
BRH1245005	1
BRH1245006	0
BRH1245007	0
BRH1245008	10
BRH1245009	3
BRH1245010	3
BRH1245011	10
BRH1245012	0
BRH1245013	10
BRH1245014	0
BRH1245015	2
BRH1245016	5

EP 3 449 255 B1

ULCERATIVE COLITIS POPULATION	
Sample ID	# of Positive Results Based on 95th Percentile

NON-ULCERATIVE COLITIS POPULATION	
Sample ID	# of Positive Results Based on 95th Percentile
BRH1245017	0
BRH1245018	0
BRH1245019	5
BRH1245020	13
BRH1245021	0
BRH1245022	15
BRH1245023	1
BRH1245024	1
BRH1245025	6
BRH1245026	5
BRH1245027	13
BRH1245029	1
BRH1245030	1
BRH1245031	3
BRH1245032	0
BRH1245033	1
BRH1245034	2
BRH1245035	0
BRH1245036	6
BRH1245037	0
BRH1245038	4
BRH1245039	6
BRH1245040	0
BRH1245041	0
BRH1267327	3
BRH1267329	2
BRH1267330	2
BRH1267331	1
BRH1267333	1
BRH1267334	13
BRH1267335	7
BRH1267337	4
BRH1267338	0
BRH1267339	3
BRH1267340	14
BRH1267341	0
BRH1267342	1
BRH1267343	6
BRH1267345	0
BRH1267346	0
BRH1267347	0
BRH1267349	2

5
10
15
20
25
30
35
40
45
50
55

EP 3 449 255 B1

ULCERATIVE COLITIS POPULATION	
Sample ID	# of Positive Results Based on 95th Percentile

NON-ULCERATIVE COLITIS POPULATION	
Sample ID	# of Positive Results Based on 95th Percentile

No of Observations	163
Average Number	2.9
Median Number	1

# of Patients w/ 0 Pos Results	50
% Subjects w/ 0 pos results	30.7

Table 5B

Summary statistics

[0059]

Variable	Ulcerative Colitis 90th percentile	
Sample size		103
Lowest value		0.0000
Highest value		53.0000
Arithmetic mean		12.7282
95% CI for the mean		10.3973 to 15.0590
Median		8.0000
95% CI for the median		7.0000 to 11.0000
Variance		142.2391
Standard deviation		11.9264
Relative standard deviation		0.9370 (93.70%)
Standard error of the mean		1.1751
Coefficient of Skewness		1.3143 (P<0.0001)
Coefficient of Kurtosis		1.2515 (P=0.0379)
D'Agostino-Pearson test for Normal distribution		reject Normality (P<0.0001)
Percentiles		95% Confidence interval
2.5	0.07500	
5	1.0000	0.0000 to 1.3540
10	1.8000	1.0000 to 2.0000
25	4.0000	2.0000 to 5.0730
75	19.0000	13.9270 to 25.0000
90	29.8000	25.0000 to 37.0000
95	37.0000	31.5842 to 50.5298
97.5	42.7750	

Table 6A

Summary statistics

Variable	Ulcerative Colitis_95th_percentile Ulcerative Colitis 95th percentile	
Sample size	103	
Lowest value	0.0000	
Highest value	47.0000	
Arithmetic mean	8.1165	
95% CI for the mean	6.2898 to 9.9432	
Median	5.0000	
95% CI for the median	4.0000 to 6.9228	
Variance	87.3588	
Standard deviation	9.3466	
Relative standard deviation	1.1516 (115.16%)	
Standard error of the mean	0.9209	
Coefficient of Skewness	1.9463 (P<0.0001)	
Coefficient of Kurtosis	4.4608 (P<0.0001)	
D'Agostino-Pearson test for Normal distribution	reject Normality (P<0.0001)	
Percentiles		95% Confidence interval
2.5	0.0000	
5	0.0000	0.0000 to 0.0000
10	0.0000	0.0000 to 1.0000
25	1.0000	1.0000 to 3.0000
75	11.0000	8.0000 to 16.0956
90	22.0000	16.8954 to 27.4692
95	26.7000	22.0000 to 46.1766
97.5	30.9250	

Table 6B

Summary statistics		
Variable	Non-Ulcerative Colitis 90th percentile Non-Ulcerative Colitis 90th percentile	
Sample size	163	
Lowest value	0.0000	
Highest value	43.0000	
Arithmetic mean	5.6687	
95% CI for the mean	4.5255 to 5.8119	
Median	3.0000	
95% CI for the median	2.0000 to 4.0000	
Variance	54.6303	
Standard deviation	7.3912	
Relative standard deviation	1.3039 (130.39%)	
Standard error of the mean	0.5789	
Coefficient of Skewness	2.3467 (P<0.0001)	
Coefficient of Kurtosis	6.6923 (P<0.0001)	
D'Agostino-Pearson test for Normal distribution	reject Normality (P<0.0001)	
Percentiles		95% Confidence interval
2.5	0.0000	0.0000 to 0.0000
5	0.0000	0.0000 to 0.0000
10	0.0000	0.0000 to 0.0000
25	1.0000	0.0000 to 1.0000
75	8.0000	5.6997 to 10.0000
90	15.0000	11.0000 to 19.2863
95	20.3500	16.5173 to 23.1987
97.5	26.0000	20.1327 to 41.9327

Table 7A

Summary statistics		
Variable	Non-Ulcerative Colitis 95th percentile	
Sample size	163	
Lowest value	0.0000	
Highest value	31.0000	
Arithmetic mean	2.8528	
95% CI for the mean	2.1867 to 3.5189	
Median	1.0000	
95% CI for the median	1.0000 to 2.0000	
Variance	18.5461	
Standard deviation	4.3065	
Relative standard deviation	1.5096 (150.96%)	
Standard error of the mean	0.3373	
Coefficient of Skewness	2.9508 (P<0.0001)	
Coefficient of Kurtosis	12.1761 (P<0.0001)	
D'Agostino-Pearson test for Normal distribution	reject Normality (P<0.0001)	
Percentiles		95% Confidence interval
2.5	0.0000	0.0000 to 0.0000
5	0.0000	0.0000 to 0.0000
10	0.0000	0.0000 to 0.0000
25	0.0000	0.0000 to 1.0000
75	3.0000	3.0000 to 5.0000
90	7.2000	5.0000 to 13.0000
95	13.0000	10.0000 to 15.3141
97.5	14.4250	13.0000 to 28.0115

Table 7B

Summary statistics

Variable	Ulcerative Colitis_90th_percentile_1	
Back-transformed after logarithmic transformation.		
Sample size		103
Lowest value		0.1000
Highest value		53.0000
Geometric mean		7.3070
95% CI for the mean		5.7021 to 9.3637
Median		8.0000
95% CI for the median		7.0000 to 11.0000
Coefficient of Skewness		-1.1403 (P<0.0001)
Coefficient of Kurtosis		2.0327 (P=0.0056)
D'Agostino-Pearson test for Normal distribution		reject Normality (P<0.0001)
Percentiles		95% Confidence interval
2.5	0.1189	
5	1.0000	0.10000 to 1.2781
10	1.7411	1.0000 to 2.0000
25	4.0000	2.0000 to 5.0670
75	19.0000	13.9245 to 25.0000
90	29.7592	25.0000 to 37.0000
95	37.0000	31.5247 to 50.6003
97.5	42.7754	

Table 8A

Summary statistics

Variable	Ulcerative_Colitis_95th_percentile_1	
Back-transformed after logarithmic transformation.		
Sample size		103
Lowest value		0.1000
Highest value		47.0000
Geometric mean		3.4690
95% CI for the mean		2.5190 to 4.7773
Median		5.0000
95% CI for the median		4.0000 to 6.9172
Coefficient of Skewness		-0.9013 (P=0.0005)
Coefficient of Kurtosis		0.1763 (P=0.5802)
D'Agostino-Pearson test for Normal distribution		reject Normality (P=0.0022)
Percentiles		95% Confidence interval
2.5	0.10000	
5	0.10000	0.10000 to 0.10000
10	0.10000	0.10000 to 1.0000
25	1.0000	1.0000 to 3.0000
75	11.0000	8.0000 to 16.0930
90	22.0000	16.8926 to 27.4547
95	26.6832	22.0000 to 46.1750
97.5	30.9316	

Table 8B

Summary statistics

Variable	Non_Ulcerative_Colitis_90th_percentile_1 Non-Ulcerative Colitis 90th percentile_1	
Back-transformed after logarithmic transformation.		
Sample size		163
Lowest value		0.1000
Highest value		43.0000
Geometric mean		2.1011
95% CI for the mean		1.6075 to 2.7463
Median		3.0000
95% CI for the median		2.0000 to 4.0000
Coefficient of Skewness		-0.6312 (P=0.0016)
Coefficient of Kurtosis		-0.6026 (P=0.0328)
D'Agostino-Pearson test for Normal distribution		reject Normality (P=0.0007)
Percentiles		95% Confidence interval
2.5	0.10000	0.10000 to 0.10000
5	0.10000	0.10000 to 0.10000
10	0.10000	0.10000 to 0.10000
25	1.0000	0.10000 to 1.0000
75	8.0000	5.6803 to 10.1000
90	15.0000	11.0000 to 19.3087
95	20.4105	16.5098 to 28.0218
97.5	26.0000	20.2171 to 41.8802

Table 9A

Summary statistics		
Variable	Non_Ulcerative_Colitis_95th_percentile_1 Non-Ulcerative Colitis 95th percentile 1	
Back-transformed after logarithmic transformation.		
Sample size	163	
Lowest value	0.1000	
Highest value	31.0000	
Geometric mean	0.9669	
95% CI for the mean	0.7444 to 1.2559	
Median	1.0000	
95% CI for the median	1.0000 to 2.0000	
Coefficient of Skewness	-0.1914 (P=0.3069)	
Coefficient of Kurtosis	-1.2156 (P<0.0001)	
D'Agostino-Pearson test for Normal distribution	reject Normality (P<0.0001)	
Percentiles		95% Confidence interval
2.5	0.10000	0.10000 to 0.10000
5	0.10000	0.10000 to 0.10000
10	0.10000	0.10000 to 0.10000
25	0.10000	0.10000 to 1.0000
75	3.0000	3.0000 to 5.0000
90	7.1895	5.0000 to 13.0000
95	13.0000	10.1000 to 15.3072
97.5	14.4166	13.0000 to 27.2688

Table 9B

Independent samples t-test		
Sample 1		
Variable	Non_Ulcerative_Colitis_90th_percentile_1 Non-Ulcerative Colitis 90th percentile_1	
Sample 2		
Variable	Ulcerative_Colitis_90th_percentile_1	
Back-transformed after logarithmic transformation.		
	Sample 1	Sample 2
Sample size	163	103
Geometric mean	2.1011	7.3070
95% CI for the mean	1.6075 to 2.7463	5.7021 to 9.3637
Variance of Logs	0.5654	0.3037
F-test for equal variances		P = 0.001
T-test (assuming equal variances)		
Difference on Log-transformed scale		
Difference		0.5413
Standard Error		0.08577
95% CI of difference		0.3724 to 0.7102
Test statistic t		6.311
Degrees of Freedom (DF)		264
Two-tailed probability		P < 0.0001
Back-transformed results		
Ratio of geometric means		3.4776
95% CI of ratio		2.3573 to 5.1305

Table 10A

Independent samples t-test		
Sample 1		
Variable	Non-Ulcerative Colitis 95th percentile_1 Non-Ulcerative Colitis 95th percentile_1	
Sample 2		
Variable	Ulcerative Colitis 95th percentile_1 Ulcerative Colitis 95th percentile_1	
Back-transformed after logarithmic transformation.		
	Sample 1	Sample 2
Sample size	163	103
Geometric mean	0.9669	3.4690
95% CI for the mean	0.7444 to 1.2559	2.5190 to 4.7773
Variance of Logs	0.5391	0.5057
F-test for equal variances	P = 0.731	
T-test (assuming equal variances)		
Difference on Log-transformed scale		
Difference	0.5548	
Standard Error	0.09131	
95% CI of difference	0.3751 to 0.7346	
Test statistic t	6.077	
Degrees of Freedom (DF)	264	
Two-tailed probability	P < 0.0001	
Back-transformed results		
Ratio of geometric means	3.5879	
95% CI of ratio	2.3717 to 5.4278	

Table 10B

Mann-Whitney test (independent samples)		
Sample 1		
Variable	Non-Ulcerative Colitis 90th percentile Non-Ulcerative Colitis 90th percentile	
Sample 2		
Variable	Ulcerative Colitis 90th percentile Ulcerative Colitis 90th percentile	
	Sample 1	Sample 2
Sample size	163	103
Lowest value	0.0000	0.0000
Highest value	43.0000	53.0000
Median	3.0000	8.0000
95% CI for the median	2.0000 to 4.0000	7.0000 to 11.0000
Interquartile range	1.0000 to 8.0000	4.0000 to 19.0000
Mann-Whitney test (independent samples)		
Average rank of first group		110.8681
Average rank of second group		169.3155
Mann-Whitney U		4705.50
Test statistic Z (corrected for ties)		6.053
Two-tailed probability		P < 0.0001

Table 11A

Mann-Whitney test (independent samples)		
Sample 1		
Variable	Non-Ulcerative Colitis 95th percentile Non-Ulcerative Colitis 95th percentile	
Sample 2		
Variable	Ulcerative Colitis 95th percentile Ulcerative Colitis 95th percentile	
	Sample 1	Sample 2
Sample size	153	103
Lowest value	0.0000	0.0000
Highest value	31.0000	47.0000
Median	1.0000	5.0000
95% CI for the median	1.0000 to 2.0000	4.0000 to 6.9228
Interquartile range	0.0000 to 3.0000	1.0000 to 11.0000
Mann-Whitney test (independent samples)		
Average rank of first group		110.9939
Average rank of second group		169.1165
Mann-Whitney U		4726.00
Test statistic Z (corrected for ties)		6.068
Two-tailed probability		P < 0.0001

Table 11B

ROC curve	
Variable	Ulcerative_Colitis_Test_90th Ulcerative Colitis Test 90th
Classification variable	Diagnosis__1_Ulcerative_Colitis_0_Non_Ulcerative_Colitis_ Diagnosis(1 Ulcerative Colitis 0 Non-Ulcerative Colitis)
Sample size	266
Positive group ^a	103 (38.72%)
Negative group ^b	163 (61.28%)
^a Diagnosis__1_Ulcerative_Colitis_0_Non_Ulcerative_Colitis_ = 1 ^b Diagnosis__1_Ulcerative_Colitis_0_Non_Ulcerative_Colitis_ = 0	
Disease prevalence (%)	unknown
Area under the ROC curve (AUC)	
Area under the ROC curve (AUC)	0.720
Standard Error ^a	0.0315
95% Confidence interval ^b	0.662 to 0.773
z statistic	6.966
Significance level P (Area=0.5)	<0.0001
^a DeLong et al., 1988 ^b Binomial exact	
Youden index	
Youden index J	0.3412
95% Confidence interval ^a	0.2311 to 0.4414
Associated criterion	>5
95% Confidence interval ^a	>2 to >9
Sensitivity	68.02
Specificity	68.10
^a BC _a bootstrap confidence interval (1000 iterations; random number seed: 978).	

