(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
29 May 2008 (29.05.2008)

PCT

(10) International Publication Number
WO 2008/064336 A2

(51) International Patent Classification:
G01N 33/53 (2006.01)

(21) International Application Number:
PCT/US2007/085432

(22) International Filing Date:
21 November 2007 (21.11.2007)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/867,022 22 November 2006 (22.11.2006) US

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

(84) Designated States *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:
— *without international search report and to be republished upon receipt of that report*

WO 2008/064336 A2

(54) Title: AUTOIMMUNE DISEASE BIOMARKERS

(57) Abstract: Provided herein are novel panels of biomarkers for the diagnosis of autoimmune diseases, and methods and kits for detecting these biomarkers in samples of individuals suspected of having an autoimmune disease. Also provided are methods of monitoring the progression of an autoimmune disease and methods of monitoring the efficacy and side effects of a treatment for an autoimmune disease.

AUTOIMMUNE DISEASE BIOMARKERS

CROSS-REFERENCE TO RELATED APPLICATIONS

[001] This application claims benefit of U.S. Provisional Application no. 60/867,022, filed November 22, 2006, which is incorporated by reference in its entirety herein to the extent that there is no inconsistency with the present disclosure.

BACKGROUND OF THE INVENTION

[002] This invention generally relates to biomarkers associated with autoimmune diseases, specifically Rheumatoid Arthritis (RA), Systemic Lupus Erythematosus (SLE) and Anti-Neutrophil Cytoplasmic Antibody (ANCA) associated diseases, and methods, compositions and kits for the diagnosis, prognosis, and monitoring the progression of autoimmune diseases.

[003] The development of autoantibodies is observed in autoimmune disorders and numerous cancers. Because of this, proteins targeted by autoantibodies (herein referred to as "autoantigens") are effective biomarkers and form the basis of potential diagnostic and prognostic assays, as well as approaches for monitoring disease progression and response to treatment. The effective use of autoantigen biomarkers for these applications, however, is often contingent upon the identification of not one but multiple biomarkers. This is a consequence of the observation that the development of autoantibodies to any given protein is typically seen only in a fraction of patients (A. Fossa et al., Prostate 59, 440-7 (Jun 1, 2004); S. S. Van Rhee et al., Blood 105, 3939-3944 (2005)). Current methods for the identification of autoantigens are cumbersome, technically challenging, have low sensitivity, and poor reproducibility. It is therefore cumbersome and time-consuming to identify panels of disease-specific markers that could facilitate diagnosing and treating diseases.

[004] One widely utilized approach for autoantigen identification is SEREX: serological analysis of cDNA expression libraries. This approach is most appropriate

for cancer autoantigen identification, and involves the generation of tumor-specific lambda GT11 cDNA expression libraries, followed by immunological screening of plaque lifts using patient sera. The SEREX approach was successfully used to identify the cancer autoantigen NY-ESO-1, a protein that is autoantigenic in ~20-50% of patients overexpressing NY-ESO-1 (Y. T. Chen et al., Proc Natl Acad Sci U S A 94, 1914-8 (1997)). However, while clearly useful, SEREX is not a high throughput approach, it is expensive, labor-intensive, requiring expertise in sophisticated molecular biological techniques, typically has a high false positive rate and, because it relies on bacterial protein expression, cannot identify autoantigens requiring post-translational modifications (U. Sahin et al., Proc Natl Acad Sci U S A 92, 11810-3 (1995)). More recently, reverse phase protein microarrays have been used to identify colon cancer and lung cancer autoantigens (M. J. Nam et al., Proteomics 3, 2108-15 (2003); F. M. Brichory et al., Proc Natl Acad Sci U S A 98, 9824-9 (2001)). These arrays are made by fractionating cancer cell homogenates, arraying them in spots on a microarray, probing them with patient sera, and detecting antibody binding. Mass-spectrometry based techniques are subsequently used to identify the actual autoantigen – a process which can be both time-consuming and tedious.

[005] Functional protein microarrays are another method that may be used to identify biomarkers. These protein microarrays empower investigators with defined high-protein content for profiling serum samples to identify autoantigen biomarkers. Human protein microarrays may contain as many as 1800, 3000, 4000, 5000, 6000, 7000, 8000, 9000, 10,000, 100,000, 500,000 or 1,000,000 or more purified human proteins immobilized on nitrocellulose-coated glass slides. The protein microarrays may be probed with serum from a diseased individual to identify reactive proteins that are potential biomarkers for the disease. Human protein microarrays that contain proteins that are expressed in insect cells are expected to contain appropriate post-translational modifications. Because all proteins are purified under native conditions, immobilized proteins are expected to maintain their native conformations (B. Schweitzer, P. Predki, M. Snyder, Proteomics 3, 2190-9 (2003)).

[006] Autoimmune diseases arise from an overactive immune response against the body's own cells and tissues. Today there are many human diseases classified as either definite or probable autoimmune diseases, the prominent examples being

Systemic Lupus Erythematosus, Sjögren's syndrome and Rheumatoid Arthritis. The causes of autoimmune diseases are often unknown and the symptoms can appear without warning or apparent cause. Diagnosis of autoimmune diseases can be difficult because symptoms can vary greatly from person to person and are easily confused with other disorders. Diagnosis of autoimmune disorders largely rests on accurate medical history and physical examination of the patient in conjunction with abnormalities observed in routine laboratory tests. In several systemic disorders, serological assays which can detect specific autoantibodies can be employed. However, current tests are often inconclusive and inaccurate. The ability to screen a patient for multiple biomarkers associated with autoimmune diseases would improve diagnosis and treatment of the diseases.

[007] Rheumatoid arthritis (RA) is a chronic, inflammatory autoimmune disease that causes the immune system to attack the joints. It is a disabling and painful inflammatory condition, which can lead to substantial loss of mobility due to pain and joint destruction. The disease is also systemic in that it often also affects many extra-articular tissues throughout the body including the skin, blood vessels, heart, lungs, and muscles. Rheumatoid arthritis can be difficult to diagnose. Symptoms differ from person to person and can be more severe in some people than in others. Within the same person, the full range of symptoms may develop over time, and only a few symptoms may be present in the early stages. Also, symptoms can be similar to those of other types of arthritis and joint conditions, and it may take some time for other conditions to be ruled out. Additionally, there is no single test for the disease. One common test used to help diagnose RA is for rheumatoid factor, an antibody that is present eventually in the blood of most people with the disease. Not all people with RA test positive for rheumatoid factor, however, especially early in the disease. Also, some people test positive for rheumatoid factor, yet never develop the disease. Another test assesses the presence of anti-citrullinated protein (ACP) antibodies. Other common laboratory tests include a white blood cell count, a blood test for anemia, and a test of the erythrocyte sedimentation rate, which measures inflammation in the body.

[008] Systemic lupus erythematosus (SLE or lupus) is a chronic, potentially debilitating or fatal autoimmune disease in which the immune system attacks the

body's cells and tissue, resulting in inflammation and tissue damage. SLE can affect any part of the body, but often harms the heart, joints (rheumatological), skin, kidneys, lungs, blood vessels and brain/nervous system. Some of the most common symptoms of the disease include extreme fatigue, painful or swollen joints (arthritis), unexplained fever, skin rashes, and kidney problems; however, no two cases of lupus are exactly alike. Signs and symptoms vary considerably from person to person, may come on suddenly or develop slowly, may be mild or severe, and may be temporary or permanent. Even the distinctive rash that gives the disease its name does not occur in every case. Additionally, the problems associated with the disease change over time and overlap with those of many other disorders. For these reasons, doctors may not initially consider lupus until the signs and symptoms become more obvious. Even then, lupus can be challenging to diagnose because nearly all people with lupus experience fluctuations in disease activity. Lupus can be effectively treated with drugs, mainly with immunosuppression, though there is currently no cure for this disease.

[009] Currently, no single test can determine whether a person has lupus, but several laboratory tests may help a physician to make a diagnosis. For example, the antinuclear antibody (ANA) test is commonly used to look for autoantibodies that react against components of the cell nucleus. Most people with lupus test positive for ANA; however, there are a number of other causes of a positive ANA besides lupus, including infections, other autoimmune diseases, and a positive ANA may occasionally be found in healthy individuals. The ANA test is thus not definitive for lupus, but is only one of a number of considerations used in making a diagnosis. Other laboratory tests are used to monitor the progress of lupus or its symptoms, once it has been diagnosed. A complete blood count, urinalysis, blood chemistries, and the erythrocyte sedimentation rate (ESR) test can provide valuable information on the stage or progression of the disease. Another common test measures the blood level of proteins of the complement system. People with lupus often have increased ESRs and low complement levels, especially during flare-ups of the disease.

[0010] Anti-neutrophil cytoplasmic antibodies (ANCAs) are antibodies against molecules in the cytoplasm of neutrophil granulocytes and monocyte lysosomes

(Niles et al., Arch Intern Med 156, 440-5 (1996)). They are detected in a number of autoimmune disorders, but are particularly associated with systemic vasculitis. ANCA-associated vasculitis is the most common primary systemic small-vessel vasculitis to occur in adults (I. Mansi, A. Opran, and F. Rosner, American Family Physician 65, 1615-20 (2002)). ANCA-associated small-vessel vasculitis includes microscopic polyangiitis, Wegener's granulomatosis, Churg-Strauss syndrome, and drug-induced vasculitis. Rapid diagnosis of ANCA-associated diseases is critically important, because life-threatening injury to organs often develops quickly and is mitigated dramatically by immunosuppressive treatment. Less than 10% of patients with clinically and pathologically identical diseases do not have ANCA, and at least 90% of patients with Wegener's granulomatosis, microscopic polyangiitis, and the Churg-Strauss syndrome have either MPO-ANCA or PR3-ANCA (R. Falk and J.C. Jennette, J Am Soc Nephrol 13,1977-1979 (2002)). Thus, there is a loose correlation between ANCA titer and disease activity; however, these studies may be hampered by the imprecision of the ANCA assays themselves. In general, serologic testing for ANCA is recommended for patients with glomerulonephritis, pulmonary hemorrhage, especially pulmonary-renal syndrome, cutaneous vasculitis with systemic features, mononeuritis multiplex or other peripheral neuropathy, long-standing sinusitis or otitis, subglottic tracheal stenosis, and retro-orbital mass.

[0011] The ability to screen a patient for multiple biomarkers associated with autoimmune diseases would improve diagnosis and treatment of the diseases. However, it is unlikely that a single individual marker can accomplish this task. Assay experience with autoimmune diseases and cancer patients has demonstrated that a single antigen is not sufficient to characterize all sera and to differentiate between healthy and diseased individuals. An approach that can identify as many autoimmune biomarkers as possible to generate a serological test will be beneficial so that patients can be selected for therapy based on accurate information regarding their antigenic profile. There is a need in the art for the identification of new biomarkers that can be used in the care and management of autoimmune diseases, for example by the development of a non-invasive, accurate, fast and sensitive assay that utilizes multiple biomarkers for the detection, diagnosis, staging, and monitoring of autoimmune diseases in individuals.

SUMMARY OF THE INVENTION

[0012] The present invention recognizes the need for a reliable test for autoimmune diseases, and in particular for a minimally invasive test that can detect RA, SLE and ANCA.

[0013] The invention is based in part on the discovery of a collection of autoantibody biomarkers for the detection, diagnosis, prognosis, staging, and monitoring of RA, SLE and ANCA. The invention provides biomarkers for autoimmune disease, particularly autoantibody biomarkers, and biomarker detection panels. Furthermore, the invention provides methods of detecting, diagnosing, prognosing, staging, and monitoring RA, SLE and ANCA by detecting biomarkers of the invention in a test sample of an individual.

[0014] The present invention identifies numerous biomarkers that are useful for the detection, diagnosis, staging, and monitoring of autoimmune diseases in individuals. A determination of the presence or absence of an autoimmune disease in an individual does not necessarily require that antibodies against all of the identified antigen biomarkers are present or absent. Similarly, a determination of the presence or absence of an autoimmune disease in an individual does not require that all of the target antigens biomarkers be present in increased or decreased amounts. Art-recognized statistical methods can be used to determine the significance of a specific pattern of antibodies against a plurality of the listed antigen biomarkers, or the significance of a specific pattern of increased or decreased amounts of biomarkers.

[0015] In one aspect of the invention, serum from patients diagnosed with RA, SLE and ANCA as well as healthy patients were profiled against a human protein microarray containing thousands of human proteins used as biomarkers. Numerous proteins on the array were bound by antibodies from patients diagnosed with RA, SLE and ANCA, but not healthy patients. Many of the proteins were selective for RA, SLE or ANCA antibodies showing little or no binding in one or both of the other disease groups. Additionally, serum from patients diagnosed with RA were profiled against a high throughput human protein microarray before and after treatment with a drug used to treat auto-immune disorders. Several proteins had altered patient

antibody levels after treatment compared to the antibody levels for the target proteins before treatment.

[0016] One embodiment of the invention is a method of detecting autoantibodies in a test sample from an individual suspected of having an autoimmune disease by contacting the test sample from the individual with one or more target antigens each comprising an autoantigen of Table 1 (provided below) or a fragment thereof comprising an epitope; and detecting binding of the one or more target antigens, wherein the binding of the one or more target antigens detects the presence of the one or more antibodies in the test sample. In a further embodiment, at least 10%; at least 25%; at least 50%; at least 80%; or at least 95% of the target antigens are bound by one or more antibodies from the test sample. The sample used in the detection and diagnosis methods of the invention can be any type of sample, but preferably is a saliva sample or a blood sample, or a fraction thereof, such as plasma or serum.

[0017] Another embodiment is a method of diagnosing RA in an individual comprising contacting a test sample from the individual with one or more target antigens and detecting binding of the one or more target antigens to one or more antibodies in the test sample, wherein the presence of the one or more antibodies against the one or more target antigens is indicative of rheumatoid arthritis, wherein the one or more target antigens are selected from the group comprising of Table 2 (as provided below) or a fragment thereof comprising an epitope.

[0018] Another embodiment is a method of diagnosing SLE in an individual comprising contacting a test sample from the individual with one or more biomarkers; and detecting binding of the one or more biomarkers to one or more antibodies in the test sample, wherein the presence of the one or more antibodies against the one or more biomarkers is indicative of SLE, wherein the one or more biomarkers are selected from the group comprising of Table 3 (as provided below) or a fragment thereof comprising an epitope.

[0019] Another embodiment is a method of diagnosing ANCA in an individual comprising contacting a test sample from the individual with one or more target

antigens; and detecting binding of the one or more target antigens to one or more antibodies in the test sample, wherein the presence of the one or more antibodies against the one or more target antigens is indicative of ANCA, wherein the one or more target antigens are selected from the group comprising of Table 5 (as provided below) or a fragment thereof comprising an epitope.

[0020] Another embodiment of the present invention is a composition comprising one or more human antibodies from an individual with an autoimmune disease, wherein each antibody is bound to one or more target antigens each comprising an autoantigen of Table 1 or fragments thereof comprising an epitope. The target antigens may be immobilized on a solid support or may be part of a protein microarray. Another embodiment of the present invention is a solid support comprising two or more target antigens each comprising an autoantigen of Table 1 or fragments thereof comprising an epitope; and an immobilized human antibody control, wherein the human antibody control is a positive control for immunodetection.

[0021] The invention also provides kits that include one or more test antigens or one or more target antigens provided herein. The kits can include one or more reagents for detecting binding of an antibody from a sample. In some embodiments, the one or more test antigens or one or more target antigens of a kit are provided bound to a solid support. The invention includes kits that include biomarker detection panels of the invention, including biomarker detection panels in which the target antigens are bound to one or more solid supports. In some embodiments of kits, the kit provides a biomarker detection panel in which the target antigens of the detection panel are bound to a chip or array.

[0022] In some embodiments, the invention provides compositions, kits and methods for detecting one or more identified biomarkers as a diagnostic indicator for an autoimmune disease, such as RA, SLE, or ANCA. Additional uses of the invention include, among others: 1) the detection of one or more identified antigen biomarkers as a tool to select an appropriate therapeutic approach for treatment of a patient with a disease; 2) the use of one or more detected biomarkers as a vaccine candidate or therapeutic target; 3) the use of one or more identified biomarkers as a

screening tool for use in the development of new therapeutics including antibodies; 4) the detection of one or more identified biomarkers as a tool for stratifying patients prior to infliximab (Remicade®) treatment; 5) the detection of one or more identified biomarkers for the early identification of the development of an SLE-like response in RA patients undergoing infliximab treatment; 6) the detection of observed anti-TNFα autoantibody response for the development of improved anti-TNF therapies; and 7) the detection of observed anti-TNFα autoantibody response as a surrogate marker for monitoring patient immune response to infliximab therapy.

BRIEF DESCRIPTION OF THE DRAWINGS

[0023] Figure 1shows a protein microarray comprised of more than 5,000 purified human proteins arrayed in duplicate on nitrocellulose-coated glass slides. Array features are arranged in 48 distinct subarrays, each of which includes unique human proteins and common control elements. An individual subarray is shown in the right panel.

[0024] Figure 2A shows a panel of 12 samples, including sera from healthy donors, as well as lupus, ANCA, and rheumatoid arthritis patients profiled on the 5,000 protein microarrays of Figure 1 at three dilutions and the distribution of signals evaluated. Signal intensity is plotted as a function of the number of features giving rise to signals in the specified range. Figure 2B shows the average background signals plotted for each dilution.

[0025] Figures 3A-3C show three-part statistical analysis of protein microarray data. Background-subtracted signal intensity data was evaluated using three independent statistical approaches, including M-statistics applied to quantile normalized data (Figure 3A), volcano analysis applied to non-normalized data (Figure 3B), and fold change calculations applied to quantile normalized data (Figure 3C). Candidate biomarkers were selected based on the indicated threshold values developed for each analytical measure. The overlap in candidate autoantigens identified using each statistical approach is shown.

[0026] Figure 4 shows signals from immunoreactive proteins identified in the SLE or healthy population based on either M-statistics or volcano analysis (classification

statistic). Proteins ranking in the top 100 on the custom array assays were evaluated against the original 5,000-protein array data to assess the reproducibility of immunoreactive signals. The number of proteins with a calculated p-value <0.01 or a Signal Used difference >1500 that were included on the focused arrays are indicated (solid bars). Values calculated from the custom array data were used to generate a rank order, and proteins ranking in the top 100 on the custom arrays, sorted by either p-value or Signal Used difference, are indicated with hatched bars. The percentage of proteins identified as significant in the original assays that are also in the top 100 on the custom arrays (by each metric) are indicated.

[0027] Figure 5 illustrates separation of populations using Principle Component Analysis. Principle component analysis was carried out on non-normalized signal intensity data derived from all 5,000 human proteins (left panel), a set of 10 SLE-annotated autoantigens (middle panel), or a set of 18 candidate autoantigens (right panel). Three-dimensional representations of the first three principle components are shown. To ensure accurate reporting of the data, each plot is represented as two 180 degree planar rotations. Black spots correspond to normal samples, red spots correspond to SLE samples. Depth cues are provided through changes in color intensity (black to gray and red to pink).

[0028] Figures 6A-6C show immunological profiling using Luminex® technology. Figure 6A shows Luminex® beads from four color regions coupled to goat anti-GST antibody. Anti-GST-conjugated beads from one region were incubated in independent reactions with increasing concentrations of purified recombinant GST. Beads from all four regions were then mixed together and incubated with a second fluorescently labeled anti-GST antibody. Signals were obtained from each bead region and plotted as a function of GST concentration. Figure 6B shows Luminex® beads from eighteen color regions were coupled to goat anti-GST antibody. Anti-GST-conjugated beads from all color regions were incubated in independent reactions with purified recombinant GST-tagged candidate autoantigens. Beads from all regions were then mixed together and incubated with increasing dilutions of serum samples in duplicate. Serum IgG bound to the GST-tagged proteins was detected using a fluorescently labeled anti-human IgG antibody. Median Fluorescence Intensity data for one representative protein is plotted across all serum

dilutions. Error bars indicate standard deviations calculated across the duplicate assays. Figure 6C shows Pearson's Correlation Coefficients calculated from the Median Fluorescence Intensity data generated through Experiment 5 relative to the background-subtracted signal intensity data generated through immunological profiling on the custom arrays.

DETAILED DESCRIPTION OF THE INVENTION

[0029] The invention is based on the identification of autoantigens for autoimmune diseases. Serum samples from healthy individuals as well as patients with autoimmune diseases, such as RA, SLE, and ANCA were profiled on ProtoArray™ human protein micoarrays (Invitrogen Corporation, Carlsbad, CA), to identify multiple disease-specific biomarkers. The extensive content of the arrays, including lower abundance proteins, native conformation, and insect cell-derived post-translational modifications, enabled the identification of biomarkers not previously known to be associated with RA, SLE and/or ANCA.

[0030] A list of antigen biomarkers (profiled using the ProtoArray™ human protein micoarray) that were bound by antibodies from sera from patients diagnosed with an autoimmune disease is shown in Table 1. Proteins that were bound by antibodies from RA, SLE, and ANCA patients, which were not present in normal, healthy individuals, are shown in Tables 2, 3 and 5, respectively. Microarrays, or other assay formats, containing these biomarkers are able to detect the presence of antibodies in a patient sample that bind the biomarkers, enabling the diagnosis and monitoring of the diseases. Microarrays or other assays can contain specific biomarkers or a specific group of biomarkers, such as those associated with RA in Table 2, for detection of antibodies for a specific disease.

[0031] One embodiment of the present invention is a method of detecting one or more target antibodies in a test sample of an individual suspected of having an autoimmune disease comprising: a) contacting the test sample from the individual with one or more target antigens each comprising an autoantigen of Table 1 or a fragment thereof comprising an epitope; and b) detecting binding of the one or more target antigens, wherein the binding of the one or more target antigens detects the presence of the one or more target antibodies in the test sample. In a further

embodiment, the test sample is contacted with two or more; ten or more; twenty or more; fifty or more; or all of the autoantigens of Table 1 or fragments thereof comprising an epitope. In a further embodiment, the quantitative amount of antibodies that bind to each biomarker is determined.

[0032] In a further embodiment, at least 1, 2, 3, 4, 5, 10, 20, 35, 50, 75, 100, 150 or 200 antigen biomarkers must be bound by an antibody from the test sample to indicate the presence of an autoimmune disease.

[0033] Autoimmune diseases, including RA, SLE and ANCA, will have several autoantigens in common with other autoimmune diseases. Autoimmune diseases will also have antigens that are selective for that particular autoimmune disease. The binding of one or more of the autoantigens from Table 1 by an antibody from a patient's test sample will indicate the presence of an autoimmune disease. However, binding of one or more specific autoantigens selective for a particular autoimmune disease may be required to determine which autoimmune disease is present.

[0034] Another embodiment of the present invention is a method of diagnosing rheumatoid arthritis in an individual comprising: a) contacting a test sample from the individual with one or more target antigens, each comprising an autoantigen of Table 2 or a fragment thereof comprising an epitope; and b) detecting binding of the one or more target antigens to one or more antibodies in the test sample, wherein the presence of the one or more antibodies bound against the one or more target antigens is indicative of rheumatoid arthritis. In a further embodiment, the test sample is contacted with two or more; ten or more; twenty or more; or all of the autoantigens listed in Table 2 or fragment thereof comprising an epitope. In a further embodiment, the amount of antibodies that bind to each antigen is determined.

[0035] In a further embodiment, at least 1, 2, 3, 4, 5, 10, 20, or 35 of the RA antigens are bound by an antibody from the test sample to indicate the presence of rheumatoid arthritis. One autoantigen, leukocyte receptor cluster member 12 (BC033195) is selective for RA but not SLE or ANCA. In a further embodiment, a kit and a method for diagnosing RA comprises contacting a test sample with one or

more autoantigens, wherein one of the biomarkers is leukocyte receptor cluster member 12.

[0036] Another embodiment of the present invention is a method of diagnosing systemic lupus erythematosus in an individual comprising: a) contacting a test sample from the individual with one or more target antigens, each comprising an autoantigen of Table 3 or fragments thereof comprising an epitope; and b) detecting binding of the one or more target antigens to one or more antibodies in the test sample, wherein the presence of the one or more antibodies bound against the one or more target antigens is indicative of systemic lupus erythematosus. In a further embodiment, the test sample is contacted with two or more; ten or more; twenty or more; fifty or more; or all of the autoantigens listed in Table 3. In a further embodiment, the amount of antibodies that bind to each antigen is determined.

[0037] In a further embodiment, at least 1, 2, 3, 4, 5, 10, 20, 35, 50, 75, 100 or 150 of the SLE antigens are bound by an antibody from the test sample to indicate the presence of systemic lupus erythematosus. In a further embodiment, a kit and a method for diagnosing SLE comprises contacting a test sample with one or more antigens, wherein one or more of the antigens are selected from the autoantigens in Table 4 or fragments thereof comprising an epitope.

[0038] Another embodiment of the present invention is a method of diagnosing anti-neutrophil cytoplasmic antibody associated diseases in an individual comprising: a) contacting a test sample from the individual with one or more target antigens, each comprising an autoantigen of Table 5 or fragments thereof comprising an epitope; and

b) detecting binding of the one or more target antigens to one or more antibodies in the test sample, wherein the presence of the one or more antibodies bound against the one or more target antigens is indicative of anti-neutrophil cytoplasmic antibody associated diseases. In a further embodiment, the test sample is contacted with two or more; ten or more; twenty or more; fifty or more; or all of the autoantigens listed in Table 5. In a further embodiment, the amount of antibodies that bind to each antigen is determined.

[0039] In a further embodiment, at least 1, 2, 3, 4, 5, 10, 20, 35, 50, 75, or all of the ANCA autoantigens are bound by an antibody from the test sample to indicate the presence of anti-neutrophil cytoplasmic antibody associated diseases. In a further embodiment, a kit and a method for diagnosing ANCA comprises contacting a test sample with one or more antigens, wherein one or more of the antigens are selected from the autoantigens in Table 6 or fragments thereof comprising an epitope.

[0040] The progression or remission of a disease can be monitored by contacting test samples from an individual taken at different times with the panel of antigens. For example, a second test sample is taken from the patient and contacted with the antigen panel days or weeks after the first test sample. Alternatively, the second or subsequent test samples can be taken from the patient and tested against the panel of antigens at regular intervals, such as daily, weekly, monthly, quarterly, semi-annually, or annually. By testing the patient's test samples at different times, the presence of antibodies and therefore the stage of the disease can be compared. A further embodiment of the invention is a method of monitoring one or more target antibodies in test samples from an individual diagnosed as having an autoimmune disease comprising: a) contacting a first test sample from the individual with a first set of one or more target antigens; b) detecting binding of the one or more target antigens, wherein the binding of the one or more target antigens detects the presence of the one or more target antibodies in the first test sample; c) contacting a second test sample from the individual with a second set of the one or more target antigens; d) detecting binding of the one or more target antigens, wherein the binding of the one or more target antigens detects the presence of the one or more target antibodies in the second test sample; and e) comparing the presence of the one or more antibodies bound against the one or more target antigens from the first test sample with the one or more antibodies bound against the one or more target antigens from the second test sample, wherein each of the one or more target antigens comprises an autoantigen of Table 1 or fragments thereof comprising an epitope. In other embodiments of the invention, the one or more target antigens comprise an autoantigen of Table 2, Table 3, or Table 5 or fragments thereof.

[0041] The progression of the disease is further monitored by quantitatively comparing the amounts of antibodies that bind to the autoantigens. Accordingly, another embodiment of the invention further comprises detecting the amount of the one or more antibodies against the one or more antigens in the first test sample and the second test sample; and comparing the amount of the one or more antibodies from the first test sample with the amount of the one or more antibodies from the second test sample.

[0042] Another embodiment of the invention is a mixture comprising one or more target antigens each comprising an autoantigen of Table 1 or a fragment thereof comprising an epitope; and a test sample from an individual suspected of having an autoimmune disease. The mixture optionally further comprises a control antibody against one or more of the target antigens. In a further embodiment, the mixture comprises two or more; ten or more; twenty or more; fifty or more; one hundred or more; or all of the autoantigens of Table 1 or fragments thereof comprising an epitope. The test sample includes, but is not limited to, cells, tissues, or bodily fluids from an individual.

[0043] The present invention identifies >300 proteins that are selectively recognized by antibodies in RA, ANCA, or SLE patient sera which represent an important pool of novel candidates for potential diagnostic markers or therapeutic targets. The present invention further identifies a panel of antigens that exhibit increased or decreased autoantibody response in RA patients following infilximab (Remicade®) treatment, which represents an important group of novel biomarkers for utility in patient stratification and monitoring treatment efficacy. These proteins also can facilitate early identification of patients progressing towards infilximab-induced SLE-like syndrome.

[0044] Infliximab (Remicade®) is an injectable antibody used to treat autoimmune disorders like Crohn's disease, ulcerative colitis, psoriatic arthritis and rheumatoid arthritis. The drug reduces the amount of active TNF-α (tumour necrosis factor alpha) in the body by binding to it and preventing it from signaling the receptors for TNF-α on the surface of cells. Autoantibodies directed against the cytokine tumor necrosis factor alpha (TNF-α) comprise the most statistically significant differentiator

of untreated RA patients relative to patients after 20 weeks of infilximab treatment. Detection of an anti-TNFα autoantibody response serves as a tool for improvements to anti-TNF antibody-based therapies, the development of adjuvant therapies designed to mitigate this response, as well as a marker for monitoring host-response to infilximab.

[0045] Infliximab has also been reported to be helpful in reducing the joint inflammation of juvenile rheumatoid arthritis, ankylosing spondylitis, uveitis, psoriasis, and for sarcoidosis that is not responding to traditional therapies. Treatment with infliximab may increase the risk of developing certain types of cancer or autoimmune disorders (such as a lupus-like syndrome).

[0046] Another embodiment of the invention comprises a method of monitoring one or more target antibodies in test samples from an individual receiving treatment for an autoimmune disease comprising a) contacting a first test sample from an individual with a first set of one or more target antigens; b) detecting binding of the one or more target antigens to one or more antibodies in the first test sample, wherein the presence of the one or more antibodies bound against the one or more target antigens detects the one or more target antibodies; c) administering a treatment for the autoimmune disease to the individual; d) after the administration of the treatment, contacting a second test sample from the individual with a second set of the one or more target antigens; e) detecting binding of the one or more target antigens to one or more antibodies in the second test sample, wherein the presence of the one or more antibodies bound against the one or more target antigens detects the one or more target antibodies; and f) comparing the presence of the one or more antibodies against the one or more target antigens from the first sample with the one or more antibodies against the one or more target antigens from the second sample, wherein each of the one or more target antigens comprises an autoantigen of Table 1 or fragments thereof comprising an epitope.

[0047] The binding levels of the antibodies to the one or more antigens may increase or decrease as a result of the treatment. In one embodiment, the decrease of binding levels to autoantigens of Table 7A is indicative of the presence of autoimmune disease in the patient. In another embodiment, the increase of binding

levels to autoantigens of Table 7B is indicative of the presence of autoimmune disease.

[0048] By administering treatment, it is meant to encompass any therapeutic drug, procedure, or combination thereof administered to a patient to alleviate an autoimmune disease, including, but not limited to, administering a drug orally or intravenously to a patient. Where the autoimmune disease is rheumatoid arthritis, the treatment may comprise intravenously administering the drug infliximab to the patient. The treatment may be continuous, that is, administered to the patient at regular intervals. Multiple test samples can be taken from the patient during the course of the treatment. Preferably, the first test sample is taken from the patient before treatment begins.

[0049] In a further embodiment, the amount of the one or more antibodies against the one or more antigens in each test sample is detected; and the amount of the one or more antibodies from the first test sample is compared with the amount of one or more antibodies from the second test sample.

[0050] In one embodiment, the treatment is for rheumatoid arthritis and the one or more target antigens each comprise an autoantigen of Table 2 or a fragment thereof comprising an epitope. Preferably, the treatment is the administration of infliximab to a patient.

[0051] The invention also provides a method of staging autoimmune disease in an individual. This method comprises identifying a human patient having an autoimmune disease and analyzing cells, tissues or bodily fluid from such human patient for the autoimmune disease-associated biomarkers of the present invention. The presence or level of the biomarker is then compared to the level of the biomarker in the same cells, tissues or bodily fluid type of a healthy control individual, or with a reference range of the level of biomarker obtained from at least one healthy control individual. An elevated level of immune reactivity against a biomarker protein identified as being present in elevated amounts in autoimmune disease patients, when compared to the control or reference range, is associated with the presence of autoimmune disease in the test individual. A decreased level of

immune reactivity against a biomarker protein identified as being present in decreased amounts in autoimmune disease patients, when compared to the control or reference range, is associated with the presence of autoimmune disease in the test individual.

Definitions

[0052] The term "about" as used herein refers to a value within 10% of the underlying parameter (i.e., plus or minus 10%), and is sometimes a value within 5% of the underlying parameter (i.e., plus or minus 5%), a value sometimes within 2.5% of the underlying parameter (i.e., plus or minus 2.5%), or a value sometimes within 1% of the underlying parameter (i.e., plus or minus 1%), and sometimes refers to the parameter with no variation. Thus, a distance of "about 20 nucleotides in length" includes a distance of 19 or 21 nucleotides in length (i.e., within a 5% variation) or a distance of 20 nucleotides in length (i.e., no variation) in some embodiments.

[0053] As used herein, the article "a" or "an" can refer to one or more of the elements it precedes (e.g., a protein microarray "a" protein may comprise one protein sequence or multiple proteins).

[0054] The term "or" is not meant to be exclusive to one or the terms it designates. For example, as it is used in a phrase of the structure "A or B" may denote A alone, B alone, or both A and B.

[0055] By "biomarker" it is meant a biochemical characteristic that can be used to detect, diagnose, prognose, direct treatment, or to measure the progress of a disease or condition, or the effects of treatment of a disease or condition. Biomarkers include, but are not limited to, the presence of a nucleic acid, protein, carbohydrate, or antibody, or combination thereof, associated with the presence of a disease in an individual. The present invention provides biomarkers for RA, SLE and ANCA that are antibodies present in the sera of subjects diagnosed with RA, SLE and ANCA. The biomarker antibodies in the present invention are the autoantibodies displaying increased reactivity in individuals with an autoimmune disease, most likely as a consequence of their increased abundance. The autoantibodies can be detected with autoantigens, human proteins that are

specifically bound by the antibodies. Importantly, biomarkers need not be expressed in a majority of disease individuals to have clinical value. The receptor tyrosine kinase Her2 is known to be over-expressed in approximately 25% of all breast cancers (J. S. Ross et al., Mol Cell Proteomics 3, 379-98 (Apr, 2004)), and yet is a clinically important indicator of disease progression as well as specific therapeutic options.

[0056] "Biomolecule" refers to an organic molecule of biological origin, e.g., steroids, fatty acids, amino acids, nucleotides, sugars, peptides, polypeptides, antibodies, polynucleotides, complex carbohydrates or lipids.

[0057] The phrase "differentially present" refers to differences in the quantity of a biomolecule (such as an antibody) present in a sample taken from patients having an autoimmune disease as compared to a comparable sample taken from patients who do not have an autoimmune disease (e.g., normal or healthy patients). A biomolecule is differentially present between the two samples if the amount of the polypeptide in one sample is significantly different from the amount of the polypeptide in the other sample. For example, a polypeptide is differentially present between the two samples if it is present in an amount (e.g., concentration, mass, molar amount, etc.) at least about 150%, at least about 200%, at least about 500% or at least about 1000% greater or lesser than it is present in the other sample, or if it is detectable (gives a signal significantly greater than background or a negative control) in one sample and not detectable in the other. Any biomolecules that are differentially present in samples taken from autoimmune disease patients as compared to subjects who do not have an autoimmune disease can be used as biomarkers.

[0058] "Antibody" refers to a polypeptide ligand substantially encoded by an immunoglobulin gene or immunoglobulin genes, or fragments thereof, which specifically binds and recognizes an epitope (e.g., an antigen). The recognized immunoglobulin genes include the kappa and lambda light chain constant region genes, the alpha, gamma, delta, epsilon and mu heavy chain constant region genes, and the myriad immunoglobulin variable region genes. Antibodies exist, e.g., as intact immunoglobulins or as a number of well characterized fragments produced by

digestion with various peptidases. This includes, e.g., Fab' and F(ab)'.sub.2 fragments. The term "antibody," as used herein, also includes antibody fragments either produced by the modification of whole antibodies or those synthesized de novo using recombinant DNA methodologies. It also includes polyclonal antibodies, monoclonal antibodies, chimeric antibodies, humanized antibodies, or single chain antibodies. "Fc" portion of an antibody refers to that portion of an immunoglobulin heavy chain that comprises one or more heavy chain constant region domains, CH1, CH2 and CH3, but does not include the heavy chain variable region. An "autoantibody" is an antibody that is directed against the host's own proteins or other molecules. In the present invention, high throughput microarrays have been used to detect autoantibodies from RA, SLE and ANCA patients that are not typically present in normal patients.

[0059] The term "antigen" or "test antigen" as used herein refers to proteins or polypeptides to be used as targets for screening test samples obtained from subjects for the presence of autoantibodies. "Autoantigen" is used to denote antigens for which the presence of antibodies in a sample of an individual has been detected. These antigens, test antigens, or autoantigens are contemplated to include any fragments thereof of the so-identified proteins, in particular, immunologically detectable fragments. They are also meant to include immunologically detectable products of proteolysis of the proteins, as well as processed forms, post-translationally modified forms, such as, for example, "pre," "pro," or "prepro" forms of markers, or the "pre," "pro," or "prepro" fragment removed to form the mature marker, as well as allelic variants and splice variants of the antigens, test antigens, or autoantigens. The identification or listing of antigens, test antigens, and autoantigens also includes amino acid sequence variants of these, for example, sequence variants that include a fragment, domain, or epitope that shares immune reactivity with the identified antigen, test antigen, and autoantigen protein. Similarly, an "autoantigen" refers to a molecule, such as a protein, endogenous to the host that is recognized by an autoantibody.

[0060] An "epitope" is a site on an antigen, such as an autoantigen disclosed herein, recognized by an antibody.

[0061] As used herein, the word “protein” refers to a full-length protein, a portion of a protein, or a peptide. Proteins can be produced via fragmentation of larger proteins, or chemically synthesized. Proteins may, for example, be prepared by recombinant overexpression in a species such as, but not limited to, bacteria, yeast, insect cells, and mammalian cells. Proteins to be placed in a protein microarray of the invention, may be, for example, are fusion proteins, for example with at least one affinity tag to aid in purification and/or immobilization. In certain aspects of the invention, at least 2 tags are present on the protein, one of which can be used to aid in purification and the other can be used to aid in immobilization. In certain illustrative aspects, the tag is a His tag, a GST tag, or a biotin tag. Where the tag is a biotin tag, the tag can be associated with a protein in vitro or in vivo using commercially available reagents (Invitrogen, Carlsbad, CA). In aspects where the tag is associated with the protein in vitro, a Bioease tag can be used (Invitrogen, Carlsbad, CA).

