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(54) **Title**: COMPOSITIONS, DEVICES, AND METHODS OF IBS SENSITIVITY TESTING

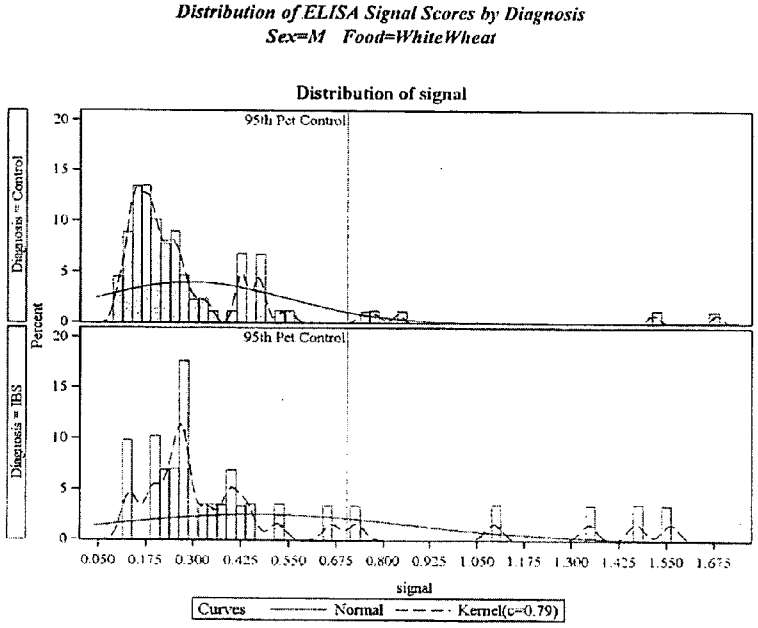


Figure 1A

(57) **Abstract**: Contemplated test kits and methods for food sensitivity are based on rational-based selection of food preparations with established discriminatory p-value. Particularly preferred kits include those with a minimum number of food preparations that have an average discriminatory p-value of ≤ 0.07 as determined by their raw p-value or an average discriminatory p-value of ≤ 0.10 as determined by FDR multiplicity adjusted p-value. In further contemplated aspects, compositions and methods for food sensitivity are also stratified by gender to further enhance predictive value.

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COMPOSITIONS, DEVICES, AND METHODS OF IBS SENSITIVITY TESTING

[0001] This application claims priority to our U.S. provisional patent application with the serial number 62/079783 filed November 14, 2014 which is incorporated by reference herein in its entirety.

Field of the Invention

[0002] 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 irritable bowel syndrome.

Background

[0003] 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.

[0004] Food sensitivity, especially as it relates to irritable bowel syndrome (IBS), often presents with chronic abdominal pain, discomfort, bloating, and/or change in bowel habits and is not well understood in the medical community. Most typically, IBS is diagnosed by elimination of other pathological conditions (*e.g.*, bacterial or protozoan infection, lactose intolerance, etc.) that may have similar or overlapping symptoms. However, IBS 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.

[0005] 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. For example, not all IBS patients show positive response to food A, and not all IBS patients show negative response to food B. Thus, even if an IBS patient shows positive response to food A, removal of food A from the patient's diet may not relieve the patient's IBS 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 IBS.

[0006] Many have made efforts to select food items or allergens to include in the test panel for immunoassay tests. For example, US Patent Application No. 2007/0122840 to Cousins discloses selection of 29 food allergens that are included in the test panel for ELISA assay. The 29 food allergens are selected based on the frequency of IgG positivity in preliminary experiments with a larger panel of food allergens. However, Cousins fails to teach any quantitative and/or statistical analysis for the selected antigens and as such fails to provide any rationale for the selection. Indeed, Cousin's method to select 29 food allergens for test panel has been criticized that the selection is rather arbitrary. For example, Croft criticized in a paper titled "IgG food antibodies and irritating the bowel", published in Gastroenterology, Vol. 128, Issue 4, p.1135–1136, that Cousin's method is not clear whether the quantity and range of food antibodies being measured are similar or completely different to non-IBS patients or non-food intolerant patients because it lacks controls (normal or non-IBS control subject). Thus, it is at best unclear if Cousins achieves any improvement with respect to false positive and false negative results.

[0007] For another example, US Patent Application No. 2011/0306898 to Stierstorfer discloses selection of 41 food substances as test materials on skin patches. The 41 food substances are selected based on chemical compounds included in the food substances (e.g., vanillin, cinnamic aldehyde, sorbic acid, etc.). The food substances are tested on IBS patients or IBS-suspected patients for allergic contact dermatitis. However, Stierstorfer also fails to disclose how the false positive or false negative food allergens are eliminated and whether the food allergens are selected based on the gender stratification among IgG positivity results.

[0008] All publications identified herein are incorporated by reference to the same extent as if each individual publication or patent application were specifically and individually indicated to

be incorporated by reference. Where a definition or use of a term in an incorporated reference is inconsistent or contrary to the definition of that term provided herein, the definition of that term provided herein applies and the definition of that term in the reference does not apply.

[0009] 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 IBS.

Summary of The Invention

[0010] The inventive subject matter provides systems and methods for testing food intolerance in patients diagnosed with or suspected to have irritable bowel syndrome. One aspect of the invention is a test kit with for testing food intolerance in patients diagnosed with or suspected to have irritable bowel syndrome. The test kit includes a plurality of distinct food preparations coupled to individually addressable respective solid carriers. 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.

[0011] Another aspect of the invention includes a method of testing food intolerance in patients diagnosed with or suspected to have irritable bowel syndrome. The method includes a step of contacting a food preparation with a bodily fluid of a patient that is diagnosed with or suspected to have irritable bowel syndrome. The bodily fluid is associated with a gender identification. It is especially preferred that 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. The method continues with a step of measuring IgG bound to the at least one component of the food preparation to obtain a signal, and then comparing the signal to a gender-stratified reference value for the food preparation using the gender identification to obtain a result. Then, the method also includes a step of updating or generating a report using the result.

[0012] Another aspect of the invention includes a method of generating a test for food intolerance in patients diagnosed with or suspected to have irritable bowel syndrome. The method includes a step of obtaining test results for a plurality of distinct food preparations. The test results are based on bodily fluids of patients diagnosed with or suspected to have irritable

bowel syndrome and bodily fluids of a control group not diagnosed with or not suspected to have irritable bowel syndrome. The method also includes a step of stratifying the test results by gender for each of the distinct food preparations. Then the method continues with a step of assigning for a predetermined percentile rank a different cutoff value for male and female patients for each of the distinct food preparations.

[0013] Still another aspect of the invention includes a use of a plurality of distinct food preparations coupled to individually addressable respective solid carriers in a diagnosis of irritable bowel syndrome. The plurality of distinct food preparations are selected based on their 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.

[0014] Various objects, features, aspects and advantages of the inventive subject matter 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

[0015] Table 1 shows a list of food items from which food preparations can be prepared.

[0016] Table 2 shows statistical data of foods ranked according to 2-tailed FDR multiplicity-adjusted p-values.

[0017] Table 3 shows statistical data of ELISA score by food and gender.

[0018] Table 4 shows cutoff values of foods for a predetermined percentile rank.

[0019] Figure 1A illustrates ELISA signal score of male IBS patients and control tested with white wheat.

[0020] Figure 1B illustrates a distribution of percentage of male IBS subjects exceeding the 90th and 95th percentile tested with white wheat.

[0021] Figure 1C illustrates a signal distribution in women along with the 95th percentile cutoff as determined from the female control population tested with white wheat.

[0022] Figure 1D illustrates a distribution of percentage of female IBS subjects exceeding the 90th and 95th percentile tested with white wheat.

[0023] Figure 2A illustrates ELISA signal score of male IBS patients and control tested with cocoa.

[0024] Figure 2B illustrates a distribution of percentage of male IBS subjects exceeding the 90th and 95th percentile tested with cocoa.

[0025] Figure 2C illustrates a signal distribution in women along with the 95th percentile cutoff as determined from the female control population tested with cocoa.

[0026] Figure 2D illustrates a distribution of percentage of female IBS subjects exceeding the 90th and 95th percentile tested with cocoa.

[0027] Figure 3A illustrates ELISA signal score of male IBS patients and control tested with rye.

[0028] Figure 3B illustrates a distribution of percentage of male IBS subjects exceeding the 90th and 95th percentile tested with rye.

[0029] Figure 3C illustrates a signal distribution in women along with the 95th percentile cutoff as determined from the female control population tested with rye.

[0030] Figure 3D illustrates a distribution of percentage of female IBS subjects exceeding the 90th and 95th percentile tested with rye.

[0031] Figure 4A illustrates ELISA signal score of male IBS patients and control tested with black tea.

[0032] Figure 4B illustrates a distribution of percentage of male IBS subjects exceeding the 90th and 95th percentile tested with black tea.

[0033] Figure 4C illustrates a signal distribution in women along with the 95th percentile cutoff as determined from the female control population tested with black tea.

[0034] Figure 4D illustrates a distribution of percentage of female IBS subjects exceeding the 90th and 95th percentile tested with black tea.

[0035] Figures 5A-5B illustrate distributions of IBS subjects by number of foods that were identified as trigger foods at the 90th percentile and 95th percentile.

[0036] Table 5 shows raw data of IBS patients and control with number of positive results based on the 90th percentile.

[0037] Table 6 shows statistical data summarizing the raw data of IBS patient populations shown in Table 5.

[0038] Table 7 shows statistical data summarizing the raw data of control populations shown in Table 5.

[0039] Table 8 shows statistical data summarizing the raw data of IBS patient populations shown in Table 5 transformed by logarithmic transformation.

[0040] Table 9 shows statistical data summarizing the raw data of control populations shown in Table 5 transformed by logarithmic transformation.

[0041] Table 10 shows statistical data of an independent T-test to compare the geometric mean number of positive foods between the IBS and non- IBS samples.

[0042] Table 11 shows statistical data of a Mann-Whitney test to compare the geometric mean number of positive foods between the IBS and non- IBS samples.

[0043] Figure 6A illustrates a box and whisker plot of data shown in Table 5.

[0044] Figure 6B illustrates a notched box and whisker plot of data shown in Table 5.

[0045] Figure 7 illustrates the ROC curve corresponding to the statistical data shown in Table 12.

[0046] Table 12 shows statistical data of a Receiver Operating Characteristic (ROC) curve analysis of data shown in Tables 5-11.

[0047] **Table 13** shows statistical data of performance metrics in predicting IBS status among female patients from number of positive foods.

[0048] **Table 14** shows statistical data of performance metrics in predicting IBS status among male patients from number of positive foods.

Detailed Description

[0049] The inventors have discovered that food preparations used in food tests to identify trigger foods in patients diagnosed with or suspected to have IBS are not equally well predictive and/or associated with IBS/IBS symptoms. Indeed, various experiments have revealed that among a wide variety of food items certain food items are highly predictive/associated with IBS whereas others have no statistically significant association with IBS.

[0050] 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 IBS. 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 IBS signs and symptoms.

[0051] 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.

[0052] 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. 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.

[0053] 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.

[0054] 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.

[0055] Groupings of alternative elements or embodiments of the invention disclosed herein are not to be construed as limitations. Each group member can be referred to and claimed individually or in any combination with other members of the group or other elements found herein. One or more members of a group can be included in, or deleted from, a group for reasons of convenience and/or patentability. When any such inclusion or deletion occurs, the specification is herein deemed to contain the group as modified thus fulfilling the written description of all Markush groups used in the appended claims.

[0056] In one especially preferred aspect, the inventors therefore contemplate a test kit or test panel that is suitable for testing food intolerance in patients where the patient is diagnosed with

or suspected to have irritable bowel syndrome. Most preferably, such test kit or panel will include a plurality of distinct food preparations (*e.g.*, raw or processed extract, preferably aqueous extract with optional co-solvent, which may or may not be filtered) that are coupled to individually addressable respective solid carriers (*e.g.*, in a form of an array or a micro well plate), wherein the 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. As used herein, processed extracts includes food extracts made of food items that are mechanically or chemically modified (e.g., minced, heated, boiled, fermented, smoked, etc.).

[0057] 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 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.

[0058] 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 IBS. Particularly suitable food preparations may be identified by the experimental procedures outlined below. Thus, it should be appreciated that the food items need not be limited to the items described herein, but that all items are contemplated that can be identified by the methods

presented herein. Therefore, exemplary food preparations include at least two, at least four, at least eight, or at least 12 food preparations prepared from cocoa, tea (e.g. green, black, etc.), oat, cabbage, cow milk, onion (e.g. yellow, white, maui, etc.), honey, rye, corn, yeast, wheat (e.g. red, white, etc.), soybean, egg, tuna, lemon, pineapple, cucumber, orange, halibut, walnut, grapefruit, cane sugar, chicken, blueberry, or shrimp (e.g. US Gulf white, Thai, Tiger, etc.). Additionally contemplated food preparations are prepared from Crab (e.g. Dungeness, Blue, Alaskan King, etc.), Barley, Strawberry, Pork, Rice (e.g. Brown, White, etc.), Beef, Cashew, Codfish, Potato, White Sesame, Broccoli, Almond, Turkey, Scallop, and/or Salmon. Still further especially contemplated food items and food additives from which food preparations can be prepared are listed in **Table 1**.

[0059] Using bodily fluids from patients diagnosed with or suspected to have irritable bowel syndrome and healthy control group individuals (*i.e.*, those not diagnosed with or not suspected to have irritable bowel syndrome), numerous additional food items may be identified. Preferably, such identified food items will have high discriminatory power and as such have a p-value of ≤ 0.15, more preferably ≤ 0.10, and most preferably ≤ 0.05 as determined by raw p-value, and/or a p-value of ≤ 0.10, more preferably ≤ 0.08, and most preferably ≤ 0.07 as determined by False Discovery Rate (FDR) multiplicity adjusted p-value.

[0060] Therefore, where a panel has multiple food preparations, it is contemplated that the plurality of distinct food preparations has an average discriminatory p-value of ≤ 0.05 as determined by raw p-value or an average discriminatory p-value of ≤ 0.08 as determined by FDR multiplicity adjusted p-value, or even more preferably an average discriminatory p-value of ≤ 0.025 as determined by raw p-value or an average discriminatory p-value of ≤ 0.07 as determined by FDR multiplicity adjusted p-value. In further preferred aspects, it should be appreciated that the FDR multiplicity adjusted p-value may be adjusted for at least one of age and gender, and most preferably adjusted for both age and gender. On the other hand, where a test kit or panel is stratified for use with a single gender, it is also contemplated that in a test kit or panel at least 50% (and more typically 70% or all) of the plurality of distinct food preparations, when adjusted for a single gender, 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. Furthermore, it should be appreciated that other

stratifications (*e.g.*, dietary preference, ethnicity, place of residence, genetic predisposition or family history, etc.) are also contemplated, and the PHOSITA will be readily appraised of the appropriate choice of stratification.

[0061] 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 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.

[0062] 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, a microfluidic device, dip sticks, membrane-bound arrays, etc. Consequently, the solid carrier to which the food preparations are coupled may include wells of a multiwall plate, a microfluidic device, a (*e.g.*, color-coded or magnetic) bead, or an adsorptive film (*e.g.*, nitrocellulose or micro/nanoporous polymeric film), a chemical sensor, or an electrical sensor, (*e.g.* a printed copper sensor or microchip). In some embodiments, it is also contemplated that a suitable solid carrier for molecular absorption and signal detection by a light detector (e.g., surface plasmon resonance, etc.) can be used.

[0063] Consequently, the inventors also contemplate a method of testing food intolerance in patients that are diagnosed with or suspected to have irritable bowel syndrome. Most typically, such methods will include a step of contacting a food preparation with a bodily fluid (e.g., whole blood, plasma, serum, saliva, or a fecal suspension) of a patient that is diagnosed with or suspected to have irritable bowel syndrome, and wherein the bodily fluid is associated with a gender identification. As noted before, the step of contacting is preferably performed under conditions that allow IgG (or IgE or IgA or IgM) from the bodily fluid to bind to at least one

component of the food preparation, and the IgG bound to the component(s) of the food preparation are then quantified/measured to obtain a signal. Most preferably, the signal is then compared against a gender-stratified reference value (e.g., at least a 90th percentile value) for the food preparation using the gender identification to obtain a result, which is then used to update or generate a report. Preferably, the report can be generated as an aggregate result of individual assay results.

[0064] Most commonly, such methods will not be limited to a single food preparation, but will employ multiple different food preparations. As noted before, suitable food preparations can be identified using various methods as described below, however, especially preferred food preparations include cocoa, tea (e.g. green, black, etc.), oat, cabbage, cow milk, onion (e.g. yellow, white, maui, etc.), honey, rye, corn, yeast, wheat (e.g. red, white, etc.), soybean, egg, tuna, lemon, pineapple, cucumber, orange, halibut, walnut, grapefruit, cane sugar, chicken, blueberry, or shrimp (e.g. US Gulf white, Thai, Tiger, etc.). Additionally contemplated food preparations are prepared from Crab (e.g. Dungeness, Blue, Alaskan King, etc.), Barley, Strawberry, Pork, Rice (e.g. Brown, White, etc.), Beef, Cashew, Codfish, Potato, White Sesame, Broccoli, Almond, Turkey, Scallop, and/or Salmon, and/or items of Table 1. As also noted above, it is generally preferred that at least some, or all of the different food preparations have an average discriminatory p-value of ≤ 0.07 (or ≤ 0.05, or ≤ 0.025) as determined by raw p-value, and/or or an average discriminatory p-value of ≤ 0.10 (or ≤ 0.08, or ≤ 0.07) as determined by FDR multiplicity adjusted p-value.

[0065] While it is preferred that food preparations are prepared from a 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 lime, a mixture of crabs comprising blue crab, king crab and Dungeness crab, a mixture of wheat comprising a white wheat and red wheat, a mixture of shrimp comprising US Gulf white, Thai and Tiger shrimps, etc). In some embodiments, it is also contemplated that food preparations can be prepared from purified food antigens or recombinant food antigens.

[0066] 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 or

other type of antibody bound to the component of the food preparation is performed via an immunoassay test (e.g., ELISA test, antibody capture enzyme immunoassay, other types of antibody capture assays, etc.)

[0067] Viewed from a different perspective, the inventors also contemplate a method of generating a test for food intolerance in patients diagnosed with or suspected to have irritable bowel syndrome. Because the test is applied to patients already diagnosed with or suspected to have irritable bowel syndrome, the authors do not contemplate that the method has a primary diagnostic purpose for IBS. Instead, the method is for identifying triggering food items among already diagnosed or suspected IBS patients. Such test will typically include a step of obtaining one or more test results (e.g., ELISA, antibody capture enzyme immunoassay) for various distinct food preparations, wherein the test results are based on bodily fluids (e.g., blood saliva, fecal suspension) of patients diagnosed with or suspected to have irritable bowel syndrome and bodily fluids of a control group not diagnosed with or not suspected to have irritable bowel syndrome. Most preferably, the test results are then stratified by gender for each of the distinct food preparations, a different cutoff value for male and female patients for each of the distinct food preparations (e.g., cutoff value for male and female patients has a difference of at least 10% (abs)) is assigned for a predetermined percentile rank (e.g., 90th or 95th percentile).

[0068] As noted earlier, and while not limiting to the inventive subject matter, it is contemplated that the distinct food preparations include at least two (or six, or ten, or 15) food preparations prepared from food items selected from the group consisting of cocoa, tea (e.g. green, black, etc.), oat, cabbage, cow milk, onion (e.g. yellow, white, maui, etc.), honey, rye, corn, yeast, wheat (e.g. red, white, etc.), soybean, egg, tuna, lemon, pineapple, cucumber, orange, halibut, walnut, grapefruit, cane sugar, chicken, blueberry, or shrimp (e.g. US Gulf white, Thai, Tiger, etc.). Additionally contemplated food preparations are prepared from Crab (e.g. Dungeness, Blue, Alaskan King, etc.), Barley, Strawberry, Pork, Rice (e.g. Brown, White, etc.), Beef, Cashew, Codfish, Potato, White Sesame, Broccoli, Almond, Turkey, Scallop, and/or Salmon, and/or items of Table 1. On the other hand, where new food items are tested, it should be appreciated that the distinct food preparations include a food preparation prepared from a food items other than cocoa, tea (e.g. green, black, etc.), oat, cabbage, cow milk, onion (e.g. yellow, white, maui, etc.), honey, rye, corn, yeast, wheat (e.g. red, white, etc.), soybean, egg, tuna,

lemon, pineapple, cucumber, orange, halibut, walnut, grapefruit, cane sugar, chicken, blueberry, or shrimp (e.g. US Gulf white, Thai, Tiger, etc.).. Regardless of the particular choice of food items, it is generally preferred however, that the distinct food preparations have an average discriminatory p-value of ≤ 0.07 (or ≤ 0.05, or ≤ 0.025) as determined by raw p-value or an average discriminatory p-value of ≤ 0.10 (or ≤ 0.08, or ≤ 0.07) as determined by FDR multiplicity adjusted p-value. Exemplary aspects and protocols, and considerations are provided in the experimental description below.

[0069] 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 IBS.

Experiments

[0070] 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.

[0071] For some food extracts, the inventors found that food extracts prepared with specific procedures to generate food extracts provides more superior results in detecting elevated IgG reactivity in IBS 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.

[0072] 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.

[0073] 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.

[0074] Blocking of ELISA plates: To optimize signal to noise, plates were 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, were attempted but could not provide adequate signal to noise and low assay variability required.

[0075] 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.

[0076] Methodology to determine ranked food list in order of ability of ELISA signals to distinguish IBS 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 the a larger more 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, Thailand Shrimp could be dropped in favor of U.S. Gulf White Shrimp as representative of the "shrimp" food group, or King Crab could be dropped in favor of Dungeness Crab as representative of the "crab" food group In further preferred aspects, the final list foods is shorter than 50 food items, and more preferably equal or less than of 40 food items.

[0077] Since the foods ultimately selected for the food intolerance panel will not be specific for a particular gender, a gender-neutral food list was necessary. Since the observed sample was imbalanced by gender (*e.g.*, Controls: 22% female, IBS: 64% female), differences in ELISA signal magnitude strictly due to gender were 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 were compared between IBS and controls using a permutation test on a two-sample t-test with 50,000 resamplings. The Satterthwaite approximation was used for the denominator degrees of freedom to account for lack of homogeneity of variances, and the 2-tailed permuted p-value represented the raw p-value for each food. False Discovery Rates (FDR) among the comparisons, were adjusted by any acceptable statistical procedures (e.g., Benjamini-Hochberg, Family-wise Error Rate (FWER), Per Comparison Error Rate (PCER), etc.).

[0078] 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 were deemed to have significantly higher signal scores among IBS 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.

[0079] Notably, the inventors discovered that even for the same food preparation tested, the ELISA score for at least several food items varied dramatically, and exemplary raw data are provided in **Table 3**. As will 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 stratified the data by gender as described below.

[0080] Statistical Method for Cutpoint Selection for each Food: The determination of what ELISA signal scores would constitute a "positive" response was made by summarizing the distribution of signal scores among the Control subjects. For each food, IBS subjects who had have observed scores greater than or equal to selected quantiles of the Control subject distribution were deemed "positive". To attenuate the influence of any one subject on cutpoint determination, each food-specific and gender-specific dataset was bootstrap resampled 1000 times. Within each bootstrap replicate, the 90th and 95th percentiles of the Control signal scores were determined. Each IBS subject in the bootstrap sample was 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 were computed as the average 90th and 95th percentiles across the 1000 samples. The number of foods for which each IBS subject was rated as "positive" was computed by pooling data across foods. Using such method, the inventors were 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**.

[0081] Typical examples for the gender difference in IgG response in blood with respect to wheat 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 IBS 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 IBS subjects exceeding the 90th and 95th percentile. In the same fashion, **Figures 2A-2D** exemplarily depict the differential response to cocoa, **Figures 3A-3D** exemplarily depict the differential response to rye, and **Figures 4A-4D** exemplarily depict the differential response to black tea. **Figures 5A-5B** show the distribution of IBS 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 were notably distinct.

[0082] It should be noted that nothing in the art have provided any predictable food groups related to IBS 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 IBS patients have been significantly improved.

[0083] Normalization of IgG Response Data: While the raw data of the patient's IgG response results can be use 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 Dungeness crab and IgG specific to egg) can be normalized to the patient's total IgG. The normalized value of the patient's IgG specific to Dungeness crab can be 0.1 and the normalized value of the patient's IgG specific to egg can be 0.3. In this scenario, the relative strength of the patient's response to egg is three times higher compared to Dungeness crab. Then, the patient's sensitivity to egg and Dungeness crab can be indexed as such.

[0084] 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.

[0085] Methodology to determine the subset of IBS patients with food sensitivities that underlie IBS: While it is suspected that food sensitivities plays a substantial role in signs and symptoms of IBS, some IBS patients may not have food sensitivities that underlie IBS. Those patients would not be benefit from dietary intervention to treat signs and symptoms of IBS. To determine the subset of such patients, body fluid samples of IBS patients and non- IBS patients can be tested with ELISA test using test devices with 24 food samples.

[0086] **Table 5** provides exemplary raw data. As should be readily appreciated, data indicates number of positive results out of 24 sample foods based on 90th percentile value. From the raw data shown in Table 5, average and standard deviation of the number of positive foods was computed for IBS and non-IBS patients. Additionally, the number and percentage of patients with zero positive foods was calculated for both IBS and non-IBS. The number and percentage of patients with zero positive foods is about 5 fold lower in the IBS population than in the non-IBS population (6% vs. 38%, respectively). Thus, it can be easily appreciated that the IBS patient having sensitivity to zero positive foods is unlikely to have food sensitivities underlying their signs and symptoms of IBS.

[0087] **Table 6** and **Table 7** show exemplary statistical data summarizing the raw data of two patient populations shown in Table 5. 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 IBS population and the non-IBS population.

[0088] **Table 8** and **Table 9** show another exemplary statistical data summarizing the raw data of two patient populations shown in Table 5. In Tables 8 and 9, the raw data was transformed by logarithmic transformation to improve the data interpretation.

[0089] **Table 10** and **Table 11** show exemplary statistical data of an independent T-test (Table 10, logarithmically transformed data) and a Mann-Whitney test (Table 11) to compare the geometric mean number of positive foods between the IBS and non- IBS samples. The data shown in Table 10 and Table 11 indicates statistically significant differences in the geometric mean of positive number of foods between the IBS population and the non-IBS population. In both statistical tests, it is shown that the number of positive responses with 24 food samples is significantly higher in the IBS population than in the non-IBS population with an average discriminatory p-value of ≤ 0.001. 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**.

[0090] **Table 12** shows exemplary statistical data of a Receiver Operating Characteristic (ROC) curve analysis of data shown in Tables 5-11 to determine the diagnostic power of the test used in Table 5 at discriminating IBS from non- IBS subjects. When a cutoff criterion of more than 2 positive foods is used, the test yields a data with 72.4% sensitivity and 72.2% specificity, with an area under the curve (AUROC) of 0.771. The p-value for the ROC is significant at a p-value of <0.0001. **Figure 7** illustrates the ROC curve corresponding to the statistical data shown in Table 12. Because the statistical difference between the IBS population and the non-IBS population is significant when the test results are cut off to positive number of 2, the number of foods that a patient tests positive could be used as a confirmation of the primary clinical diagnosis IBS, and whether it is likely that food sensitivities underlies on the patient's signs and symptoms of IBS. Therefore, the above test can be used as another 'rule in' test to add to currently available clinical criteria for diagnosis for IBS.

[0091] Method for determining distribution of per-person number of foods declared "positive": To determine the distribution of number of "positive" foods per son and measure the diagnostic performance, the analysis was performed with 24 food items from the Table 1, which shows most positive responses to IBS patients. The 24 food items includes Cocoa, Black Tea, Oat, Cabbage, Cow's Milk, Yellow Onion, Honey, Rye, Corn, Yeast White Wheat, Soybean, Egg,

Tuna, Lemon, Pineapple, Cucumber, Orange, Halibut, Walnut, Grapefruit, Cane Sugar, Chicken, US Gulf White Shrimp. To attenuate the influence of any one subject on this analysis, each food-specific and gender-specific dataset was bootstrap resampled 1000 times. Then, for each food item in the bootstrap sample, sex-specific cutpoint was determined using the 90th and 95th percentiles of the control population. Once the sex-specific cutpoints were determined, the sex-specific cutpoints was compared with the observed ELISA signal scores for both control and IBS subjects. In this comparison, if the observed signal is equal or more than the cutpoint value, then it is determined "positive" food, and if the observed signal is less than the cutpoint value, then it is determined "negative" food.

[0092] Once all food items were determined either positive or negative, the results of the 48(24 foods x 2 cutpoints) calls for each subject were saved within each bootstrap replicate. Then, for each subject, 24 calls were summed using 90th percentile as cutpoint to get "Number of Positive Foods(90th)," and the rest of 24 calls were 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)" were 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 pretended 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 historgrams were generated for both "Number of Positive Foods(90th)" and "Number of Positive Foods(95th)" for both genders and for both IBS subjects and control subjects using programs "a_pos_foods.sas, a_pos_foods_by_dx.sas".

[0093] Method for measuring diagnostic performance: To measure diagnostic performance for each food items for each subject, we used 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 is called "Has IBS." If a subject has less than one

"Number of Positive Foods (90th)", then the subject is called "Does Not Have IBS." 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 were 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.

[0094] To increase the accuracy, the analysis above was repeated by incrementing cutpoint from 2 up to 24, and repeated for each of the 1000 bootstrap replicates. Then the performance metrics across the 1000 bootstrap replicates were 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 Table 13 (female) and Table 14 (male).

[0095] Of course, it should be appreciated that certain variations in the food preparations may be made without altering the inventive subject matter presented herein. For example, where the food item was yellow onion, that item should be understood to also include other onion varieties that were demonstrated to have equivalent activity in the tests. Indeed, the inventors have noted that for each tested food preparation, certain other related food preparations also tested in the same or equivalent manner (data not shown). Thus, it should be appreciated that each tested and claimed food preparation will have equivalent related preparations with demonstrated equal or equivalent reactions in the test.

[0096] It should be apparent to those skilled in the art that many more modifications besides those already described are possible without departing from the inventive concepts herein. The inventive subject matter, therefore, is not to be restricted except in the spirit of the appended claims. Moreover, in interpreting both the specification and the claims, all terms should be interpreted in the broadest possible manner consistent with the context. In particular, the terms "comprises" and "comprising" should be interpreted as referring to elements, components, or steps in a non-exclusive manner, indicating that the referenced elements, components, or steps may be present, or utilized, or combined with other elements, components, or steps that are not

expressly referenced. Where the specification claims refers to at least one of something selected from the group consisting of A, B, C .... and N, the text should be interpreted as requiring only one element from the group, not A plus N, or B plus N, etc.

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 (S. cerevisiae)
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	Carrageneenan
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	
Cola nut	Millet	Tobacco	
Corn	Mung bean	Tomato	
Cottage cheese	Mushroom	Trout	
Cow's milk	Mustard seed	Tuna	
Crab	Oat	Turkey	
Cucumber	Olive	Vanilla	

Table 1

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

Rank	*Food*	*Raw p-value*	*FDR Multiplicity-adj p-value*
1	Cocoa	0.0000	0.0000
2	Black Tea	0.0001	0.0020
3	Oat	0.0002	0.0032
4	Cabbage	0.0004	0.0032
5	Cows Milk	0.0004	0.0032
6	Yellow Onion	0.0006	0.0041
7	Honey	0.0008	0.0044
8	Rye	0.0010	0.0044
9	Corn	0.0010	0.0044
10	Yeast	0.0012	0.0047
11	White Wheat	0.0015	0.0055
12	Soybean	0.0020	0.0066
13	Egg	0.0022	0.0069
14	Tuna	0.0029	0.0084
15	Lemon	0.0036	0.0096
16	Pineapple	0.0045	0.0103
17	Cucumber	0.0046	0.0103
18	Orange	0.0046	0.0103
19	Halibut	0.0057	0.0120
20	Walnut	0.0062	0.0125
21	Grapefruit	0.0085	0.0161
22	Cane Sugar	0.0174	0.0316
23	Chicken	0.0184	0.0321
24	Blueberry	0.0218	0.0363
25	US Gulf White Shrimp	0.0230	0.0367
26	Dungeness Crab	0.0346	0.0533
27	Barley	0.0440	0.0652
28	Strawberry	0.0555	0.0793
29	Pork	0.0976	0.1312
30	Brown Rice	0.0984	0.1312

Rank	*Food*	*Raw p-value*	*FDR Multiplicity-adj p-value*
31	Beef	0.1067	0.1377
32	Cashew	0.1375	0.1718
33	Codfish	0.1741	0.2111
34	Potato	0.2443	0.2825
35	White Sesame	0.2472	0.2825
36	Broccoli	0.2589	0.2876
37	Almond	0.3174	0.3432
38	Turkey	0.4028	0.4240
39	Scallop	0.7149	0.7332
40	Salmon	0.9352	0.9352

Table 2

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

				ELISA Score			
Sex	*Food*	*Diagnosis*	*N*	*Mean*	*SD*	*Min*	*Max*
F	Almond	Control	26	0.227	0.124	0.100	0.565
		IBS	46	0.358	0.474	0.078	3.065
		Diff (1-2)	_	-0.132	0.387	_	_
	Barley	Control	26	0.255	0.144	0.093	0.725
		IBS	46	0.450	0.361	0.118	1.676
		Diff (1-2)	_	-0.195	0.302	_	_
	Beef	Control	26	0.170	0.081	0.086	0.439
		IBS	45	0.190	0.090	0.072	0.467
		Diff (1-2)	_	-0.020	0.087	_	_
	Black Tea	Control	26	0.179	0.075	0.069	0.307
		IBS	46	0.272	0.086	0.115	0.508
		Diff (1-2)	_	-0.093	0.083	_	_
	Blueberry	Control	26	0.425	0.190	0.233	1.061
		IBS	46	0.480	0.143	0.239	0.867
		Diff (1-2)	_	-0.055	0.162	_	_
	Broccoli	Control	26	0.220	0.127	0.118	0.620
		IBS	46	0.280	0.174	0.106	1.042
		Diff (1-2)	_	-0.059	0.159	_	_
	Brown Rice	Control	26	0.236	0.118	0.082	0.449
		IBS	46	0.253	0.136	0.101	0.690
		Diff (1-2)	_	-0.018	0.130	_	_
	Cabbage	Control	26	0.285	0.161	0.086	0.642
		IBS	46	0.432	0.173	0.132	1.033
		Diff (1-2)	_	-0.147	0.169	_	_
	Cane Sugar	Control	26	0.377	0.272	0.070	0.835
		IBS	46	0.521	0.234	0.107	0.975
		Diff (1-2)	_	-0.143	0.248	_	_
	Cashew	Control	26	0.249	0.277	0.080	1.528
		IBS	46	0.286	0.215	0.081	1.183
		Diff (1-2)	_	-0.037	0.239	_	_
	Chicken	Control	25	0.123	0.064	0.056	0.314
		IBS	46	0.156	0.097	0.062	0.579
		Diff (1-2)	_	-0.033	0.087	_	_
	Cocoa	Control	26	0.345	0.151	0.142	0.656

				ELISA Score			
Sex	*Food*	*Diagnosis*	*N*	*Mean*	*SD*	*Min*	*Max*
		IBS	46	0.587	0.349	0.208	2.030
		Diff (1-2)	_	-0.242	0.294	_	_
	Codfish	Control	26	0.202	0.081	0.083	0.392
		IBS	46	0.182	0.180	0.048	1.069
		Diff (1-2)	_	0.020	0.152	_	_
	Corn	Control	26	0.416	0.221	0.114	0.923
		IBS	47	0.562	0.333	0.146	1.686
		Diff (1-2)	_	-0.146	0.298	_	_
	Cow Milk	Control	26	0.676	0.538	0.074	2.212
		IBS	46	1.191	0.845	0.134	3.035
		Diff (1-2)	_	-0.515	0.750	_	_
	Cucumber	Control	26	0.168	0.083	0.079	0.317
		IBS	46	0.211	0.071	0.088	0.460
		Diff (1-2)	_	-0.043	0.075	_	_
	Dungeness Crab	Control	26	0.321	0.187	0.107	0.757
		IBS	46	0.390	0.226	0.082	1.285
		Diff (1-2)	_	-0.068	0.213	_	_
	Egg	Control	26	0.336	0.296	0.060	1.119
		IBS	46	0.903	0.858	0.115	3.274
		Diff (1-2)	_	-0.567	0.710	_	_
	Grapefruit	Control	25	0.154	0.088	0.069	0.458
		IBS	46	0.203	0.148	0.085	1.014
		Diff (1-2)	_	-0.049	0.130	_	_
	Halibut	Control	26	0.246	0.125	0.093	0.544
		IBS	46	0.348	0.198	0.103	0.941
		Diff (1-2)	_	-0.101	0.175	_	_
	Honey	Control	26	0.584	0.306	0.152	1.463
		IBS	46	0.805	0.364	0.200	1.638
		Diff (1-2)	_	-0.220	0.344	_	_
	Lemon	Control	26	0.282	0.157	0.080	0.635
		IBS	45	0.444	0.297	0.120	1.567
		Diff (1-2)	_	-0.162	0.255	_	_
	Oat	Control	26	0.282	0.253	0.071	1.116
		IBS	47	0.693	0.680	0.086	2.934
		Diff (1-2)	_	-0.411	0.567	_	_
	Orange	Control	26	0.222	0.119	0.080	0.549
		IBS	46	0.313	0.166	0.106	1.044
		Diff (1-2)	_	-0.091	0.151	_	_