Table 12A

EP 3 449 255 B1

ROC curve

Variable	Ulcerative Colitis Test 95th Ulcerative Colitis Test 95th
Classification variable	Diagnosis_1_Ulcerative_Colitis_0_Non_Ulcerative_Colitis_ Diagnosis(1_Ulcerative_Colitis_0_Non-Ulcerative Colitis)
Sample size	266
Positive group ^a	103 (38.72%)
Negative group ^b	163 (61.28%)
^a Diagnosis_1_Ulcerative_Colitis_0_Non_Ulcerative_Colitis_ = 1	
^b Diagnosis_1_Ulcerative_Colitis_0_Non_Ulcerative_Colitis_ = 0	
Disease prevalence (%)	unknown

Area under the ROC curve (AUC)

Area under the ROC curve (AUC)	0.719
Standard Error ^a	0.0325
95% Confidence interval ^b	0.660 to 0.772
z statistic	6.715
Significance level P (Area=0.5)	<0.0001

^a DeLong et al., 1988
^b Binomial exact

Youden index

Youden index J	0.3565
95% Confidence interval ^a	0.2058 to 0.4465
Associated criterion	>3
95% Confidence interval ^a	>2 to >5
Sensitivity	60.19
Specificity	75.46

^a BC_a bootstrap confidence interval (1000 iterations; random number seed: 978).

Table 12B

Performance Metrics in Predicting Ulcerative Colitis Status from Number of Positive Foods Using 90th Percentile of ELISA Signal to determine Positive

[0060]

Table 13A

Sex	No. of Positive Foods as Cutoff	Sensitivity	Specificity	Positive Predictive Value	Negative Predictive Value	Overall Percent Agreement
FEMALE	1	0.97	0.14	0.49	0.83	0.52
	2	0.92	0.29	0.52	0.80	0.58
	3	0.85	0.40	0.55	0.75	0.61
	4	0.76	0.49	0.56	0.71	0.62
	5	0.69	0.57	0.58	0.68	0.62
	6	0.62	0.62	0.58	0.65	0.62
	7	0.55	0.66	0.58	0.63	0.61
	8	0.49	0.69	0.57	0.61	0.60
	9	0.44	0.72	0.57	0.60	0.59
	10	0.39	0.75	0.58	0.59	0.58
	11	0.34	0.78	0.58	0.58	0.58
	12	0.31	0.81	0.59	0.58	0.58
	13	0.28	0.83	0.59	0.57	0.58
	14	0.25	0.84	0.58	0.56	0.57
	15	0.23	0.85	0.57	0.56	0.56

EP 3 449 255 B1

(continued)

	Sex	No. of Positive Foods as Cutoff	Sensitivity	Specificity	Positive Predictive Value	Negative Predictive Value	Overall Percent Agreement
5		16	0.21	0.86	0.57	0.56	0.56
		17	0.20	0.87	0.57	0.56	0.56
		18	0.19	0.88	0.58	0.56	0.56
10		19	0.18	0.90	0.60	0.56	0.56
		20	0.17	0.91	0.63	0.56	0.57
		21	0.16	0.93	0.64	0.56	0.57
		22	0.15	0.93	0.67	0.56	0.57
		23	0.15	0.95	0.67	0.56	0.57
15		24	0.14	0.95	0.71	0.56	0.57
		25	0.13	0.95	0.71	0.56	0.57
		26	0.11	0.96	0.71	0.56	0.57
		27	0.11	0.97	0.75	0.56	0.57
20		28	0.09	0.98	0.75	0.55	0.57
		29	0.08	0.98	0.80	0.55	0.57
		30	0.08	1.00	1.00	0.55	0.57
		31	0.08	1.00	1.00	0.55	0.57
		32	0.07	1.00	1.00	0.55	0.57
25		33	0.07	1.00	1.00	0.55	0.57
		34	0.06	1.00	1.00	0.55	0.56
		35	0.06	1.00	1.00	0.55	0.56
		36	0.06	1.00	1.00	0.55	0.56
30		37	0.05	1.00	1.00	0.55	0.56
		38	0.05	1.00	1.00	0.55	0.56
		39	0.05	1.00	1.00	0.55	0.56
		40	0.03	1.00	1.00	0.55	0.55
		41	0.03	1.00	1.00	0.54	0.55
35		42	0.03	1.00	1.00	0.54	0.55
		43	0.03	1.00	1.00	0.54	0.55
		44	0.03	1.00	1.00	0.54	0.55
		45	0.03	1.00	1.00	0.54	0.55
40		46	0.03	1.00	1.00	0.54	0.55
		47	0.03	1.00	1.00	0.54	0.55
		48	0.03	1.00	1.00	0.54	0.55
		49	0.03	1.00	1.00	0.54	0.55
		50	0.03	1.00	1.00	0.54	0.55
45		51	0.03	1.00	1.00	0.54	0.55
		52	0.03	1.00	1.00	0.54	0.54
		53	0.02	1.00	1.00	0.54	0.54
		54	0.00	1.00	1.00	0.54	0.54
50		55	0.00	1.00	1.00	0.54	0.54
		56	0.00	1.00	1.00	0.54	0.54
		57	0.00	1.00	.	0.53	0.53
		58	0.00	1.00	.	0.53	0.53

55 **Performance Metrics in Predicting Ulcerative Colitis Status from Number of Positive Foods Using 90th Percentile of ELISA Signal to determine Positive**

[0061]

EP 3 449 255 B1

Table 13B

	<i>Sex</i>	<i>No. of Positive Foods as Cutoff</i>	<i>Sensitivity</i>	<i>Specificity</i>	<i>Positive Predictive Value</i>	<i>Negative Predictive Value</i>	<i>Overall Percent Agreement</i>
5	MALE	1	0.97	0.15	0.35	0.90	0.41
		2	0.94	0.29	0.38	0.91	0.49
		3	0.88	0.42	0.42	0.88	0.57
10		4	0.84	0.50	0.45	0.87	0.61
		5	0.81	0.56	0.47	0.86	0.64
		6	0.77	0.63	0.49	0.85	0.67
		7	0.72	0.68	0.51	0.84	0.69
15		8	0.67	0.72	0.53	0.82	0.71
		9	0.64	0.76	0.56	0.81	0.72
		10	0.59	0.79	0.57	0.80	0.73
		11	0.56	0.82	0.59	0.80	0.73
		12	0.54	0.84	0.62	0.79	0.74
20		13	0.52	0.86	0.64	0.79	0.75
		14	0.50	0.87	0.65	0.78	0.75
		15	0.46	0.89	0.67	0.78	0.75
		16	0.44	0.90	0.68	0.77	0.75
25		17	0.42	0.92	0.71	0.77	0.76
		18	0.39	0.93	0.71	0.76	0.76
		19	0.38	0.93	0.71	0.76	0.75
		20	0.36	0.94	0.73	0.75	0.75
		21	0.34	0.94	0.73	0.75	0.75
30		22	0.32	0.95	0.73	0.75	0.75
		23	0.31	0.95	0.75	0.74	0.75
		24	0.30	0.95	0.75	0.74	0.74
		25	0.28	0.95	0.75	0.74	0.74
		26	0.27	0.96	0.75	0.73	0.73
35		27	0.23	0.96	0.75	0.73	0.73
		28	0.21	0.97	0.73	0.72	0.72
		29	0.18	0.97	0.71	0.71	0.71
		30	0.16	0.97	0.70	0.71	0.71
40		31	0.14	0.97	0.67	0.71	0.71
		32	0.13	0.97	0.67	0.70	0.70
		33	0.12	0.97	0.67	0.70	0.70
		34	0.11	0.97	0.67	0.70	0.70
		35	0.10	0.98	0.67	0.70	0.70
45		36	0.08	0.98	0.67	0.69	0.69
		37	0.07	0.98	0.67	0.69	0.69
		38	0.06	0.98	0.50	0.69	0.68
		39	0.04	0.98	0.50	0.69	0.68
50		40	0.03	0.98	0.50	0.68	0.68
		41	0.03	0.98	0.50	0.68	0.68
		42	0.00	0.98	0.00	0.68	0.68
		43	0.00	0.98	0.00	0.68	0.67
		44	0.00	0.98	0.00	0.68	0.67
55		45	0.00	0.99	0.00	0.68	0.67
		46	0.00	1.00	0.00	0.68	0.67
		47	0.00	1.00	0.00	0.68	0.67

EP 3 449 255 B1

(continued)

	Sex	No. of Positive Foods as Cutoff	Sensitivity	Specificity	Positive Predictive Value	Negative Predictive Value	Overall Percent Agreement
5		48	0.00	1.00	0.00	0.68	0.67
		49	0.00	1.00	0.00	0.68	0.68
		50	0.00	1.00	0.00	0.68	0.68
10		51	0.00	1.00	0.00	0.68	0.68
		52	0.00	1.00	0.00	0.68	0.68
		53	0.00	1.00	0.00	0.68	0.68
		54	0.00	1.00	0.00	0.68	0.68
		55	0.00	1.00	0.00	0.68	0.68
15		56	0.00	1.00	-	0.68	0.68
		57	0.00	1.00	-	0.68	0.68
		58	0.00	1.00	-	0.68	0.68

20 **Performance Metrics in Predicting Ulcerative Colitis Status from Number of Positive Foods Using 95th Percentile of ELISA Signal to determine Positive**

[0062]

25 **Table 14A**

	Sex	No. of Positive Foods as Cutoff	Sensitivity	Specificity	Positive Predictive Value	Negative Predictive Value	Overall Percent Agreement
30	FEMALE	1	0.89	0.27	0.51	0.74	0.56
		2	0.75	0.45	0.54	0.68	0.59
		3	0.65	0.58	0.57	0.66	0.61
		4	0.55	0.65	0.58	0.63	0.61
		5	0.49	0.72	0.60	0.62	0.62
35		6	0.44	0.76	0.61	0.61	0.61
		7	0.38	0.80	0.63	0.60	0.61
		8	0.33	0.83	0.63	0.59	0.60
		9	0.29	0.85	0.63	0.58	0.59
		10	0.25	0.87	0.63	0.57	0.58
40		11	0.22	0.88	0.62	0.57	0.58
		12	0.19	0.90	0.63	0.56	0.57
		13	0.18	0.91	0.64	0.56	0.57
		14	0.18	0.93	0.67	0.56	0.58
45		15	0.17	0.94	0.70	0.57	0.58
		16	0.15	0.95	0.75	0.57	0.58
		17	0.14	0.97	0.80	0.57	0.58
		18	0.13	0.98	0.83	0.56	0.58
		19	0.11	0.98	0.88	0.56	0.58
50		20	0.11	1.00	1.00	0.56	0.58
		21	0.09	1.00	1.00	0.56	0.58
		22	0.08	1.00	1.00	0.56	0.57
		23	0.08	1.00	1.00	0.55	0.57
55		24	0.06	1.00	1.00	0.55	0.57
		25	0.06	1.00	1.00	0.55	0.56
		26	0.06	1.00	1.00	0.55	0.56
		27	0.06	1.00	1.00	0.55	0.56

EP 3 449 255 B1

(continued)

	Sex	No. of Positive Foods as Cutoff	Sensitivity	Specificity	Positive Predictive Value	Negative Predictive Value	Overall Percent Agreement
5		28	0.06	1.00	1.00	0.55	0.56
		29	0.05	1.00	1.00	0.55	0.56
		30	0.05	1.00	1.00	0.55	0.56
10		31	0.05	1.00	1.00	0.55	0.56
		32	0.05	1.00	1.00	0.55	0.56
		33	0.03	1.00	1.00	0.55	0.55
		34	0.03	1.00	1.00	0.54	0.55
		35	0.03	1.00	1.00	0.54	0.55
15		36	0.03	1.00	1.00	0.54	0.55
		37	0.03	1.00	1.00	0.54	0.55
		38	0.03	1.00	1.00	0.54	0.55
		39	0.03	1.00	1.00	0.54	0.55
20		40	0.03	1.00	1.00	0.54	0.55
		41	0.03	1.00	1.00	0.54	0.55
		42	0.03	1.00	1.00	0.54	0.55
		43	0.03	1.00	1.00	0.54	0.55
		44	0.03	1.00	1.00	0.54	0.55
25		45	0.03	1.00	1.00	0.54	0.55
		46	0.03	1.00	1.00	0.54	0.55
		47	0.03	1.00	1.00	0.54	0.54
		48	0.00	1.00	1.00	0.54	0.54
30		49	0.00	1.00	1.00	0.54	0.54
		50	0.00	1.00	1.00	0.54	0.54
		51	0.00	1.00	1.00	0.54	0.54
		52	0.00	1.00	1.00	0.54	0.54
		53	0.00	1.00	1.00	0.53	0.53
35		54	0.00	1.00	1.00	0.53	0.53
		55	0.00	1.00	1.00	0.53	0.53
		56	0.00	1.00	-	0.53	0.53
		57	0.00	1.00	-	0.53	0.53
40		58	0.00	1.00	-	0.53	0.53

