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(54) **RAPID EXTRACELLULAR ANTIBODY PROFILING (REAP) FOR THE DISCOVERY AND USE OF SAID ANTIBODIES**

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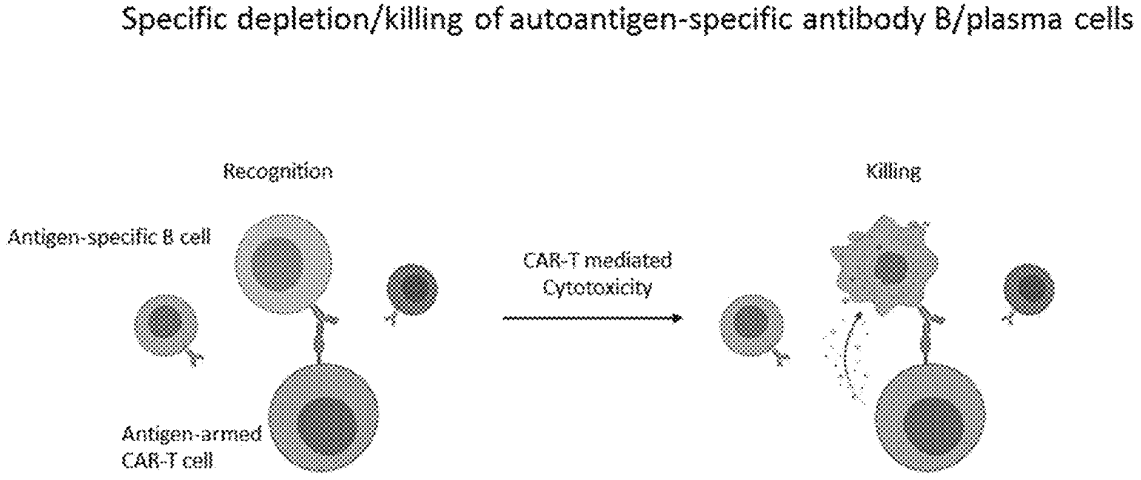
CPC ***C12N 15/1037*** (2013.01); ***C12N 15/1065*** (2013.01)

(57) **ABSTRACT**

The present invention relates to methods for a sensitive and high-throughput detection of various antibodies and targets thereof. For example, in one aspect, methods of the present invention can successfully detect autoantibodies against extracellular and secreted proteins. In various embodiments, the present invention provides methods of diagnosing, assessing prognosis, preventing, and treating diseases or disorders associated with antibodies or targets thereof detected via the high-throughput detection methods of the present invention.

Specification includes a Sequence Listing.