				ELISA Score			
Sex	*Food*	*Diagnosis*	*N*	*Mean*	*SD*	*Min*	*Max*
	Pineapple	Control	26	0.924	0.853	0.098	3.467
		IBS	47	1.624	1.015	0.206	3.721
		Diff (1-2)	_	-0.700	0.961	_	_
	Pork	Control	26	0.392	0.266	0.107	1.285
		IBS	46	0.466	0.283	0.064	1.248
		Diff (1-2)	_	-0.074	0.277	_	_
	Potato	Control	26	0.209	0.104	0.075	0.441
		IBS	46	0.266	0.089	0.087	0.474
		Diff (1-2)	_	-0.057	0.095	_	_
	Rye	Control	26	0.138	0.054	0.073	0.299
		IBS	47	0.249	0.193	0.080	1.248
		Diff (1-2)	_	-0.111	0.159	_	_
	Salmon	Control	26	0.230	0.140	0.102	0.684
		IBS	46	0.196	0.100	0.058	0.444
		Diff (1-2)	_	0.034	0.116	_	_
	Scallop	Control	25	0.283	0.205	0.086	1.025
		IBS	46	0.277	0.173	0.102	0.860
		Diff (1-2)	_	0.005	0.185	_	_
	Soybean	Control	26	0.508	0.228	0.210	0.849
		IBS	46	0.658	0.230	0.252	1.101
		Diff (1-2)	_	-0.150	0.229	_	_
	Strawberry	Control	26	0.145	0.059	0.060	0.259
		IBS	46	0.176	0.056	0.075	0.370
		Diff (1-2)	_	-0.031	0.057	_	_
	Tuna	Control	26	0.588	0.297	0.202	1.375
		IBS	46	0.859	0.431	0.181	1.875
		Diff (1-2)	_	-0.271	0.388	_	_
	Turkey	Control	26	0.248	0.110	0.072	0.583
		IBS	46	0.267	0.110	0.112	0.691
		Diff (1-2)	_	-0.019	0.110	_	_
	US Gulf White Shrimp	Control	26	0.563	0.325	0.188	1.693
		IBS	45	0.834	0.459	0.210	2.135
		Diff (1-2)	_	-0.271	0.415	_	_
	Walnut	Control	26	0.194	0.070	0.096	0.315
		IBS	46	0.273	0.123	0.135	0.944
		Diff (1-2)	_	-0.079	0.107	_	_
	White Sesame	Control	26	0.705	0.524	0.190	2.663
		IBS	46	0.734	0.393	0.126	1.967

				ELISA Score			
Sex	*Food*	*Diagnosis*	*N*	*Mean*	*SD*	*Min*	*Max*
		Diff (1-2)	_	-0.029	0.444	_	_
	White Wheat	Control	26	0.228	0.125	0.106	0.576
		IBS	47	0.427	0.355	0.096	1.872
		Diff (1-2)	_	-0.198	0.295	_	_
	Yeast	Control	25	0.963	0.624	0.157	2.364
		IBS	46	1.291	0.844	0.247	3.438
		Diff (1-2)	_	-0.327	0.775	_	_
	Yellow Onion	Control	26	0.570	0.442	0.105	1.497
		IBS	46	0.911	0.439	0.129	1.791
		Diff (1-2)	_	-0.341	0.440	_	_
M	Almond	Control	89	0.335	0.391	0.077	2.342
		IBS	29	0.361	0.341	0.069	1.442
		Diff (1-2)	_	-0.026	0.379	_	_
	Barley	Control	89	0.419	0.430	0.110	2.242
		IBS	29	0.525	0.499	0.092	1.935
		Diff (1-2)	_	-0.106	0.448	_	_
	Beef	Control	73	0.184	0.127	0.081	0.979
		IBS	27	0.222	0.102	0.078	0.555
		Diff (1-2)	_	-0.038	0.121	_	_
	Black Tea	Control	89	0.209	0.088	0.080	0.522
		IBS	29	0.242	0.076	0.118	0.395
		Diff (1-2)	_	-0.033	0.086	_	_
	Blueberry	Control	89	0.425	0.228	0.216	2.031
		IBS	29	0.517	0.207	0.278	1.424
		Diff (1-2)	_	-0.092	0.223	_	_
	Broccoli	Control	89	0.242	0.204	0.096	1.747
		IBS	29	0.263	0.194	0.133	1.116
		Diff (1-2)	_	-0.021	0.201	_	_
	Brown Rice	Control	89	0.237	0.123	0.081	0.714
		IBS	29	0.288	0.122	0.090	0.554
		Diff (1-2)	_	-0.051	0.122	_	_
	Cabbage	Control	89	0.322	0.173	0.089	0.873
		IBS	29	0.409	0.192	0.105	0.878
		Diff (1-2)	_	-0.087	0.178	_	_
	Cane Sugar	Control	89	0.375	0.255	0.076	1.097
		IBS	29	0.446	0.230	0.098	0.804
		Diff (1-2)	_	-0.071	0.249	_	_
	Cashew	Control	89	0.230	0.157	0.078	1.152

			ELISA Score				
Sex	*Food*	*Diagnosis*	*N*	*Mean*	*SD*	*Min*	*Max*
		IBS	29	0.291	0.167	0.072	0.686
		Diff (1-2)	_	-0.062	0.160	_	_
	Chicken	Control	88	0.134	0.069	0.055	0.339
		IBS	29	0.172	0.087	0.055	0.385
		Diff (1-2)	_	-0.037	0.074	_	_
	Cocoa	Control	89	0.399	0.198	0.158	1.386
		IBS	29	0.623	0.294	0.209	1.310
		Diff (1-2)	_	-0.224	0.225	_	_
	Codfish	Control	89	0.198	0.191	0.072	1.759
		IBS	29	0.146	0.053	0.071	0.325
		Diff (1-2)	_	0.053	0.169	_	_
	Corn	Control	89	0.414	0.240	0.137	1.185
		IBS	29	0.618	0.330	0.183	1.310
		Diff (1-2)	_	-0.204	0.265	_	_
	Cow Milk	Control	89	0.805	0.621	0.095	2.416
		IBS	29	1.309	0.946	0.128	3.525
		Diff (1-2)	_	-0.504	0.713	_	_
	Cucumber	Control	89	0.167	0.069	0.070	0.343
		IBS	29	0.197	0.070	0.079	0.322
		Diff (1-2)	_	-0.030	0.069	_	_
	Dungeness Crab	Control	89	0.342	0.175	0.104	1.047
		IBS	29	0.431	0.249	0.082	0.992
		Diff (1-2)	_	-0.089	0.195	_	_
	Egg	Control	89	0.407	0.385	0.071	1.799
		IBS	29	0.609	0.681	0.094	2.589
		Diff (1-2)	_	-0.202	0.474	_	_
	Grapefruit	Control	88	0.182	0.100	0.063	0.613
		IBS	29	0.260	0.185	0.058	0.658
		Diff (1-2)	_	-0.079	0.126	_	_
	Halibut	Control	89	0.284	0.153	0.105	0.751
		IBS	29	0.379	0.267	0.112	1.477
		Diff (1-2)	_	-0.095	0.187	_	_
	Honey	Control	89	0.644	0.358	0.210	2.059
		IBS	29	0.911	0.557	0.227	2.635
		Diff (1-2)	_	-0.267	0.415	_	_
	Lemon	Control	89	0.358	0.239	0.091	1.254
		IBS	29	0.503	0.375	0.082	1.709
		Diff (1-2)	_	-0.146	0.278	_	_

				ELISA Score			
Sex	*Food*	*Diagnosis*	*N*	*Mean*	*SD*	*Min*	*Max*
	Oat	Control	89	0.384	0.378	0.066	1.972
		IBS	29	0.745	0.666	0.101	2.614
		Diff (1-2)	_	-0.361	0.464	_	_
	Orange	Control	89	0.265	0.152	0.079	0.831
		IBS	29	0.358	0.252	0.076	1.126
		Diff (1-2)	_	-0.093	0.181	_	_
	Pineapple	Control	89	1.053	0.915	0.123	3.617
		IBS	29	1.354	0.883	0.287	3.126
		Diff (1-2)	_	-0.301	0.908	_	_
	Pork	Control	89	0.388	0.219	0.110	1.216
		IBS	29	0.462	0.244	0.126	1.057
		Diff (1-2)	_	-0.075	0.225	_	_
	Potato	Control	89	0.249	0.170	0.069	1.408
		IBS	29	0.253	0.125	0.100	0.578
		Diff (1-2)	_	-0.004	0.161	_	_
	Rye	Control	89	0.178	0.100	0.079	0.610
		IBS	29	0.237	0.129	0.088	0.651
		Diff (1-2)	_	-0.060	0.108	_	_
	Salmon	Control	89	0.206	0.132	0.073	0.897
		IBS	29	0.229	0.185	0.114	1.065
		Diff (1-2)	_	-0.022	0.147	_	_
	Scallop	Control	88	0.294	0.187	0.095	0.973
		IBS	29	0.320	0.222	0.067	1.161
		Diff (1-2)	_	-0.026	0.196	_	_
	Soybean	Control	89	0.523	0.292	0.175	1.653
		IBS	29	0.715	0.490	0.187	2.583
		Diff (1-2)	_	-0.191	0.351	_	_
	Strawberry	Control	89	0.151	0.058	0.062	0.311
		IBS	29	0.161	0.053	0.077	0.252
		Diff (1-2)	_	-0.010	0.057	_	_
	Tuna	Control	89	0.725	0.369	0.183	1.752
		IBS	29	0.899	0.459	0.213	1.952
		Diff (1-2)	_	-0.174	0.393	_	_
	Turkey	Control	89	0.252	0.109	0.100	0.711
		IBS	29	0.265	0.099	0.109	0.510
		Diff (1-2)	_	-0.013	0.107	_	_
	US Gulf White Shrimp	Control	89	0.709	0.366	0.226	1.982
		IBS	29	0.797	0.422	0.222	1.550

				ELISA Score			
Sex	*Food*	*Diagnosis*	*N*	*Mean*	*SD*	*Min*	*Max*
		Diff (1-2)	_	-0.089	0.380	_	_
	Walnut	Control	89	0.216	0.110	0.095	0.839
		IBS	29	0.244	0.085	0.101	0.428
		Diff (1-2)	_	-0.029	0.104	_	_
	White Sesame	Control	89	0.620	0.375	0.112	1.855
		IBS	29	0.744	0.412	0.153	1.970
		Diff (1-2)	_	-0.124	0.385	_	_
	White Wheat	Control	89	0.290	0.250	0.095	1.681
		IBS	29	0.463	0.400	0.130	1.561
		Diff (1-2)	_	-0.173	0.293	_	_
	Yeast	Control	88	0.940	0.624	0.172	3.157
		IBS	29	1.481	0.788	0.416	2.892
		Diff (1-2)	_	-0.541	0.668	_	_
	Yellow Onion	Control	89	0.558	0.418	0.094	1.672
		IBS	29	0.760	0.417	0.098	1.507
		Diff (1-2)	_	-0.203	0.418	_	_

Table 3

Upper Quantiles of ELISA Signal Scores among Control Subjects as Candidates for Test Cutpoints in Determining "Positive" or "Negative"

Top 24 Foods Ranked by Descending order of Discriminatory Ability using Permutation Test

			Cutpoint	
Food Ranking	*Food*	*Sex*	*90th percentile*	*95th percentile*
1	Cocoa	F	0.544	0.587
		M	0.581	0.721
2	BlackTea	F	0.281	0.296
		M	0.337	0.379
3	Oat	F	0.647	0.813
		M	0.880	1.187
4	Cabbage	F	0.507	0.573
		M	0.542	0.644
5	CowsMilk	F	1.373	1.611
		M	1.872	2.133
6	YellowOnion	F	1.109	1.214
		M	1.142	1.328
7	Honey	F	1.022	1.189
		M	1.111	1.422
8	Rye	F	0.209	0.237
		M	0.313	0.400
9	Corn	F	0.755	0.835
		M	0.774	0.904
10	Yeast	F	1.811	2.014
		M	1.883	2.102
11	WhiteWheat	F	0.409	0.477
		M	0.492	0.704
12	Soybean	F	0.778	0.806
		M	0.891	1.076
13	Egg	F	0.794	0.932
		M	0.988	1.270
14	Tuna	F	1.054	1.208
		M	1.276	1.472
15	Lemon	F	0.533	0.585
		M	0.705	0.885
16	Pineapple	F	2.139	2.646
		M	2.651	3.030
17	Cucumber	F	0.289	0.305

			Cutpoint	
Food Ranking	*Food*	*Sex*	*90th percentile*	*95th percentile*
		M	0.265	0.301
18	Orange	F	0.389	0.456
		M	0.483	0.589
19	Halibut	F	0.451	0.497
		M	0.506	0.600
20	Walnut	F	0.288	0.297
		M	0.319	0.387
21	Grapefruit	F	0.267	0.333
		M	0.328	0.380
22	CaneSugar	F	0.739	0.775
		M	0.746	0.834
23	Chicken	F	0.214	0.249
		M	0.250	0.275
24	Blueberry	F	0.676	0.807
		M	0.630	0.787

Table 4

IBS Population	
Sample ID	# of Positive Results based on 90th Percentile
IBS-3	5
IBS-5	0
IBS-11	1
IBS-12	9
IBS-14	0
IBS-18	0
IBS-19	1
IBS-23	11
IBS-24	1
IBS-30	9
IBS-33	8
IBS-35	7
IBS-38	6
IBS-40	3
IBS-42	6
IBS-43	2
BRH-698596	4
BHR-698597	9
BRH-698598	4
BRH-698599	18
BRH-698600	3
BRH-698621	12
BRH-698622	7
BRH-698623	5
BRH-698624	1
BRH-698625	9
BRH-774496	17
BRH-763476	0
BRH-768030	0
IBS-2	1
IBS-4	1
IBS-6	1
IBS-7	9
IBS-8	9
IBS-9	1
IBS-10	14
IBS-13	19
IBS-15	9
IBS-16	1
IBS-17	9
IBS-20	16
IBS-21	23
IBS-22	20
IBS-25	2

Non-IBS Population	
Sample ID	# of Positive Results based on 90th
BRH-768035	0
BRH-768034	1
BRH-768033	1
BRH-768032	1
BRH-768031	1
BRH-763484	0
BRH-768029	10
BRH-768028	8
BRH-763510	4
BRH-768036	0
BRH-768037	1
BRH-768038	1
BRH-768039	0
BRH-768040	0
BRH-768041	1
BRH-768042	1
BRH-768043	5
BRH-768044	3
BRH-768055	1
BRH-768054	1
BRH-764371	0
BRH-768056	2
BRH-764372	2
BRH-764377	5
BRH-764378	2
BRH-763531	1
BRH-764329	0
BRH-763533	0
BRH-763529	0
BRH-763553	12
BRH-763528	0
BRH-763509	0
BRH-763517	2
BRH-763500	0
BRH-764332	0
BRH-764338	1
BRH-764337	3
BRH-764341	1
BRH-764340	1
BRH-764342	0
BRH-764347	1
BRH-764343	5
BRH-774498	1
BRH-768027	12

IBS Population	
IBS-26	16
IBS-27	8
IBS-28	10
IBS-29	8
IBS-31	4
IBS-32	2
IBS-34	0
IBS-36	3
IBS-37	5
IBS-39	19
IBS-41	5
IBS-44	5
BRH-698601	10
BRH-698602	3
BRH-698603	13
BRH-698604	10
BRH-698605	8
BRH-698606	4
BRH-698607	2
BRH-698608	4
BRH-698609	1
BRH-698610	1
BRH-698611	3
BRH-698612	3
BRH-698613	12
BRH-698614	11
BRH-698615	4
BRH-698616	5
BRH-698617	11
BRH-698618	6
BRH-698619	9
BRH-698620	6

No of observation	76
Average # of	6.63
SD	5.54

Non-IBS Population	
BRH-768000	1
BRH-774499	12
BRH-774502	4
BRH-774504	8
BRH-767999	0
BRH-764350	0
BRH-763534	0
BRH-763506	0
BRH-774495	2
BRH-764353	0
BRH-764355	0
BRH-764356	0
BRH-764361	1
BRH-764368	1
BRH-768053	2
BRH-764370	1
BRH-764346	0
BRH-768052	0
BRH-764335	10
BRH-774510	2
BRH-774511	0
BRH-768001	2
BRH-768007	0
BRH-768008	3
BRH-767995	0
BRH-767992	3
BRH-767991	0
BRH-764344	2
BRH-764386	0
BRH-763513	7
BRH-763530	5
BRH-764345	1
BRH-764336	0
BRH-764352	4
BRH-764360	0
BRH-764339	4
BRH-763527	17
BRH-764334	1
BRH-764349	0
BRH-764380	0
BRH-764366	0
BRH-763526	19
BRH-764351	2
BRH-763503	3
BRH-764365	3
BRH-764381	0
BRH-763523	0
BRH-774500	3

Non-IBS Population	
BRH-774501	1
BRH-774505	6
BRH-774503	2
BRH-774494	0
BRH-774493	0
BRH-774492	1
BRH-774491	0
BRH-764357	2
BRH-764358	0
BRH-768045	0
BRH-768047	1
BRH-768048	8
BRH-768049	12
BRH-768051	0
BRH-768050	5
BRH-774506	11
BRH-774507	0
BRH-774509	0
BRH-774512	0
BRH-774513	4
BRH-774514	1
BRH-764359	3
BRH-763524	1

No of observation	115
Average # of	2.37
SD	3.67

Table 5

Variable	IBS IBS

Sample size	76
Lowest value	0.0000
Highest value	23.0000
Arithmetic mean	6.6316
95% CI for the mean	5.3651 to 7.8980
Median	5.0000
95% CI for the median	4.0000 to 8.0000
Variance	30.7158
Standard deviation	5.5422
Relative standard deviation	0.8357 (83.57%)
Standard error of the mean	0.6357
Coefficient of Skewness	0.9423 (P=0.0017)
Coefficient of Kurtosis	0.3684 (P=0.4053)
D'Agostino-Pearson test for Normal distribution	reject Normality (P=0.0051)

Percentiles		95% Confidence Interval
2.5	0.0000	
5	0.0000	0.0000 to 1.0000
10	1.0000	0.0000 to 1.0000
25	2.0000	1.0000 to 3.1043
75	9.0000	8.8957 to 11.6255
90	15.8000	11.0000 to 19.0000
95	18.7000	15.2303 to 22.7004
97.5	19.6000	

Table 6

Variable	Non_IBS Non-IBS
Sample size	115
Lowest value	0.0000
Highest value	19.0000
Arithmetic mean	2.3652
95% CI for the mean	1.6879 to 3.0426
Median	1.0000
95% CI for the median	1.0000 to 1.0000
Variance	13.4444
Standard deviation	3.6667
Relative standard deviation	1.5502 (155.02%)
Standard error of the mean	0.3419
Coefficient of Skewness	2.3537 (P<0.0001)
Coefficient of Kurtosis	5.8546 (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 0.0000
25	0.0000	0.0000 to 0.0000
75	3.0000	2.0000 to 4.0000
90	8.0000	5.0000 to 11.8759
95	11.7500	8.0000 to 16.1360
97.5	12.0000	

Table 7

Variable	IBS_1 IBS 1

Back-transformed after logarithmic transformation.

Sample size	76
Lowest value	0.1000
Highest value	23.0000
Geometric mean	3.7394
95% CI for the mean	2.7247 to 5.1321
Median	5.0000
95% CI for the median	4.0000 to 8.0000
Coefficient of Skewness	-1.3159 (P=0.0001)
Coefficient of Kurtosis	1.3551 (P=0.0481)
D'Agostino-Pearson test for Normal distribution	reject Normality (P<0.0001)

Percentiles		95% Confidence Interval
2.5	0.1000	
5	0.1000	0.1000 to 1.0000
10	1.0000	0.1000 to 1.0000
25	2.0000	1.0000 to 3.0914
75	9.0000	8.8901 to 11.6153
90	15.7878	11.0000 to 19.0000
95	18.6943	15.1985 to 22.6812
97.5	19.5938	

Table 8

Variable	non_IBS_1 non-IBS 1

Back-transformed after logarithmic transformation.

Sample size	115
Lowest value	0.1000
Highest value	19.0000
Geometric mean	0.7278
95% CI for the mean	0.5297 to 1.0001
Median	1.0000
95% CI for the median	1.0000 to 1.0000
Coefficient of Skewness	0.04343 (P=0.8428)
Coefficient of Kurtosis	-1.4006 (P<0.0001)
D'Agostino-Pearson test for Normal distribution	reject Normality (P<0.0001)

Percentiles		95% Confidence Interval
2.5	0.1000	
5	0.1000	0.1000 to 0.1000
10	0.1000	0.1000 to 0.1000
25	0.1000	0.1000 to 0.1000
75	3.0000	2.0000 to 4.0000
90	8.0000	5.0000 to 11.8711
95	11.7418	8.0000 to 16.0070
97.5	12.0000	

Table 9

Sample 1		
Variable	IBS_1 IBS 1	
Sample 2		
Variable	non_IBS_1 non-IBS 1	
Back-transformed after logarithmic transformation.		
	Sample 1	Sample 2
Sample size	76	115
Geometric mean	3.7394	0.7278
95% CI for the mean	2.7247 to 5.1321	0.5297 to 1.0001
Variance of Logs	0.3620	0.5582
F-test for equal variances		P = 0.045
T-test (assuming equal variances)		
Difference on Log-transformed scale		
Difference		-0.7108
Standard Error		0.1025
95% CI of difference		-0.9129 to -0.5087
Test statistic t		-6.937
Degrees of Freedom (DF)		189
Two-tailed probability		P < 0.0001
Back-transformed results		
Ratio of geometric means		0.1946
95% CI of ratio		0.1222 to 0.3100

Table 10

Sample 1	
Variable	IBS_1 IBS 1
Sample 2	
Variable	non_IBS_1 non-IBS 1

	Sample 1	Sample 2
Sample size	76	115
Lowest value	0.1000	0.1000
Highest value	23.0000	19.0000
Median	5.0000	1.0000
95% CI for the median	4.0000 to 8.0000	1.0000 to 1.0000
Interquartile range	2.0000 to 9.0000	0.1000 to 3.0000

Mann-Whitney test (independent samples)

Average rank of first group	127.1382
Average rank of second group	75.4217
Mann-Whitney U	2003.50
Test statistic Z (corrected for ties)	6.410
Two-tailed probability	P < 0.0001

Table 11

Variable	IBS_Test IBS Test
Classification variable	Diag Diag

Sample size		191
Positive group :	Diag = 1	76
Negative group :	Diag = 0	115

Disease prevalence (%)	unknown

Area under the ROC curve (AUC)

Area under the ROC curve (AUC)	0.771
Standard Error[a]	0.0346
95% Confidence interval[b]	0.705 to 0.828
z statistic	7.829
Significance level P (Area=0.5)	<0.0001

[a] DeLong et al., 1988
[b] Binomial exact

Youden index

Youden index J	0.4454
95% Confidence interval[a]	0.2976 to 0.5542
Associated criterion	>2
95% Confidence interval[a]	0 to 2

[a] BC_a bootstrap interval (1000 iterations).

Summary Table

Estimated specificity at fixed sensitivity			
Sensitivity	Specificity	95% CI[a]	Criterion
80.00	57.90	43.98 to 74.43	>0.8364
90.00	41.68	30.23 to 52.71	>0.1455
95.00	38.26	27.83 to 46.09	>0
97.50	38.26	27.83 to 46.09	>0
Estimated sensitivity at fixed specificity			
Specificity	Sensitivity	95% CI[a]	Criterion
80.00	62.89	47.37 to 76.32	>3.2
90.00	39.91	15.58 to 59.59	>7.1667
95.00	15.62	5.83 to 32.66	>11.0625
97.50	13.73	3.95 to 29.91	>11.7812

[a] BC_a bootstrap interval (1000 iterations).

Criterion values and coordinates of the ROC curve [Hide]

Criterion	Sensitivity	95% CI	Specificity	95% CI	+LR	95% CI	-LR	95% CI
≥0	100.00	95.3 - 100.0	0.00	0.0 - 3.2	1.00	1.0 - 1.0		
>0	92.11	83.6 - 97.0	38.26	29.4 - 47.8	1.49	1.3 - 1.7	0.21	0.09 - 0.5
>1	77.63	66.6 - 86.4	61.74	52.2 - 70.6	2.03	1.6 - 2.6	0.36	0.2 - 0.6
>2	72.37	60.9 - 82.0	72.17	63.0 - 80.1	2.60	1.9 - 3.6	0.38	0.3 - 0.6
>3	64.47	52.7 - 75.1	79.13	70.6 - 86.1	3.09	2.1 - 4.6	0.45	0.3 - 0.6
>4	56.58	44.7 - 67.9	83.48	75.4 - 89.7	3.42	2.2 - 5.4	0.52	0.4 - 0.7
>5	48.68	37.0 - 60.4	87.83	80.4 - 93.2	4.00	2.3 - 6.9	0.58	0.5 - 0.7
>6	43.42	32.1 - 55.3	88.70	81.4 - 93.8	3.84	2.2 - 6.8	0.64	0.5 - 0.8

Table 12

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

Sex	No. of Positive Foods as Cutoff	Sensitivity	Specificity	Positive Predictive Value	Negative Predictive Value	Overall Percent Agreement
F	1	0.96	0.35	0.73	0.80	0.74
	2	0.82	0.53	0.76	0.64	0.72
	3	0.77	0.62	0.78	0.60	0.71
	4	0.68	0.67	0.79	0.54	0.68
	5	0.63	0.71	0.80	0.50	0.66
	6	0.57	0.76	0.81	0.50	0.64
	7	0.52	0.81	0.83	0.48	0.62
	8	0.46	0.85	0.84	0.46	0.60
	9	0.41	0.88	0.85	0.45	0.57
	10	0.34	0.88	0.85	0.43	0.54
	11	0.28	0.90	0.85	0.42	0.51
	12	0.21	0.94	0.85	0.40	0.48
	13	0.18	0.94	0.86	0.39	0.46
	14	0.15	0.95	0.89	0.39	0.45
	15	0.13	1.00	1.00	0.39	0.44
	16	0.11	1.00	1.00	0.38	0.43
	17	0.10	1.00	1.00	0.38	0.42
	18	0.07	1.00	1.00	0.38	0.41
	19	0.06	1.00	1.00	0.37	0.40
	20	0.04	1.00	1.00	0.37	0.39
	21	0.03	1.00	1.00	0.37	0.38
	22	0.03	1.00	1.00	0.36	0.37
	23	0.00	1.00	1.00	0.36	0.36
	24	0.00	1.00	1.00	0.36	0.36

Table 13

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

Sex	No. of Positive Foods as Cutoff	Sensitivity	Specificity	Positive Predictive Value	Negative Predictive Value	Overall Percent Agreement
M	1	0.81	0.35	0.29	0.85	0.46
	2	0.71	0.57	0.35	0.86	0.61
	3	0.67	0.68	0.41	0.86	0.68
	4	0.62	0.75	0.45	0.86	0.72
	5	0.53	0.80	0.48	0.84	0.74
	6	0.47	0.85	0.50	0.83	0.76
	7	0.39	0.88	0.50	0.82	0.76
	8	0.30	0.90	0.50	0.80	0.75
	9	0.25	0.92	0.50	0.79	0.75
	10	0.18	0.93	0.43	0.78	0.74
	11	0.14	0.94	0.43	0.77	0.74
	12	0.11	0.95	0.40	0.77	0.75
	13	0.10	0.96	0.43	0.76	0.75
	14	0.07	0.97	0.50	0.76	0.75
	15	0.06	0.97	0.50	0.76	0.75
	16	0.06	0.98	0.50	0.76	0.75
	17	0.05	0.98	0.33	0.76	0.75
	18	0.00	0.98	0.00	0.75	0.75
	19	0.00	0.98	0.00	0.75	0.75
	20	0.00	1.00	0.00	0.75	0.75
	21	0.00	1.00	0.00	0.75	0.75
	22	0.00	1.00	0.00	0.75	0.75
	23	0.00	1.00	0.00	0.75	0.75
	24	0.00	1.00		0.75	0.75

Table 14

What is claimed is:

1. A test kit with for testing food intolerance in patients diagnosed with or suspected to have irritable bowel syndrome, comprising:

a plurality of distinct food preparations coupled to individually addressable respective solid carriers;

wherein 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.

2. The test kit of claim 1 wherein the plurality of food preparations includes at least two food preparations prepared from food items of Table 1 or selected from a group consisting of cocoa, tea, oat, cabbage, cow milk, onion, honey, rye, corn, yeast, wheat, soybean, egg, tuna, lemon, pineapple, cucumber, orange, halibut, walnut, grapefruit, cane sugar, chicken, blueberry, and shrimp, and optionally from a group consisting of crab, barley, strawberry, pork, rice, beef, cashew, codfish, potato, white Sesame, broccoli, almond, turkey, scallop, and Salmon.

3. The test kit of claim 1 wherein the plurality of food preparations includes at least four food preparations prepared from food items of Table 1 or selected from a group consisting of cocoa, tea, oat, cabbage, cow milk, onion, honey, rye, corn, yeast, wheat, soybean, egg, tuna, lemon, pineapple, cucumber, orange, halibut, walnut, grapefruit, cane sugar, chicken, blueberry, and shrimp, and optionally from a group consisting of crab, barley, strawberry, pork, rice, beef, cashew, codfish, potato, white Sesame, broccoli, almond, turkey, scallop, and Salmon.

4. The test kit of claim 1 wherein the plurality of food preparations includes at least eight food preparations prepared from food items of Table 1 or selected from a group consisting of cocoa, tea, oat, cabbage, cow milk, onion, honey, rye, corn, yeast, wheat, soybean, egg, tuna, lemon, pineapple, cucumber, orange, halibut, walnut, grapefruit, cane sugar, chicken, blueberry, and shrimp, and optionally from a group consisting of crab, barley, strawberry,

pork, rice, beef, cashew, codfish, potato, white Sesame, broccoli, almond, turkey, scallop, and salmon.

5. The test kit of claim 1 wherein the plurality of food preparations includes at least 12 food preparations prepared from food items of Table 1 or selected from a group consisting of cocoa, tea, oat, cabbage, cow milk, onion, honey, rye, corn, yeast, wheat, soybean, egg, tuna, lemon, pineapple, cucumber, orange, halibut, walnut, grapefruit, cane sugar, chicken, blueberry, and shrimp, and optionally from a group consisting of crab, barley, strawberry, pork, rice, beef, cashew, codfish, potato, white Sesame, broccoli, almond, turkey, scallop, and salmon.

6. The test kit of claim 1 wherein the plurality of distinct food preparations has an average discriminatory p-value of ≤ 0.05 as determined by raw p-value or an average discriminatory p-value of ≤ 0.08 as determined by FDR multiplicity adjusted p-value.

7. The test kit of any one of claims 1-5 wherein the plurality of distinct food preparations has an average discriminatory p-value of ≤ 0.05 as determined by raw p-value or an average discriminatory p-value of ≤ 0.08 as determined by FDR multiplicity adjusted p-value.

8. The test kit of claim 1 wherein the plurality of distinct food preparations has an average discriminatory p-value of ≤ 0.025 as determined by raw p-value or an average discriminatory p-value of ≤ 0.07 as determined by FDR multiplicity adjusted p-value.

9. The test kit of any one of claims 1-5 wherein the plurality of distinct food preparations has an average discriminatory p-value of ≤ 0.025 as determined by raw p-value or an average discriminatory p-value of ≤ 0.07 as determined by FDR multiplicity adjusted p-value.

10. The test kit of claim 1 wherein FDR multiplicity adjusted p-value is adjusted for at least one of age and gender.

11. The test kit of any one of claims 1-8 wherein FDR multiplicity adjusted p-value is adjusted for at least one of age and gender.

12. The test kit of claim 1 wherein FDR multiplicity adjusted p-value is adjusted for age and gender.

13. The test kit of any one of claims 1-8 wherein FDR multiplicity adjusted p-value is adjusted for age and gender.

14. The test kit of claim 1 wherein at least 50% of the plurality of distinct food preparations, when adjusted for a single gender, has 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.

15. The test kit of any one of claims 1-13 wherein at least 50% of the plurality of distinct food preparations, when adjusted for a single gender, has 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.

16. The test kit of claim 1 wherein at least 70% of the plurality of distinct food preparations, when adjusted for a single gender, has 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.

17. The test kit of any one of the claims 1-13 wherein at least 70% of the plurality of distinct food preparations, when adjusted for a single gender, has 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.

18. The test kit of claim 1 wherein all of the plurality of distinct food preparations, when adjusted for a single gender, has 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.

19. The test kit of any one of the claims 1-17 wherein all of the plurality of distinct food preparations, when adjusted for a single gender, has 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.

20. The test kit of claim 1 wherein the plurality of distinct food preparations is crude aqueous extracts.

21. The test kit of any one of the claims 1-19 wherein the plurality of distinct food preparations is crude aqueous extracts.

22. The test kit of claim 1 wherein the plurality of distinct food preparations is processed aqueous extracts.

23. The test kit of any one of the claims 1-21 wherein the plurality of distinct food preparations is processed aqueous extracts.

24. The test kit of claim 1 wherein the solid carrier is a well of a multiwall plate, a bead, an electrical sensor, a chemical sensor, a microchip or an adsorptive film.

25. The test kit of any one of the claims 1-23 wherein the solid carrier is a well of a multiwall plate, a bead, an electrical sensor, a chemical sensor, a microchip or an adsorptive film.

26. A method of testing food intolerance in patients diagnosed with or suspected to have irritable bowel syndrome, comprising:

contacting a food preparation with a bodily fluid of a patient that is diagnosed with or suspected to have irritable bowel syndrome, and wherein the bodily fluid is associated with a gender identification;

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.

27. The method of claim 26 wherein the bodily fluid of the patient is whole blood, plasma, serum, saliva, or a fecal suspension.

28. The method of claim 26 wherein the step of contacting a food preparation is performed with a plurality of distinct food preparations.

29. The method of claim 26 or claim 27 wherein the step of contacting a food preparation is performed with a plurality of distinct food preparations.

30. The method of claim 28 wherein the plurality of distinct food preparations is prepared from food items of Table 1 or selected from a group consisting of cocoa, tea, oat, cabbage, cow milk, onion, honey, rye, corn, yeast, wheat, soybean, egg, tuna, lemon, pineapple, cucumber, orange, halibut, walnut, grapefruit, cane sugar, chicken, blueberry, and shrimp, and optionally from a group consisting of crab, barley, strawberry, pork, rice, beef, cashew, codfish, potato, white Sesame, broccoli, almond, turkey, scallop, and salmon.

31. The method of any of the claims 28-29 wherein the plurality of distinct food preparations is prepared from food items of Table 1 or selected from a group consisting of cocoa, tea, oat, cabbage, cow milk, onion, honey, rye, corn, yeast, wheat, soybean, egg, tuna, lemon, pineapple, cucumber, orange, halibut, walnut, grapefruit, cane sugar, chicken, blueberry, and shrimp, and optionally from a group consisting of crab, barley, strawberry, pork, rice, beef, cashew, codfish, potato, white Sesame, broccoli, almond, turkey, scallop, and salmon.

32. The method of claim 28 wherein the plurality of distinct food preparations has 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.

33. The method of any of the claims 28-29 wherein the plurality of distinct food preparations has 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.

34. The method of claim 28 wherein the plurality of distinct food preparations has an average discriminatory p-value of ≤ 0.05 as determined by raw p-value or an average discriminatory p-value of ≤ 0.08 as determined by FDR multiplicity adjusted p-value.

35. The method of any of the claims 28-29 wherein the plurality of distinct food preparations has an average discriminatory p-value of ≤ 0.05 as determined by raw p-value or an average discriminatory p-value of ≤ 0.08 as determined by FDR multiplicity adjusted p-value.