[0062] As used herein, the term “peptide,” “oligopeptide,” and "polypeptide" are used interchangeably with protein herein and refer to a sequence of contiguous amino acids linked by peptide bonds. As used herein, the term “protein” refers to a polypeptide that can also include post-translational modifications that include the modification of amino acids of the protein and may include the addition of chemical groups or biomolecules that are not amino acid-based. The terms apply to amino acid polymers in which one or more amino acid residue is an analog or mimetic of a corresponding naturally occurring amino acid, as well as to naturally occurring amino acid polymers. Polypeptides can be modified, e.g., by the addition of carbohydrate residues to form glycoproteins. The terms "polypeptide," "peptide" and "protein" include glycoproteins, as well as non-glycoproteins.

[0063] A "variant" of a polypeptide or protein, as used herein, refers to an amino acid sequence that is altered with respect to the referenced polypeptide or protein by one or more amino acids. In the present invention, a variant of a polypeptide retains the antigenicity, or antibody-binding property, of the referenced protein. In preferred aspects of the invention, a variant of a polypeptide or protein can be bound by the same population of autoantibodies that are able to bind the referenced protein. Preferably a variant of a polypeptide has at least 60% identity to the referenced

protein over a sequence of at least 15 amino acids. More preferably a variant of a polypeptide is at least 70% identical to the referenced protein over a sequence of at least 15 amino acids. Protein variants can be, for example, at least 80%, at least 90%, at least 95%, or at least 99% identical to referenced polypeptide over a sequence of at least 15 amino acids. Protein variants of the invention can be, for example, at least 80%, at least 90%, at least 95%, or at least 99% identical to referenced polypeptide over a sequence of at least 20 amino acids. The variant may have "conservative" changes, wherein a substituted amino acid has similar structural or chemical properties (e.g., replacement of leucine with isoleucine). A variant may also have "nonconservative" changes (e.g., replacement of glycine with tryptophan). Analogous minor variations may also include amino acid deletions or insertions, or both. Guidance in determining which amino acid residues may be substituted, inserted, or deleted without abolishing immunological reactivity may be found using computer programs well known in the art, for example, DNASTAR software.

[0064] Protein biomarkers used in a protein array of the present invention may be the full protein or fragments of the full protein. Protein fragments are suitable for use as part of the protein array as long as the fragments contain the epitope recognized by the antibodies. The required epitope for a given full protein can be mapped using protein microarrays, and with ELISPOT or ELISA techniques. It is understood that the antigen biomarkers provided by the present invention are meant to encompass the full protein as well as fragments thereof comprising an epitope. Typically, suitable protein fragments comprise at least 5%; at least 10%; at least 20%; or at least 50% of the full length protein amino acid sequence. In one embodiment of the present invention, protein fragments of target autoantigens contain at least 6 contiguous amino acids; at least 10 contiguous amino acids; at least 20 contiguous amino acids; at least 50 contiguous amino acids; at least 100 contiguous amino acids; or at least 200 contiguous amino acids of the full length protein.

[0065] As used herein, a “biomarker detection panel” or “biomarker panel” refers to a set of biomarkers that are provided together for detection, diagnosis, prognosis, staging, or monitoring of a disease or condition, based on detection values for the set (panel) of biomarkers.

[0066] The methods of the present invention are carried out on test samples derived from patients, including individuals suspected of having an autoimmune disease and those who have been diagnosed to have a disease. A "test sample" as used herein can be any type of sample, such as a sample of cells or tissue, or a sample of bodily fluid, preferably from an animal, most preferably a human. The sample can be a tissue sample, such as a swab or smear, or a pathology or biopsy sample of tissue, including tumor tissue. Samples can also be tissue extracts, for example from tissue biopsy or autopsy material. A sample can be a sample of bodily fluids, such as but not limited to blood, plasma, serum, sputum, semen, synovial fluid, cerebrospinal fluid, urine, lung aspirates, nipple aspirates, tears, or a lavage. Samples can also include, for example, cells or tissue extracts such as homogenates, cell lysates or solubilized tissue obtained from a patient. A preferred sample is a blood or serum sample.

[0067] By "blood" is meant to include whole blood, plasma, serum, or any derivative of blood. A blood sample may be, for example, serum.

[0068] A "patient" is an individual diagnosed with a disease or being tested for the presence of disease. A patient tested for a disease can have one or more indicators of a disease state, or can be screened for the presence of disease in the absence of any indicators of a disease state. As used herein an individual "suspected" of having a disease can have one or more indicators of a disease state or can be part of a population routinely screened for disease in the absence of any indicators of a disease state.

[0069] Autoimmune diseases are diseases characterized by an immune response against the body's own cells and tissues. Rheumatoid arthritis (RA) is a chronic, inflammatory autoimmune disease that causes the immune system to attack the joints. Systemic lupus erythematosus (SLE or lupus) is a chronic, potentially debilitating or fatal autoimmune disease in which the immune system attacks the body's cells and tissue, resulting in inflammation and tissue damage. ANCA refers to any autoimmune disease characterized by the presence of anti-neutrophil cytoplasmic antibodies, such as small-vessel vasculitis and including, but not limited

to, microscopic polyangiitis, Wegener's granulomatosis, Churg-Strauss syndrome, and drug-induced vasculitis.

[0070] By “an individual suspected of having an autoimmune disease,” is meant an individual who has been diagnosed with an autoimmune disease, such as RA, SLE or ANCA, or who has at least one indicator of autoimmune disease, or who is at an increased risk of developing autoimmune disease due to age, environmental and/or nutritional factors, or genetic factors.

[0071] As used herein, the term “array” refers to an arrangement of entities in a pattern on a substrate. Although the pattern is typically a two-dimensional pattern, the pattern may also be a three-dimensional pattern. In a protein array, the entities are proteins. In certain embodiments, the array can be a microarray or a nanoarray. A "nanoarray” is an array in which separate entities are separated by 0.1nm to 10 μm, for example from 1 nm to 1μm. A “microarray” is an array in the density of entities on the array is at least 100/cm^2. On microarrays separate entities can be separated, for example, by more than 1 μm.

[0072] The term "protein array" as used herein refers to a protein array, a protein microarray or a protein nanoarray. A protein array may include, for example, but is not limited to, a “ProtoArray™,” protein high density array (Invitrogen, Carlsbad, CA, available on the Internet at Invitrogen.com). The ProtoArray™ high density protein array can be used to screen complex biological mixtures, such as serum, to assay for the presence of autoantibodies directed against human proteins. Alternatively, a custom protein array that includes autoantigens, such as those provided herein, for the detection of autoantibody biomarkers, can be used to assay for the presence of autoantibodies directed against human proteins. In certain disease states including autoimmune diseases and cancer, autoantibodies are expressed at altered levels relative to those observed in healthy individuals.

[0073] The term "protein chip" is used in the present application synonymously with protein array or microarray.

[0074] The phrase "diagnosis" as used herein refers to methods by which the skilled artisan can estimate and/or determine whether or not a patient is suffering from a given disease or condition. The skilled artisan often makes a diagnosis on the basis of one or more diagnostic indicators, i.e., a marker, the presence, absence, or amount of which is indicative of the presence, severity, or absence of the condition, physical features (lumps or hard areas in or on tissue), or histological or biochemical analysis of biopsied or sampled tissue or cells, or a combination of these.

[0075] Similarly, a prognosis is often determined by examining one or more "prognostic indicators", the presence or amount of which in a patient (or a sample obtained from the patient) signal a probability that a given course or outcome will occur. For example, when one or more prognostic indicators reach a sufficiently high level in samples obtained from such patients, the level may signal that the patient is at an increased probability of having a disease or condition in comparison to a similar patient exhibiting a lower marker level. A level or a change in level of a prognostic indicator, which in turn is associated with an increased probability of morbidity or death, is referred to as being "associated with an increased predisposition to an adverse outcome" in a patient. For example, preferred prognostic markers can predict the onset of an autoimmune disease in a patient with one or more target antibodies of Table 1, or a more advanced stage of an autoimmune disease in a patient diagnosed with the disease.

[0076] The term "correlating," as used herein in reference to the use of diagnostic and prognostic indicators, refers to comparing the presence or amount of the indicator in a patient to its presence or amount in persons known to suffer from, or known to be at risk of, a given condition; or in persons known to be free of a given condition. As discussed above, a marker level in a patient sample can be compared to a level known to be associated with autoimmune disease. The sample's marker level is said to have been correlated with a diagnosis; that is, the skilled artisan can use the marker level to determine whether the patient has an autoimmune disease, and respond accordingly. Alternatively, the sample's marker level can be compared to a marker level known to be associated with a good outcome (e.g., the absence of

autoimmune disease, etc.). In preferred embodiments, a profile of marker levels are correlated to a global probability or a particular outcome using ROC curves.

[0077] The phrase "determining the prognosis" as used herein refers to methods by which the skilled artisan can predict the course or outcome of a condition in a patient. The term "prognosis" does not refer to the ability to predict the course or outcome of a condition with 100% accuracy, or even that a given course or outcome is more likely to occur than not. Instead, the skilled artisan will understand that the term "prognosis" refers to an increased probability that a certain course or outcome will occur; that is, that a course or outcome is more likely to occur in a patient exhibiting a given condition, when compared to those individuals not exhibiting the condition. For example, in individuals not exhibiting the condition, the chance of a given outcome may be about 3%. In preferred embodiments, a prognosis is about a 5% chance of a given outcome, about a 7% chance, about a 10% chance, about a 12% chance, about a 15% chance, about a 20% chance, about a 25% chance, about a 30% chance, about a 40% chance, about a 50% chance, about a 60% chance, about a 75% chance, about a 90% chance, and about a 95% chance. The term "about" in this context refers to +/-1%.

[0078] "Diagnostic" means identifying the presence or nature of a pathologic condition. Diagnostic methods differ in their sensitivity and specificity. While a particular diagnostic method may not provide a definitive diagnosis of a condition, it suffices if the method provides a positive indication that aids in diagnosis.

[0079] "Sensitivity" is defined as the percent of diseased individuals (individuals with autoimmune disease) in which the biomarker of interest is detected (true positive number / total number of diseased x 100). Nondiseased individuals diagnosed by the test as diseased are “false positives”.

[0080] "Specificity" is defined as the percent of nondiseased individuals for which the biomarker of interest is not detected (true negative / total number without disease x 100). Diseased individuals not detected by the assay are "false negatives." Subjects who are not diseased and who test negative in the assay, are termed "true negatives."

[0081] A "diagnostic amount" of a marker refers to an amount of a marker in a subject's sample that is consistent with a diagnosis of autoimmune disease. A diagnostic amount can be either in absolute amount (e.g., X nanogram/ml) or a relative amount (e.g. relative intensity of signals).

[0082] A "test amount" of a marker refers to an amount of a marker present in a sample being tested. A test amount can be either in absolute amount (e.g., X nanogram/ml) or a relative amount (e.g., relative intensity of signals).

[0083] A "control amount" of a marker can be any amount or a range of amount which is to be compared against a test amount of a marker. For example, a control amount of a marker can be the amount of a marker (e.g., seminal basic protein) in an autoimmune disease patient, or a normal patient. A control amount can be either in absolute amount (e.g., X nanogram/ml) or a relative amount (e.g., relative intensity of signals).

[0084] "Detect" refers to identifying the presence, absence or amount of the object to be detected.

[0085] "Label" or a "detectable moiety" refers to a composition detectable by spectroscopic, photochemical, biochemical, immunochemical, or chemical means. For example, useful labels include radiolabels such as ^{32}P, ^{35}S, or ^{125}I; fluorescent dyes; chromophores, electron-dense reagents; enzymes that generate a detectable signal (e.g., as commonly used in an ELISA); or spin labels. The label or detectable moiety has or generates a measurable signal, such as a radioactive, chromogenic, or fluorescent signal, that can be used to quantify the amount of bound detectable moiety in a sample. The detectable moiety can be incorporated in or attached to a primer or probe either covalently, or through ionic, van der Waals or hydrogen bonds, e.g., incorporation of radioactive nucleotides, or biotinylated nucleotides that are recognized by streptavidin. The label or detectable moiety may be directly or indirectly detectable. Indirect detection can involve the binding of a second directly or indirectly detectable moiety to the detectable moiety. For example, the detectable moiety can be the ligand of a binding partner, such as biotin, which is a binding

partner for streptavidin, or a nucleotide sequence, which is the binding partner for a complementary sequence, to which it can specifically hybridize. The binding partner may itself be directly detectable, for example, an antibody may be itself labeled with a fluorescent molecule. The binding partner also may be indirectly detectable, for example, a nucleic acid having a complementary nucleotide sequence can be a part of a branched DNA molecule that is in turn detectable through hybridization with other labeled nucleic acid molecules. (See, e.g., P. D. Fahrlander and A. Klausner, Bio/Technology 6:1165 (1988)). Quantitation of the signal is achieved by, e.g., scintillation counting, densitometry, or flow cytometry.

[0086] "Measure" in all of its grammatical forms, refers to detecting, quantifying or qualifying the amount (including molar amount), concentration or mass of a physical entity or chemical composition either in absolute terms in the case of quantifying, or in terms relative to a comparable physical entity or chemical composition.

[0087] "Immunoassay" is an assay in which an antibody specifically binds an antigen to provide for the detection and/or quantitation of the antibody or antigen. An immunoassay is characterized by the use of specific binding properties of a particular antibody to isolate, target, and/or quantify the antigen.

[0088] The phrase "specifically (or selectively) binds" to an antibody or "specifically (or selectively) immunoreactive with," when referring to a protein or peptide, refers to a binding reaction that is determinative of the presence of the protein in a heterogeneous population of proteins and other biologics. Thus, under designated immunoassay conditions, the specified antibodies bind to a particular protein at least two times the background and do not substantially bind in a significant amount to other proteins present in the sample. Specific binding to an antibody under such conditions may require an antibody that is selected for its specificity for a particular protein. For example, polyclonal antibodies raised to seminal basic protein from specific species such as rat, mouse, or human can be selected to obtain only those polyclonal antibodies that are specifically immunoreactive with seminal basic protein and not with other proteins, except for polymorphic variants and alleles of seminal basic protein. This selection may be achieved by subtracting out antibodies that cross-react with seminal basic protein

molecules from other species. A variety of immunoassay formats may be used to select antibodies specifically immunoreactive with a particular protein. For example, solid-phase ELISA immunoassays are routinely used to select antibodies specifically immunoreactive with a protein (see, e.g., Harlow & Lane, Antibodies, A Laboratory Manual (1988), for a description of immunoassay formats and conditions that can be used to determine specific immunoreactivity). Typically a specific or selective reaction will be at least twice background signal or noise and more typically more than 10 to 100 times background.

[0089] "Immune reactivity" as used herein means the presence or level of binding of an antibody or antibodies in a sample to one or more target antigens. A "pattern of immune reactivity" refers to the profile of binding of antibodies in a sample to a plurality of target antigens.

[0090] As used herein, "target antigen" refers to a protein, or to a portion, fragment, variant, isoform, processing product thereof having immunoreactivity of the protein, that is used to determine the presence, absence, or amount of an antibody in a sample from a subject. A "test antigen" is a protein evaluated for use as a target antigen. A test antigen is therefore a candidate target antigen, or a protein used to determine whether a portion of a test population has antibodies reactive against it. Use of the terms "target antigen", "test antigen", "autoantigen", and, simply, "antigen" is meant to include the complete wild type mature protein, or can also denote a precursor, processed form (including, a proteolytically processed or otherwise cleaved form) unprocessed form, post-translationally modified, or chemically modified form of the protein indicated, in which the target antigen, test antigen, or antigen retains or possesses the specific binding characteristics of the referenced protein to one or more autoantibodies of a test sample. The protein can have, for example, one or more modifications not typically found in the protein produced by normal cells, including aberrant processing, cleavage or degradation, oxidation of amino acid residues, atypical glycosylation pattern, etc. The use of the terms "target antigen", "test antigen", "autoantigen", or "antigen" also include splice isoforms or allelic variants of the referenced proteins, or can be sequence variants of the referenced protein, with the proviso that the "target antigen", "test antigen", "autoantigen", or "antigen" retains or possesses the immunological reactivity of the

referenced protein to one or more autoantibodies of a test sample. Use of the term "target antigen", "test antigen", "autoantigen", or simply "antigen" specifically encompasses fragments of a referenced protein ("antigenic fragments") that have the antibody binding specificity of the reference protein.

Methods

[0091] The invention provides, in one aspect, a method of detecting one or more target antibodies in a test sample from an individual. The method includes: contacting the test sample from the individual with one or more target antigens of the invention, each comprising an autoantigen of Table 1, or a fragment thereof that includes an epitope recognized by a target antibody; and detecting binding of one or more antibodies in the sample to one or more target antigens, thereby detecting the presence of the one or more target antibodies in the sample. The target antigen can be any of the target antigens provided in Table 1, or a fragment thereof that includes an epitope. Furthermore, the target antigen can be a panel of target antigens that includes, for example, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25, 50, or all target antigens of Table 1. The method can be carried out using virtually any immunoassay method. Non-limiting examples of immunoassay methods are provided below.

[0092] The individual from whom the test sample is taken can be any individual, healthy or suspected of having an autoimmune disease, and in some embodiments is an individual that is being screened for RA, SLE or ANCA.

[0093] Binding is typically detected using an immunoassay, which can be in various formats as described in detail below. Detection of binding in certain illustrative embodiments makes use of one or more solid supports to which the test antigen is immobilized on a substrate to which the sample from an individual, typically a human subject, is applied. After incubation of the sample with the immobilized antigen, or optionally, concurrently with the incubation of the sample, an antibody that is reactive against human antibodies (for example, an anti-human IgG antibody that is from a species other than human, for example, goat, rabbit, pig, mouse, etc.) can be applied to the solid support with which the sample is incubated. The non-human antibody is directly or indirectly labeled. After removing nonspecifically bound antibody, signal from the label that is significantly above

background level is indicative of binding of a human antibody from the sample to a test antigen on the solid support.

[0094] In the methods provided herein, the sample can be any sample of cells or tissue, or of bodily fluid. Since the autoantibodies being screened for circulate in the blood and are fairly stable in blood sample, in certain illustrative embodiments, the test sample is blood or a fraction thereof, such as, for example, serum. The sample can be unprocessed prior to contact with the test antigen, or can be a sample that has undergone one or more processing steps. For example, a blood sample can be processed to remove red blood cells and obtain serum.

[0095] The test sample can be contacted with a test antigen provided in solution phase, or the test antigen can be provided bound to a solid support. In preferred embodiments, the detection is performed by an immunoassay, as described in more detail below. Detection of binding of the target sample to a test antigen indicates the presence of an autoantibody that specifically binds the test antigen in the sample. Identifying an autoantibody present in a sample from an individual can be used to identify biomarkers of a disease or condition, or to diagnose a disease or condition.

[0096] The detection can be performed on any solid support, such as a bead, dish, plate, well, sheet, membrane, slide, chip, or array, such as a protein array, which can be a microarray, and can optionally be a high density microarray.

[0097] The detection method can provide a positive/negative binding result, or can give a value that can be a relative or absolute value for the level of the autoantibody biomarker in the sample. The result can provide a diagnosis, prognosis, or be used as an indicator for conducting further tests or evaluation that may or may not result in a diagnosis or prognosis.

[0098] The method includes detecting more than one autoantibody in a sample from an individual, in which one or more of the test antigens used to detect autoantibodies is a test antigen of Table 1.

[0099] A fragment that includes an epitope recognized by an antibody can be at least 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 20, 25, 30, 35, 40, 45, 50, 75, 100, 150, 200, 250, 300, 350, 400, 450, 500, 750, or 1000 amino acids in length. The fragment can also be between 5, 10, 15, 20, 25, 50, 75, 100, 150, 200, or 250 and one amino acid less than the entire length of an autoantigen. Typically, such epitopes are characterized in advance such that it is known that autoantibodies for a given autoantigen recognize the epitope. Methods for epitope mapping are well known in the art.

[00100] In some embodiments, the detection is performed on a protein array, which can be a microarray, and can optionally be a microarray that includes proteins at a concentration of at least 100/cm^2 or 1000/cm^2, or greater than 400/cm^2.

[00101] The detection method can provide a positive/negative binding result, or can give a value that can be a relative or absolute value for the level of the autoantibody biomarker in the sample.

[00102] The method can be repeated over time, for example, to monitor a pre-disease state, to monitor progression of a disease, or to monitor a treatment regime. The results of a diagnostic test that determines the immune reactivity of a patient sample to a test antigen can be compared with the results of the same diagnostic test done at an earlier time. Significant differences in immune reactivity over time can contribute to a diagnosis or prognosis of autoimmune disease.

[00103] In some preferred embodiments, the biomarker detection panel has an ROC/AUC of 0.550 or greater, of 0.600 or greater, 0.650 or greater, 0.700 or greater, 0.750 or greater, 0.800 or greater, 0.850 or greater, or 0.900 or greater for distinguishing between a normal state and a disease state in a subject.

[00104] A target antigen present in a biomarker detection panel can be an entire mature form of a protein, such as a protein referred to as a target antigen (for example, a target antigen listed in Table 1, Table 2, Table 3 or Table 5), or can be a precursor, processed form, unprocessed form, isoforms, variant, a fragment thereof that includes an epitope, or allelic variant thereof, providing that the modified,

processed, or variant for of the protein has the ability to bind autoantigens present in samples from individuals.

[00105] In some embodiments, a biomarker detection panel used to detect autoimmune disease comprises one or more target antigens of Table 1. In some embodiments, a biomarker detection panel used to detect autoimmune disease comprises two or more target antigens of Table 1. In some embodiments, a biomarker detection panel used to detect autoimmune disease comprises three or more target antigens of Table 1. In some embodiments, a biomarker detection panel used to detect autoimmune disease comprises four or more target antigens of Table 1. In some embodiments, the test sample is contacted with a biomarker detection panel comprising five or more target antigens of Table 1. In some embodiments, the biomarker detection panel used in the methods of the invention includes six, seven, eight, nine, ten, eleven or twelve target antigens of Table 1. In some embodiments, the biomarker detection panel used in the methods of the invention includes 12, 13, 14, 15, 16, 17, 18, 19, 20, or more target antigens of Table 1. In some embodiments, the test sample is contacted with a biomarker detection panel comprising 21, 22, 23, 24, 25, 26, 27, 28, 29, or 30 antigens of Table 1. A biomarker detection panel can comprise between 30 and 35 antigens of Table 1, between 35 and 40 antigens of Table 1, between 40 and 45 antigens of Table 1, between 45 and 50 antigens of Table 1, between 50 and 55 antigens of Table 1, between 55 and 60 antigens of Table 1, between 60 and 65 antigens of Table 1, between 65 and 70 antigens of Table 1, between 70 and 75 antigens of Table 1, between 75 and 80 antigens of Table 1, between 80 and 85 antigens of Table 1, between 85 and 90 antigens of Table 1, between 90 and 95 antigens of Table 1, between 95 and 100 antigens of Table 1, between 100 and 105 antigens of Table 1, or between 105 and 108 antigens of Table 1. In all of the previous embodiments, one or more of the test antigens of Table 1 present in the biomarker detection panel can be a target antigen of Table 2, Table 3 or Table 5.

Immunoassays

[00106] Virtually any immunoassay technique known in the art can be used to detect antibodies that bind an antigen according to methods and kits of the present invention. Such immunoassay methods include, without limitation,

radioimmunoassays, immunohistochemistry assays, competitive-binding assays, Western Blot analyses, ELISA assays, sandwich assays, two-dimensional gel electrophoresis (2D electrophoresis) and non-gel based approaches such as mass spectrometry or protein interaction profiling, all known to those of ordinary skill in the art. These methods may be carried out in an automated manner, as is known in the art. Such immunoassay methods may also be used to detect the binding of antibodies in a sample to a target antigen.

[00107] In one example of an ELISA method, the method includes incubating a sample with a target protein and incubating the reaction product formed with a binding partner, such as a secondary antibody, that binds to the reaction product by binding to an antibody from the sample that associated with the target protein to form the reaction product. In some cases these may comprise two separate steps, in others, the two steps may be simultaneous, or performed in the same incubation step. Examples of methods of detection of the binding of the target protein to an antibody, is the use of an anti-human IgG (or other) antibody or protein A. This detection antibody may be linked to, for example, a peroxidase, such as horseradish peroxidase.

[00108] Using protein arrays for immunoassays allows the simultaneous analysis of multiple proteins. For example, target antigens or antibodies that recognize biomarkers that may be present in a sample are immobilized on microarrays. Then, the biomarker antibodies or proteins, if present in the sample, are captured on the cognate spots on the array by incubation of the sample with the microarray under conditions favoring specific antigen-antibody interactions. The binding of protein or antibody in the sample can then be determined using secondary antibodies or other binding labels, proteins, or analytes. Comparison of proteins or antibodies found in two or more different samples can be performed using any means known in the art. For example, a first sample can be analyzed in one array and a second sample analyzed in a second array that is a replica of the first array.

[00109] The term "sandwich assay" refers to an immunoassay where the antigen is sandwiched between two binding reagents, which are typically antibodies. The first binding reagent/antibody is attached to a surface and the second binding

reagent/antibody comprises a detectable moiety or label. Examples of detectable moieties include, for example and without limitation: fluorochromes, enzymes, epitopes for binding a second binding reagent (for example, when the second binding reagent/antibody is a mouse antibody, which is detected by a fluorescently-labeled anti-mouse antibody), for example an antigen or a member of a binding pair, such as biotin. The surface may be a planar surface, such as in the case of a typical grid-type array (for example, but without limitation, 96-well plates and planar microarrays), as described herein, or a non-planar surface, as with coated bead array technologies, where each "species" of bead is labeled with, for example, a fluorochrome (such as the Luminex technology described herein and in U.S. Pat. Nos. 6,599,331, 6,592,822 and 6,268,222), or quantum dot technology (for example, as described in U.S. Pat. No. 6,306,610).

[00110] A variety of different solid phase substrates can be used to detect a protein or antibody in a sample, or to quantitate or determine the concentration of a protein or antibody in a sample. The choice of substrate can be readily made by those of ordinary skill in the art, based on convenience, cost, skill, or other considerations. Useful substrates include without limitation: beads, bottles, surfaces, substrates, fibers, wires, framed structures, tubes, filaments, plates, sheets, and wells. These substrates can be made from: polystyrene, polypropylene, polycarbonate, glass, plastic, metal, alloy, cellulose, cellulose derivatives, nylon, coated surfaces, acrylamide or its derivatives and polymers thereof, agarose, or latex, or combinations thereof. This list is illustrative rather than exhaustive.

[00111] Other methods of protein detection and measurement described in the art can be used as well. For example, a single antibody can be coupled to beads or to a well in a microwell plate, and quantitated by immunoassay. In this assay format, a single protein can be detected in each assay. The assays can be repeated with antibodies to many analytes to arrive at essentially the same results as can be achieved using the methods of this invention. Bead assays can be multiplexed by employing a plurality of beads, each of which is uniquely labeled in some manner. For example each type of bead can contain a pre-selected amount of a fluorophore. Types of beads can be distinguished by determining the amount of fluorescence (and/or wavelength) emitted by a bead. Such fluorescently labeled beads are

commercially available from Luminex Corporation (Austin, Tex.; see the worldwide web address of luminexcorp.com). The Luminex assay is very similar to a typical sandwich ELISA assay, but utilizes Luminex microspheres conjugated to antibodies or proteins (Vignali, J. Immunol. Methods 243:243-255 (2000)).

[00112] The methodology and steps of various antibody assays are known to those of ordinary skill in the art. Additional information may be found, for example, in Antibodies: A Laboratory Manual, Cold Spring Harbor Laboratory, Chap. 14 (1988); Bolton and Hunter, "Radioimmunoassay and Related Methods," in Handbook of Experimental Immunology (D. M. Weir, ed.), Blackwell Scientific Publications, 1996; and Current Protocols in Immunology, (John E. Coligan, et al., eds) (1993).

[00113] The antibodies used to perform the foregoing assays can include polyclonal antibodies, monoclonal antibodies and fragments thereof as described supra. Monoclonal antibodies can be prepared according to established methods (see, e.g., Kohler and Milstein (1975) Nature 256:495; and Harlow and Lane (1988) Antibodies: A Laboratory Manual (C.H.S.P., N.Y.)).

[00114] An antibody can be a complete immunoglobulin or an antibody fragment. Antibody fragments used herein, typically are those that retain their ability to bind an antigen. Antibodies subtypes include IgG, IgM, IgA, IgE, or an isotype thereof (e.g., IgG1, IgG2a, IgG2b or IgG3). Antibody preparations can by polyclonal or monoclonal, and can be chimeric, humanized or bispecific versions of such antibodies. Antibody fragments include but are not limited to Fab, Fab', F(ab)'2, Dab, Fv and single-chain Fv (ScFv) fragments. Bifunctional antibodies sometimes are constructed by engineering two different binding specificities into a single antibody chain and sometimes are constructed by joining two Fab' regions together, where each Fab' region is from a different antibody (e.g., U.S. Patent No. 6,342,221). Antibody fragments often comprise engineered regions such as CDR-grafted or humanized fragments. Antibodies sometimes are derivitized with a functional molecule, such as a detectable label (e.g., dye, fluorophore, radioisotope, light scattering agent (e.g., silver, gold)) or binding agent (e.g., biotin, streptavidin), for example.

[00115] In certain embodiments, one or more diagnostic (or prognostic) biomarkers, such as one or more autoantibody biomarkers, are correlated to a condition or disease by the presence or absence of the biomarker(s). In other embodiments, threshold level(s) of a diagnostic or prognostic biomarker(s) can be established, and the level of the biomarker(s) in a sample can simply be compared to the threshold level(s).

[00116] As will be understood, for any particular biomarker, a distribution of biomarker levels for subjects with and without a disease will likely overlap. Under such conditions, a test does not absolutely distinguish normal from disease with 100% accuracy, and the area of overlap indicates where the test cannot distinguish normal from disease. A threshold is selected, above which (or below which, depending on how a biomarker changes with the disease) the test is considered to be abnormal and below which the test is considered to be normal. Receiver Operating Characteristic curves, or "ROC" curves, are typically generated by plotting the value of a variable versus its relative frequency in "normal" and "disease" populations. The area under the ROC curve is a measure of the probability that the perceived measurement will allow correct identification of a condition. ROC curves can also be generated using relative, or ranked, results. Methods of generating ROC curves and their use are well known in the art. See, e.g., Hanley et al., Radiology 143: 29-36 (1982).

[00117] One or more test antigens may have relatively low diagnostic or prognostic value when considered alone, but when used as part of a panel that includes other reagents for biomarker detection (such as but not limited to other test antigens), such test antigens can contribute to making a particular diagnosis or prognosis. In preferred embodiments, particular threshold values for one or more test antigens in a biomarker detection panel are not relied upon to determine if a profile of marker levels obtained from a subject are indicative of a particular diagnosis or prognosis. Rather, the present invention may utilize an evaluation of the entire marker profile of a biomarker detection panel, for example by plotting ROC curves for the sensitivity of a particular biomarker detection panel. In these methods, a profile of biomarker measurements from a sample of an individual is considered together to provide an overall probability (expressed either as a numeric score or as a percentage risk) that

an individual has an autoimmune disease, for example. In such embodiments, an increase in a certain subset of biomarkers (such as a subset of biomarkers that includes one or more autoantibodies) may be sufficient to indicate a particular diagnosis (or prognosis) in one patient, while an increase in a different subset of biomarkers (such as a subset of biomarkers that includes one or more autoantibodies) may be sufficient to indicate the same or a different diagnosis (or prognosis) in another patient. Weighting factors may also be applied to one or more biomarkers being detected. As one example, when a biomarker is of particularly high utility in identifying a particular diagnosis or prognosis, it may be weighted so that at a given level it alone is sufficient to indicate a positive diagnosis. In another example, a weighting factor may provide that no given level of a particular marker is sufficient to signal a positive result, but only signals a result when another marker also contributes to the analysis.

[00118] In preferred embodiments, markers and/or marker panels are selected to exhibit at least 70% sensitivity, more preferably at least 80% sensitivity, even more preferably at least 85% sensitivity, still more preferably at least 90% sensitivity, and most preferably at least 95% sensitivity, combined with at least 70% specificity, more preferably at least 80% specificity, even more preferably at least 85% specificity, still more preferably at least 90% specificity, and most preferably at least 95% specificity. In particularly preferred embodiments, both the sensitivity and specificity are at least 75%, more preferably at least 80%, even more preferably at least 85%, still more preferably at least 90%, and most preferably at least 95%.

[00119] Using various subsets of the test antigens provided in Table 1, the present invention provides test antibodies for detecting autoantibodies in a sample from an individual, antibodies for detecting autoimmune disease in an individual, and biomarker detection panels comprising combinations of the test antigens of Table 1 that can be used to detect and/or diagnose autoimmune disease, specifically RA, SLE and ANCA, with high sensitivity and specificity. Accordingly, methods, compositions, and kits are provided herein for the detection, diagnosis, staging, and monitoring of prostate cancer in individuals.

[00120] Automated systems for performing immunoassays, such as those utilized in the methods herein, are widely known and used in medical diagnostics. For example, random-mode or batch analyzer immunoassay systems can be used, as are known in the art. These can utilize magnetic particles or non-magnetic particles or microparticles and can utilize a fluorescence or chemiluminescence readout, for example. As non-limiting examples, the automated system can be an automated microarray hybridization station, an automated liquid handling robot, the Beckman ACCESS paramagnetic-particle, an chemiluminescent immunoassay, the Bayer ACS:180 chemiluminescent immunoassay or the Abbott AxSYM microparticle enzyme immunoassay. Such automated systems can be designed to perform methods provided herein for an individual antigen or for multiple antigens without multiple user interventions.

Biomarker detection panels

[00121] The invention also provides biomarker detection panels for diagnosing, prognosing, monitoring, or staging autoimmune disease, in which the biomarker detection panels comprise two or more target antigens selected from Table 1, in which at least 50% of the proteins of the test panel are proteins of Table 1. In some preferred embodiments, the proteins of the biomarker detection panel are provided on one or more solid supports, in which at least 50% of the proteins on the one or more solid supports to which the proteins of the panel are bound are of Table 1. Proteins of a biomarker detection panel can be provided bound to a solid support in the form of a bead, matrix, dish, well, plate, slide, sheet, membrane, filter, fiber, chip, or array. In some preferred embodiments, the proteins of the biomarker detection panel are provided on a protein array in which 50% or more of the proteins on the array are target antigens of the biomarker detection panel.

[00122] The set of biomarkers in a biomarker detection panel are associated, either electronically, or preferably physically. For example, each biomarker of a biomarker detection panel can be provided in isolated form, in separate tubes that are sold and/or shipped together, for example as part of a kit. In certain embodiments, isolated biomarkers are formed into a detection panel by attaching them to the same solid support. The biomarkers of a biomarker panel can also be mixed together in the same solution.

[00123] The invention also provides biomarker detection panels for diagnosing, prognosing, monitoring, or staging autoimmune disease, in which the biomarker detection panels comprise 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25, 30, 35, 40, 45, 50 or more target antigens selected from Table 1, or in certain preferred embodiments, Table 2, Table 3 or Table 5, in which at least 55%, 60%, 65%, 70%, or 75% of the proteins of the test panel are proteins of Table 1, Table 2, Table 3 or Table 5 respectively. In some preferred embodiments, the proteins of the biomarker detection panel are provided on one or more solid supports, in which at least 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95% or 100% of the proteins on the one or more solid supports to which the proteins of the panel are bound are of Table 1, Table 2, Table 3 or Table 5. In some preferred embodiments, the proteins of the biomarker detection panel are provided on a protein array in which at least 55%, 60%, 65%, 70%, or 75%, 80%, 85%, 90%, 95% or 100% of the proteins on the array are target antigens of the biomarker detection panel.

[00124] In some embodiments, the biomarker detection panel used in the methods of the invention includes 6, 7, 8, 9, 10, 11, or 12 target antigens of Table 1. In some embodiments, the biomarker detection panel used in the methods of the invention includes 13, 14, 15, 16, 17, 18, 19, 20, or more target antigens of Table 1. In some embodiments, the test sample is contacted with a biomarker detection panel comprising 21, 22, 23, 24, 25, 26, 27, 28, 29, or 30 antigens of Table 1. A biomarker detection panel can comprise between 30 and 35 antigens of Table 1, between 35 and 40 antigens of Table 1, between 40 and 45 antigens of Table 1, between 45 and 50 antigens of Table 1, between 50 and 55 antigens of Table 1, between 55 and 60 antigens of Table 1, between 60 and 65 antigens of Table 1, between 65 and 70 antigens of Table 1, between 70 and 75 antigens of Table 1, between 75 and 80 antigens of Table 1, between 80 and 85 antigens of Table 1, between 85 and 90 antigens of Table 1, between 90 and 95 antigens of Table 1, between 95 and 100 antigens of Table 1, between 100 and 105 antigens of Table 1, or between 105 and 108 antigens of Table 1.

[00125] Also included in the invention is a composition that comprises a biomarker detection panel for diagnosing, prognosing, monitoring, or staging autoimmune

disease that comprises two or more target antigens selected from Table 1, in which at least one of the two or more target antigens is bound to an autoantibody from a sample of an individual. The invention also includes a biomarker detection panel for diagnosing, prognosing, monitoring, or staging autoimmune disease that comprises 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30 or more target antigens selected from Table 1, in which at least one of the two or more target antigens is bound to an autoantibody from a sample of an individual. Also included in the invention is a composition that comprises a biomarker detection panel for diagnosing, prognosing, monitoring, or staging autoimmune disease that comprises two or more target antigens selected from Table 2, Table 3 or Table 5, in which at least one of the target antigens of the array is bound to an autoantibody from a sample of an individual. The arrays having bound antibody from a sample can be arrays in which at least 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, of 95% of the protein bound to the arrays are proteins of Table 1.