Performance Metrics in Predicting Ulcerative Colitis Status from Number of Positive Foods Using 95th Percentile of ELISA Signal to determine Positive

[0063]

Table 14B

	Sex	No. of Positive Foods as Cutoff	Sensitivity	Specificity	Positive Predictive Value	Negative Predictive Value	Overall Percent Agreement
50	MALE	1	0.90	0.25	0.36	0.85	0.46
		2	0.83	0.48	0.43	0.86	0.59
		3	0.79	0.64	0.51	0.87	0.69
55		4	0.74	0.72	0.55	0.85	0.72
		5	0.64	0.78	0.58	0.82	0.73
		6	0.58	0.83	0.62	0.80	0.75
		7	0.53	0.87	0.65	0.79	0.76

EP 3 449 255 B1

(continued)

	Sex	No. of Positive Foods as Cutoff	Sensitivity	Specificity	Positive Predictive Value	Negative Predictive Value	Overall Percent Agreement
5		8	0.48	0.89	0.67	0.78	0.76
		9	0.44	0.91	0.69	0.77	0.76
		10	0.40	0.92	0.69	0.76	0.75
10		11	0.36	0.92	0.69	0.75	0.74
		12	0.33	0.93	0.69	0.75	0.74
		13	0.31	0.93	0.69	0.74	0.73
		14	0.30	0.94	0.70	0.74	0.73
		15	0.28	0.95	0.73	0.74	0.73
15		16	0.27	0.95	0.73	0.73	0.73
		17	0.24	0.96	0.75	0.73	0.73
		18	0.22	0.97	0.75	0.72	0.73
		19	0.20	0.97	0.75	0.72	0.72
20		20	0.19	0.97	0.75	0.72	0.72
		21	0.17	0.97	0.75	0.71	0.72
		22	0.14	0.98	0.75	0.71	0.71
		23	0.12	0.98	0.75	0.70	0.70
		24	0.10	0.98	0.67	0.70	0.70
25		25	0.08	0.98	0.67	0.69	0.70
		26	0.07	0.98	0.67	0.69	0.69
		27	0.06	0.98	0.67	0.69	0.69
		28	0.04	0.98	0.67	0.69	0.69
30		29	0.04	0.98	0.50	0.69	0.68
		30	0.03	0.98	0.50	0.68	0.68
		31	0.03	0.98	0.50	0.68	0.68
		32	0.00	0.99	0.50	0.68	0.68
		33	0.00	1.00	0.00	0.68	0.68
35		34	0.00	1.00	0.00	0.68	0.68
		35	0.00	1.00	0.00	0.68	0.67
		36	0.00	1.00	0.00	0.68	0.67
		37	0.00	1.00	0.00	0.68	0.68
		38	0.00	1.00	0.00	0.68	0.68
40		39	0.00	1.00	0.00	0.68	0.68
		40	0.00	1.00	0.00	0.68	0.68
		41	0.00	1.00	0.00	0.68	0.68
		42	0.00	1.00	0.00	0.68	0.68
45		43	0.00	1.00	0.00	0.68	0.68
		44	0.00	1.00	0.00	0.68	0.68
		45	0.00	1.00	0.00	0.68	0.68
		46	0.00	1.00	-	0.68	0.68
		47	0.00	1.00	-	0.68	0.68
50		48	0.00	1.00	-	0.68	0.68
		49	0.00	1.00	-	0.68	0.68
		50	0.00	1.00	-	0.68	0.68
		51	0.00	1.00	-	0.68	0.68
55		52	0.00	1.00	-	0.68	0.68
		53	0.00	1.00	-	0.68	0.68
		54	0.00	1.00	-	0.68	0.68
		55	0.00	1.00	-	0.68	0.68

(continued)

Sex	No. of Positive Foods as Cutoff	Sensitivity	Specificity	Positive Predictive Value	Negative Predictive Value	Overall Percent Agreement
	56	0.00	1.00	-	0.68	0.68
	57	0.00	1.00	-	0.68	0.68
	58	0.00	1.00	-	0.68	0.68

Claims

1. A test panel for testing food intolerance in patients diagnosed with or suspected to have ulcerative colitis, comprising: a plurality of distinct food preparations, wherein each food preparation is independently coupled to an individually addressable solid carrier; wherein the plurality of distinct food preparations consists of green pea, cantaloupe, pinto bean, cucumber, green pepper, grapefruit, carrot, orange, almond, sardine, sweet potato, broccoli, garlic, lima bean, squashes, celery, string bean, tomato, cauliflower, black walnut, sunflower seed, cane sugar, buck wheat, soybean, lemon, barley, oat, oyster, mustard, rye, peach, chili pepper, spinach, peanut, avocado, shrimp, pineapple, cola nut, rice, cabbage, butter, eggplant, apple, egg, wheat, cottage cheese, sole, cashew, olive, parsley, corn, honey, chocolate, cow's milk, potato, onion, tea, and tobacco.
2. The test panel of claim 1, wherein the distinct food preparations are crude filtered aqueous extracts or processed aqueous extracts.
3. The test panel claim 1 or claim 2, wherein the solid carrier is a well of a multiwell plate, a bead, an electrical sensor, a chemical sensor, a microchip or an adsorptive film.
4. An *in vitro* method of testing food intolerance in patients diagnosed with or suspected to have ulcerative colitis, comprising:
 - contacting a food preparation with a bodily fluid of a patient that is diagnosed with or suspected to have ulcerative colitis, wherein the bodily fluid is associated with a gender identification, and wherein the step of contacting is performed under conditions that allow IgG from the bodily fluid to bind to at least one component of the food preparation;
 - measuring IgG bound to the at least one component of the food preparation to obtain a signal;
 - comparing the signal to a gender-stratified reference value for the food preparation using the gender identification to obtain a result; and
 - updating or generating a report using the result,
 wherein the step of contacting a food preparation is performed with a plurality of distinct food preparations, and wherein the plurality of distinct food preparations consists of green pea, cantaloupe, pinto bean, cucumber, green pepper, grapefruit, carrot, orange, almond, sardine, sweet potato, broccoli, garlic, lima bean, squashes, celery, string bean, tomato, cauliflower, black walnut, sunflower seed, cane sugar, buck wheat, soybean, lemon, barley, oat, oyster, mustard, rye, peach, chili pepper, spinach, peanut, avocado, shrimp, pineapple, cola nut, rice, cabbage, butter, eggplant, apple, egg, wheat, cottage cheese, sole, cashew, olive, parsley, corn, honey, chocolate, cow's milk, potato, onion, tea, and tobacco.
5. The method of claim 4, wherein the bodily fluid of the patient is whole blood, plasma, serum, saliva, or a fecal suspension.
6. The method of claim 4 or claim 5, wherein the gender-stratified reference value for each of the food preparations is the 90th percentile rank, or higher, of signals obtained by contacting bodily fluid from a control group of subjects that is not diagnosed with or suspected of having ulcerative colitis with the food preparation.

Patentansprüche

1. Testpanel zum Testen einer Nahrungsmittelunverträglichkeit bei Patienten mit Diagnose von oder Verdacht auf Colitis ulcerosa, umfassend:

eine Vielzahl unterschiedlicher Nahrungsmittelzubereitungen, wobei jede Nahrungsmittelzubereitung unabhängig an einen einzeln adressierbaren festen Träger gekoppelt ist; wobei die Vielzahl unterschiedlicher Nahrungsmittelzubereitungen aus grüner Erbse, Cantaloupe-Melone, Pin-tobohne, Gurke, grüner Paprika, Grapefruit, Karotte, Orange, Mandel, Sardine, Süßkartoffel, Brokkoli, Knob-lauch, Limabohne, Kürbissen, Sellerie, Gartenbohne, Tomate, Blumenkohl, Schwarznuss, Sonnenblumenker-nen, Rohrzucker, Buchweizen, Sojabohne, Zitrone, Gerste, Hafer, Auster, Senf, Roggen, Pfirsich, Chilischote, Spinat, Erdnuss, Avocado, Garnele, Ananas, Kolanuss, Reis, Kohl, Butter, Aubergine, Apfel, Ei, Weizen, Hüt-tenkäse, Seezunge, Cashew, Olive, Petersilie, Mais, Honig, Schokolade, Kuhmilch, Kartoffel, Zwiebel, Tee und Tabak besteht.

2. Testpanel nach Anspruch 1, wobei die unterschiedlichen Nahrungsmittelzubereitungen rohe gefilterte wässrige Extrakte oder verarbeitete wässrige Extrakte sind.

3. Testpanel nach Anspruch 1 oder Anspruch 2, wobei der feste Träger eine Vertiefung einer Mikrotiterplatte, eine Perle, ein elektrischer Sensor, ein chemischer Sensor, ein Mikrochip oder eine Adsorptionsfolie ist.

4. In-vitro-Verfahren zum Testen einer Nahrungsmittelunverträglichkeit bei Patienten mit Diagnose oder Verdacht auf Colitis ulcerosa, umfassend:

Inkontaktbringen einer Nahrungsmittelzubereitung mit einer Körperflüssigkeit eines Patienten, der eine Diag-nose von oder ein Verdacht auf Colitis ulcerosa aufweist, wobei die Körperflüssigkeit mit einer Geschlecht-sidentifikation in Zusammenhang steht und wobei der Schritt des Inkontaktbringens unter Bedingungen durch-geführt wird, die ein Binden von IgG aus der Körperflüssigkeit an mindestens einen Bestandteil der Nahrungs-mittelzubereitung ermöglichen;

Messen von an den mindestens einen Bestandteil der Nahrungsmittelzubereitung gebundenem IgG, um ein Signal zu erhalten;

Vergleichen des Signals mit einem nach Geschlecht stratifizierten Referenzwert für die Nahrungsmittelzube-reitung unter Verwendung der Geschlechtsidentifikation, um ein Ergebnis zu erhalten; und

Aktualisieren oder Erstellen eines Berichts unter Verwendung des Ergebnisses,

wobei der Schritt des Inkontaktbringens einer Nahrungsmittelzubereitung mit einer Vielzahl unterschiedlicher Nahrungsmittelzubereitungen durchgeführt wird, und

wobei die Vielzahl unterschiedlicher Nahrungsmittelzubereitungen aus grüner Erbse, Cantaloupe-Melone, Pin-tobohne, Gurke, grüner Paprika, Grapefruit, Karotte, Orange, Mandel, Sardine, Süßkartoffel, Brokkoli, Knob-lauch, Limabohne, Kürbissen, Sellerie, Gartenbohne, Tomate, Blumenkohl, Schwarznuss, Sonnenblumenker-nen, Rohrzucker, Buchweizen, Sojabohne, Zitrone, Gerste, Hafer, Auster, Senf, Roggen, Pfirsich, Chilischote, Spinat, Erdnuss, Avocado, Garnele, Ananas, Kolanuss, Reis, Kohl, Butter, Aubergine, Apfel, Ei, Weizen, Hüt-tenkäse, Seezunge, Cashew, Olive, Petersilie, Mais, Honig, Schokolade, Kuhmilch, Kartoffel, Zwiebel, Tee und Tabak besteht.

5. Verfahren nach Anspruch 4, wobei die Körperflüssigkeit des Patienten Vollblut, Plasma, Serum, Speichel oder eine Stuhlsuspension ist.

6. Verfahren nach Anspruch 4 oder Anspruch 5, wobei der nach Geschlecht stratifizierte Referenzwert für jede der Nahrungsmittelzubereitungen der 90. Perzentilrang oder höher von Signalen ist, die durch das Inkontaktbringen von Körperflüssigkeit von einer Kontrollgruppe von Subjekten, die keine Diagnose von oder Verdacht auf Colitis ulcerosa aufweisen, mit der Nahrungsmittelzubereitung erhalten werden.

Revendications

1. Panel de test pour tester l'intolérance alimentaire chez des patients diagnostiqués ou suspectés de souffrir de colite ulcéreuse, comprenant :

EP 3 449 255 B1

une pluralité de préparations alimentaires distinctes, dans lequel chaque préparation alimentaire est couplée indépendamment à un support solide adressable individuellement ;

dans lequel la pluralité de préparations alimentaires distinctes est constituée de pois verts, cantaloup, haricots pinto, concombre, poivron vert, pamplemousse, carotte, orange, amande, sardine, patate douce, brocoli, ail, haricot de Lima, courges, céleri, haricot vert, tomate, chou-fleur, noix noire, graines de tournesol, sucre de canne, sarrasin, soja, citron, orge, avoine, huître, moutarde, seigle, pêche, piment, épinards, arachide, avocat, crevette, ananas, noix de cola, riz, chou, beurre, aubergine, pomme, oeuf, blé, fromage blanc, sole, noix de cajou, olive, persil, maïs, miel, chocolat, lait de vache, pomme de terre, oignon, thé et tabac.

5

10 **2.** Panel de test selon la revendication 1, dans lequel les préparations alimentaires distinctes sont des extraits aqueux bruts filtrés ou des extraits aqueux traités.

15 **3.** Panel de test selon la revendication 1 ou la revendication 2, dans lequel le support solide est un puits d'une plaque multipuits, une bille, un capteur électrique, un capteur chimique, une micropuce ou un film adsorbant.