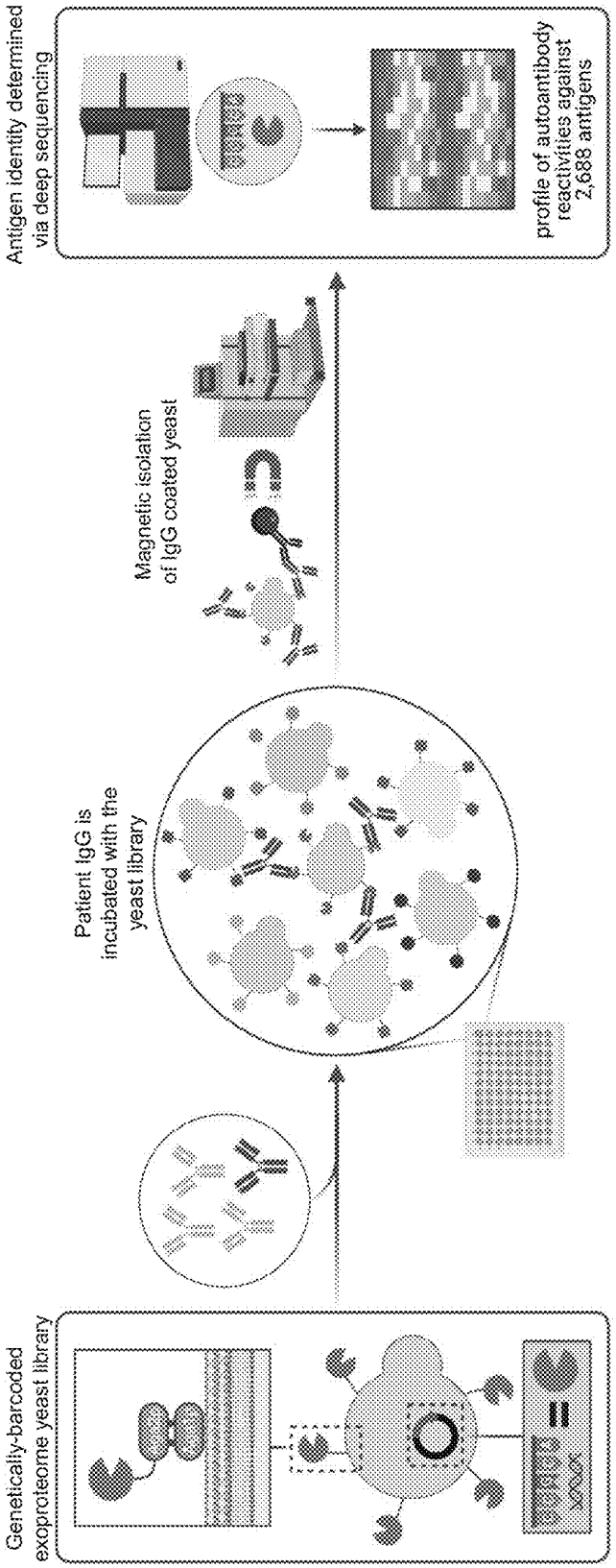

Genetically-barcoded exoproteome yeast library
Patient IgG is incubated with the yeast library
Magnetic isolation of IgG coated yeast
Antigen identity determined via deep sequencing
profile of autoantibody reactivities against 2,688 antigens

Figure 1

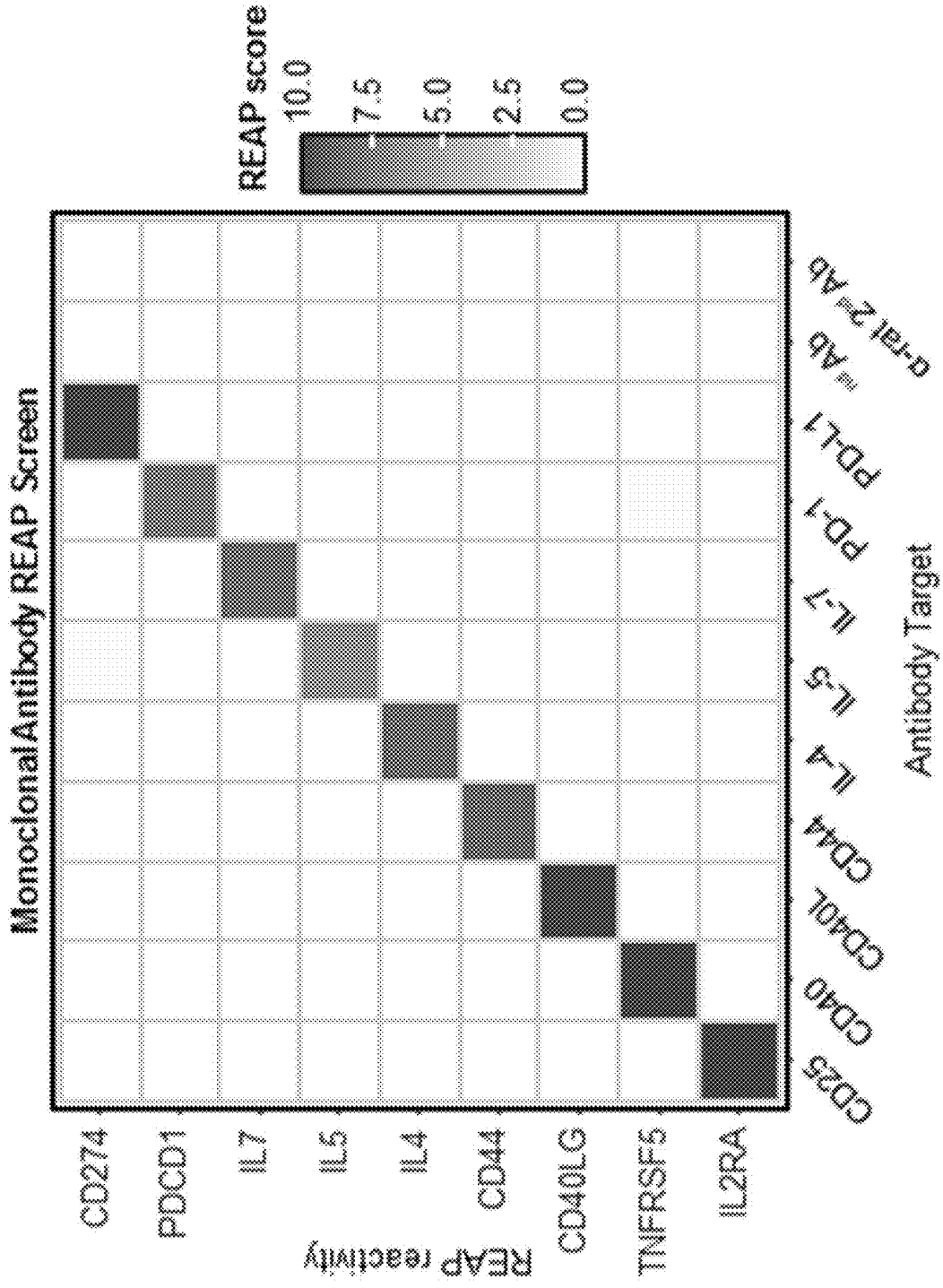

Monoclonal Antibody REAP Screen
REAP score
10.0
7.5
5.0
2.5
0.0
REAP reactivity
CD274
PDCD1
IL7
IL5
IL4
CD44
CD40LG
TNFRSF5
IL2RA
CD25
CD40
CD40L
CD44
IL4
IL5
IL7
PD-1
PD-L1
α-rat 2° Ab
Antibody Target