36. The method of claim 28 wherein the plurality of distinct food preparations has an average discriminatory p-value of ≤ 0.025 as determined by raw p-value or an average discriminatory p-value of ≤ 0.07 as determined by FDR multiplicity adjusted p-value.

37. The method of any of the claims 28-29 wherein the plurality of distinct food preparations has an average discriminatory p-value of ≤ 0.025 as determined by raw p-value or an average discriminatory p-value of ≤ 0.07 as determined by FDR multiplicity adjusted p-value.

38. The method of claim 28 wherein all of the plurality of distinct food preparations has 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.

39. The method of any of the claims 28-29 wherein all of the plurality of distinct food preparations has 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.

40. The method of claim 26 wherein the food preparation is immobilized on a solid surface, optionally in an addressable manner.

41. The method of any of the claims 26-39 wherein the food preparation is immobilized on a solid surface, optionally in an addressable manner.

42. The method of claim 26 wherein the step of measuring IgG bound to the at least one component of the food preparation is performed via an immunoassay test.

43. The method of any of the claims 26-41 wherein the step of measuring IgG bound to the at least one component of the food preparation is performed via immunoassay test.

44. The method of claim 26 wherein the gender-stratified reference value for the food preparation is an at least a 90th percentile value.

45. The method of any of the claims 26-43 wherein the gender-stratified reference value for the food preparation is an at least a 90th percentile value.

46. A method of generating a test for food intolerance in patients diagnosed with or suspected to have irritable bowel syndrome, comprising:

obtaining test results for a plurality of distinct food preparations, wherein the test results are based on bodily fluids of patients diagnosed with or suspected to have irritable bowel syndrome and bodily fluids of a control group not diagnosed with or not suspected to have irritable bowel syndrome;

stratifying the test results by gender for each of the distinct food preparations; and

assigning for a predetermined percentile rank a different cutoff value for male and female patients for each of the distinct food preparations.

47. The method of claim 46 wherein the test result is an ELISA result.

48. The method of claim 46 wherein the plurality of distinct food preparations includes at least two food preparations prepared from food items of Table 1 or selected from a group consisting of cocoa, tea, oat, cabbage, cow milk, onion, honey, rye, corn, yeast, wheat, soybean, egg, tuna, lemon, pineapple, cucumber, orange, halibut, walnut, grapefruit, cane sugar, chicken, blueberry, and shrimp, and optionally from a group consisting of crab, barley, strawberry, pork, rice, beef, cashew, codfish, potato, white Sesame, broccoli, almond, turkey, scallop, and salmon..

49. The method of claim 46 or claim 47 wherein the plurality of distinct food preparations includes at least two food preparations prepared from food items of Table 1 or selected from a group consisting of cocoa, tea, oat, cabbage, cow milk, onion, honey, rye, corn, yeast, wheat, soybean, egg, tuna, lemon, pineapple, cucumber, orange, halibut, walnut, grapefruit, cane sugar, chicken, blueberry, and shrimp, and optionally from a group consisting of crab, barley, strawberry, pork, rice, beef, cashew, codfish, potato, white Sesame, broccoli, almond, turkey, scallop, and salmon..

50. The method of claim 46 wherein the plurality of distinct food preparations includes at least six food preparations prepared from food items of Table 1 or selected from a group consisting of cocoa, tea, oat, cabbage, cow milk, onion, honey, rye, corn, yeast, wheat, soybean, egg, tuna, lemon, pineapple, cucumber, orange, halibut, walnut, grapefruit, cane sugar, chicken, blueberry, and shrimp, and optionally from a group consisting of crab, barley, strawberry, pork, rice, beef, cashew, codfish, potato, white Sesame, broccoli, almond, turkey, scallop, and salmon..

51. The method of any of claim 46 or claim 47 wherein the plurality of distinct food preparations includes at least six food preparations prepared from food items of Table 1 or selected from a group consisting of cocoa, tea, oat, cabbage, cow milk, onion, honey, rye, corn, yeast, wheat, soybean, egg, tuna, lemon, pineapple, cucumber, orange, halibut, walnut, grapefruit, cane sugar, chicken, blueberry, and shrimp, and optionally from a group consisting of crab, barley, strawberry, pork, rice, beef, cashew, codfish, potato, white Sesame, broccoli, almond, turkey, scallop, and salmon..

52. The method of claim 46 wherein the plurality of distinct food preparations includes a food preparation prepared from food items of Table 1 or selected from a group consisting of cocoa, tea, oat, cabbage, cow milk, onion, honey, rye, corn, yeast, wheat, soybean, egg, tuna, lemon, pineapple, cucumber, orange, halibut, walnut, grapefruit, cane sugar, chicken, blueberry, and shrimp, and optionally from a group consisting of crab, barley, strawberry, pork, rice, beef, cashew, codfish, potato, white Sesame, broccoli, almond, turkey, scallop, and salmon..

53. The method of any of claim 46 or 47 wherein the plurality of distinct food preparations includes a food preparation prepared from food items of Table 1 or selected from a group consisting of cocoa, tea, oat, cabbage, cow milk, onion, honey, rye, corn, yeast, wheat, soybean, egg, tuna, lemon, pineapple, cucumber, orange, halibut, walnut, grapefruit, cane sugar, chicken, blueberry, and shrimp, and optionally from a group consisting of crab, barley, strawberry, pork, rice, beef, cashew, codfish, potato, white Sesame, broccoli, almond, turkey, scallop, and salmon.

54. The method of claim 46 wherein the plurality of distinct food preparations has 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. The method of any of claims 46-53 wherein the plurality of distinct food preparations has 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.

56. The method of claim 46 wherein the plurality of different food preparations has an average discriminatory p-value of ≤ 0.05 as determined by raw p-value or an average discriminatory p-value of ≤ 0.08 as determined by FDR multiplicity adjusted p-value.

57. The method of any of claims 46-53 wherein the plurality of different food preparations has an average discriminatory p-value of ≤ 0.05 as determined by raw p-value or an average discriminatory p-value of ≤ 0.08 as determined by FDR multiplicity adjusted p-value.

58. The method of claim 46 wherein the plurality of different food preparations has an average discriminatory p-value of ≤ 0.025 as determined by raw p-value or an average discriminatory p-value of ≤ 0.07 as determined by FDR multiplicity adjusted p-value.

59. The method of any of claims 46-53 wherein the plurality of different food preparations has an average discriminatory p-value of ≤ 0.025 as determined by raw p-value or an average discriminatory p-value of ≤ 0.07 as determined by FDR multiplicity adjusted p-value.

60. The method of claim 46 wherein the bodily fluid of the patient is whole blood, plasma, serum, saliva, or a fecal suspension.

61. The method of any of claims 46-59 wherein the bodily fluid of the patient is whole blood, plasma, serum, saliva, or a fecal suspension.

62. The method of claim 46 wherein the predetermined percentile rank is an at least 90th percentile rank.

63. The method of any of claims 46-61 wherein the predetermined percentile rank is an at least 90th percentile rank.

64. The method of claim 46 wherein the cutoff value for male and female patients has a difference of at least 10% (abs).

65. The method of any of claims 46-63 wherein the cutoff value for male and female patients has a difference of at least 10% (abs).

66. The method of claim 26 or 46, further comprising a step of normalizing the result to the patient's total IgG.

67. The method of any of claims 26-65, further comprising a step of normalizing the result to the patient's total IgG.

68. The method of claim 26 or 46, further comprising a step of normalizing the result to the global mean of the patient's food specific IgG results.

69. The method of any of claims 26-65, further comprising a step of normalizing the result to the global mean of the patient's food specific IgG results.

70. The method of claim 26 or 46, further comprising a step of identifying a subset of patients, wherein the subset of patients' sensitivities to the food preparations underlies IBS by raw p-value or an average discriminatory p-value of ≤ 0.01.

71. The method of any of claims 26-65, further comprising a step of identifying a subset of patients, wherein the subset of patients' sensitivities to the food preparations underlies IBS by raw p-value or an average discriminatory p-value of ≤ 0.01.

72. The method of claim 26 or 46, further comprising a step of determining numbers of the food preparations, wherein the numbers of the food preparations can be used to confirm IBS by raw p-value or an average discriminatory p-value of ≤ 0.01.

73. The method of any of claims 26-65, further comprising a step of determining numbers of the food preparations, wherein the numbers of the food preparations can be used to confirm IBS by raw p-value or an average discriminatory p-value of ≤ 0.01.

74. Use of a plurality of distinct food preparations coupled to individually addressable respective solid carriers in a diagnosis of irritable bowel syndrome, wherein 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.

75. Use of claim 74 wherein the plurality of food preparations includes at least two food preparations prepared from food items of Table 1 or selected from a group consisting of cocoa, tea, oat, cabbage, cow milk, onion, honey, rye, corn, yeast, wheat, soybean, egg, tuna, lemon, pineapple, cucumber, orange, halibut, walnut, grapefruit, cane sugar, chicken, blueberry, and shrimp, and optionally from a group consisting of crab, barley, strawberry, pork, rice, beef, cashew, codfish, potato, white Sesame, broccoli, almond, turkey, scallop, and salmon.

76. Use of claim 74 wherein the plurality of food preparations includes at least four food preparations prepared from food items of Table 1 or selected from a group consisting of cocoa, tea, oat, cabbage, cow milk, onion, honey, rye, corn, yeast, wheat, soybean, egg, tuna, lemon, pineapple, cucumber, orange, halibut, walnut, grapefruit, cane sugar, chicken, blueberry, and shrimp, and optionally from a group consisting of crab, barley, strawberry, pork, rice, beef, cashew, codfish, potato, white Sesame, broccoli, almond, turkey, scallop, and salmon.

77. Use of claim 74 wherein the plurality of food preparations includes at least eight food preparations prepared from food items of Table 1 or selected from a group consisting of cocoa, tea, oat, cabbage, cow milk, onion, honey, rye, corn, yeast, wheat, soybean, egg, tuna, lemon, pineapple, cucumber, orange, halibut, walnut, grapefruit, cane sugar, chicken, blueberry, and shrimp, and optionally from a group consisting of crab, barley, strawberry, pork, rice, beef, cashew, codfish, potato, white Sesame, broccoli, almond, turkey, scallop, and salmon.

78. Use of claim 74 wherein the plurality of food preparations includes at least 12 food preparations prepared from food items of Table 1 or selected from a group consisting of cocoa, tea, oat, cabbage, cow milk, onion, honey, rye, corn, yeast, wheat, soybean, egg, tuna,

lemon, pineapple, cucumber, orange, halibut, walnut, grapefruit, cane sugar, chicken, blueberry, and shrimp, and optionally from a group consisting of crab, barley, strawberry, pork, rice, beef, cashew, codfish, potato, white Sesame, broccoli, almond, turkey, scallop, and salmon.

79. Use of claim 74 wherein the plurality of distinct food preparations has an average discriminatory p-value of ≤ 0.05 as determined by raw p-value or an average discriminatory p-value of ≤ 0.08 as determined by FDR multiplicity adjusted p-value.

80. Use of any one of claims 74-78, wherein the plurality of distinct food preparations has an average discriminatory p-value of ≤ 0.05 as determined by raw p-value or an average discriminatory p-value of ≤ 0.08 as determined by FDR multiplicity adjusted p-value.

81. Use of claim of claim 74 wherein the plurality of distinct food preparations has an average discriminatory p-value of ≤ 0.025 as determined by raw p-value or an average discriminatory p-value of ≤ 0.07 as determined by FDR multiplicity adjusted p-value.

82. Use of any one of claims 74-78 wherein the plurality of distinct food preparations has an average discriminatory p-value of ≤ 0.025 as determined by raw p-value or an average discriminatory p-value of ≤ 0.07 as determined by FDR multiplicity adjusted p-value.

83. Use of claim 74 wherein FDR multiplicity adjusted p-value is adjusted for at least one of age and gender.

84. Use of any one of claims 74-82 wherein FDR multiplicity adjusted p-value is adjusted for at least one of age and gender.

85. Use of claim 74 wherein FDR multiplicity adjusted p-value is adjusted for age and gender.

86. Use of any one of claims 74-82 wherein FDR multiplicity adjusted p-value is adjusted for age and gender.

87. Use of claim 74 wherein at least 50% of the plurality of distinct food preparations, when adjusted for a single gender, has 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.

88. Use of any one of claims 74-86 wherein at least 50% of the plurality of distinct food preparations, when adjusted for a single gender, has 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.

89. Use of claim 74 wherein at least 70% of the plurality of distinct food preparations, when adjusted for a single gender, has 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.

90. Use of any one of the claims 74-86 wherein at least 70% of the plurality of distinct food preparations, when adjusted for a single gender, has 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.

91. Use of claim 74 wherein all of the plurality of distinct food preparations, when adjusted for a single gender, has 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.

92. Use of any one of the claims 74-86 wherein all of the plurality of distinct food preparations, when adjusted for a single gender, has 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.

93. Use of claim 74 wherein the plurality of distinct food preparations is crude filtered aqueous extracts.

94. Use of any one of the claims 74-92 wherein the plurality of distinct food preparations is crude filtered aqueous extracts.

95. Use of claim 74 wherein the plurality of distinct food preparations is processed aqueous extracts.

96. Use of any one of the claims 74-94 wherein the plurality of distinct food preparations is processed aqueous extracts.

97. Use of claim 74 wherein the solid carrier is a well of a multiwall plate, a bead, an electrical sensor, a chemical sensor, a microchip, or an adsorptive film.

98. Use of any one of the claims 74-96 wherein the solid carrier is a well of a multiwall plate, a bead, an electrical sensor, a chemical sensor, a microchip, or an adsorptive film.

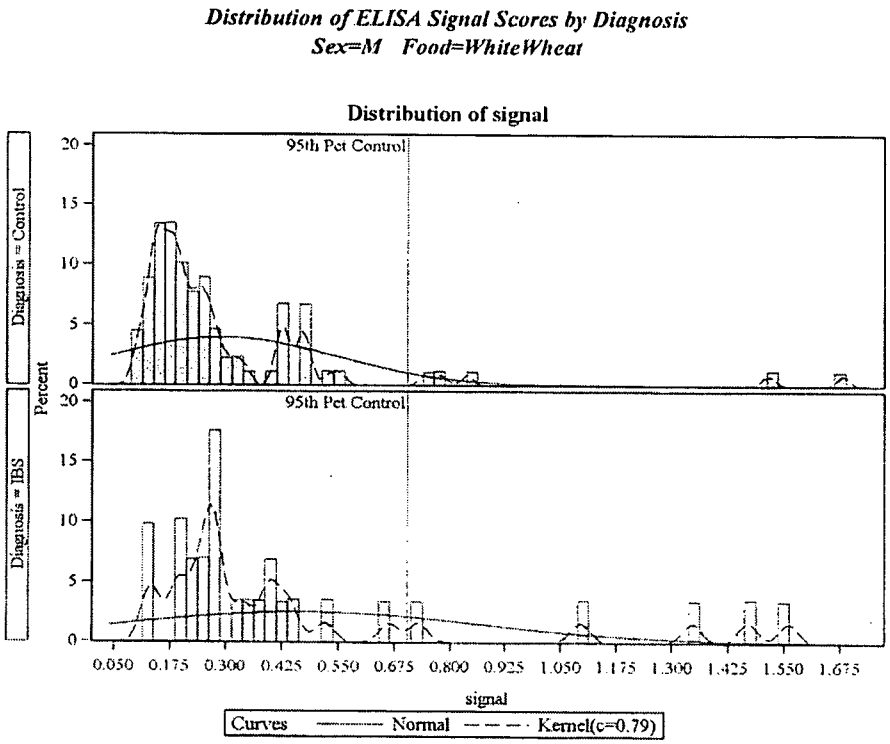


Figure 1A

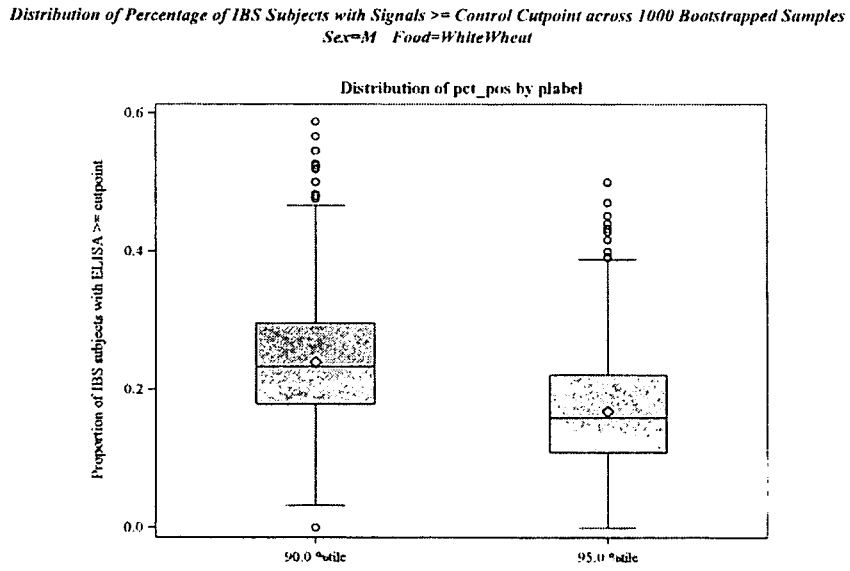


Figure 1B

Distribution of ELISA Signal Scores by Diagnosis
Sex=F Food=WhiteWheat

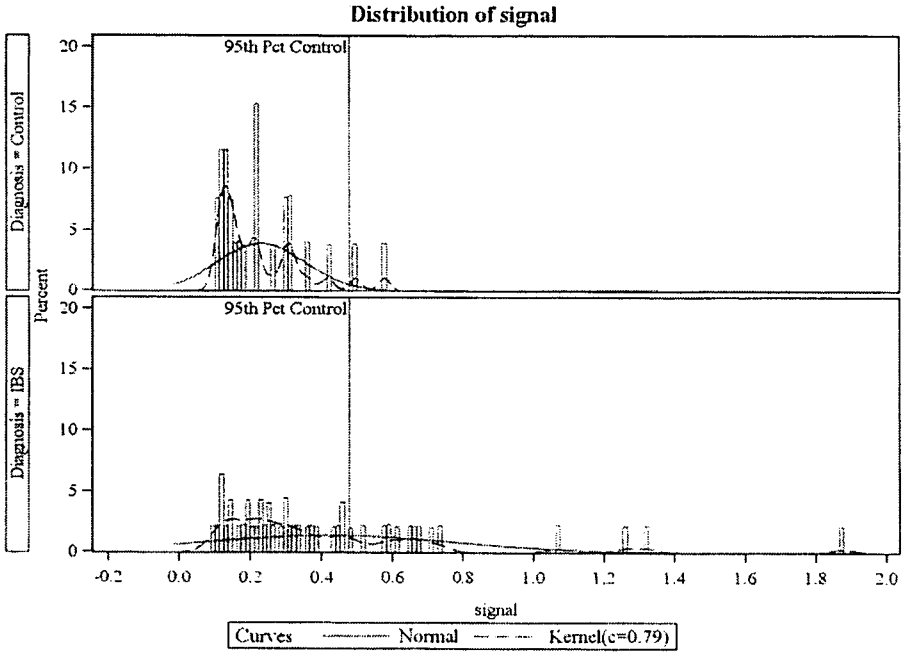


Figure 1C

Distribution of Percentage of IBS Subjects with Signals >= Control Cutpoint across 1000 Bootstrapped Samples
Sex=F Food=WhiteWheat

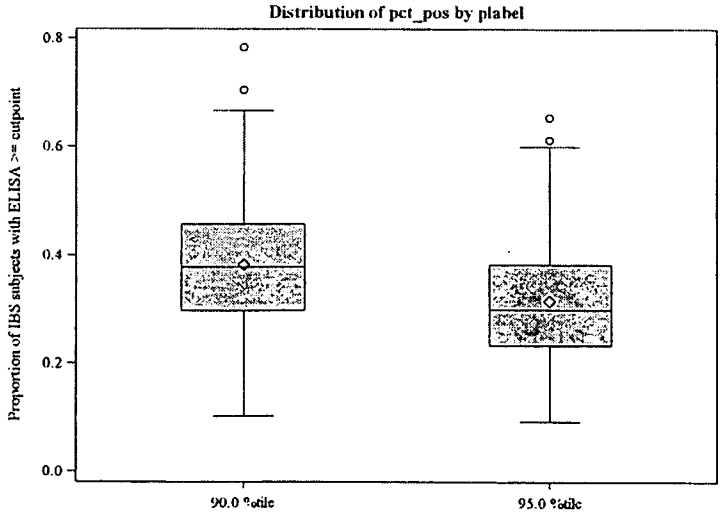


Figure 1D

Distribution of ELISA Signal Scores by Diagnosis
Sex=M Food=Cocoa

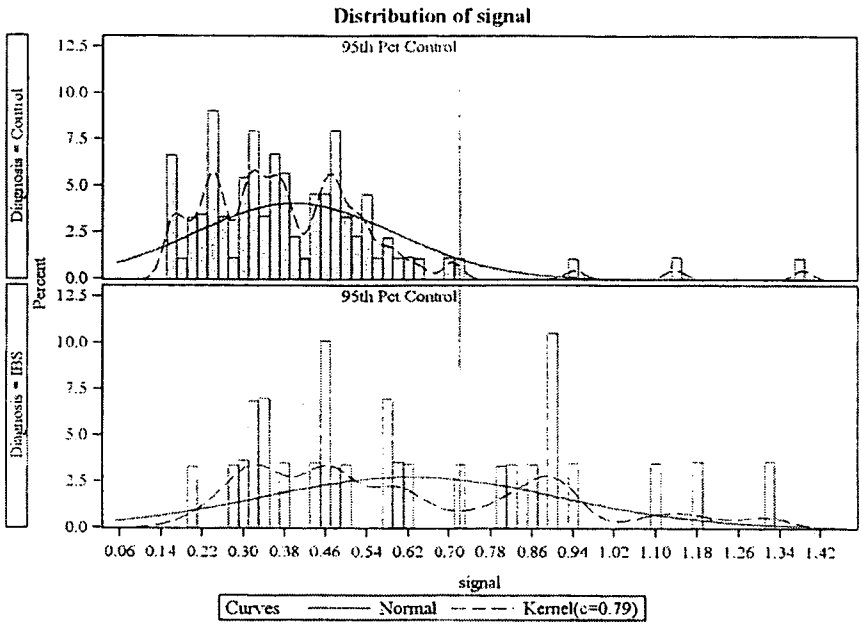


Figure 2A

Distribution of Percentage of IBS Subjects with Signals >= Control Cutpoint across 1000 Bootstrapped Samples
Sex=M Food=Cocoa

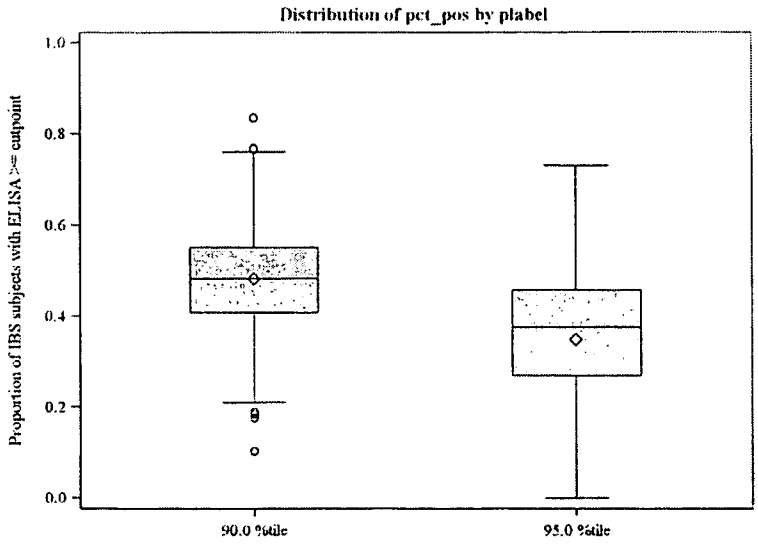


Figure 2B

Distribution of ELISA Signal Scores by Diagnosis
Sex=F Food=Cocoa

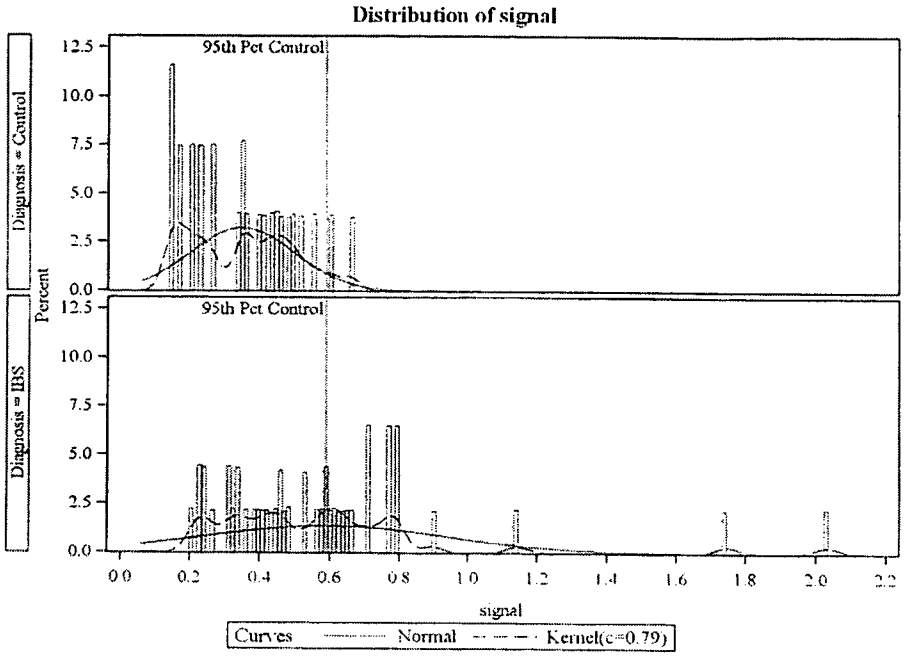


Figure 2C

Distribution of Percentage of IBS Subjects with Signals >= Control Cutpoint across 1000 Bootstrapped Samples
Sex=F Food=Cocoa

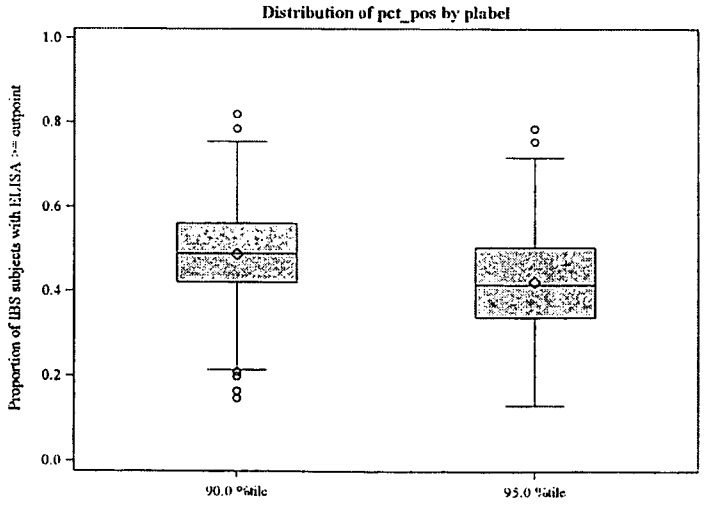


Figure 2D

Distribution of ELISA Signal Scores by Diagnosis
Sex=M Food=Rye

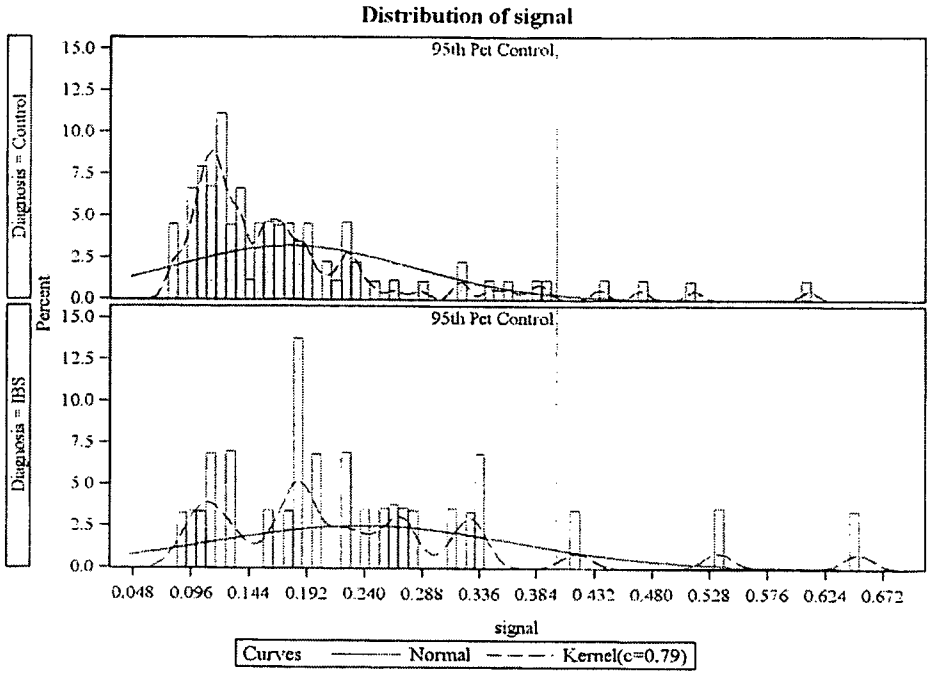


Figure 3A

Distribution of Percentage of IBS Subjects with Signals >= Control Cutpoint across 1000 Bootstrapped Samples
Sex=M Food=Rye

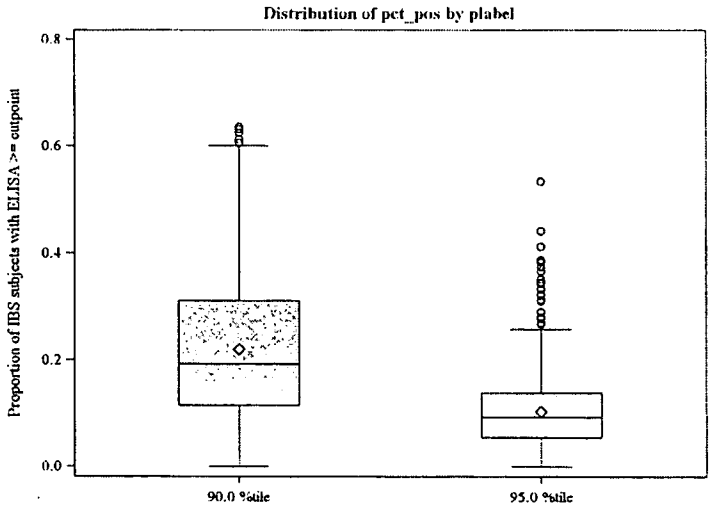


Figure 3B

Distribution of ELISA Signal Scores by Diagnosis
Sex=F Food=Rye

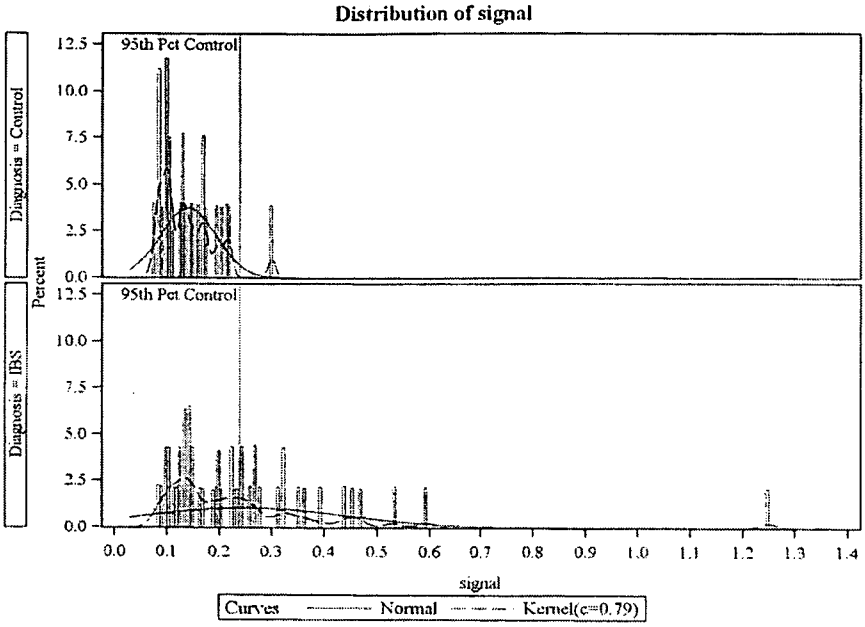


Figure 3C

Distribution of Percentage of IBS Subjects with Signals >= Control Cutpoint across 1000 Bootstrapped Samples
Sex=F Food=Rye

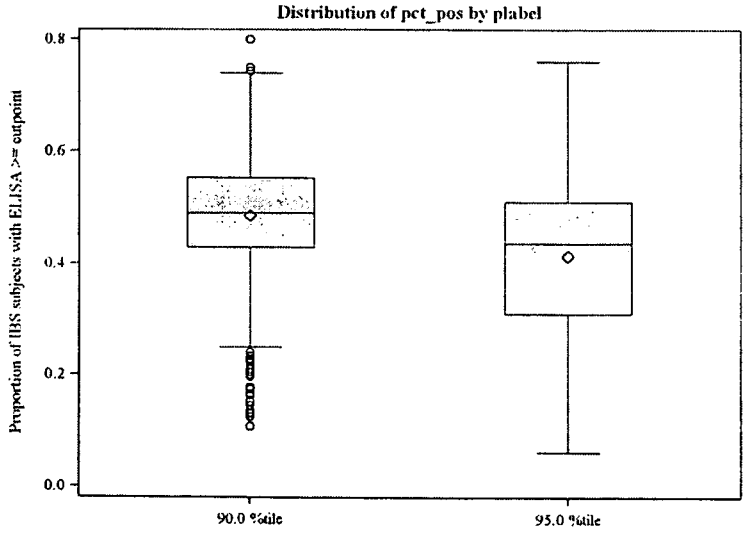


Figure 3D

Distribution of ELISA Signal Scores by Diagnosis
Sex=M Food=BlackTea

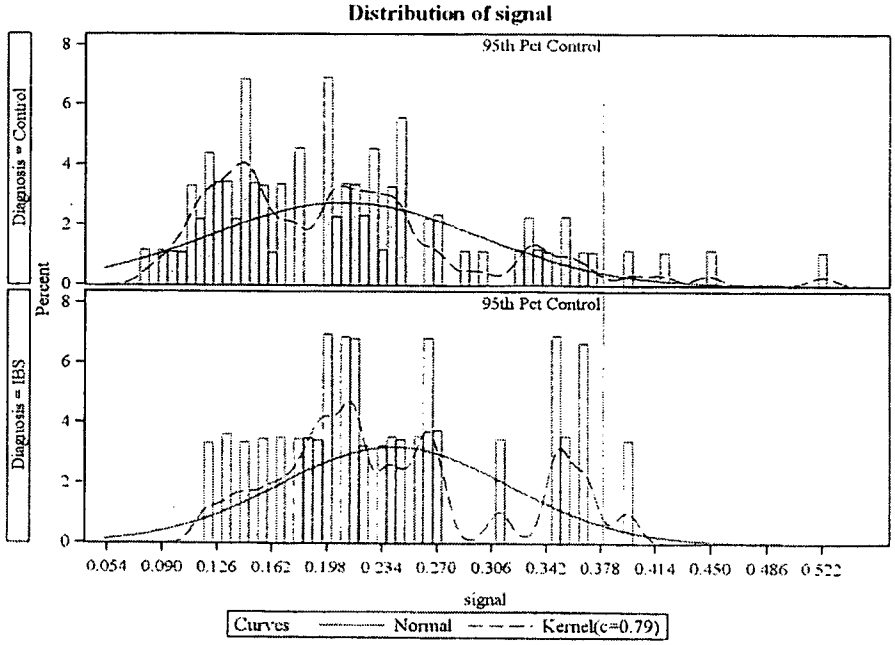


Figure 4A

Distribution of Percentage of IBS Subjects with Signals >= Control Cutpoint across 1000 Bootstrapped Samples
Sex=M Food=BlackTea