4. Procédé in vitro de test d'intolérance alimentaire chez des patients diagnostiqués ou suspectés de souffrir de colite ulcéreuse, comprenant :

20 la mise en contact d'une préparation alimentaire avec un fluide corporel d'un patient qui est diagnostiqué ou suspecté de souffrir de colite ulcéreuse, dans lequel le fluide corporel est associé à une identification de genre, et dans lequel l'étape de mise en contact est réalisée dans des conditions qui permettent aux IgG provenant du fluide corporel de se lier à au moins un composant de la préparation alimentaire ;

la mesure des IgG liés à l'au moins un composant de la préparation alimentaire pour obtenir un signal ;

25 la comparaison du signal à une valeur de référence stratifiée par genre pour la préparation alimentaire à l'aide de l'identification de genre pour obtenir un résultat ; et

la mise à jour ou la génération d'un rapport en utilisant le résultat,

dans lequel l'étape de mise en contact d'une préparation alimentaire est réalisée avec une pluralité de préparations alimentaires distinctes, et

30 dans lequel la pluralité de préparations alimentaires distinctes est constituée de pois verts, cantaloup, haricots pinto, concombre, poivron vert, pamplemousse, carotte, orange, amande, sardine, patate douce, brocoli, ail, haricot de Lima, courges, céleri, haricot vert, tomate, chou-fleur, noix noire, graines de tournesol, sucre de canne, sarrasin, soja, citron, orge, avoine, huître, moutarde, seigle, pêche, piment, épinards, arachide, avocat, crevette, ananas, noix de cola, riz, chou, beurre, aubergine, pomme, oeuf, blé, fromage blanc, sole, noix de cajou, olive, persil, maïs, miel, chocolat, lait de vache, pomme de terre, oignon, thé et tabac.

35 **5.** Procédé selon la revendication 4, dans lequel le fluide corporel du patient est du sang total, du plasma, du sérum, de la salive ou une suspension fécale.

40 **6.** Procédé selon la revendication 4 ou la revendication 5, dans lequel la valeur de référence stratifiée par genre pour chacune des préparations alimentaires est le rang du 90e percentile, ou plus, des signaux obtenus en mettant en contact un fluide corporel provenant d'un groupe témoin de sujets qui n'ont été diagnostiqué ou suspectés de souffrir de colite ulcéreuse avec la préparation alimentaire.

45

50

55

*Distribution of ELISA Signal Scores by Diagnosis
Sex=MALE Food=Green Pea*

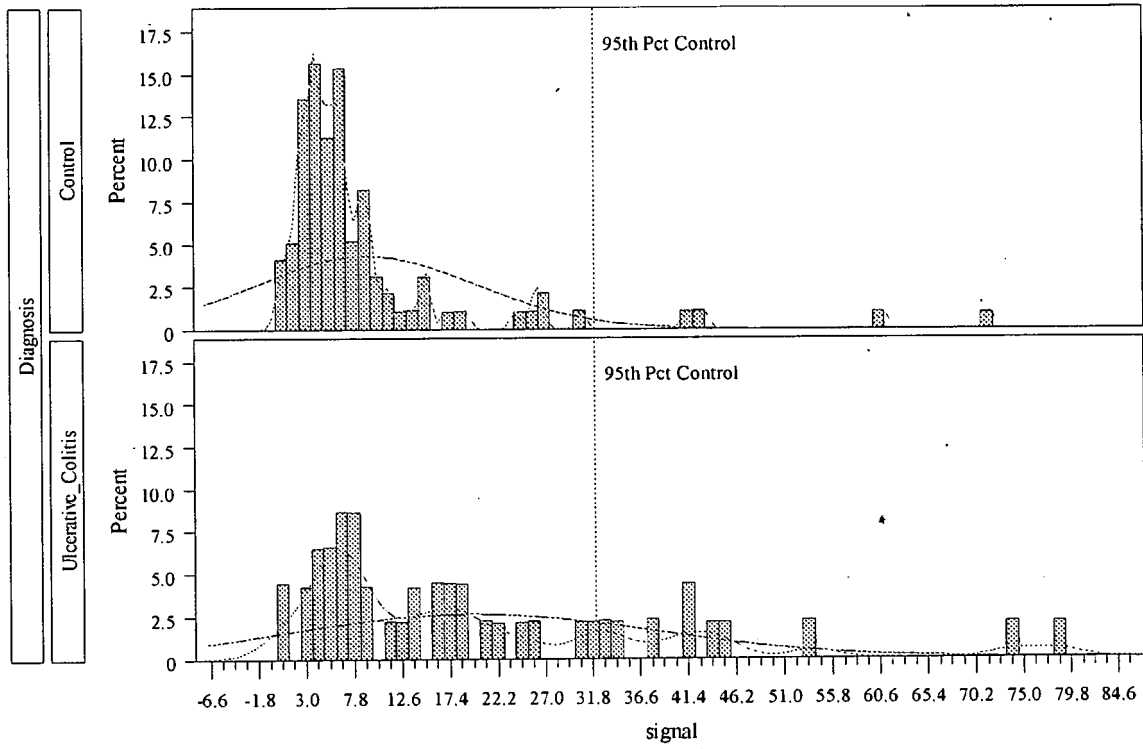


Figure 1A

Distribution of Percentage of Ulcerative Colitis Subjects with Signals \geq Control Cutpoint across 1000 Bootstrapped Samples

Sex=MALE Food=Green Pea

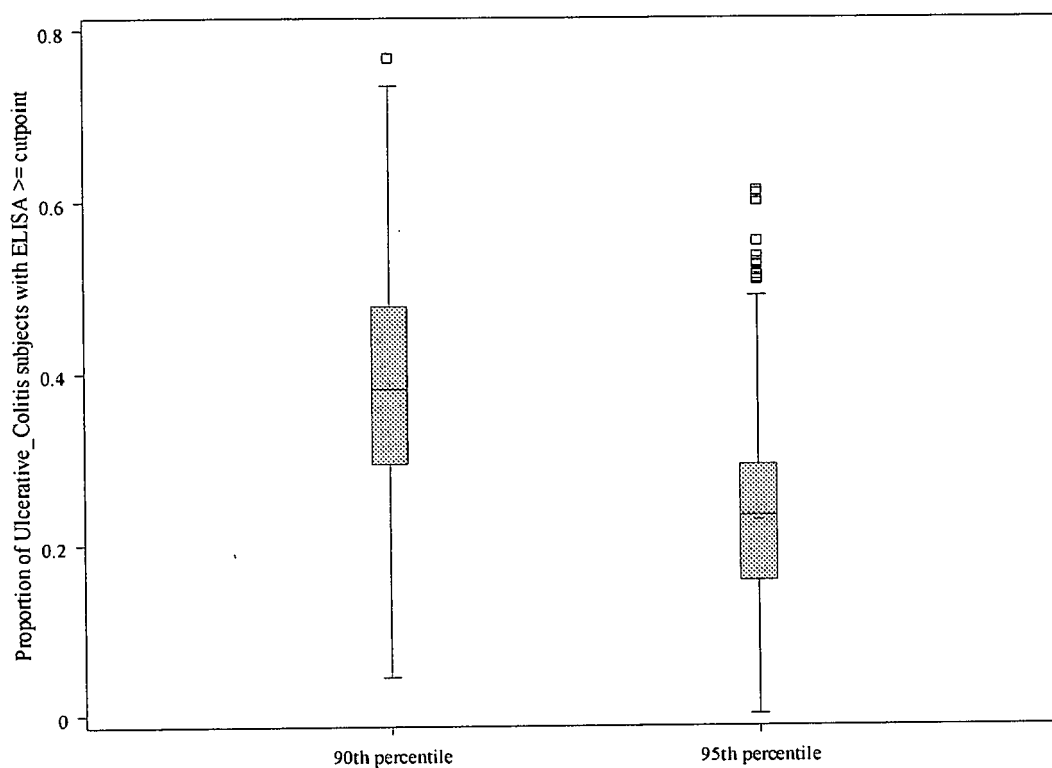


Figure 1B

*Distribution of ELISA Signal Scores by Diagnosis
Sex=FEMALE Food=Green Pea*

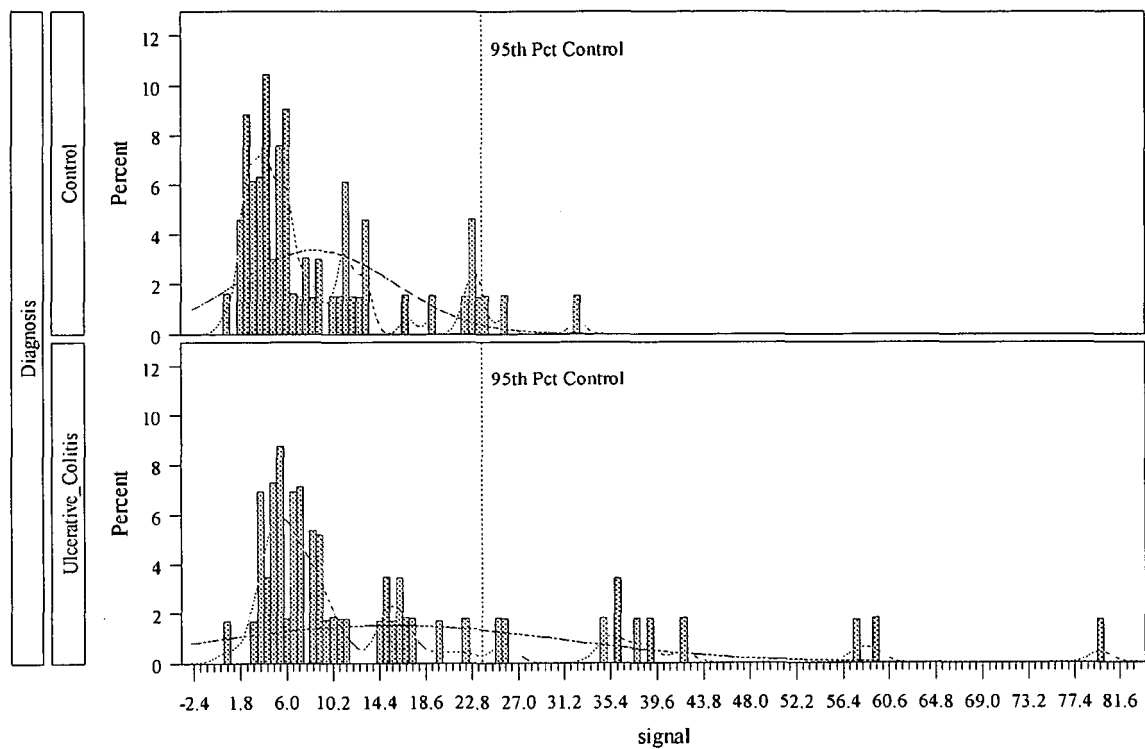


Figure 1C

Distribution of Percentage of Ulcerative Colitis Subjects with Signals \geq Control Cutpoint across 1000 Bootstrapped Samples