Figure 2A

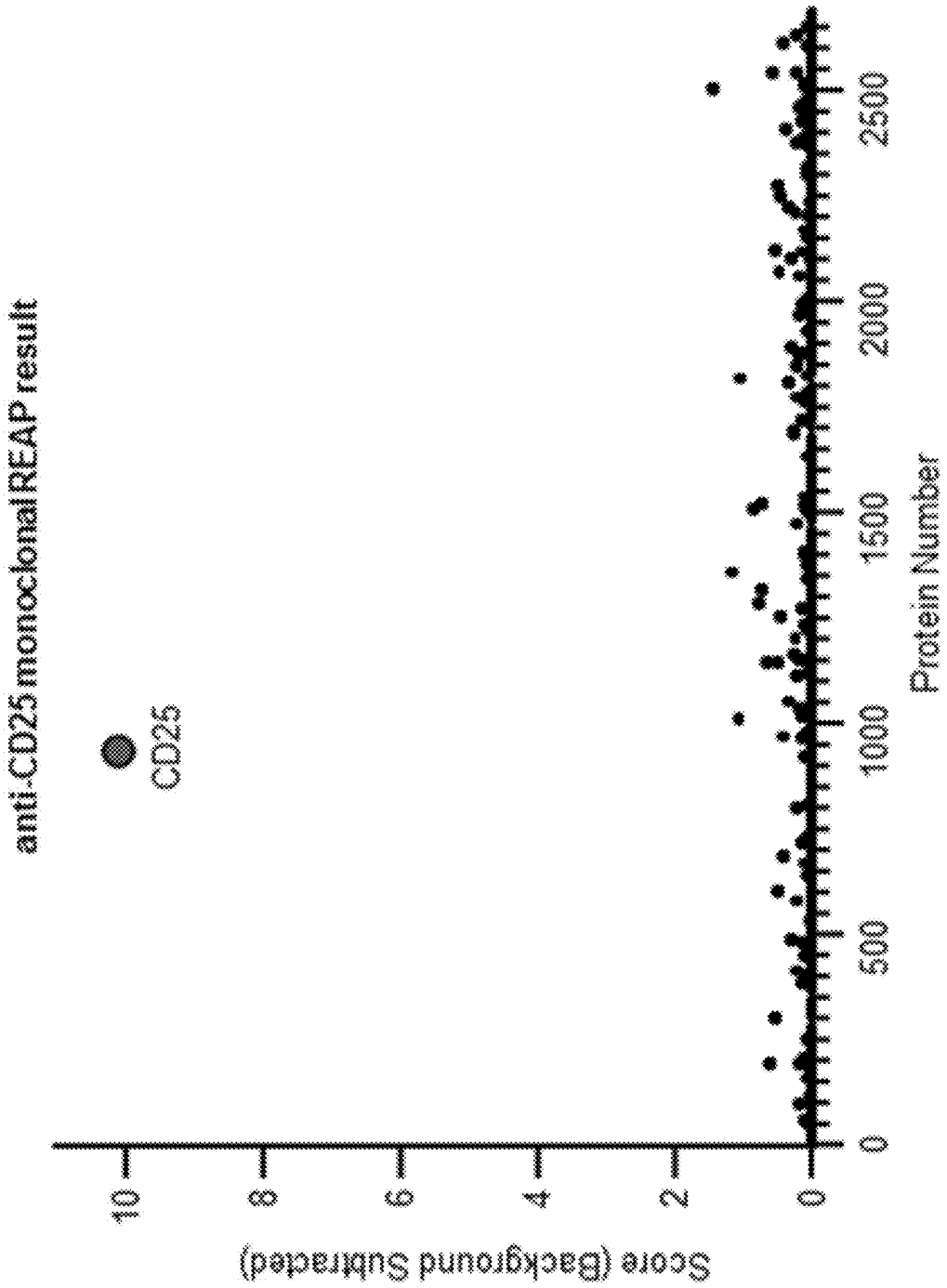