Method for Synthesizing Protein Antigens

[00126] The methods, kits, and systems provided herein include autoantigens, which typically are protein antigens. To obtain protein antigens to be used in the methods provided herein, known methods can be used for making and isolating viral, prokaryotic or eukaryotic proteins in a readily scalable format, amenable to high-throughput analysis. For example, methods include synthesizing and purifying proteins in an array format compatible with automation technologies. Therefore, in one embodiment, protein micrarrays for the invention a method for making and isolating eukaryotic proteins comprising the steps of growing a eukaryotic cell transformed with a vector having a heterologous sequence operatively linked to a regulatory sequence, contacting the regulatory sequence with an inducer that enhances expression of a protein encoded by the heterologous sequence, lysing the cell, contacting the protein with a binding agent such that a complex between the protein and binding agent is formed, isolating the complex from cellular debris, and isolating the protein from the complex, wherein each step is conducted in a 96-well format.

[00127] In a particular embodiment, eukaryotic proteins are made and purified in a 96-array format (*i.e.*, each site on the solid support where processing occurs is one of 96 sites), *e.g.*, in a 96-well microtiter plate. In another embodiment, the solid support does not bind proteins (*e.g.*, a non-protein-binding microtiter plate).

[00128] In certain embodiments, proteins are synthesized by *in vitro* translation according to methods commonly known in the art. For example, proteins can be expressed using a wheat germ, rabbit reticulocyte, or bacterial extract, such as the Expressway.

[00129] Any expression construct having an inducible promoter to drive protein synthesis can be used in accordance with the methods of the invention. The expression construct may be, for example, tailored to the cell type to be used for transformation. Compatibility between expression constructs and host cells are known in the art, and use of variants thereof are also encompassed by the invention.

[00130] In a particular embodiment, the fusion proteins have GST tags and are affinity purified by contacting the proteins with glutathione beads. In further embodiment, the glutathione beads, with fusion proteins attached, can be washed in a 96-well box without using a filter plate to ease handling of the samples and prevent cross contamination of the samples.

[00131] In addition, fusion proteins can be eluted from the binding compound (*e.g.*, glutathione bead) with elution buffer to provide a desired protein concentration. In a specific embodiment, fusion proteins are eluted from the glutathione beads with 30 µl of elution buffer to provide a desired protein concentration.

[00132] For purified proteins that will eventually be spotted onto microscope slides, the glutathione beads are separated from the purified proteins. In one example, all of the glutathione beads are removed to avoid blocking of the microarrays pins used to spot the purified proteins onto a solid support. In one embodiment, the glutathione beads are separated from the purified proteins using a filter plate, for example,

comprising a non-protein-binding solid support. Filtration of the eluate containing the purified proteins should result in greater than 90% recovery of the proteins.

[00133] The elution buffer may, for example, comprise a liquid of high viscosity such as, for example, 15% to 50% glycerol, for example, about 25% glycerol. The glycerol solution stabilizes the proteins in solution, and prevents dehydration of the protein solution during the printing step using a microarrayer.

[00134] Purified proteins may, for example, be stored in a medium that stabilizes the proteins and prevents desiccation of the sample. For example, purified proteins can be stored in a liquid of high viscosity such as, for example, 15% to 50% glycerol, for example, in about 25% glycerol. In one example, samples may be aliquoted containing the purified proteins, so as to avoid loss of protein activity caused by freeze/thaw cycles.

[00135] The skilled artisan can appreciate that the purification protocol can be adjusted to control the level of protein purity desired. In some instances, isolation of molecules that associate with the protein of interest is desired. For example, dimers, trimers, or higher order homotypic or heterotypic complexes comprising an overproduced protein of interest can be isolated using the purification methods provided herein, or modifications thereof. Furthermore, associated molecules can be individually isolated and identified using methods known in the art (*e.g.*, mass spectroscopy).

[00136] The protein antigens once produced can be used in the biomarker panels, methods and kits provided herein as part of a "positionally addressable" array. The array includes a plurality of target antigens, with each target antigen being at a different position on a solid support. The array can include, for example 1, 2, 3, 4, 5, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 40, 50, 100, 200, 300, 400, or 500 different proteins. The array can include 1, 2, 3, 4, 5, 10, 15, 20, 25, 50, 100 or all the proteins of Table 1. In one aspect, the majority of proteins on an array include proteins identified as autoantigens that can have

diagnostic value for a particular disease or medical condition when provided together autoantigen biomarker detection panel.

[00137] In one aspect, the protein array is a bead-based array. In another aspect, the protein array is a planar array. Methods for making protein arrays, such as by contact printing, are well known. In some embodiments, the detection is performed on a protein array, which can be a microarray, and can optionally be a microarray that includes proteins at a concentration of at least 100/cm^2 or 1000/cm^2, or greater than 400/cm^2.

Kits

[00138] In certain embodiments of the invention, kits are provided. Thus, in some embodiments, a kit is provided that comprises 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30-34, 35-39, 40-44, 45-49, 50-54, 55-59, 60-64, 65-69, 70-74, 75-79, 80-84, 85-89, 90-94, 95-100, 100-105, or 106-108 of the test antigen proteins provided in Table 1. In certain aspects the kit includes up to 10, 50, 100, or 108 of the test antigen proteins of Table 1. A kit of the invention can include any of the biomarker detection panels disclosed herein, including, but not limited to, a biomarker panel comprising two or more test antigens of Table 1, and a biomarker panel comprising two or more test antigens of Table 2, Table 3, or Table 5.

[00139] In one embodiment, a kit for diagnosing an autoimmune disease comprises one or more, two or more, ten or more, twenty or more, fifty or more, or all of the autoantigens of Table 1 or a fragment thereof comprising an epitope; and means for detecting if one or more molecules in a test sample binds to one or more of the antigens. In some embodiments, the kits and protein arrays of the present invention contain less than 1,000 polypeptides, or less than 100 polypeptides. In a further embodiment, the kit further comprises a control antibody against one or more of the antigens.

[00140] In a further embodiment, the kit comprises one or more, two or more, ten or more, twenty or more, fifty or more, or all of the antigens selected from the group comprising of Table 2 or fragments thereof comprising an epitope. In a related

embodiment, the kit consists essentially of one or more, two or more, ten or more, twenty or more, fifty or more, or all of the antigens selected from the group comprising of Table 2 or fragments thereof comprising an epitope.

[00141] In another embodiment, the kit comprises one or more, two or more, ten or more, twenty or more, fifty or more, or all of the antigens selected from the group comprising of Table 3 or fragments thereof comprising an epitope. In a related embodiment, the kit consists essentially of one or more, two or more, ten or more, twenty or more, fifty or more, or all of the antigens selected from the group comprising of Table 3 or fragments thereof comprising an epitope.

[00142] In another embodiment, the kit comprises one or more, two or more, ten or more, twenty or more, fifty or more, or all of the antigens selected from the group comprising of Table 5 or fragments thereof comprising an epitope. In a related embodiment, the kit consists essentially of one or more, two or more, ten or more, twenty or more, fifty or more, or all of the antigens selected from the group comprising of Table 5 or fragments thereof comprising an epitope.

[00143] In another embodiment, the kit comprises one or more, two or more, ten or more, twenty or more, fifty or more, or all of the antigens selected from the group comprising of Table 2 or fragments thereof comprising an epitope, in combination with one or more, two or more, ten or more, twenty or more, fifty or more, or all of the antigens selected from the group comprising of Table 3 or fragments thereof comprising an epitope.

[00144] In another embodiment, the kit comprises one or more, two or more, ten or more, twenty or more, fifty or more, or all of the antigens selected from the group comprising of Table 2 or fragments thereof comprising an epitope, in combination with one or more, two or more, ten or more, twenty or more, fifty or more, or all of the antigens selected from the group comprising of Table 5 or fragments thereof comprising an epitope.

[00145] In another embodiment, the kit comprises one or more, two or more, ten or more, twenty or more, fifty or more, or all of the antigens selected from the group

comprising of Table 3 or fragments thereof comprising an epitope, in combination with one or more, two or more, ten or more, twenty or more, fifty or more, or all of the antigens selected from the group comprising of Table 5 or fragments thereof comprising an epitope.

[00146] The kit can include one or more positive controls, one or more negative controls, and/or one or more normalization controls.

[00147] The proteins of the kit may, for example, be immobilized on a solid support or surface. The proteins may, for example, be immobilized in an array. The protein microarray may use bead technology, such as the Luminex technology (Luminex Corp., Austin, TX). The test protein array may or may not be a high-density protein microarray that includes at least 100 proteins/cm^2. The kit can provide a biomarker detection panel of proteins as described herein immobilized on an array. At least 50%, at least 55%, at least 60%, at least 65%, at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, or at least 95% of the proteins immobilized on the array can be proteins of the biomarker test pane. The array can include immobilized on the array one or more positive control proteins, one or more negative controls, and/or one or more normalization controls.

[00148] A kit may further comprise a reporter reagent to detect binding of human antibody to the proteins, such as, for example, an antibody that binds to human antibody, linked to a detectable label. A kit may further comprise reagents useful for various immune reactivity assays, such as ELISA, or other immunoassay techniques known to those of skill in the art. The assays in which the kit reagents can be used may be competitive assays, sandwich assays, and the label may be selected from the group of well-known labels used for radioimmunoassay, fluorescent or chemiluminescence immunoassay.

[00149] A kit can include reagents described herein in any combination. For example, in one aspect, the kit includes a biomarker detection panel as provided herein immobilized on a solid support and anti-human antibodies for detection in solution. The detection antibodies can comprise labels.

[00150] The kit can also include a program in computer readable form to analyze results of methods performed using the kits to practice the methods provided herein.

[00151] The kits of the present invention may also comprise one or more of the components in any number of separate containers, packets, tubes, vials, microtiter plates and the like, or the components may be combined in various combinations in such containers.

[00152] The kits of the present invention may also comprise instructions for performing one or more methods described herein and/or a description of one or more compositions or reagents described herein. Instructions and/or descriptions may be in printed form and may be included in a kit insert. A kit also may include a written description of an Internet location that provides such instructions or descriptions.

EXAMPLES

[00153] The examples set forth below illustrate, but do not limit the invention.

Example 1

[00154] Serum from ten healthy control individuals, twelve individuals with RA prior to and following initiation of Remicade® treatment, twenty individuals with SLE, and twenty individuals with ANCA were profiled against a high throughput human protein array. Serum samples were diluted 1:150 and used to probe human ProtoArray™. Specifically, arrays were blocked for 1 hour, incubated with dilute serum solution for 90 minutes, washed 3 X 10 minutes, incubated with anti-human IgG antibody conjugated to AlexaFluor 647 for 90 minutes, washed as above, dried, and scanned. Following scanning, data was acquired using specialized software. Background-subtracted signals from each population were normalized utilizing a quantile normalization strategy. All possible pairwise comparisons were performed between all groups of samples included in the study utilizing an M-statistics algorithm in which the M-statistic is identified that is associated with the lowest possible p-value for a particular pairwise comparison of sample populations.

[00155] Proteins of interest identified as significant interactors with antibodies present in the serum from autoimmune disease patients included a number of known autoantigens including proteinase-3, myeloperoxidase, CCP peptide, and ssDNA, as well as a number of candidate novel autoantigens. These autoantigens are listed in Table 1 and are further classified according to the corresponding autoimmune disease: RA (Table 2), SLE (Table 3), and ANCA (Table 5). Pairwise comparisons performed between RA at various timepoint pre-and post-Remicade® treatment identified a number of known and novel autoantigens for which either an increased or decreased autoantibody response is observed over the treatment timecourse as described above (Tables 7A and 7B).

Example 2

[00156] Serum samples from healthy individuals as well as individuals with autoimmune diseases including RA (Rheumatoid Arthritis), SLE (Systemic Lupus Erythrematosus) and ANCA (Anti-Neutrophil Cytoplasmic Antibody) were profiled on ProtoArray™ human protein microarrays as described in Example 1. Utilizing the calculations as described below, a number of potential antigen biomarkers were identified for autoimmune diseases. These proteins have the potential to serve as important diagnostic or prognostic indicators. Instead of an assay containing thousands or tens of thousands of proteins, a test sample can be profiled against an assay containing just the antigens associated with autoimmune disease, or a specific autoimmune disease. The tables below identify the autoantigens for RA, SLE, and ANCA.

[00157] Tables 1 - 7 identify antigens according to Genbank ID number for the nucleotide sequence that encodes the antigens. It is understood that an antigen of Tables 1-7 refers to a protein or fragments thereof that is encoded by the nucleotide sequence associated with the nucleotide ID number. Table 1 lists autoantigens associated with RA, SLE and ANCA. The autoantigens in Tables 2, 3 and 5 separately list the autoantigens associated with RA, SLE and ANCA, respectively, and are each a subset of the autoantigens of Table 1.

[00158] Table 1 is a list of autoantigens that were bound more often by antibodies from sera from RA, SLE and ANCA individuals than by antibodies from healthy individuals.

Table 1. Autoimmune disease patients vs. healthy patients

Genbank ID number of nucleic acid coding for the protein	Normal Count	RA, SLE or ANCA Count	p-value	Name or description
BC000052.1	0	9	0.0117396	Similar to peroxisome proliferative activated receptor, alpha
BC000103.1	3	17	0.0048444	NCK adaptor protein 2
BC000175.2	1	12	0.0111660	Hermansky-Pudlak syndrome 1, transcript variant 3
BC000381.2	1	13	0.0055970	TBP-like 1, mRNA
BC000442.1	1	13	0.0055972	serine/threonine kinase 12
BC000809.1	2	7	0.0185217	transcription elongation factor A (SII)-like 1
BC000914.1	1	15	0.0010990	splicing factor, arginine/serine-rich 3
BC000914.1	0	12	0.0014564	splicing factor, arginine/serine-rich 3
BC000997.2	1	12	0.0111660	splicing factor, arginine/serine-rich 7, 35kDa
BC001120.1	10	11	0.0117396	lectin, galactoside-binding, soluble, 3 (galectin 3)
BC001371.2	0	9	0.0117396	chromosome 20 open reading frame 31, mRNA
BC001396.1	3	17	0.0048440	AD-003 protein
BC001662.1	0	9	0.0117396	mitogen-activated protein kinase-activated protein kinase 3
BC001662.1	1	6	0.0173851	mitogen-activated protein kinase-activated protein kinase 3
BC002637.1	0	5	0.0108359	tribbles homolog 2
BC002733.2	1	12	0.0111660	mRNA, complete cds.
BC002880.1	1	14	0.0025987	cysteinyl-tRNA synthetase
BC003168.1	0	9	0.0117396	oxysterol binding protein-like 10,
BC004514.1	1	12	0.0111658	hypothetical protein FLJ12584
BC004514.1	1	7	0.0048821	hypothetical protein FLJ12584
BC005248.1	0	11	0.0030750	eukaryotic translation initiation factor 1A, Y-linked
BC005332.1	0	11	0.00307	cDNA clone MGC:12418 IMAGE:3934658,

			47	complete cds
BC006105.1	2	14	0.01309 35	chromosome 6 open reading frame 134, mRNA
BC006376.1	0	10	0.00614 90	N-myristoyltransferase 2
BC006456.1	10	11	0.01174 00	KIAA0592 protein
BC006793.1	0	10	0.00614 90	GATA binding protein 3
BC007228.1	0	9	0.01174 00	Taxol resistant associated protein 3 (TRAG-3)
BC007411.2	2	15	0.00623 97	diaphanous homolog 1 (Drosophila)
BC007411.2	2	7	0.01852 17	diaphanous homolog 1 (Drosophila)
BC007833.2	0	9	0.01174 00	phosphatidylinositol-4-phosphate 5-kinase, type I, alpha, mRNA
BC007863.1	0	5	0.01083 59	platelet-activating factor acetylhydrolase, isoform Ib, gamma subunit (29kD)
BC007888.1	2	14	0.01309 30	eukaryotic translation initiation factor 2, subunit 2 (beta, 38kD)
BC007949.1	0	9	0.01173 96	eukaryotic translation elongation factor 1 gamma
BC008623.1	0	12	0.00145 60	hypothetical protein FLJ21044 similar to Rbig1, cloneMGC:16823 IMAGE:4177689, mRNA,complete cds.
BC009623.1	0	9	0.01174 00	nucleophosmin (nucleolar phosphoprotein B23, numatrin)
BC009762.2	0	9	0.01174 00	mRNA, complete cds.
BC009873.1	NA	NA	NA	clone MGC:16442 IMAGE:3946787
BC010642.1	0	9	0.01174 00	zinc finger protein 22 (KOX 15),
BC011379.1	2	15	0.00624 00	DKFZP434H132 protein
BC011498.1	4	18	0.00723 50	Unknown (protein for MGC:17017)
BC011668.1	1	12	0.01116 60	Similar to casein kinase 2, alpha 1 polypeptide
BC011707.1	10	11	0.01174 00	nuclear receptor binding factor 2, mRNA
BC011804.2	4	17	0.01839 00	chromosome 1 open reading frame 165, mRNA
BC011863.2	2	7	0.01852 17	Unknown (protein for MGC:20604)
BC012105.1	3	8	0.01488 45	nuclear VCP-like, mRNA
BC012120.1	0	9	0.01174 00	nuclear factor I/C (CCAAT-binding transcription factor)
BC012472.1	1	12	0.01116 60	ubiquitin D, mRNA
BC012876.1	0	14	0.00026 65	clone MGC:17259 IMAGE:4149333
BC012924.1	NA	NA	NA	dual adaptor of phosphotyrosine and 3-phosphoinositides
BC013073.1	0	10	0.00614 90	chromosome 1 open reading frame 37, mRNA
BC013103.1	1	6	0.01738 51	Similar to hypothetical protein FLJ20435, cloneMGC:16997 IMAGE:4343882,

				mRNAcomplete cds.
BC013171.1	10	11	0.0117396	cDNA clone MGC:17065 IMAGE:4344401, complete cds
BC013567.1	10	11	0.0117400	hypothetical protein FLJ11328
BC014271.2	1	14	0.0025987	endoglin (Osler-Rendu-Weber syndrome 1), mRNA
BC014435.1	0	5	0.0108359	Unknown (protein for MGC:22922)
BC014452.1	4	17	0.0183900	cDNA clone IMAGE:4903661
BC014975.1	2	7	0.0185217	hypothetical protein FLJ14668, mRNA
BC014991.1	0	9	0.0117396	N-methylpurine-DNA glycosylase
BC015008.1	4	17	0.0183900	hydroxyacylglutathione hydrolase-like, mRNA
BC015497.1	1	12	0.0111660	cDNA clone MGC:9014 IMAGE:3913870, complete cds
BC015715.1	1	12	0.0111660	makorin, ring finger protein, 2
BC015833.1	4	17	0.0183901	cDNA clone MGC:27152 IMAGE:4691630, complete cds
BC016057.1	10	11	0.0117396	Usher syndrome 1C (autosomal recessive, severe), mRNA
BC016312.1	10	11	0.0117396	chromosome 15 open reading frame 15, mRNA
BC016380.1	1	14	0.0025987	cDNA clone MGC:27376 IMAGE:4688477, complete cds
BC016381.1	0	13	0.0006473	cDNA clone MGC:27378 IMAGE:4688865, complete cds
BC016381.1	1	6	0.0173851	cDNA clone MGC:27378 IMAGE:4688865, complete cds
BC016764.1	4	20	0.0003540	ribulose-5-phosphate-3-epimerase, transcript variant 1
BC016764.1	3	16	0.0116173	ribulose-5-phosphate-3-epimerase, transcript variant 1
BC016778.1	2	14	0.0130930	HIV-1 rev binding protein 2, mRNA
BC016842.1	1	12	0.0111660	family with sequence similarity 61, member A, mRNA
BC017114.1	0	10	0.0061490	hypothetical protein FLJ22833
BC017865.1	0	11	0.0030747	Fc fragment of IgG, low affinity IIIa, receptor (CD16a), mRNA
BC018142.1	3	8	0.0148845	caspase recruitment domain family, member 14, mRNA
BC018302.1	0	9	0.0117396	TRM1 tRNA methyltransferase 1 homolog (S. cerevisiae), mRNA
BC018302.1	0	6	0.0030960	TRM1 tRNA methyltransferase 1 homolog (S. cerevisiae), mRNA
BC019337.1	10	11	0.0117400	immunoglobulin heavy constant gamma 1 (G1m marker), mRNA
BC019337.1	4	19	0.0021220	immunoglobulin heavy constant gamma 1 (G1m marker), mRNA
BC020622.1	1	13	0.0055972	zinc finger, A20 domain containing 1, mRNA, complete cds.
BC020647.1	2	14	0.0130930	HSPC128 protein, mRNA

BC020962.1	0	9	0.0117396	similar to glucosamine-6-sulfatases
BC022098.1	0	10	0.0061493	cDNA clone MGC:31944 IMAGE:4878869, complete cds
BC022231.1	1	12	0.0111660	Ets2 repressor factor, mRNA
BC022325.1	0	16	0.0000333	hypothetical protein FLJ12729
BC022362.1	1	14	0.0025987	cDNA clone MGC:23888 IMAGE:4704496, complete cds
BC023569.1	0	9	0.0117400	UPF3 regulator of nonsense transcripts homolog A (yeast), transcript variant 2
BC024289.1	0	10	0.0061493	cDNA clone MGC:39273 IMAGE:5440834, complete cds
BC024289.1	1	7	0.0048821	cDNA clone MGC:39273 IMAGE:5440834, complete cds
BC025314.1	3	17	0.0048444	immunoglobulin heavy constant gamma 1 (G1m marker), mRNA
BC025314.1	1	6	0.0173851	immunoglobulin heavy constant gamma 1 (G1m marker), mRNA
BC025345.1	4	19	0.0021220	mRNA similar to LOC149651 (cDNA clone MGC:39393 IMAGE:4862156), complete cds
BC025996.2	0	13	0.0006470	cDNA clone MGC:26787 IMAGE:4838986
BC027607.1	1	12	0.0111660	clone MGC:26892 IMAGE:4828241
BC028039.1	1	6	0.0173851	hypothetical protein MGC39900
BC028151.1	0	9	0.0117400	DNA segment on chromosome X and Y (unique) 155 expressed sequence, mRNA
BC028237.1	1	12	0.0111660	growth differentiation factor 10, mRNA
BC028301.1	0	12	0.0014560	mRNA similar to LOC147447
BC029046.1	4	17	0.0183900	H1 histone family, member 0, mRNA
BC029444.1	0	11	0.0030747	cDNA clone MGC:32714 IMAGE:4692138, complete cds
BC029609.1	0	10	0.0061493	cDNA clone MGC:39831 IMAGE:5302675
BC029827.1	0	9	0.0117400	Down syndrome critical region gene 9, mRNA
BC029891.1	0	10	0.0061490	transcription factor EC, mRNA
BC030219.1	1	14	0.0025990	RAD51-like 1 (S. cerevisiae)
BC030219.1	1	6	0.0173851	RAD51-like 1 (S. cerevisiae)
BC030590.1	1	12	0.0111658	retinoblastoma binding protein 8, mRNA
BC030702.1	0	10	0.0061490	hypothetical protein FLJ12847
BC030814.1	0	14	0.0002665	immunoglobulin kappa variable 1-5, mRNA
BC030983.1	2	17	0.0009742	immunoglobulin lambda constant 1 (Mcg marker), mRNA
BC030984.1	2	19	0.0000636	cDNA clone MGC:32654 IMAGE:4701898, complete cds
BC031074.1	1	16	0.00041	poly (ADP-ribose) polymerase family, member 16,

			41	mRNA
BC032124.1	1	6	0.01738 51	bromodomain containing 3
BC032334.1	0	5	0.01083 59	putative homeodomain transcription factor 2, mRNA, complete cds.
BC032452.1	10	11	0.01174 00	immunoglobulin lambda constant 1 (Mcg marker), mRNA
BC032462.1	0	10	0.00614 90	vacuolar protein sorting 29 (yeast), mRNA
BC032485.1	0	9	0.01174 00	hypothetical protein FLJ30473,
BC032485.1	1	16	0.00041 41	hypothetical protein FLJ30473
BC032852.2	4	18	0.00723 50	melanoma antigen family B, 4, mRNA
BC032866.2	1	13	0.00559 72	eukaryotic translation initiation factor 5, transcript variant 2, mRNA
BC033195.1	1	6	0.01738 51	leukocyte receptor cluster (LRC) member 12
BC033856.1	3	17	0.00484 40	Similar to RIKEN cDNA 3110040D16 gene, cloneMGC:45395 IMAGE:5123380, mRNA,completecds.
BC034401.1	10	11	0.01174 00	Similar to LOC161981
BC034954.2	2	7	0.01852 17	nucleosome assembly protein 1-like 3, mRNA
BC035314.1	4	17	0.01839 00	brix domain containing 1
BC035568.1	0	9	0.01174 00	acylphosphatase 1, erythrocyte (common) type
BC036075.1	0	9	0.01173 96	GIPC PDZ domain containing family, member 2, mRNA
BC036723.1	1	12	0.01116 58	Fc fragment of IgG, low affinity IIIa, receptor (CD16a), mRNA
BC037906.1	2	7	0.01852 17	hypothetical protein FLJ11017, mRNA
BC038105.2	1	14	0.00259 90	membrane protein, palmitoylated 7 (MAGUK p55 subfamily member 7)
BC039814.1	1	17	0.00013 40	zinc finger protein 265, transcript variant 2, mRNA
BC040844.1	1	14	0.00259 90	synaptotagmin binding, cytoplasmic RNA interacting protein, mRNA
BC041037.1	0	7	0.00071 45	immunoglobulin heavy constant mu, mRNA
BC041157.1	0	11	0.00307 47	thromboxane A synthase 1 (platelet, cytochrome P450, family 5, subfamily A), transcript variantTXS-I, mRNA
BC042625.1	1	13	0.00559 70	LUC7-like 2 (S. cerevisiae), mRNA
BC044584.1	0	11	0.00307 47	DnaJ (Hsp40) homolog, subfamily C, member 4, mRNA
BC050428.1	5	19	0.00884 20	katanin p60 (ATPase-containing) subunit A 1, mRNA
BC051301.1	0	10	0.00614 90	TEA domain family member 2, mRNA
BC052806.1	0	9	0.01174 00	cDNA clone MGC:61802 IMAGE:5730155
BC053656.1	10	11	0.01174 00	EGF-like repeats and discoidin I-like domains 3, mRNA

BC053656.1	1	17	0.00013 40	EGF-like repeats and discoidin I-like domains 3, mRNA
BC053664.1	0	12	0.00145 64	complete cds.
BC053866.1	0	9	0.01174 00	endothelin 3, transcript variant 2
BC053872.1	0	9	0.01174 00	copine V, mRNA
BC053984.1	3	18	0.00165 72	cDNA clone MGC:59926 IMAGE:5480266, complete cds
BC054034.1	1	12	0.01116 60	U11/U12 snRNP 35K, transcript variant 2
BC055314.1	0	10	0.00614 90	C2f protein
BC056256.1	1	16	0.00041 41	immunoglobulin kappa constant, mRNA
BC057774.1	1	12	0.01116 60	hypothetical protein FLJ31455, mRNA
BC058903.1	0	9	0.01174 00	intercellular adhesion molecule 3, mRNA
BC063275.1	1	15	0.00109 90	eukaryotic translation initiation factor 2C, 1, mRNA
BC063479.1	1	15	0.00109 90	La ribonucleoprotein domain family, member 4, mRNA
BC066938.1	4	17	0.01839 01	DEAD (Asp-Glu-Ala-Asp) box polypeptide 43, mRNA
BC066987.1	0	9	0.01173 96	cDNA clone MGC:87634 IMAGE:4838596, complete cds
BC067446.1	0	9	0.01174 00	disabled homolog 1 (Drosophila), mRNA
CTL1093	6	20	0.00766 28	Human IgG
CTL1094	10	11	0.01174 00	Influenza A
CTL2110	0	11	0.00307 50	DNA TOPOISIMERASE(Scl-70)
CTL2112	3	17	0.00484 40	ssDNA
CTL2130	1	18	0.00003 51	proteinase-3
CTL2132	1	12	0.01116 60	myeloperoxidase
CTL2132	1	6	0.01738 51	myeloperoxidase_100ug/ml_S
CTL2136	1	13	0.00559 70	U1-snRNP 68 PROTEIN
CTL2137	1	15	0.00109 95	La/SS-B (La)
CTL2138	0	14	0.00026 70	RNP COMPLEX
CTL2142	4	19	0.00212 20	ssDNA
CTL2145	0	14	0.00026 70	RIBOSOMAL RNA
CTL2152	2	14	0.01309 30	RNA POLYMERASE
NM_000997.	0	9	0.01174 00	ribosomal protein L37 (RPL37)
NM_001014.	1	14	0.00259	ribosomal protein S10 (RPS10)

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NM_001015.2	10	11	0.0117396	ribosomal protein S11 (RPS11)
NM_001106.2	1	12	0.0111660	activin A receptor, type IIB (ACVR2B)
NM_001124.1	0	10	0.0061490	adrenomedullin (ADM), mRNA
NM_001280.1	0	9	0.0117400	cold inducible RNA binding protein (CIRBP), mRNA
NM_001616.2	0	13	0.0006470	activin A receptor, type II (ACVR2)
NM_001663.2	2	16	0.0026547	ADP-ribosylation factor 6 (ARF6), mRNA
NM_001697.1	1	12	0.0111660	ATP synthase, H+ transporting, mitochondrial F1 complex, O subunit (oligomycin sensitivityconferring protein) (ATP5O)
NM_001826.1	2	9	0.0005954	DC28 protein kinase 1, clone MGC:12835 IMAGE:4110344, mRNA, complete cds.
NM_001894.2	0	9	0.0117400	casein kinase 1, epsilon (CSNK1E)
NM_001894.2	0	13	0.0006473	casein kinase 1, epsilon (CSNK1E)
NM_001896.1	0	10	0.0061490	casein kinase 2, alpha prime polypeptide (CSNK2A2)
NM_001896.2	0	10	0.0061490	casein kinase 2, alpha prime polypeptide (CSNK2A2), mRNA
NM_002019.1	10	11	0.0117396	fms-related tyrosine kinase 1 (vascular endothelial growth factor/vascular permeability factorreceptor) (FLT1)
NM_002103.3	0	10	0.0061493	glycogen synthase 1 (muscle) (GYS1), mRNA
NM_002129.2	0	10	0.0061490	high-mobility group box 2 (HMGB2), mRNA
NM_002387.1	10	11	0.0117400	mutated in colorectal cancers (MCC), mRNA
NM_002462.2	1	12	0.0111658	myxovirus (influenza virus) resistance 1, interferon-inducible protein p78 (mouse) (MX1), mRN
NM_003045.3	1	12	0.0111658	solute carrier family 7 (cationic amino acid transporter, y+ system), member 1 (SLC7A1),mRNA
NM_003049.1	0	9	0.0117396	solute carrier family 10 (sodium/bile acid cotransporter family), member 1 (SLC10A1),mRNA
NM_003295.1	0	10	0.0061490	tumor protein, translationally-controlled 1 (TPT1), mRNA
NM_003495.2	0	9	0.0117400	histone 1, H4i (HIST1H4I), mRNA
NM_003516.2	6	20	0.0076630	histone 2, H2aa (HIST2H2AA), mRNA
NM_003583.2	2	15	0.0062400	dual-specificity tyrosine-(Y)-phosphorylation regulated kinase 2 (DYRK2), transcript variant 1 mRNA
NM_003600.1	0	9	0.0117400	Serine/threonine kinase 6 (STK6)
NM_003662.1	2	7	0.0185217	Pirin (PIR)
NM_003897.2	0	11	0.0030750	immediate early response 3 (IER3), transcript variant short, mRNA

NM_003907.1	3	8	0.0148845	Eukaryotic translation initiation factor 2B, subunit 5 epsilon, 82kDa (EIF2B5), mRNA
NM_004055.3	3	17	0.0048444	calpain 5 (CAPN5), mRNA
NM_004055.3	3	8	0.0148845	calpain 5 (CAPN5), mRNA
NM_004214.3	1	15	0.0010990	fibroblast growth factor (acidic) intracellular binding protein (FIBP)
NM_004217.1	0	10	0.0061493	aurora kinase B (AURKB)
NM_004567.2	10	11	0.0117400	6-phosphofructo-2-kinase/fructose-2,6-biphosphatase 4 (PFKFB4), mRNA
NM_004596.1	0	13	0.0006470	small nuclear ribonucleoprotein polypeptide A (SNRPA
NM_004635.2	1	6	0.0173851	mitogen-activated protein kinase-activated protein kinase 3 (MAPKAPK3)
NM_004645.1	4	17	0.0183900	coilin (COIL),
NM_004656.2	2	15	0.0062400	BRCA1 associated protein-1 (ubiquitin carboxy-terminal hydrolase) (BAP1), mRNA
NM_004732.1	4	17	0.0183901	potassium voltage-gated channel, shaker-related subfamily, beta member 3 (KCNAB3)
NM_004765.2	0	10	0.0061490	B-cell CLL/lymphoma 7C (BCL7C), mRNA
NM_005157.2	1	6	0.0173851	v-abl Abelson murine leukemia viral oncogene homolog 1 (ABL1), transcript variant a
NM_005240.1	1	12	0.0111660	ets variant gene 3 (ETV3), mRNA
NM_005435.2	2	7	0.0185217	Rho guanine nucleotide exchange factor (GEF) 5 (ARHGEF5)
NM_005522.3	0	11	0.0030747	homeo box A1 (HOXA1), transcript variant 1, mRNA
NM_006205.1	3	18	0.0016570	phosphodiesterase 6H, cGMP-specific, cone, gamma (PDE6H), mRNA
NM_006205.1	0	6	0.0030960	phosphodiesterase 6H, cGMP-specific, cone, gamma (PDE6H), mRNA
NM_006223.1	3	16	0.0116170	protein (peptidyl-prolyl cis/trans isomerase) NIMA-interacting, 4 (parvulin) (PIN4)
NM_006298.2	1	13	0.0055970	zinc finger protein 192 (ZNF192), mRNA
NM_006298.2	10	11	0.0117396	zinc finger protein 192 (ZNF192), mRNA
NM_006388.2	3	17	0.0048440	HIV-1 Tat interacting protein, 60kDa (HTATIP), transcript variant 2, mRNA
NM_006433.2	0	9	0.0117400	granulysin (GNLY), transcript variant NKG5, mRNA
NM_006607.1	4	17	0.0183900	pituitary tumor-transforming 2 (PTTG2), mRNA
NM_006857.1	1	12	0.0111660	putative nucleic acid binding protein RY-1 (RY1), mRNA
NM_006869.1	0		0.0117396	centaurin, alpha 1 (CENTA1), mRNA
NM_007285.5	3	16	0.0116170	GABA(A) receptor-associated protein-like 2 (GABARAPL2)
NM_007311.2	10	11	0.0117400	benzodiazapine receptor (peripheral) (BZRP), transcript variant PBR-S
NM_012163.1	0	9	0.0117400	F-box and leucine-rich repeat protein 9 (FBXL9)
NM_012163.	0	10	0.00614	F-box and leucine-rich repeat protein 9 (FBXL9)

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NM_012241.2	1	13	0.00559 72	sirtuin (silent mating type information regulation 2 homolog) 5 (S. cerevisiae) (SIRT5), transcript variant 1, mRNA
NM_012321.1	2	14	0.01309 30	U6 snRNA-associated Sm-like protein (LSM4)
NM_013322.2	3	8	0.01488 45	sorting nexin 10 (SNX10), mRNA
NM_014765.1	0	5	0.01083 59	translocase of outer mitochondrial membrane 20 homolog (yeast) (TOMM20), mRNA
NM_015488.1	3	16	0.01161 70	myofibrillogenesis regulator 1 (MR-1)
NM_015640.1	4	18	0.00723 50	PAI-1 mRNA-binding protein (PAI-RBP1)
NM_015987.2	0	13	0.00064 70	heme binding protein 1 (HEBP1)
NM_016207.2	10	11	0.01174 00	cleavage and polyadenylation specific factor 3, 73kDa (CPSF3), mRNA
NM_016355.3	1	14	0.00259 90	DEAD (Asp-Glu-Ala-Asp) box polypeptide 47 (DDX47), transcript variant 1, mRNA
NM_016483.3	1	15	0.00109 90	PHD finger protein 7 (PHF7)
NM_016505.2	4	19	0.00212 20	putative S1 RNA binding domain protein (PS1D), mRNA
NM_016576.2	0	10	0.00614 93	guanosine monophosphate reductase 2 (GMPR2)
NM_016836.1	0	5	0.01083 59	RNA binding motif, single stranded interacting protein 1 (RBMS1), transcript variant YC1
NM_016940.1	1	12	0.01116 60	chromosome 21 open reading frame 6 (C21orf6), mRNA
NM_018032.2	1	13	0.00559 70	LUC7-like (S. cerevisiae) (LUC7L)
NM_018047.1	0	9	0.01174 00	RNA binding motif protein 22 (RBM22), mRNA
NM_018047.1	0	9	0.01173 96	RNA binding motif protein 22 (RBM22), mRNA
NM_018107.2	1	14	0.00259 90	RNA-binding region (RNP1, RRM) containing 4 (RNPC4)
NM_018153.2	2	14	0.01309 35	anthrax toxin receptor 1 (ANTXR1), transcript variant 3, mRNA
NM_018184.1	0	10	0.00614 93	ADP-ribosylation factor-like 10C (ARL10C)
NM_018679.2	0	10	0.00614 93	t-complex 11 (mouse) (TCP11), mRNA
NM_019021.1	0	12	0.00145 64	hypothetical protein FLJ20010 (FLJ20010), mRNA
NM_020239.2	1	12	0.01116 60	small protein effector 1 of Cdc42
NM_020317.2	NA	NA	NA	hypothetical protein dJ465N24.2.1
NM_020367.2	0	9	0.01173 96	chromosome 12 open reading frame 6 (C12orf6)
NM_020381.2	1	14	0.00259 87	chromosome 6 open reading frame 210 (C6orf210), mRNA
NM_020444.2	10	11	0.01174 00	KIAA1191 protein (KIAA1191), mRNA
NM_020661.1	1	13	0.00559 70	activation-induced cytidine deaminase (AICDA), mRNA
NM_020804.	0	9	0.01173	protein kinase C and casein kinase substrate in