Sex=FEMALE Food=Green Pea

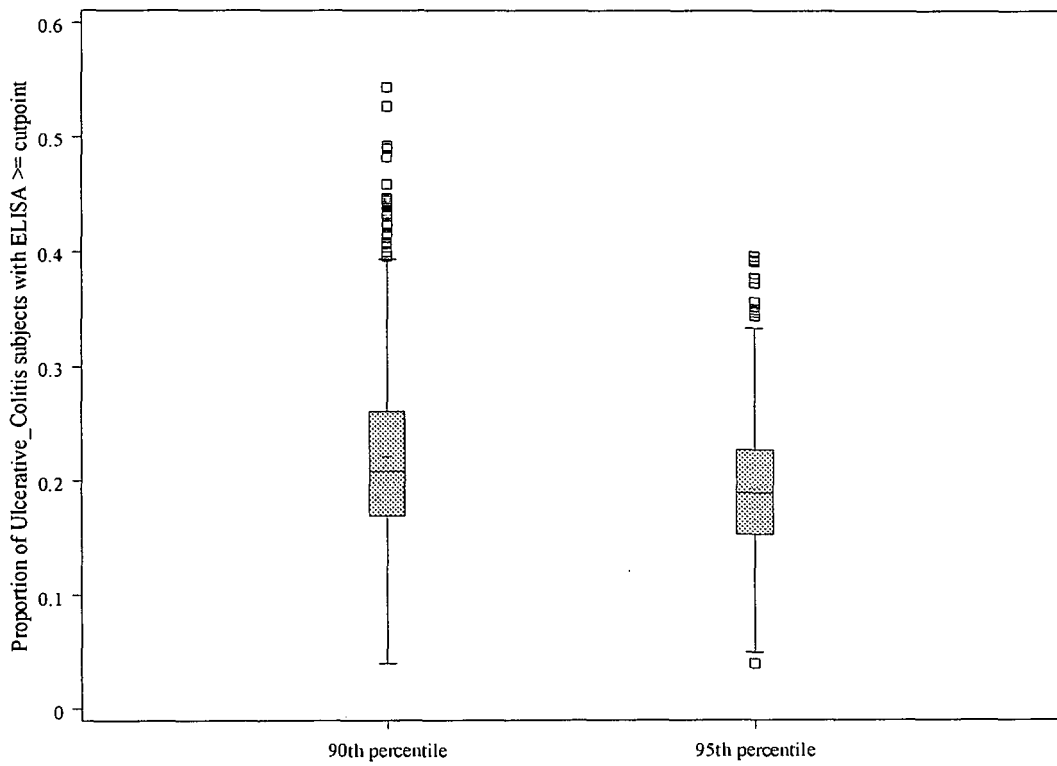


Figure 1D

Distribution of ELISA Signal Scores by Diagnosis
Sex=MALE Food=Cantaloupe

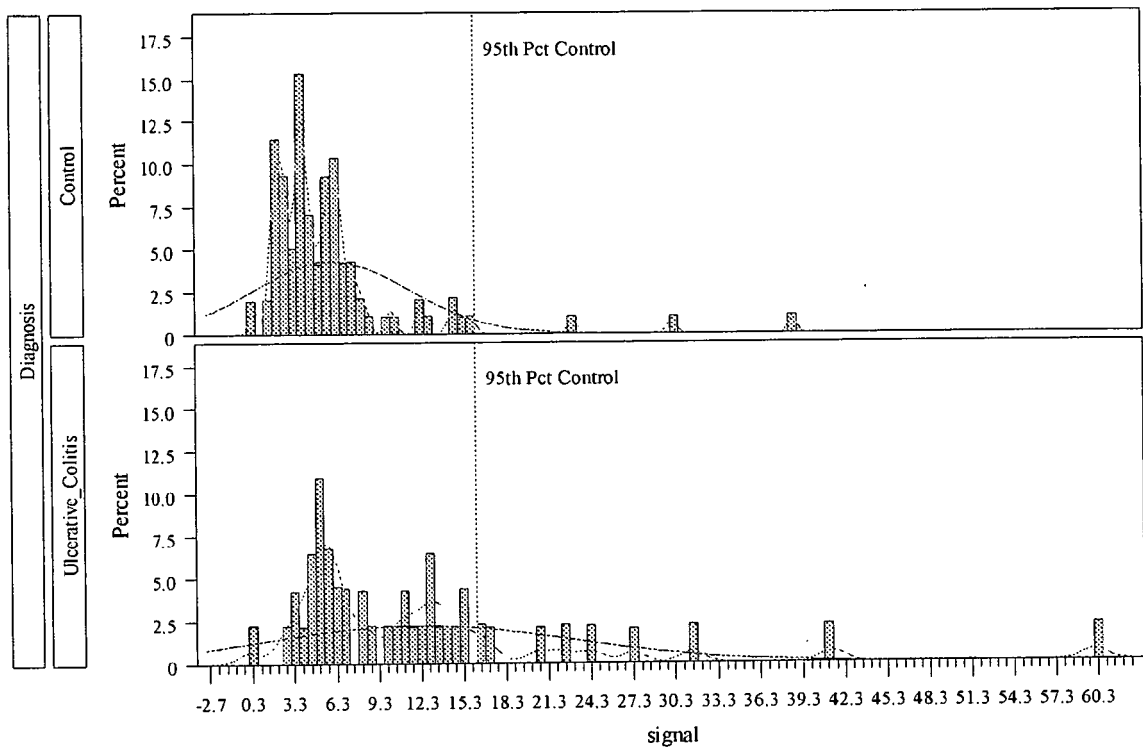


Figure 2A

Distribution of Percentage of Ulcerative Colitis Subjects with Signals \geq Control Cutpoint across 1000 Bootstrapped Samples

Sex=MALE Food=Cantaloupe

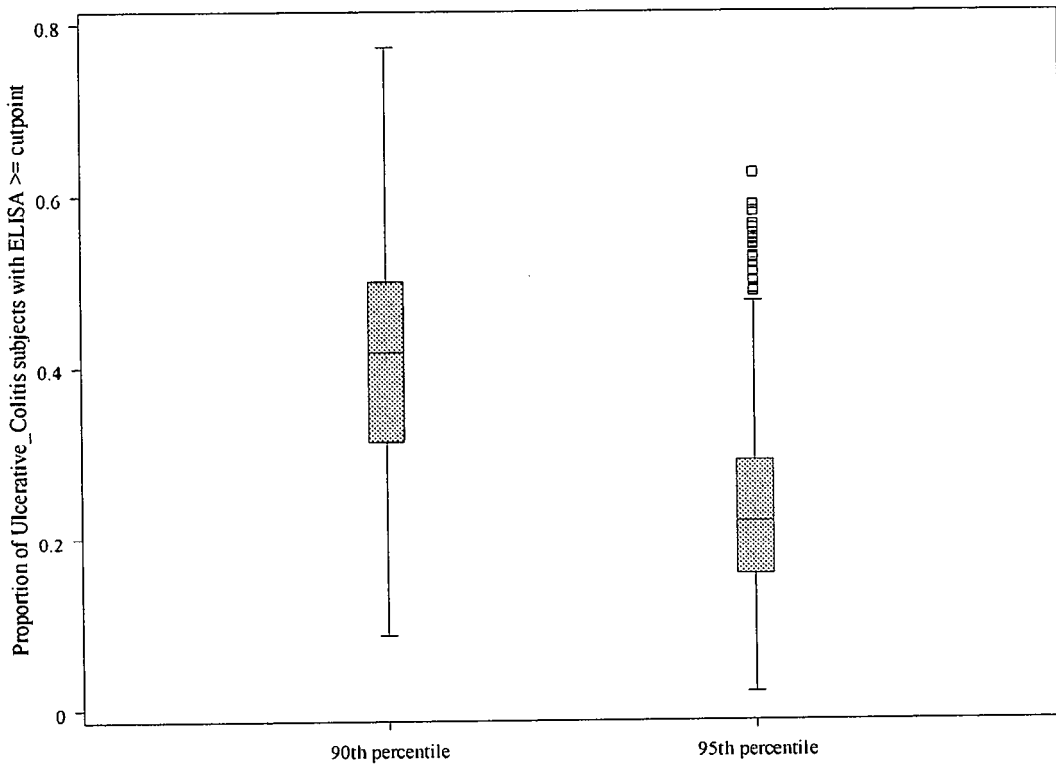


Figure 2B

Distribution of ELISA Signal Scores by Diagnosis
Sex=FEMALE Food=Cantaloupe

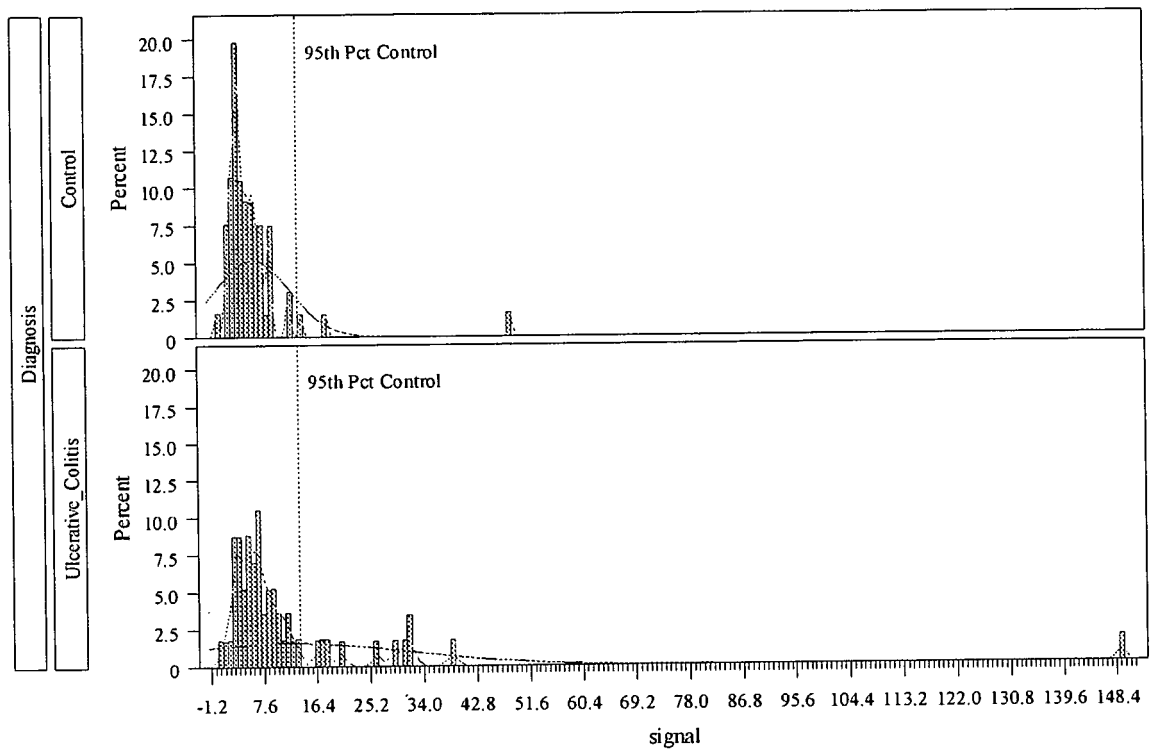


Figure 2C

Distribution of Percentage of Ulcerative Colitis Subjects with Signals \geq Control Cutpoint across 1000 Bootstrapped Samples

Sex=FEMALE Food=Cantaloupe

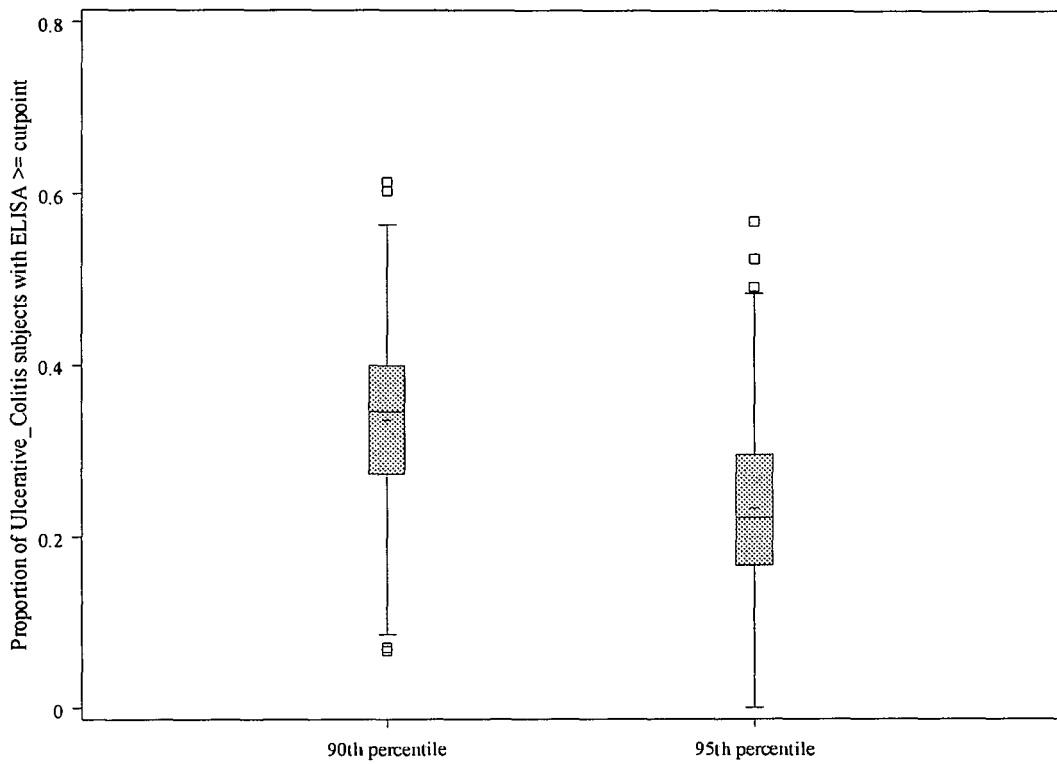


Figure 2D

*Distribution of ELISA Signal Scores by Diagnosis
Sex=MALE Food=Pinto Bean*

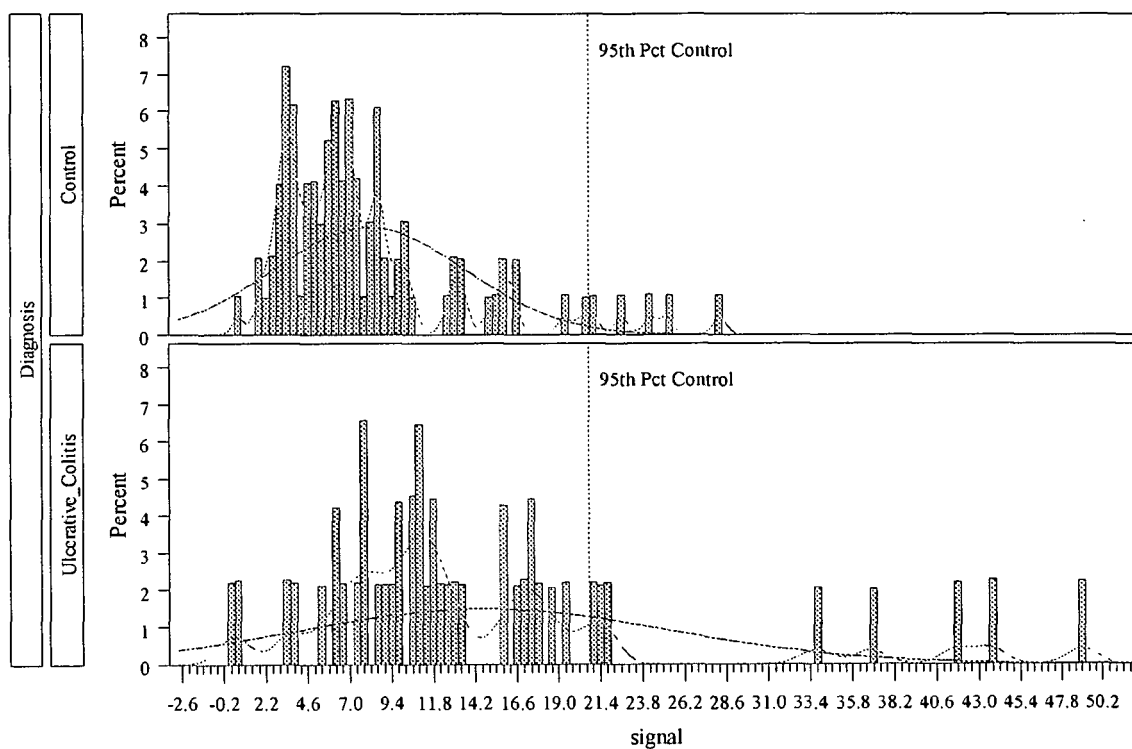


Figure 3A

*Distribution of Percentage of Ulcerative Colitis Subjects with Signals \geq Control
Cutpoint across 1000 Bootstrapped Samples
Sex=MALE Food=Pinto Bean*