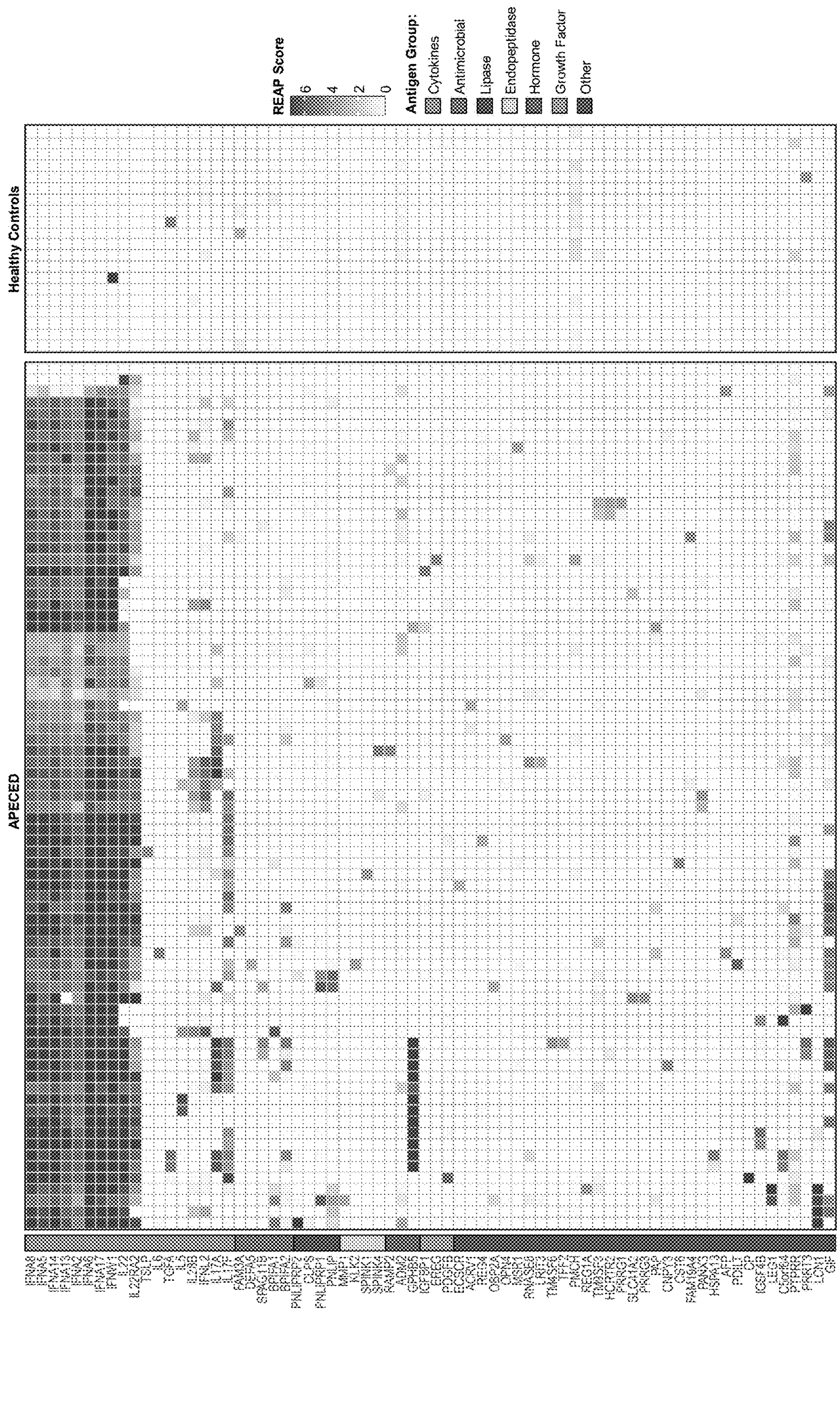