2			96	neurons 1 (PACSIN1), mRNA
NM_020898.1	2	7	0.0185217	KIAA1536 protein (KIAA1536), mRNA
NM_021104.1	1	13	0.0055970	ribosomal protein L41 (RPL41), mRNA
NM_021130.1	10	11	0.0117396	peptidylprolyl isomerase A (cyclophilin A) (PPIA)
NM_021133.1	3	16	0.0116173	ribonuclease L (2',5'-oligoisoadenylate synthetase-dependent) (RNASEL),
NM_021639.2	0	5	0.0108359	hypothetical protein SP192 (SP192)
NM_021709.1	0	10	0.0061493	CD27-binding (Siva) protein (SIVA), transcript variant 2, mRNA
NM_021822.1	0	9	0.0117400	apolipoprotein B mRNA editing enzyme, catalytic polypeptide-like 3G (APOBEC3G), mRNA
NM_022100.1	0	9	0.0117400	mitochondrial ribosomal protein S14 (MRPS14), nuclear gene encoding mitochondrial protein, mRNA
NM_022787.2	4	19	0.0021220	nicotinamide nucleotide adenylyltransferase 1 (NMNAT1), mRNA
NM_022787.2	4	17	0.0183901	nicotinamide nucleotide adenylyltransferase 1 (NMNAT1), mRNA
NM_023940.1	10	11	0.0117400	hypothetical protein MGC2827
NM_024292.2	0	5	0.0108359	ubiquitin-like 5, mRNA, complete cds.
NM_024625.3	0	9	0.0117400	zinc finger CCCH type, antiviral 1 (ZC3HAV1), transcript variant 2, mRNA
NM_031465.2	0	11	0.0030750	hypothetical protein , mRNA
NM_031473.1	2	7	0.0185217	carnitine deficiency-associated gene expressed in ventricle 1 (CDV-1)
NM_032042.2	0	12	0.0014560	hypothetical protein DKFZp564D172 (DKFZP564D172)
NM_032042.2	1	6	0.0173851	hypothetical protein DKFZp564D172
NM_032328.1	0	5	0.0108359	hypothetical protein , mRNA
NM_032345.1	0	10	0.0061490	PYM protein (PYM), mRNA
NM_032350.3	0	9	0.0117400	hypothetical protein , mRNA
NM_032855.1	0	12	0.0014564	hematopoietic SH2 protein (HSH2)
NM_032855.1	1	6	0.0173851	hematopoietic SH2 protein (HSH2)
NM_032906.2	2	15	0.0062400	hypothetical protein , mRNA
NM_033030.2	1	12	0.0111660	bol, boule-like (Drosophila) (BOLL)
NM_033122.1	3	8	0.0148845	testis development protein NYD-SP26 (NYD-SP26),
NM_052822.1	0	9	0.0117396	secretory carrier membrane protein 1 (SCAMP1), transcript variant 2
NM_052877.1	0	12	0.0014564	mediator of RNA polymerase II transcription, subunit 8 homolog (yeast) (MED8)
NM_054016.1	1	14	0.0025990	FUS interacting protein (serine-arginine rich) 1 (FUSIP1), transcript variant 2, mRNA
NM_138551.	3	16	0.01161	thymic stromal lymphopoietin (TSLP), transcript

1			70	variant 2
NM_138775.1	1	12	0.0111660	hypothetical protein BC015183 (LOC91801), mRNA
NM_144982.1	2	15	0.0062400	hypothetical protein MGC23401 (MGC23401)
NM_145020.1	NA	NA	NA	hypothetical protein FLJ32743
NM_145315.2	10	11	0.0117396	lactation elevated 1 (LACE1)
NM_145810.1	0	9	0.0117400	cell division cycle associated 7 (CDCA7), transcript variant 2, mRNA
NM_152688.1	0	11	0.0030750	KH domain containing, RNA binding, signal transduction associated 2 (KHDRBS2), mRNA
NM_152688.1	0	10	0.0061493	KH domain containing, RNA binding, signal transduction associated 2 (KHDRBS2), mRNA
NM_152697.2	3	16	0.0116173	hypothetical protein , mRNA
NM_152769.1	0	11	0.0030750	chromosome 19 open reading frame 26 (C19orf26), mRNA
NM_152770.1	1	12	0.0111660	hypothetical protein , mRNA
NM_152770.1	0	5	0.0108359	hypothetical protein , mRNA
NM_153207.2	2	15	0.0062400	AE binding protein 2 (AEBP2)
NM_153215.1	1	17	0.0001340	hypothetical protein FLJ38608 (FLJ38608), mRNA
NM_153332.2	4	19	0.0021220	3' exoribonuclease (3'HEXO), mRNA
NM_173474.2	0	5	0.0108359	N-terminal asparagine amidase (NTAN1), mRNA
NM_173519.1	0	5	0.0108359	hypothetical protein , mRNA
NM_173545.1	0	9	0.0117400	chromosome 2 open reading frame 13 (C2orf13), mRNA
NM_175923.2	1	12	0.0111660	hypothetical protein MGC42630 (MGC42630)
NM_177996.1	1	12	0.0111660	erythrocyte membrane protein band 4.1-like 1 (EPB41L1), transcript variant 2, mRNA
NM_177996.1	1	6	0.0173851	erythrocyte membrane protein band 4.1-like 1 (EPB41L1), transcript variant 2, mRNA
NM_178496.2	1	13	0.0055972	similar to BcDNA:GH11415 gene product (LOC151963), mRNA
NM_182623.1	4	18	0.0072350	hypothetical protein FLJ36766 (FLJ36766), mRNA
NM_182665.1	0	12	0.0014564	Ras association (RalGDS/AF-6) domain family 5 (RASSF5), transcript variant 3, mRNA
NM_198395.1	0	9	0.0117400	Ras-GTPase-activating protein SH3-domain-binding protein (G3BP), transcript variant 2
NM_198490.1	0	11	0.0030747	RAB43, member RAS oncogene family (RAB43), mRNA
NM_203326.1	0	9	0.0117396	5-azacytidine induced 2 (AZI2), transcript variant 2
NM_203326.1	0	5	0.0108359	5-azacytidine induced 2 (AZI2), transcript variant 2
NM_212492.1	0	10	0.0061493	G protein pathway suppressor 1 (GPS1), transcript variant 1, mRNA

[00159] Table 2 is a list of autoantigens that were bound by antibodies in sera from individuals with RA (before treatment with infliximab) more often than by antibodies in sera from healthy individuals. The normal count and RA count are presented along with the corresponding p-value.

Table 2. RA vs. healthy patients

Genbank ID number of nucleic acid coding for the protein	Normal Count	RA Count	p-value	Name or description
BC000809.1	2	7	0.018522	transcription elongation factor A (SII)-like 1
BC001662.1	1	6	0.017385	mitogen-activated protein kinase-activated protein kinase 3
BC002637.1	0	5	0.010836	tribbles homolog 2
BC004514.1	1	7	0.004882	hypothetical protein FLJ12584
BC007411.2	2	7	0.018522	diaphanous homolog 1 (Drosophila)
BC007863.1	0	5	0.010836	platelet-activating factor acetylhydrolase, isoform Ib, gamma subunit (29kD)
BC011863.2	2	7	0.018522	Unknown (protein for MGC:20604)
BC012105.1	3	8	0.014884	nuclear VCP-like, mRNA
BC013103.1	1	6	0.017385	Similar to hypothetical protein FLJ20435, cloneMGC:16997 IMAGE:4343882, mRNA, complete cds.
BC014435.1	0	5	0.010836	Unknown (protein for MGC:22922)
BC014975.1	2	7	0.018522	hypothetical protein FLJ14668, mRNA
BC016381.1	1	6	0.017385	cDNA clone MGC:27378 IMAGE:4688865, complete cds
BC018142.1	3	8	0.014884	caspase recruitment domain family, member 14, mRNA
BC018302.1	0	6	0.003096	TRM1 tRNA methyltransferase 1 homolog (S. cerevisiae), mRNA
BC024289.1	1	7	0.004882	cDNA clone MGC:39273 IMAGE:5440834, complete cds
BC025314.1	1	6	0.017385	immunoglobulin heavy constant gamma 1 (G1m marker), mRNA
BC028039.1	1	6	0.017385	hypothetical protein MGC39900
BC030219.1	1	6	0.017385	RAD51-like 1 (S. cerevisiae)
BC032124.1	1	6	0.017385	bromodomain containing 3
BC032334.1	0	5	0.010836	putative homeodomain transcription factor 2, mRNA, complete cds.
BC033195.1	1	6	0.017385	leukocyte receptor cluster (LRC) member 12
BC034954.2	2	7	0.018522	nucleosome assembly protein 1-like 3, mRNA
BC037906.1	2	7	0.018522	hypothetical protein FLJ11017, mRNA
BC041037.1	0	7	0.000714	immunoglobulin heavy constant mu, mRNA
CTL2132	1	6	0.017385	myeloperoxidase_100ug/ml_S
NM_001826.1	2	9	0.000595	CDC28 protein kinase 1, clone MGC:12835 IMAGE:4110344, mRNA, complete cds.
NM_003662.1	2	7	0.018522	Pirin (PIR)
NM_003907.1	3	8	0.014884	eukaryotic translation initiation factor 2B, subunit 5

				epsilon, 82kDa (EIF2B5), mRNA
NM_004055.3	3	8	0.014884	calpain 5 (CAPN5), mRNA
NM_004635.2	1	6	0.017385	mitogen-activated protein kinase-activated protein kinase 3 (MAPKAPK3)
NM_005157.2	1	6	0.017385	v-abl Abelson murine leukemia viral oncogene homolog 1 (ABL1), transcript variant a
NM_005435.2	2	7	0.018522	Rho guanine nucleotide exchange factor (GEF) 5 (ARHGEF5)
NM_006205.1	0	6	0.003096	phosphodiesterase 6H, cGMP-specific, cone, gamma (PDE6H), mRNA
NM_013322.2	3	8	0.014884	sorting nexin 10 (SNX10), mRNA
NM_014765.1	0	5	0.010836	translocase of outer mitochondrial membrane 20 homolog (yeast) (TOMM20), mRNA
NM_016836.1	0	5	0.010836	RNA binding motif, single stranded interacting protein 1 (RBMS1), transcript variant YC1
NM_020898.1	2	7	0.018522	KIAA1536 protein (KIAA1536), mRNA
NM_021639.2	0	5	0.010836	hypothetical protein SP192 (SP192)
NM_024292.2	0	5	0.010836	ubiquitin-like 5, mRNA, complete cds.
NM_031473.1	2	7	0.018522	carnitine deficiency-associated gene expressed in ventricle 1 (CDV-1)
NM_032042.2	1	6	0.017385	hypothetical protein DKFZp564D172
NM_032328.1	0	5	0.010836	hypothetical protein , mRNA
NM_032855.1	1	6	0.017385	hematopoietic SH2 protein (HSH2)
NM_033122.1	3	8	0.014884	testis development protein NYD-SP26 (NYD-SP26),
NM_152770.1	0	5	0.010836	hypothetical protein , mRNA
NM_173474.2	0	5	0.010836	N-terminal asparagine amidase (NTAN1), mRNA
NM_173519.1	0	5	0.010836	hypothetical protein , mRNA
NM_177996.1	1	6	0.017385	erythrocyte membrane protein band 4.1-like 1 (EPB41L1), transcript variant 2, mRNA
NM_203326.1	0	5	0.010836	5-azacytidine induced 2 (AZI2), transcript variant 2

[00160] Table 3 is a list of autoantigens that were bound more often by antibodies in sera from individuals with SLE than by antibodies in sera from healthy individuals. The normal count and SLE count are presented along with the corresponding p-value.

Table 3. SLE vs. healthy patients

Genbank ID number of nucleic acid coding for the protein	Normal Count	SLE Count	p-value	Name or description
BC000175.2	1	12	0.011166	Hermansky-Pudlak syndrome 1, transcript variant 3
BC000381.2	1	13	0.005597	TBP-like 1, mRNA
BC000914.1	1	15	0.001099	splicing factor, arginine/serine-rich 3
BC000997.2	1	12	0.011166	splicing factor, arginine/serine-rich 7, 35kDa
BC001396.1	3	17	0.004844	AD-003 protein
BC002733.2	1	12	0.011166	mRNA, complete cds.

BC005248.1	0	11	0.003075	eukaryotic translation initiation factor 1A, Y-linked
BC006376.1	0	10	0.006149	N-myristoyltransferase 2
BC006456.1	10	11	0.01174	KIAA0592 protein
BC006793.1	0	10	0.006149	GATA binding protein 3
BC007228.1	0	9	0.01174	Taxol resistant associated protein 3 (TRAG-3)
BC007833.2	0	9	0.01174	phosphatidylinositol-4-phosphate 5-kinase, type I, alpha, mRNA
BC007888.1	2	14	0.013093	eukaryotic translation initiation factor 2, subunit 2 (beta, 38kD)
BC008623.1	0	12	0.001456	hypothetical protein FLJ21044 similar to Rbig1, cloneMGC:16823 IMAGE:4177689, mRNA, complete cds.
BC009623.1	0	9	0.01174	nucleophosmin (nucleolar phosphoprotein B23, numatrin)
BC009762.2	0	9	0.01174	mRNA, complete cds.
BC009873.1	NA	NA	NA	clone MGC:16442 IMAGE:3946787
BC010642.1	0	9	0.01174	zinc finger protein 22 (KOX 15),
BC011379.1	2	15	0.00624	DKFZP434H132 protein
BC011498.1	4	18	0.007235	Unknown (protein for MGC:17017)
BC011668.1	1	12	0.011166	Similar to casein kinase 2, alpha 1 polypeptide
BC011707.1	10	11	0.01174	nuclear receptor binding factor 2, mRNA
BC011804.2	4	17	0.01839	chromosome 1 open reading frame 165, mRNA
BC012120.1	0	9	0.01174	nuclear factor I/C (CCAAT-binding transcription factor)
BC012472.1	1	12	0.011166	ubiquitin D, mRNA
BC012924.1	NA	NA	NA	dual adaptor of phosphotyrosine and 3-phosphoinositides
BC013073.1	0	10	0.006149	chromosome 1 open reading frame 37, mRNA
BC013567.1	10	11	0.01174	hypothetical protein FLJ11328
BC014452.1	4	17	0.01839	cDNA clone IMAGE:4903661
BC015008.1	4	17	0.01839	hydroxyacylglutathione hydrolase-like, mRNA
BC015497.1	1	12	0.011166	cDNA clone MGC:9014 IMAGE:3913870, complete cds
BC015715.1	1	12	0.011166	makorin, ring finger protein, 2
BC016764.1	4	20	0.000354	ribulose-5-phosphate-3-epimerase, transcript variant 1
BC016778.1	2	14	0.013093	HIV-1 rev binding protein 2, mRNA
BC016842.1	1	12	0.011166	family with sequence similarity 61, member A, mRNA
BC017114.1	0	10	0.006149	hypothetical protein FLJ22833
BC019337.1	10	11	0.01174	immunoglobulin heavy constant gamma 1 (G1m marker), mRNA
BC020647.1	2	14	0.013093	HSPC128 protein, mRNA
BC022231.1	1	12	0.011166	Ets2 repressor factor, mRNA
BC022325.1	0	16	3.33E-05	hypothetical protein FLJ12729
BC023569.1	0	9	0.01174	UPF3 regulator of nonsense transcripts homolog A (yeast), transcript variant 2
BC025996.2	0	13	0.000647	cDNA clone MGC:26787 IMAGE:4838986
BC027607.1	1	12	0.011166	clone MGC:26892 IMAGE:4828241
BC028151.1	0	9	0.01174	DNA segment on chromosome X and Y (unique) 155 expressed sequence, mRNA

BC028237.1	1	12	0.011166	growth differentiation factor 10, mRNA
BC028301.1	0	12	0.001456	mRNA similar to LOC147447
BC029046.1	4	17	0.01839	H1 histone family, member 0, mRNA
BC029827.1	0	9	0.01174	Down syndrome critical region gene 9, mRNA
BC029891.1	0	10	0.006149	transcription factor EC, mRNA
BC030219.1	1	14	0.002599	RAD51-like 1 (S. cerevisiae)
BC030702.1	0	10	0.006149	hypothetical protein FLJ12847
BC032452.1	10	11	0.01174	immunoglobulin lambda constant 1 (Mcg marker), mRNA
BC032462.1	0	10	0.006149	vacuolar protein sorting 29 (yeast), mRNA
BC032485.1	0	9	0.01174	hypothetical protein FLJ30473,
BC032852.2	4	18	0.007235	melanoma antigen family B, 4, mRNA
BC033856.1	3	17	0.004844	Similar to RIKEN cDNA 3110040D16 gene, cloneMGC:45395 IMAGE:5123380, mRNA, complete cds.
BC034401.1	10	11	0.01174	Similar to LOC161981
BC035314.1	4	17	0.01839	brix domain containing 1
BC035568.1	0	9	0.01174	acylphosphatase 1, erythrocyte (common) type
BC038105.2	1	14	0.002599	membrane protein, palmitoylated 7 (MAGUK p55 subfamily member 7)
BC040844.1	1	14	0.002599	synaptotagmin binding, cytoplasmic RNA interacting protein, mRNA
BC042625.1	1	13	0.005597	LUC7-like 2 (S. cerevisiae), mRNA
BC050428.1	5	19	0.008842	katanin p60 (ATPase-containing) subunit A 1, mRNA
BC051301.1	0	10	0.006149	TEA domain family member 2, mRNA
BC052806.1	0	9	0.01174	cDNA clone MGC:61802 IMAGE:5730155
BC053656.1	10	11	0.01174	EGF-like repeats and discoidin I-like domains 3, mRNA
BC053866.1	0	9	0.01174	endothelin 3, transcript variant 2
BC053872.1	0	9	0.01174	copine V, mRNA
BC054034.1	1	12	0.011166	U11/U12 snRNP 35K, transcript variant 2
BC055314.1	0	10	0.006149	C2f protein
BC057774.1	1	12	0.011166	hypothetical protein FLJ31455, mRNA
BC058903.1	0	9	0.01174	intercellular adhesion molecule 3, mRNA
BC063275.1	1	15	0.001099	eukaryotic translation initiation factor 2C, 1, mRNA
BC063479.1	1	15	0.001099	La ribonucleoprotein domain family, member 4, mRNA
BC067446.1	0	9	0.01174	disabled homolog 1 (Drosophila), mRNA
CTL1094	10	11	0.01174	Influenza A
CTL2110	0	11	0.003075	DNA TOPOISIMERASE(Scl-70)
CTL2112	3	17	0.004844	ssDNA
CTL2132	1	12	0.011166	myeloperoxidase
CTL2136	1	13	0.005597	U1-snRNP 68 PROTEIN
CTL2138	0	14	0.000267	RNP COMPLEX
CTL2142	4	19	0.002122	ssDNA
CTL2145	0	14	0.000267	RIBOSOMAL RNA
CTL2152	2	14	0.013093	RNA POLYMERASE
NM_000997.2	0	9	0.01174	ribosomal protein L37 (RPL37)
NM_001014.2	1	14	0.002599	ribosomal protein S10 (RPS10)

NM_001106.2	1	12	0.011166	activin A receptor, type IIB (ACVR2B)
NM_001124.1	0	10	0.006149	adrenomedullin (ADM), mRNA
NM_001280.1	0	9	0.01174	cold inducible RNA binding protein (CIRBP), mRNA
NM_001616.2	0	13	0.000647	activin A receptor, type II (ACVR2)
NM_001697.1	1	12	0.011166	ATP synthase, H+ transporting, mitochondrial F1 complex, O subunit (oligomycin sensitivity conferring protein) (ATP5O)
NM_001894.2	0	9	0.01174	casein kinase 1, epsilon (CSNK1E)
NM_001896.1	0	10	0.006149	casein kinase 2, alpha prime polypeptide (CSNK2A2)
NM_001896.2	0	10	0.006149	casein kinase 2, alpha prime polypeptide (CSNK2A2), mRNA
NM_002129.2	0	10	0.006149	high-mobility group box 2 (HMGB2), mRNA
NM_002387.1	10	11	0.01174	mutated in colorectal cancers (MCC), mRNA
NM_003295.1	0	10	0.006149	tumor protein, translationally-controlled 1 (TPT1), mRNA
NM_003495.2	0	9	0.01174	histone 1, H4i (HIST1H4I), mRNA
NM_003516.2	6	20	0.007663	histone 2, H2aa (HIST2H2AA), mRNA
NM_003583.2	2	15	0.00624	dual-specificity tyrosine-(Y)-phosphorylation regulated kinase 2 (DYRK2), transcript variant 1, mRNA
NM_003600.1	0	9	0.01174	serine/threonine kinase 6 (STK6)
NM_003897.2	0	11	0.003075	immediate early response 3 (IER3), transcript variant short, mRNA
NM_004214.3	1	15	0.001099	fibroblast growth factor (acidic) intracellular binding protein (FIBP)
NM_004567.2	10	11	0.01174	6-phosphofructo-2-kinase/fructose-2,6-biphosphatase 4 (PFKFB4), mRNA
NM_004596.1	0	13	0.000647	small nuclear ribonucleoprotein polypeptide A (SNRPA
NM_004645.1	4	17	0.01839	coilin (COIL),
NM_004656.2	2	15	0.00624	BRCA1 associated protein-1 (ubiquitin carboxy-terminal hydrolase) (BAP1), mRNA
NM_004765.2	0	10	0.006149	B-cell CLL/lymphoma 7C (BCL7C), mRNA
NM_005240.1	1	12	0.011166	ets variant gene 3 (ETV3), mRNA
NM_006205.1	3	18	0.001657	phosphodiesterase 6H, cGMP-specific, cone, gamma (PDE6H), mRNA
NM_006223.1	3	16	0.011617	protein (peptidyl-prolyl cis/trans isomerase) NIMA-interacting, 4 (parvulin) (PIN4)
NM_006298.2	1	13	0.005597	zinc finger protein 192 (ZNF192), mRNA
NM_006388.2	3	17	0.004844	HIV-1 Tat interacting protein, 60kDa (HTATIP), transcript variant 2, mRNA
NM_006433.2	0	9	0.01174	granulysin (GNLY), transcript variant NKG5, mRNA
NM_006607.1	4	17	0.01839	pituitary tumor-transforming 2 (PTTG2), mRNA
NM_006857.1	1	12	0.011166	putative nucleic acid binding protein RY-1 (RY1), mRNA
NM_007285.5	3	16	0.011617	GABA(A) receptor-associated protein-like 2 (GABARAPL2)
NM_007311.2	10	11	0.01174	benzodiazapine receptor (peripheral) (BZRP), transcript variant PBR-S
NM_012163.1	0	9	0.01174	F-box and leucine-rich repeat protein 9 (FBXL9)

NM_012321.1	2	14	0.013093	U6 snRNA-associated Sm-like protein (LSM4)
NM_015488.1	3	16	0.011617	myofibrillogenesis regulator 1 (MR-1)
NM_015640.1	4	18	0.007235	PAI-1 mRNA-binding protein (PAI-RBP1)
NM_015987.2	0	13	0.000647	heme binding protein 1 (HEBP1)
NM_016207.2	10	11	0.01174	cleavage and polyadenylation specific factor 3, 73kDa (CPSF3), mRNA
NM_016355.3	1	14	0.002599	DEAD (Asp-Glu-Ala-Asp) box polypeptide 47 (DDX47), transcript variant 1, mRNA
NM_016483.3	1	15	0.001099	PHD finger protein 7 (PHF7)
NM_016505.2	4	19	0.002122	putative S1 RNA binding domain protein (PS1D), mRNA
NM_016940.1	1	12	0.011166	chromosome 21 open reading frame 6 (C21orf6), mRNA
NM_018032.2	1	13	0.005597	LUC7-like (S. cerevisiae) (LUC7L)
NM_018047.1	0	9	0.01174	RNA binding motif protein 22 (RBM22), mRNA
NM_018107.2	1	14	0.002599	RNA-binding region (RNP1, RRM) containing 4 (RNPC4)
NM_020239.2	1	12	0.011166	small protein effector 1 of Cdc42
NM_020317.2	NA	NA	NA	hypothetical protein dJ465N24.2.1
NM_020444.2	10	11	0.01174	KIAA1191 protein (KIAA1191), mRNA
NM_020661.1	1	13	0.005597	activation-induced cytidine deaminase (AICDA), mRNA
NM_021104.1	1	13	0.005597	ribosomal protein L41 (RPL41), mRNA
NM_021822.1	0	9	0.01174	apolipoprotein B mRNA editing enzyme, catalytic polypeptide-like 3G (APOBEC3G), mRNA
NM_022100.1	0	9	0.01174	mitochondrial ribosomal protein S14 (MRPS14), nuclear gene encoding mitochondrial protein, mRNA
NM_022787.2	4	19	0.002122	nicotinamide nucleotide adenylyltransferase 1 (NMNAT1), mRNA
NM_023940.1	10	11	0.01174	hypothetical protein MGC2827
NM_024625.3	0	9	0.01174	zinc finger CCCH type, antiviral 1 (ZC3HAV1), transcript variant 2, mRNA
NM_031465.2	0	11	0.003075	hypothetical protein , mRNA
NM_032042.2	0	12	0.001456	hypothetical protein DKFZp564D172 (DKFZP564D172)
NM_032345.1	0	10	0.006149	PYM protein (PYM), mRNA
NM_032350.3	0	9	0.01174	hypothetical protein , mRNA
NM_032906.2	2	15	0.00624	hypothetical protein , mRNA
NM_033030.2	1	12	0.011166	bol, boule-like (Drosophila) (BOLL)
NM_054016.1	1	14	0.002599	FUS interacting protein (serine-arginine rich) 1 (FUSIP1), transcript variant 2, mRNA
NM_138551.1	3	16	0.011617	thymic stromal lymphopoietin (TSLP), transcript variant 2
NM_138775.1	1	12	0.011166	hypothetical protein BC015183 (LOC91801), mRNA
NM_144982.1	2	15	0.00624	hypothetical protein MGC23401 (MGC23401)
NM_145020.1	NA	NA	NA	hypothetical protein FLJ32743
NM_145810.1	0	9	0.01174	cell division cycle associated 7 (CDCA7), transcript variant 2, mRNA

NM_152688.1	0	11	0.003075	KH domain containing, RNA binding, signal transduction associated 2 (KHDRBS2), mRNA
NM_152769.1	0	11	0.003075	chromosome 19 open reading frame 26 (C19orf26), mRNA
NM_152770.1	1	12	0.011166	hypothetical protein , mRNA
NM_153207.2	2	15	0.00624	AE binding protein 2 (AEBP2)
NM_153332.2	4	19	0.002122	3' exoribonuclease (3'HEXO), mRNA
NM_173545.1	0	9	0.01174	chromosome 2 open reading frame 13 (C2orf13), mRNA
NM_175923.2	1	12	0.011166	hypothetical protein MGC42630 (MGC42630)
NM_177996.1	1	12	0.011166	erythrocyte membrane protein band 4.1-like 1 (EPB41L1), transcript variant 2, mRNA
NM_182623.1	4	18	0.007235	hypothetical protein FLJ36766 (FLJ36766), mRNA
NM_198395.1	0	9	0.01174	Ras-GTPase-activating protein SH3-domain-binding protein (G3BP), transcript variant 2

[00161] The autoantigens listed in Table 4 are selective for SLE, but not RA or ANCA. Table 4 is a list of autoantigens that were bound by an antibody from sera from an individual with SLE but not healthy, RA or ANCA patients.

Table 4. SLE vs. all

Genbank ID number of nucleic acid coding for the protein	**Name or Description**
BC000381.2	TBP-like 1, mRNA
BC002733.2	mRNA, complete cds.
BC006376.1	N-myristoyltransferase 2
BC007833.2	phosphatidylinositol-4-phosphate 5-kinase, type I, alpha, mRNA
BC008623.1	hypothetical protein FLJ21044 similar to Rbig1, cloneMGC:16823 IMAGE:4177689, mRNA, complete cds.
BC009623.1	Similar to nucleophosmin (nucleolar phosphoprotein B23, numatrin)
BC009762.2	mRNA, complete cds.
BC010642.1	zinc finger protein 22 (KOX 15)
BC011498.1	histone deacetylase 6
BC012472.1	ubiquitin D, mRNA
BC014452.1	cDNA clone IMAGE:4903661
BC015008.1	hydroxyacylglutathione hydrolase-like, mRNA
BC016842.1	family with sequence similarity 61, member A, mRNA
BC017114.1	hypothetical protein FLJ22833
BC020647.1	HSPC128 protein, mRNA
BC022325.1	hypothetical protein FLJ12729

BC025996.2	CDNA clone MGC:26787 IMAGE:4838986
BC027607.1	clone MGC:26892 IMAGE:4828241
BC028301.1	mRNA similar to LOC147447
BC029046.1	H1 histone family, member 0, mRNA
BC032852.2	melanoma antigen family B, 4, mRNA
BC033856.1	Similar to RIKEN cDNA 3110040D16 gene, cloneMGC:45395 IMAGE:5123380, mRNA, complete cds.
BC038105.2	membrane protein, palmitoylated 7 (MAGUK p55 subfamily member 7)
BC042625.1	LUC7-like 2 (S. cerevisiae), mRNA
BC052806.1	cDNA clone MGC:61802 IMAGE:5730155
BC053866.1	endothelin 3, transcript variant 2
BC054034.1	U11/U12 snRNP 35K, transcript variant 2
BC055314.1	C2f protein
BC063275.1	eukaryotic translation initiation factor 2C, 1, mRNA
CTL2110	DNA TOPOISIMERASE(Scl-70)
CTL2112	ssDNA
CTL2138	RNP COMPLEX
CTL2142	ssDNA
CTL2145	RIBOSOMAL RNA
NM_000997.2	ribosomal protein L37 (RPL37
NM_001014.2	ribosomal protein S10 (RPS10)
NM_001124.1	adrenomedullin (ADM), mRNA
NM_001896.1	casein kinase 2, alpha prime polypeptide (CSNK2A2)
NM_001896.2	casein kinase 2, alpha prime polypeptide (CSNK2A2), mRNA
NM_002129.2	high-mobility group box 2 (HMGB2), mRNA
NM_003516.2	histone 2, H2aa (HIST2H2AA), mRNA
NM_004214.3	fibroblast growth factor (acidic) intracellular binding protein (FIBP)
NM_004596.1	Small nuclear ribonucleoprotein polypeptide A (SNRPA)
NM_004645.1	coilin (COIL)
NM_006298.2	zinc finger protein 192 (ZNF192), mRNA
NM_007285.5	GABA(A) receptor-associated protein-like 2 (GABARAPL2)
NM_015488.1	myofibrillogenesis regulator 1 (MR-1),
NM_015640.1	PAI-1 mRNA-binding protein (PAI-RBP1)
NM_015987.2	Heme binding protein 1 (HEBP1)
NM_016355.3	DEAD (Asp-Glu-Ala-Asp) box polypeptide 47 (DDX47), transcript variant 1, mRNA
NM_016483.3	PHD finger protein 7 (PHF7)
NM_016505.2	putative S1 RNA binding domain protein (PS1D), mRNA
NM_016940.1	chromosome 21 open reading frame 6 (C21orf6), mRNA
NM_018032.2	LUC7-like (S. cerevisiae) (LUC7L)
NM_020239.2	small protein effector 1 of Cdc42 (SPEC1)

NM_020661.1	activation-induced cytidine deaminase (AICDA), mRNA
NM_032345.1	PYM protein (PYM), mRNA
NM_054016.1	FUS interacting protein (serine-arginine rich) 1 (FUSIP1), transcript variant 2, mRNA
NM_138775.1	hypothetical protein BC015183 (LOC91801), mRNA
NM_144982.1	hypothetical protein MGC23401 (MGC23401)
NM_152769.1	chromosome 19 open reading frame 26 (C19orf26), mRNA
NM_153207.2	AE binding protein 2 (AEBP2)
NM_153332.2	3' exoribonuclease (3'HEXO), mRNA

[00162] Table 5 is a list of autoantigens that were bound more often by antibodies in sera from individuals with ANCA than by antibodies in sera from healthy individuals. The normal count and ANCA count are presented along with the corresponding p-value.

Table 5. ANCA vs. healthy patients

Genbank ID number of nucleic acid coding for the protein	Normal Count	ANCA Count	p-value	Name or description
BC000052.1	0	9	0.01174	Similar to peroxisome proliferative activated receptor, alpha
BC000103.1	3	17	0.004844	NCK adaptor protein 2
BC000442.1	1	13	0.005597	serine/threonine kinase 12
BC000914.1	0	12	0.001456	splicing factor, arginine/serine-rich 3
BC001120.1	10	11	0.01174	lectin, galactoside-binding, soluble, 3 (galectin 3)
BC001371.2	0	9	0.01174	chromosome 20 open reading frame 31, mRNA
BC001662.1	0	9	0.01174	mitogen-activated protein kinase-activated protein kinase 3
BC002880.1	1	14	0.002599	cysteinyl-tRNA synthetase
BC003168.1	0	9	0.01174	oxysterol binding protein-like 10,
BC004514.1	1	12	0.011166	hypothetical protein FLJ12584
BC005332.1	0	11	0.003075	cDNA clone MGC:12418 IMAGE:3934658, complete cds
BC006105.1	2	14	0.013093	chromosome 6 open reading frame 134, mRNA
BC007411.2	2	15	0.00624	diaphanous homolog 1 (Drosophila)
BC007949.1	0	9	0.01174	eukaryotic translation elongation factor 1 gamma
BC012876.1	0	14	0.000267	clone MGC:17259 IMAGE:4149333
BC013171.1	10	11	0.01174	cDNA clone MGC:17065 IMAGE:4344401, complete cds
BC014271.2	1	14	0.002599	endoglin (Osler-Rendu-Weber syndrome 1), mRNA

BC014991.1	0	9	0.01174	N-methylpurine-DNA glycosylase
BC015833.1	4	17	0.01839	cDNA clone MGC:27152 IMAGE:4691630, complete cds
BC016057.1	10	11	0.01174	Usher syndrome 1C (autosomal recessive, severe), mRNA
BC016312.1	10	11	0.01174	chromosome 15 open reading frame 15, mRNA
BC016380.1	1	14	0.002599	cDNA clone MGC:27376 IMAGE:4688477, complete cds
BC016381.1	0	13	0.000647	cDNA clone MGC:27378 IMAGE:4688865, complete cds
BC016764.1	3	16	0.011617	ribulose-5-phosphate-3-epimerase, transcript variant 1
BC017865.1	0	11	0.003075	Fc fragment of IgG, low affinity IIIa, receptor (CD16a), mRNA
BC018302.1	0	9	0.01174	TRM1 tRNA methyltransferase 1 homolog (S. cerevisiae), mRNA
BC019337.1	4	19	0.002122	immunoglobulin heavy constant gamma 1 (G1m marker), mRNA
BC020622.1	1	13	0.005597	zinc finger, A20 domain containing 1, mRNA, complete cds.
BC020962.1	0	9	0.01174	similar to glucosamine-6-sulfatases
BC022098.1	0	10	0.006149	cDNA clone MGC:31944 IMAGE:4878869, complete cds
BC022362.1	1	14	0.002599	cDNA clone MGC:23888 IMAGE:4704496, complete cds
BC024289.1	0	10	0.006149	cDNA clone MGC:39273 IMAGE:5440834, complete cds
BC025314.1	3	17	0.004844	immunoglobulin heavy constant gamma 1 (G1m marker), mRNA
BC025345.1	4	19	0.002122	mRNA similar to LOC149651 (cDNA clone MGC:39393 IMAGE:4862156), complete cds
BC029444.1	0	11	0.003075	cDNA clone MGC:32714 IMAGE:4692138, complete cds
BC029609.1	0	10	0.006149	cDNA clone MGC:39831 IMAGE:5302675
BC030590.1	1	12	0.011166	retinoblastoma binding protein 8, mRNA
BC030814.1	0	14	0.000267	immunoglobulin kappa variable 1-5, mRNA
BC030983.1	2	17	0.000974	immunoglobulin lambda constant 1 (Mcg marker), mRNA
BC030984.1	2	19	6.36E-05	cDNA clone MGC:32654 IMAGE:4701898, complete cds
BC031074.1	1	16	0.000414	poly (ADP-ribose) polymerase family, member 16, mRNA
BC032485.1	1	16	0.000414	hypothetical protein FLJ30473
BC032866.2	1	13	0.005597	eukaryotic translation initiation factor 5, transcript variant 2, mRNA
BC036075.1	0	9	0.01174	GIPC PDZ domain containing family, member 2, mRNA
BC036723.1	1	12	0.011166	Fc fragment of IgG, low affinity IIIa, receptor (CD16a), mRNA
BC039814.1	1	17	0.000134	zinc finger protein 265, transcript variant 2, mRNA

BC041157.1	0	11	0.003075	thromboxane A synthase 1 (platelet, cytochrome P450, family 5, subfamily A), transcript variant TXS-I, mRNA
BC044584.1	0	11	0.003075	DnaJ (Hsp40) homolog, subfamily C, member 4, mRNA
BC053656.1	1	17	0.000134	EGF-like repeats and discoidin I-like domains 3, mRNA
BC053664.1	0	12	0.001456	complete cds.
BC053984.1	3	18	0.001657	cDNA clone MGC:59926 IMAGE:5480266, complete cds
BC056256.1	1	16	0.000414	immunoglobulin kappa constant, mRNA
BC066938.1	4	17	0.01839	DEAD (Asp-Glu-Ala-Asp) box polypeptide 43, mRNA
BC066987.1	0	9	0.01174	cDNA clone MGC:87634 IMAGE:4838596, complete cds
CTL1093	6	20	0.007663	Human IgG
CTL2130	1	18	3.51E-05	proteinase-3
CTL2137	1	15	0.001099	La/SS-B (La)
NM_001015.2	10	11	0.01174	ribosomal protein S11 (RPS11)
NM_001663.2	2	16	0.002655	ADP-ribosylation factor 6 (ARF6), mRNA
NM_001894.2	0	13	0.000647	casein kinase 1, epsilon (CSNK1E)
NM_002019.1	10	11	0.01174	fms-related tyrosine kinase 1 (vascular endothelial growth factor/vascular permeability factor receptor) (FLT1)
NM_002103.3	0	10	0.006149	glycogen synthase 1 (muscle) (GYS1), mRNA
NM_002462.2	1	12	0.011166	myxovirus (influenza virus) resistance 1, interferon-inducible protein p78 (mouse) (MX1), mRNA
NM_003045.3	1	12	0.011166	solute carrier family 7 (cationic amino acid transporter, y+ system), member 1 (SLC7A1), mRNA
NM_003049.1	0	9	0.01174	solute carrier family 10 (sodium/bile acid cotransporter family), member 1 (SLC10A1), mRNA
NM_004055.3	3	17	0.004844	calpain 5 (CAPN5), mRNA
NM_004217.1	0	10	0.006149	aurora kinase B (AURKB)
NM_004732.1	4	17	0.01839	potassium voltage-gated channel, shaker-related subfamily, beta member 3 (KCNAB3)
NM_005522.3	0	11	0.003075	homeo box A1 (HOXA1), transcript variant 1, mRNA
NM_006298.2	10	11	0.01174	zinc finger protein 192 (ZNF192), mRNA
NM_006869.1	0	9	0.01174	centaurin, alpha 1 (CENTA1), mRNA
NM_012163.1	0	10	0.006149	F-box and leucine-rich repeat protein 9 (FBXL9)
NM_012241.2	1	13	0.005597	sirtuin (silent mating type information regulation 2 homolog) 5 (S. cerevisiae) (SIRT5), transcript variant 1, mRNA
NM_016576.2	0	10	0.006149	guanosine monophosphate reductase 2 (GMPR2)
NM_018047.1	0	9	0.01174	RNA binding motif protein 22 (RBM22), mRNA
NM_018153.2	2	14	0.013093	anthrax toxin receptor 1 (ANTXR1), transcript variant 3, mRNA
NM_018184.1	0	10	0.006149	ADP-ribosylation factor-like 10C (ARL10C)
NM_018679.2	0	10	0.006149	t-complex 11 (mouse) (TCP11), mRNA
NM_019021.1	0	12	0.001456	hypothetical protein FLJ20010 (FLJ20010), mRNA
NM_020367.2	0	9	0.01174	chromosome 12 open reading frame 6 (C12orf6)
NM_020381.2	1	14	0.002599	chromosome 6 open reading frame 210 (C6orf210), mRNA

NM_020804.2	0	9	0.01174	protein kinase C and casein kinase substrate in neurons 1 (PACSIN1), mRNA
NM_021130.1	10	11	0.01174	peptidylprolyl isomerase A (cyclophilin A) (PPIA)
NM_021133.1	3	16	0.011617	ribonuclease L (2',5'-oligoisoadenylate synthetase-dependent) (RNASEL),
NM_021709.1	0	10	0.006149	CD27-binding (Siva) protein (SIVA), transcript variant 2, mRNA
NM_022787.2	4	17	0.01839	nicotinamide nucleotide adenylyltransferase 1 (NMNAT1), mRNA
NM_032855.1	0	12	0.001456	hematopoietic SH2 protein (HSH2)
NM_052822.1	0	9	0.01174	secretory carrier membrane protein 1 (SCAMP1), transcript variant 2
NM_052877.1	0	12	0.001456	mediator of RNA polymerase II transcription, subunit 8 homolog (yeast) (MED8)
NM_145315.2	10	11	0.01174	lactation elevated 1 (LACE1)
NM_152688.1	0	10	0.006149	KH domain containing, RNA binding, signal transduction associated 2 (KHDRBS2), mRNA
NM_152697.2	3	16	0.011617	hypothetical protein , mRNA
NM_153215.1	1	17	0.000134	hypothetical protein FLJ38608 (FLJ38608), mRNA
NM_178496.2	1	13	0.005597	similar to BcDNA:GH11415 gene product (LOC151963), mRNA
NM_182665.1	0	12	0.001456	Ras association (RalGDS/AF-6) domain family 5 (RASSF5), transcript variant 3, mRNA
NM_198490.1	0	11	0.003075	RAB43, member RAS oncogene family (RAB43), mRNA
NM_203326.1	0	9	0.01174	5-azacytidine induced 2 (AZI2), transcript variant 2
NM_212492.1	0	10	0.006149	G protein pathway suppressor 1 (GPS1), transcript variant 1, mRNA

[00163] The autoantibodies listed in Table 6 are selective for ANCA, but not RA or SLE. Table 6 is a list of autoantibodies that were bound by an antibody from sera from an individual with ANCA but not healthy, RA or SLE patients.