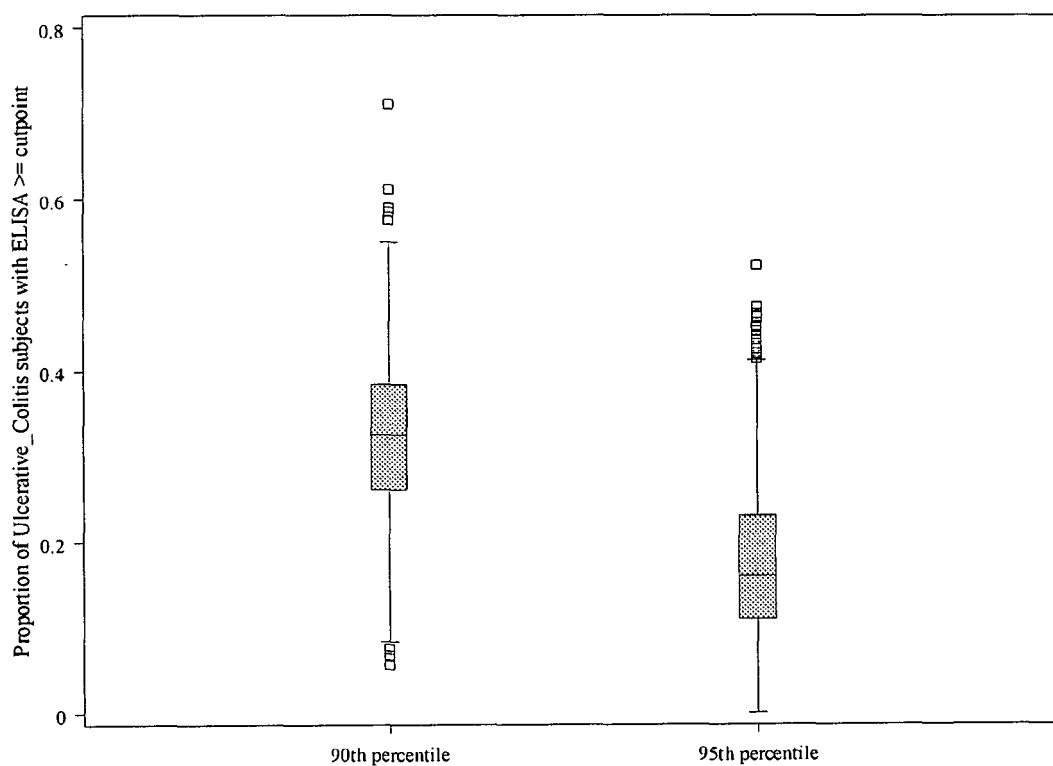


Figure 3B

Distribution of ELISA Signal Scores by Diagnosis
Sex=FEMALE Food=Pinto Bean

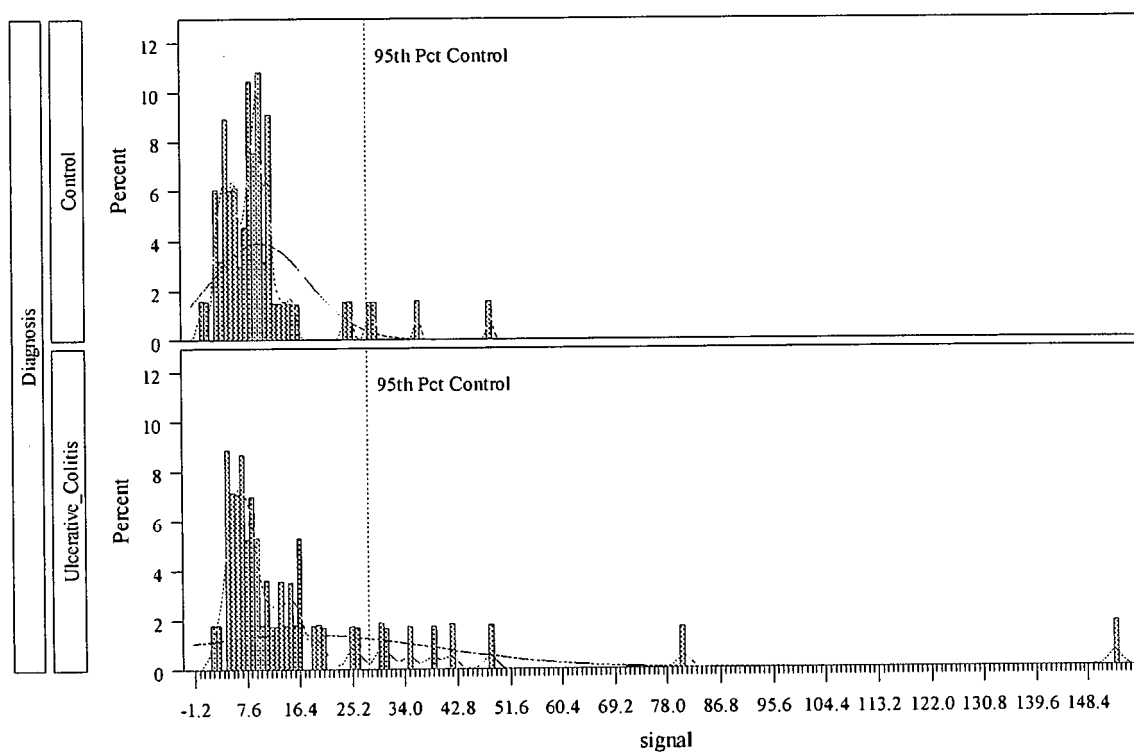


Figure 3C

Distribution of Percentage of Ulcerative Colitis Subjects with Signals \geq Control Cutpoint across 1000 Bootstrapped Samples

Sex=FEMALE Food=Pinto Bean

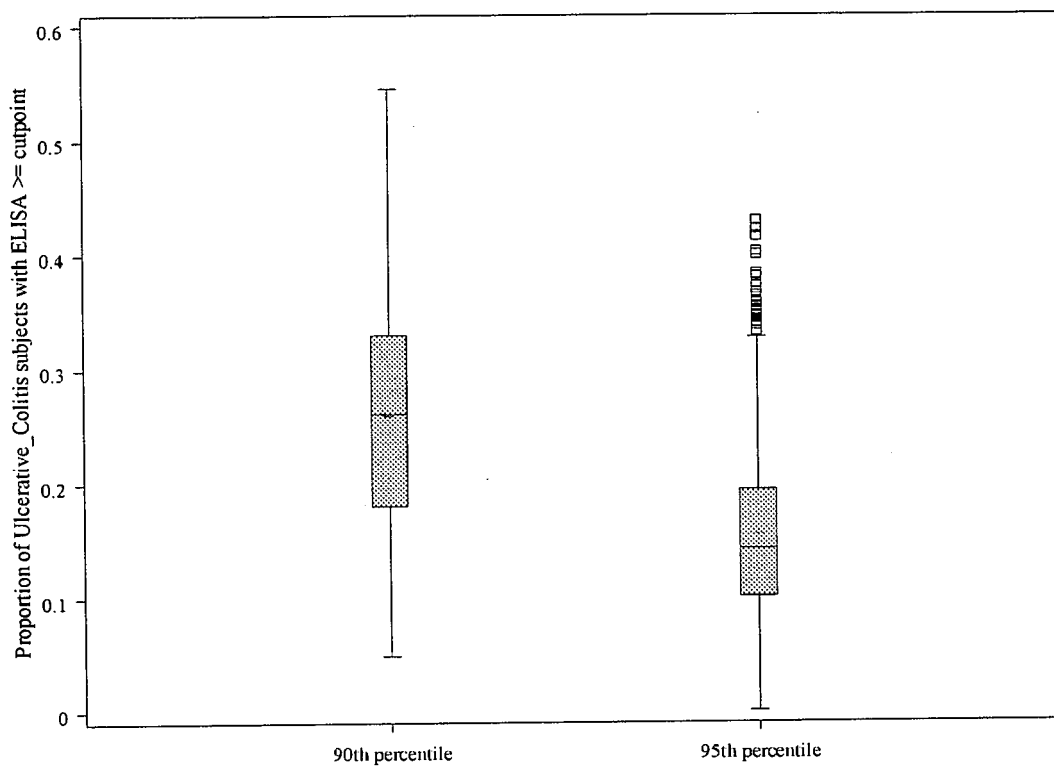


Figure 3D

Distribution of ELISA Signal Scores by Diagnosis
Sex=MALE Food=Cucumber

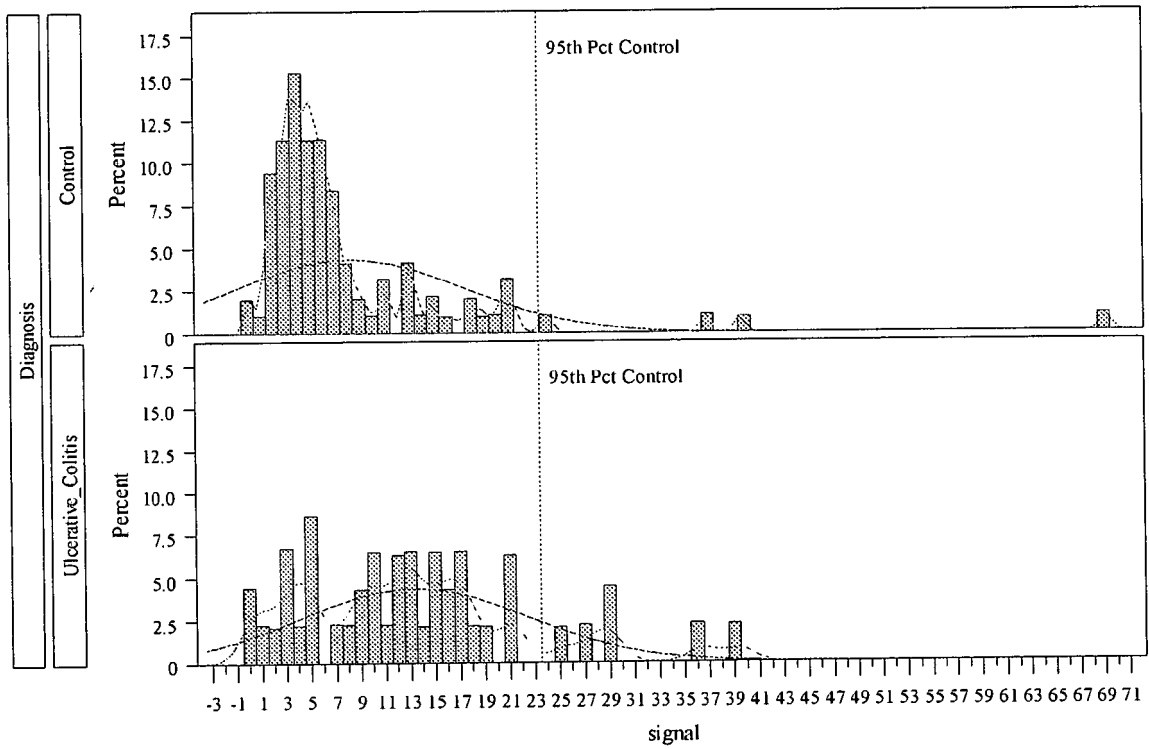


Figure 4A

*Distribution of Percentage of Ulcerative Colitis Subjects with Signals \geq Control
Cutpoint across 1000 Bootstrapped Samples
Sex=MALE Food=Cucumber*