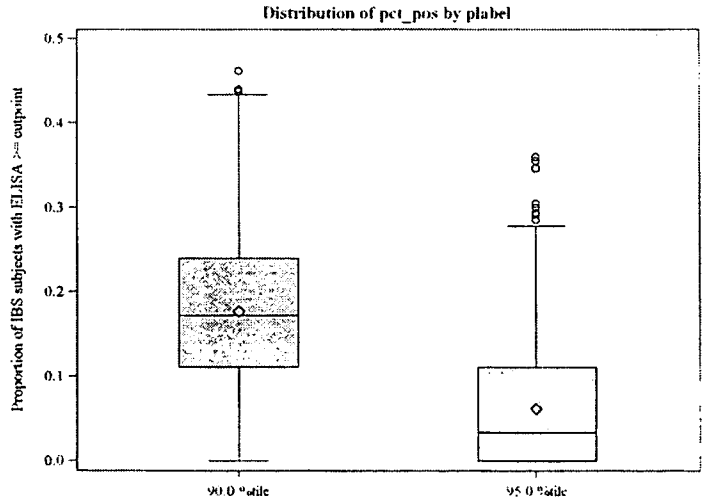


Figure 4B

Distribution of ELISA Signal Scores by Diagnosis
Sex=F Food=BlackTea

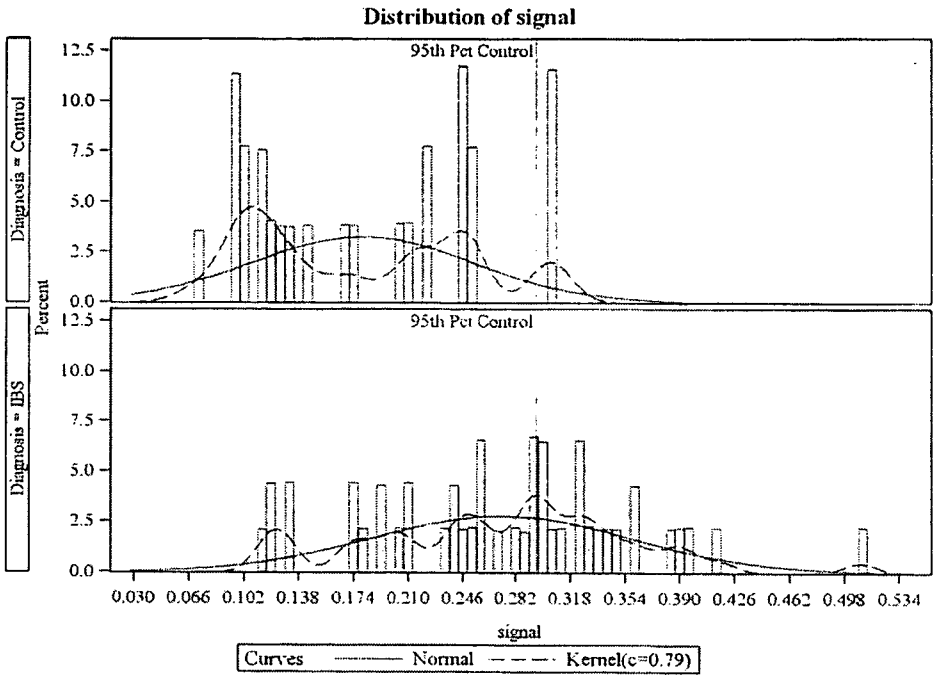


Figure 4C

Distribution of Percentage of IBS Subjects with Signals >= Control Cutpoint across 1000 Bootstrapped Samples
Sex=F Food=BlackTea

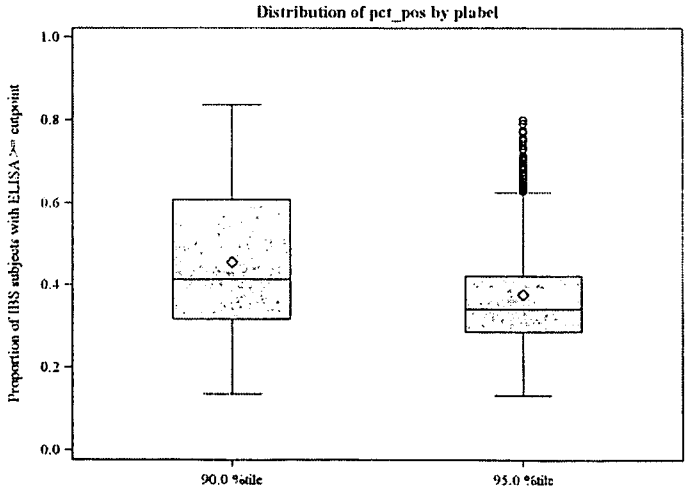


Figure 4D

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

90th Percentile as Cutpoint

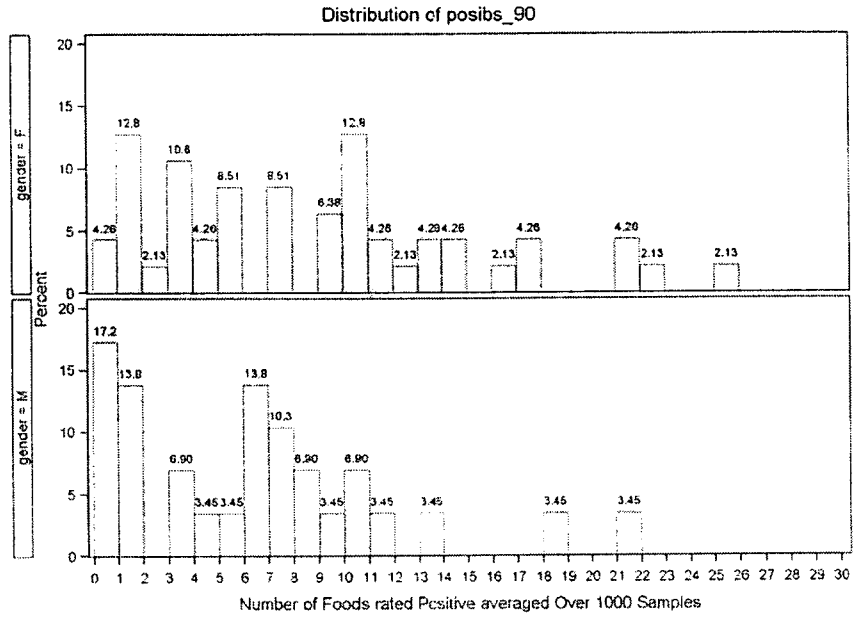


Figure 5A

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

95th Percentile as Cutpoint

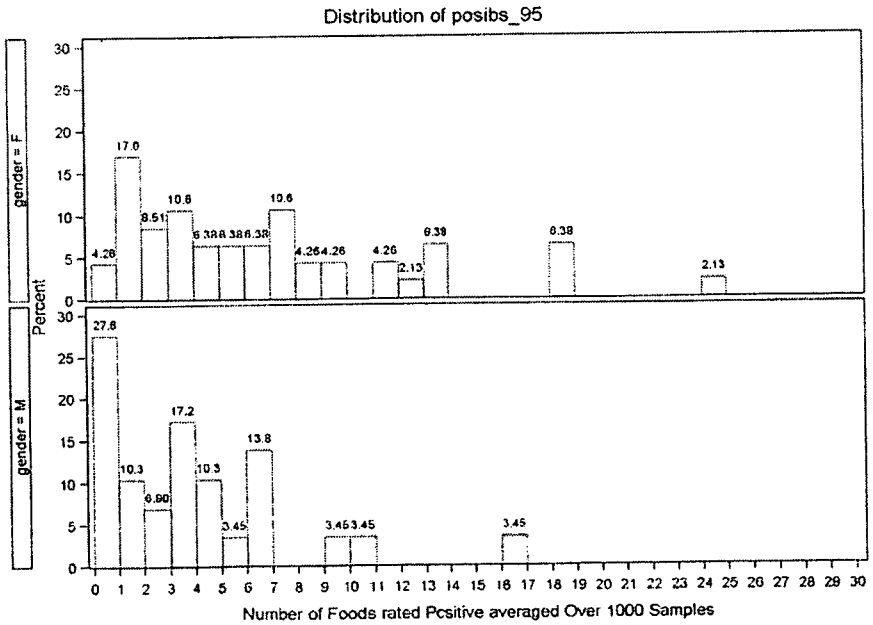


Figure 5B

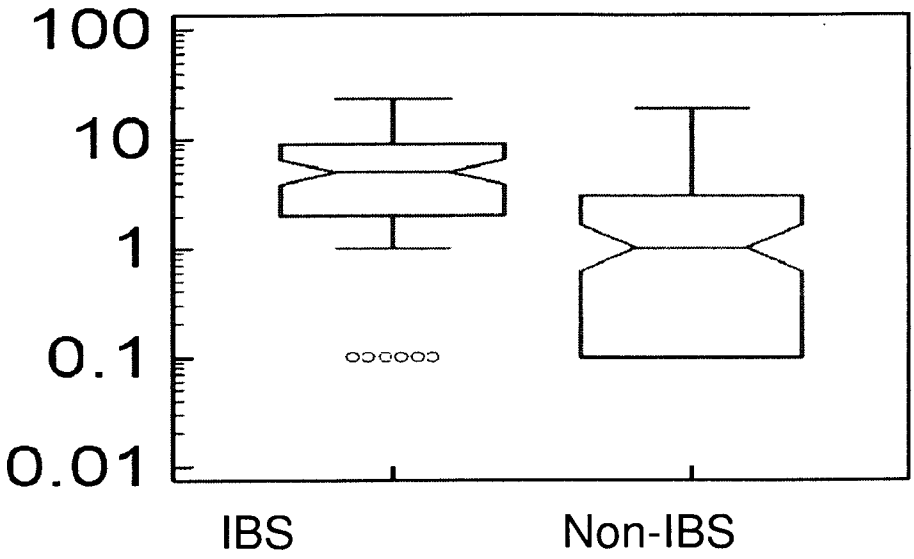


Figure 6A

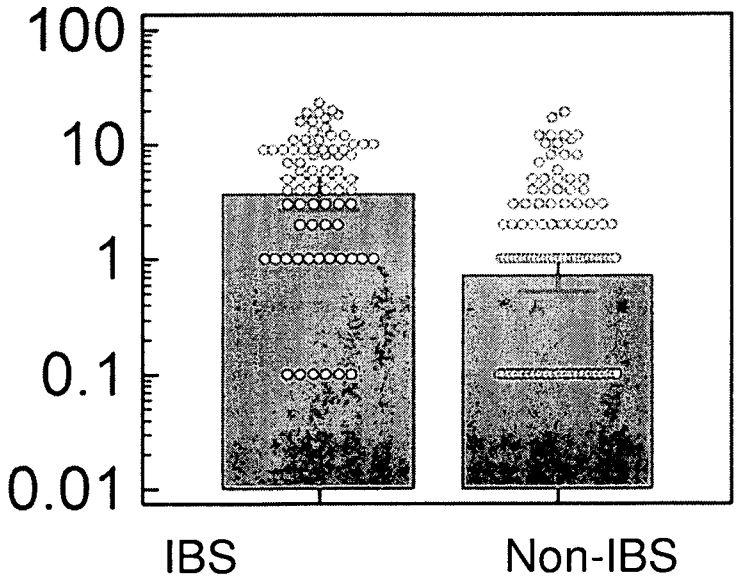


Figure 6B

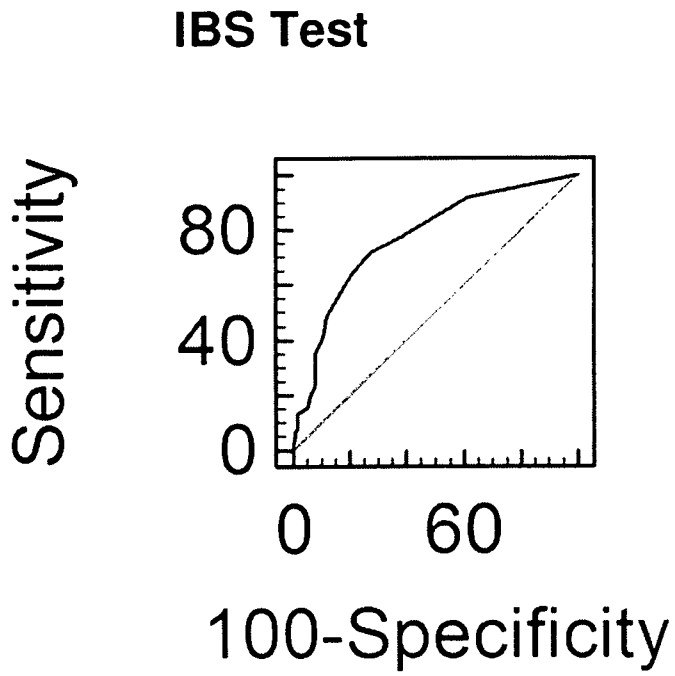


Figure 7

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2015/060759

A. CLASSIFICATION OF SUBJECT MATTER

G01N 33/53(2006.01)i, G01N 33/543(2006.01)i, A61B 10/00(2006.01)i

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
G01N 33/53; C12M 3/00; G01N 33/543; A61B 10/00

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
Korean utility models and applications for utility models
Japanese utility models and applications for utility models

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
eKOMPASS(KIPO internal) & Keywords: irritable bowel syndrome (IBS), food intolerance, p-value, FDR (false discovery rate), gender-stratified reference value

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	ZENG, QIANG et al., 'Variable food-specific IgG antibody levels in healthy and symptomatic Chinese adults', PloS One, 2013, Vol.8, Issue No.1, e53612 (internal pages 1-9) See page 1-2, 5; and figures 2-4.	1-10,12,14,16,18,20,22,24,26-30,32,34,36,38,40,42,44,46-54,56,58,60,62,64,66,68,70,72,74-83,85,87,89,91,93,95,97
A	ATKINSON, W. et al., 'Food elimination based on IgG antibodies in irritable bowel syndrome: a randomised controlled trial', Gut, 2004, Vol.53, Issue No.10, pp.1459-1464 See pages 1459-1461; figure 4; and Tables 1-4.	1-10,12,14,16,18,20,22,24,26-30,32,34,36,38,40,42,44,46-54,56,58,60,62,64,66,68,70,72,74-83,85,87,89,91,93,95,97

☒ Further documents are listed in the continuation of Box C. ☒ See patent family annex.

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

Date of the actual completion of the international search	Date of mailing of the international search report
29 February 2016 (29.02.2016)	**29 February 2016 (29.02.2016)**

Name and mailing address of the ISA/KR
International Application Division
Korean Intellectual Property Office
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Authorized officer
COMMISSIONER
Telephone No. +82-42-481-8116

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2015/060759

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	MONSBAKKEN, K. W. et al., 'Perceived food intolerance in subjects with irritable bowel syndrome-etiology, prevalence and consequences', European Journal of Clinical Nutrition, 2006, Vol.60, No.5, pp.667-672 See the whole document.	1-10,12,14,16,18,20,22,24,26-30,32,34,36,38,40,42,44,46-54,56,58,60,62,64,66,68,70,72,74-83,85,87,89,91,93,95,97
A	US 2007-0122840 A1 (COUSINS, PETER DAVID GEORGE) 31 May 2007 See the whole document.	1-10,12,14,16,18,20,22,24,26-30,32,34,36,38,40,42,44,46-54,56,58,60,62,64,66,68,70,72,74-83,85,87,89,91,93,95,97
A	WO 2009-035529 A1 (IMMUNOHEALTH INTERNATIONAL, LLC) 19 March 2009 See the whole document.	1-10,12,14,16,18,20,22,24,26-30,32,34,36,38,40,42,44,46-54,56,58,60,62,64,66,68,70,72,74-83,85,87,89,91,93,95,97

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2015/060759

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

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

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. ☒ Claims Nos.: See extra sheet.
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

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

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required addtional search fees were timely paid by the applicant, this international search report covers all searchable claims.

2. ☐ As all searchable claims could be searched without effort justifying an additional fees, this Authority did not invite payment of any additional fees.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.

☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.

☐ No protest accompanied the payment of additional search fees.

3. Claims 11, 13, 15, 17, 19, 21, 23, 25, 31, 33, 35, 37, 39, 41, 43, 45, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 84, 86, 88, 90, 92, 94, 96, 98

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No.

PCT/US2015/060759

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 2007-0122840 A1	31/05/2007	AU 2004-236863 A1	18/11/2004
		CA 2524579 A1	18/11/2004
		EP 1623233 A1	08/02/2006
		GB 0310522 D0	11/06/2003
		WO 2004-099785 A1	18/11/2004
WO 2009-035529 A1	19/03/2009	US 2010-0227340 A1	09/09/2010

(19)中华人民共和国国家知识产权局

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(10)申请公布号 CN 107110855 A
(43)申请公布日 2017.08.29

(21)申请号 201580066420.2

(22)申请日 2015.11.13

(30)优先权数据
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(85)PCT国际申请进入国家阶段日
2017.06.06

(86)PCT国际申请的申请数据
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(87)PCT国际申请的公布数据
WO2016/077808 EN 2016.05.19

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扎克瑞·伊拉尼-科恩

(74)专利代理机构 北京国昊天诚知识产权代理有限公司 11315
代理人 许志勇 李有财

(51)Int.Cl.
G01N 33/543(2006.01)
G01N 33/68(2006.01)

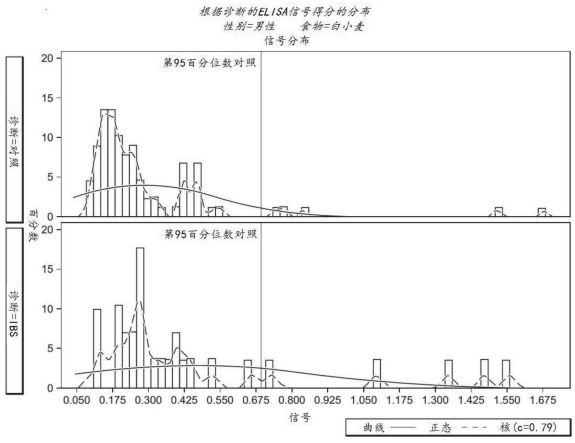
权利要求书7页 说明书33页 附图15页

(54)发明名称

IBS 敏感度测试的组合物、设备以及方法

(57)摘要

所设想的用于食物敏感度的测试试剂盒和方法以基于合理地选择具有确立的判别p值的食物制备物为基础。特别优选的试剂盒包括具有最少数量的食物制备物的试剂盒，食物制备物具有由它们的原始p值确定的平均判别p值≤0.07，或由FDR多重校正的p值确定的平均判别p值≤0.10。在另外设想的方面，用于食物敏感度的组合物和方法还根据性别来分层以进一步增强预测值。



CN 107110855 A

1.一种用于测试被诊断为或疑似罹患肠易激综合征的患者的食物不耐受的测试试剂盒,包括:

多个不同的食物制备物,其耦合到可单独寻址的各固相载体;

其中所述多个不同的食物制备物具有由原始p值确定的平均判别p值≤0.07,或由FDR多重校正的p值确定的平均判别p值≤0.10。

2.如权利要求1所述的测试试剂盒,其中所述多个食物制备物包括由表1的食物项目制备的或由选自由可可、茶、麦片、卷心菜、牛奶、洋葱、蜂蜜、黑麦、玉米、酵母、小麦、大豆、鸡蛋、金枪鱼、柠檬、菠萝、黄瓜、柑橘、大比目鱼、胡桃、葡萄柚、蔗糖、鸡肉、蓝莓以及虾组成的组,且可选地选自由蟹、大麦、草莓、猪肉、稻米、牛肉、腰果、鳕鱼、马铃薯、白芝麻、花椰菜、杏仁、火鸡、扇贝以及鲑鱼组成的组的食物项目制备的至少两个食物制备物。

3.如权利要求1所述的测试试剂盒,其中所述多个食物制备物包括由表1的食物项目制备的或由选自由可可、茶、麦片、卷心菜、牛奶、洋葱、蜂蜜、黑麦、玉米、酵母、小麦、大豆、鸡蛋、金枪鱼、柠檬、菠萝、黄瓜、柑橘、大比目鱼、胡桃、葡萄柚、蔗糖、鸡肉、蓝莓以及虾组成的组,且可选地选自由蟹、大麦、草莓、猪肉、稻米、牛肉、腰果、鳕鱼、马铃薯、白芝麻、花椰菜、杏仁、火鸡、扇贝以及鲑鱼组成的组的食物项目制备的至少四个食物制备物。

4.如权利要求1所述的测试试剂盒,其中所述多个食物制备物包括由表1的食物项目制备的或由选自由可可、茶、麦片、卷心菜、牛奶、洋葱、蜂蜜、黑麦、玉米、酵母、小麦、大豆、鸡蛋、金枪鱼、柠檬、菠萝、黄瓜、柑橘、大比目鱼、胡桃、葡萄柚、蔗糖、鸡肉、蓝莓以及虾组成的组,且可选地选自由蟹、大麦、草莓、猪肉、稻米、牛肉、腰果、鳕鱼、马铃薯、白芝麻、花椰菜、杏仁、火鸡、扇贝以及鲑鱼组成的组的食物项目制备的至少八个食物制备物。

5.如权利要求1所述的测试试剂盒,其中所述多个食物制备物包括由表1的食物项目制备的或由选自由可可、茶、麦片、卷心菜、牛奶、洋葱、蜂蜜、黑麦、玉米、酵母、小麦、大豆、鸡蛋、金枪鱼、柠檬、菠萝、黄瓜、柑橘、大比目鱼、胡桃、葡萄柚、蔗糖、鸡肉、蓝莓以及虾组成的组,且可选地选自由蟹、大麦、草莓、猪肉、稻米、牛肉、腰果、鳕鱼、马铃薯、白芝麻、花椰菜、杏仁、火鸡、扇贝以及鲑鱼组成的组的食物项目制备的至少十二个食物制备物。

6.如权利要求1所述的测试试剂盒,其中所述多个不同的食物制备物具有由原始p值确定的平均判别p值≤0.05,或由FDR多重校正的p值确定的平均判别p值≤0.08。

7.如权利要求1-5中任一项所述的测试试剂盒,其中所述多个不同的食物制备物具有由原始p值确定的平均判别p值≤0.05,或由FDR多重校正的p值确定的平均判别p值≤0.08。

8.如权利要求1所述的测试试剂盒,其中所述多个不同的食物制备物具有由原始p值确定的平均判别p值≤0.025,或由FDR多重校正的p值确定的平均判别p值≤0.07。

9.如权利要求1-5中任一项所述的测试试剂盒,其中所述多个不同的食物制备物具有由原始p值确定的平均判别p值≤0.025,或由FDR多重校正的p值确定的平均判别p值≤0.07。

10.如权利要求1所述的测试试剂盒,其中FDR多重校正的p值是针对年龄和性别中的至少一个来校正。

11.如权利要求1-8中任一项所述的测试试剂盒,其中FDR多重校正的p值是针对年龄和性别中的至少一个来校正。

12.如权利要求1所述的测试试剂盒,其中FDR多重校正的p值是针对年龄和性别来校

正。

13.如权利要求1-8中任一项所述的测试试剂盒，其中FDR多重校正的p值是针对年龄和性别来校正。

14.如权利要求1所述的测试试剂盒，其中当针对单个性别来校正时，所述多个不同的食物制备物中的至少50％具有由原始p值确定的平均判别p值≤0.07，或由FDR多重校正的p值确定的平均判别p值≤0.10。

15.如权利要求1-13中任一项所述的测试试剂盒，其中当针对单个性别来校正时，所述多个不同的食物制备物中的至少50％具有由原始p值确定的平均判别p值≤0.07，或由FDR多重校正的p值确定的平均判别p值≤0.10。

16.如权利要求1所述的测试试剂盒，其中当针对单个性别来校正时，所述多个不同的食物制备物中的至少70％具有由原始p值确定的平均判别p值≤0.07，或由FDR多重校正的p值确定的平均判别p值≤0.10。

17.如权利要求1-13中任一项所述的测试试剂盒，其中当针对单个性别来校正时，所述多个不同的食物制备物中的至少70％具有由原始p值确定的平均判别p值≤0.07，或由FDR多重校正的p值确定的平均判别p值≤0.10。

18.如权利要求1所述的测试试剂盒，其中当针对单个性别来校正时，所有所述多个不同的食物制备物具有由原始p值确定的平均判别p值≤0.07，或由FDR多重校正的p值确定的平均判别p值≤0.10。

19.如权利要求1-17中任一项所述的测试试剂盒，其中当针对单个性别来校正时，所有所述多个不同的食物制备物具有由原始p值确定的平均判别p值≤0.07，或由FDR多重校正的p值确定的平均判别p值≤0.10。

20.如权利要求1所述的测试试剂盒，其中所述多个不同的食物制备物是粗的含水提取物。

21.如权利要求1-19中任一项所述的测试试剂盒，其中所述多个不同的食物制备物是粗的含水提取物。

22.如权利要求1所述的测试试剂盒，其中所述多个不同的食物制备物是处理过的含水提取物。

23.如权利要求1-21中任一项所述的测试试剂盒，其中所述多个不同的食物制备物是处理过的含水提取物。

24.如权利要求1所述的测试试剂盒，其中所述固相载体是多壁板的孔、珠、电传感器、化学传感器、微芯片或吸附膜。

25.如权利要求1-23中任一项所述的测试试剂盒，其中所述固相载体是多壁板的孔、珠、电传感器、化学传感器、微芯片或吸附膜。

26.一种测试被诊断为或疑似罹患肠易激综合征的患者的食物不耐受的方法，包括：

使食物制备物与被诊断为或疑似罹患肠易激综合征的患者的体液接触，且其中所述体液与性别确认相关联；

其中接触步骤在允许来自所述体液的IgG结合到所述食物制备物的至少一种组分的条件下进行；

测量结合到所述食物制备物的所述至少一种组分的IgG以获得信号；

比较所述信号与使用所述性别确认得到的所述食物制备物的性别分层的参考值以获得结果;以及

利用所述结果更新或生成报告。

27.如权利要求26所述的方法,其中所述患者的所述体液是全血、血浆、血清、唾液或粪便悬液。

28.如权利要求26所述的方法,其中接触食物制备物的所述步骤由多个不同的食物制备物来进行。

29.如权利要求26或权利要求27所述的方法,其中接触食物制备物的所述步骤由多个不同的食物制备物进行。

30.如权利要求28所述的方法,其中所述多个不同的食物制备物由表1的食物项目制备或由选自由可可、茶、麦片、卷心菜、牛奶、洋葱、蜂蜜、黑麦、玉米、酵母、小麦、大豆、鸡蛋、金枪鱼、柠檬、菠萝、黄瓜、柑橘、大比目鱼、胡桃、葡萄柚、蔗糖、鸡肉、蓝莓以及虾组成的组,且可选地选自由蟹、大麦、草莓、猪肉、稻米、牛肉、腰果、鳕鱼、马铃薯、白芝麻、花椰菜、杏仁、火鸡、扇贝以及鲑鱼组成的组的食物项目制备。

31.如权利要求28-29中任一项所述的方法,其中所述多个食物制备物由表1的食物项目制备或由选自由可可、茶、麦片、卷心菜、牛奶、洋葱、蜂蜜、黑麦、玉米、酵母、小麦、大豆、鸡蛋、金枪鱼、柠檬、菠萝、黄瓜、柑橘、大比目鱼、胡桃、葡萄柚、蔗糖、鸡肉、蓝莓以及虾组成的组,且可选地选自由蟹、大麦、草莓、猪肉、稻米、牛肉、腰果、鳕鱼、马铃薯、白芝麻、花椰菜、杏仁、火鸡、扇贝以及鲑鱼组成的组的食物项目制备。

32.如权利要求28所述的方法,其中所述多个不同的食物制备物具有由原始p值确定的平均判别p值≤0.07,或由FDR多重校正的p值确定的平均判别p值≤0.10。

33.如权利要求28-29中任一项所述的方法,其中所述多个不同的食物制备物具有由原始p值确定的平均判别p值≤0.07,或由FDR多重校正的p值确定的平均判别p值≤0.10。

34.如权利要求28所述的方法,其中所述多个不同的食物制备物具有由原始p值确定的平均判别p值≤0.05,或由FDR多重校正的p值确定的平均判别p值≤0.08。

35.如权利要求28-29中任一项所述的方法,其中所述多个不同的食物制备物具有由原始p值确定的平均判别p值≤0.05,或由FDR多重校正的p值确定的平均判别p值≤0.08。

36.如权利要求28所述的方法,其中所述多个不同的食物制备物具有由原始p值确定的平均判别p值≤0.025,或由FDR多重校正的p值确定的平均判别p值≤0.07。

37.如权利要求28-29中任一项所述的方法,其中所述多个不同的食物制备物具有由原始p值确定的平均判别p值≤0.025,或由FDR多重校正的p值确定的平均判别p值≤0.07。

38.如权利要求28所述的方法,其中所有所述多个不同的食物制备物具有由原始p值确定的平均判别p值≤0.07,或由FDR多重校正的p值确定的平均判别p值≤0.10。

39.如权利要求28-29中任一项所述的方法,其中所有所述多个不同的食物制备物具有由原始p值确定的平均判别p值≤0.07,或由FDR多重校正的p值确定的平均判别p值≤0.10。

40.如权利要求26所述的方法,其中所述食物制备物被固定在固体表面上,可选地以可寻址的方式进行固定。

41.如权利要求26-39中任一项所述的方法,其中所述食物制备物被固定在固体表面上,可选地以可寻址的方式进行固定。

42.如权利要求26所述的方法，其中测量结合到所述食物制备物的至少一种组分的IgG的步骤经由免疫测定测试来进行。

43.如权利要求26-41中任一项所述的方法，其中测量结合到所述食物制备物的至少一种组分的IgG的步骤经由免疫测定测试来进行。

44.如权利要求26所述的方法，其中所述食物制备物的所述性别分层的参考值是至少第90百分位数值。

45.如权利要求26-43中任一项所述的方法，其中所述食物制备物的所述性别分层的参考值是至少第90百分位数值。

46.一种生成用于被诊断为或疑似罹患肠易激综合征的患者的食物不耐受的测试的方法，包括：

获得多个不同的食物制备物的测试结果，其中所述测试结果基于被诊断为或疑似罹患肠易激综合征的患者的体液和未被诊断为或不是疑似罹患肠易激综合征的对照组的体液；

针对每一个所述不同的食物制备物，根据性别分层所述测试结果；以及

针对每一个所述不同的食物制备物，为预定的百分位数排名分配用于男性患者和女性患者的不同的分界值。

47.如权利要求46所述的方法，其中所述测试结果是ELISA结果。

48.如权利要求46所述的方法，其中所述多个食物制备物包括由表1的食物项目制备的或由选自由可可、茶、麦片、卷心菜、牛奶、洋葱、蜂蜜、黑麦、玉米、酵母、小麦、大豆、鸡蛋、金枪鱼、柠檬、菠萝、黄瓜、柑橘、大比目鱼、胡桃、葡萄柚、蔗糖、鸡肉、蓝莓以及虾组成的组，且可选地选自由蟹、大麦、草莓、猪肉、稻米、牛肉、腰果、鳕鱼、马铃薯、白芝麻、花椰菜、杏仁、火鸡、扇贝以及鲑鱼组成的组的食物项目制备的至少两个食物制备物。

49.如权利要求46或权利要求47所述的方法，其中所述多个食物制备物包括由表1的食物项目制备的或由选自由可可、茶、麦片、卷心菜、牛奶、洋葱、蜂蜜、黑麦、玉米、酵母、小麦、大豆、鸡蛋、金枪鱼、柠檬、菠萝、黄瓜、柑橘、大比目鱼、胡桃、葡萄柚、蔗糖、鸡肉、蓝莓以及虾组成的组，且可选地选自由蟹、大麦、草莓、猪肉、稻米、牛肉、腰果、鳕鱼、马铃薯、白芝麻、花椰菜、杏仁、火鸡、扇贝以及鲑鱼组成的组的食物项目制备的至少两个食物制备物。

50.如权利要求46所述的方法，其中所述多个食物制备物包括由表1的食物项目制备的或由选自由可可、茶、麦片、卷心菜、牛奶、洋葱、蜂蜜、黑麦、玉米、酵母、小麦、大豆、鸡蛋、金枪鱼、柠檬、菠萝、黄瓜、柑橘、大比目鱼、胡桃、葡萄柚、蔗糖、鸡肉、蓝莓以及虾组成的组，且可选地选自由蟹、大麦、草莓、猪肉、稻米、牛肉、腰果、鳕鱼、马铃薯、白芝麻、花椰菜、杏仁、火鸡、扇贝以及鲑鱼组成的组的食物项目制备的至少六个食物制备物。

51.如权利要求46或权利要求47所述的方法，其中所述多个食物制备物包括由表1的食物项目制备的或由选自由可可、茶、麦片、卷心菜、牛奶、洋葱、蜂蜜、黑麦、玉米、酵母、小麦、大豆、鸡蛋、金枪鱼、柠檬、菠萝、黄瓜、柑橘、大比目鱼、胡桃、葡萄柚、蔗糖、鸡肉、蓝莓以及虾组成的组，且可选地选自由蟹、大麦、草莓、猪肉、稻米、牛肉、腰果、鳕鱼、马铃薯、白芝麻、花椰菜、杏仁、火鸡、扇贝以及鲑鱼组成的组的食物项目制备的至少六个食物制备物。

52.如权利要求46所述的方法，其中所述多个不同的食物制备物包括由表1的食物项目制备的或由选自由可可、茶、麦片、卷心菜、牛奶、洋葱、蜂蜜、黑麦、玉米、酵母、小麦、大豆、鸡蛋、金枪鱼、柠檬、菠萝、黄瓜、柑橘、大比目鱼、胡桃、葡萄柚、蔗糖、鸡肉、蓝莓以及虾组成

的组，且可选地选自由蟹、大麦、草莓、猪肉、稻米、牛肉、腰果、鳕鱼、马铃薯、白芝麻、花椰菜、杏仁、火鸡、扇贝以及鲑鱼组成的组的食物项目制备的食物制备物。

53.如权利要求46或47中任一项所述的方法，其中所述多个不同的食物制备物包括由表1的食物项目制备的或由选自由可可、茶、麦片、卷心菜、牛奶、洋葱、蜂蜜、黑麦、玉米、酵母、小麦、大豆、鸡蛋、金枪鱼、柠檬、菠萝、黄瓜、柑橘、大比目鱼、胡桃、葡萄柚、蔗糖、鸡肉、蓝莓以及虾组成的组，且可选地选自由蟹、大麦、草莓、猪肉、稻米、牛肉、腰果、鳕鱼、马铃薯、白芝麻、花椰菜、杏仁、火鸡、扇贝以及鲑鱼组成的组的食物项目制备的食物制备物。

54.如权利要求46所述的方法，其中所述多个不同的食物制备物包括具有由原始p值确定的平均判别p值≤0.07，或由FDR多重校正的p值确定的平均判别p值≤0.10。

55.如权利要求46-53中任一项所述的方法，其中所述多个不同的食物制备物具有由原始p值确定的平均判别p值≤0.07，或由FDR多重校正的p值确定的平均判别p值≤0.10。

56.如权利要求46所述的方法，其中所述多个不同的食物制备物具有由原始p值确定的平均判别p值≤0.05，或由FDR多重校正的p值确定的平均判别p值≤0.08。

57.如权利要求46-53中任一项所述的方法，其中所述多个不同的食物制备物具有由原始p值确定的平均判别p值≤0.05，或由FDR多重校正的p值确定的平均判别p值≤0.08。

58.如权利要求46所述的方法，其中所述多个不同的食物制备物具有由原始p值确定的平均判别p值≤0.025，或由FDR多重校正的p值确定的平均判别p值≤0.07。

59.如权利要求46-53中任一项所述的方法，其中所述多个不同的食物制备物具有由原始p值确定的平均判别p值<0.025，或由FDR多重校正的p值确定的平均判别p值<0.07。

60.如权利要求46所述的方法，其中所述患者的所述体液是全血、血浆、血清、唾液或粪便悬液。

61.如权利要求46-59中任一项所述的方法，其中所述患者的所述体液是全血、血浆、血清、唾液或粪便悬液。

62.如权利要求46所述的方法，其中所述预定的百分位数排名是至少第90百分位数排名。

63.如权利要求46-61中任一项所述的方法，其中所述预定的百分位数排名是至少第90百分位数排名。

64.如权利要求46所述的方法，其中用于男性患者和女性患者的所述分界值具有至少10％(绝对值)的差。

65.如权利要求46-63中任一项所述的方法，其中用于男性患者和女性患者的所述分界值具有至少10％(绝对值)的差。

66.如权利要求26或46所述的方法，还包括将所述结果归一化为患者的总IgG的步骤。

67.如权利要求26-65中任一项所述的方法，还包括将所述结果归一化为患者的总IgG的步骤。

68.如权利要求26或46所述的方法，还包括将所述结果归一化为患者的食物特异性IgG结果的全局均值的步骤。

69.如权利要求26-65中任一项所述的方法，还包括将所述结果归一化为患者的食物特异性IgG结果的全局均值的步骤。

70.如权利要求26或46所述的方法，还包括确认患者的子集的步骤，其中所述患者的子

集对所述食物制备物的敏感度根据原始p值或平均判别p值≤0.01构成IBS的基础。

71.如权利要求26-65中任一项所述的方法，还包括确认患者的子集的步骤，其中所述患者的子集对所述食物制备物的敏感度根据原始p值或平均判别p值≤0.01构成IBS的基础。