Table 6. ANCA vs. all

Genbank ID number of nucleic acid coding for the protein	Name or description
BC002880.1	cysteinyl-tRNA synthetase
BC003168.1	oxysterol binding protein-like 10,
BC005332.1	cDNA clone MGC:12418 IMAGE:3934658, complete cds
BC006105.1	chromosome 6 open reading frame 134, mRNA
BC020962.1	similar to glucosamine-6-sulfatases
BC022098.1	cDNA clone MGC:31944 IMAGE:4878869, complete cds
BC029444.1	cDNA clone MGC:32714 IMAGE:4692138, complete cds
BC030814.1	immunoglobulin kappa variable 1-5, mRNA
BC030983.1	immunoglobulin lambda constant 1 (Mcg marker), mRNA

BC030984.1	cDNA clone MGC:32654 IMAGE:4701898, complete cds
BC039814.1	zinc finger protein 265, transcript variant 2, mRNA
BC044584.1	DnaJ (Hsp40) homolog, subfamily C, member 4, mRNA
BC053664.1	complete cds.
BC056256.1	immunoglobulin kappa constant, mRNA
CTL2130	proteinase-3
CTL2137	La/SS-B (La)
NM_004732.1	potassium voltage-gated channel, shaker-related subfamily, beta member 3 (KCNAB3)
NM_006869.1	centaurin, alpha 1 (CENTA1), mRNA
NM_012241.2	sirtuin (silent mating type information regulation 2 homolog) 5 (S. cerevisiae) (SIRT5), transcript variant 1, mRNA
NM_020381.2	chromosome 6 open reading frame 210 (C6orf210), mRNA
NM_052877.1	mediator of RNA polymerase II transcription, subunit 8 homolog (yeast) (MED8)
NM_153215.1	hypothetical protein FLJ38608 (FLJ38608), mRNA

Example 3

[00164] Serum from twelve individuals with RA prior to and following initiation of infilximab (Remicade®) treatment were profiled against a high throughput human protein array as described in Example 1. Table 7A is a list of autoantigens that were bound by antibodies from RA patient sera and showed a decrease count after twenty weeks of infliximab treatment. Table 7B is a list of autoantigens that were bound by antibodies from RA patient sera and showed an increase count after twenty weeks of infliximab treatment.

Table 7A. RA biomarkers showing a decrease count following treatment.

Genbank ID number of nucleic acid coding for the protein	**RA_T0**	**RA_T20**	**p-value**	**Name or description**
BC012105.1	5	0	0.006192	nuclear VCP-like, mRNA
BC025314.1	6	0	0.001548	immunoglobulin heavy constant gamma 1 (G1m marker), mRNA
BC028039.1	7	2	0.008454	hypothetical protein MGC39900
BC041037.1	6	1	0.008978	immunoglobulin heavy constant mu, mRNA
NM_003848.1	5	0	0.006192	succinate-CoA ligase, GDP-forming, beta subunit (SUCLG2), mRNA
NM_020367.2	6	1	0.008978	chromosome 12 open reading frame 6 (C12orf6)
NM_133484.1	5	0	0.006192	TRAF family member-associated NFKB activator (TANK), transcript variant 2, mRNA

Table 7B. RA biomarkers showing an increase count following treatment.

Genbank ID number of nucleic acid coding for the protein	RA_T0	RA_T20	p-value	Name or description
BC001132.1	0	6	0.017028	DEAD (Asp-Glu-Ala-Asp) box polypeptide 54
BC005382.1	3	11	0.008978	SPANX family, member E, mRNA
BC006550.1	4	12	0.006192	RNA binding motif protein, X chromosome
BC009894.2	4	12	0.006192	3'-phosphoadenosine 5'-phosphosulfate synthase 2
BC011792.1	0	6	0.017028	Clone MGC:19561 IMAGE:4300082
BC016609.1	1	10	0.001718	cytidine monophosphate N-acetylneuraminic acid synthetase, mRNA
BC034247.1	0	6	0.017028	chromosome 9 open reading frame 105, mRNA
BC053557.1	0	6	0.017028	cDNA clone MGC:61706 IMAGE:6162269
BC064367.1	0	6	0.017028	sterile alpha motif domain containing 6, mRNA
NM_000594.2	0	10	0.000187	tumor necrosis factor (TNF superfamily, member 2) (TNF), mRNA
NM_001449.2	1	8	0.015905	four and a half LIM domains 1 (FHL1)
NM_004217.1	1	8	0.015905	aurora kinase B (AURKB)
NM_005926.2	1	10	0.001718	microfibrillar-associated protein 1 (MFAP1), mRNA
NM_012101.2	0	7	0.006811	tripartite motif-containing 29 (TRIM29), transcript variant 1, mRNA
NM_058163.1	0	7	0.006811	hypothetical protein DT1P1A10 (DT1P1A10), mRNA
NM_183241.1	0	6	0.017028	hypothetical protein LOC286257 (LOC286257), mRNA

Example 4

[00165] Serum samples from individuals with autoimmune diseases including RA (Rheumatoid Arthritis), SLE (Systemic Lupus Erythrematosus) and ANCA (Anti-Neutrophil Cytoplasmic Antibody) were profiled on ProtoArray™ human protein microarrays as described in Example 1. Utilizing the calculations as described below, the antigen biomarkers for each autoimmune disease were compared with one another to identify biomarkers selective for each particular disease. The tables below identify the autoantigens which are present for one autoimmune disease, such as RA, SLE, and ANCA, but are not present for another disease.

[00166] Tables 8 - 13 identify antigens according to Genbank ID number for the nucleotide sequence that encodes the antigens. It is understood that an antigen of Tables 8-13 refers to a protein or fragments thereof that is encoded by the nucleotide sequence associated with the nucleotide ID number. Table 8 lists antigens that were bound by an antibody from RA patient sera but not by an antibody from SLE patient

sera. Table 9 lists antigens that were bound by an antibody from RA patient sera but not by an antibody from ANCA patient sera. Table 10 lists antigens that were bound by an antibody from SLE patient sera but not by an antibody from RA patient sera. Table 11 lists antigens that were bound by an antibody from SLE patient sera but not by an antibody from ANCA patient sera. Table 12 lists antigens that were bound by an antibody from ANCA patient sera but not by an antibody from SLE patient sera. Table 13 lists antigens that were bound by an antibody from ANCA patient sera but not by an antibody from RA patient sera.

Table 8. Table 8 is a list of proteins that were bound by an antibody from RA patient sera but not SLE patients.

Genbank ID number of nucleic acid coding for the protein	RA Count	SLE Count	p-value	Name or description
BC001120.1	8	4	0.000862	lectin, galactoside-binding, soluble, 3 (galectin 3)
BC001286.1	5	0	0.001061	dCMP deaminase, mRNA
BC001694.1	8	7	0.009495	clone MGC:2299 IMAGE:2967519
BC005332.1	4	0	0.005305	cDNA clone MGC:12418 IMAGE:3934658, complete cds
BC012105.1	8	7	0.009495	nuclear VCP-like, mRNA
BC012576.1	8	7	0.009495	Unknown (protein for MGC:13472)
BC012876.1	4	0	0.005305	clone MGC:17259 IMAGE:4149333
BC014271.2	4	0	0.005305	endoglin (Osler-Rendu-Weber syndrome 1), mRNA
BC014435.1	8	5	0.002128	Unknown (protein for MGC:22922)
BC016380.1	4	0	0.005305	cDNA clone MGC:27376 IMAGE:4688477, complete cds
BC016381.1	6	1	0.001099	cDNA clone MGC:27378 IMAGE:4688865, complete cds
BC018111.1	9	8	0.002427	pim-2 oncogene
BC019337.1	5	0	0.001061	immunoglobulin heavy constant gamma 1 (G1m marker), mRNA
BC022098.1	9	7	0.001142	cDNA clone MGC:31944 IMAGE:4878869, complete cds
BC022429.1	5	2	0.016438	cDNA clone MGC:24679 IMAGE:4270959, complete cds
BC024289.1	7	1	0.00017	cDNA clone MGC:39273 IMAGE:5440834, complete cds
BC025314.1	6	0	0.000177	immunoglobulin heavy constant gamma 1 (G1m marker), mRNA
BC028039.1	8	7	0.009495	hypothetical protein MGC39900
BC029444.1	6	2	0.003888	cDNA clone MGC:32714 IMAGE:4692138, complete cds

BC032451.1	7	2	0.000701	cDNA clone MGC:40426 IMAGE:5178085, complete cds
BC033195.1	4	0	0.005305	hypothetical gene FLJ00060
BC041037.1	7	0	2.31E-05	immunoglobulin heavy constant mu, mRNA
BC051885.1	7	4	0.005343	chromosome 14 open reading frame 106, mRNA, complete cds.
BC053984.1	6	0	0.000177	cDNA clone MGC:59926 IMAGE:5480266, complete cds
CTL2131	5	2	0.016438	CCP peptide 1% BSA_1mg/ml
CTL2134	9	7	0.001142	dsDNA
NM_000431.1	5	2	0.016438	mevalonate kinase (mevalonic aciduria) (MVK), mRNA
NM_001157.2	5	2	0.016438	annexin A11 (ANXA11), transcript variant a, mRNA
NM_001667.1	8	7	0.009495	ADP-ribosylation factor-like 2 (ARL2), mRNA
NM_002476.2	9	7	0.001142	myosin, light polypeptide 4, alkali; atrial, embryonic (MYL4)
NM_002963.2	9	8	0.002427	S100 calcium binding protein A7 (psoriasin 1) (S100A7), mRNA
NM_004722.2	8	7	0.009495	adaptor-related protein complex 4, mu 1 subunit (AP4M1), mRNA
NM_005435.2	7	5	0.011617	Rho guanine nucleotide exchange factor (GEF) 5 (ARHGEF5)
NM_005697.3	6	1	0.001099	secretory carrier membrane protein 2 (SCAMP2), mRNA
NM_006002.2	9	7	0.001142	ubiquitin carboxyl-terminal esterase L3 (ubiquitin thiolesterase) (UCHL3),
NM_006169.1	5	2	0.016438	nicotinamide N-methyltransferase (NNMT)
NM_013322.2	8	6	0.004698	sorting nexin 10 (SNX10), mRNA
NM_016207.2	8	6	0.004698	cleavage and polyadenylation specific factor 3, 73kDa (CPSF3), mRNA
NM_019023.1	8	7	0.009495	protein arginine N-methyltransferase 7 (PRMT7), mRNA
NM_024610.2	8	7	0.009495	HSPB (heat shock 27kDa) associated protein 1 (HSPBAP1)
NM_032781.2	8	7	0.009495	protein tyrosine phosphatase, non-receptor type 5 (striatum-enriched) (PTPN5), mRNA
NM_033064.1	8	7	0.009495	ataxia, cerebellar, Cayman type (caytaxin) (ATCAY)
NM_033161.2	8	6	0.004698	surfeit 4 (SURF4), mRNA
NM_080876.2	8	7	0.009495	dual specificity phosphatase 19 (DUSP19), mRNA
NM_152653.1	4	0	0.005305	ubiquitin-conjugating enzyme E2E 2 (UBC4/5 homolog, yeast) (UBE2E2), mRNA

Table 9. Table 9 is a list of proteins that were bound by an antibody from RA patient sera but not ANCA patients.

Genbank ID number of nucleic acid coding for the protein	RA Count	ANCA Count	p-value	Name or description
BC001120.1	9	8	0.016771	lectin, galactoside-binding, soluble, 3 (galectin 3
BC001286.1	4	0	0.005305	dCMP deaminase, mRNA
BC007347.2	4	0	0.005305	Unknown (protein for MGC:1566)
BC008715.2	4	0	0.005305	microtubule-associated protein 4, mRNA
BC010697.1	6	3	0.010263	amylase, alpha 2B; pancreatic
BC013567.1	4	0	0.005305	hypothetical protein FLJ11328
BC014218.2	4	0	0.005305	cDNA clone IMAGE:3954254
BC017570.1	4	0	0.005305	chromosome 9 open reading frame 78, mRNA
BC031281.1	4	0	0.005305	tetratricopeptide repeat domain 16, mRNA
BC032334.1	5	0	0.001061	putative homeodomain transcription factor 2, mRNA, complete cds.
BC033195.1	6	2	0.003888	hypothetical gene FLJ00060
BC036107.1	5	1	0.016438	heat shock 70kDa protein 2, mRNA
CTL2132	6	1	0.001099	myeloperoxidase_100ug/ml_S
NM_002476.2	4	0	0.005305	myosin, light polypeptide 4, alkali; atrial, embryonic
NM_002540.3	6	3	0.010263	outer dense fiber of sperm tails 2 (ODF2), transcript variant 1, mRNA
NM_003576.2	9	4	0.016771	serine/threonine kinase 24 (STE20 homolog, yeast)
NM_003662.1	4	0	0.005305	Pirin (PIR)
NM_003691.1	8	7	0.009495	serine/threonine kinase 16 (STK16)
NM_006169.1	5	0	0.001061	nicotinamide N-methyltransferase (NNMT)
NM_012425.2	4	0	0.005305	Ras suppressor protein 1 (RSU1)
NM_016520.1	4	0	0.005305	chromosome 9 open reading frame 78 (C9orf78), mRNA
NM_022822.1	4	0	0.005305	likely ortholog of kinesin light chain 2 (KLC2), mRNA
NM_024053.1	5	1	0.016438	chromosome 22 open reading frame 18 (C22orf18)
NM_024779.2	9	5	0.002427	hypothetical protein , mRNA
NM_032781.2	8	7	0.017848	hypothetical protein (FLJ32384), mRNA
NM_033064.1	5	2	0.016438	hypothetical protein , mRNA
NM_052848.1	4	0	0.005305	ubiquitin-conjugating enzyme E2E 2 (UBC4/5 homolog, yeast) (UBE2E2), mRNA
NM_144608.1	4	0	0.005305	Meis1, myeloid ecotropic viral integration site 1 homolog 2 (mouse) (MEIS2), transcript variant d, mRNA
NM_152362.1	6	1	0.003888	hypothetical protein , mRNA
NM_152653.1	4	0	0.005305	ubiquitin-conjugating enzyme E2E 2 (UBC4/5 homolog, yeast) (UBE2E2)
NM_170676.2	5	2	0.016438	Meis1, myeloid ecotropic viral integration site 1 homolog 2 (mouse) (MEIS2), transcript variant d
NM_173519.1	5	1	0.005482	hypothetical protein MGC34646 (MGC34646)

Table 10. Table 10 is a list of proteins that were bound by an antibody from SLE patient sera but not RA patients.

Genbank ID number of nucleic acid coding for the protein	SLE Count	RA Count	p-value	Name or description
BC000084.1	0	9	0.016771	hypothetical protein FLJ10357
BC000238.1	0	9	0.016771	hypothetical protein FLJ10415, mRNA
BC000381.2	0	10	0.009224	TBP-like 1, mRNA
BC000442.1	0	10	0.009224	serine/threonine kinase 12
BC000463.1	0	13	0.001142	splicing factor 3b, subunit 3, 130kD
BC000557.1	9	11	0.016771	phosphatidylethanolamine N-methyltransferase
BC000691.1	9	10	0.009224	brain specific protein
BC000877.1	1	14	0.004698	vasopressin-induced transcript
BC000921.2	0	10	0.009224	methyltransferase like 5, mRNA
BC000979.2	9	10	0.009224	DEAD (Asp-Glu-Ala-Asp) box polypeptide 49,
BC001280.1	0	11	0.004855	serine/threonine kinase 6, transcript variant 1
BC001280.1	0	9	0.016771	serine/threonine kinase 6, transcript variant 1
BC001294.1	0	9	0.016771	Similar to x 006 protein
BC001396.1	0	10	0.009224	AD-003 protein, clone MGC:783 IMAGE:3050940
BC002509.1	0	9	0.016771	clone MGC:2941 IMAGE:3051214
BC002606.1	0	9	0.016771	Similar to hypothetical protein, clone MGC:2992 IMAGE:3160695
BC002733.2	3	17	0.010263	mRNA, complete cds.
BC003360.1	0	11	0.004855	DEAD (Asp-Glu-Ala-Asp) box polypeptide 18, mRNA
BC004301.1	0	9	0.016771	core promoter element binding protein, mRNA
BC005004.1	0	10	0.009224	family with sequence similarity 64, member A, mRNA
BC005955.1	0	10	0.009224	hypothetical protein MGC14595
BC006376.1	0	10	0.009224	N-myristoyltransferase 2, clone MGC:12700
BC006550.1	0	12	0.002427	RNA binding motif protein, X chromosome
BC007320.2	9	11	0.016771	annexin A10
BC007833.2	1	14	0.004698	phosphatidylinositol-4-phosphate 5-kinase, type I, alpha, mRNA
BC008077.2	0	11	0.004855	signal recognition particle receptor ('docking protein'), mRNA
BC008623.1	0	10	0.009224	hypothetical protein FLJ21044 similar to Rbig1, cloneMGC:16823 IMAGE:4177689, mRNA, complete cds.
BC009294.1	0	9	0.016771	clone MGC:16644 IMAGE:4123062
BC009348.2	0	9	0.016771	cirrhosis, autosomal recessive 1A (cirhin), mRNA
BC009623.1	0	15	0.0002	Similar to nucleophosmin (nucleolar phosphoprotein B23, numatrin)
BC009762.2	0	12	0.002427	mRNA, complete cds.

BC009819.1	0	10	0.009224	hypothetical protein FLJ23591
BC009829.1	0	13	0.001142	hypothetical protein FLJ11526
BC009894.2	5	20	0.005305	3'-phosphoadenosine 5'-phosphosulfate synthase 2
BC010074.2	0	11	0.004855	FUS interacting protein (serine/arginine-rich) 1, mRNA
BC010176.1	9	11	0.016771	clone MGC:20533 IMAGE:3342874
BC010467.1	1	14	0.004698	cDNA clone MGC:17410 IMAGE:4156035
BC010501.1	0	11	0.004855	catenin (cadherin-associated protein), delta 1
BC010642.1	0	9	0.016771	zinc finger protein 22 (KOX 15)
BC010947.1	0	9	0.016771	signal recognition particle 19kDa, mRNA
BC011498.1	1	13	0.009495	Unknown (protein for MGC:17017)
BC011668.1	0	10	0.009224	Similar to casein kinase 2, alpha 1 polypeptide
BC011792.1	0	13	0.001142	clone MGC:19561 IMAGE:4300082
BC011842.2	0	13	0.001142	hypothetical protein FLJ11184, mRNA
BC011885.1	9	10	0.009224	eukaryotic translation initiation factor (eIF) 2A, mRNA
BC012472.1	1	17	0.000302	ubiquitin D, mRNA
BC012566.1	0	9	0.016771	nucleophosmin (nucleolar phosphoprotein B23, numatrin), mRNA
BC012865.1	0	11	0.004855	retinoic acid induced 16
BC013073.1	0	10	0.009224	chromosome 1 open reading frame 37, mRNA
BC013319.1	0	9	0.016771	Similar to hypothetical protein FLJ11183, cloneMGC:13390 IMAGE:4286103, mRNA, complete cds.
BC013900.1	0	9	0.016771	hypothetical protein FLJ20436
BC013966.2	0	10	0.009224	family with sequence similarity 64, member A, mRNA
BC014441.1	0	11	0.004855	NOL1/NOP2/Sun domain family, member 4, mRNA
BC014452.1	0	10	0.009224	cDNA clone IMAGE:4903661
BC014949.1	0	9	0.016771	likely ortholog of mouse D11lgp2, mRNA
BC014991.1	4	18	0.016438	N-methylpurine-DNA glycosylase
BC015008.1	1	16	0.000862	hydroxyacylglutathione hydrolase-like, mRNA
BC015497.1	0	11	0.004855	cDNA clone MGC:9014 IMAGE:3913870, complete cds
BC015569.1	0	9	0.016771	Similar to SRp25 nuclear protein
BC015715.1	1	13	0.009495	makorin, ring finger protein, 2
BC016276.1	0	11	0.004855	KIAA0008 gene product, clone MGC:768 IMAGE:3537754
BC016609.1	1	12	0.017848	cytidine monophosphate N-acetylneuraminic acid synthetase, mRNA
BC016764.1	3	20	0.000177	ribulose-5-phosphate-3-epimerase
BC016768.1	0	9	0.016771	nucleophosmin (nucleolar phosphoprotein B23, numatrin), mRNA
BC016842.1	0	9	0.016771	family with sequence similarity 61, member A, mRNA
BC017114.1	0	14	0.0005	hypothetical protein FLJ22833
BC017212.2	0	9	0.016771	PHD finger protein 11, mRNA
BC017296.2	9	11	0.016771	sestrin 3, mRNA
BC017943.1	0	9	0.016771	protein phosphatase 1 regulatory subunit 1A
BC018630.1	0	9	0.016771	Similar to KIAA0471 gene product, clone MGC:32006 IMAGE:4308560

BC018749.1	9	11	0.016771	immunoglobulin lambda variable 2-14, mRNA
BC018823.2	2	15	0.011617	splicing factor, arginine/serine-rich 5
BC019598.1	0	10	0.009224	zinc finger, matrin type 4, mRNA
BC020597.1	0	10	0.009224	general transcription factor IIB
BC020647.1	0	10	0.009224	HSPC128 protein, mRNA
BC020962.1	2	16	0.005343	similar to glucosamine-6-sulfatases
BC021121.1	3	20	0.000177	protein kinase, lysine deficient 1
BC021263.1	9	11	0.016771	RAB24, member RAS oncogene family
BC021282.1	1	13	0.009495	zinc finger protein 444
BC021930.1	0	10	0.009224	Unknown (protein for MGC:32072)
BC021983.1	1	15	0.002128	nucleophosmin (nucleolar phosphoprotein B23, numatrin), transcript variant 1, mRNA
BC022077.1	2	15	0.011617	hypothetical protein MGC33338
BC022325.1	1	17	0.000302	hypothetical protein FLJ12729
BC022361.1	0	9	0.016771	chromosome 14 open reading frame 111
BC024184.2	0	11	0.004855	germ cell-less homolog 1 (Drosophila)-like, mRNA
BC025996.2	0	9	0.016771	cDNA clone MGC:26787 IMAGE:4838986
BC026104.2	0	9	0.016771	programmed cell death 4 (neoplastic transformation inhibitor), transcript variant 1, mRNA
BC027607.1	0	10	0.009224	clone MGC:26892 IMAGE:4828241,
BC028040.1	0	15	0.0002	2',3'-cyclic nucleotide 3' phosphodiesterase, mRNA
BC028301.1	1	14	0.004698	mRNA similar to LOC147447
BC028672.1	0	9	0.016771	chromosome 15 open reading frame 15, mRNA
BC028711.2	0	13	0.001142	hypothetical protein MGC27005
BC029046.1	1	12	0.017848	H1 histone family, member 0, mRNA
BC029406.1	9	11	0.016771	angiopoietin 1, mRNA, complete cds.
BC029775.1	0	9	0.016771	hypothetical protein LOC199964
BC029891.1	0	10	0.009224	transcription factor EC, mRNA
BC030702.1	0	13	0.001142	hypothetical protein FLJ12847
BC030711.2	1	13	0.009495	chromosome 2 open reading frame 13
BC030783.1	0	11	0.004855	glycerol-3-phosphate acyltransferase, mitochondrial, mRNA
BC031682.1	1	12	0.017848	hypothetical protein MGC10433, mRNA
BC032347.1	0	11	0.004855	chromosome 8 open reading frame 59, mRNA
BC032852.2	3	17	0.010263	melanoma antigen family B, 4, mRNA
BC033242.1	1	12	0.017848	methyl-CpG binding domain protein 1, transcript variant 3, mRNA
BC033621.2	0	12	0.002427	hypothetical protein DKFZp434G1415, mRNA
BC033758.1	0	10	0.009224	centaurin, alpha 2, mRNA
BC033856.1	0	11	0.004855	Similar to RIKEN cDNA 3110040D16 gene, cloneMGC:45395 IMAGE:5123380, mRNA, complete cds.
BC034236.1	9	11	0.016771	hypothetical protein MGC39821
BC034401.1	9	10	0.009224	Similar to LOC161981
BC035314.1	0	9	0.016771	brix domain containing 1
BC036365.1	0	12	0.002427	hypothetical protein FLJ23537
BC038105.2	2	17	0.002135	membrane protein, palmitoylated 7 (MAGUK p55 subfamily member 7)
BC038808.1	0	12	0.002427	apolipoprotein B mRNA editing enzyme, catalytic polypeptide-like 3F, transcript variant 1, mRNA
BC039711.1	0	11	0.004855	translokin, mRNA

BC040177.2	1	14	0.004698	protein phosphatase 1H (PP2C domain containing), mRNA
BC042625.1	1	15	0.002128	LUC7-like 2 (S. cerevisiae), mRNA
BC044953.1	1	15	0.002128	zinc finger protein 620
BC045535.1	0	9	0.016771	chromosome 1 open reading frame 25, mRNA
BC047472.1	9	11	0.016771	mRNA similar to RIKEN cDNA 4832415H08 gene, complete cds.
BC050428.1	0	13	0.001142	katanin p60 (ATPase-containing) subunit A 1, mRNA
BC050563.1	2	15	0.011617	hypothetical protein LOC202051, mRNA
BC050603.1	0	12	0.002427	hypothetical protein MGC3329, mRNA
BC051790.1	0	10	0.009224	mRNA similar to hypothetical protein FLJ20651 (cDNAclone MGC:57594 IMAGE:6190506), complete cds.
BC052806.1	0	11	0.004855	cDNA clone MGC:61802 IMAGE:5730155
BC053365.1	0	9	0.016771	ribosomal protein S6 kinase, 70kDa, polypeptide 1, mRNA
BC053557.1	0	10	0.009224	cDNA clone MGC:61706 IMAGE:6162269
BC053866.1	3	17	0.010263	endothelin 3, transcript variant 2
BC054031.2	0	11	0.004855	mitochondrial ribosomal protein S17
BC054034.1	1	14	0.004698	U11/U12 snRNP 35K
BC054892.1	9	11	0.016771	dynein, cytoplasmic, light polypeptide 2B, mRNA
BC055314.1	1	14	0.004698	C2f protein
BC056148.1	0	10	0.009224	nuclear receptor subfamily 1, group D, member 1
BC057809.1	0	9	0.016771	complete cds.
BC061699.1	0	10	0.009224	glycosyltransferase-like domain containing 1, mRNA
BC063275.1	0	14	0.0005	eukaryotic translation initiation factor 2C, 1, mRNA
BC063463.1	9	10	0.009224	coenzyme Q3 homolog, methyltransferase (yeast), mRNA
BC064367.1	0	9	0.016771	sterile alpha motif domain containing 6, mRNA
BC064841.1	0	9	0.016771	complete cds.
CTL2110	1	15	0.002128	DNA TOPOISIMERASE(Scl-70)
CTL2112	0	13	0.001142	ssDNA
CTL2138	0	15	0.0002	RNP COMPLEX
CTL2142	1	14	0.004698	ssDNA
CTL2144	9	11	0.016771	TRANSGLUTAMINASE
CTL2145	0	13	0.001142	RIBOSOMAL RNA
CTL2150	1	14	0.004698	SMITH ANTIGEN
CTL2151	0	9	0.016771	Ro-52
NM_000107.1	0	10	0.009224	damage-specific DNA binding protein 2, 48kDa (DDB2), mRNA
NM_000327.2	9	11	0.016771	retinal outer segment membrane protein 1 (ROM1), mRNA
NM_000723.3	2	15	0.011617	calcium channel, voltage-dependent, beta 1 subunit (CACNB1), transcript variant 1, mRNA
NM_000970.2	0	10	0.009224	ribosomal protein L6 (RPL6)
NM_000975.2	1	15	0.002128	ribosomal protein L11 (RPL11), mRNA
NM_000984.2	1	12	0.017848	ribosomal protein L23a (RPL23A)
NM_000993.	0	9	0.016771	ribosomal protein L31 (RPL31), mRNA

2				
NM_000997.2	0	10	0.009224	ribosomal protein L37 (RPL37)
NM_001002913.1	0	11	0.004855	chromosome 9 open reading frame 115 (C9orf115), mRNA
NM_001013.2	0	14	0.0005	ribosomal protein S9 (RPS9)
NM_001014.2	0	15	0.0002	ribosomal protein S10 (RPS10)
NM_001022.3	1	16	0.000862	ribosomal protein S19 (RPS19), mRNA
NM_001023.2	0	9	0.016771	ribosomal protein S20 (RPS20), mRNA
NM_001029.2	0	9	0.016771	ribosomal protein S26 (RPS26)
NM_001124.1	0	12	0.002427	adrenomedullin (ADM), mRNA
NM_001203.1	0	11	0.004855	bone morphogenetic protein receptor, type IB (BMPR1B), mRNA
NM_001280.1	1	13	0.009495	cold inducible RNA binding protein (CIRBP), mRNA
NM_001626.2	9	11	0.016771	v-akt murine thymoma viral oncogene homolog 2 (AKT2)
NM_001662.2	0	9	0.016771	ADP-ribosylation factor 5 (ARF5), mRNA
NM_001697.1	0	15	0.0002	ATP synthase, H+ transporting, mitochondrial F1 complex, O subunit (oligomycin sensitivity conferring protein) (ATP5O)
NM_001759.2	9	10	0.009224	cyclin D2 (CCND2), mRNA
NM_001894.2	0	12	0.002427	casein kinase 1, epsilon (CSNK1E)
NM_001896.1	3	17	0.010263	casein kinase 2, alpha prime polypeptide (CSNK2A2)
NM_001896.2	1	14	0.004698	casein kinase 2, alpha prime polypeptide (CSNK2A2), mRNA
NM_001896.2	0	9	0.016771	casein kinase 2, alpha prime polypeptide (CSNK2A2)
NM_001952.2	0	10	0.009224	E2F transcription factor 6 (E2F6)
NM_001997.2	1	12	0.017848	Finkel-Biskis-Reilly murine sarcoma virus (FBR-MuSV) ubiquitously expressed (fox derived); ribosomal protein S30 (FAU)
NM_002129.2	0	9	0.016771	high-mobility group box 2 (HMGB2), mRNA
NM_002159.2	0	9	0.016771	histatin 1, mRNA,complete cds.
NM_002412.1	0	11	0.004855	O-6-methylguanine-DNA methyltransferase (MGMT)
NM_002788.1	0	9	0.016771	proteasome (prosome, macropain) subunit, alpha type, 3 (PSMA3)
NM_003092.3	2	16	0.005343	small nuclear ribonucleoprotein polypeptide B" (SNRPB2), transcript variant 1, mRNA
NM_003321.3	0	9	0.016771	Tu translation elongation factor, mitochondrial (TUFM), mRNA

NM_003516.2	0	10	0.009224	histone 2, H2aa (HIST2H2AA), mRNA
NM_003600.1	0	11	0.004855	serine/threonine kinase 6 (STK6)
NM_003910.2	0	9	0.016771	maternal G10 transcript (G10), mRNA
NM_003915.2	0	9	0.016771	copine I (CPNE1), transcript variant 3, mRNA
NM_004114.2	0	14	0.0005	fibroblast growth factor 13 (FGF13), transcript variant 1A, mRNA
NM_004214.3	1	16	0.000862	fibroblast growth factor (acidic) intracellular binding protein (FIBP)
NM_004217.1	1	15	0.002128	aurora kinase B (AURKB),
NM_004596.1	0	16	7.14E-05	small nuclear ribonucleoprotein polypeptide A (SNRPA)
NM_004635.2	0	10	0.009224	mitogen-activated protein kinase-activated protein kinase 3 (MAPKAPK3)
NM_004645.1	0	9	0.016771	coilin (COIL)
NM_004656.2	1	14	0.004698	BRCA1 associated protein-1 (ubiquitin carboxy-terminal hydrolase) (BAP1), mRNA
NM_004718.2	0	9	0.016771	cytochrome c oxidase subunit VIIa polypeptide 2 like (COX7A2L), nuclear gene encoding mitochondrial protein, mRNA
NM_004873.1	0	9	0.016771	BCL2-associated athanogene 5 (BAG5)
NM_004906.3	0	10	0.009224	Wilms tumor 1 associated protein (WTAP), transcript variant 1, mRNA
NM_004966.2	2	15	0.011617	heterogeneous nuclear ribonucleoprotein F (HNRPF), mRNA
NM_005011.2	0	10	0.009224	nuclear respiratory factor 1 (NRF1), mRNA
NM_005240.1	0	10	0.009224	ets variant gene 3 (ETV3), mRNA
NM_006205.1	0	9	0.016771	phosphodiesterase 6H, cGMP-specific, cone, gamma (PDE6H), mRNA
NM_006251.4	0	9	0.016771	protein kinase, AMP-activated, alpha 1 catalytic subunit (PRKAA1), transcript variant 1, mRNA
NM_006298.2	0	9	0.016771	zinc finger protein 192 (ZNF192), mRNA
NM_006299.2	9	11	0.016771	zinc finger protein 193 (ZNF193), mRNA
NM_006337.3	0	10	0.009224	microspherule protein 1 (MCRS1), mRNA
NM_006428.3	0	9	0.016771	mitochondrial ribosomal protein L28 (MRPL28), nuclear gene encoding mitochondrial protein, mRNA
NM_006701.2	0	12	0.002427	thioredoxin-like 4A (TXNL4A), mRNA
NM_006775.1	9	11	0.016771	quaking homolog, KH domain RNA binding (mouse) (QKI), transcript variant 1, mRNA
NM_006869.1	0	9	0.016771	centaurin, alpha 1 (CENTA1), mRNA
NM_006931.1	0	9	0.016771	solute carrier family 2 (facilitated glucose transporter), member 3 (SLC2A3), mRNA

NM_007054.1	0	13	0.001142	kinesin family member 3A (KIF3A)
NM_007285.5	0	12	0.002427	GABA(A) receptor-associated protein-like 2 (GABARAPL2)
NM_012153.1	0	10	0.009224	ets homologous factor (EHF)
NM_012179.2	9	10	0.009224	F-box only protein 7 (FBXO7)
NM_012279.1	0	9	0.016771	double-stranded RNA-binding zinc finger protein JAZ (JAZ)
NM_013257.2	0	9	0.016771	serum/glucocorticoid regulated kinase-like (SGKL)
NM_013375.2	0	9	0.016771	activator of basal transcription 1 (ABT1), mRNA
NM_013401.2	0	9	0.016771	RAB3A interacting protein (rabin3)-like 1 (RAB3IL1), mRNA
NM_014047.1	1	14	0.004698	HSPC023 protein (HSPC023), mRNA
NM_014466.2	9	10	0.009224	tektin 2 (testicular) (TEKT2), mRNA
NM_014763.2	0	10	0.009224	mitochondrial ribosomal protein L19 (MRPL19), nuclear gene encoding mitochondrial protein, mRNA
NM_014878.2	0	13	0.001142	KIAA0117 protein (KIAA0117), mRNA
NM_015014.1	0	12	0.002427	KIAA0117 protein (KIAA0117)
NM_015414.2	0	9	0.016771	ribosomal protein L36 (RPL36), transcript variant 2
NM_015464.1	2	16	0.005343	sclerostin domain containing 1 (SOSTDC1), mRNA
NM_015488.1	1	12	0.017848	myofibrillogenesis regulator 1 (MR-1)
NM_015640.1	0	14	0.0005	PAI-1 mRNA-binding protein (PAI-RBP1)
NM_015698.2	9	11	0.016771	T54 protein (T54)
NM_015933.1	0	14	0.0005	hypothetical protein HSPC016 (HSPC016)
NM_015971.2	1	12	0.017848	mitochondrial ribosomal protein S7 (MRPS7), nuclear gene encoding mitochondrial protein, mRNA
NM_015987.2	1	14	0.004698	heme binding protein 1 (HEBP1)
NM_016073.2	0	9	0.016771	hepatoma-derived growth factor, related protein 3 (HDGFRP3), mRNA
NM_016321.1	0	9	0.016771	Rhesus blood group, C glycoprotein (RHCG), mRNA
NM_016355.3	0	9	0.016771	DEAD (Asp-Glu-Ala-Asp) box polypeptide 47 (DDX47), transcript variant 1, mRNA
NM_016483.3	2	15	0.011617	PHD finger protein 7 (PHF7)
NM_016487.1	0	10	0.009224	HSPC230 gene (HSPC230)
NM_016505.2	1	15	0.002128	putative S1 RNA binding domain protein (PS1D), mRNA
NM_016940.1	0	12	0.002427	chromosome 21 open reading frame 6 (C21orf6), mRNA