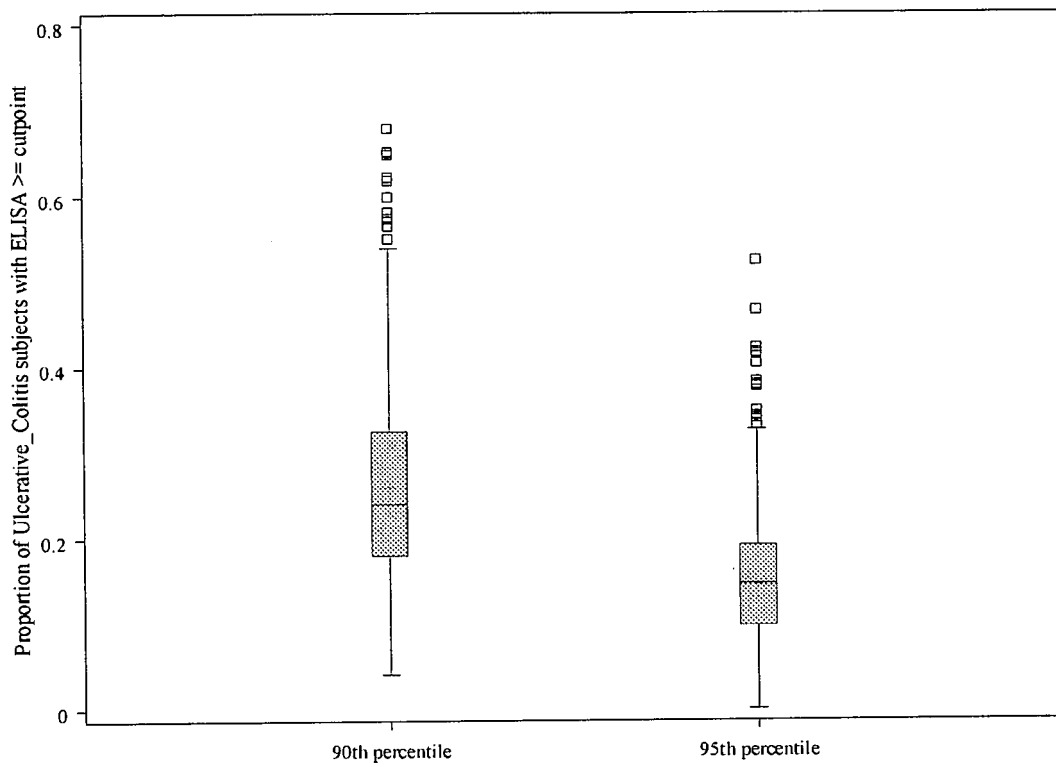


Figure 4B

Distribution of ELISA Signal Scores by Diagnosis
Sex=FEMALE Food=Cucumber

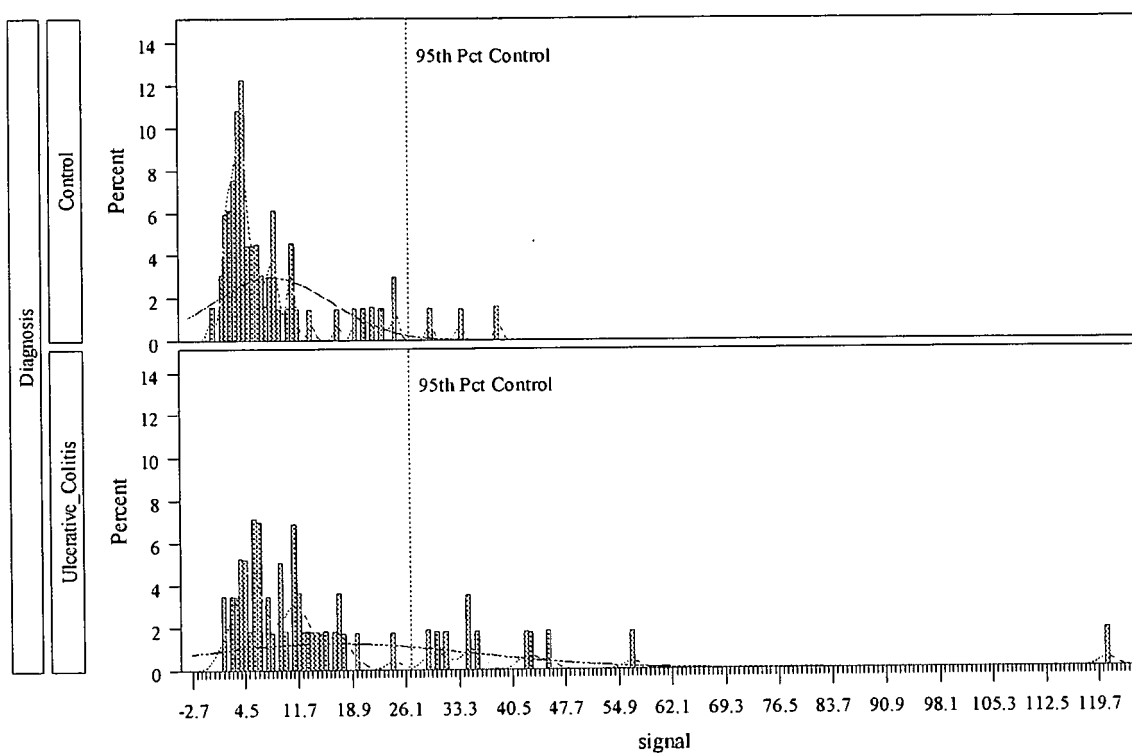


Figure 4C

*Distribution of Percentage of Ulcerative Colitis Subjects with Signals \geq Control
Cutpoint across 1000 Bootstrapped Samples
Sex=FEMALE Food=Cucumber*

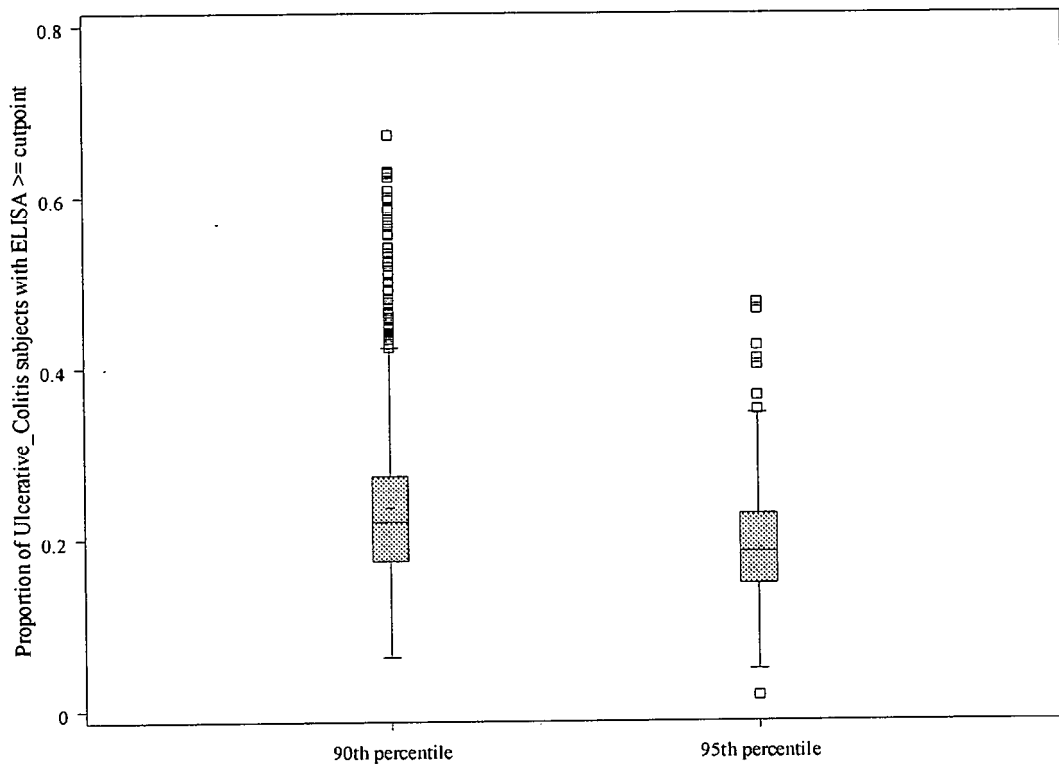


Figure 4D

Distribution of Ulcerative Colitis Subjects by Number of Foods in which they were rated as "Positive" by Sex

90th Percentile as Cutpoint

Distribution of posibs_90

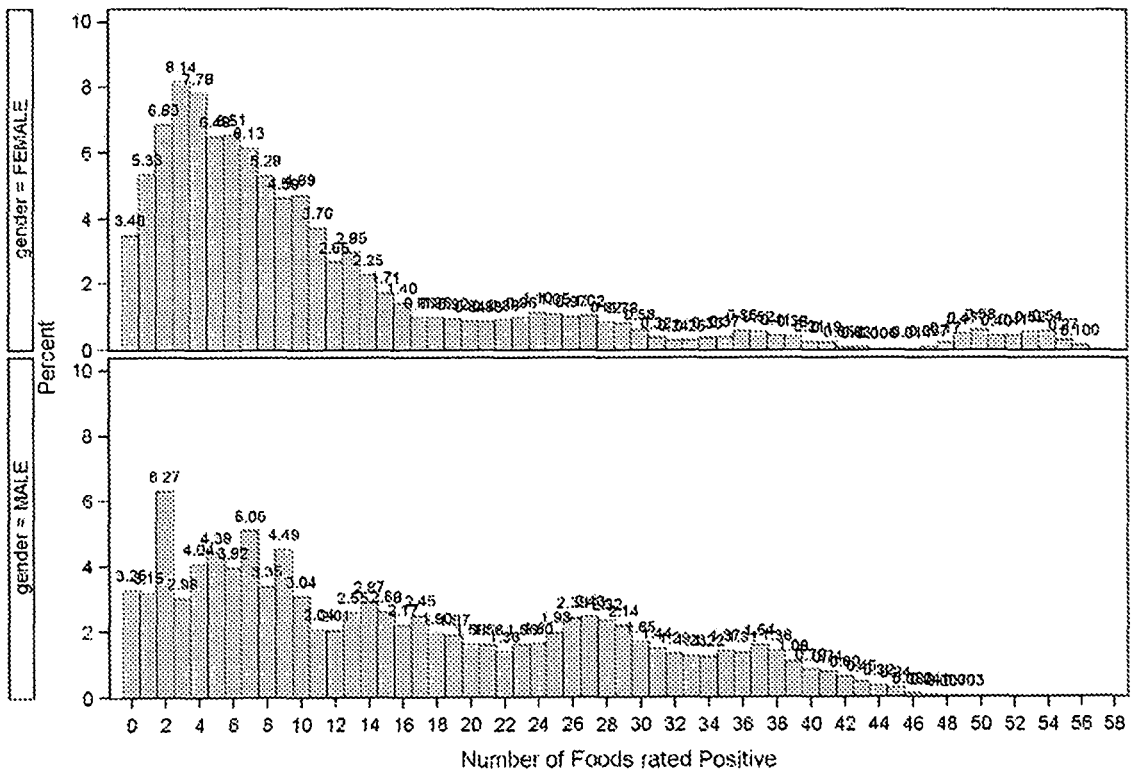


Figure 5A

Distribution of Ulcerative Colitis Subjects by Number of Foods in which they were rated as "Positive" by Sex