72.如权利要求26或46所述的方法，还包括确定所述食物制备物的数量的步骤，其中所述食物制备物的数量能够用于根据原始p值或平均判别p值≤0.01证实IBS。

73.如权利要求26-65中任一项所述的方法，还包括确定所述食物制备物的数量的步骤，其中所述食物制备物的数量能够用于根据原始p值或平均判别p值≤0.01证实IBS。

74.耦合到可单独寻址的各固相载体的多个不同的食物制备物在诊断肠易激综合征中的用途，其中所述多个不同的食物制备物具有由原始p值确定的平均判别p值≤0.07，或由FDR多重校正的p值确定的平均判别p值≤0.10。

75.如权利要求74所述的用途，其中所述多个食物制备物包括由表1的食物项目制备的或由选自由可可、茶、麦片、卷心菜、牛奶、洋葱、蜂蜜、黑麦、玉米、酵母、小麦、大豆、鸡蛋、金枪鱼、柠檬、菠萝、黄瓜、柑橘、大比目鱼、胡桃、葡萄柚、蔗糖、鸡肉、蓝莓以及虾组成的组，且可选地选自由蟹、大麦、草莓、猪肉、稻米、牛肉、腰果、鳕鱼、马铃薯、白芝麻、花椰菜、杏仁、火鸡、扇贝以及鲑鱼组成的组的食物项目制备的至少两个食物制备物。

76.如权利要求74所述的用途，其中所述多个食物制备物包括由表1的食物项目制备的或由选自由可可、茶、麦片、卷心菜、牛奶、洋葱、蜂蜜、黑麦、玉米、酵母、小麦、大豆、鸡蛋、金枪鱼、柠檬、菠萝、黄瓜、柑橘、大比目鱼、胡桃、葡萄柚、蔗糖、鸡肉、蓝莓以及虾组成的组，且可选地选自由蟹、大麦、草莓、猪肉、稻米、牛肉、腰果、鳕鱼、马铃薯、白芝麻、花椰菜、杏仁、火鸡、扇贝以及鲑鱼组成的组的食物项目制备的至少四个食物制备物。

77.如权利要求74所述的用途，其中所述多个食物制备物包括由表1的食物项目制备的或由选自由可可、茶、麦片、卷心菜、牛奶、洋葱、蜂蜜、黑麦、玉米、酵母、小麦、大豆、鸡蛋、金枪鱼、柠檬、菠萝、黄瓜、柑橘、大比目鱼、胡桃、葡萄柚、蔗糖、鸡肉、蓝莓以及虾组成的组，且可选地选自由蟹、大麦、草莓、猪肉、稻米、牛肉、腰果、鳕鱼、马铃薯、白芝麻、花椰菜、杏仁、火鸡、扇贝以及鲑鱼组成的组的食物项目制备的至少八个食物制备物。

78.如权利要求74所述的用途，其中所述多个食物制备物包括由表1的食物项目制备的或由选自由可可、茶、麦片、卷心菜、牛奶、洋葱、蜂蜜、黑麦、玉米、酵母、小麦、大豆、鸡蛋、金枪鱼、柠檬、菠萝、黄瓜、柑橘、大比目鱼、胡桃、葡萄柚、蔗糖、鸡肉、蓝莓以及虾组成的组，且可选地选自由蟹、大麦、草莓、猪肉、稻米、牛肉、腰果、鳕鱼、马铃薯、白芝麻、花椰菜、杏仁、火鸡、扇贝以及鲑鱼组成的组的食物项目制备的至少十二个食物制备物。

79.如权利要求74所述的用途，其中所述多个不同的食物制备物具有由原始p值确定的平均判别p值≤0.05，或由FDR多重校正的p值确定的平均判别p值≤0.08。

80.如权利要求74-78中任一项所述的用途，其中所述多个不同的食物制备物具有由原始p值确定的平均判别p值≤0.05，或由FDR多重校正的p值确定的平均判别p值≤0.08。

81.如权利要求74所述的用途，其中所述多个不同的食物制备物具有由原始p值确定的平均判别p值≤0.025，或由FDR多重校正的p值确定的平均判别p值≤0.07。

82.如权利要求74-78中任一项所述的用途，其中所述多个不同的食物制备物具有由原始p值确定的平均判别p值≤0.025，或由FDR多重校正的p值确定的平均判别p值≤0.07。

83.如权利要求74所述的用途，其中FDR多重校正的p值是针对年龄和性别中的至少一个来校正。

84.如权利要求74-82中任一项所述的用途，其中FDR多重校正的p值是针对年龄和性别中的至少一个来校正。

85.如权利要求74所述的用途，其中FDR多重校正的p值是针对年龄和性别来校正。

86.如权利要求74-82中任一项所述的用途，其中FDR多重校正的p值是针对年龄和性别来校正。

87.如权利要求74所述的用途，其中当针对单个性别来校正时，所述多个不同的食物制备物中的至少50％具有由原始p值确定的平均判别p值≤0.07，或由FDR多重校正的p值确定的平均判别p值≤0.10。

88.如权利要求74-86中任一项所述的用途，其中当针对单个性别来校正时，所述多个不同的食物制备物中的至少50％具有由原始p值确定的平均判别p值≤0.07，或由FDR多重校正的p值确定的平均判别p值≤0.10。

89.如权利要求74所述的用途，其中当针对单个性别来校正时，所述多个不同的食物制备物中的至少70％具有由原始p值确定的平均判别p值≤0.07，或由FDR多重校正的p值确定的平均判别p值≤0.10。

90.如权利要求74-86中任一项所述的用途，其中当针对单个性别来校正时，所述多个不同的食物制备物中的至少70％具有由原始p值确定的平均判别p值≤0.07，或由FDR多重校正的p值确定的平均判别p值≤0.10。

91.如权利要求74所述的用途，其中当针对单个性别来校正时，所有所述多个不同的食物制备物具有由原始p值确定的平均判别p值≤0.07，或由FDR多重校正的p值确定的平均判别p值≤0.10。

92.如权利要求74-86中任一项所述的用途，其中当针对单个性别来校正时，所有所述多个不同的食物制备物具有由原始p值确定的平均判别p值≤0.07，或由FDR多重校正的p值确定的平均判别p值≤0.10。

93.如权利要求74所述的用途，其中所述多个不同的食物制备物是粗过滤的含水提取物。

94.如权利要求74-92中任一项所述的用途，其中所述多个不同的食物制备物是粗过滤的含水提取物。

95.如权利要求74所述的用途，其中所述多个不同的食物制备物是处理过的含水提取物。

96.如权利要求74-94中任一项所述的用途，其中所述多个不同的食物制备物是处理过的含水提取物。

97.如权利要求74所述的用途，其中所述固相载体多壁板的孔、珠、电传感器、化学传感器、微芯片或吸附膜。

98.如权利要求74-96中任一项所述的用途，其中所述固相载体是多壁板的孔、珠、电传感器、化学传感器、微芯片或吸附膜。

IBS敏感度测试的组合物、设备以及方法

[0001] 本申请要求享有2014年11月14日提交的、属于本申请人的、序列号为62/079783的美国临时专利申请的优先权，该临时专利申请在此通过引用全文并入。

技术领域

[0002] 本发明的领域是用于食物不耐受(food intolerance)的敏感度测试(sensitivity test)，且尤其涉及测试且可能地排除所选择的作为用于被诊断为或疑似罹患肠易激综合征的患者的诱发食物(trigger food)的食物项目(food item)。

背景技术

[0003] 本背景描述包括可以用于理解本发明的信息。本背景并不是承认本文提供的任何信息是现有技术或与目前要求保护的本发明相关，或不承认具体或隐含引用的出版物是现有技术。

[0004] 食物敏感度，尤其当其与肠易激综合征(IBS)有关时，通常表现出慢性腹痛、不舒服、胃气胀和/或排便习惯变化且在医学界还未得到充分了解。更通常地，IBS通过排除可能具有类似症状或重叠症状的其他病理条件(如细菌或原生动物感染、乳糖不耐受症等)来进行诊断。然而，就诱发症状的食谱项目而言，IBS是非常多样的，且还未获知帮助识别具有合理的确定程度的诱发食物项目的标准测试，使这样的患者通常要进行反复试验。

[0005] 虽然有一些市售的测试和实验室来帮助识别诱发食物，但是这些实验室的测试结果的质量通常较差，如消费者权益保护组织(如http://www.which.co.uk/news/2008/08/food-allergy-tests-could-risk-your-health-154711/)所报道的。更显著地，与这些测试和实验室相关的问题是高的假阳性率、高的假阴性率、高的患者内变化性以及实验之间的变化性，使得这样的测试几乎是无用的。类似地，另外不确定的且高度变化的测试结果也在其他地方有所报道(Alternative Medicine Review，第9卷，第2期，2004:第198-207页)，且作者推断这可能是因为食物反应和食物敏感度经由许多不同的机理发生。例如，并不是所有的IBS患者显示出对食物A的阳性响应，且并不是所有的IBS患者显示出对食物B的阴性响应。因而即使IBS患者显示出对食物A的阳性响应，从患者的食谱中剔除食物A也可能不会减轻患者的IBS症状。换句话说，还未充分确定目前可用的测试中所采用的食物样本是否基于使对那些食物样本的敏感度与IBS相关的高的可能性被合适地选择。

[0006] 许多人努力来选择食物项目或变应原以包括在用于免疫测定测试的测试板(test panel)中。例如，Cousins的美国专利申请第2007/0122840号公开了选择了29种被包括在用于ELISA测定的测试板中的食物变应原。这29种食物变应原是基于在具有更大组的食物变应原的初步试验中IgG阳性的频率来选择。然而，Cousins未能教导选定抗原的任何量化和/或统计分析且因此未能提供任何选择的基本原理。当然，Cousin选择了29种用于测试板的食物变应原的方法已经受到了批评，因为其选择是相当随意的。例如，Croft在题目为“IgG food antibodies and irritating the bowel”(Gastroenterology出版，第128卷，第4期，第1135-1136页)的文章中批评到Cousin的方法还不清楚被测量的食物抗体的数量和范围

是否类似于或完全不同于非IBS患者或非食物不耐受患者，因为其缺乏对照(正常的或非IBS对照受治疗者)。因而，至少是不清楚Cousin在关于假阳性率和假阴性率结果方面是否获得了任何改进。

[0007] 关于另一个例子，Stierstorfer的美国专利申请第2011/0306898号公开了选择41种食物物质作为对皮肤贴剂的测试材料。这41种食物物质基于食物物质中包含的化合物(如香草醛、肉桂醛、山梨酸等)被选择。对IBS患者或IBS疑似患者针对变应性接触性生皮炎来测试食物物质。然而，Stierstorfer也未能公开假阳性或假阴性食物变应原如何被排除和食物变应原是否基于IgG阳性结果中的性别分层被选择。

[0008] 本文中的所有出版物通过引用被并入到以下程度：好像每一个单独的出版物或专利申请被具体地且单独地表示为通过引用被并入。如果并入的参考文献中的术语的定义或应用与本文提供的该术语的定义不一致或相反，那么以本文提供的该术语的定义适用为准，而参考文献中的该术语的定义并不适用。

[0009] 因而，即使本领域已知用于食物敏感度的各种测试，所有或几乎所有这些测试存在一种或多种不足。因此，仍存在对用于食物敏感度测试的改进的组合物、设备以及方法的需求，尤其是确认且可能地排除确认为或疑似罹患IBS的患者的诱发食物。

发明内容

[0010] 本发明的主题是提出了一种用于测试被诊断为或疑似罹患肠易激综合征的患者的食物不耐受的系统和方法。本发明的一个方面是一种用于测试被诊断为或疑似罹患肠易激综合征的患者的食物不耐受的测试试剂盒。该测试试剂盒包括耦合到可单独寻址的各固相载体(solid carrier)的多个不同的食物制备物。多个不同的食物制备物具有由原始p值确定的平均判别p值≤0.07，或由FDR多重校正的p值确定的平均判别p值≤0.10。

[0011] 本发明的另一个方面包括一种用于测试被诊断为或疑似罹患肠易激综合征的患者的食物不耐受的方法。该方法包括使食物制备物与被诊断为或疑似罹患肠易激综合征的患者的体液接触的步骤。体液与性别确认相关联。特别优选地，接触步骤在允许来自体液的IgG结合到食物制备物的至少一种组分的条件下进行。该方法继续测量结合到食物制备物的至少一种组分的IgG的步骤以获得信号，且随后比较信号与使用性别确认得到的食物制备物的性别分层的参考值以获得结果。接着，该方法还包括利用该结果更新或生成报告的步骤。

[0012] 本发明的另一个方面包括一种生成被诊断为或疑似罹患肠易激综合征的患者的食物不耐受的测试的方法。该方法包括获得多个不同的食物制备物的测试结果的步骤。测试结果是基于被诊断为或疑似罹患肠易激综合征的患者的体液和未被诊断为或不是疑似罹患肠易激综合征的对照组的体液。该方法还包括针对每一个不同的食物制备物，根据性别对测试结果分层的方法的步骤。随后，该方法继续以下步骤：针对每一个不同的食物制备物，将用于男性患者和女性患者的不同的分界值(cutoffvalue)分配给预定的百分位数排名。

[0013] 本发明其它方面包括耦合到可单独寻址的各固相载体的多个不同的食物制备物在诊断肠易激综合征中的用途。多个不同的食物制备物基于它们的由原始p值确定的平均判别p值≤0.07，或由FDR多重校正的p值确定的平均判别p值≤0.10来选择。

[0014] 本发明主题的各种目的、特征、方面和优点将从以下对优选实施方案以及附图的详细描述中变得更加明显，其中相同的附图标记表示相同的部件。

附图说明

[0015] 表1显示了食物项目的列表，食物制备物可以由这些食物项目制备。

[0016] 表2显示了根据双尾FDR多重校正的p值排名的食物的统计数据。

[0017] 表3显示了根据食物和性别的ELISA得分的统计数据。

[0018] 表4显示了用于预定的百分位数排名的食物的分界值。

[0019] 图1A图示了用白小麦测试的男性IBS患者和对照的ELISA信号得分。

[0020] 图1B图示了用白小麦测试的超过第90百分位数和第95百分位数的男性IBS受治疗者的百分数分布。

[0021] 图1C图示了用白小麦测试的女性的信号分布以及由女性对照群体确定的第95百分位数分界。

[0022] 图1D图示了用白小麦测试的超过第90百分位数和第95百分位数的女性IBS受治疗者的百分数分布。

[0023] 图2A图示了用可可测试的男性IBS患者和对照的ELISA信号得分。

[0024] 图2B图示了用可可测试的超过第90百分位数和第95百分位数的男性IBS受治疗者的百分数分布。

[0025] 图2C图示了用可可测试的女性的信号分布以及由女性对照群体确定的第95百分位数分界。

[0026] 图2D图示了用可可测试的超过第90百分位数和第95百分位数的女性IBS受治疗者的百分数分布。

[0027] 图3A图示了用黑麦测试的男性IBS患者和对照的ELISA信号得分。

[0028] 图3B图示了用黑麦测试的超过第90百分位数和第95百分位数的男性IBS受治疗者的百分数分布。

[0029] 图3C图示了用黑麦测试的女性的信号分布以及由女性对照群体确定的第95百分位数分界。

[0030] 图3D图示了用黑麦测试的超过第90百分位数和第95百分位数的女性IBS受治疗者的百分数分布。

[0031] 图4A图示了用黑茶测试的男性IBS患者和对照的ELISA信号得分。

[0032] 图4B图示了用黑茶测试的超过第90百分位数和第95百分位数的男性IBS受治疗者的百分数分布。

[0033] 图4C图示了用黑茶测试的女性的信号分布以及由女性对照群体确定的第95百分位数分界。

[0034] 图4D图示了用黑茶测试的超过第90百分位数和第95百分位数的女性IBS受治疗者的百分数分布。

[0035] 图5A-5B图示了IBS受治疗者的根据第90百分位数和第95百分位数被确认为诱发食物的食物的数量的分布。

[0036] 表5显示了IBS患者和对照的具有基于第90百分位数的阳性结果的数量的原始数

据。

[0037] 表6显示出汇总了表5所示的IBS患者群体的原始数据的统计数据。

[0038] 表7显示出汇总了表5所示的对照群体的原始数据的统计数据。

[0039] 表8显示出汇总了表5所示的IBS患者群体的原始数据经过对数变换所变换的统计数据。

[0040] 表9显示出汇总了表5所示的对照群体的原始数据经过对数变换所变换的统计数据。

[0041] 表10显示出比较了IBS样本与非IBS样本之间的阳性食物的几何平均数的独立T检验的统计数据。

[0042] 表11显示出比较了IBS样本与非IBS样本之间的阳性食物的几何平均数的Mann-Whitney检验的统计数据。

[0043] 图6A图示了表5所示数据的箱形图和须形图。

[0044] 图6B图示了表5所示数据的缺口箱形(notchedbox)图和须形图。

[0045] 图7图示了对应于表12中所示的统计数据的ROC曲线。

[0046] 表12显示了表5-11中所示的数据的接受者工作特征(ROC)曲线分析的统计数据。

[0047] 表13显示出从阳性食物的数量预测女性患者中的IBS状态的性能指标的统计数据。

[0048] 表14显示出从阳性食物的数量预测男性患者中的IBS状态的性能指标的统计数据。

具体实施方式

[0049] 发明人已经发现食物测试中采用的用于确认被诊断为或疑似罹患IBS的患者的诱发食物的食物制备物并不具有同样良好的预测性和/或不与IBS/IBS症状相关联。的确，多种实验已经揭示出在非常广泛的食物项目中，某些食物项目是高度预测性的/与IBS高度相关联，而另一些食物项目与IBS的统计学关联并不显著。

[0050] 甚至更意想不到的是，发明人发现除了食物项目的高度变化外，测试中对于响应的性别差异性在测定食物项目与IBS的关联性方面也发挥着重要作用。因此，基于发明人的发现和另外的设想，现在提供了在选择因IBS症候和症状的减轻而能够被排除的食物项目方面具有明显更高的预测能力的测试试剂盒和方法。

[0051] 以下讨论提供了本发明主题的多个示例性实施方案。尽管每个实施方案都表示本发明要素的单一组合，但本发明主题被认为包括所公开要素的所有可能的组合。因此，如果一个实施方案包括要素A、B和C，并且第二实施方案包括要素B和D，则即使未明确地公开，本发明的主题也被认为包括A、B、C或D的其他剩余组合。

[0052] 在一些实施方案中，用于描述并要求保护本发明的某些实施方案的表达量或范围的数字被理解为在某些情形中由术语“约”修饰。因此，在一些实施方案中，书面描述和所附权利要求中描述的数值参数是近似值，可以根据特定实施方案寻求获得的期望性质变化。在一些实施方案中，数值参数应该根据所报告的有效数字的位数且通过应用常规的舍入技术来解释。尽管这样，描述本发明某些实施方案的宽范围的数值范围和参数是近似值，而具体实施例中描述的数值被尽可行地精确报告。本发明的一些实施方案中提出的数值可以包

含从它们各自的测试测量中存在的标准偏差所无法避免的某些误差。除非上下文做出相反表示，本文描述的所有范围应该被解释为包括它们的端点且开放式范围应该被解释为仅包括商业上可实施的值。类似地，所有列出的值应该被认为包括中间值，除非上下文做出相反表示。

[0053] 如在本文的说明书和贯穿下面的权利要求中所使用的，除非上下文另有明确规定，否则“一个(a)”、“一个(an)”和“该(the)”的含义包括复数指代。此外，如本文的说明书中所使用的那样，除非上下文另有明确规定，否则“在…内(in)”的含义包括“在…内(in)”和“在…上(on)”。

[0054] 本文描述的所有方法可以以任何合适的顺序被执行，除非本文另外表示或另外与上下文明显矛盾的。关于本文中某些实施方案提供的任何和所有示例或示例性语言(例如“诸如”)的使用仅旨在更好地说明本发明，并且不对所要求保护的本发明的范围构成限制。说明书中的任何语言不应被解释为表示对本发明的实践必不可少的、任何非要求保护的要素。

[0055] 本文公开的本发明的可选要素或实施方案的分组不应被解释为限制性的。每个组成员可以单独地或与组中的其他成员或本文中找到的其它要素的任何组合被引用和要求保护。出于简洁和/或可专利性的原因，组中的一个或多个成员可被包括在组中或从组中删除。当发生任何此类包括或删除时，本说明书被视为包括经修改的组，从而满足所附权利要求中使用的所有马库什组合的书面描述。

[0056] 在一个特别优选的方面中，发明人因此设想了适用于测试患者的食物不耐受的测试试剂盒或测试板，其中患者被诊断为或疑似罹患肠易激综合征。更优选地，这样的测试试剂盒或板将包括多个不同的食物制备物(如，原始的或处理过的提取物，优选具有任选的共溶剂的含水提取物，其可以被或可以不被过滤)，这些食物制备物被偶联至可单独寻址的各固相载体(如，呈阵列或微孔板的形式)，其中不同的食物制备物具有由原始p值确定的平均判别p值≤0.07，或由FDR多重校正的p值确定的平均判别p值≤0.10。正如本文中使用的，处理过的提取物包括由经过机械或化学改性的(如切碎的、加热的、沸腾的、发酵的、烟熏的等)的食物项目制成的食物提取物。

[0057] 在一些实施方案中，用于描述并要求保护本发明的某些实施方案的表达成分的量、性质诸如浓度、反应条件等的数字被理解为在某些情形中由术语“约”修饰。因此，在一些实施方案中，书面描述和所附权利要求中描述的数值参数是近似值，可以根据特定实施方案寻求获得的期望性质变化。在一些实施方案中，数值参数应该根据所报告的有效数字的位数且通过应用常规的舍入技术来解释。尽管这样，描述本发明某些实施方案的宽范围的数值范围和参数是近似值，而具体实施例中描述的数值被尽可行地精确报告。本发明的一些实施方案中提出的数值可以包含某些误差，从它们各自的测试测量中存在的标准偏差所无法避免的。类似地，除非上下文做出相反表示，本文描述的所有范围应该被解释为包括它们的端点且开放式范围应该被解释为仅包括商业上可实施的值。类似地，所有列出的值应该被认为包括中间值，除非上下文做出相反表示。

[0058] 虽然并不限制本发明的主题，但是食物制备物将通常由通常已知或疑似为诱发IBS的症候或症状的食物得到。特别合适的食物制备物可以通过下面概括的实验过程来确认。因而，应理解，食物项目不需要被限制到本文描述的项目，而是所有项目可以被设想，且

它们可以通过本文提供的方法被确认。因此，示例性的食物制备物包括由可可、茶(如绿茶、黑茶等)、麦片、卷心菜、牛奶、洋葱(如黄洋葱、白洋葱、maui洋葱等)、蜂蜜、黑麦、玉米、酵母、小麦(如红小麦、白小麦等)、大豆、鸡蛋、金枪鱼、柠檬、菠萝、黄瓜、柑橘、大比目鱼、胡桃、葡萄柚、蔗糖、鸡肉、蓝莓或虾(如美国海湾白虾、泰国虾、虎虾等)制备的至少两个、至少四个、至少八个或至少十二个食物制备物。另外设想的食物制备物由蟹(如珍宝蟹、蓝蟹、阿拉斯加帝王蟹等)、大麦、草莓、猪肉、稻米(如棕色、白色等)、牛肉、腰果、鳕鱼、马铃薯、白芝麻、花椰菜、杏仁、火鸡、扇贝和/或鲑鱼制备。仍另外特别设想的食物项目和食物添加剂列在表1中，食物制备物可以由这些食物项目和食物添加剂制备。

[0059] 使用来自被诊断为或疑似罹患肠易激综合征的患者的体液和来自健康的对照组个体(即未被诊断为或不是疑似罹患肠易激综合征的那些人)的体液，可以确认许多额外的食物项目。优选地，这样确认的食物项目将具有高的判别能力且因此具有由原始p值确定的p值≤0.15，更优选≤0.10以及最优选≤0.05，和/或由错误发现率(FDR)多重校正的p值确定的p值≤0.10，更优选≤0.08以及最优选≤0.07。

[0060] 因此，如果板具有多种食物制备物，设想多个不同的食物制备物具有由原始p值确定的平均判别p值≤0.05，或由FDR多重校正的p值确定的平均判别p值≤0.08，或甚至更优选具有由原始p值确定的平均判别p值≤0.025，或由FDR多重校正的p值确定的平均判别p值≤0.07。在另外优选的方面中，应理解，FDR多重校正的p值可以根据年龄和性别中的至少一个来校正，且最优选根据年龄和性别两者来校正。另一方面，如果测试试剂盒或板被分层以与单个性别一起使用，还设想在测试试剂盒或板中，当针对单个性别被校正时，多个不同的食物制备物中的至少50％(且更通常70％或全部)具有由原始p值确定的平均判别p值≤0.07，或由FDR多重校正的p值确定的平均判别p值≤0.10。此外，应理解，其他分层(如饮食偏好、种族、居住地、遗传倾向性或家族史等)也被设想，且PHOSITA将被易于评价为合适的分层选择。

[0061] 本文中对值的范围的叙述仅仅意在作为落在该范围内的每个单独值的简略说法。除非另有说明，否则将在一定范围内每个单独的值并入本说明书中，如同在本文中单独列举一样。本文所述的所有方法可以以任何合适的顺序进行，除非本文另有说明或者与上下文明显矛盾。关于本文中某些实施方案提供的任何和所有示例或示例性语言(例如“诸如”)的使用仅旨在更好地说明本发明，并且不对所要求保护的本发明的范围构成限制。说明书中的任何语言不应被解释为表示对本发明的实践必不可少的、任何非要求保护的要素。

[0062] 当然，应注意，特定格式的测试试剂盒或板可以显著变化且设想的格式包括微孔板、微流体设备、浸量尺、膜结合阵列等。因此，耦合食物制备物的固相载体可以包括多壁板的孔、微流体设备、(如颜色编码的或磁性的)珠，或吸附膜(如硝化纤维素或微孔/纳米孔聚合物膜)、化学传感器或电传感器(如印刷的铜传感器或微芯片)。在一些实施方案中，还设想用于分子吸收和通过光检测器(如表面等离子体共振等)的信号检测的合适的固相载体可以被使用。

[0063] 因此，发明人还设想一种测试被诊断为或疑似罹患肠易激综合征的患者的食物不耐受的方法。更通常地，这样的方法将包括使食物制备物与被诊断为或疑似罹患肠易激综合征的患者的体液(如全血、血浆、血清、唾液或粪便悬液)接触的步骤，且其中体液与性别确认相关联。如前所述，接触步骤优选地在允许来自体液的IgG(或IgE或IgA或IgM)结合到

食物制备物的至少一种组分的条件下进行，且结合到食物制备物的组分的IgG随后被量化/测量以获得信号。最优选地，该信号随后与使用性别确认得到的食物制备物的性别分层的参考值(如至少第90百分位数的值)比较以获得结果，该结果随后用于更新或生成报告。优选地，报告可以作为单个测定结果的集合结果来生成。

[0064] 更通常地，这样的方法将不会被限制到单个食物制备物，而是将采用多个不同的食物制备物。如前所述，合适的食物制备物可以使用下面描述的各种方法被确认，然而，尤其优选的食物制备物包括可可、茶(如绿茶、黑茶等)、麦片、卷心菜、牛奶、洋葱(如黄洋葱、白洋葱、maui洋葱等)、蜂蜜、黑麦、玉米、酵母、小麦(如红小麦、白小麦等)、大豆、鸡蛋、金枪鱼、柠檬、菠萝、黄瓜、柑橘、大比目鱼、胡桃、葡萄柚、蔗糖、鸡肉、蓝莓或虾(如美国海湾白虾、泰国虾、虎虾等)。另外设想的食物制备物由蟹(如珍宝蟹、蓝蟹、阿拉斯加帝王蟹等)、大麦、草莓、猪肉、稻米(如棕色、白色等)、牛肉、腰果、鳕鱼、马铃薯、白芝麻、花椰菜、杏仁、火鸡、扇贝和/或鲑鱼，和/或表1的项目制备。正如上面还注意到的，通常优选至少一些或所有的不同的食物制备物具有由原始p值确定的平均判别p值≤0.07(或≤0.05，或≤0.025)，和/或由FDR多重校正的p值确定的平均判别p值≤0.10(或≤0.08，或≤0.07)。

[0065] 虽然优选食物制备物由作为粗提取物，或粗过滤的提取物的单个食物项目来制备，但是设想食物制备物可以由多个食物项目的混合物(如包括柠檬、柑橘和酸橙的柑橘属的混合物、包括蓝蟹、帝王蟹以及珍宝蟹的蟹类的混合物、包括白小麦和红小麦的小麦的混合物、包括美国海湾白虾、泰国虾以及虎虾的虾的混合物等)来制备。在一些实施方案中，还设想食物制备物可以由纯化的食物抗原或重组体食物抗原来制备。

[0066] 正如通常优选地，食物制备物被固定到固体表面上(通常以可寻址的方式)，设想测量结合到食物制备物的组分的IgG或其他类型的抗体的步骤经由免疫测定测试(如ELISA测试、抗体捕捉酶免疫测定、其他类型的抗体捕捉测定等)来进行。

[0067] 从不同的角度看，发明人还设想一种生成用于被诊断为或疑似罹患肠易激综合征的患者的食物不耐受的测试的方法。由于测试被应用于已经被诊断为或疑似罹患肠易激综合征的患者，因而作者并不设想该方法具有对IBS的初步诊断目的。相反，该方法用于确认已经被确诊的或疑似的IBS患者中的诱发食物项目。这样的测试通常将包括获得不同食物制备物的一个或多个测试结果(如ELISA、抗体捕捉酶免疫测定)的步骤，其中测试结果基于被诊断为或疑似罹患肠易激综合征的患者的体液(如血液、唾液、粪便悬液)和未被诊断为或不是疑似罹患肠易激综合征的对照组的体液。更优选地，针对每一种不同的食物制备物，测试结果被根据性别分层，针对每一种不同的食物制备物，用于男性患者和女性患者的不同的分界值(如用于男性患者和女性患者的分界值具有至少10％(绝对值)的差)被分配给预定的百分位数排名(如第90百分位数或第95百分位数)。

[0068] 正如前面注意到的，且虽然不限于本发明的主题，但是设想不同的食物制备物包括由选自由可可、茶(如绿茶、黑茶等)、麦片、卷心菜、牛奶、洋葱(黄洋葱、白洋葱、maui洋葱等)、蜂蜜、黑麦、玉米、酵母、小麦(如红小麦、白小麦等)、大豆、鸡蛋、金枪鱼、柠檬、菠萝、黄瓜、柑橘、大比目鱼、胡桃、葡萄柚、蔗糖、鸡肉、蓝莓或虾(如美国海湾白虾、泰国虾、虎虾等)组成的组的食物项目制备的至少两个(或六个、或十个、或十五个)食物制备物。另外设想的食物制备物由蟹(如珍宝蟹、蓝蟹阿拉斯加帝王蟹等)、大麦、草莓、猪肉、稻米(如棕色、白色等)、牛肉、腰果、鳕鱼、马铃薯、白芝麻、花椰菜、杏仁、火鸡、扇贝和/或鲑鱼，和/或表1中的

项目制备。在另一方面，如果新的食物项目被测试，则应理解，不同的食物制备物包括由不是可可、茶(如绿茶、黑茶等)、麦片、卷心菜、牛奶、洋葱(如黄洋葱、白洋葱、maui洋葱等)、蜂蜜、黑麦、玉米、酵母、小麦(如红色、白色等)、大豆、鸡蛋、金枪鱼、柠檬、菠萝、黄瓜、柑橘、大比目鱼、胡桃、葡萄柚、蔗糖、鸡肉、蓝莓或虾(如美国海湾白虾、泰国虾、虎虾等)的食物项目制备的食物制备物。不考虑食物项目的具体选择，然而通常优选，不同的食物制备物具有由原始p值确定的平均判别p值≤0.07(或≤0.05，或≤0.025)，或由FDR多重校正的p值确定的平均判别p值≤0.10(或≤0.08，或≤0.07)。示例性的方面和方案以及考虑被提供给在下面的实验描述中。

[0069] 因而，应理解，通过具有本文描述的高置信度检验系统，可以显著降低假阳性率和假阴性率，且尤其是如果检验系统和方法是针对性别差异被性别分层的或校正的(如下显示)。因此，这样的优势还未被认识到且期望本文提供的系统和方法将会显著增强用于被诊断为或疑似罹患IBS的患者的食物敏感度测试的预测能力。

[0070] 实验

[0071] 用于产生食物制备物的一般方案：市售的由各种生鲜食物的可食用部分制备的食物提取物(可从Biomerica Inc.,17571 Von KarmanAve,Irvine,CA 92614获得)用于按照制造商的说明书来制备ELISA板。

[0072] 对于一些食物提取物，发明人发现由产生食物提取物的特定过程制备的食物提取物比市售的食物提取物在检测IBS患者的升高的IgG反应性方面提供了更优异的结果。例如，对于谷物和坚果，优选产生食物提取物的三步过程。第一步是脱脂步骤。在此步骤中，通过使谷物和坚果的粉末与非极性溶剂接触并收集残余物来提取谷物和坚果中的脂质。然后，通过使脱脂的谷物或坚果粉末与升高的pH接触以获得混合物并从该混合物除去固体以获得液体提取物来提取该粉末。一旦产生液体提取物，则添加水性制剂来稳定该液体提取物。在优选的实施方案中，水性制剂包括糖醇、金属螯合剂、蛋白酶抑制剂、矿物盐以及20-50mM的4-9pH的缓冲液的缓冲液组分。此制剂允许-70℃下长期存储和多次冻融而不会损失活性。

[0073] 对于另一个实施例，对于肉类和鱼，优选产生食物提取物的两步过程。第一步是提取步骤。在此步骤中，通过在高冲击压力处理器中，在水性缓冲制剂中乳化生的、未蒸煮的肉类或鱼来产生源自生的未蒸煮的肉类或鱼的提取物。接着，除去固体材料以获得液体提取物。一旦产生液体提取物，则添加水性制剂来稳定该液体提取物。在优选的实施方案中，水性制剂包括糖醇、金属螯合剂、蛋白酶抑制剂、矿物盐以及20-50mM的4-9pH的缓冲液的缓冲液组分。此制剂允许-70℃下长期存储和多次冻融而不会损失活性。

[0074] 对于另外的实施例，对于水果和蔬菜，优选产生食物提取物的两步过程。第一步是提取步骤。在此步骤中，使用提取器(如原汁榨汁机等)以粉碎食物和提取汁液来产生源自水果或蔬菜的液体提取物。接着，除去固体材料以获得液体提取物。一旦产生液体提取物，则添加水性制剂来稳定该液体提取物。在优选的实施方案中，水性制剂包括糖醇、金属螯合剂、蛋白酶抑制剂、矿物盐以及20-50mM的4-9pH的缓冲液的缓冲液组分。此制剂允许-70℃下长期存储和多次冻融而不会损失活性。

[0075] ELISA板的封闭：为了优化信噪，用专卖的封闭缓冲液来封闭板。在优选的实施方案中，封闭缓冲液包括20-50mM的4-9pH的缓冲液、动物源的蛋白以及短链醇。包括几种商用

制备物的其他封闭缓冲液也被尝试使用，但未能提供足够的信噪和所要求的低的测定变化性。

[0076] ELISA制备和样本测试：将食物抗原制备物按照制造商的说明书固定到各微量测试孔上。为了测定，使食物抗原与患者的血清中存在的抗体反应，且通过洗涤步骤除去过量的血清蛋白。为了检测IgG抗体结合，使酶标记的抗IgG抗体共轭物与抗原-抗体复合物反应。通过添加与偶联酶反应的底物来显现颜色。测量颜色强度且与对特定食物抗原是特异性的IgG抗体的浓度成正比。

[0077] 确定按照区分IBS与对照受治疗者的ELISA信号的能力的顺序排名的食物列表的方法：从初始选择中(如，100种食物项目或150种食物项目，或甚至更多)，可以因预期群体的低消耗而在分析之前排除一些样本。此外，特定的食物项目可以被用作更大范围的同属的食物组的代表，如果现有测试已经确立了同属组内的不同物质之间的相关性(最优选两个性别，但也适合于单个性别的相关性)尤其如此。例如，泰国虾可以被去掉，而支持美国海湾白虾作为“虾”食物组的代表，或帝王蟹可以被去掉而支持珍宝蟹作为“蟹”食物组的代表。在另外优选的方面中，最终的列表食物不到50种食物项目，且更优选等于或少于40种食物项目。