NM_017503.2	0	9	0.016771	surfeit 2 (SURF2), mRNA
NM_017588.1	0	10	0.009224	WD repeat domain 5 (WDR5), transcript variant 1
NM_017692.1	0	10	0.009224	aprataxin (APTX)
NM_017838.2	0	11	0.004855	nucleolar protein family A, member 2 (H/ACA small nucleolar RNPs) (NOLA2)
NM_017846.3	0	11	0.004855	tRNA selenocysteine associated protein (SECP43), mRNA
NM_017866.3	0	9	0.016771	hypothetical protein FLJ20533 (FLJ20533), mRNA
NM_017868.2	0	9	0.016771	tetratricopeptide repeat domain 12 (TTC12)
NM_018032.2	1	15	0.002128	LUC7-like (S. cerevisiae) (LUC7L)
NM_018047.1	0	15	0.0002	RNA binding motif protein 22 (RBM22), mRNA
NM_018454.4	0	11	0.004855	nucleolar and spindle associated protein 1 (NUSAP1)
NM_018683.2	9	11	0.016771	zinc finger protein 313 (ZNF313)
NM_019021.1	1	13	0.009495	hypothetical protein FLJ20010 (FLJ20010), mRNA
NM_019069.3	0	10	0.009224	WD repeat domain 5B (WDR5B), mRNA
NM_019099.1	0	9	0.016771	hypothetical protein LOC55924 (LOC55924)
NM_020239.2	1	14	0.004698	small protein effector 1 of Cdc42 (SPEC1)
NM_020317.2	9	10	0.009224	hypothetical protein dJ465N24.2.1
NM_020530.2	1	14	0.004698	oncostatin M (OSM)
NM_020661.1	0	9	0.016771	activation-induced cytidine deaminase (AICDA), mRNA
NM_021218.1	2	16	0.005343	chromosome 9 open reading frame 80 (C9orf80), mRNA
NM_021627.2	0	9	0.016771	SUMO1/sentrin/SMT3 specific protease 2 (SENP2), mRNA
NM_021925.1	9	11	0.016771	hypothetical protein FLJ21820 (FLJ21820), mRNA
NM_022100.1	0	13	0.001142	mitochondrial ribosomal protein S14 (MRPS14), nuclear gene encoding mitochondrial protein, mRNA
NM_022107.1	0	9	0.016771	G-protein signalling modulator 3 (AGS3-like, C. elegans) (GPSM3), mRNA
NM_022787.2	1	16	0.000862	nicotinamide nucleotide adenylyltransferase 1 (NMNAT1), mRNA
NM_022839.2	0	14	0.0005	mitochondrial ribosomal protein S11 (MRPS11), nuclear gene encoding mitochondrial protein, transcript variant 1, mRNA
NM_024313.1	0	9	0.016771	hypothetical protein MGC3731 (MGC3731)
NM_024749.1	9	10	0.009224	hypothetical protein FLJ12505
NM_025061.	0	9	0.016771	hypothetical protein FLJ23420 (FLJ23420)

2				
NM_031452.1	0	9	0.016771	hypothetical protein MGC2560 (MGC2560)
NM_031465.2	0	10	0.009224	hypothetical protein , mRNA
NM_031473.1	9	10	0.009224	carnitine deficiency-associated gene expressed in ventricle 1 (CDV-1),
NM_031910.2	1	16	0.000862	C1q and tumor necrosis factor related protein 6 (C1QTNF6)
NM_031991.1	0	11	0.004855	polypyrimidine tract binding protein 1 (PTBP1), transcript variant 3
NM_032111.2	0	10	0.009224	mitochondrial ribosomal protein L14 (MRPL14), nuclear gene encoding mitochondrial protein, mRNA
NM_032284.1	0	9	0.016771	hypothetical protein FLJ14936 (FLJ14936)
NM_032338.2	0	9	0.016771	hypothetical protein , mRNA
NM_032345.1	0	10	0.009224	PYM protein (PYM), mRNA
NM_032359.1	0	12	0.002427	hypothetical protein MGC4308
NM_032459.1	0	9	0.016771	embryonal Fyn-associated substrate (EFS), transcript variant 2, mRNA
NM_032848.1	0	11	0.004855	hypothetical protein FLJ14827 (FLJ14827), mRNA
NM_032855.1	9	11	0.016771	hematopoietic SH2 protein (HSH2)
NM_033048.1	0	9	0.016771	CPX chromosome region, candidate 1 (CPXCR1)
NM_033177.2	1	12	0.017848	HLA-B associated transcript 4 (BAT4), mRNA
NM_033345.1	0	10	0.009224	regulator of G-protein signalling 8 (RGS8)
NM_033416.1	0	10	0.009224	IMP4, U3 small nucleolar ribonucleoprotein, homolog (yeast) (IMP4), mRNA
NM_052844.1	9	11	0.016771	hypothetical protein MGC20486
NM_052848.1	9	10	0.009224	hypothetical protein , mRNA
NM_054016.1	1	12	0.017848	FUS interacting protein (serine-arginine rich) 1 (FUSIP1), transcript variant 2, mRNA
NM_138451.1	0	9	0.016771	IQ motif containing D (IQCD), mRNA
NM_138612.1	9	11	0.016771	hyaluronan synthase 3 (HAS3), transcript variant 2, mRNA
NM_138775.1	0	11	0.004855	hypothetical protein BC015183 (LOC91801), mRNA
NM_138777.1	0	9	0.016771	mitochondrial ribosome recycling factor (MRRF)
NM_138959.1	1	13	0.009495	vang-like 1
NM_144595.1	0	9	0.016771	hypothetical protein FLJ30046
NM_144679.1	0	9	0.016771	hypothetical protein FLJ31528 (FLJ31528), mRNA
NM_144714.	0	10	0.009224	hypothetical protein MGC27069

1				
NM_144769.1	0	9	0.016771	forkhead box I1 (FOXI1), transcript variant 2, mRNA
NM_144971.1	0	15	0.0002	hypothetical protein MGC26641 (MGC26641)
NM_144982.1	2	18	0.000701	hypothetical protein MGC23401 (MGC23401)
NM_145204.1	9	11	0.016771	NEDD8-specific protease 1 (SENP8)
NM_145691.3	0	9	0.016771	ATP synthase mitochondrial F1 complex assembly factor 2 (ATPAF2), nuclear gene encoding mitochondrial protein, mRNA
NM_145802.1	4	19	0.005482	septin 6 (SEPT6)
NM_145810.1	2	15	0.011617	cell division cycle associated 7 (CDCA7), transcript variant 2
NM_152255.1	0	9	0.016771	proteasome (prosome, macropain) subunit, alpha type, 7 (PSMA7), transcript variant 2
NM_152324.1	0	9	0.016771	hypothetical protein , mRNA
NM_152376.2	0	9	0.016771	UBX domain containing 3 (UBXD3), mRNA
NM_152397.1	0	10	0.009224	IQ motif containing F1 (IQCF1), mRNA
NM_152474.2	0	14	0.0005	chromosome 19 open reading frame 18 (C19orf18), mRNA
NM_152638.2	0	11	0.004855	chromosome 12 open reading frame 12 (C12orf12), mRNA
NM_152769.1	1	16	0.000862	chromosome 19 open reading frame 26 (C19orf26), mRNA
NM_153207.2	0	10	0.009224	AE binding protein 2 (AEBP2)
NM_153332.2	0	10	0.009224	3' exoribonuclease (3'HEXO), mRNA
NM_173519.1	9	11	0.016771	hypothetical protein , mRNA
NM_175923.2	2	17	0.002135	hypothetical protein MGC42630
NM_178496.2	9	11	0.016771	similar to BcDNA:GH11415 gene product (LOC151963), mRNA
NM_182692.1	0	11	0.004855	SFRS protein kinase 2 (SRPK2), transcript variant 1, mRNA
NM_199334.2	0	10	0.009224	thyroid hormone receptor, alpha (erythroblastic leukemia viral (v-erb-a) oncogene homolog, avian) (THRA), transcript variant 1, mRNA
NM_199415.1	9	10	0.009224	U-box domain containing 5 (UBOX5), transcript variant 2, mRNA
NM_203454.1	0	9	0.016771	hypothetical protein , mRNA
NM_206834.1	0	9	0.016771	chromosome 6 open reading frame 201 (C6orf201), mRNA

Table 11. Table 11 is a list of proteins that were bound by an antibody from SLE patient sera but not ANCA patients.

Genbank ID number of nucleic acid coding for the protein	SLE Count	ANCA Count	p-value	Name or description
AB065619.1	3	18	0.000122	gene for seven transmembrane helix receptor,
AB065812.1	1	12	0.011239	gene for seven transmembrane helix receptor, complete cds, isolate:CBRC7TM_375
BC000166.2	3	12	0.003956	cDNA clone IMAGE:2901054
BC000381.2	0	10	0.000218	TBP-like 1, mRNA
BC000877.1	2	10	0.006907	vasopressin-induced transcript
BC000934.2	0	6	0.010098	eukaryotic translation initiation factor 2, subunit 2 beta, 38kDa, mRNA
BC000954.1	6	17	0.009351	chromobox homolog 3 (HP1 gamma homolog, Drosophila), transcript variant 1
BC000997.2	0	11	7.27E-05	splicing factor, arginine/serine-rich 7, 35kDa
BC001280.1	1	9	0.015475	serine/threonine kinase 6, transcript variant 1
BC002424.1	0	8	0.001638	integral membrane protein 2C, transcript variant 1, mRNA
BC002559.1	2	12	0.0011	high-glucose-regulated protein 8, clone MGC:739 IMAGE:3139250
BC002606.1	6	15	0.012421	Similar to hypothetical protein, clone MGC:2992 IMAGE:3160695
BC002733.2	3	12	0.003956	mRNA, complete cds.
BC005248.1	3	11	0.009351	eukaryotic translation initiation factor 1A, Y-linked
BC005955.1	3	12	0.011239	hypothetical protein MGC14595
BC006376.1	0	7	0.004158	N-myristoyltransferase 2
BC006793.1	4	13	0.012421	GATA binding protein 3
BC007228.1	4	19	0.000624	similar to Taxol resistant associated protein 3 (TRAG-3)
BC007347.2	1	11	0.002868	Unknown (protein for MGC:1566)
BC007833.2	0	14	1.97E-05	phosphatidylinositol-4-phosphate 5-kinase, type I, alpha, mRNA
BC007888.1	11	19	0.004181	eukaryotic translation initiation factor 2, subunit 2 (beta, 38kD)
BC008623.1	1	8	0.009828	hypothetical protein FLJ21044 similar to Rbig1, cloneMGC:16823 IMAGE:4177689, mRNA, complete cds.
BC008730.2	0	7	0.004158	hexokinase 1, transcript variant 1, mRNA
BC008741.1	1	8	0.009828	LIM protein (similar to rat protein kinase C-binding enigma)
BC009350.1	1	9	0.015475	clone MGC:14871 IMAGE:4137621
BC009623.1	3	14	0.000532	Similar to nucleophosmin (nucleolar phosphoprotein B23, numatrin)
BC009650.1	1	10	0.001671	mRNA, complete cds.
BC009762.2	4	13	0.004765	mRNA, complete cds.

BC009819.1	3	12	0.003956	hypothetical protein FLJ23591
BC010074.2	5	17	0.003956	FUS interacting protein (serine/arginine-rich) 1, mRNA
BC010356.1	2	9	0.015475	gi|14714460 hypothetical protein
BC010360.1	6	17	0.003956	Unknown (protein for MGC:13386)
BC010467.1	8	18	0.002868	cDNA clone MGC:17410 IMAGE:4156035
BC010642.1	2	10	0.006907	zinc finger protein 22 (KOX 15)
BC010697.1	1	11	0.000624	amylase, alpha 2B; pancreatic
BC010907.1	0	9	0.015475	PAK1 interacting protein 1, mRNA
BC010947.1	0	11	7.27E-05	signal recognition particle 19kDa, mRNA
BC011379.1	2	11	0.002868	DKFZP434H132 protein
BC011498.1	0	6	0.010098	Unknown (protein for MGC:17017)
BC011600.1	0	6	0.010098	Similar to RD RNA-binding protein, clone MGC:2263
BC011804.2	2	11	0.009351	chromosome 1 open reading frame 165, mRNA
BC011842.2	1	11	0.000624	hypothetical protein FLJ11184, mRNA
BC012462.1	0	6	0.010098	clone MGC:21750 IMAGE:4537558
BC012472.1	6	18	0.000122	ubiquitin D, mRNA
BC012566.1	0	6	0.010098	nucleophosmin (nucleolar phosphoprotein B23, numatrin), mRNA
BC012865.1	1	9	0.015475	retinoic acid induced 16
BC012926.1	1	9	0.004181	EPS8-like 3, transcript variant 1, mRNA
BC013051.1	0	7	0.004158	LIM domain kinase 2
BC013437.1	2	9	0.015475	Similar to MADS box transcription enhancer factor 2, polypeptide A (myocyte enhancer factor 2A)
BC014218.2	2	12	0.011239	cDNA clone IMAGE:3954254
BC014298.1	2	11	0.002868	likely ortholog of mouse C114 dsRNA-binding protein
BC014452.1	4	16	0.000616	cDNA clone IMAGE:4903661
BC015008.1	8	16	0.011239	hydroxyacylglutathione hydrolase-like, mRNA
BC016609.1	0	8	0.009828	cytidine monophosphate N-acetylneuraminic acid synthetase, mRNA
BC016768.1	2	11	0.002868	nucleophosmin (nucleolar phosphoprotein B23, numatrin), mRNA
BC016778.1	2	10	0.006907	HIV-1 rev binding protein 2, mRNA
BC016842.1	2	11	0.002868	family with sequence similarity 61, member A, mRNA
BC017020.1	4	15	0.012421	single-stranded DNA binding protein 2
BC017114.1	6	18	0.0011	hypothetical protein FLJ22833,
BC017163.1	2	13	0.004765	CGI-74 protein, mRNA (cDNA clone MGC:8819 IMAGE:3920377)
BC018823.2	5	16	0.000616	splicing factor, arginine/serine-rich
BC020647.1	0	7	0.004158	HSPC128 protein, mRNA
BC021930.1	4	15	0.005193	Unknown (protein for MGC:32072)
BC021983.1	0	8	0.001638	nucleophosmin (nucleolar phosphoprotein B23, numatrin), transcript variant 1, mRNA
BC022077.1	2	13	0.000386	hypothetical protein MGC33338
BC022231.1	1	8	0.009828	Ets2 repressor factor, mRNA
BC022325.1	0	17	1.28E-08	hypothetical protein FLJ12729
BC022361.1	0	6	0.010098	chromosome 14 open reading frame 111,

BC025996.2	4	16	0.001821	cDNA clone MGC:26787 IMAGE:4838986
BC027178.1	8	18	0.015475	formin binding protein 3, mRNA
BC027607.1	6	15	0.012421	clone MGC:26892 IMAGE:4828241
BC028301.1	0	9	0.000614	similar to LOC147447
BC028396.1	0	6	0.010098	polyhomeotic-like 2 (Drosophila)
BC028425.1	0	6	0.010098	KIAA0027 protein
BC029046.1	3	12	0.003956	H1 histone family, member 0, mRNA
BC029427.1	2	12	0.0011	hypothetical protein LOC374969
BC030219.1	3	13	0.012421	RAD51-like 1 (S. cerevisiae)
BC030711.2	2	9	0.015475	chromosome 2 open reading frame 13
BC031010.1	0	6	0.010098	SET and MYND domain containing 3, mRNA
BC031281.1	3	13	0.004765	tetratricopeptide repeat domain 16, mRNA
BC032334.1	7	16	0.004765	putative homeodomain transcription factor 2, mRNA, complete cds.
BC032449.1	0	8	0.001638	paralemmin, mRNA
BC032852.2	10	18	0.006907	melanoma antigen family B, 4, mRNA
BC033088.1	0	6	0.010098	lamin A/C, mRNA
BC033159.1	10	19	0.009828	DnaJ (Hsp40) homolog, subfamily C, member 8, mRNA
BC033629.1	1	8	0.009828	chromosome 20 open reading frame 77, mRNA
BC033856.1	3	15	0.000164	Similar to RIKEN cDNA 3110040D16 gene, cloneMGC:45395 IMAGE:5123380, mRNA, complete cds.
BC038105.2	4	16	0.000616	membrane protein, palmitoylated 7 (MAGUK p55 subfamily member 7)
BC038808.1	11	20	0.001638	apolipoprotein B mRNA editing enzyme, catalytic polypeptide-like 3F, transcript variant 1, mRNA
BC042625.1	0	9	0.000614	LUC7-like 2 (S. cerevisiae), mRNA
BC043564.1	13	20	0.010098	potassium voltage-gated channel, shaker-related subfamily, member 2, mRNA
BC052806.1	4	14	0.001821	cDNA clone MGC:61802
BC053343.1	1	11	0.009351	karyopherin alpha 2 (RAG cohort 1, importin alpha 1), mRNA
BC053557.1	6	15	0.005193	cDNA clone MGC:61706 IMAGE:6162269
BC053866.1	2	11	0.009351	endothelin 3, transcript variant 2
BC054034.1	0	7	0.004158	U11/U12 snRNP 35K, transcript variant 2
BC055314.1	1	11	0.002868	C2f protein
BC056508.1	1	12	0.0011	variable charge, Y-linked 1B
BC058912.1	3	12	0.011239	butyrate-induced transcript 1, mRNA
BC060758.1	0	12	0.003956	complete cds.
BC063275.1	4	16	0.004765	eukaryotic translation initiation factor 2C, 1, mRNA
BC065525.1	0	6	0.010098	adducin 2 (beta), mRNA
BC067446.1	1	8	0.009828	disabled homolog 1 (Drosophila), mRNA
CTL2110	0	11	7.27E-05	DNA TOPOISIMERASE(Scl-70)
CTL2112	3	18	8.32E-06	ssDNA
CTL2121	1	8	0.009828	Ro-52
CTL2132	1	11	0.000624	myeloperoxidase
CTL2136	1	11	0.000624	U1-snRNP 68 PROTEIN
CTL2138	0	14	1.67E-06	RNP COMPLEX

CTL2139	1	10	0.001671	UNFRAC. WHOLE HISTONE
CTL2142	1	14	1.97E-05	ssDNA
CTL2143	12	19	0.009828	CENTROMERE PRO B
CTL2145	0	12	2.25E-05	RIBOSOMAL RNA
CTL2147	0	7	0.004158	dsDNA
CTL2150	6	16	0.004765	SMITH ANTIGEN
CTL2151	2	12	0.0011	Ro-52
NM_000723.3	1	10	0.001671	calcium channel, voltage-dependent, beta 1 subunit (CACNB1), transcript variant 1, mRNA
NM_000975.2	1	10	0.006907	ribosomal protein L11 (RPL11), mRNA
NM_000979.2	11	19	0.009828	ribosomal protein L18 (RPL18), mRNA
NM_000984.2	1	8	0.009828	ribosomal protein L23a (RPL23A)
NM_000989.2	0	7	0.004158	ribosomal protein L30 (RPL30), mRNA
NM_000997.2	1	12	0.011239	ribosomal protein L37 (RPL37)
NM_000999.2	0	6	0.010098	ribosomal protein L38 (RPL38)
NM_001014.2	1	14	1.97E-05	ribosomal protein S10 (RPS10)
NM_001015.2	0	7	0.004158	ribosomal protein S11 (RPS11)
NM_001020.2	5	16	0.004765	ribosomal protein S16 (RPS16)
NM_001022.3	2	11	0.002868	ribosomal protein S19 (RPS19), mRNA
NM_001023.2	0	6	0.010098	ribosomal protein S20 (RPS20), mRNA
NM_001106.2	4	12	0.011239	activin A receptor, type IIB (ACVR2B),
NM_001124.1	2	9	0.015475	adrenomedullin (ADM), mRNA
NM_001616.2	4	13	0.004765	activin A receptor, type II (ACVR2)
NM_001722.2	4	12	0.011239	polymerase (RNA) III (DNA directed) polypeptide D, 44kDa (POLR3D), mRNA
NM_001896.1	2	10	0.006907	casein kinase 2, alpha prime polypeptide (CSNK2A2)
NM_001896.2	2	10	0.006907	casein kinase 2, alpha prime polypeptide (CSNK2A2), mRNA
NM_001997.2	2	10	0.006907	Finkel-Biskis-Reilly murine sarcoma virus (FBR-MuSV) ubiquitously expressed (fox derived); ribosomal protein S30 (FAU)
NM_002129.2	0	8	0.001638	high-mobility group box 2 (HMGB2), mRNA
NM_002446.2	5	16	0.000616	mitogen-activated protein kinase kinase kinase 10 (MAP3K10)
NM_002677.1	4	14	0.012822	peripheral myelin protein 2 (PMP2)
NM_002734.1	1	9	0.004181	protein kinase, cAMP-dependent, regulatory, type I, alpha (tissue specific extinguisher 1) (PRKAR1A)

NM_003092.3	5	13	0.012421	small nuclear ribonucleoprotein polypeptide B" (SNRPB2), transcript variant 1, mRNA
NM_003123.1	8	17	0.009351	sialophorin (gpL115, leukosialin, CD43) (SPN)
NM_003295.1	0	7	0.004158	tumor protein, translationally-controlled 1 (TPT1), mRNA
NM_003390.2	1	9	0.004181	WEE1 homolog (S. pombe) (WEE1)
NM_003516.2	9	20	0.001638	histone 2, H2aa (HIST2H2AA), mRNA
NM_003621.1	0	8	0.001638	PTPRF interacting protein, binding protein 2 (liprin beta 2) (PPFIBP2), mRNA
NM_003688.1	10	19	0.004181	calcium/calmodulin-dependent serine protein kinase (MAGUK family) (CASK)
NM_003992.1	1	9	0.004181	CDC-like kinase 3 (CLK3), transcript variant phclk3
NM_004114.2	5	13	0.012421	fibroblast growth factor 13 (FGF13), transcript variant 1A, mRNA
NM_004214.3	0	14	1.67E-06	fibroblast growth factor (acidic) intracellular binding protein (FIBP)
NM_004286.2	2	9	0.015475	GTP binding protein 1 (GTPBP1)
NM_004310.2	3	12	0.011239	ras homolog gene family, member H (RHOH), mRNA
NM_004596.1	0	13	6.44E-06	small nuclear ribonucleoprotein polypeptide A (SNRPA)
NM_004645.1	0	7	0.004158	coilin (COIL)
NM_004966.2	1	9	0.004181	heterogeneous nuclear ribonucleoprotein F (HNRPF), mRNA
NM_005441.2	2	10	0.006907	chromatin assembly factor 1, subunit B (p60) (CHAF1B), mRNA
NM_005517.2	0	7	0.004158	high-mobility group nucleosomal binding domain 2 (HMGN2), mRNA
NM_006298.2	7	18	0.000386	zinc finger protein 192 (ZNF192), mRNA
NM_006528.2	1	8	0.009828	tissue factor pathway inhibitor 2 (TFPI2), mRNA
NM_006681.1	6	17	0.009351	neuromedin U (NMU), mRNA
NM_006695.2	2	9	0.015475	RaP2 interacting protein 8 (RPIP8)
NM_006701.2	1	9	0.004181	thioredoxin-like 4A (TXNL4A), mRNA
NM_006788.2	0	7	0.004158	ralA binding protein 1 (RALBP1)
NM_006791.1	1	12	0.0011	mortality factor 4 like 1 (MORF4L1)
NM_006857.1	0	8	0.001638	putative nucleic acid binding protein RY-1 (RY1), mRNA
NM_006937.2	0	6	0.010098	SMT3 suppressor of mif two 3 homolog 2 (yeast) (SMT3H2)
NM_007054.1	3	19	1.97E-05	kinesin family member 3A (KIF3A)

NM_007173.3	0	6	0.010098	protease, serine, 23 (PRSS23), mRNA
NM_007285.5	5	16	0.004765	GABA(A) receptor-associated protein-like 2 (GABARAPL2)
NM_012153.1	3	12	0.003956	ets homologous factor (EHF)
NM_012279.1	12	19	0.009828	double-stranded RNA-binding zinc finger protein JAZ (JAZ),
NM_012316.2	0	6	0.010098	karyopherin alpha 6 (importin alpha 7) (KPNA6)
NM_012321.1	0	10	0.001671	U6 snRNA-associated Sm-like protein (LSM4)
NM_012425.2	1	9	0.015475	Ras suppressor protein 1 (RSU1)
NM_013293.1	0	12	0.000216	transformer-2 alpha (TRA2A)
NM_014047.1	6	16	0.004765	HSPC023 protein (HSPC023), mRNA
NM_014765.1	9	18	0.015475	translocase of outer mitochondrial membrane 20 homolog (yeast) (TOMM20), mRNA
NM_015014.1	8	16	0.011239	KIAA0117 protein (KIAA0117), mRNA
NM_015149.2	0	7	0.004158	ral guanine nucleotide dissociation stimulator-like 1 (RGL1), mRNA
NM_015464.1	1	11	0.000624	sclerostin domain containing 1 (SOSTDC1), mRNA
NM_015488.1	6	17	0.001528	myofibrillogenesis regulator 1 (MR-1)
NM_015640.1	3	13	0.001528	PAI-1 mRNA-binding protein (PAI-RBP1)
NM_015933.1	2	13	0.000386	hypothetical protein HSPC016 (HSPC016)
NM_015971.2	0	6	0.010098	mitochondrial ribosomal protein S7 (MRPS7), nuclear gene encoding mitochondrial protein, mRNA
NM_015987.2	4	18	8.32E-06	heme binding protein 1 (HEBP1)
NM_016000.2	0	6	0.010098	tRNA nucleotidyl transferase, CCA-adding, 1 (TRNT1), mRNA
NM_016303.1	5	14	0.012822	pp21 homolog (LOC51186)
NM_016321.1	5	13	0.012421	Rhesus blood group, C glycoprotein (RHCG), mRNA
NM_016355.3	0	13	6.44E-06	DEAD (Asp-Glu-Ala-Asp) box polypeptide 47 (DDX47), transcript variant 1, mRNA
NM_016483.3	2	15	0.000164	PHD finger protein 7 (PHF7)
NM_016505.2	1	13	6.85E-05	putative S1 RNA binding domain protein (PS1D), mRNA
NM_016520.1	1	8	0.009828	chromosome 9 open reading frame 78 (C9orf78), mRNA
NM_016606.2	9	20	0.001638	chromosome 5 open reading frame 19 (C5orf19), mRNA
NM_016940.1	4	18	0.000386	chromosome 21 open reading frame 6 (C21orf6), mRNA

NM_017588.1	2	14	0.000122	WD repeat domain 5 (WDR5), transcript variant 1
NM_017692.1	0	7	0.004158	aprataxin (APTX)
NM_017838.2	1	14	1.97E-05	nucleolar protein family A, member 2 (H/ACA small nucleolar RNPs) (NOLA2)
NM_017846.3	0	8	0.001638	tRNA selenocysteine associated protein (SECP43), mRNA
NM_018032.2	2	13	0.000386	LUC7-like (S. cerevisiae) (LUC7L)
NM_018105.1	3	11	0.009351	THAP domain containing, apoptosis associated protein 1 (THAP1)
NM_018107.2	4	14	0.001821	RNA-binding region (RNP1, RRM) containing 4 (RNPC4)
NM_018710.1	13	20	0.010098	hypothetical protein DKFZp762O076 (DKFZp762O076), mRNA
NM_019099.1	2	10	0.006907	hypothetical protein LOC55924
NM_020239.2	1	11	0.000624	small protein effector 1 of Cdc42 (SPEC1)
NM_020530.2	7	17	0.009351	oncostatin M (OSM)
NM_020648.3	14	20	0.010098	twisted gastrulation homolog 1 (Drosophila) (TWSG1), mRNA
NM_020661.1	0	9	0.000614	activation-induced cytidine deaminase (AICDA), mRNA
NM_021104.1	0	6	0.010098	ribosomal protein L41 (RPL41), mRNA
NM_022142.3	1	12	0.011239	epididymal sperm binding protein 1 (ELSPBP1), mRNA
NM_022839.2	3	11	0.009351	mitochondrial ribosomal protein S11 (MRPS11), nuclear gene encoding mitochondrial protein, transcript variant 1, mRNA
NM_024068.1	1	10	0.001671	hypothetical protein MGC2731 (MGC2731)
NM_024482.1	0	7	0.004158	glucocorticoid modulatory element binding protein 1 (GMEB1), transcript variant 2, mRNA
NM_024625.3	1	14	0.000532	zinc finger CCCH type, antiviral 1 (ZC3HAV1), transcript variant 2, mRNA
NM_031412.1	0	10	0.000218	GABA(A) receptor-associated protein like 1 (GABARAPL1)
NM_031452.1	5	15	0.012421	hypothetical protein MGC2560
NM_031910.2	6	17	0.000532	C1q and tumor necrosis factor related protein 6 (C1QTNF6)
NM_031991.1	9	20	0.000614	polypyrimidine tract binding protein 1 (PTBP1), transcript variant 3
NM_032042.2	6	15	0.005193	hypothetical protein DKFZp564D172
NM_032338.2	1	8	0.009828	hypothetical protein , mRNA
NM_032345.1	4	16	0.00018	PYM protein (PYM), mRNA

NM_032883.1	1	10	0.001671	chromosome 20 open reading frame 100 (C20orf100), mRNA
NM_033048.1	3	13	0.012421	CPX chromosome region, candidate 1 (CPXCR1)
NM_033177.2	2	12	0.011239	HLA-B associated transcript 4 (BAT4), mRNA
NM_033642.1	2	9	0.015475	fibroblast growth factor 13 (FGF13), transcript variant 1B, mRNA
NM_054016.1	1	10	0.001671	FUS interacting protein (serine-arginine rich) 1 (FUSIP1), transcript variant 2, mRNA
NM_058199.1	2	12	0.003956	olfactomedin 1 (OLFM1), transcript variant 3
NM_138775.1	2	15	0.000164	hypothetical protein BC015183 (LOC91801), mRNA
NM_144590.1	0	9	0.004181	ankyrin repeat domain 22 (ANKRD22), mRNA
NM_144608.1	0	9	0.000614	hypothetical protein (FLJ32384), mRNA
NM_144659.1	0	8	0.001638	t-complex 10 (mouse)-like (TCP10L)
NM_144971.1	3	11	0.009351	hypothetical protein MGC26641
NM_144982.1	3	13	0.001528	hypothetical protein MGC23401
NM_145010.1	9	20	0.000218	hypothetical protein MGC26778
NM_152362.1	0	8	0.001638	hypothetical protein , mRNA
NM_152397.1	0	9	0.000614	IQ motif containing F1 (IQCF1), mRNA
NM_152638.2	1	8	0.009828	chromosome 12 open reading frame 12 (C12orf12), mRNA
NM_152769.1	1	8	0.009828	chromosome 19 open reading frame 26 (C19orf26), mRNA
NM_153207.2	10	18	0.006907	AE binding protein 2 (AEBP2)
NM_153332.2	4	16	0.000616	3' exoribonuclease (3'HEXO), mRNA
NM_170676.2	2	11	0.002868	Meis1, myeloid ecotropic viral integration site 1 homolog 2 (mouse) (MEIS2), transcript variant d, mRNA
NM_173545.1	1	8	0.009828	chromosome 2 open reading frame 13 (C2orf13), mRNA
NM_177924.1	1	8	0.009828	N-acylsphingosine amidohydrolase (acid ceramidase) 1 (ASAH1), transcript variant 1, mRNA
NM_178861.3	4	17	0.001528	zinc finger protein 183-like 1 (ZNF183L1), mRNA
NM_182623.1	12	20	0.010098	hypothetical protein FLJ36766 (FLJ36766), mRNA
NM_198395.1	8	18	0.0011	Ras-GTPase-activating protein SH3-domain-binding protein (G3BP), transcript variant 2

NM_199334.2	0	6	0.010098	thyroid hormone receptor, alpha (erythroblastic leukemia viral (v-erb-a) oncogene homolog, avian) (THRA), transcript variant 1, mRNA
NM_203350.1	1	9	0.004181	zinc finger protein 265 (ZNF265), transcript variant 1, mRNA

Table 12. Table 12 is a list of proteins that were bound by an antibody from ANCA patient sera but not SLE patients.