anti-CD25 monoclonal REAP result
CD25
Score (Background Subtracted)
0
2
4
6
8
10
0
500
1000
1500
2000
2500
Protein Number

Figure 2B



APECED
Healthy Controls
REAP Score
6
4
2
0
Antigen Group:
Cytokines
Antimicrobial
Lipase
Endopeptidase
Hormone
Growth Factor
Other

Figure 3

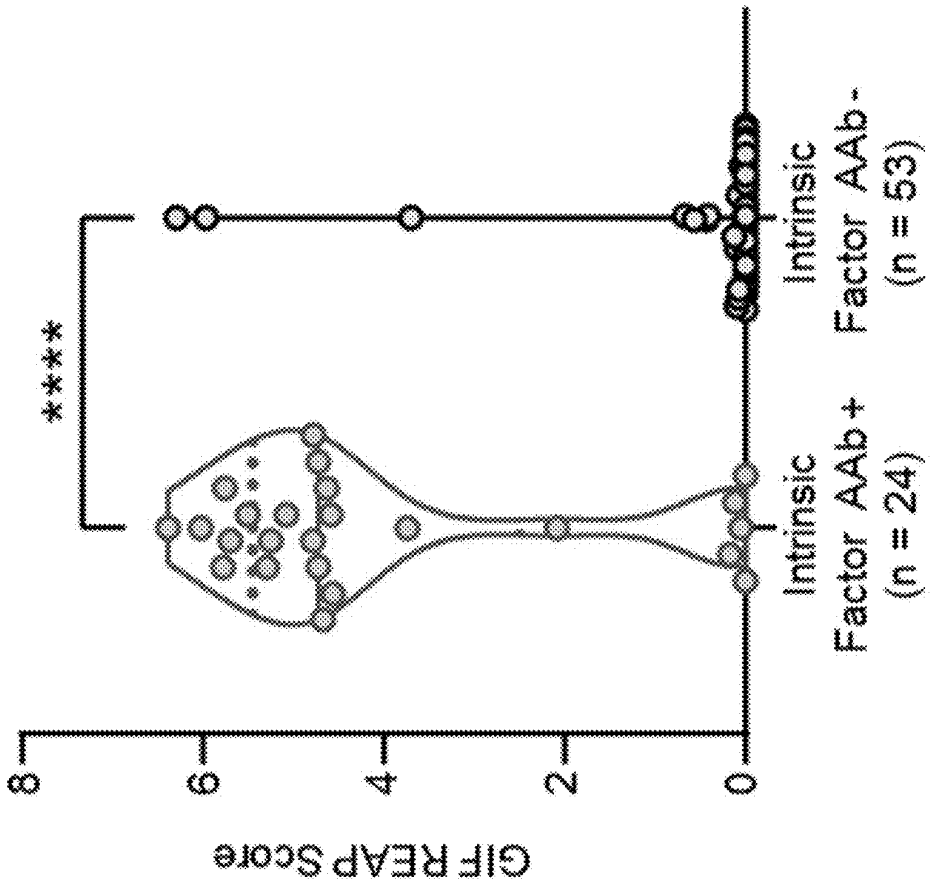

GIF REAP Score
0
2
4
6
8
****
Intrinsic Factor AAb+ (n = 24)
Intrinsic Factor AAb- (n = 53)