[0078] 由于最终选择的用于食物不耐受小组的食物将不会对特定的性别是特异性的，因而需要性别-中立的食物列表。由于所观察的样本是性别失衡的(如，对照：22％的女性，IBS：64％的女性)，则通过使用双样本t检验来对针对性别的信号得分建模型并存储残余物供进一步的分析来消除完全因性别引起的ELISA信号幅度的差。对于每一种受测试的食物，采用具有50,000重抽样的对双样本t检验的排列检验(permutation test)来比较IBS与对照之间的残余信号得分。萨特思韦特(Satterthwaite)近似被用于分母自由度以解释方差齐性的缺乏，且双尾排列的(2-tailedpermuted)p值代表每一种食物的原始p值。比较中的错误发现率(FDR)由任何可接受的统计程序(如Benjamini-Hochberg、族系错误率(FWER)、每次比较错误率(PCER)等)来校正。

[0079] 根据食物的双尾FDR多重校正的p值来对食物排名。具有等于或小于期望的FDR阈值的校正p值的食物被认为在IBS中比在对照受治疗者中具有明显更高的信号得分，且因此被认为是包括在食物不耐受小组中的候选者。表2提供了代表统计程序的结果的典型结果。此处，食物的排名是根据经FDR校正的双尾排列T检验的p值。

[0080] 值得注意地，发明人发现甚至对于受测试的同一个食物制备物，至少好几种食物项目的ELISA得分显著变化，且示例性的原始数据提供在表3中。因此，正如将容易理解的，如果同样的分界值被应用于男性数据和女性数据的原始数据，则没有根据性别分层的数据将丧失重要的解释能力。为了克服此缺陷，发明人按照下面的描述根据性别来对数据分层。

[0081] 每一种食物的分界点(cutpoint)选择的统计方法：通过使对照受治疗者中的信号得分的分布汇总来确定何种ELISA信号得分将构成“阳性”响应。对于每一种食物，具有所观察的得分大于或等于对照受治疗者分布的选定分位数的IBS受治疗者被认为是“阳性的”。为了减少任一个受治疗者对分界点确定的影响，每一种食物-特异性的和性别-特异性的数据集被自助(bootstrap)重抽样1000次。在每一次自助重复中(bootstrap replicate)，确定对照信号得分的第90百分位数和第95百分位数。自助样本中的每一位IBS受治疗者与第90百分位数和第95百分位数比较以确定他/她是否具有“阳性”响应。每一种食物和性别的

最终的基于第90百分位数和第95百分位数的分界点被计算为整个1000份样本中的平均第90百分位数和第95百分位数。通过池化(pooling)整个食物的数据来计算每一位IBS受治疗者被认为对食物是“阳性的”食物的数量。采用这样的方法，发明人现在能够确认预定的百分位数排名的分界值，该值在大多数情形中是显著不同的，正如可以从表4看到的。

[0082] 图1A-1D显示了相对于小麦的、血液中的IgG响应的性别差异的典型示例，其中图1A显示了男性的信号分布以及由男性对照群体确定的第95百分位数分界。图1B显示了超过第90百分位数和第95百分位数的男性IBS受治疗者的百分数分布，而图1C显示了女性的信号分布以及由女性对照群体确定的第95百分位数分界。图1D显示了超过第90百分位数和第95百分位数的女性IBS受治疗者的百分数分布。以同样的方式，图2A-2D示例性地描绘了对可可的不同响应，图3A-3D示例性地描绘了对黑麦的不同响应以及图4A-4D示例性地描绘了对黑茶的不同响应。图5A-5B显示了IBS受治疗者的根据在第90百分位数(5A)和第95百分位数(5B)下被确认为诱发食物的食物的数量的分布。发明人设想不考虑特定的食物项目，男性和女性响应是显著不同的。

[0083] 应注意，本领域未提供与IBS有关的被性别分层的任何可预测的食物组。因而，发现对性别显示出不同响应的食物项目是出人意料的结果，显然，基于所有先前可获得的技术也无法预期到这样的结果。换句话说，基于性别分层选择食物项目提供了出人意料的技术效果，使得作为男性或女性IBS患者的诱发食物的特定食物项目的统计学显著性得以显著改进。

[0084] IgG响应数据的归一化：虽然患者的IgG响应结果的原始数据可以用于比较给定食物间的响应强度，但是还设想患者的IgG响应结果被归一化并被指数化(indexed)以产生无量纲的数值以便比较对给定食物的相对响应强度。例如，患者的食物特异性的IgG结果(如对珍宝蟹特异性的IgG和对鸡蛋特异性的IgG)中的一个或多个可以被归一化为患者的总IgG。患者的对珍宝蟹特异性的IgG的归一化值可以是0.1且患者的对鸡蛋特异性的IgG的归一化值可以是0.3。在此情形中，患者对鸡蛋的响应的相对强度是珍宝蟹的3倍。于是，患者对鸡蛋和珍宝蟹的敏感度可以这样被指数化。

[0085] 在其他实施例中，患者的食物特异性IgG结果(如对虾特异性的IgG和对猪肉特异性的IgG)中的一个或多个可以被归一化为患者的食物特异性IgG结果的全局均值。患者的食物特异性IgG的全局均值可以通过患者的食物特异性IgG的总量来测量。在此情形中，患者对虾的特异性IgG可以被归一化为患者的总食物特异性IgG(如对虾、猪肉、珍宝蟹、鸡肉、豌豆等的IgG水平的平均值)的平均值。然而，还设想患者的食物特异性IgG的全局均值可以通过患者的对特定种类的食物的IgG水平经由多次测试来测量。如果之前已经针对患者测试了5次对虾的敏感度且测试了7次对猪肉的敏感度，那么患者的对虾或对猪肉的新的IgG值被归一化为对虾的5次测试结果的平均值或对猪肉的7次测试结果的平均值。患者的对虾特异性的IgG的归一化值可以是6.0且患者的对猪肉特异性的IgG的归一化值可以是1.0。在此情形中，患者此时对虾的敏感度是对虾的平均敏感度的6倍，但具有基本上类似的对猪肉的敏感度。然后，患者对虾和猪肉的敏感度可以基于这样的比较被指数化。

[0086] 确定具有构成IBS基础的食物敏感度的IBS患者的子集的方法：虽然怀疑食物敏感度在IBS的症候和症状方面起着重要作用，但是一些IBS患者可能不具有构成IBS基础的食物敏感度。那些患者将不会获益于饮食干预来治疗IBS的症候和症状。为了确定这样的患者

的子集，IBS患者和非IBS患者的体液样本可以采用使用具有24份食物样本的测试设备进行的ELISA测试来测试。

[0087] 表5提供了示例性的原始数据。正如应该被容易理解的，数据表示了基于第90百分位数值的24份样本食物中的阳性结果的数量。从表5显示的原始数据看，计算了IBS患者和非IBS患者的阳性食物数量的平均偏差和标准偏差。另外，计算了IBS患者和非IBS患者的具有零阳性食物的患者的数量和百分数。IBS群体中的具有零阳性食物的患者的数量和百分数不到非IBS群体中的约五分之一(分别为6％对比38％)。因而，可以容易理解，对零阳性食物具有敏感度的IBS患者不可能具有构成他们的IBS症候和症状的基础的食物敏感度。

[0088] 表6和表7显示出汇总了表5所示的两类患者群体的原始数据的示例性的统计数据。统计数据包括正态性(normality)、算术平均值、中值、百分位数以及代表IBS群体和非IBS群体中的阳性食物的数量的平均值和中值的95％置信区间(CI)。

[0089] 表8和表9显示出汇总了表5所示的两类患者群体的原始数据的另一个示例性统计数据。在表8和9中，原始数据通过对数变换进行变换以改善数据解释。

[0090] 表10和表11显示了独立的T检验(表10，经过对数变换的数据)和Mann-Whitney检验(表11)的示例性统计数据以比较IBS样本与非IBS样本之间的阳性食物的数量的几何平均值。表10和表11中显示的数据表明IBS群体与非IBS群体之间的食物的阳性数量的几何平均值的显著统计学差异。在两种统计检验中，显示了关于24份食物样本的阳性响应的数量在IBS群体中比在非IBS群体中明显更高且平均判别p值≤0.001。这些统计数据还图示为图6A中的箱形图和须形图，和图6B中的缺口箱形图和须形图。

[0091] 表12显示了表5-11所显示的数据的接受者工作特征(ROC)曲线分析的示例性统计数据以确定表5中采用的测试在区分IBS受治疗者与非IBS受治疗者方面的诊断能力。当采用超过2种阳性食物的分界标准时，测试得到72.4％敏感度和72.2％特异度的数据，且具有0.771的曲线下面积(AUROC)。ROC的p值在<0.0001的p值时是显著的。图7图示了对应于表12所示的统计数据的ROC曲线。由于IBS群体与非IBS群体之间的统计学差异是显著的，当测试结果被以2个阳性数量分界时，患者测试阳性的食物的数量可以被用作初步临床诊断IBS的证实，和食物敏感度是否可以构成患者的IBS的症候和症状的基础的证实。因此，上述测试可以被用作另一种“划入”测试以添加到目前可用的诊断IBS的临床标准中。

[0092] 用于确定每人的称为“阳性”食物的数量的分布的方法：为了确定每人的“阳性”食物的数量分布并测量诊断性能，用表1中的24种食物项目进行分析，这显示了对IBS患者的最阳性的响应。24种食物项目包括可可、黑茶、麦片、卷心菜、牛奶、黄洋葱、蜂蜜、黑麦、玉米、酵母、白小麦、大豆、鸡蛋、金枪鱼、柠檬、菠萝、黄瓜、柑橘、大比目鱼、胡桃、葡萄柚、蔗糖、鸡肉、美国海湾白虾。为了减少任一个受治疗者对此分析的影响，每一种食物特异性的和性别特异性的数据集被自助重抽样1000次。接着，对于此自助样本中的每一种食物项目，使用对照群体的第90百分位数和第95百分位数来确定性别特异性的分界点。一旦确定了性别特异性的分界点，则性别特异性的分界点与所观察到的对照和IBS受治疗者的ELISA信号得分比较。在此比较中，如果观察到的信号等于或大于分界点值，则认为是“阳性”食物，且如果观察到的信号小于分界点值，则认为是“阴性”食物。

[0093] 一旦所有的食物项目被认为是阳性的或阴性的，则每位受治疗者的48次(24种食物×2个分界点)呼叫(call)的结果被保存在每一个自助重复中。然后，对于每一位受治疗

者，24次呼叫被采用作为分界点的第90百分位数来求和以得到“阳性食物(第90)的数量”，且剩余24次呼叫被采用第95百分位数来求和以得到“阳性食物(第95)的数量”。接着，在每一个重复中，汇总整个受治疗者的“阳性食物(第90)的数量”和“阳性食物(第95)的数量”以得到如下所述的每个重复的描述性统计量：1)总体平均值等于平均值的平均值；2)总体标准偏差等于标准偏差的平均值；3)总体中值等于中值的平均值；4)总体最小值等于最小值的最小值；以及5)总体最大值等于最大值的最大值。在此分析中，当计算频率分布和直方图时，为了避免非整数的“阳性食物的数量”，作者假设相同的原始数据集的1000次重复实际上是添加到原始样本中的具有相同尺度的999个集的新的受治疗者。一旦完成数据的汇总，就采用程序“a_pos_foods.sas、a_pos_foods_by_dx.sas”生成有关两种性别和有关IBS受治疗者和对照受治疗者两者的“阳性食物(第90)的数量”和“阳性食物(第95)的数量”的频率分布和直方图。

[0094] 测量诊断性能的方法：为了测量每一位受治疗者的针对每一种食物项目的诊断性能，我们使用上述每一个自助重复中的每一位受治疗者的“阳性食物(第90)的数量”和“阳性食物(第95)的数量”的数据。在此分析中，分界点被设定为1。因而，如果受治疗者具有一个或多个“阳性食物(第90)的数量”，则受治疗者被呼叫为“罹患IBS”。如果受治疗者具有小于1个“阳性食物(第90)的数量”，则受治疗者被呼叫为“未罹患IBS”。当建立了所有呼叫时，呼叫与实际的诊断进行比较以确定呼叫是否是真阳性(TP)、真阴性(TN)、假阳性(FP)或假阴性(FN)。当分界点被设定为1用于每一种方法时，汇总整个受治疗者的比较以得到“阳性食物(第90)的数量”和“阳性食物(第95)的数量”的敏感度、特异度、阳性预测值以及阴性预测值的性能指标。每一(敏感度、1-特异度)对成为在ROC曲线上用于此重复的点。

[0095] 为了提高准确度，上述分析通过将分界点从2个增加到高达24个，且重复用于1000个自助重复中的每一个来被重复。于是，1000个自助重复中的性能指标通过采用程序“t_pos_foods_by_dx.sas”计算平均值被汇总。女性和男性的诊断性能的结果显示在表13(女性)和表14(男性)中。

[0096] 当然，应理解，可以对食物制备物做出某些变化而不会改变本文提供的本发明的主题。例如，如果食物项目是黄洋葱，则该项目应该被理解为还包括被证明在测试中具有等同活性的其他洋葱种类。的确，发明人注意到，对于每一个所测试的食物制备物，某些其他相关的食物制备物也以相同或等同的方式(数据未显示)被测试。因而，应理解，每一个受测试的且要求保护的食物制备物将存在与具有经验证的测试中的相同或等同反应的的制备物相关联的等同物。

[0097] 对于本领域技术人员应该明显的是除了已经描述的那些之外，还可以在不脱离本文的发明构思的前提下进行更多的修改。因此，除了所附权利要求的精神外，本发明的主题不受限制。此外，在解释说明书和权利要求书时，所有术语应以符合上下文的最广泛的方式进行解释。特别地，术语“包括(comprises)”和“包括(comprising)”应被解释为以非排他性方式指代要素、部件或步骤，指示参考要素、部件或步骤可以与未明确引用的其他要素、部件或步骤存在或使用或组合。如果说明书声明指代选自由A、B、C...和N组成的组中的至少一种，则文本应该被解释为仅需要组中的一个要素，而不是A加N或B加N等。

[0098]

鲍鱼	成熟干酪	洋葱	胡桃，黑
薏仁	墨鱼	柑橘	西瓜
杏仁	鸭肉	牡蛎	Welch 洋葱
美国干酪	榴莲	番木瓜	小麦
苹果	鳗鱼	红辣椒	小麦麦麸
朝鲜蓟	蛋白(单独的)	欧芹	酵母(酿酒酵母)
芦笋	蛋黄(单独的)	桃	酸奶
鳄梨	蛋白/蛋黄(组合)	花生	

[0099]

小白菜	茄子	梨	**食物添加剂**
竹笋	大蒜	胡椒，黑	阿拉伯树胶
香蕉	姜	菠萝	羧甲基纤维素
大麦，全谷物	麸质-麦醇溶蛋白	黑白斑豆	角叉菜胶
牛肉	羊奶	李子	FD&C 蓝#1
甜菜	葡萄，白/康科德	猪肉	FD&C 红#3
β-乳球蛋白	葡萄柚	马铃薯	FD&C 红#40
蓝莓	草鱼	兔肉	FD&C 黄#5
花椰菜	绿洋葱	稻米	FD&C 黄#6
荞麦	青豆	洛克福乳酪	明胶
黄油	青椒	黑麦	瓜尔胶
卷心菜	番石榴	糖精	麦芽糖糊精
蔗糖	带鱼	红花籽	果胶
香瓜	鳕鱼类	鲑鱼	乳清
香菜	大比目鱼	沙丁鱼	黄原胶
胡萝卜	榛子	扇贝	
酪蛋白	蜂蜜	芝麻	
腰果	海草	鱼翅	
菜花	芸豆	羊奶	
芹菜	奇异果	虾	
糖莴苣	羊羔	鳎鱼	
车达奶酪	韭葱	大豆	
鹰嘴豆	柠檬	菠菜	
鸡肉	小扁豆	南瓜属	
红辣椒	莴苣，卷心	乌贼	
巧克力	利马豆	草莓	
肉桂	龙虾	菜豆	
蛤蜊	桂圆	向日葵籽	
可可豆	鲭鱼	甜马铃薯	
椰子	麦芽	瑞士干酪	
鳕鱼	芒果	芋头	
咖啡	马郁兰	茶，黑	
可拉果	粟	烟草	
玉米	绿豆	西红柿	
松软干酪	蘑菇	鳟鱼	
牛奶	芥菜籽	金枪鱼	
蟹	麦片	火鸡	
黄瓜	橄榄	香草	

[0100] 表1

[0101] 根据经FDR校正的双尾排列T检验的p值的食物的排名

[0102]

排名	食物	原始p值	FDR多重校正的p值
1	可可	0.0000	0.0000
2	黑茶	0.0001	0.0020
3	麦片	0.0002	0.0032
4	卷心菜	0.0004	0.0032
5	牛奶	0.0004	0.0032
6	黄洋葱	0.0006	0.0041
7	蜂蜜	0.0008	0.0044
8	黑麦	0.0010	0.0044
9	玉米	0.0010	0.0044
10	酵母	0.0012	0.0047
11	白小麦	0.0015	0.0055
12	大豆	0.0020	0.0066
13	鸡蛋	0.0022	0.0069
14	金枪鱼	0.0029	0.0084
15	柠檬	0.0036	0.0096
16	菠萝	0.0045	0.0103
17	黄瓜	0.0046	0.0103
18	柑橘	0.0046	0.0103
19	大比目鱼	0.0057	0.0120
20	胡桃	0.0062	0.0125
21	葡萄柚	0.0085	0.0161
22	蔗糖	0.0174	0.0316
23	鸡肉	0.0184	0.0321
24	蓝莓	0.0218	0.0363
25	美国海湾白虾	0.0230	0.0367
26	珍宝蟹	0.0346	0.0533
27	大麦	0.0440	0.0652
28	草莓	0.0555	0.0793
29	猪肉	0.0976	0.1312
30	棕稻米	0.0984	0.1312
31	牛肉	0.1067	0.1377
32	腰果	0.1375	0.1718
33	鳕鱼	0.1741	0.2111
34	马铃薯	0.2443	0.2825
35	白芝麻	0.2472	0.2825
36	花椰菜	0.2589	0.2876
37	杏仁	0.3174	0.3432
38	火鸡	0.4028	0.4240
39	扇贝	0.7149	0.7332
40	鲑鱼	0.9352	0.9352

[0103] 表2

[0104] 根据食物和性别的ELISA得分的基本描述性统计量比较IBS与对照

[0105]

				ELISA 得分			
性别	食物	诊断	数量	平均值	SD	最小	最大
F	杏仁	对照	26	0.227	0.124	0.100	0.565
		IBS	46	0.358	0.474	0.078	3.065
		差(1-2)	_	-0.132	0.387	_	_
	大麦	对照	26	0.255	0.144	0.093	0.725
		IBS	46	0.450	0.361	0.118	1.676
		差(1-2)	_	-0.195	0.302	_	_
	牛肉	对照	26	0.170	0.081	0.086	0.439
		IBS	45	0.190	0.090	0.072	0.467
		差(1-2)	_	-0.020	0.087	_	_
	黑茶	对照	26	0.179	0.075	0.069	0.307
		IBS	46	0.272	0.086	0.115	0.508
		差(1-2)	-	-0.093	0.083	-	-
	蓝莓	对照	26	0.425	0.190	0.233	1.061
		IBS	46	0.480	0.143	0.239	0.867
		差(1-2)	-	-0.055	0.162	-	-
	花椰菜	对照	26	0.220	0.127	0.118	0.620
		IBS	46	0.280	0.174	0.106	1.042
		差(1-2)	-	-0.059	0.159	-	-
	棕稻米	对照	26	0.236	0.118	0.082	0.449
		IBS	46	0.253	0.136	0.101	0.690
		差(1-2)	-	-0.018	0.130	-	-
	卷心菜	对照	26	0.285	0.161	0.086	0.642
		IBS	46	0.432	0.173	0.132	1.033
		差(1-2)	-	-0.147	0.169	-	-
	蔗糖	对照	26	0.377	0.272	0.070	0.835
		IBS	46	0.521	0.234	0.107	0.975
		差(1-2)	-	-0.143	0.248	-	-
	腰果	对照	26	0.249	0.277	0.080	1.528
		IBS	46	0.286	0.215	0.081	1.183
		差(1-2)	-	-0.037	0.239	-	-
	鸡肉	对照	25	0.123	0.064	0.056	0.314
		IBS	46	0.156	0.097	0.062	0.579
		差(1-2)	-	-0.033	0.087	-	-
	可可	对照	26	0.345	0.151	0.142	0.656
		IBS	46	0.587	0.349	0.208	2.030
		差(1-2)	-	-0.242	0.294	-	-
	鳕鱼	对照	26	0.202	0.081	0.083	0.392
		IBS	46	0.182	0.180	0.048	1.069
		差(1-2)	-	0.020	0.152	-	-
	玉米	对照	26	0.416	0.221	0.114	0.923
		IBS	47	0.562	0.333	0.146	1.686
		差(1-2)	-	-0.146	0.298	-	-
	牛奶	对照	26	0.676	0.538	0.074	2.212

				ELISA 得分			
性别	食物	诊断	数量	平均值	SD	最小	最大
		IBS	46	1.191	0.845	0.134	3.035
		差(1-2)	-	-0.515	0.750	-	-
	黄瓜	对照	26	0.168	0.083	0.079	0.317
		IBS	46	0.211	0.071	0.088	0.460
		差(1-2)	-	-0.043	0.075	-	-
	珍宝蟹	对照	26	0.321	0.187	0.107	0.757
		IBS	46	0.390	0.226	0.082	1.285
		差(1-2)	-	-0.068	0.213	-	-
	鸡蛋	对照	26	0.336	0.296	0.060	1.119
		IBS	46	0.903	0.858	0.115	3.274
		差(1-2)	-	-0.567	0.710	-	-
	葡萄柚	对照	25	0.154	0.088	0.069	0.458
		IBS	46	0.203	0.148	0.085	1.014
		差(1-2)	-	-0.049	0.130	-	-
	大比目鱼	对照	26	0.246	0.125	0.093	0.544
		IBS	46	0.348	0.198	0.103	0.941
		差(1-2)	-	-0.101	0.175	-	-
	蜂蜜	对照	26	0.584	0.306	0.152	1.463
		IBS	46	0.805	0.364	0.200	1.638
		差(1-2)	-	-0.220	0.344	-	-
	柠檬	对照	26	0.282	0.157	0.080	0.635
[0106]		IBS	45	0.444	0.297	0.120	1.567
		差(1-2)	-	-0.162	0.255	-	-
	麦片	对照	26	0.282	0.253	0.071	1.116
		IBS	47	0.693	0.680	0.086	2.934
		差(1-2)	-	-0.411	0.567	-	-
	柑橘	对照	26	0.222	0.119	0.080	0.549
		IBS	46	0.313	0.166	0.106	1.044
		差(1-2)	-	-0.091	0.151	-	-
	菠萝	对照	26	0.924	0.853	0.098	3.467
		IBS	47	1.624	1.015	0.206	3.721
		差(1-2)	-	-0.700	0.961	-	-
	猪肉	对照	26	0.392	0.266	0.107	1.285
		IBS	46	0.466	0.283	0.064	1.248
		差(1-2)	-	-0.074	0.277	-	-
	马铃薯	对照	26	0.209	0.104	0.075	0.441
		IBS	46	0.266	0.089	0.087	0.474
		差(1-2)	-	-0.057	0.095	-	-
	黑麦	对照	26	0.138	0.054	0.073	0.299
		IBS	47	0.249	0.193	0.080	1.248
		差(1-2)	-	-0.111	0.159	-	-
	鲑鱼	对照	26	0.230	0.140	0.102	0.684
		IBS	46	0.196	0.100	0.058	0.444
		差(1-2)	-	0.034	0.116	-	-
	扇贝	对照	25	0.283	0.205	0.086	1.025

				ELISA 得分			
性别	食物	诊断	数量	平均值	SD	最小	最大
		IBS	46	0.277	0.173	0.102	0.860
		差(1-2)	-	0.005	0.185	-	-
	大豆	对照	26	0.508	0.228	0.210	0.849
		IBS	46	0.658	0.230	0.252	1.101
		差(1-2)	-	-0.150	0.229	-	-
	草莓	对照	26	0.145	0.059	0.060	0.259
		IBS	46	0.176	0.056	0.075	0.370
		差(1-2)	-	-0.031	0.057	-	-
	金枪鱼	对照	26	0.588	0.297	0.202	1.375
		IBS	46	0.859	0.431	0.181	1.875
		差(1-2)	-	-0.271	0.388	-	-
	火鸡	对照	26	0.248	0.110	0.072	0.583
		IBS	46	0.267	0.110	0.112	0.691
		差(1-2)	-	-0.019	0.110	-	-
	美国海湾白虾	对照	26	0.563	0.325	0.188	1.693
		IBS	45	0.834	0.459	0.210	2.135
		差(1-2)	-	-0.271	0.415	-	-
	胡桃	对照	26	0.194	0.070	0.096	0.315
		IBS	46	0.273	0.123	0.135	0.944
		差(1-2)	-	-0.079	0.107	-	-
	白芝麻	对照	26	0.705	0.524	0.190	2.663
[0107]		IBS	46	0.734	0.393	0.126	1.967
		差(1-2)	-	-0.029	0.444	-	-
	白小麦	对照	26	0.228	0.125	0.106	0.576
		IBS	47	0.427	0.355	0.096	1.872
		差(1-2)	-	-0.198	0.295	-	-
	酵母	对照	25	0.963	0.624	0.157	2.364
		IBS	46	1.291	0.844	0.247	3.438
		差(1-2)	-	-0.327	0.775	-	-
	黄洋葱	对照	26	0.570	0.442	0.105	1.497
		IBS	46	0.911	0.439	0.129	1.791
		差(1-2)	-	-0.341	0.440	-	-
M	杏仁	对照	89	0.335	0.391	0.077	2.342
		IBS	29	0.361	0.341	0.069	1.442
		差(1-2)	-	-0.026	0.379	-	-
	大麦	对照	89	0.419	0.430	0.110	2.242
		IBS	29	0.525	0.499	0.092	1.935
		差(1-2)	-	-0.106	0.448	-	-
	牛肉	对照	73	0.184	0.127	0.081	0.979
		IBS	27	0.222	0.102	0.078	0.555
		差(1-2)	-	-0.038	0.121	-	-
	黑茶	对照	89	0.209	0.088	0.080	0.522
		IBS	29	0.242	0.076	0.118	0.395
		差(1-2)	-	-0.033	0.086	-	-
	蓝莓	对照	89	0.425	0.228	0.216	2.031

[0108]

性别	食物	诊断	数量	ELISA 得分 平均值	SD	最小	最大
		IBS	29	0.517	0.207	0.278	1.424
		差(1-2)	-	-0.092	0.223	-	-
	花椰菜	对照	89	0.242	0.204	0.096	1.747
		IBS	29	0.263	0.194	0.133	1.116
		差(1-2)	-	-0.021	0.201	-	-
	棕稻米	对照	89	0.237	0.123	0.081	0.714
		IBS	29	0.288	0.122	0.090	0.554
		差(1-2)	-	-0.051	0.122	-	-
	卷心菜	对照	89	0.322	0.173	0.089	0.873
		IBS	29	0.409	0.192	0.105	0.878
		差(1-2)	-	-0.087	0.178	-	-
	蔗糖	对照	89	0.375	0.255	0.076	1.097
		IBS	29	0.446	0.230	0.098	0.804
		差(1-2)	-	-0.071	0.249	-	-
	腰果	对照	89	0.230	0.157	0.078	1.152
		IBS	29	0.291	0.167	0.072	0.686
		差(1-2)	-	-0.062	0.160	-	-
	鸡肉	对照	88	0.134	0.069	0.055	0.339
		IBS	29	0.172	0.087	0.055	0.385
		差(1-2)	-	-0.037	0.074	-	-
	可可	对照	89	0.399	0.198	0.158	1.386
		IBS	29	0.623	0.294	0.209	1.310
		差(1-2)	-	-0.224	0.225	-	-
	鳕鱼	对照	89	0.198	0.191	0.072	1.759
		IBS	29	0.146	0.053	0.071	0.325
		差(1-2)	-	0.053	0.169	-	-
	玉米	对照	89	0.414	0.240	0.137	1.185
		IBS	29	0.618	0.330	0.183	1.310
		差(1-2)	-	-0.204	0.265	-	-
	牛奶	对照	89	0.805	0.621	0.095	2.416
		IBS	29	1.309	0.946	0.128	3.525
		差(1-2)	-	-0.504	0.713	-	-
	黄瓜	对照	89	0.167	0.069	0.070	0.343
		IBS	29	0.197	0.070	0.079	0.322
		差(1-2)	-	-0.030	0.069	-	-
	珍宝蟹	对照	89	0.342	0.175	0.104	1.047
		IBS	29	0.431	0.249	0.082	0.992
		差(1-2)	-	-0.089	0.195	-	-
	鸡蛋	对照	89	0.407	0.385	0.071	1.799
		IBS	29	0.609	0.681	0.094	2.589
		差(1-2)	-	-0.202	0.474	-	-
	葡萄柚	对照	88	0.182	0.100	0.063	0.613
		IBS	29	0.260	0.185	0.058	0.658
		差(1-2)	-	-0.079	0.126	-	-
	大比目鱼	对照	89	0.284	0.153	0.105	0.751

				ELISA 得分			
性别	食物	诊断	数量	平均值	SD	最小	最大
		IBS	29	0.379	0.267	0.112	1.477
		差(1-2)	-	-0.095	0.187	-	-
	蜂蜜	对照	89	0.644	0.358	0.210	2.059
		IBS	29	0.911	0.557	0.227	2.635
		差(1-2)	-	-0.267	0.415	-	-
	柠檬	对照	89	0.358	0.239	0.091	1.254
		IBS	29	0.503	0.375	0.082	1.709
		差(1-2)	-	-0.146	0.278	-	-
	麦片	对照	89	0.384	0.378	0.066	1.972
		IBS	29	0.745	0.666	0.101	2.614
		差(1-2)	-	-0.361	0.464	-	-
	柑橘	对照	89	0.265	0.152	0.079	0.831
		IBS	29	0.358	0.252	0.076	1.126
		差(1-2)	-	-0.093	0.181	-	-
	菠萝	对照	89	1.053	0.915	0.123	3.617
		IBS	29	1.354	0.883	0.287	3.126
		差(1-2)	-	-0.301	0.908	-	-
	猪肉	对照	89	0.388	0.219	0.110	1.216
		IBS	29	0.462	0.244	0.126	1.057
		差(1-2)	-	-0.075	0.225	-	-
	马铃薯	对照	89	0.249	0.170	0.069	1.408
[0109]		IBS	29	0.253	0.125	0.100	0.578
		差(1-2)	-	-0.004	0.161	-	-
	黑麦	对照	89	0.178	0.100	0.079	0.610
		IBS	29	0.237	0.129	0.088	0.651
		差(1-2)	-	-0.060	0.108	-	-
	鲑鱼	对照	89	0.206	0.132	0.073	0.897
		IBS	29	0.229	0.185	0.114	1.065
		差(1-2)	-	-0.022	0.147	-	-
	扇贝	对照	88	0.294	0.187	0.095	0.973
		IBS	29	0.320	0.222	0.067	1.161
		差(1-2)	-	-0.026	0.196	-	-
	大豆	对照	89	0.523	0.292	0.175	1.653
		IBS	29	0.715	0.490	0.187	2.583
		差(1-2)	-	-0.191	0.351	-	-
	草莓	对照	89	0.151	0.058	0.062	0.311
		IBS	29	0.161	0.053	0.077	0.252
		差(1-2)	-	-0.010	0.057	-	-
	金枪鱼	对照	89	0.725	0.369	0.183	1.752
		IBS	29	0.899	0.459	0.213	1.952
		差(1-2)	-	-0.174	0.393	-	-
	火鸡	对照	89	0.252	0.109	0.100	0.711
		IBS	29	0.265	0.099	0.109	0.510
		差(1-2)	-	-0.013	0.107	-	-
	美国海湾白虾	对照	89	0.709	0.366	0.226	1.982

				ELISA 得分			
性别	食物	诊断	数量	平均值	SD	最小	最大
		IBS	29	0.797	0.422	0.222	1.550
		差(1-2)	-	-0.089	0.380	-	-
	胡桃	对照	89	0.216	0.110	0.095	0.839
		IBS	29	0.244	0.085	0.101	0.428
		差(1-2)	-	-0.029	0.104	-	-
	白芝麻	对照	89	0.620	0.375	0.112	1.855
		IBS	29	0.744	0.412	0.153	1.970
[0110]		差(1-2)	-	-0.124	0.385	-	-
	白小麦	对照	89	0.290	0.250	0.095	1.681
		IBS	29	0.463	0.400	0.130	1.561
		差(1-2)	-	-0.173	0.293	-	-
	酵母	对照	88	0.940	0.624	0.172	3.157
		IBS	29	1.481	0.788	0.416	2.892
		差(1-2)	-	-0.541	0.668	-	-
	黄洋葱	对照	89	0.558	0.418	0.094	1.672
		IBS	29	0.760	0.417	0.098	1.507
		差(1-2)	-	-0.203	0.418	-	-

[0111] 表3

[0112] 作为候选者的对照受治疗者的ELISA信号得分的上侧分位数用于确定“阳性”或“阴性”的检验分界点

[0113] 使用排列检验的按区分能力的降序排名的前24种食物

			分界点	
食物排名	食物	性别	第 90 百分位数	第 95 百分位数
1	可可	F	0.544	0.587
		M	0.581	0.721
2	黑茶	F	0.281	0.296
		M	0.337	0.379
3	麦片	F	0.647	0.813
		M	0.880	1.187
4	卷心菜	F	0.507	0.573
[0114]		M	0.542	0.644
5	牛奶	F	1.373	1.611
		M	1.872	2.133
6	黄洋葱	F	1.109	1.214
		M	1.142	1.328
7	蜂蜜	F	1.022	1.189
		M	1.111	1.422
8	黑麦	F	0.209	0.237
		M	0.313	0.400
9	玉米	F	0.755	0.835
		M	0.774	0.904

[0115]

食物排名	食物	性别	分界点 第90百分位数	分界点 第95百分位数
10	酵母	F	1.811	2.014
		M	1.883	2.102
11	白小麦	F	0.409	0.477
		M	0.492	0.704
12	大豆	F	0.778	0.806
		M	0.891	1.076
13	鸡蛋	F	0.794	0.932
		M	0.988	1.270
14	金枪鱼	F	1.054	1.208
		M	1.276	1.472
15	柠檬	F	0.533	0.585
		M	0.705	0.885
16	菠萝	F	2.139	2.646
		M	2.651	3.030
17	黄瓜	F	0.289	0.305
		M	0.265	0.301
18	柑橘	F	0.389	0.456
		M	0.483	0.589
19	大比目鱼	F	0.451	0.497
		M	0.506	0.600
20	胡桃	F	0.288	0.297
		M	0.319	0.387
21	葡萄柚	F	0.267	0.333
		M	0.328	0.380
22	蔗糖	F	0.739	0.775
		M	0.746	0.834
23	鸡肉	F	0.214	0.249
		M	0.250	0.275
24	蓝莓	F	0.676	0.807
		M	0.630	0.787

[0116] 表4

[0117]

IBS 群体	
样本 ID	# 基于第 90 百分位数的阳性结果
IBS-3	5
IBS-5	0
IBS-11	1
IBS-12	9
IBS-14	0
IBS-18	0
IBS-19	1
IBS-23	11

非 IBS 群体	
样本 ID	# 基于第 90 的阳性结果
BRH-768035	0
BRH-768034	1
BRH-768033	1
BRH-768032	1
BRH-768031	1
BRH-763484	0
BRH-768029	10
BRH-768028	8

[0118]

IBS 群体	
IBS-24	1
IBS-30	9
IBS-33	8
IBS-35	7
IBS-38	6
IBS-40	3
IBS-42	6
IBS-43	2
BRH-698596	4
BHR-698597	9
BRH-698598	4
BRH-698599	18
BRH-698600	3
BRH-698621	12
BRH-698622	7
BRH-698623	5
BRH-698624	1
BRH-698625	9
BRH-774496	17
BRH-763476	0
BRH-768030	0
IBS-2	1
IBS-4	1
IBS-6	1
IBS-7	9
IBS-8	9
IBS-9	1
IBS-10	14
IBS-13	19
IBS-15	9
IBS-16	1
IBS-17	9
IBS-20	16
IBS-21	23
IBS-22	20
IBS-25	2
IBS-26	16
IBS-27	8
IBS-28	10
IBS-29	8
IBS-31	4
IBS-32	2
IBS-34	0
IBS-36	3
IBS-37	5
IBS-39	19
IBS-41	5
IBS-44	5
BRH-698601	10
BRH-698602	3
BRH-698603	13
BRH-698604	10
BRH-698605	8
BRH-698606	4
BRH-698607	2
BRH-698608	4
BRH-698609	1
BRH-698610	1
BRH-698611	3
BRH-698612	3
BRH-698613	12