Genbank ID number of nucleic acid coding for the protein	ANCA Count	SLE Count	p-value	Name or description
BC000052.1	8	1	0.009828	Similar to peroxisome proliferative activated receptor, alpha, clone MGC:2237
BC000103.1	17	6	0.0015282	NCK adaptor protein 2
BC000733.1	6	0	0.010098	eukaryotic translation initiation factor 3, subunit 4 (delta, 44kD),
BC000979.2	12	2	0.0010998	DEAD (Asp-Glu-Ala-Asp) box polypeptide 49
BC001132.1	9	2	0.0154752	DEAD (Asp-Glu-Ala-Asp) box polypeptide 54
BC001152.1	12	0	0.0002158	growth arrest-specific 7, mRNA
BC001286.1	7	0	0.004158	dCMP deaminase, mRNA
BC001669.1	20	7	6.44E-06	Similar to oxidase (cytochrome c) assembly 1-like, clone MGC:2171
BC001873.1	11	2	0.0093506	hairy/enhancer-of-split related with YRPW motif 1, mRNA
BC001907.1	18	8	0.0010998	hypothetical protein MGC2650
BC001917.1	11	2	0.0028678	malate dehydrogenase 2, NAD (mitochondrial), mRNA
BC002493.1	17	9	0.0093506	cDNA clone MGC:2575 IMAGE:3051226
BC002677.1	16	3	0.0047651	hypothetical protein, clone MGC:3375 IMAGE:3609357
BC002880.1	16	2	8.32E-06	cysteinyl-tRNA synthetase, clone MGC:11246
BC002955.1	16	6	0.0047651	ubiquitin specific peptidase 2, transcript variant 1, mRNA
BC003065.1	16	5	0.0006159	cyclin-dependent kinase 2,
BC003132.1	17	8	0.0093506	nuclear distribution gene C homolog (A. nidulans)
BC003168.1	13	3	0.0047651	oxysterol binding protein-like 10
BC004271.1	14	4	0.0018205	carnosinase 1
BC004514.1	8	1	0.009828	hypothetical protein FLJ12584
BC005297.1	9	1	0.0041809	kynurenine 3-monooxygenase (kynurenine 3-hydroxylase), mRNA
BC005332.1	18	3	1.68E-06	cDNA clone MGC:12418 IMAGE:3934658, complete cds

BC006105.1	10	0	0.000218	chromosome 6 open reading frame 134, mRNA
BC007363.1	15	6	0.0124209	clone MGC:16138 IMAGE:3630050
BC007411.2	20	11	0.001638	diaphanous homolog 1 (Drosophila)
BC007560.1	9	0	0.0154752	LIM and SH3 protein 1, mRNA
BC007581.1	8	0	0.001638	aldehyde dehydrogenase 4 family, member A1, transcript variant P5CDhL, mRNA
BC007872.1	19	9	0.009828	thymidine kinase 1, soluble
BC009189.1	12	3	0.0112387	CGI-39 protein; cell death-regulatory protein GRIM19
BC009250.1	17	6	0.0005323	nucleolar GTPase
BC009696.1	14	3	0.0005323	interferon induced transmembrane protein 2 (1-8D), mRNA
BC009712.1	8	1	0.009828	Similar to ATP-binding cassette, sub-family D (ALD), member 3
BC009894.2	17	5	0.0093506	3'-phosphoadenosine 5'-phosphosulfate synthase 2
BC010176.1	9	1	0.0041809	clone MGC:20533 IMAGE:3342874,
BC010959.1	11	2	0.0028678	BCL2/adenovirus E1B 19kDa interacting protein 1, transcript variant BNIP1, mRNA
BC011710.2	10	1	0.0069071	hypoxia-inducible factor prolyl 4-hydroxylase
BC011811.1	10	1	0.001671	clone MGC:20260 IMAGE:3028747
BC011885.1	9	1	0.0041809	eukaryotic translation initiation factor (eIF) 2A, mRNA
BC012109.1	19	10	0.001671	homer homolog 2 (Drosophila)
BC012576.1	15	3	0.0001642	Unknown (protein for MGC:13472)
BC012609.1	9	1	0.0154752	serpin peptidase inhibitor, clade B (ovalbumin), member 2, mRNA
BC012783.2	12	1	0.0010998	cDNA clone IMAGE:3949276
BC012876.1	18	4	8.32E-06	clone MGC:17259 IMAGE:4149333
BC014037.1	16	5	0.0018205	Similar to serum/glucocorticoid regulated kinase 2
BC014271.2	18	4	8.32E-06	endoglin (Osler-Rendu-Weber syndrome 1), mRNA
BC014667.1	20	9	7.27E-05	immunoglobulin heavy constant gamma 1 (G1m marker), mRNA
BC014889.1	13	2	0.0015282	requiem, apoptosis response zinc finger gene
BC015684.2	14	3	0.0005323	Similar to Sjogren syndrome antigen A1 (52kD, ribonucleoprotein autoantigen SS-A/Ro)
BC015833.1	19	4	1.10E-06	cDNA clone MGC:27152 IMAGE:4691630, complete cds
BC015848.1	11	0	7.27E-05	chromosome 17 open reading frame 25, mRNA
BC016380.1	18	4	8.32E-06	cDNA clone MGC:27376 IMAGE:4688477, complete cds
BC016381.1	15	3	0.0001642	cDNA clone MGC:27378 IMAGE:4688865, complete cds
BC016789.1	15	3	0.0051934	glycine-N-acyltransferase-like 2, mRNA

BC017115.1	8	1	0.009828	Unknown (protein for MGC:16813)
BC017237.1	6	0	0.010098	Similar to syntaxin 10
BC017344.1	11	1	0.0006238	Similar to hypothetical protein FLJ23469
BC017865.1	20	10	0.000218	Fc fragment of IgG, low affinity IIIa, receptor (CD16a), mRNA
BC017959.1	7	0	0.004158	hypothetical protein FLJ22555, mRNA
BC018749.1	8	0	0.001638	immunoglobulin lambda variable 2-14, mRNA
BC019337.1	19	3	2.03E-07	immunoglobulin heavy constant gamma 1 (G1m marker), mRNA
BC020622.1	9	2	0.0154752	zinc finger, A20 domain containing 1, mRNA, complete cds.
BC020658.1	9	0	0.0041809	transmembrane protein 40, mRNA
BC020962.1	13	1	6.85E-05	similar to glucosamine-6-sulfatases
BC020985.1	16	5	0.0018205	gi|21594102 Unknown (protein for MGC:9724)
BC021551.1	11	1	0.0006238	hypothetical protein FLJ14639
BC022098.1	18	4	8.32E-06	cDNA clone MGC:31944 IMAGE:4878869, complete cds
BC022362.1	19	6	1.97E-05	cDNA clone MGC:23888 IMAGE:4704496, complete cds
BC022454.2	11	1	0.0006238	transient receptor potential cation channel, subfamily M, member 3
BC024289.1	15	2	3.43E-05	cDNA clone MGC:39273 IMAGE:5440834, complete cds
BC024291.1	12	3	0.0039558	Similar to serine/threonine kinase 29
BC025314.1	18	4	8.32E-06	immunoglobulin heavy constant gamma 1 (G1m marker), mRNA
BC025389.1	11	2	0.0028678	hypothetical protein MGC26605
BC027486.1	8	0	0.001638	cDNA clone MGC:34907 IMAGE:5104096, complete cds
BC028039.1	16	3	4.38E-05	hypothetical protein MGC39900
BC028728.1	11	0	7.27E-05	Similar to putative ion channel protein CATSPER2,clone MGC:33346 IMAGE:4828636, mRNA, complete cds.
BC028840.1	6	0	0.010098	hypothetical protein DKFZp566D1346
BC029054.1	16	2	8.32E-06	PDZ domain containing 7, mRNA
BC029444.1	19	4	1.10E-06	cDNA clone MGC:32714 IMAGE:4692138, complete cds
BC030814.1	16	2	8.32E-06	immunoglobulin kappa variable 1-5, mRNA
BC030983.1	17	2	1.68E-06	immunoglobulin lambda constant 1 (Mcg marker), mRNA
BC030984.1	16	1	1.10E-06	cDNA clone MGC:32654 IMAGE:4701898, complete cds
BC031074.1	19	5	5.01E-06	poly (ADP-ribose) polymerase family, member 16, mRNA
BC031592.1	10	1	0.001671	serpin peptidase inhibitor, clade F (alpha-2 antiplasmin, pigment epithelium derived factor), member 2, mRNA

BC031966.1	12	1	0.0002158	cDNA clone MGC:43036 IMAGE:4839025
BC032451.1	20	8	2.25E-05	cDNA clone MGC:40426 IMAGE:5178085, complete cds
BC032452.1	18	5	3.43E-05	immunoglobulin lambda constant 1 (Mcg marker), mRNA
BC033035.1	15	5	0.0019238	similar to hypothetical protein, clone MGC:33355 IMAGE:4839231
BC033178.1	20	3	1.28E-08	immunoglobulin heavy constant gamma 3 (G3m marker), mRNA
BC034141.1	20	7	6.44E-06	immunoglobulin kappa constant, mRNA
BC034146.1	16	8	0.0112387	cDNA clone MGC:32764 IMAGE:4618950, complete cds
BC034247.1	13	1	0.0003858	chromosome 9 open reading frame 105, mRNA
BC035911.1	12	1	0.0010998	DEAD (Asp-Glu-Ala-Asp) box polypeptide 55, mRNA, complete cds.
BC036723.1	16	3	4.38E-05	Fc fragment of IgG, low affinity IIIa, receptor (CD16a), mRNA
BC038713.1	11	2	0.0093506	pleckstrin homology, Sec7 and coiled-coil domains 2 (cytohesin-2), transcript variant 1, mRNA
BC039814.1	17	4	4.38E-05	zinc finger protein 265, transcript variant 2, mRNA
BC039904.1	15	5	0.0051934	histone deacetylase 4, mRNA
BC040656.1	15	5	0.0019238	leucine rich repeat containing 3B
BC041037.1	13	0	6.44E-06	immunoglobulin heavy constant mu, mRNA
BC044584.1	16	8	0.0112387	DnaJ (Hsp40) homolog, subfamily C, member 4, mRNA
BC048125.1	10	1	0.001671	hypothetical protein FLJ32800, mRNA
BC051382.1	9	0	0.0041809	hypothetical protein MGC5987
BC051762.1	13	3	0.0015282	chromosome 20 open reading frame 96
BC051885.1	20	10	0.0006143	chromosome 14 open reading frame 106, mRNA, complete cds.
BC053656.1	17	3	9.69E-06	EGF-like repeats and discoidin I-like domains 3, mRNA
BC053664.1	14	3	0.0005323	complete cds.
BC053984.1	18	4	8.32E-06	cDNA clone MGC:59926 IMAGE:5480266, complete cds
BC056256.1	18	3	1.68E-06	immunoglobulin kappa constant, mRNA
BC057770.1	10	0	0.000218	solute carrier family 27 (fatty acid transporter), member 2, mRNA
BC064367.1	17	9	0.0093506	sterile alpha motif domain containing 6, mRNA
BC064945.1	9	1	0.0154752	SCY1-like 1 binding protein 1, mRNA
CTL2122	16	4	0.00018	RNA POLYMERASE
CTL2130	17	2	1.68E-06	Proteinase-3

CTL2134	18	6	0.0001222	dsDNA
CTL2137	13	3	0.0015282	La/SS-B
CTL2144	16	4	0.00018	TRANSGLUTAMINASE
NM_000023.1	13	3	0.0015282	sarcoglycan, alpha (50kDa dystrophin-associated glycoprotein) (SGCA), mRNA
NM_000137.1	16	7	0.0047651	fumarylacetoacetate hydrolase (fumarylacetoacetase) (FAH), mRNA
NM_001002018.1	18	11	0.0154752	host cell factor C1 regulator 1 (XPO1 dependant) (HCFC1R1), transcript variant 3, mRNA
NM_001203.1	20	11	0.0006143	bone morphogenetic protein receptor, type IB (BMPR1B), mRNA
NM_001258.1	12	2	0.0010998	cyclin-dependent kinase 3 (CDK3), mRNA
NM_001449.2	18	3	1.68E-06	four and a half LIM domains 1 (FHL1)
NM_001769.2	10	1	0.001671	CD9 antigen (p24) (CD9), mRNA
NM_001892.2	6	0	0.010098	casein kinase 1, alpha 1 (CSNK1A1),
NM_002082.1	16	6	0.0112387	G protein-coupled receptor kinase 6 (GRK6)
NM_002362.2	6	0	0.010098	melanoma antigen, family A, 4 (MAGEA4)
NM_002395.2	12	4	0.0112387	malic enzyme 1, NADP(+)-dependent, cytosolic (ME1), mRNA
NM_002431.1	15	6	0.0051934	menage a trois 1 (CAK assembly factor) (MNAT1)
NM_002436.2	6	0	0.010098	membrane protein, palmitoylated 1, 55kDa (MPP1), mRNA
NM_002576.2	11	2	0.0028678	p21/Cdc42/Rac1-activated kinase 1 (STE20 homolog, yeast) (PAK1)
NM_002578.1	20	12	0.001638	p21 (CDKN1A)-activated kinase 3 (PAK3)
NM_002613.1	12	3	0.0039558	3-phosphoinositide dependent protein kinase-1 (PDPK1)
NM_002744.2	6	0	0.010098	protein kinase C, zeta (PRKCZ)
NM_002754.3	20	7	2.25E-05	mitogen-activated protein kinase 13 (MAPK13), mRNA
NM_002774.2	13	1	6.85E-05	kallikrein 6 (neurosin, zyme) (KLK6)
NM_002963.2	13	3	0.0015282	S100 calcium binding protein A7 (psoriasin 1) (S100A7), mRNA
NM_003049.1	11	2	0.0093506	solute carrier family 10 (sodium/bile acid cotransporter family), member 1 (SLC10A1), mRNA
NM_003315.1	11	2	0.0028678	DnaJ (Hsp40) homolog, subfamily C, member 7 (DNAJC7), mRNA
NM_003476.2	12	2	0.0010998	cysteine and glycine-rich protein 3 (cardiac LIM protein) (CSRP3), mRNA
NM_003582.1	12	4	0.0112387	dual-specificity tyrosine-(Y)-phosphorylation regulated kinase 3 (DYRK3)
NM_003792.1	9	1	0.0041809	endothelial differentiation-related factor 1 (EDF1)

NM_003942.1	10	0	0.000218	ribosomal protein S6 kinase, 90kDa, polypeptide 4 (RPS6KA4)
NM_004073.2	14	3	0.0005323	polo-like kinase 3 (Drosophila) (PLK3), mRNA
NM_004078.1	12	2	0.0010998	cysteine and glycine-rich protein 1 (CSRP1), mRNA
NM_004089.1	13	3	0.0047651	delta sleep inducing peptide, immunoreactor (DSIPI)
NM_004181.2	14	3	0.0005323	ubiquitin carboxyl-terminal esterase L1 (ubiquitin thiolesterase) (UCHL1)
NM_004722.2	8	1	0.009828	adaptor-related protein complex 4, mu 1 subunit (AP4M1), mRNA
NM_004732.1	17	5	0.0005323	potassium voltage-gated channel, shaker-related subfamily, beta member 3 (KCNAB3)
NM_004759.2	12	2	0.0010998	mitogen-activated protein kinase-activated protein kinase 2 (MAPKAPK2), transcript variant 1
NM_004881.1	9	2	0.0154752	quinone oxidoreductase homolog (PIG3)
NM_004935.1	16	7	0.0112387	cyclin-dependent kinase 5 (CDK5)
NM_005157.2	16	4	0.0047651	v-abl Abelson murine leukemia viral oncogene homolog 1 (ABL1), transcript variant a
NM_005347.2	9	2	0.0154752	heat shock 70kDa protein 5 (glucose-regulated protein, 78kDa) (HSPA5), mRNA
NM_005435.2	18	10	0.0069071	Rho guanine nucleotide exchange factor (GEF) 5 (ARHGEF5)
NM_005522.3	17	3	9.69E-06	homeo box A1 (HOXA1), transcript variant 1
NM_005697.3	12	1	0.0002158	secretory carrier membrane protein 2 (SCAMP2), mRNA
NM_006002.2	8	0	0.001638	ubiquitin carboxyl-terminal esterase L3 (ubiquitin thiolesterase) (UCHL3)
NM_006552.1	8	0	0.009828	secretoglobin, family 1D, member 1 (SCGB1D1), mRNA
NM_006775.1	9	2	0.0154752	quaking homolog, KH domain RNA binding (mouse) (QKI), transcript variant 1, mRNA
NM_006869.1	20	13	0.004158	centaurin, alpha 1 (CENTA1), mRNA
NM_012097.2	11	0	0.0028678	ADP-ribosylation factor-like 5 (ARL5), transcript variant 1
NM_012101.2	13	4	0.0047651	tripartite motif-containing 29 (TRIM29), transcript variant 1, mRNA
NM_012241.2	13	1	6.85E-05	sirtuin (silent mating type information regulation 2 homolog) 5 (S. cerevisiae) (SIRT5), transcript variant 1, mRNA
NM_013254.2	15	7	0.0124209	TANK-binding kinase 1 (TBK1), mRNA
NM_013322.2	16	5	0.0018205	sorting nexin 10 (SNX10), mRNA
NM_013410.1	12	1	0.0039558	adenylate kinase 3 (AK3)
NM_014046.	8	0	0.001638	mitochondrial ribosomal protein S18B (MRPS18B),

2				nuclear gene encoding mitochondrial protein, mRNA
NM_014188.2	6	0	0.010098	HSPC182 protein (HSPC182), mRNA
NM_014251.1	11	3	0.0093506	solute carrier family 25, member 13 (citrin) (SLC25A13), mRNA
NM_016006.1	15	5	0.0124209	comparative gene identification 58 (CGI58)
NM_016052.1	12	2	0.0010998	CGI-115 protein (CGI-115)
NM_016091.1	9	1	0.0041809	eukaryotic translation initiation factor 3, subunit 6 interacting protein (EIF3S6IP)
NM_016207.2	11	0	7.27E-05	cleavage and polyadenylation specific factor 3, 73kDa (CPSF3), mRNA
NM_017503.2	7	0	0.004158	surfeit 2 (SURF2), mRNA
NM_017811.2	8	1	0.009828	ubiquitin-conjugating enzyme E2R 2 (UBE2R2)
NM_018129.1	9	2	0.0154752	pyridoxine 5'-phosphate oxidase (PNPO), mRNA
NM_018184.1	18	9	0.0154752	ADP-ribosylation factor-like 10C (ARL10C)
NM_018679.2	10	1	0.0069071	t-complex 11 (mouse) (TCP11), mRNA
NM_019103.1	7	0	0.004158	hypothetical protein LOC55954
NM_020367.2	10	1	0.001671	chromosome 12 open reading frame 6 (C12orf6)
NM_020381.2	9	0	0.0006143	chromosome 6 open reading frame 210 (C6orf210), mRNA
NM_020444.2	18	10	0.0069071	KIAA1191 protein (KIAA1191), mRNA
NM_020547.1	9	1	0.0041809	anti-Mullerian hormone receptor, type II (AMHR2)
NM_020929.1	15	3	0.0124209	netrin-G1 ligand (NGL-1), mRNA
NM_021117.1	8	0	0.001638	cryptochrome 2 (photolyase-like) (CRY2), mRNA
NM_021146.2	11	2	0.0028678	angiopoietin-like 7 (ANGPTL7), mRNA
NM_021254.1	9	2	0.0154752	chromosome 21 open reading frame 59 (C21orf59), mRNA
NM_021709.1	13	2	0.0015282	CD27-binding (Siva) protein (SIVA), transcript variant 2, mRNA
NM_021945.1	13	2	0.0015282	hypothetical protein FLJ22174
NM_022777.1	11	1	0.0006238	RAB, member RAS oncogene family-like 5 (RABL5), mRNA
NM_024041.1	19	8	0.0002158	sodium channel modifier 1 (SCNM1)
NM_024096.1	9	1	0.0041809	XTP3-transactivated protein A (XTP3TPA), mRNA
NM_024348.2	8	1	0.009828	dynactin 3 (p22) (DCTN3), transcript variant 2, mRNA
NM_024419.2	7	0	0.004158	phosphatidylglycerophosphate synthase (PGS1)

NM_024749.1	16	6	0.0018205	hypothetical protein FLJ12505
NM_024770.1	12	3	0.0112387	hypothetical protein FLJ13984 (FLJ13984), mRNA
NM_024786.1	15	6	0.0124209	zinc finger, DHHC domain containing 11 (ZDHHC11), mRNA
NM_024893.1	12	0	2.25E-05	chromosome 20 open reading frame 39 (C20orf39), mRNA
NM_030773.1	10	2	0.0069071	tubulin, beta 1 (TUBB1)
NM_032146.2	17	9	0.0093506	ADP-ribosylation factor-like 6 (ARL6)
NM_032731.2	13	1	6.85E-05	thioredoxin-like 5 (TXNL5), mRNA
NM_032855.1	18	5	3.43E-05	hematopoietic SH2 protein (HSH2)
NM_052844.1	11	1	0.0006238	hypothetical protein MGC20486
NM_052848.1	8	1	0.009828	hypothetical protein , mRNA
NM_052877.1	20	9	7.27E-05	mediator of RNA polymerase II transcription, subunit 8 homolog (yeast) (MED8)
NM_058163.1	12	4	0.0112387	hypothetical protein DT1P1A10 (DT1P1A10), mRNA
NM_058217.1	15	6	0.0051934	RAD51 homolog C (S. cerevisiae) (RAD51C), transcript variant 3
NM_138355.1	14	3	0.0128224	secernin 2 (Ses2)
NM_138432.1	12	2	0.0010998	serine dehydratase related sequence 1 (SDS-RS1)
NM_138455.1	16	5	0.0018205	collagen triple helix repeat containing 1
NM_138470.1	13	1	0.0047651	hypothetical protein BC008131 (LOC142937)
NM_139240.2	11	1	0.0006238	LOC92346 (LOC92346), mRNA
NM_145063.1	20	14	0.010098	chromosome 6 open reading frame 130 (C6orf130)
NM_145109.1	16	6	0.0112387	mitogen-activated protein kinase kinase 3 (MAP2K3), transcript variant B, mRNA
NM_145792.1	12	2	0.0010998	microsomal glutathione S-transferase 1 (MGST1), transcript variant 1a
NM_148975.1	10	2	0.0069071	membrane-spanning 4-domains, subfamily A, member 4 (MS4A4A), transcript variant 2, mRNA
NM_152421.2	6	0	0.010098	hypothetical protein , mRNA
NM_152690.1	12	1	0.0002158	dolichyl-phosphate mannosyltransferase polypeptide 2, regulatory subunit (DPM2), transcript variant 2
NM_152772.1	16	6	0.0112387	hypothetical protein , mRNA
NM_153215.1	19	5	1.97E-05	hypothetical protein FLJ38608 (FLJ38608), mRNA
NM_173519.1	17	6	0.0093506	hypothetical protein , mRNA

NM_175907.3	20	8	2.25E-05	zinc binding alcohol dehydrogenase, domain containing 2 (ZADH2), mRNA
NM_178496.2	19	7	0.001671	similar to BcDNA:GH11415 gene product (LOC151963), mRNA
NM_178832.2	16	4	0.0112387	chromosome 10 open reading frame 83 (C10orf83), mRNA
NM_181738.1	12	2	0.0010998	peroxiredoxin 2 (PRDX2), nuclear gene encoding mitochondrial protein, transcript variant 3, mRNA
NM_183059.1	13	4	0.0047651	chromosome 1 open reading frame 36 (C1orf36), mRNA
NM_197964.1	14	6	0.0128224	hypothetical protein HSPC268 (HSPC268), mRNA
NM_198490.1	9	1	0.0154752	RAB43, member RAS oncogene family (RAB43), mRNA
NP_005219.2	15	7	0.0124209	epidermal growth factor receptor (erthroblastic leukemia viral (v-erb-b) oncogene homolog, avian) (EGFR), mutant isoform L861Q

Table 13. A list of proteins that were bound by an antibody from ANCA patient sera but not RA patients.

Genbank ID number of nucleic acid coding for the protein	**ANCA Count**	**RA Count**	**p-value**	**Name or description**
BC000442.1	0	13	0.001142	serine/threonine kinase 12
BC000463.1	1	19	0.00017	splicing factor 3b, subunit 3, 130kD
BC001709.1	0	9	0.016771	NAD kinase, mRNA
BC002880.1	0	15	0.0002	cysteinyl-tRNA synthetase
BC003065.1	2	18	0.000701	cyclin-dependent kinase 2
BC003168.1	1	13	0.009495	oxysterol binding protein-like 10
BC005332.1	0	11	0.004855	cDNA clone MGC:12418 IMAGE:3934658, complete cds
BC006105.1	2	16	0.005343	chromosome 6 open reading frame 134, mRNA
BC006550.1	0	10	0.009224	RNA binding motif protein, X chromosome
BC007363.1	0	14	0.0005	clone MGC:16138 IMAGE:3630050
BC007581.1	0	14	0.0005	aldehyde dehydrogenase 4 family, member A1, transcript variant P5CDhL, mRNA
BC009894.2	1	16	0.000862	3'-phosphoadenosine 5'-phosphosulfate synthase 2
BC011792.1	0	10	0.009224	clone MGC:19561 IMAGE:4300082
BC012783.2	0	9	0.016771	cDNA clone IMAGE:3949276
BC020962.1	0	14	0.0005	similar to glucosamine-6-sulfatases
BC021121.1	3	20	0.000177	mRNA, complete cds.
BC022098.1	0	9	0.016771	cDNA clone MGC:31944 IMAGE:4878869, complete cds

BC025345.1	2	19	0.00017	mRNA similar to LOC149651 (cDNA clone MGC:39393 IMAGE:4862156), complete cds
BC028040.1	4	20	0.001061	2',3'-cyclic nucleotide 3' phosphodiesterase, mRNA
BC029444.1	0	11	0.004855	cDNA clone MGC:32714 IMAGE:4692138, complete cds
BC030814.1	2	16	0.005343	immunoglobulin kappa variable 1-5, mRNA
BC030983.1	3	19	0.001099	immunoglobulin lambda constant 1 (Mcg marker), mRNA
BC030984.1	3	19	0.001099	cDNA clone MGC:32654 IMAGE:4701898, complete cds
BC031650.1	1	13	0.009495	clone MGC:35144 IMAGE:5169239
BC032452.1	3	17	0.010263	immunoglobulin lambda constant 1 (Mcg marker), mRNA
BC032485.1	3	17	0.010263	hypothetical protein FLJ30473
BC033178.1	5	20	0.005305	immunoglobulin heavy constant gamma 3 (G3m marker), mRNA
BC033856.1	4	19	0.005482	Similar to RIKEN cDNA 3110040D16 gene, cloneMGC:45395 IMAGE:5123380, mRNA, complete cds.
BC034141.1	2	17	0.002135	immunoglobulin kappa constant, mRNA
BC034247.1	0	9	0.016771	chromosome 9 open reading frame 105, mRNA
BC039814.1	1	14	0.004698	zinc finger protein 265, transcript variant 2, mRNA
BC044584.1	0	14	0.0005	DnaJ (Hsp40) homolog, subfamily C, member 4, mRNA
BC053664.1	1	12	0.017848	complete cds.
BC056256.1	2	15	0.011617	immunoglobulin kappa constant, mRNA
BC064367.1	0	15	0.0002	sterile alpha motif domain containing 6, mRNA
CTL2130	2	18	0.000701	proteinase-3
CTL2137	1	15	0.002128	La/SS-B
NM_001001550.1	2	18	0.003888	growth factor receptor-bound protein 10 (GRB10), transcript variant 3, mRNA
NM_001203.1	0	16	7.14E-05	bone morphogenetic protein receptor, type IB (BMPR1B), mRNA
NM_001258.1	0	11	0.004855	cyclin-dependent kinase 3 (CDK3), mRNA
NM_001280.1	3	18	0.003888	cold inducible RNA binding protein (CIRBP), mRNA
NM_001449.2	1	18	8.64E-05	four and a half LIM domains 1
NM_001894.2	0	10	0.009224	casein kinase 1, epsilon (CSNK1E)
NM_003582.1	1	15	0.002128	dual-specificity tyrosine-(Y)-phosphorylation regulated kinase 3 (DYRK3)
NM_003942.1	2	15	0.011617	ribosomal protein S6 kinase, 90kDa, polypeptide 4 (RPS6KA4)
NM_004073.2	0	14	0.0005	polo-like kinase 3 (Drosophila) (PLK3), mRNA
NM_004217.	1	16	0.000862	aurora kinase B (AURKB)

1				
NM_004497.1	0	10	0.009224	forkhead box A3 (FOXA3)
NM_004732.1	3	17	0.010263	potassium voltage-gated channel, shaker-related subfamily, beta member 3 (KCNAB3)
NM_004906.3	0	10	0.009224	Wilms tumor 1 associated protein (WTAP), transcript variant 1, mRNA
NM_006428.3	0	10	0.009224	mitochondrial ribosomal protein L28 (MRPL28), nuclear gene encoding mitochondrial protein, mRNA
NM_006869.1	0	19	1.81E-05	centaurin, alpha 1 (CENTA1), mRNA
NM_012241.2	0	14	0.0005	sirtuin (silent mating type information regulation 2 homolog) 5 (S. cerevisiae) (SIRT5), transcript variant 1, mRNA
NM_014481.2	2	16	0.005343	APEX nuclease (apurinic/apyrimidinic endonuclease) 2 (APEX2), nuclear gene encoding mitochondrial protein, mRNA
NM_016584.2	0	9	0.016771	interleukin 23, alpha subunit p19 (IL23A), mRNA
NM_017503.2	0	10	0.009224	surfeit 2 (SURF2), mRNA
NM_018047.1	0	13	0.001142	RNA binding motif protein 22 (RBM22), mRNA
NM_020381.2	2	15	0.011617	chromosome 6 open reading frame 210 (C6orf210), mRNA
NM_021117.1	0	9	0.016771	cryptochrome 2 (photolyase-like) (CRY2), mRNA
NM_021945.1	2	16	0.005343	hypothetical protein FLJ22174 (FLJ22174)
NM_024041.1	1	18	8.64E-05	sodium channel modifier 1
NM_052877.1	5	20	0.005305	mediator of RNA polymerase II transcription, subunit 8 homolog (yeast) (MED8)
NM_139240.2	0	10	0.009224	LOC92346 (LOC92346), mRNA
NM_152376.2	0	10	0.009224	UBX domain containing 3 (UBXD3), mRNA
NM_152697.2	0	14	0.004698	hypothetical protein , mRNA
NM_153215.1	4	18	0.016438	hypothetical protein FLJ38608 (FLJ38608), mRNA
NM_175907.3	1	17	0.000302	zinc binding alcohol dehydrogenase, domain containing 2 (ZADH2), mRNA

Example 5

[00167] This study utilized high-content protein microarrays comprised of more than 5,000 human proteins, including 25 known autoantigens, to evaluate

immunological profiles across panels of serum samples derived from healthy donors and Systemic Lupus Erythemasosus (SLE) patients.

[00168] The microarrays were designed to include more than 5,000 recombinant human proteins, purified under non-denaturing conditions from a insect cell expression system. Most of the protein features included an N-terminal GST tag to facilitate protein purification as well as quality control assays designed to validate protein immobilization on the microarrays. In addition, more than 25 known autoantigens were integrated with the array features. These included autoantigens designated by the ARA as diagnostic for SLE in combination with other clinical symptoms (Table 14a). The arrays were spotted using contact printing technology, in which proteins were deposited as adjacent duplicates arranged in 48 individual subarrays, with each subarray including control elements designed to facilitate data acquisition and serve as indicators of assay performance (Figure 1).

Table 14a. Annotated autoantigens included on the 5,000-protein microarray. Autoantigens consistent with the ARA diagnostic criteria are indicated.

Autoantigen	ARA Diagnostic
purified vimentin	
pyruvate dehydrogenase	
transglutaminase	
single stranded DNA	
double stranded DNA	X
unfractionated whole histone	
RNA polymerase (E. coli)	
cardiolipin	X
ribosomal RNA	X
Ro-52	X
Jo-1	
thyroglobulin	
Smith antigen (Sm)	X
RNP complex	X
histone H2a(f2a2)	
Centromere Protein B (CENP B)	
La/SS-B (La)	X
DNA Topoisomerase I (Scl-70; full length)	
U1-snRNP 68 Protein (68 kDa)	X
beta-2-glycoprotein 1	
myeloperoxidase	
proteinase-3	

ds plasmid DNA	X
myeloperoxidase	
proteinase-3	
Cyclic citruillinated peptide	

[00169] Three three statistical approaches were applied in parallel to identify more than 230 candidate biomarkers for SLE (Table 14b). Independent expression and purification of these putative autoantigens was carried out in order to develop custom protein microarrays for use in validation studies. A global ranking scheme was developed for the >230 candidate SLE biomarkers through the use of a scoring system in which proteins were assigned a point for each of the specified threshold criteria they met. The scoring metric factored in a number of statistical parameters including Z-factor, M-statistics p-value, Signal Used difference, and Signal Used ratio, with 18 of the proteins generating the maximum score (Table 15). (It should be noted that the 18 proteins present in Table 15 are included in Table 3.)

Table 14b. Candidate biomarkers tested for presence in SLE patients

Database ID	Database ID	Database ID	Database ID	Database ID
BC000381.2	BC017114.1	BC051762.1	NM_004214.3	NM_020239.2
BC000979.2	BC017344.1	BC051885.1	NM_004383.1	NM_020317.2
BC001120.1	BC018749.1	BC052806.1	NM_004578.2	NM_020661.1
BC001129.1	BC018929.1	BC055314.1	NM_004582.2	NM_020664.3
BC001396.1	BC020597.1	BC056256.1	NM_004596.1	NM_021146.2
BC001907.1	BC020647.1	BC063275.1	NM_004645.1	NM_021254.1
BC001917.1	BC020962.1	BC063479.1	NM_004656.2	NM_022777.1
BC002733.2	BC022098.1	BC067446.1	NM_004765.2	NM_022787.2
BC002880.1	BC022325.1	BC067735.1	NM_004881.1	NM_024041.1
BC003132.1	BC022362.1	BC068460.1	NM_005368.1	NM_024096.1
BC004271.1	BC022454.2	NM_000801.2	NM_005441.2	NM_024114.1
BC005248.1	BC023982.1	NM_000993.2	NM_005522.3	NM_024749.1
BC006192.1	BC024289.1	NM_001014.2	NM_005558.2	NM_024893.1
BC006376.1	BC024291.1	NM_001029.2	NM_005697.3	NM_025055.2
BC006793.1	BC025281.1	NM_001106.2	NM_006002.2	NM_031412.1
BC007581.1	BC025389.1	NM_001124.1	NM_006169.1	NM_031465.2
BC007872.1	BC025996.2	NM_001219.2	NM_006205.1	NM_031910.2
BC007888.1	BC027486.1	NM_001280.1	NM_006251.4	NM_032042.2
BC008623.1	BC027607.1	NM_001449.2	NM_006298.2	NM_032146.2
BC009623.1	BC028301.1	NM_001501.1	NM_006374.2	NM_032345.1
BC009696.1	BC028728.1	NM_001616.2	NM_006388.2	NM_032350.3
BC009762.2	BC029046.1	NM_001697.1	NM_006607.1	NM_032855.1
BC009873.1	BC029054.1	NM_001769.2	NM_007008.1	NM_033642.1

BC010947.1	BC029444.1	NM_001894.2	NM_007162.1	NM_052848.1
BC011379.1	BC030219.1	NM_001896.1	NM_007240.1	NM_054016.1
BC011668.1	BC030702.1	NM_001896.2	NM_012163.1	NM_138414.1
BC011811.1	BC031966.1	NM_002053.1	NM_013375.2	NM_138419.1
BC011842.2	BC032347.1	NM_002129.2	NM_014176.1	NM_138771.1
BC011885.1	BC032451.1	NM_002287.2	NM_014685.1	NM_144982.1
BC011888.1	BC032462.1	NM_002362.2	NM_015640.1	NM_145020.1
BC012120.1	BC032485.1	NM_002436.2	NM_015987.2	NM_145063.1
BC012575.1	BC032852.2	NM_002443.2	NM_016091.1	NM_145315.2
BC012576.1	BC033035.1	NM_002576.2	NM_016289.2	NM_145792.1
BC012783.2	BC033178.1	NM_002578.1	NM_016355.3	NM_148975.1
BC012924.1	BC033856.1	NM_002613.1	NM_016360.1	NM_152430.1
BC013073.1	BC034141.1	NM_002754.3	NM_016483.3	NM_152638.2
BC013567.1	BC034146.1	NM_002774.2	NM_016505.2	NM_152690.1
BC014244.1	BC034247.1	NM_003130.1	NM_017495.3	NM_152769.1
BC014452.1	BC038105.2	NM_003295.1	NM_017503.2	NM_153207.2
BC014949.1	BC038713.1	NM_003463.2	NM_017588.1	NM_153332.2
BC015008.1	BC040656.1	NM_003476.2	NM_017811.2	NM_173519.1
BC015497.1	BC041037.1	NM_003583.2	NM_017838.2	NM_175907.3
BC015833.1	BC041157.1	NM_003621.1	NM_017846.3	NM_175923.2
BC015904.1	BC042625.1	NM_003792.1	NM_018032.2	NM_177996.1
BC016380.1	BC042864.1	NM_003897.2	NM_018047.1	
BC016764.1	BC048125.1	NM_004089.1	NM_018129.1	
BC016842.1	BC050428.1	NM_004181.2	NM_018457.1	

Table 15. Candidate SLE biomarkers achieving the maximum score in a ranking metric applied to protein microarray data.

	Database ID	Description
1	NM_001106.2	activin A receptor, type IIB
2	BC038105.2	membrane protein, palmitoylated 7 (MAGUK p55 subfamily member 7)
3	BC055314.1	C2f protein
4	BC063275.1	eukaryotic translation initiation factor 2C, 1
5	NM_001616.2	activin A receptor, type II
6	NM_020317.2	hypothetical protein dJ465N24.2.1
7	BC042625.1	LUC7-like 2
8	NM_145020.1	hypothetical protein FLJ32743
9	BC009873.1	clone MGC:16442 IMAGE:3946787
10	NM_022787.2	nicotinamide nucleotide adenylyltransferase 1
11	BC025996.2	cDNA clone MGC:26787 IMAGE:4838986
12	NM_004596.1	small nuclear ribonucleoprotein polypeptide A
13	NM_018032.2	LUC7-like
14	BC012924.1	dual adaptor of phosphotyrosine and 3-phosphoinositides
15	BC022325.1	polyhomeotic like 3
16	NM_015640.1	PAI-1 mRNA-binding protein
17	NM_001014.2	ribosomal protein S10
18	NM_004765.2	B-cell CLL/lymphoma 7C

[00170] Luminex®-bead sets were prepared for validation studies using these 18 candidate SLE autoantigens. A validation rate of approximately 70% was observed across both microarray and Luminex X-MAP® technology platforms when the same set of disease and normal serum samples were used as probes. Improved discrimination between the two populations was observed when Principal Component Analysis was applied to data derived from 18 novel, protein microarray-defined proteins relative to autoantigens with annotated associated with SLE. Leave-one-out cross-validation analysis using support vector machine learning calculated a classification error rate of 3.3% for the array-defined candidate biomarkers, relative to an error rate of 13.3% calculated for the annotated SLE biomarkers. Taken together, this study provides the experimental and statistical framework to support the adoption of protein microarray technology as a tool for immunological profiling for disease biomarker discovery.

[00171] Diagnostic assays directed towards detection of the ARA-designated SLE autoantigens are typically performed at serum dilutions ranging from 1:10 – 1:100 to minimize false positive and false negative signals. Previous work on autoantigen arrays has suggested that this platform may be more sensitive, thus requiring a greater dilution factor to produce optimal signals and maximal dynamic range. To confirm this observation, a panel of 12 samples including serum from healthy individuals and SLE patients was evaluated on the high content human ProtoArray® at three dilutions: 1:150, 1:640, and 1:2560. Following the assays, high resolution images were obtained for each array and pixel intensity data was obtained corresponding to defined circular features and as well as local background. Histograms were generated for each sample representing the frequency with which background-subtracted signal intensity values were observed across the dynamic range. A representative signal distribution plot corresponding to one SLE sample is shown in Figure 2. The majority of signals across all three dilutions were observed below 10,000 Relative Fluorescence Units (RFU); however, a significant increase in the number of array features giving rise to signals above 5,000 RFU were observed at the 1:150 dilution relative to the two higher dilutions, suggesting that larger dilutions may increase the likelihood of false negatives in the assay. Although signals observed above 20,000 RFU were fewer in total across all dilutions tested, a

significantly greater number of array features gave rise to high intensity signals at the 1:150 dilution (Figure 2, right panel). Median pixel intensity values corresponding to local background were calculated for each array across the three dilutions tested, and average background values across all arrays were calculated. The maximum measurable signal on the scanner used in these assays is 65,000 RFU. The average background values across the three dilutions tested differed by less than 4-fold, suggesting a similar available dynamic range (Figure 2B). Based on these results, the 1:150 dilution was selected for use in profiling an expanded panel of serum samples. Twenty serum samples drawn from SLE patients, and ten sera drawn from healthy individuals were diluted 1:150 and profiled on the 5,000-protein microarrays. High resolution images were obtained on a fluorescent microarray scanner and pixel intensity data was captured through image analysis.

[00172] Three statistical approaches were applied to the data and the results of these analyses were compared. One of the methods employed in the analysis of the protein microarray data utilized M-statistics applied to quantile-normalized signal intensity data. This algorithm provides a count corresponding to the number of assays in one group for which a signal value for a specified protein is larger then the largest observed signal value for this protein in another group (Figure 3A, red ellipse). Subsequent calculations specify the number of arrays in one population with signals arising from this protein that are larger than the *second largest* signal in the other population (Figure 3A, violet ellipse), *third largest* etc., proceeding iteratively through the data set for all proteins on the array. The M "I" order statistic for the group y of size n_y compared to group x of size n_x is given by:

$$M^{y}_{i,above,between} = \sum_{k=1}^{n_y} 1_{\{y_k > x_{(i)} + between\}} 1_{\{y_k > above\}}$$

where $x_{(i)}$ is the i^{th} largest value of the group x, and above and between are the calculation parameters. The p-value is calculated as a probability of having an M value greater or equal then M_i. The M statistic with the lowest p-value was selected, and the corresponding p-value was used to establish a threshold for selection of significant biomarker candidates. A second method utilized to analyze the SLE autoantibody profiles was the 'volcano plot', in which non-normalized signal intensity data is arranged along dimensions of biological and statistical significance. The first

(horizontal) dimension represents the log-scale fold change between the two populations, and the second (vertical) axis represents the p-value for a t-test of differences between samples. The first axis indicates biological impact of the change; the second indicates the statistical evidence, or reliability of the change. The pixel intensity microarray data obtained from the SLE and healthy autoantibody profiling experiments was used in a volcano plot statistical approach in which p-Values were calculated using M-statistics. This analysis identified 48 proteins that resulted in a p-Value <0.05, and a $\log_2$ fold-change >1 (Figure 3B). It has been reported that p-Values computed using commonly used statistics including a two sample t-test, *U*- (Mann–Whitney) and *M*- statistics give rise to a largely similar rank order of array features. In the third analytical approach, a simple difference in background-subtracted signal values (Signal Used) was calculated from quantile-normalized signal intensity data, and candidate biomarkers exhibiting a difference greater than 1,500 RFU were selected for inclusion in subsequent validation studies. The overlap in candidate SLE biomarkers identified using these three statistical approaches is depicted in Figure 3C.