Figure 4

Figure 5A

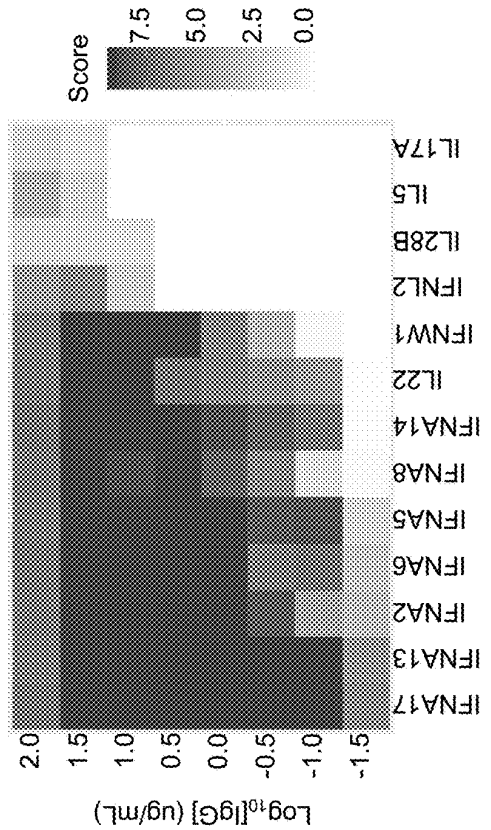


Figure 5B

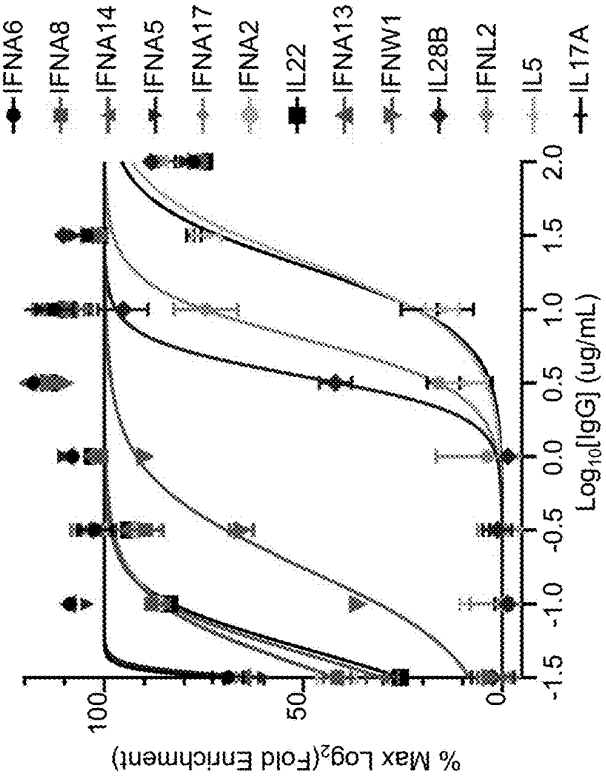


Figure 5

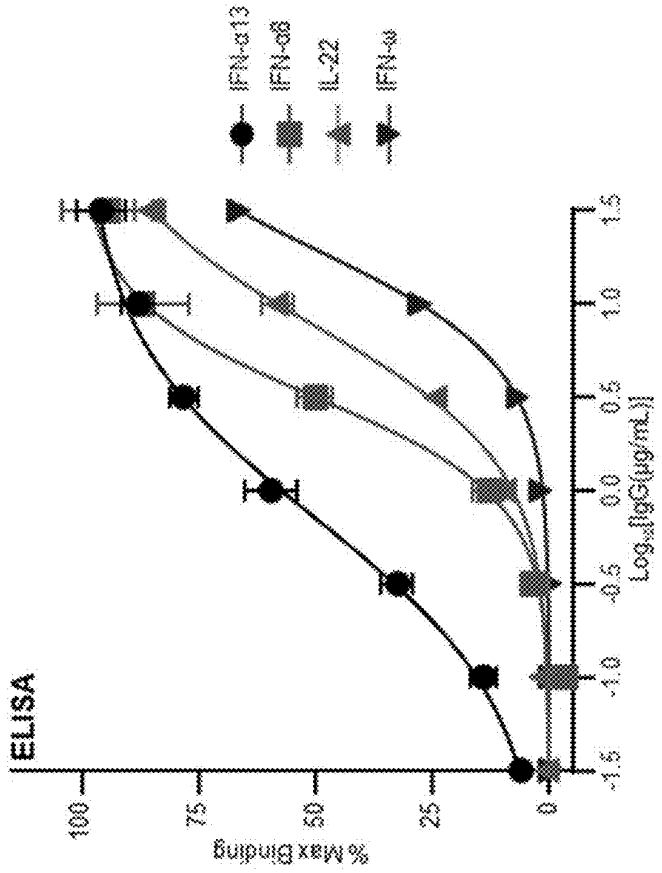


Figure 6B