95th Percentile as Cutpoint

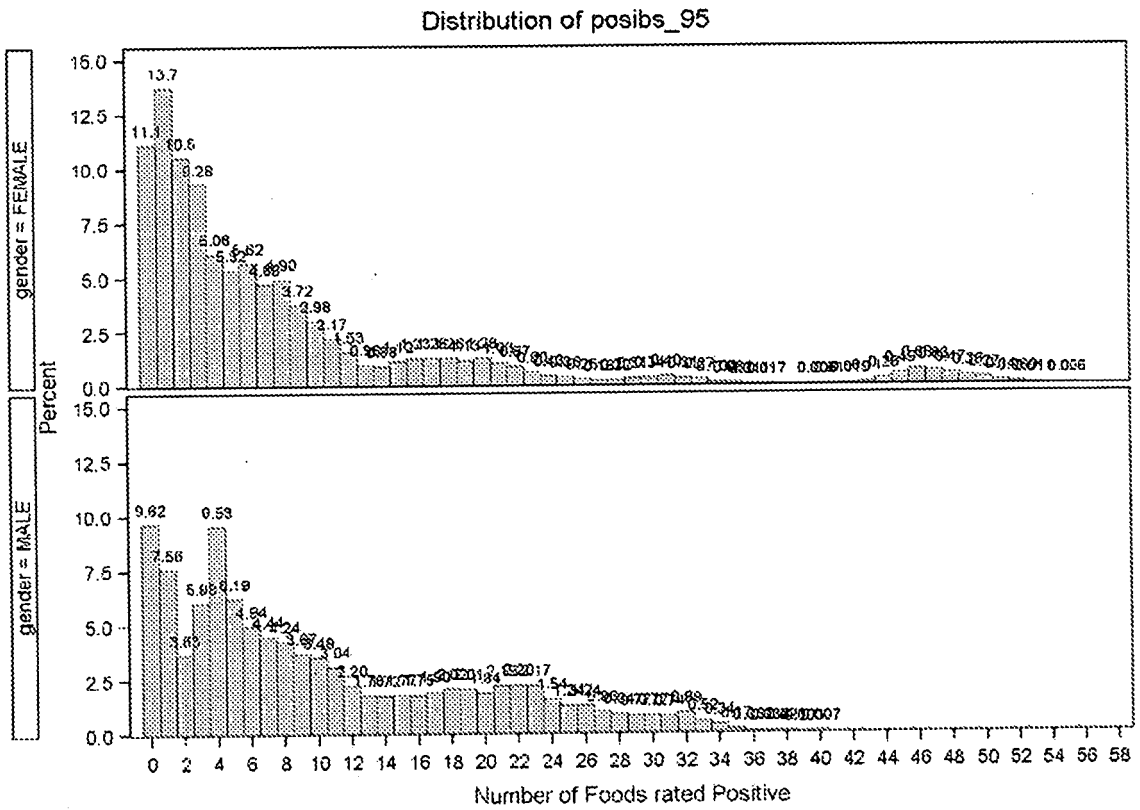


Figure 5B

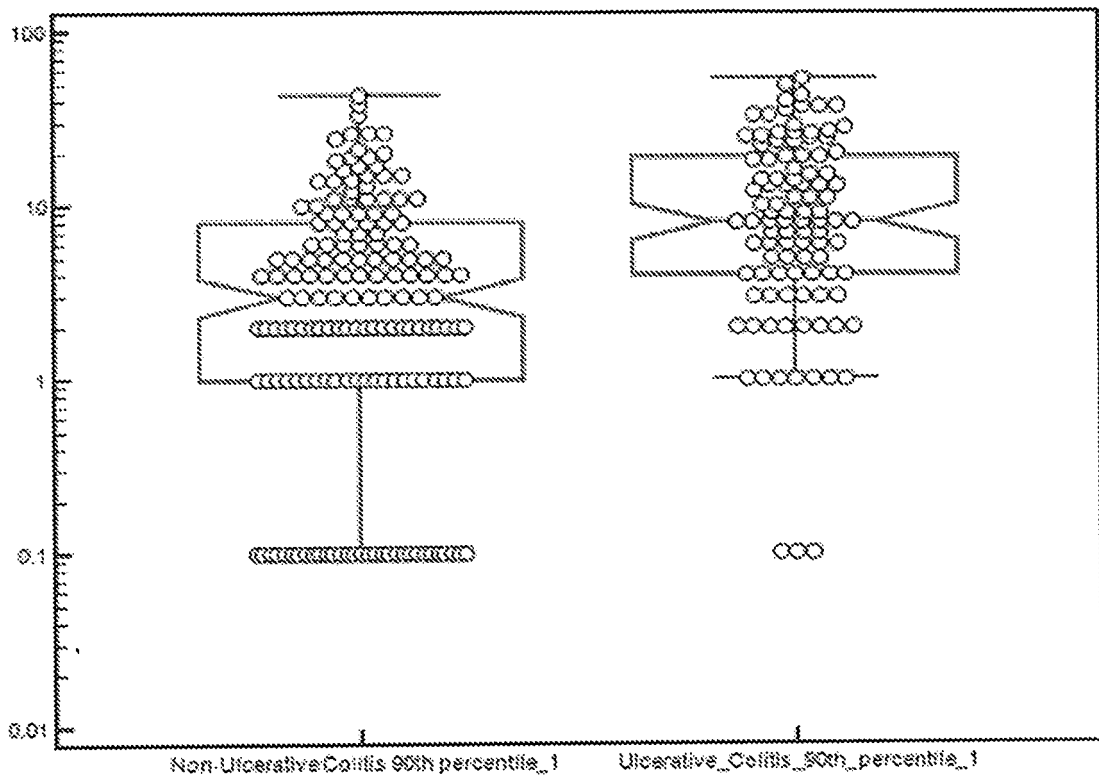


Figure 6A

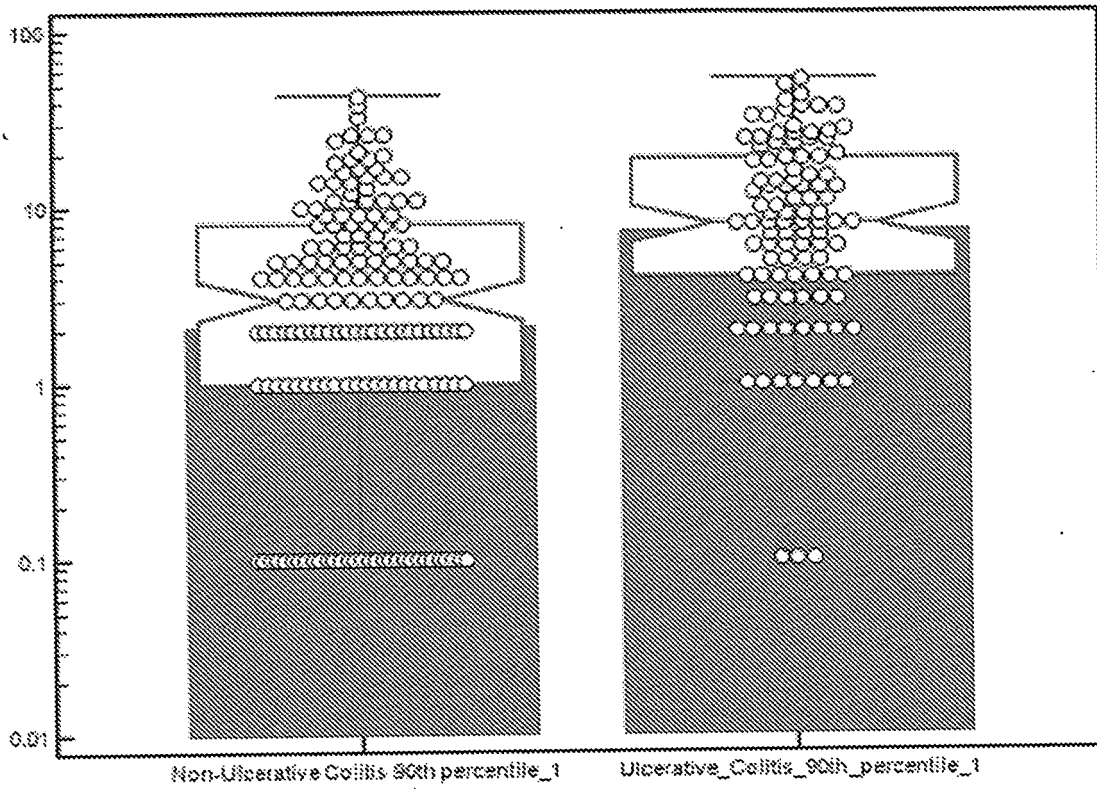


Figure 6B

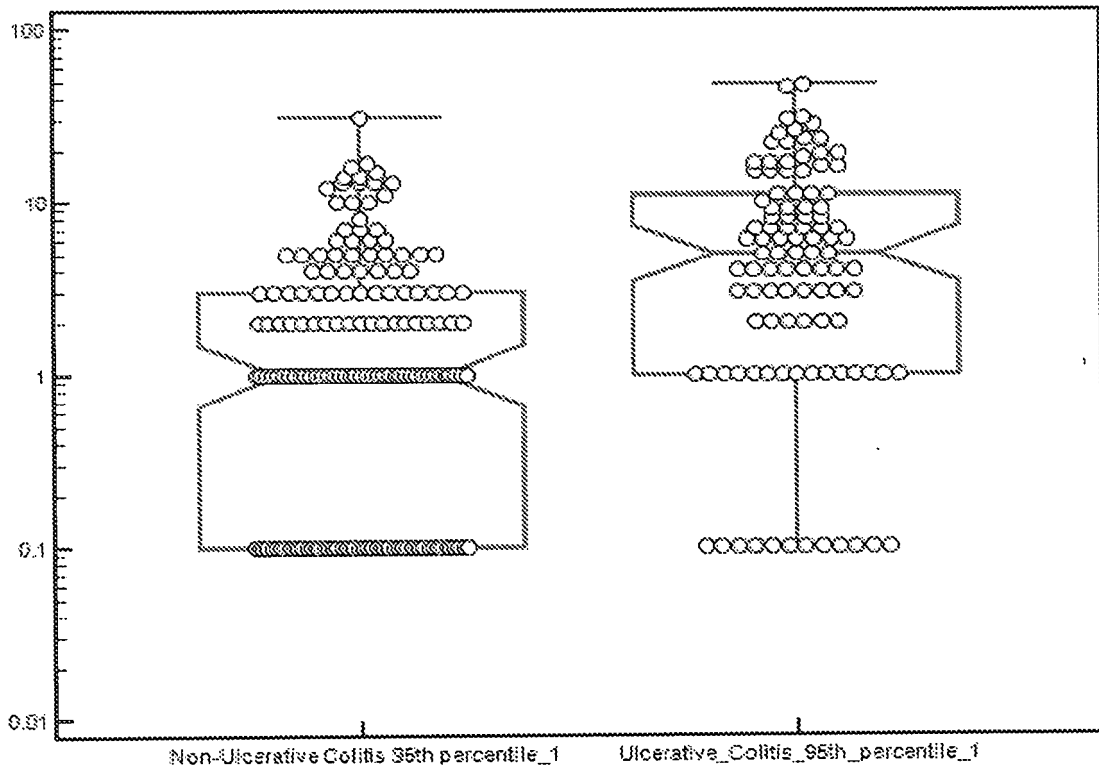


Figure 6C

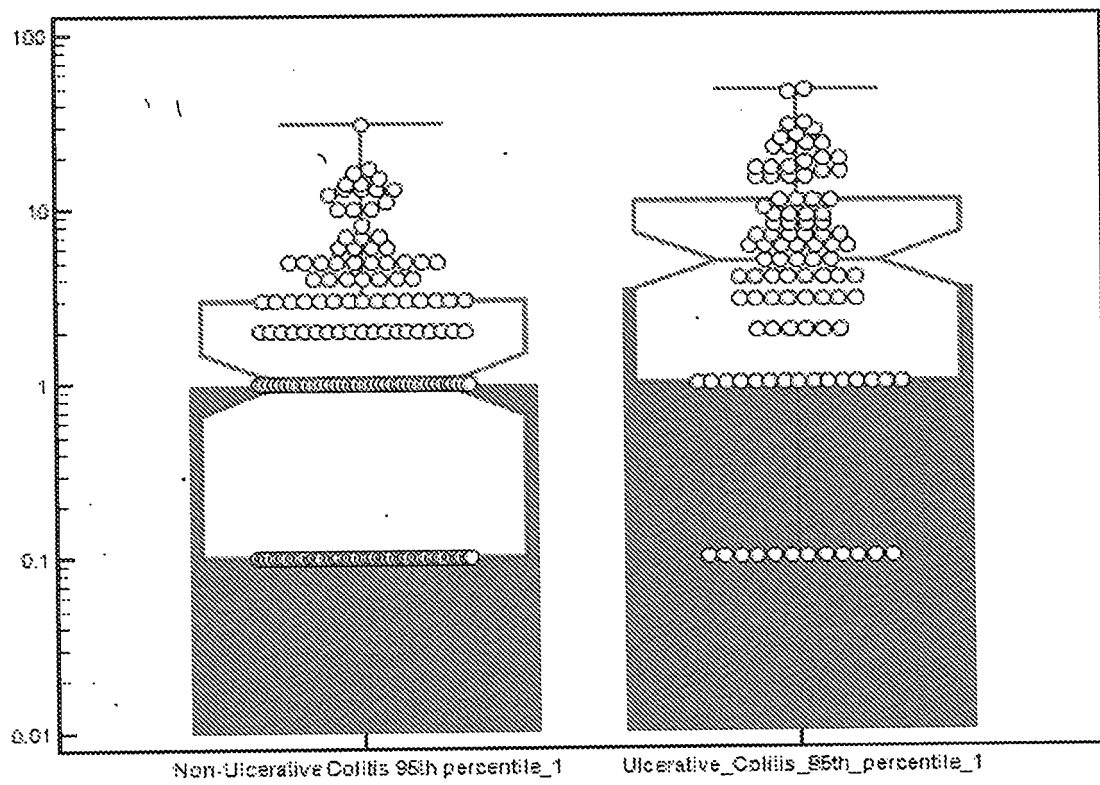


Figure 6D

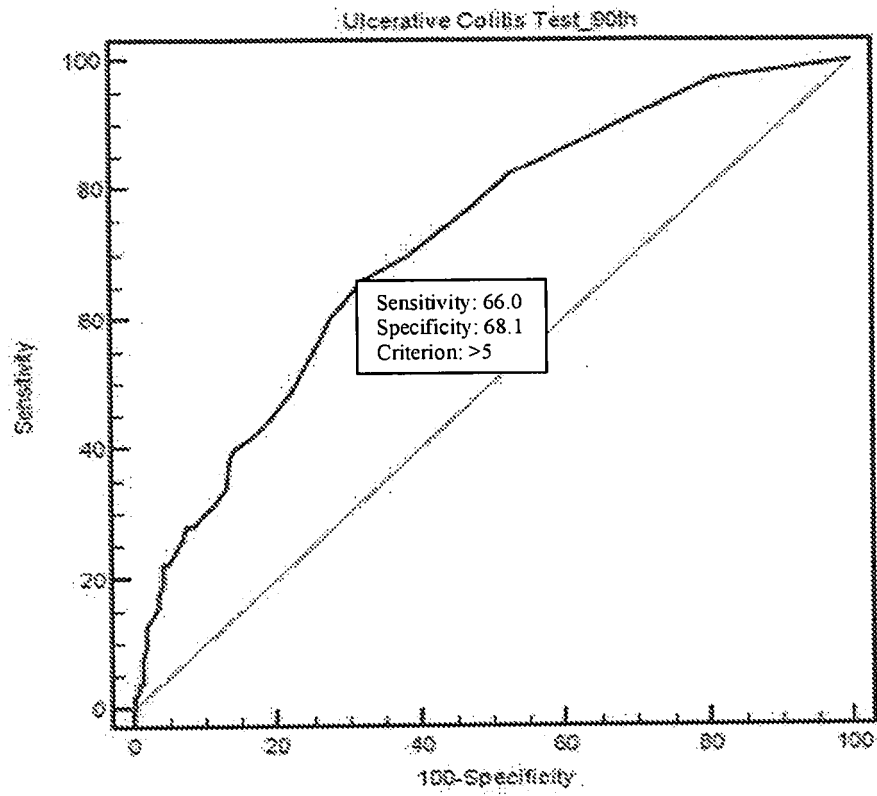


Figure 7A

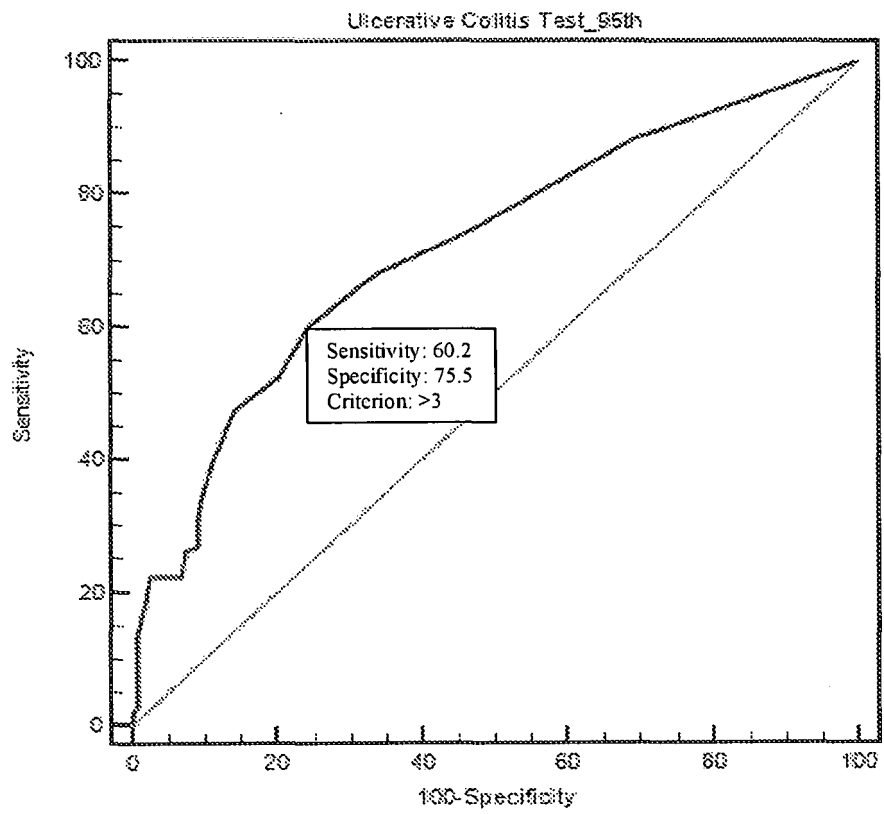


Figure 7B

REFERENCES CITED IN THE DESCRIPTION

This list of references cited by the applicant is for the reader's convenience only. It does not form part of the European patent document. Even though great care has been taken in compiling the references, errors or omissions cannot be excluded and the EPO disclaims all liability in this regard.

Patent documents cited in the description

- US 62327932 B [0036]

Non-patent literature cited in the description

- *Alternative Medicine Review*, 2004, vol. 9 (2), 198-207 [0004]