[00173] Array elements were spotted as adjacent duplicates in a 12-step, two-fold dilution series, and the resulting microarrays were probed with the original 30-sample panel, to evaluate the effectiveness of the different statistical approaches. Background-subtracted pixel intensity values were extracted from immune profiling experiments using these validation microarrays, and each array feature was subsequently classified as exhibiting elevated immune reactivity in either the SLE or the healthy population using M-statistics or volcano plot analysis as described above. Subsequent to this population assignment, array features were ranked by p-value or Signal Used difference. While a direct comparison of p-values was not possible because of the relatively small total number of features present on the validation microarrays, values calculated from the signal intensity data on these arrays were compared to the original high content array data to assess the reproducibility of immunoreactive signals. The number of proteins with a calculated p-value <0.01 or a Signal Used difference >1500 that were included on the validation arrays are indicated in Figure 4 (solid bars). P-values and Signal Used differences calculated from the validation array data were used to generate a rank order, and proteins ranking in the top 100 on the validation arrays, sorted by either metric, are

indicated with hatched bars. The percentage of proteins identified as significant in the original assays that are also in the top 100 on the custom arrays by either ranking statistic are indicated. The results of this analysis revealed a higher degree of validation between immunoreactivity observed on the original and validation microarrays for proteins eliciting an elevated immune response in the SLE population relative to the healthy population. The maximum validation rate in the SLE population was 72%, while the maximum validation rate observed in the healthy population was 58.6%. Additionally, proteins assigned to a population using M-statistics as the classification metric exhibited a higher degree of reproducibility relative to proteins assigned to a specific population using volcano analysis. The maximum validation rate observed for proteins classified by M-statistics was 72%, while the maximum validation rate observed for proteins classified by volcano analysis was only 40.8%. A global ranking scheme was developed for the list of candidate SLE biomarkers through the use of a scoring system in which proteins were assigned a point for each of the specified threshold criteria they met. The scoring metric factored in a number of statistical parameters including Z-factor, M-statistics p-value, Signal Used difference, and Signal Used ratio, with eighteen of the over 230 proteins generating the maximum score. Interestingly, 13 of these proteins were identified as SLE biomarkers by all three of the statistical approaches applied to the original data set, representing 50% of the proteins in the three-way zone of overlap (Figure 3C). Further, all of these 18 candidate autoantigens were defined as hits using M-statistics, while 16/18 (89%) and 13/18 (72%) of the 18 autoantigens were identified using Signal Used difference and volcano analysis respectively. Taken together, these results suggest that M-statistics provides a robust analytical approach for identification of an initial set of putative autoantigens from high content protein microarray data sets.

[00174] Principal Component Analysis (PCA) was used to qualitatively evaluate the separability of the two populations using either a panel of ten autoantigens that have been previously shown to be associated with SLE, or using the 18 candidate SLE biomarkers defined through the scoring analysis described above. The three-dimensional plots shown in Figure 5 represent the first three principal components, and suggest that the novel SLE biomarkers defined through this study result in

improved separation of the two populations relative to the separation achieved through Principal Component Analysis of the 10 literature-defined SLE antigens.

[00175] The results presented above demonstrated that the candidate biomarkers defined through the protein microarray assays exhibited reproducible reactivity when profiled on arrays comprised of proteins that were expressed and purified independently from those used in the original experiments. It was important, however, to validate the candidate biomarkers using an orthogonal technology. The Luminex® X-MAP technology was selected for these experiments as it is one of the few platforms that is suitable for carrying out multiplex assays in a clinical setting. A bead coupling strategy was utilized in which a goat anti-GST antibody was first conjugated to each bead region, enabling subsequent binding of the GST-tagged proteins. To evaluate the transfer of GST tagged proteins between beads post-coupling, purified GST was incubated with anti-GST-conjugated beads from one color region, and then mixed with anti-GST-conjugated beads from other color regions. As shown in Figure 6A, the migration of GST from one anti-GST-conjugated bead region to another was not observed at GST protein concentrations below 5 µg/ml. Luminex® beads corresponding to 18 unique color regions were conjugated to goat anti-GST antibodies as described above, and then incubated separately with 1 µg/ml of each of the 18 candidate SLE biomarkers identified through the scoring analysis applied to the protein microarray data. All protein-bound bead regions were then combined, and incubated in triplicate with a dilution series of each of the sera utilized in the original study, including 20 samples from SLE patients and 10 samples from a healthy control population. These assays yielded reproducible, concentration-dependent signals (Figure 6B). The relationship between the signals observed in the validation microarray assays and the signals observed in the Luminex assays were calculated using Pearson's correlation coefficient. In this experiment, signals for 13 of the 18 proteins (approximately 70%) yielded Pearson's Correlations >0.5 across all the study samples, similar to the rate of validation observed across the independent microarray experiments (Figure 6C). Notably, nine of these 13 proteins correspond to proteins were derived from the 3-way zone of overlap resulting from the parallel statistical analysis originally carried out on the high content arrays. These results confirm and extend the findings of the

autoimmune profiling carried out using protein microarrays by providing validation data using an unrelated technology platform.

Example 6

[00176] Invitrogen's proprietary ProtoArray® Prospector software includes a series of algorithms specifically designed to analyze data resulting from immune response profiling studies, with the goal of identifying proteins that can be used to statistically differentiate two populations. A general overview of the process, as well as a detailed explanation of the specific algorithms is provided below.

[00177] The general approach used in Immune Response Profiling data analysis employs a three-step process:

Single array analysis: For each protein on each array, a series of values is calculated including background subtracted signals, Z-Score, Z-Factor, CI-P value, and replicate spot coefficient of variation (see below for details regarding the CI-P value)

Group characterization: Signals for each individual protein across all samples from a given population are aligned for downstream analysis

Identify differences between treated and untreated sample populations: Utilizing M-statistics, proteins are identified for which the differential signals between two populations result in a significant p-value

CI-p-Value Calculation

[00178] The term CI-p-Value stands for Chebyshev's Inequality p-Value. The value is derived by testing the following hypothesis:

H_0: This spot comes from the Negative Control Distribution

H_a: This spot does not come from the Negative Control Distribution

[00179] In the effort to minimize assumptions about the negative control distribution, and hence the assumptions effects on the resulting p-values to test the given hypothesis, we utilize the Chebyshev's Inequality which states that if X is a random variable where $\mu = E(X)$ is the mean, $\sigma^2 = Var(X)$ is the variance where if k > 1 then,

$$P\left(\frac{|X-\mu|}{\sigma} \geq k\right) \leq \frac{1}{k^2}$$

[00180] This is an absolute bound on the probability under the null hypothesis (this means that under the null hypothesis this is the most conservative p-value estimate). Again under the null hypothesis we assume that the non-control spot comes from the negative control distribution where we will estimate the sample mean and sample standard deviation are estimated from the signals from the negative controls. Using this Inequality we calculate the,

$$\text{CI - p - Value} = \begin{cases} 1 & Y_k \leq \overline{X} + s \\ \left(\frac{s}{\left(Y_k - \overline{X}\right)}\right)^2 & Y_k > \overline{X} + s \end{cases}$$

where the mean and the standard deviation are from the observed signals in the Negative Control distribution. In this calculation Y represents the signal of the protein, s is the standard deviation of the negative controls, and k represents the kth protein, where Yk is the signal of the kth protein. Note that this is an upper bound on the true probability, since we are not making any assumptions of the distribution.

Group Designation and Characterization

[00181] The purpose of this step is to provide the Prospector software with sample identities for a specified group of assays (e.g., those from “normal” individuals) and align background-subtracted signals calculated for each of these assays into a single file. This function takes as an input single microarray results calculated with Prospector, aligns values from the ‘Signal Used’ columns of single array analysis result files and writes the resulting spreadsheet into a single result file. The output is a tab-delimited text file with name starting with “Group Characterization Results”, which may be opened in Microsoft Excel.

Group Comparison

[00182] The final set of algorithms compares two groups and identifies proteins which exhibit increased signal values in one group relative to another. M Statistics values are reported, which are described below. In addition, a p-value is calculated for each protein across a comparison that represents the probability that there is no signal increase in one group compared to another.

[00183] Analysis parameters include:

Quantile Normalization (default = on) – normalize signal values across assays being compared.

Signal must be larger than … RFUs (default is 500) – an additional parameter for M values calculation, which requires signal values to be over a specified background threshold;

Signal difference must be more then … RFUs (default is 200) – an additional parameter for M values calculation, which requires a specified gap between two signals to be considered significantly different.

[00184] Prospector reads specified group characterization files, completes calculations requested and writes resulting spreadsheet into a single result file. This tab-delimited text file, which may be opened in Microsoft Excel, contains a header detailing the analysis parameters applied. The result file contains a table with a list of probes with following columns of calculated values:

Group1 Count – The number of arrays in group 1 with signal larger than the cutoff

Group2 Count – The number of arrays in group 2 with signal larger than the cutoff

Group1 Prevalence - The estimated prevalence of the marker in group 1

Group2 Prevalence - The estimated prevalence of the marker in group 2

P-Value - The P-value for the most significant difference due to M statistic

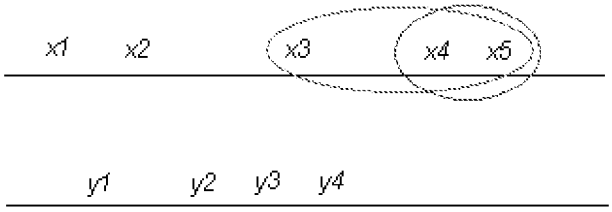
Cutoff - The cutoff signal for determining a "hit"

Normalized Signal Values – if normalization was selected, columns with normalized data (one per array) are appended to the right.

Calculations

M-Statistics

[00185] This algorithm provides a count corresponding to the number of assays in one group for which a signal value for a specified protein is larger then the largest observed signal value for this protein in another group (smaller ellipse). The software subsequently calculates the number of arrays in a specified group with signals arising from this protein that are larger then the *second largest* signal in another group (larger ellipse), *third largest* etc., proceeding iteratively through the data set for all ProtoArray® proteins.



[00186] The M "I" order statistic for the group y of size n_y compared to group x of size n_x is given by:

$$M^{y}_{i,above,between} = \sum_{k=1}^{n_y} 1_{\{y_k > x_{(i)} + between\}} 1_{\{y_k > above\}} \quad (1)$$

where $x_{(i)}$ is the i^{th} largest value of the group x, and above and between are the calculation parameters.

[00187] The p-value is calculated as a probability of having an M value greater or equal then M_i. Prospector selects the M statistic with the lowest p-value and reports this M_{max} value and order, as well as a corresponding p-value and prevalence estimate as described below.

[00188] Using a non-informative prior distribution for prevalence (i.e. assuming that the unknown prevalence of the marker is between 0 and 1) and acknowledging a binomial sampling scheme (i.e. that out of n arrays, the prevalence of the marker is

given by p, one observes X arrays that are turned on), prevalence may be estimated as

$$E(P) = \frac{M_{\max} + 1}{n_y + 2} . \qquad (2)$$

Quantile Normalization

[00189] Quantile normalization is a non-parametric procedure normalizing two or more one-channel datasets to a synthetic array. This method assumes that the distribution of signals is nearly the same in all samples. The largest signal for each array is replaced by a median value of the largest signals; the second largest signal is replaced by a median value of the second largest signals etc.

Definitions of Statistical Terms

[00190] Hypothesis Testing: Two mutually exclusive hypotheses are given, one is typically called the null hypothesis and the other is typically called the alternative hypothesis. Data is then collected to test the viability of the null hypothesis, and this data is used to determine if the null hypothesis is rejected or not.

[00191] Rejection Rule: This is a statistical method in which the observed data either rejects the null hypothesis or fails to reject the null hypothesis. It is important to note that this Rule will never "accept the null or alternative hypothesis"; it is exclusively a rule to reject. There are four possible outcomes to this approach, based on the true nature of the null hypothesis, and what is decided by the Rejection Rule. The four outcomes can be shown as:

	True Nature of H_0		
Decision by the Rejection Rule		**H_0 is True**	**H_0 is False**
	Reject H_0	Type I Error	Correct Decision
	Fail to Reject H_0	Correct Decision	Type II Error

[00192] Note that the true nature of H_0 is never really known. The actual formula for the Rejection Rule varies from hypothesis test to hypothesis test depending on the type of data, and the set of assumptions being made.

[00193] Type I Error: Typically, the probability of a Type I error is denoted as α. In general this is considered the most serious type of error to make.

[00194] Type II Error: Typically the probability of a Type II error is denoted as β. Though this is also an error, it is usually controlled by attempting to minimize the probability of Type I Error.

[00195] Precision: In a statistical terminology, precision is defined as the probability of not making a Type I Error. This can be considered as the probability of a true positive. Hence this is denoted as 1- α.

[00196] Power: In a statistical terminology, power is defined as the probability of not making a Type II Error. This can be considered the probability of a true negative. Hence this is denoted as 1- β.

[00197] Having now fully described the present invention in some detail by way of illustration and examples for purposes of clarity of understanding, it will be obvious to one of ordinary skill in the art that the same can be performed by modifying or changing the invention within a wide and equivalent range of conditions, formulations and other parameters without affecting the scope of the invention or any specific embodiment thereof, and that such modifications or changes are intended to be encompassed within the scope of the appended claims.

[00198] One of ordinary skill in the art will appreciate that starting materials, reagents, purification methods, materials, substrates, device elements, analytical methods, assay methods, mixtures and combinations of components other than those specifically exemplified can be employed in the practice of the invention without resort to undue experimentation. All art-known functional equivalents, of any such materials and methods are intended to be included in this invention. The terms and expressions which have been employed are used as terms of description and

not of limitation, and there is no intention that in the use of such terms and expressions of excluding any equivalents of the features shown and described or portions thereof, but it is recognized that various modifications are possible within the scope of the invention claimed. Thus, it should be understood that although the present invention has been specifically disclosed by preferred embodiments and optional features, modification and variation of the concepts herein disclosed may be resorted to by those skilled in the art, and that such modifications and variations are considered to be within the scope of this invention as defined by the appended claims.

[00199] As used herein, “comprising” is synonymous with "including," "containing," or "characterized by," and is inclusive or open-ended and does not exclude additional, unrecited elements or method steps. As used herein, "consisting of" excludes any element, step, or ingredient not specified in the claim element. As used herein, "consisting essentially of" does not exclude materials or steps that do not materially affect the basic and novel characteristics of the claim. In each instance herein any of the terms "comprising", "consisting essentially of" and "consisting of" may be replaced with either of the other two terms.

[00200] When a group of materials, compositions, components or compounds is disclosed herein, it is understood that all individual members of those groups and all subgroups thereof are disclosed separately. When a Markush group or other grouping is used herein, all individual members of the group and all combinations and subcombinations possible of the group are intended to be individually included in the disclosure. Every formulation or combination of components described or exemplified herein can be used to practice the invention, unless otherwise stated. Whenever a range is given in the specification, for example, a temperature range, a time range, or a composition range, all intermediate ranges and subranges, as well as all individual values included in the ranges given are intended to be included in the disclosure. In the disclosure and the claims, “and/or” means additionally or alternatively. Moreover, any use of a term in the singular also encompasses plural forms.

[00201] All references cited herein are hereby incorporated by reference in their entirety to the extent that there is no inconsistency with the disclosure of this specification. Some references provided herein are incorporated by reference to provide details concerning sources of starting materials, additional starting materials, additional reagents, additional methods of synthesis, additional methods of analysis, additional biological materials, additional nucleic acids, chemically modified nucleic acids, additional cells, and additional uses of the invention. All headings used herein are for convenience only. All patents and publications mentioned in the specification are indicative of the levels of skill of those skilled in the art to which the invention pertains, and are herein incorporated by reference to the same extent as if each individual publication, patent or patent application was specifically and individually indicated to be incorporated by reference. References cited herein are incorporated by reference herein in their entirety to indicate the state of the art as of their publication or filing date and it is intended that this information can be employed herein, if needed, to exclude specific embodiments that are in the prior art. For example, when composition of matter are claimed, it should be understood that compounds known and available in the art prior to Applicant's invention, including compounds for which an enabling disclosure is provided in the references cited herein, are not intended to be included in the composition of matter claims herein.

What is claimed is:

1. A method of detecting one or more target antibodies in a test sample of an individual suspected of having an autoimmune disease comprising:

a) contacting the test sample from the individual with one or more target antigens each comprising an autoantigen of Table 1 or a fragment thereof comprising an epitope recognized by a target antibody; and

b) detecting binding of one or more antibodies in the test sample to the one or more target antigens, thereby detecting the presence of the one or more target antibodies in the test sample.

2. The method of claim 1, wherein the one or more target antigens are immobilized on a solid support.

3. The method of claim 1, wherein the test sample is contacted with two or more target antigens of Table 1 or fragments thereof comprising an epitope.

4. The method of claim 1, wherein the test sample is contacted with twenty or more target antigens of Table 1 or fragments thereof comprising an epitope.

5. The method of claim 1, wherein the test sample is contacted with fifty or more target antigens of Table 1 or fragments thereof comprising an epitope.

6. The method of claim 1, wherein the test sample is contacted with a hundred or more target antigens of Table 1 or fragments thereof comprising an epitope.

7. The method of claim 1, wherein the test sample is contacted with all of the target antigens of Table 1 or fragments thereof comprising an epitope.

8. The method of claim 1, wherein the test sample comprises cells, tissue, or a bodily fluid from the individual.

9. The method of claim 1, wherein the test sample comprises blood, serum, plasma, synovial fluid, cerebrospinal fluid, cell lysates or saliva from the individual.

10. The method of claim 1, further comprising detecting the amount of the one or more antibodies bound to the one or more target antigens in the test sample.

11. The method of claim 1, wherein binding of the one or more target antigens to one or more antibodies in the test sample is determined using an immunoassay.

12. The method of claim 1, wherein at least ten of the one or more target antigens are bound by the one or more antibodies from the test sample.

13. The method of claim 1, wherein at least twenty of the one or more target antigens are bound by the one or more antibodies from the test sample.

14. The method of claim 1, wherein at least fifty of the one or more target antigens are bound by the one or more antibodies from the test sample.

15. A method of diagnosing rheumatoid arthritis in an individual comprising:

a) contacting a test sample from the individual with one or more target antigens, each comprising an autoantigen of Table 2 or a fragment thereof comprising an epitope; and

b) detecting binding of the one or more target antigens to one or more antibodies in the test sample, wherein the presence of the one or more antibodies bound against the one or more target antigens is indicative of rheumatoid arthritis.

16. The method of claim 15, wherein the one or more target antigens are immobilized on a solid support.

17. The method of claim 15, wherein the test sample is contacted with two or more target antigens of Table 2 or fragments thereof comprising an epitope.

18. The method of claim 15, wherein the test sample is contacted with ten or more target antigens of Table 2 or fragments thereof comprising an epitope.

19. The method of claim 15, wherein the test sample is contacted with twenty or more target antigens of Table 2 or fragments thereof comprising an epitope.

20. The method of claim 15, wherein the test sample is contacted with all of the target antigens of Table 2 or fragments thereof comprising an epitope.

21. The method of claim 15, wherein the test sample is a serum sample.

22. The method of claim 15, wherein at least ten of the one or more target antigens are bound by the one or more antibodies from the test sample.

23. The method of claim 15, wherein at least twenty of the one or more target antigens are bound by the one or more antibodies from the test sample.

24. The method of claim 15, wherein the one or more target antigens comprises leukocyte receptor cluster member 12.

25. A method of diagnosing systemic lupus erythematosus in an individual comprising:

a) contacting a test sample from the individual with one or more target antigens, each comprising an autoantigen of Table 3 or fragments thereof comprising an epitope; and

b) detecting binding of the one or more target antigens to one or more antibodies in the test sample, wherein the presence of the one or more antibodies bound against the one or more target antigens is indicative of systemic lupus erythematosus.

26. The method of claim 25, wherein the one or more target antigens are immobilized on a solid support.

27. The method of claim 25, wherein the test sample is contacted with two or more target antigens of Table 3 or fragments thereof comprising an epitope.

28. The method of claim 25, wherein the test sample is contacted with twenty or more target antigens of Table 3 or fragments thereof comprising an epitope.

29. The method of claim 25, wherein the test sample is contacted with fifty or more target antigens of Table 3 or fragments thereof comprising an epitope.

30. The method of claim 25, wherein the test sample is contacted with all of the target antigens of Table 3 or fragments thereof comprising an epitope.

31. The method of claim 25, wherein the test sample is a serum sample.

32. The method of claim 25, wherein at least ten of the one or more target antigens are bound by the one or more antibodies from the test sample.

33. The method of claim 25, wherein at least twenty of the one or more target antigens are bound by the one or more antibodies from the test sample.

34. The method of claim 25, wherein the test sample is contacted with one or more target antigens, each comprising an autoantigen of Table 4 or fragments thereof.

35. A method of diagnosing anti-neutrophil cytoplasmic antibody associated diseases in an individual comprising:

a) contacting a test sample from the individual with one or more target antigens, each comprising an autoantigen of Table 5 or fragments thereof comprising an epitope; and

b) detecting binding of the one or more target antigens to one or more antibodies in the test sample, wherein the presence of the one or more antibodies bound against the one or more target antigens is indicative of anti-neutrophil cytoplasmic antibody associated diseases.

36. The method of claim 35, wherein the one or more target antigens are immobilized on a solid support.

37. The method of claim 35, wherein the test sample is contacted with two or more target antigens of Table 5 or fragments thereof comprising an epitope.

38. The method of claim 35, wherein the test sample is contacted with twenty or more target antigens of Table 5 or fragments thereof comprising an epitope.

39. The method of claim 35, wherein the test sample is contacted with fifty or more target antigens of Table 5 or fragments thereof comprising an epitope.

40. The method of claim 35, wherein the test sample is contacted with all of the target antigens of Table 5 or fragments thereof comprising an epitope.

41. The method of claim 35, wherein the test sample is a serum sample.

42. The method of claim 35, wherein at least ten of the one or more target antigens are bound by the one or more antibodies from the test sample.

43. The method of claim 25, wherein at least twenty of the one or more target antigens are bound by the one or more antibodies from the test sample.

44. The method of claim 35, wherein the test sample is contacted with one or more target antigens, each comprising an autoantigen of Table 6 or fragments thereof.

45. A method of monitoring one or more target antibodies in test samples from an individual diagnosed as having an autoimmune disease comprising:

a) contacting a first test sample from the individual with a first set of one or more target antigens;

b) detecting binding of one or more antibodies in the test sample to the one or more target antigens, thereby detecting the presence of the one or more target antibodies in the first test sample;

c) contacting a second test sample from the individual with a second set of the one or more target antigens;

d) detecting binding of one or more antibodies in the test sample to the one or more target antigens, thereby detecting the presence of the one or more target antibodies in the second test sample; and

e) comparing the presence of the one or more antibodies from the first test sample with the presence of the one or more antibodies from the second test sample, wherein each of the one or more target antigens comprises an autoantigen of Table 1 or fragments thereof comprising an epitope.

46. The method of claim 45, wherein the second test sample is taken from the individual at a later time than the first test sample.

47. The method of claim 45, further comprising the steps:

a) detecting the amount of the one or more antibodies bound to the one or more target antigens in the first test sample and the second test sample; and

b) comparing the amount of bound antibodies from the first test sample with the amount of bound antibodies from the second test sample.

48. The method of claim 45, wherein each of the one or more target antigens comprises an autoantigen of Table 2 or fragments thereof comprising an epitope.

49. The method of claim 45, wherein each of the one or more target antigens comprises an autoantigen of Table 3 or fragments thereof comprising an epitope.

50. The method of claim 45, wherein each of the one or more target antigens comprises an autoantigen of Table 5 or fragments thereof comprising an epitope.

51. A method of monitoring one or more target antibodies in test samples from an individual receiving treatment for an autoimmune disease comprising:

a) contacting a first test sample from an individual with a first set of one or more target antigens;

b) detecting binding of one or more antibodies in the first test sample to the one or more target antigens, thereby detecting the presence of the one or more target antibodies in the first test sample;

c) administering a treatment for the autoimmune disease to the individual;

d) after the administration of the treatment, contacting a second test sample from the individual with a second set of the one or more target antigens;

e) detecting binding of one or more antibodies in the second test sample to the one or more target antigens, thereby detecting the presence of the one or more target antibodies in the first second sample; and

f) comparing the presence of the one or more antibodies from the first sample with the presence of the one or more antibodies from the second sample, wherein each of the one or more target antigens comprises an autoantigen of Table 1 or fragments thereof comprising an epitope.

52. The method of claim 52, wherein the autoimmune disease is rheumatoid arthritis.

53. The method of claim 52, wherein each of the one or more target antigens comprises an autoantigen of Table 2 or fragments thereof comprising an epitope.

54. The method of claim 52, wherein the treatment comprises administering a drug to the individual.

55. The method of claim 54, wherein the drug is infilximab.

56. The method of claim 52, wherein the treatment is continuous.

57. The method of claim 52, wherein the first test sample is taken from the individual prior to any treatment being administered to the individual.

58. The method of claim 52, further comprising contacting one or more subsequent test samples from the individual with an additional set of the one or more target antigens;

e) detecting binding of one or more antibodies in the one or more subsequent test samples to the one or more target antigens, thereby detecting the presence of the one or more target antibodies in the subsequent test samples; and

f) comparing the presence of the one or more antibodies from the subsequent test samples with the presence of one or more antibodies from the first

and second sample, wherein each of the one or more target antigens comprises an autoantigen of Table 1 or fragments thereof comprising an epitope.

59. The method of claim 52, further comprising:

a) detecting the amount of the one or more antibodies bound to the one or more target antigens in the first test sample and the second test sample; and

b) comparing the amount of bound antibodies from the first test sample with the amount of bound antibodies from the second test sample.

60. A kit for diagnosing an autoimmune disease comprising:

a) one or more target antigens each comprising an autoantigen of Table 1 or a fragment thereof comprising an epitope; and

b) means for detecting binding of one or more molecules in a test sample to the one or more target antigens.

61. The kit of claim 60, further comprising a control antibody against one or more of the target antigens.

62. The kit of claim 60, wherein the kit comprises two or more target antigens.

63. The kit of claim 60, wherein the kit comprises twenty or more target antigens.

64. The kit of claim 60, wherein the kit comprises fifty or more target antigens.

65. The kit of claim 60, wherein each of the one or more target antigens comprises an autoantigen of Table 2 or fragments thereof comprising an epitope.

66. The kit of claim 60, wherein each of the one or more target antigens comprises an autoantigen of Table 3 or fragments thereof comprising an epitope.

67. The kit of claim 60, wherein each of the one or more target antigens comprises an autoantigen of Table 5 or fragments thereof comprising an epitope.

68. The kit of claim 60, wherein the one or more target antigens are immobilized on a solid support.

69. The kit of claim 60, wherein the one or more target antigens are part of a high density protein array.

70. The kit of claim 60, wherein the one or more target antigens are immobilized on a plurality of solid supports.

71. The kit of claim 70, wherein the solid supports are flat surfaces or beads.

72. The kit of claim 60, wherein the kit comprises less than 1,000 polypeptides.

73. The kit of claim 60, wherein the kit comprises less than 100 polypeptides.

74. The kit of claim 60, wherein at least 75% of the polypeptides are autoantigens of Table 1 or a fragment thereof comprising an epitope.

75. The kit of claim 60, wherein at least 90% of the polypeptides are autoantigens of Table 1 or a fragment thereof comprising an epitope.

76. A mixture comprising:

a) one or more target antigens each comprising an autoantigen of Table 1 or a fragment thereof comprising an epitope; and

b) a test sample from an individual suspected of having an autoimmune disease.

77. The mixture of claim 76, further comprising a control antibody against one or more of the target antigens.

78. The mixture of claim 76, further comprising two or more target antigens of Table 1 or fragments thereof comprising an epitope.

79. The mixture of claim 76, further comprising twenty or more target antigens of Table 1 or fragments thereof comprising an epitope.

80. The mixture of claim 76, further comprising fifty or more target antigens of Table 1 or fragments thereof comprising an epitope.

81. The mixture of claim 76, further comprising one hundred or more target antigens of Table 1 or fragments thereof comprising an epitope.

82. The mixture of claim 76, further comprising all of the target antigens of Table 1 or fragments thereof comprising an epitope.

83. The mixture of claim 76, wherein the test sample comprises cells, tissue, or a bodily fluid from the individual.

84. The mixture of claim 76, wherein one or more antibodies of the test sample are bound to one or more of the target antigens.

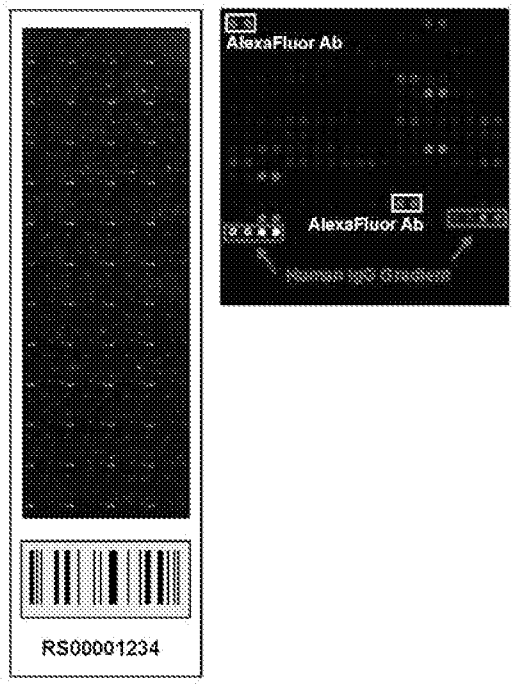


Figure 1

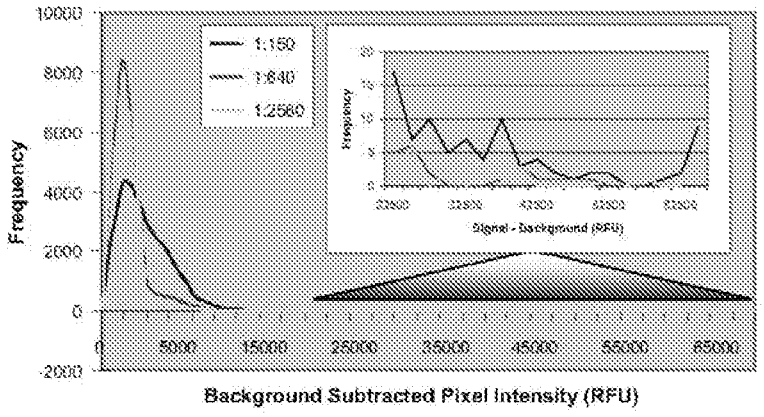


Figure 2A

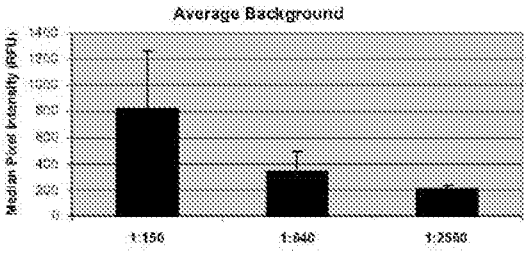


Figure 2B

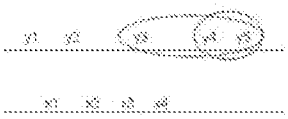


Figure 3A

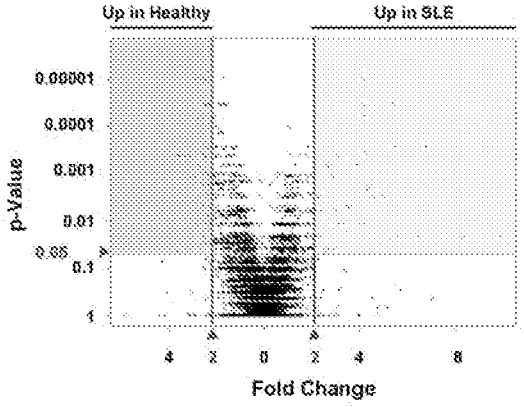


Figure 3C

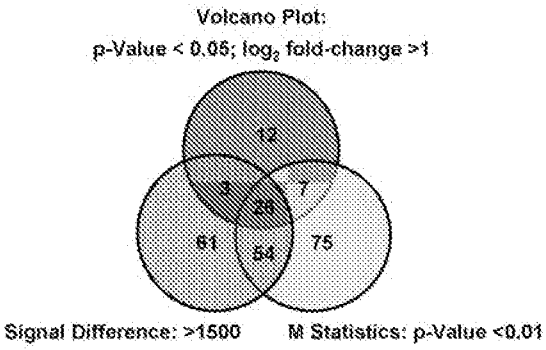


Figure 3B

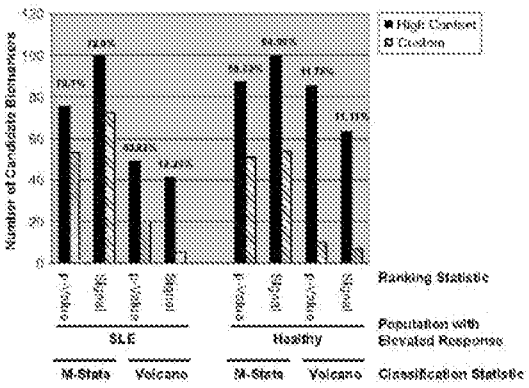

Number of Candidate Biomarkers
High Content
Custom
Ranking Statistic
SLE
Healthy
Population with Elevated Response
M-Stats
Volcano
M-Stats
Volcano
Classification Statistic

Figure 4

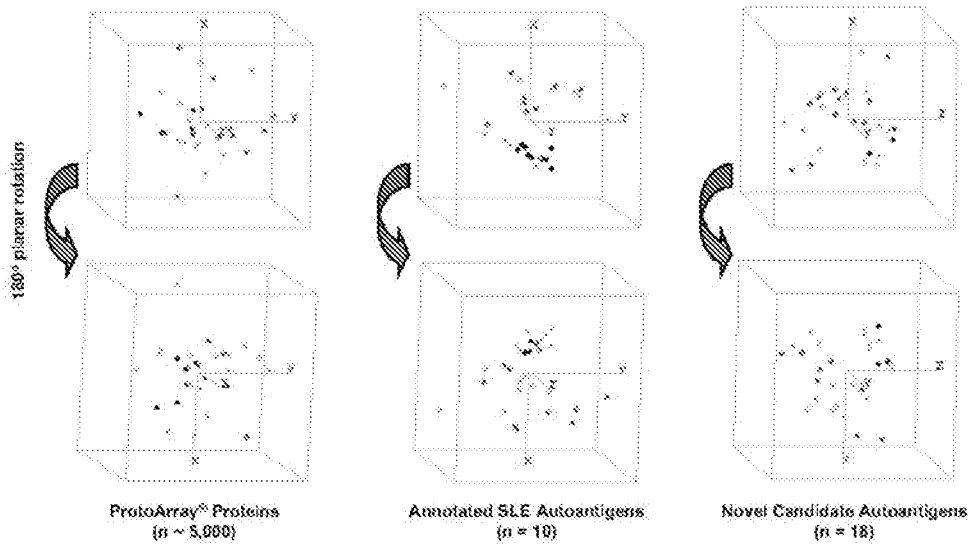

180° planar rotation
ProtoArray® Proteins
(n ~ 5,000)
Annotated SLE Autoantigens
(n = 10)
Novel Candidate Autoantigens
(n = 18)

Figure 5

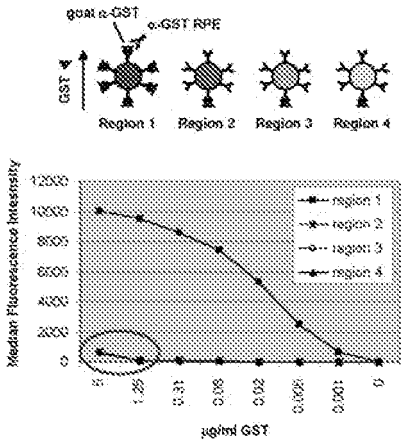


Figure 6A

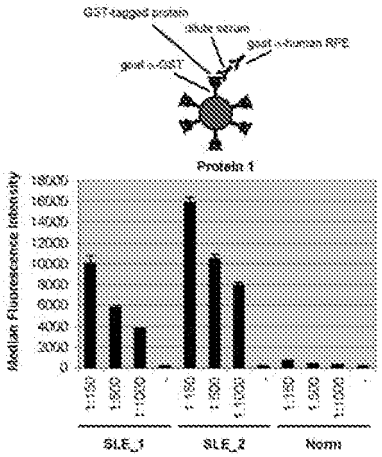


Figure 6B

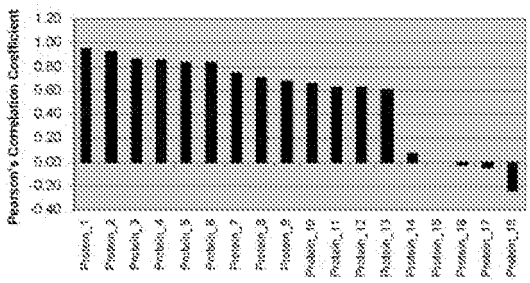


Figure 6C

专利名称(译)	自身免疫疾病生物标志物		
公开(公告)号	EP2089712A4	公开(公告)日	2010-09-22
申请号	EP2007868834	申请日	2007-11-21
[标]申请(专利权)人(译)	生命技术公司		
申请(专利权)人(译)	Life Technologies公司		
当前申请(专利权)人(译)	Life Technologies公司		
[标]发明人	MATTOON DAWN R SCHWEITZER BARRY ALCORTA DAVID PATEL DHAVEL FALK RONALD		
发明人	MATTOON, DAWN R. SCHWEITZER, BARRY ALCORTA, DAVID PATEL, DHAVEL FALK, RONALD		
IPC分类号	G01N33/53 G01N33/564		
CPC分类号	A61P19/02 A61P29/00 A61P37/06 G01N33/564 G01N2800/102 G01N2800/104		
优先权	60/867022 2006-11-22 US		
其他公开文献	EP2089712A2		
外部链接	Espacenet		

摘要(译)

本文提供了用于诊断自身免疫性疾病的新型生物标志物，以及用于检测怀疑患有自身免疫性疾病的个体样品中这些生物标志物的方法和试剂盒。 还提供了监测自身免疫疾病进展的方法和监测自身免疫疾病治疗的功效和副作用的方法。