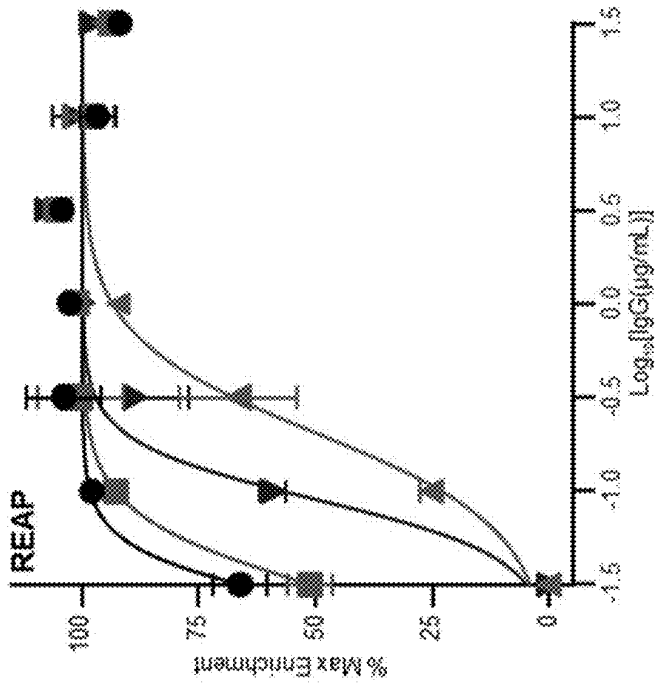


Figure 6A

Figure 6

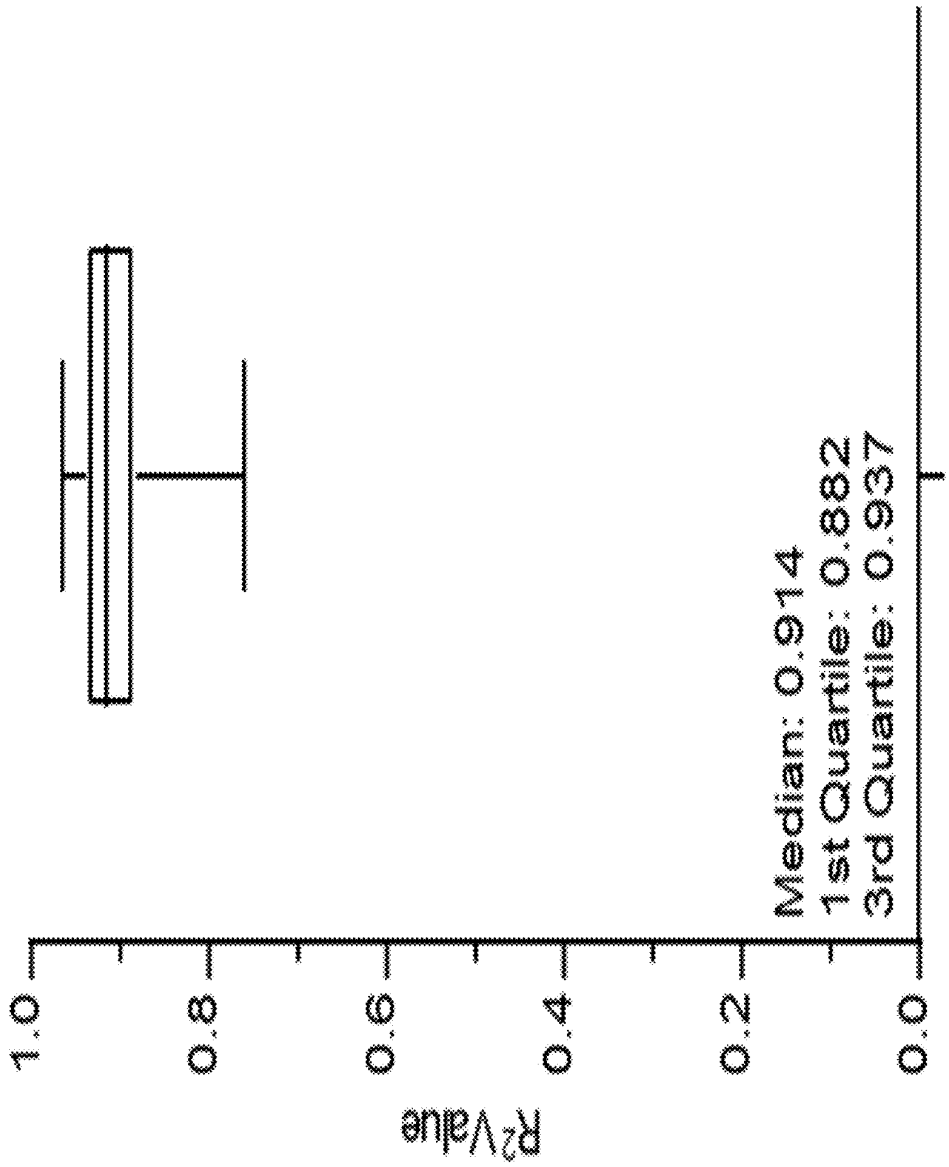

R²Value
1.0
0.8
0.6
0.4
0.2
0.0
Median: 0.914
1st Quartile: 0.882
3rd Quartile: 0.937
n = 77