非 IBS 群体	
BRH-763510	4
BRH-768036	0
BRH-768037	1
BRH-768038	1
BRH-768039	0
BRH-768040	0
BRH-768041	1
BRH-768042	1
BRH-768043	5
BRH-768044	3
BRH-768055	1
BRH-768054	1
BRH-764371	0
BRH-768056	2
BRH-764372	2
BRH-764377	5
BRH-764378	2
BRH-763531	1
BRH-764329	0
BRH-763533	0
BRH-763529	0
BRH-763553	12
BRH-763528	0
BRH-763509	0
BRH-763517	2
BRH-763500	0
BRH-764332	0
BRH-764338	1
BRH-764337	3
BRH-764341	1
BRH-764340	1
BRH-764342	0
BRH-764347	1
BRH-764343	5
BRH-774498	1
BRH-768027	12
BRH-768000	1
BRH-774499	12
BRH-774502	4
BRH-774504	8
BRH-767999	0
BRH-764350	0
BRH-763534	0
BRH-763506	0
BRH-774495	2
BRH-764353	0
BRH-764355	0
BRH-764356	0
BRH-764361	1
BRH-764368	1
BRH-768053	2
BRH-764370	1
BRH-764346	0
BRH-768052	0
BRH-764335	10
BRH-774510	2
BRH-774511	0
BRH-768001	2
BRH-768007	0
BRH-768008	3
BRH-767995	0

[0119]

IBS 群体	
BRH-698614	11
BRH-698615	4
BRH-698616	5
BRH-698617	11
BRH-698618	6
BRH-698619	9
BRH-698620	6
观察数	76
平均 #	6.63
SD	5.54

非 IBS 群体	
BRH-767992	3
BRH-767991	0
BRH-764344	2
BRH-764386	0
BRH-763513	7
BRH-763530	5
BRH-764345	1
BRH-764336	0
BRH-764352	4
BRH-764360	0
BRH-764339	4
BRH-763527	17
BRH-764334	1
BRH-764349	0
BRH-764380	0
BRH-764366	0
BRH-763526	19
BRH-764351	2
BRH-763503	3
BRH-764365	3
BRH-764381	0
BRH-763523	0
BRH-774500	3
BRH-774501	1
BRH-774505	6
BRH-774503	2
BRH-774494	0
BRH-774493	0
BRH-774492	1
BRH-774491	0
BRH-764357	2
BRH-764358	0
BRH-768045	0
BRH-768047	1
BRH-768048	8
BRH-768049	12
BRH-768051	0
BRH-768050	5
BRH-774506	11
BRH-774507	0
BRH-774509	0
BRH-774512	0
BRH-774513	4
BRH-774514	1
BRH-764359	3
BRH-763524	1
观察数	115
平均 #	2.37
SD	3.67

[0120] 表5

[0121]

变量	IBS IBS

样本数量	76
最低值	0.0000
最高值	23.0000
算数平均值	6.6316
平均值的 95% CI	5.3651 到 7.8980
中值	5.0000
中值的 95% CI	4.0000 到 8.0000
方差	30.7158
标准偏差	5.5422
相对标准偏差	0.8357 (83.57%)
平均值的标准误差	0.6357
偏度系数	0.9423 (P=0.0017)
峰度系数	0.3684 (P=0.4053)
关于正态分布的 D'Agostino-Pearson 检验	拒绝正态性 (P=0.0051)

百分位数		95%置信区间
2.5	0.0000	
5	0.0000	0.0000 到 1.0000
10	1.0000	0.0000 到 1.0000
25	2.0000	1.0000 到 3.1043
75	9.0000	8.8957 到 11.6255
90	15.8000	11.0000 到 19.0000
95	18.7000	15.2303 到 22.7004
97.5	19.6000	

[0122] 表6

[0123]

变量	非_IBS 非-IBS
样本数量	115
最低值	0.0000
最高值	19.0000
算数平均值	2.3652
平均值的 95% CI	1.6879 到 3.0426
中值	1.0000
中值的 95% CI	1.0000 到 1.0000
方差	13.4444
标准偏差	3.6667
相对标准偏差	1.5502 (155.02%)
平均值的标准误差	0.3419
偏度系数	2.3537 (P<0.0001)
峰度系数	5.8546 (P<0.0001)
关于正态分布的 D'Agostino-Pearson 检验	拒绝正态性(P<0.0001)

百分位数		95%置信区间
2.5	0.0000	
5	0.0000	0.0000 到 0.0000
10	0.0000	0.0000 到 0.0000
25	0.0000	0.0000 到 0.0000
75	3.0000	2.0000 到 4.0000
90	8.0000	5.0000 到 11.8759
95	11.7500	8.0000 到 16.1360
97.5	12.0000	

[0124] 表7

[0125]

变量	IBS_1 IBS 1
在对数变换后反变换的	
样本数量	76
最低值	0.1000
最高值	23.0000
几何平均值	3.7394
平均值的 95% CI	2.7247 到 5.1321
中值	5.0000
中值的 95% CI	4.0000 到 8.0000
偏度系数	-1.3159 (P=0.0001)
峰度系数	1.3551 (P=0.0481)
关于正态分布的 D'Agostino-Pearson 检验	拒绝正态性(P<0.0001)

百分位数		95%置信区间
2.5	0.1000	
5	0.1000	0.1000 到 1.0000
10	1.0000	0.1000 到 1.0000
25	2.0000	1.0000 到 3.0914
75	9.0000	8.8901 到 11.6153
90	15.7878	11.0000 到 19.0000
95	18.6943	15.1985 到 22.6812
97.5	19.5938	

[0126] 表8

[0127]

变量	非_IBS_1 非-IBS 1
在对数变换后反变换的	
样本数量	115
最低值	0.1000
最高值	19.0000
几何平均值	0.7278
平均值的 95% CI	0.5297 到 1.0001
中值	1.0000
中值的 95% CI	1.0000 到 1.0000
偏度系数	0.04343 (P=0.8428)
峰度系数	-1.4006 (P<0.0001)
关于正态分布的 D'Agostino-Pearson 检验	拒绝正态性(P<0.0001)

百分位数		95%置信区间
2.5	0.1000	
5	0.1000	0.1000 到 0.1000
10	0.1000	0.1000 到 0.1000
25	0.1000	0.1000 到 0.1000
75	3.0000	2.0000 到 4.0000
90	8.0000	5.0000 到 11.8711
95	11.7418	8.0000 到 16.0070
97.5	12.0000	

[0128] 表9

[0129]

样本 1	
变量	IBS_1 IBS 1
样本 2	
变量	非_IBS_1 非-IBS 1

在对数变换后反变换的		
	样本 1	样本 2
样本数量	76	115
几何平均值	3.7394	0.7278
平均值的 95% CI	2.7247 到 5.1321	0.5297 到 1.0001
对数化后方差	0.3620	0.5582

等方差性的 F 检验	P = 0.045

T 检验（假设等方差性）

对数变换比例的差	
差	-0.7108
标准误差	0.1025
差的 95% CI	-0.9129 到-0.5087
检验统计量 t	-6.937
自由度（DF）	189
双尾概率	P < 0.0001
反变换的结果	
几何平均值的比	0.1946
比的 95% CI	0.1222 到 0.3100

[0130] 表10

[0131]

样本 1	
变量	IBS_1 IBS 1
样本 2	
变量	非_IBS_1 非-IBS 1

	样本 1	样本 2le 2
样本数量	76	115
最低值	0.1000	0.1000
最高值	23.0000	19.0000
中值	5.0000	1.0000
中值的 95% CI	4.0000 到 8.0000	1.0000 到 1.0000
四分位距	2.0000 到 9.0000	0.1000 到 3.0000

Mann-Whitney检验（独立样本）

第一组的平均排名	127.1382
第二组的平均排名	75.4217
Mann-Whitney U	2003.50
检验统计量 Z（关于秩次校正的）	6.410
双尾概率	P < 0.0001

[0132] 表11

[0133]

变量	IBS_测试 IBS 测试
分类变量	诊断 诊断

样本数量		191
阳性组:	诊断 = 1	76
阴性组:	诊断 = 0	115
疾病患病率（%）		未知

ROC 曲线下的面积（AUC）

ROC 曲线下的面积（AUC）	0.771
标准误差 [a]	0.0346
95%置信区间 [b]	0.705 到 0.828
z 统计量	7.829
显著性水平 P（面积=0.5）	<0.0001

[a] DeLong 等人 1988
[b] 二项式精确

Youden 指数

Youden 指数 J	0.4454
95%置信区间 [a]	0.2976 到 0.5542
关联标准	>2
95%置信区间 [a]	0 到 2

[a] BC_a 自助区间（1000 次迭代）

总表

固定敏感度下的估计的特异度			
敏感度	特异度	95% CI [a]	标准
80.00	57.90	43.98 到 74.43	>0.8364
90.00	41.68	30.23 到 52.71	>0.1455
95.00	38.26	27.83 到 46.09	>0
97.50	38.26	27.83 到 46.09	>0
固定特异度下的估计的敏感度			
特异度	敏感度	95% CI [a]	标准
80.00	62.89	47.37 到 76.32	>3.2
90.00	39.91	15.58 到 59.59	>7.1667
95.00	15.62	5.83 到 32.66	>11.0625
97.50	13.73	3.95 到 29.91	>11.7812

[a] BC_a 自助区间（1000 次迭代）

ROC 曲线的标准值和坐标 [隐藏]

标准	敏感度	95% CI	特异度	95% CI	+LR	95% CI	-LR	95% CI
=0	100.00	95.3 - 100.0	0.00	0.0 - 3.2	1.00	1.0 - 1.0		
>0	92.11	83.6 - 97.0	38.26	29.4 - 47.8	1.49	1.3 - 1.7	0.21	0.09 - 0.5
>1	77.63	66.6 - 86.4	61.74	52.2 - 70.6	2.03	1.6 - 2.6	0.36	0.2 - 0.6
>2	72.37	60.9 - 82.0	72.17	63.0 - 80.1	2.60	1.9 - 3.6	0.38	0.3 - 0.6
>3	64.47	52.7 - 75.1	79.13	70.6 - 86.1	3.09	2.1 - 4.6	0.45	0.3 - 0.6
>4	56.58	44.7 - 67.9	83.48	75.4 - 89.7	3.42	2.2 - 5.4	0.52	0.4 - 0.7
>5	48.68	37.0 - 60.4	87.83	80.4 - 93.2	4.00	2.3 - 6.9	0.58	0.5 - 0.7
>6	43.42	32.1 - 55.3	88.70	81.4 - 93.8	3.84	2.2 - 6.8	0.64	0.5 - 0.8

[0134] 表12

[0135] 从阳性食物的数量预测IBS状态的性能指标

[0136] 使用ELISA信号的第90百分位数以确定阳性

性别	作为分界的阳性食物的编号	敏感度	特异度	阳性预测值	阴性预测值	总体百分数一致性
F	1	0.96	0.35	0.73	0.80	0.74
	2	0.82	0.53	0.76	0.64	0.72
	3	0.77	0.62	0.78	0.60	0.71
	4	0.68	0.67	0.79	0.54	0.68
	5	0.63	0.71	0.80	0.50	0.66
	6	0.57	0.76	0.81	0.50	0.64
	7	0.52	0.81	0.83	0.48	0.62
	8	0.46	0.85	0.84	0.46	0.60
	9	0.41	0.88	0.85	0.45	0.57
	10	0.34	0.88	0.85	0.43	0.54
	11	0.28	0.90	0.85	0.42	0.51
	12	0.21	0.94	0.85	0.40	0.48
	13	0.18	0.94	0.86	0.39	0.46
	14	0.15	0.95	0.89	0.39	0.45
	15	0.13	1.00	1.00	0.39	0.44
	16	0.11	1.00	1.00	0.38	0.43
	17	0.10	1.00	1.00	0.38	0.42
	18	0.07	1.00	1.00	0.38	0.41
	19	0.06	1.00	1.00	0.37	0.40
	20	0.04	1.00	1.00	0.37	0.39
	21	0.03	1.00	1.00	0.37	0.38
	22	0.03	1.00	1.00	0.36	0.37
	23	0.00	1.00	1.00	0.36	0.36
	24	0.00	1.00	1.00	0.36	0.36

[0137]

[0138] 表13

[0139] 从阳性食物的数量预测IBS状态的性能指标

[0140] 使用ELISA信号的第90百分位数以确定阳性

[0141]

性别	作为分界的阳性食物的编号	敏感度	特异度	阳性预测值	阴性预测值	总体百分数一致性
M	1	0.81	0.35	0.29	0.85	0.46
	2	0.71	0.57	0.35	0.86	0.61
	3	0.67	0.68	0.41	0.86	0.68
	4	0.62	0.75	0.45	0.86	0.72
	5	0.53	0.80	0.48	0.84	0.74
	6	0.47	0.85	0.50	0.83	0.76
	7	0.39	0.88	0.50	0.82	0.76
	8	0.30	0.90	0.50	0.80	0.75
	9	0.25	0.92	0.50	0.79	0.75
	10	0.18	0.93	0.43	0.78	0.74
	11	0.14	0.94	0.43	0.77	0.74
	12	0.11	0.95	0.40	0.77	0.75
	13	0.10	0.96	0.43	0.76	0.75
	14	0.07	0.97	0.50	0.76	0.75
	15	0.06	0.97	0.50	0.76	0.75
	16	0.06	0.98	0.50	0.76	0.75
	17	0.05	0.98	0.33	0.76	0.75
	18	0.00	0.98	0.00	0.75	0.75
	19	0.00	0.98	0.00	0.75	0.75
	20	0.00	1.00	0.00	0.75	0.75
	21	0.00	1.00	0.00	0.75	0.75
	22	0.00	1.00	0.00	0.75	0.75
	23	0.00	1.00	0.00	0.75	0.75
	24	0.00	1.00	.	0.75	0.75

[0142] 表14

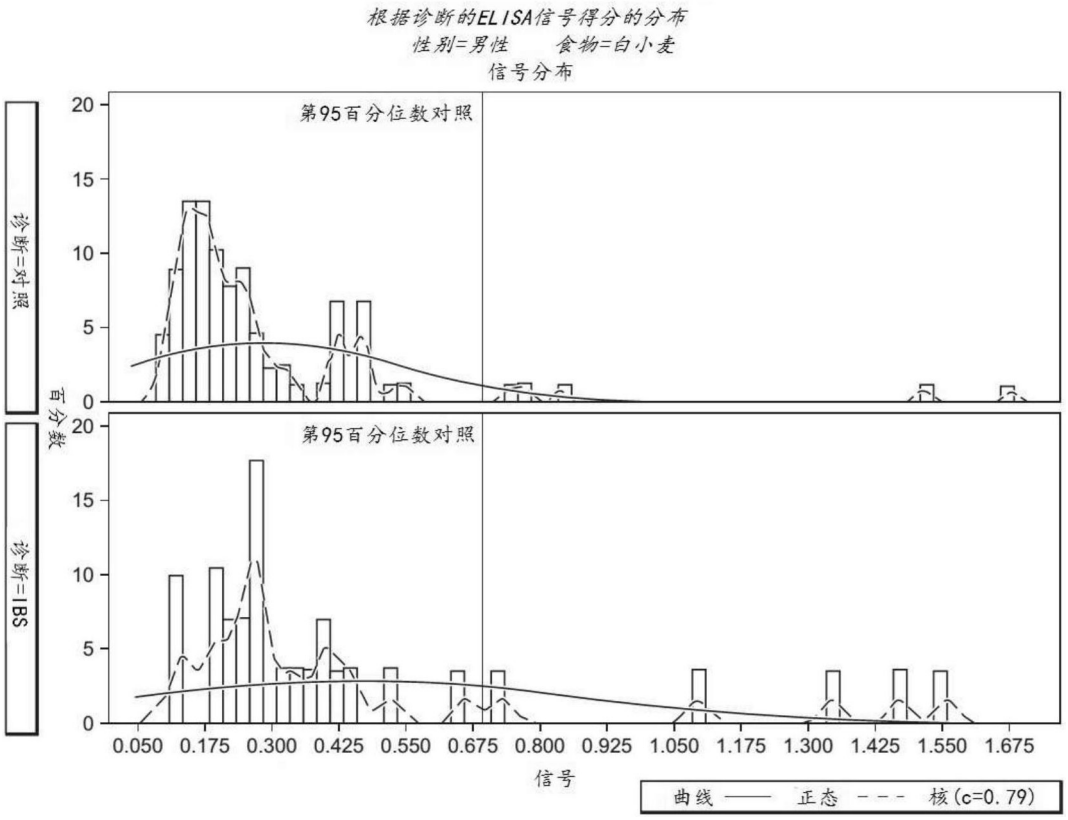

根据诊断的ELISA信号得分的分布
性别=男性 食物=白小麦
信号分布
诊断=对照
诊断=IBS
第95百分位数对照
第95百分位数对照
百分数
0.050 0.175 0.300 0.425 0.550 0.675 0.800 0.925 1.050 1.175 1.300 1.425 1.550 1.675
信号
曲线 —— 正态 - - - 核(c=0.79)

图1A

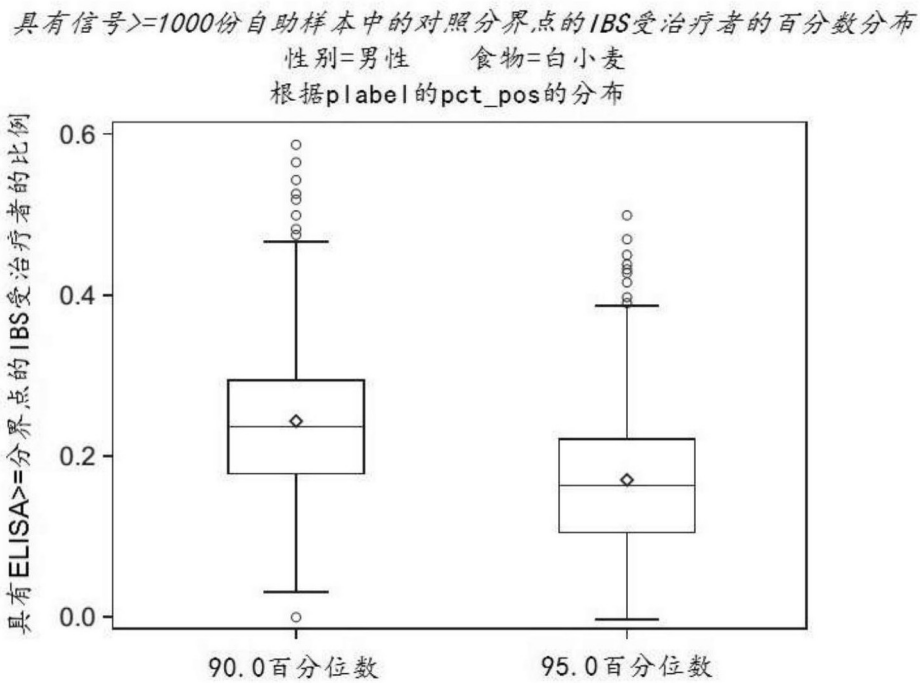

具有信号>=1000份自助样本中的对照分界点的IBS受治疗者的百分数分布
性别=男性 食物=白小麦
根据plabel的pct_pos的分布
具有ELISA>=分界点的IBS受治疗者的比例
90.0百分位数
95.0百分位数

图1B

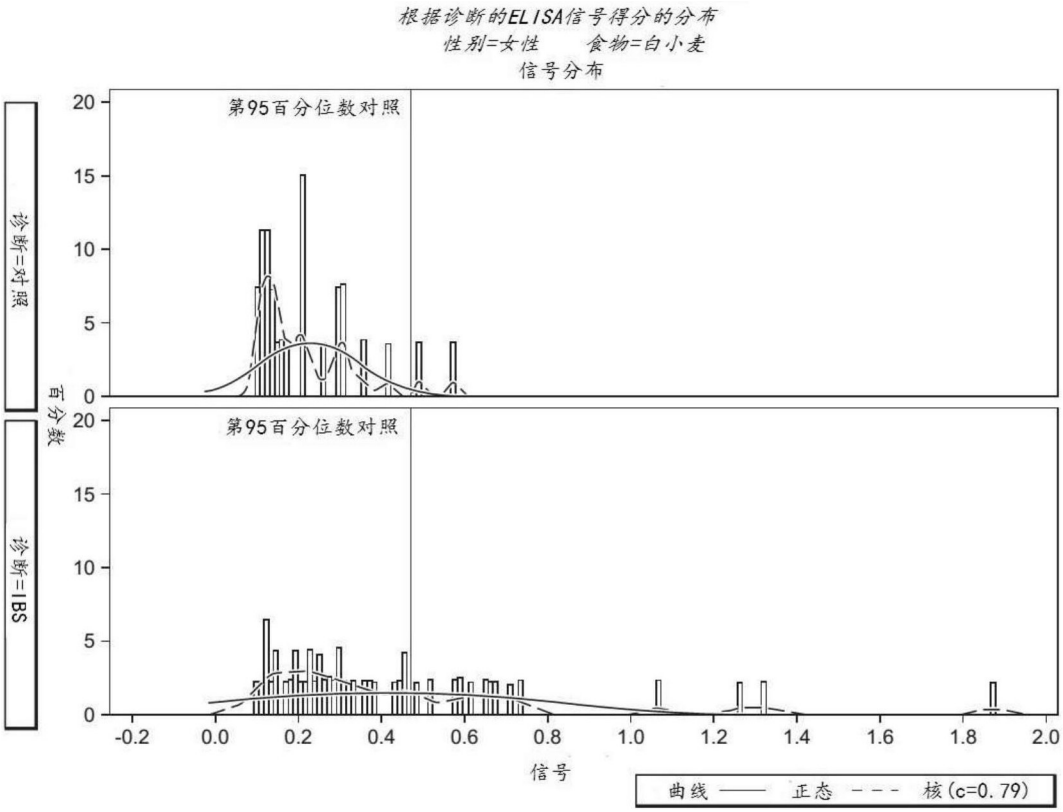

根据诊断的ELISA信号得分的分布
性别=女性 食物=白小麦
信号分布
第95百分位数对照
第95百分位数对照
诊断=对照
诊断=IBS
频率
信号
曲线 —— 正态 - - - 核(c=0.79)

图1C

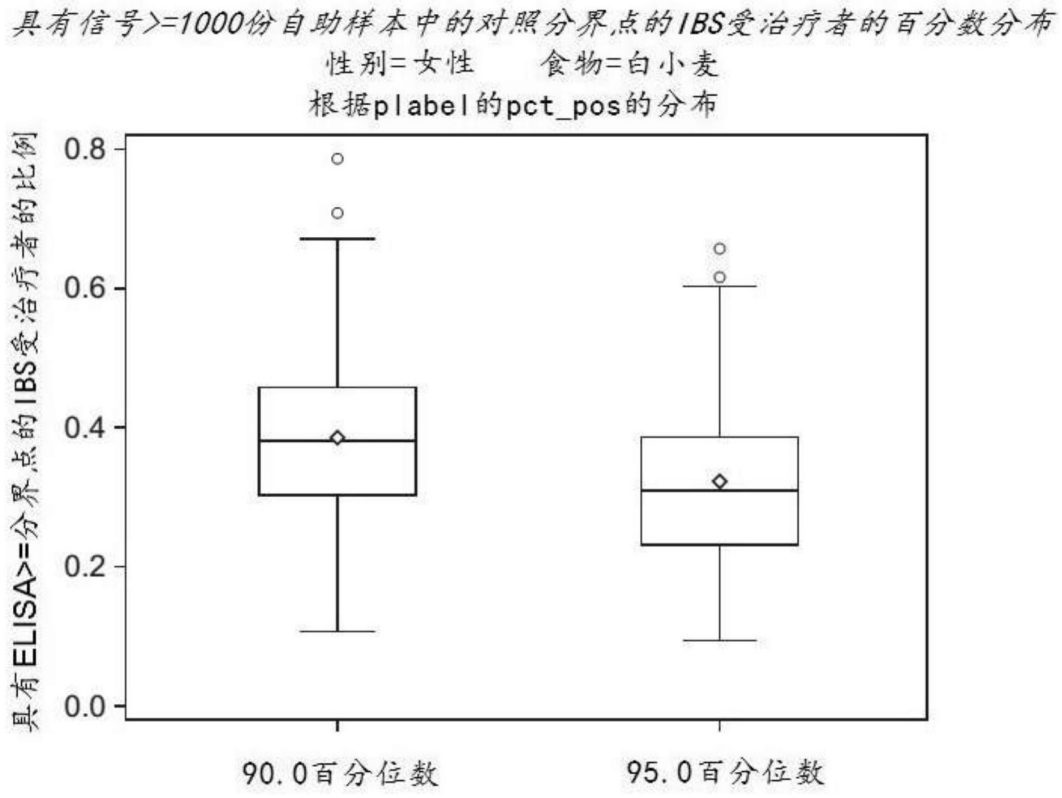

具有信号>=1000份自助样本中的对照分界点的IBS受治疗者的百分数分布
性别=女性 食物=白小麦
根据plabel的pct_pos的分布
具有ELISA>=分界点的IBS受治疗者的比例
90.0百分位数
95.0百分位数

图1D

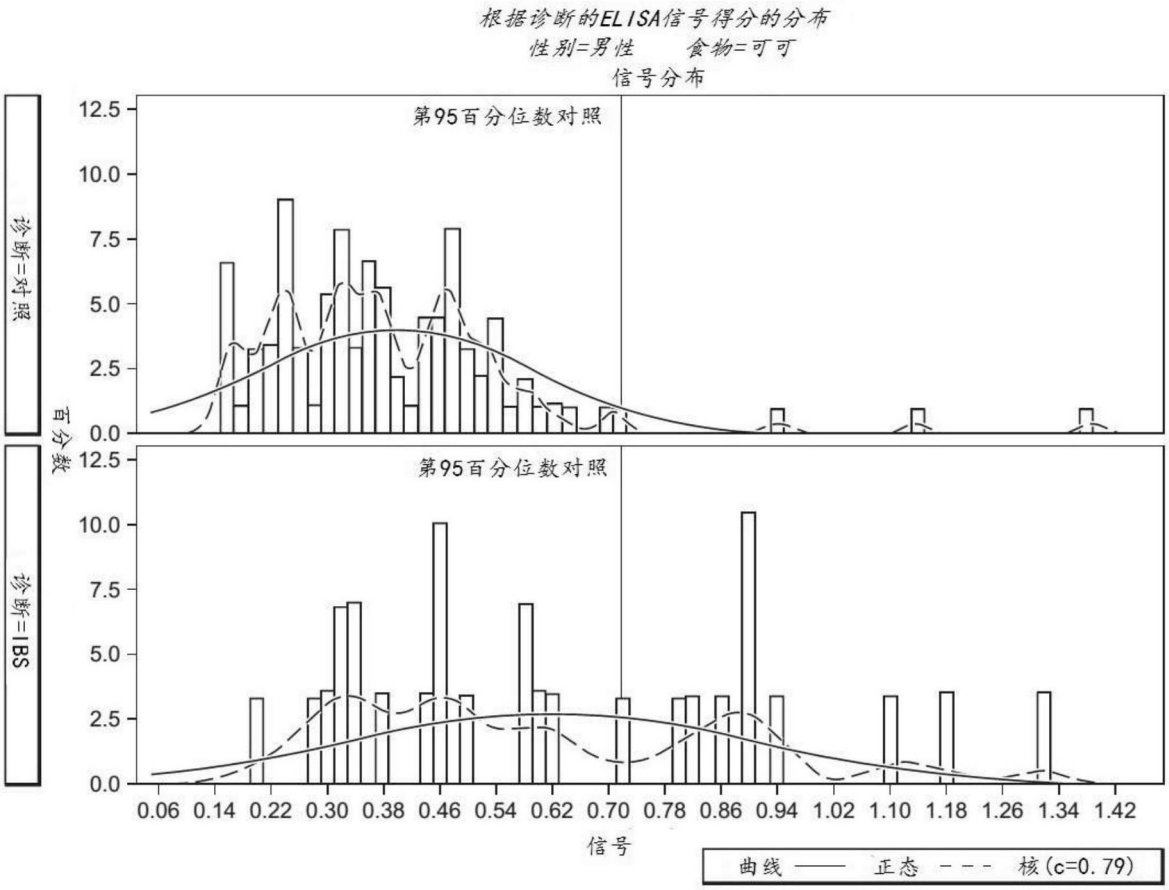

根据诊断的ELISA信号得分的分布
性别=男性 食物=可可
信号分布
诊断=对照
诊断=IBS
第95百分位数对照
第95百分位数对照
百分数
12.5
10.0
7.5
5.0
2.5
0.0
0.06 0.14 0.22 0.30 0.38 0.46 0.54 0.62 0.70 0.78 0.86 0.94 1.02 1.10 1.18 1.26 1.34 1.42
信号
曲线 —— 正态 - - - 核(c=0.79)

图2A

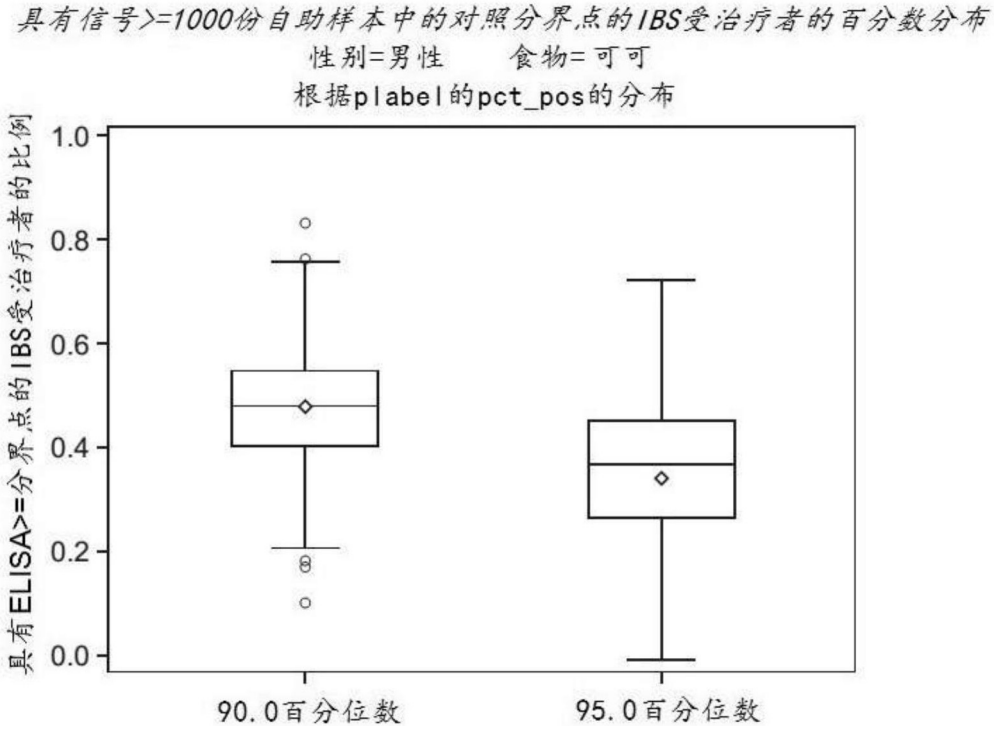

具有信号>=1000份自助样本中的对照分界点的IBS受治疗者的百分数分布
性别=男性 食物=可可
根据plabel的pct_pos的分布
具有ELISA>=分界点的IBS受治疗者的比例
1.0
0.8
0.6
0.4
0.2
0.0
90.0百分位数
95.0百分位数

图2B

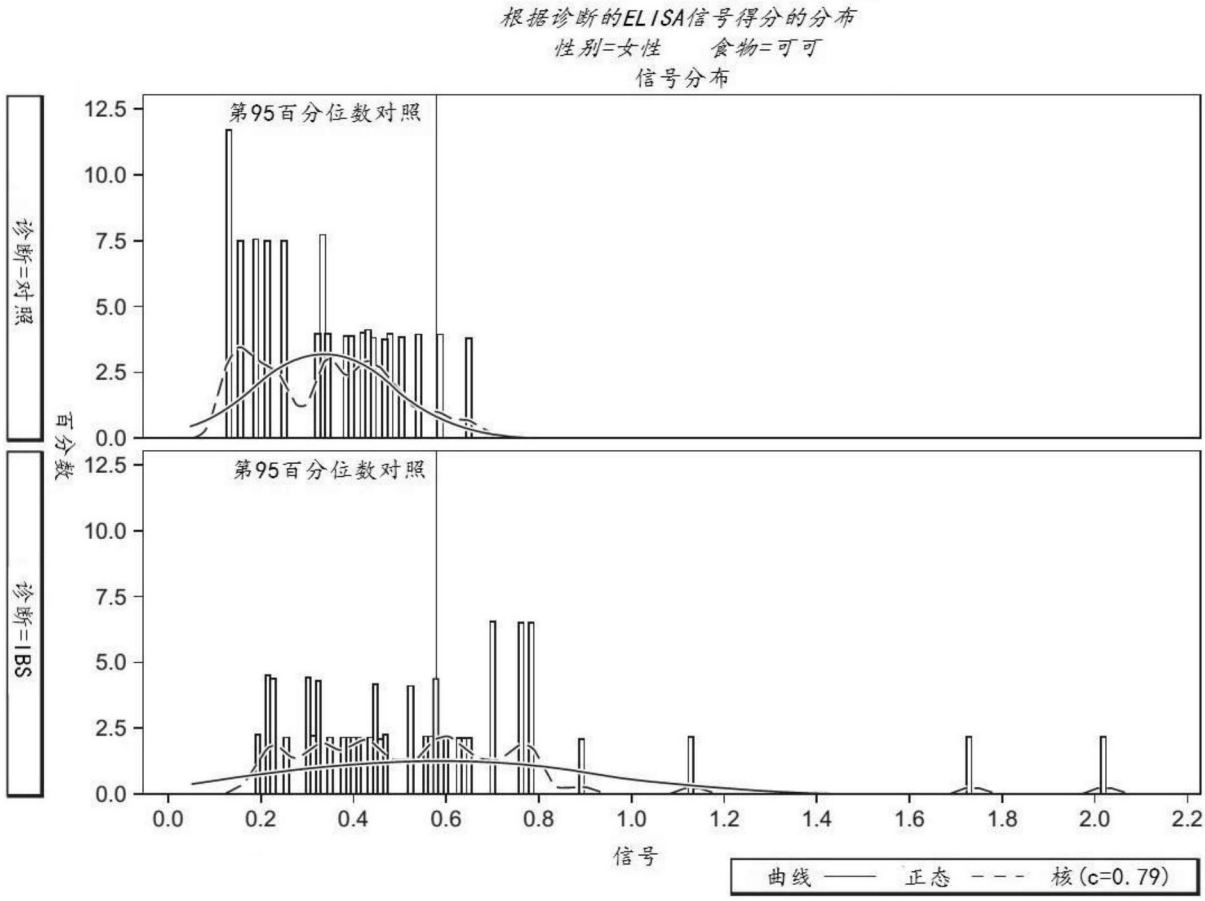

根据诊断的ELISA信号得分的分布
性别=女性 食物=可可
信号分布
诊断=对照
诊断=IBS
第95百分位数对照
第95百分位数对照
百分数
12.5
10.0
7.5
5.0
2.5
0.0
0.0
0.2
0.4
0.6
0.8
1.0
1.2
1.4
1.6
1.8
2.0
2.2
信号
曲线 —— 正态 - - - 核(c=0.79)

图2C

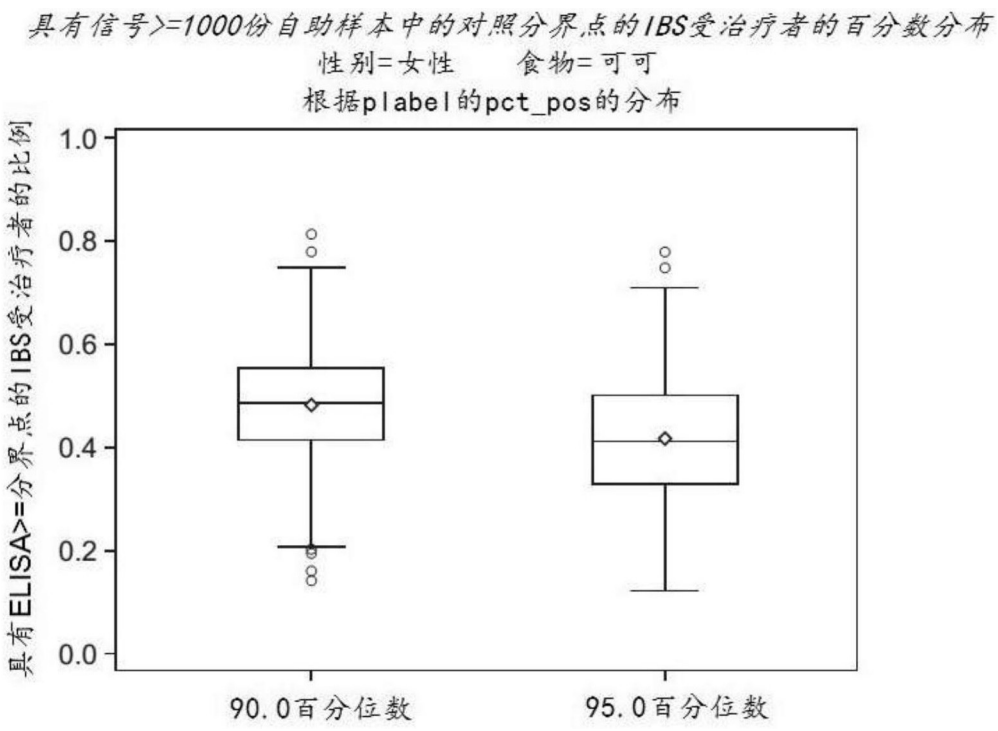

具有信号>=1000份自助样本中的对照分界点的IBS受治疗者的百分数分布
性别=女性 食物=可可
根据plabel的pct_pos的分布
具有ELISA>=分界点的IBS受治疗者的比例
1.0
0.8
0.6
0.4
0.2
0.0
90.0百分位数
95.0百分位数

图2D

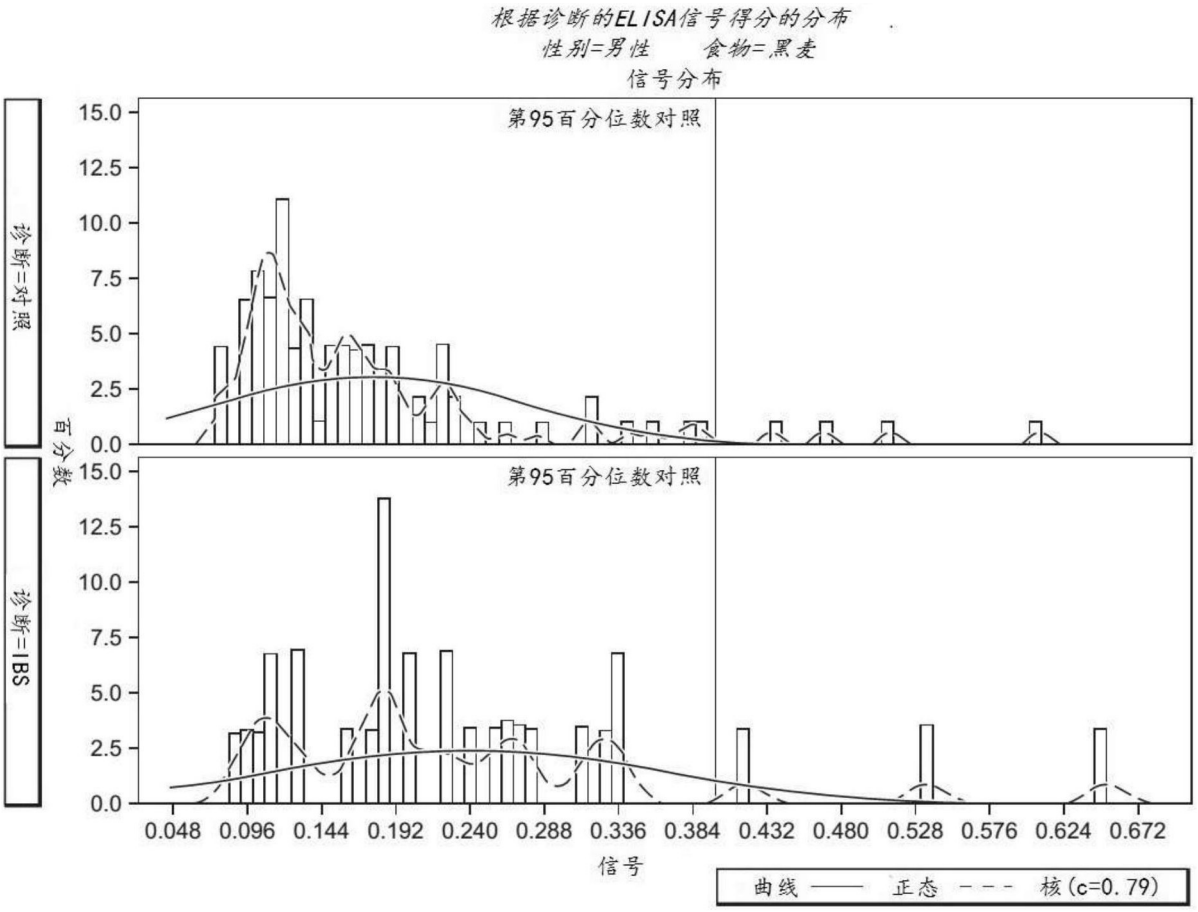

根据诊断的ELISA信号得分的分布
性别=男性 食物=黑麦
信号分布
诊断=对照
诊断=IBS
第95百分位数对照
第95百分位数对照
百分数
15.0
12.5
10.0
7.5
5.0
2.5
0.0
0.048 0.096 0.144 0.192 0.240 0.288 0.336 0.384 0.432 0.480 0.528 0.576 0.624 0.672
信号
曲线 —— 正态 - - - 核(c=0.79)

图3A

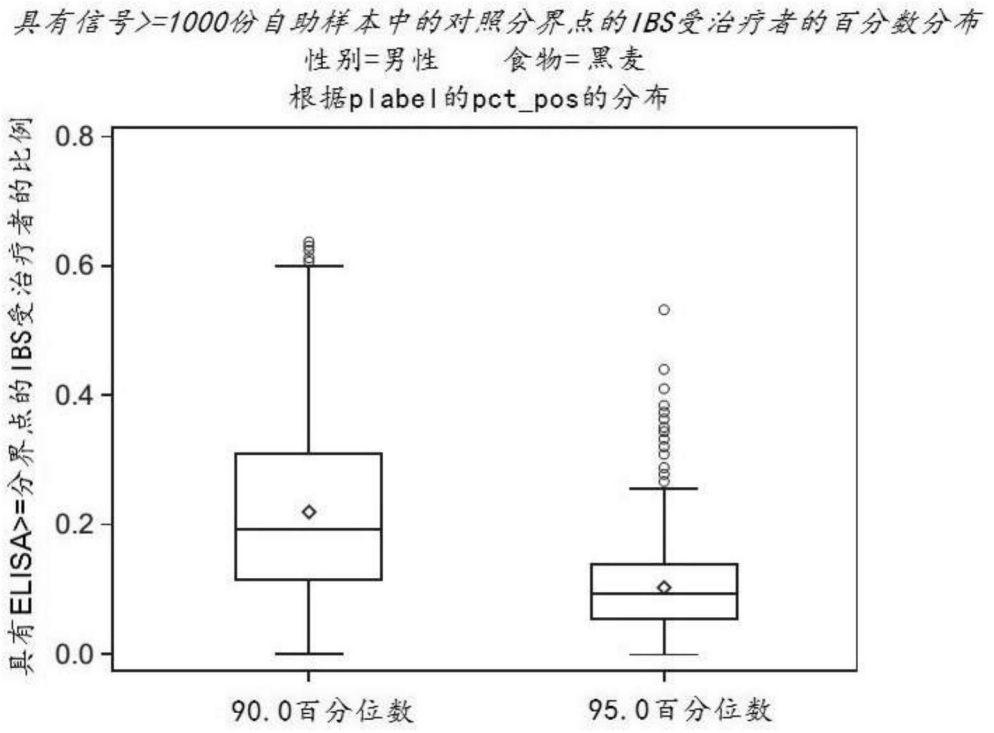

具有信号>=1000份自助样本中的对照分界点的IBS受治疗者的百分数分布
性别=男性 食物=黑麦
根据plabel的pct_pos的分布
具有ELISA>=分界点的IBS受治疗者的比例
0.8
0.6
0.4
0.2
0.0
90.0百分位数
95.0百分位数

图3B

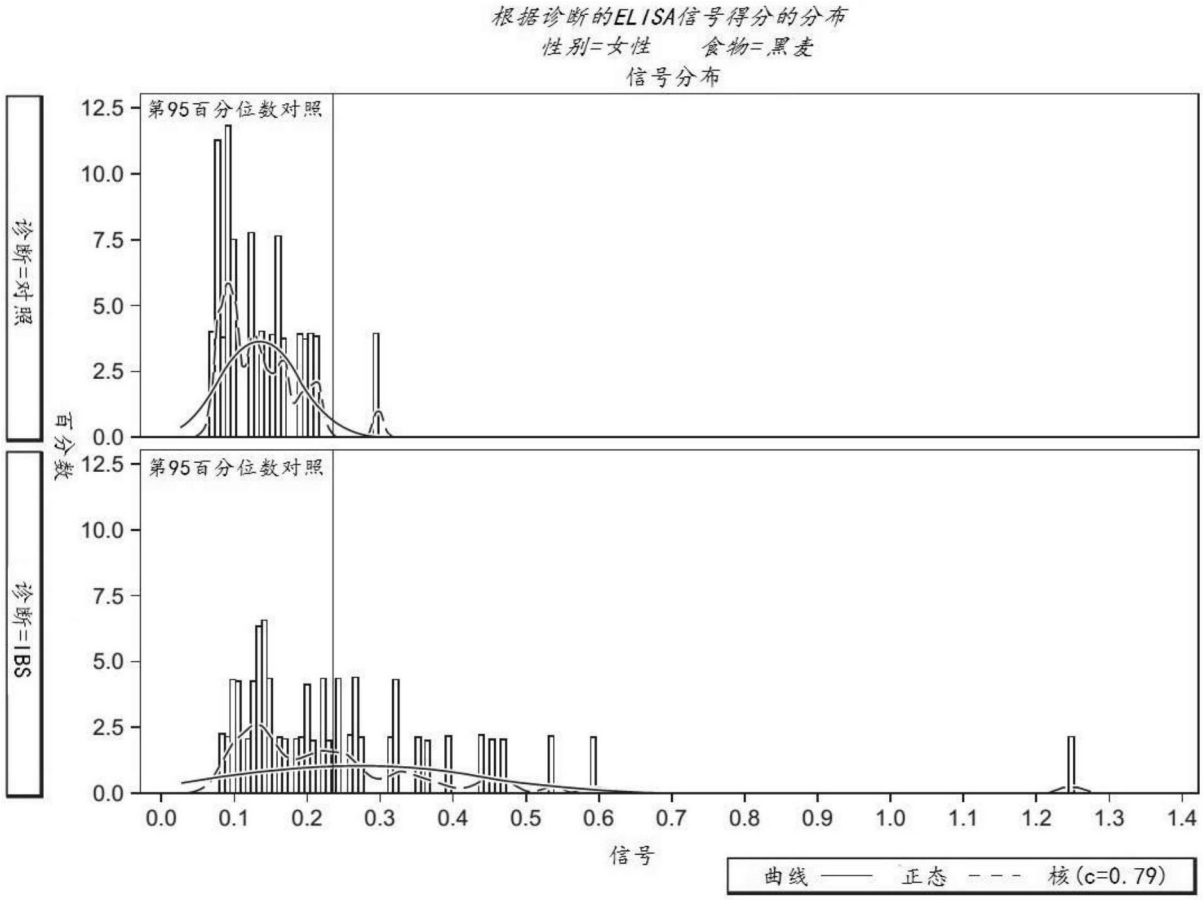

根据诊断的ELISA信号得分的分布
性别=女性 食物=黑麦
信号分布
诊断=对照
诊断=IBS
第95百分位数对照
第95百分位数对照
百分数
12.5
10.0
7.5
5.0
2.5
0.0
0.0 0.1 0.2 0.3 0.4 0.5 0.6 0.7 0.8 0.9 1.0 1.1 1.2 1.3 1.4
信号
曲线 —— 正态 - - - 核(c=0.79)

图3C

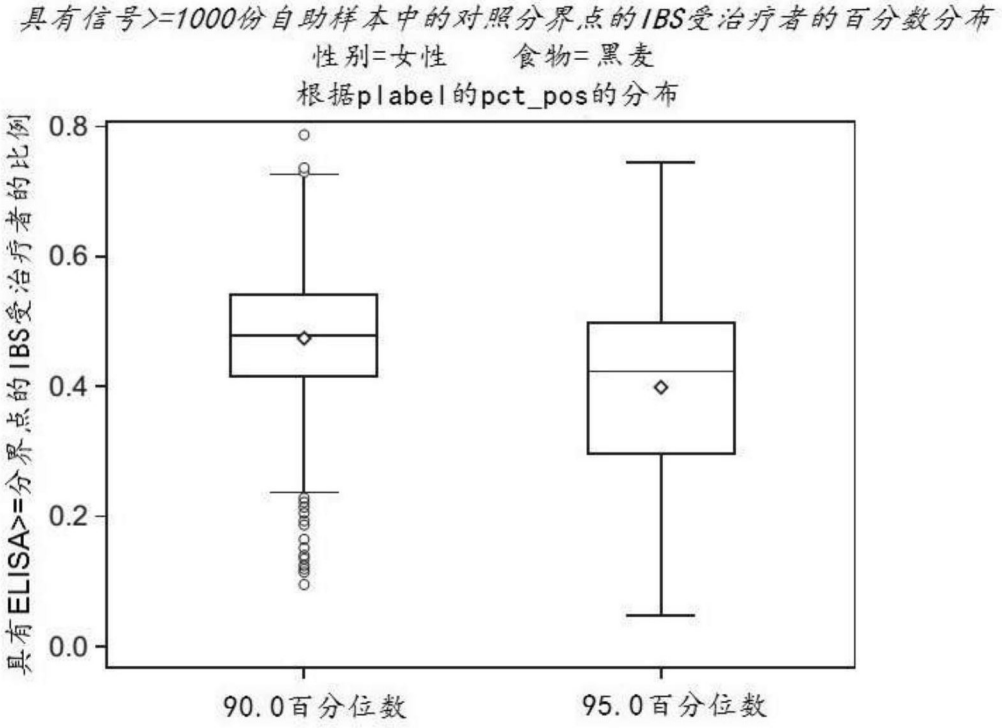

具有信号>=1000份自助样本中的对照分界点的IBS受治疗者的百分数分布
性别=女性 食物=黑麦
根据plabel的pct_pos的分布
具有ELISA>=分界点的IBS受治疗者的比例
0.8
0.6
0.4
0.2
0.0
90.0百分位数
95.0百分位数

图3D

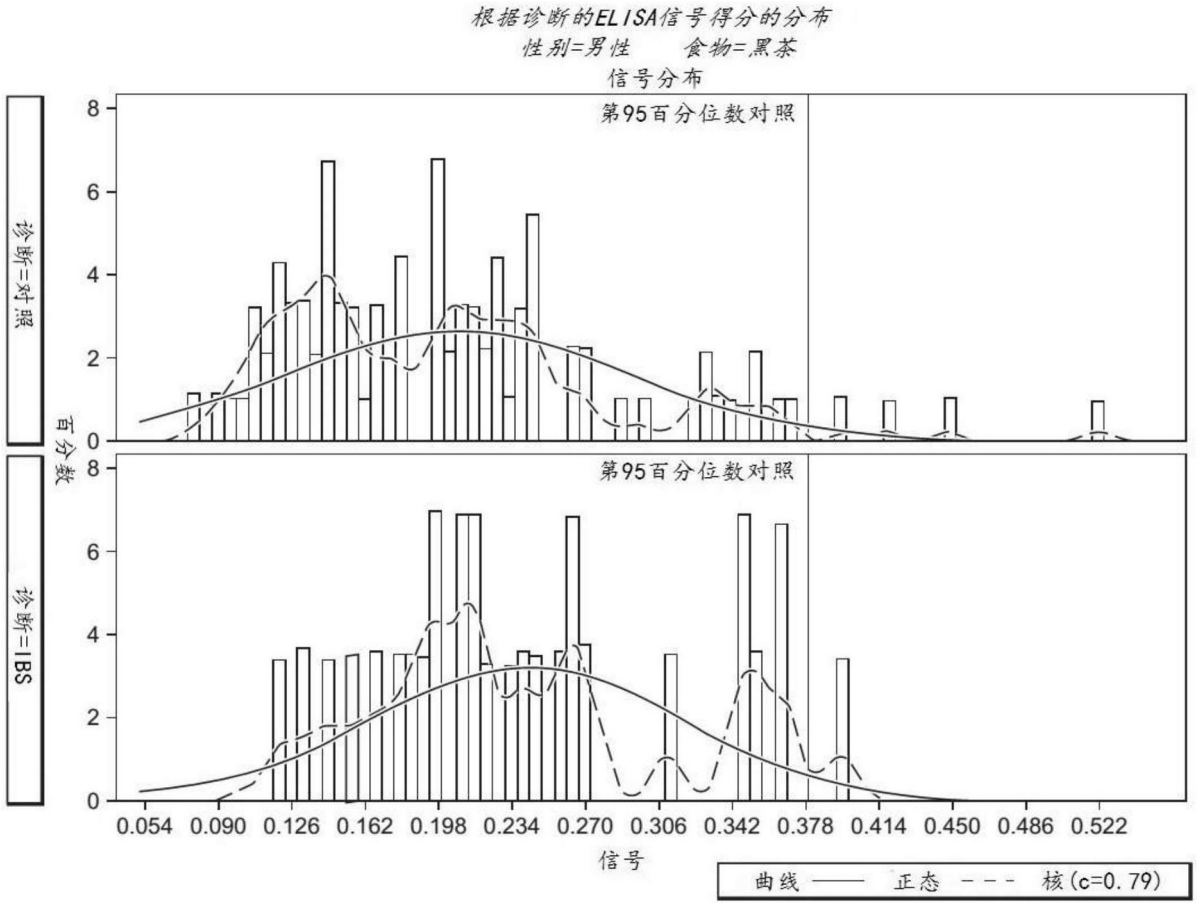

根据诊断的ELISA信号得分的分布
性别=男性 食物=黑茶
信号分布
诊断=对照
诊断=IBS
第95百分位数对照
第95百分位数对照
百分数
0
2
4
6
8
0.054 0.090 0.126 0.162 0.198 0.234 0.270 0.306 0.342 0.378 0.414 0.450 0.486 0.522
信号
曲线 —— 正态 - - - 核(c=0.79)

图4A

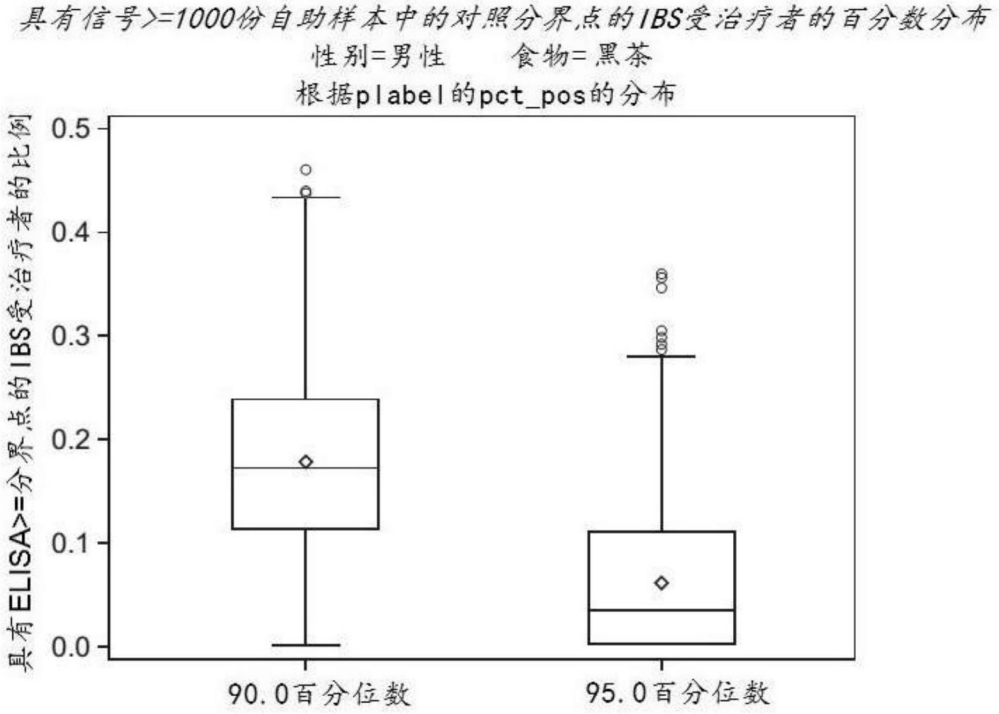

具有信号>=1000份自助样本中的对照分界点的IBS受治疗者的百分数分布
性别=男性 食物=黑茶
根据plabel的pct_pos的分布
具有ELISA>=分界点的IBS受治疗者的比例
0.5
0.4
0.3
0.2
0.1
0.0
90.0百分位数
95.0百分位数

图4B

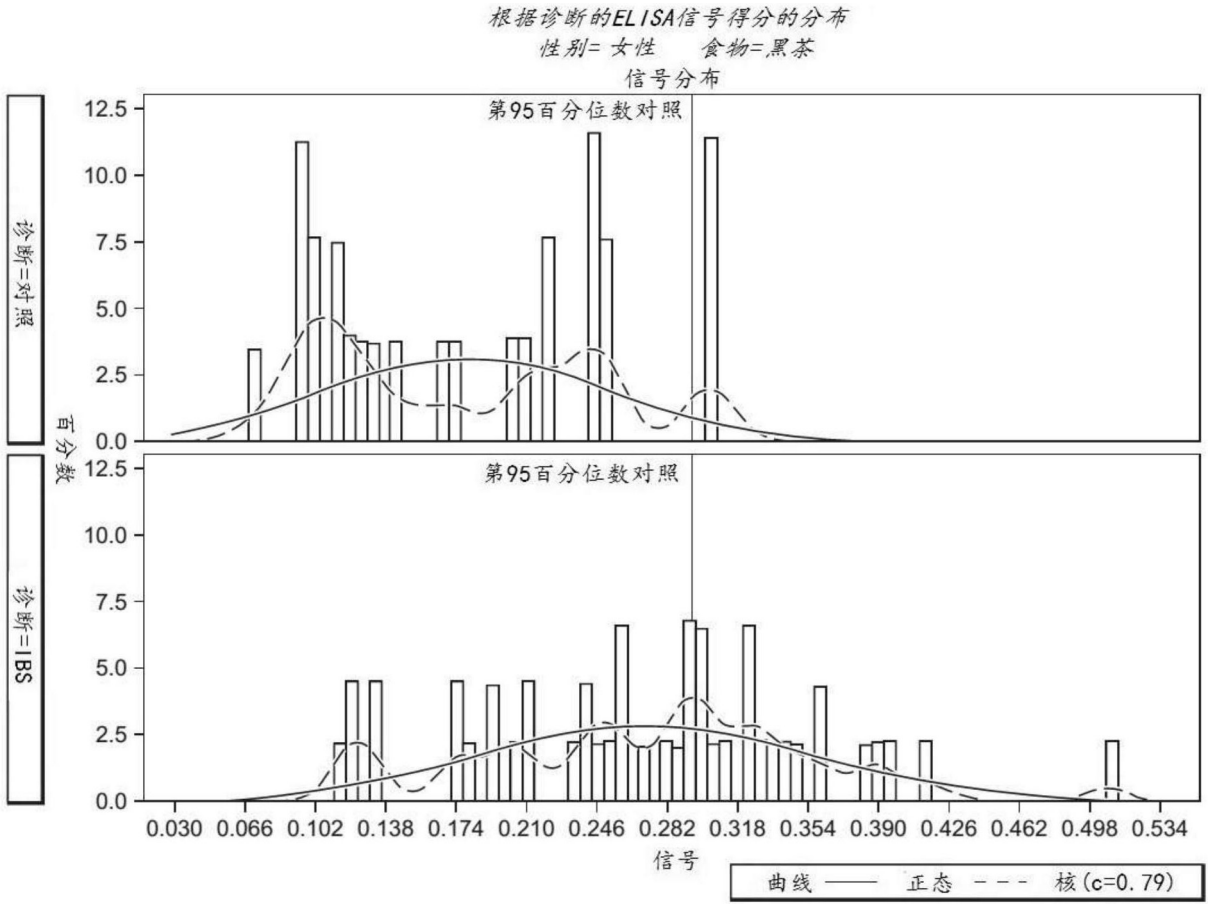

根据诊断的ELISA信号得分的分布
性别= 女性 食物=黑茶
信号分布
诊断=对照
诊断=IBS
第95百分位数对照
第95百分位数对照
百分数
12.5
10.0
7.5
5.0
2.5
0.0
0.030 0.066 0.102 0.138 0.174 0.210 0.246 0.282 0.318 0.354 0.390 0.426 0.462 0.498 0.534
信号
曲线 —— 正态 - - - 核(c=0.79)

图4C

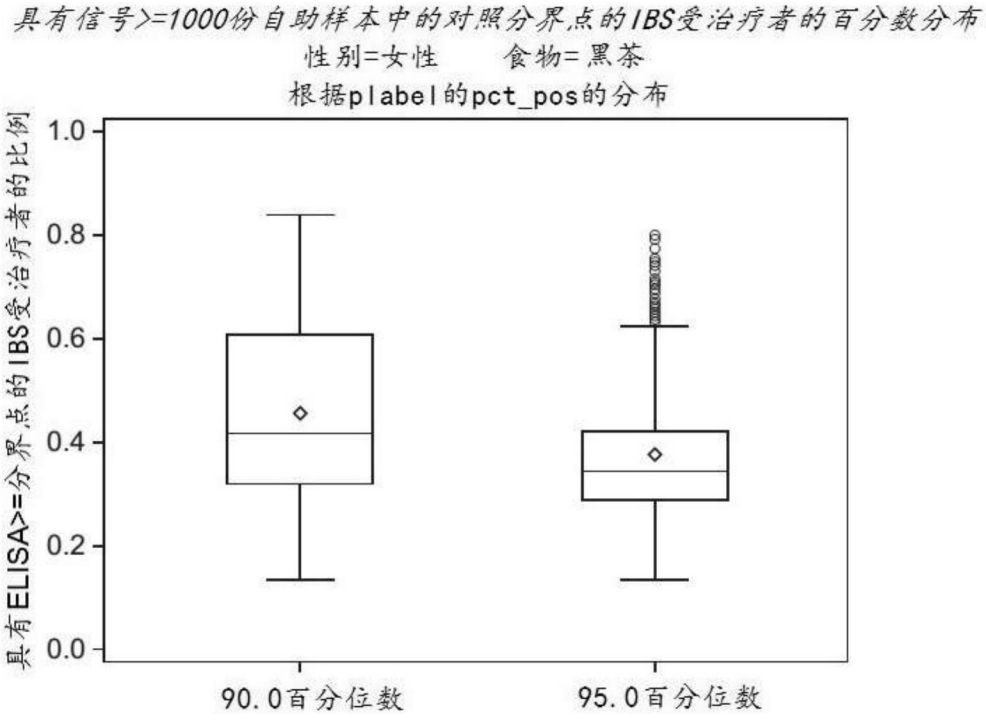

具有信号>=1000份自助样本中的对照分界点的IBS受治疗者的百分数分布
性别=女性 食物=黑茶
根据plabel的pct_pos的分布
具有ELISA>=分界点的IBS受治疗者的比例
1.0
0.8
0.6
0.4
0.2
0.0
90.0百分位数
95.0百分位数

图4D

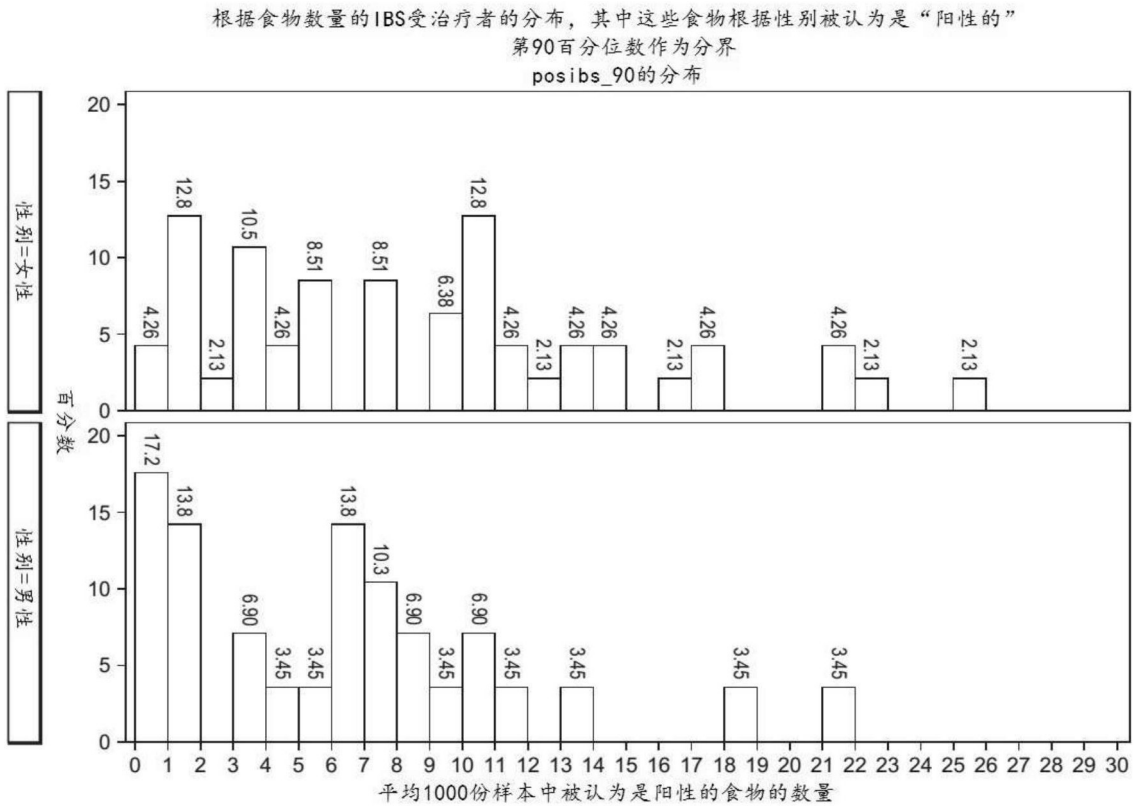

根据食物数量的IBS受治疗者的分布，其中这些食物根据性别被认为是“阳性的”
第90百分位数作为分界
posibs_90的分布
性别=女性
性别=男性
百分数
平均1000份样本中被认为是阳性的食物的数量

图5A

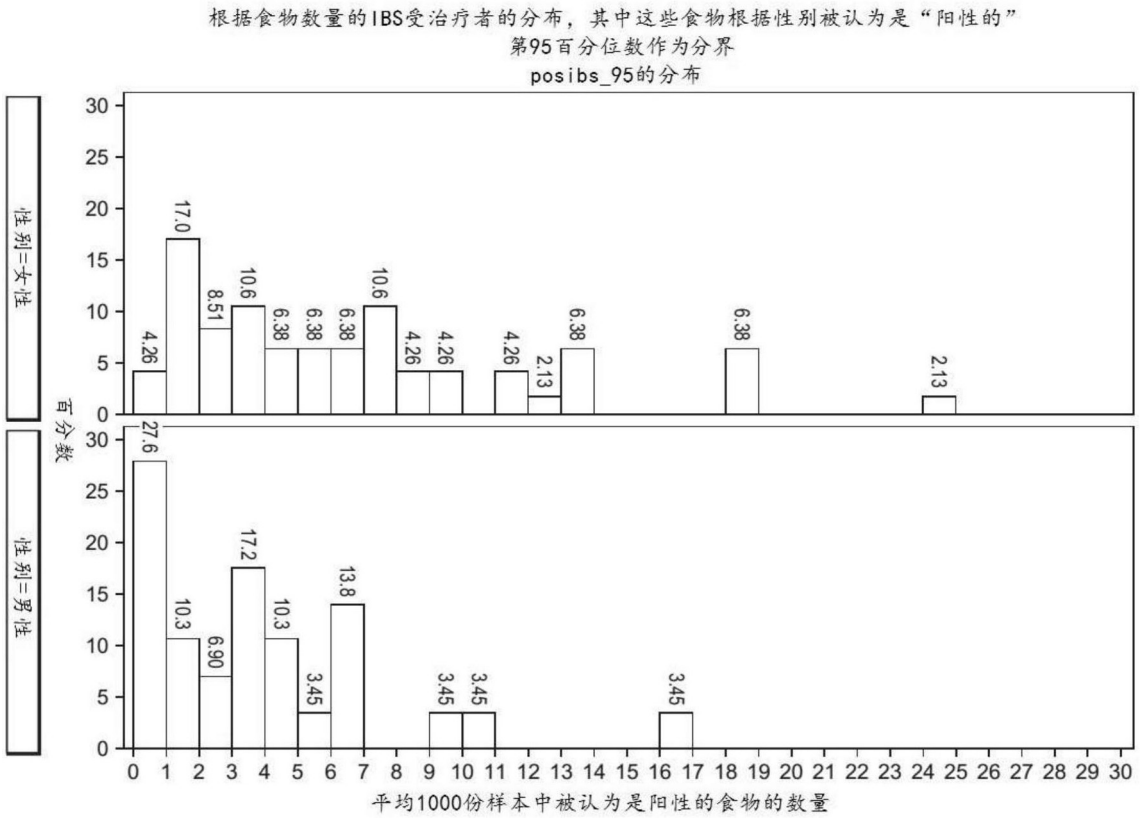

根据食物数量的IBS受治疗者的分布，其中这些食物根据性别被认为是“阳性的”
第95百分位数作为分界
posibs_95的分布
性别=女性
性别=男性
百分数
平均1000份样本中被认为是阳性的食物的数量

图5B

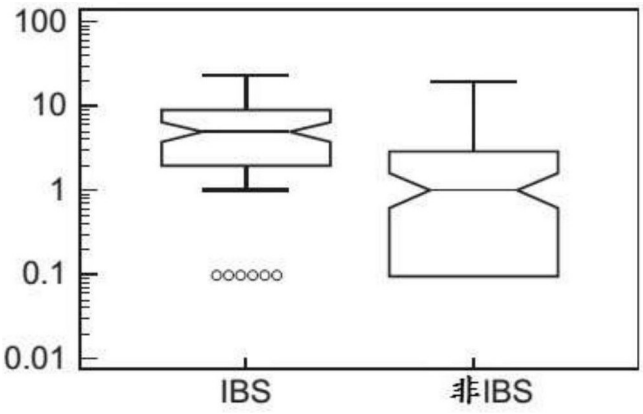

IBS
非IBS

图6A

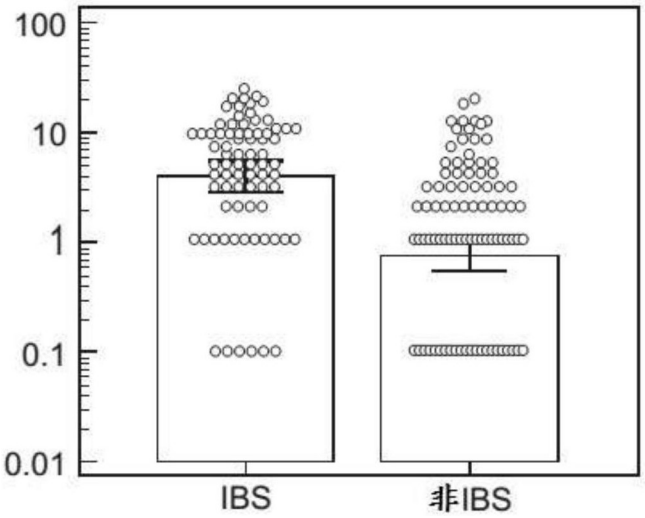


图6B

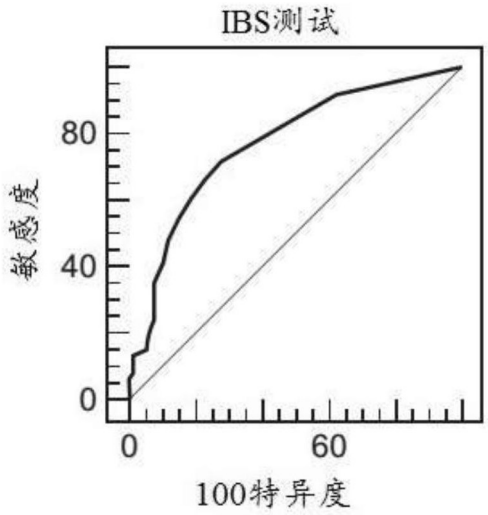


图7