Figure 7

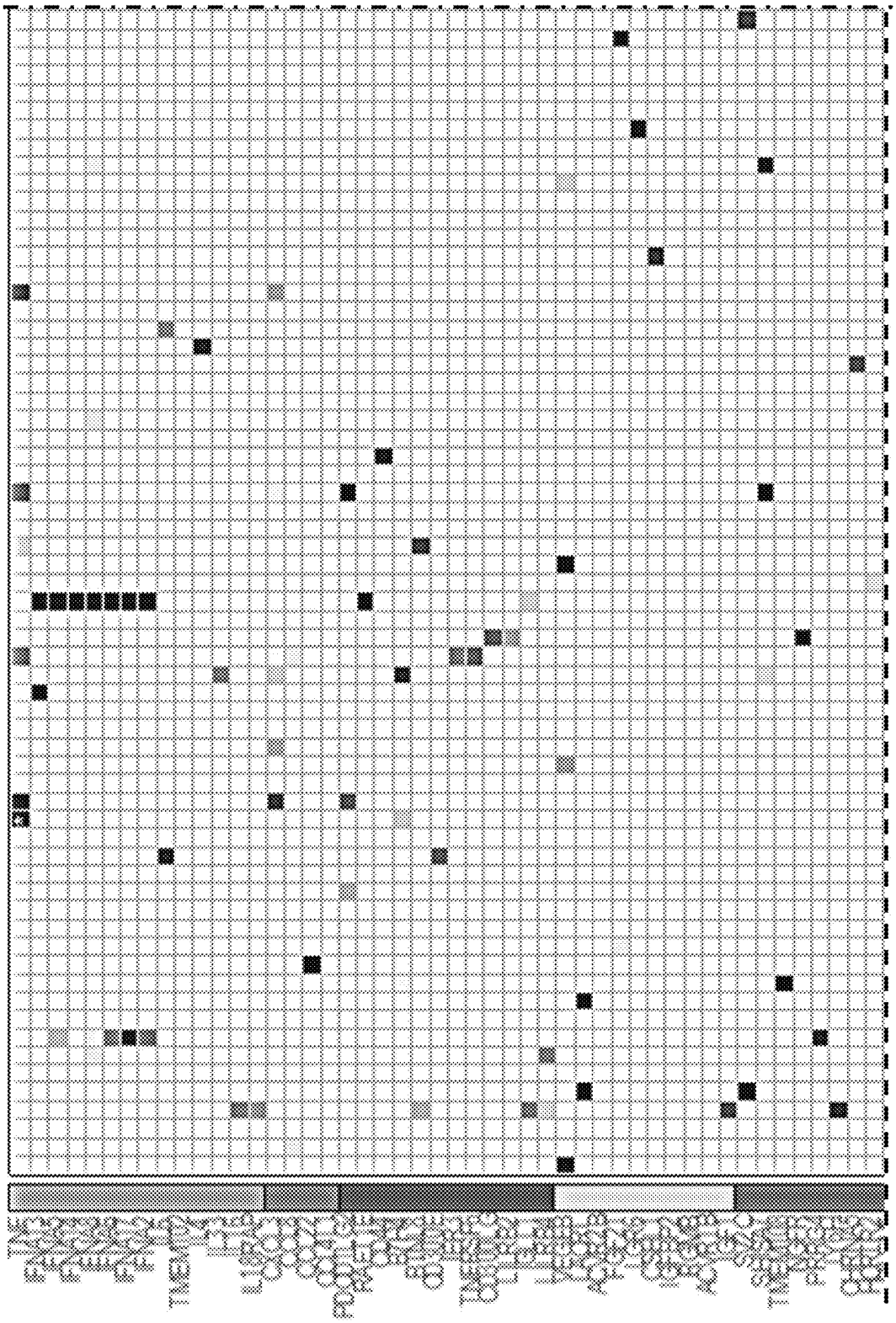


Figure 8

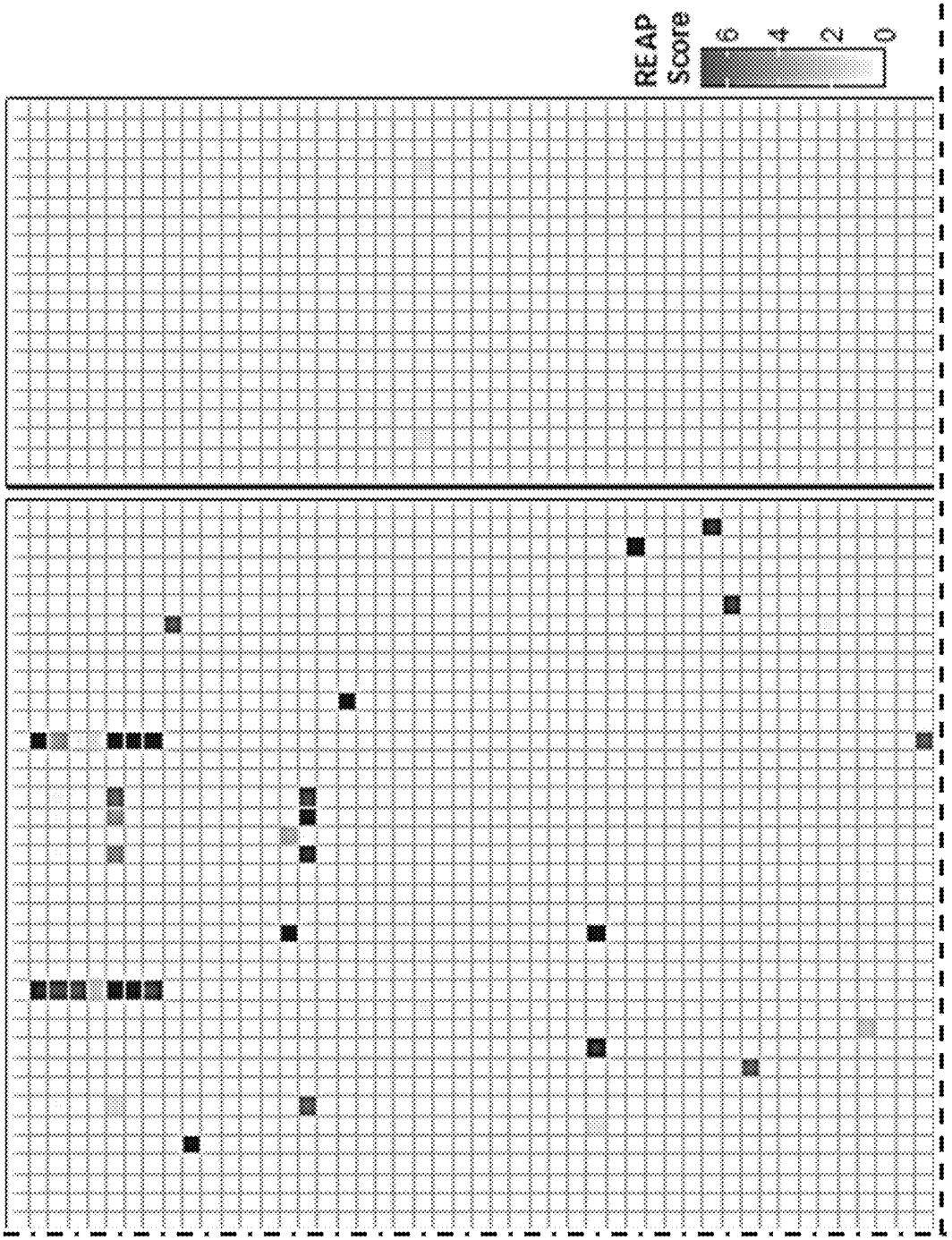


Figure 8 (cont.)

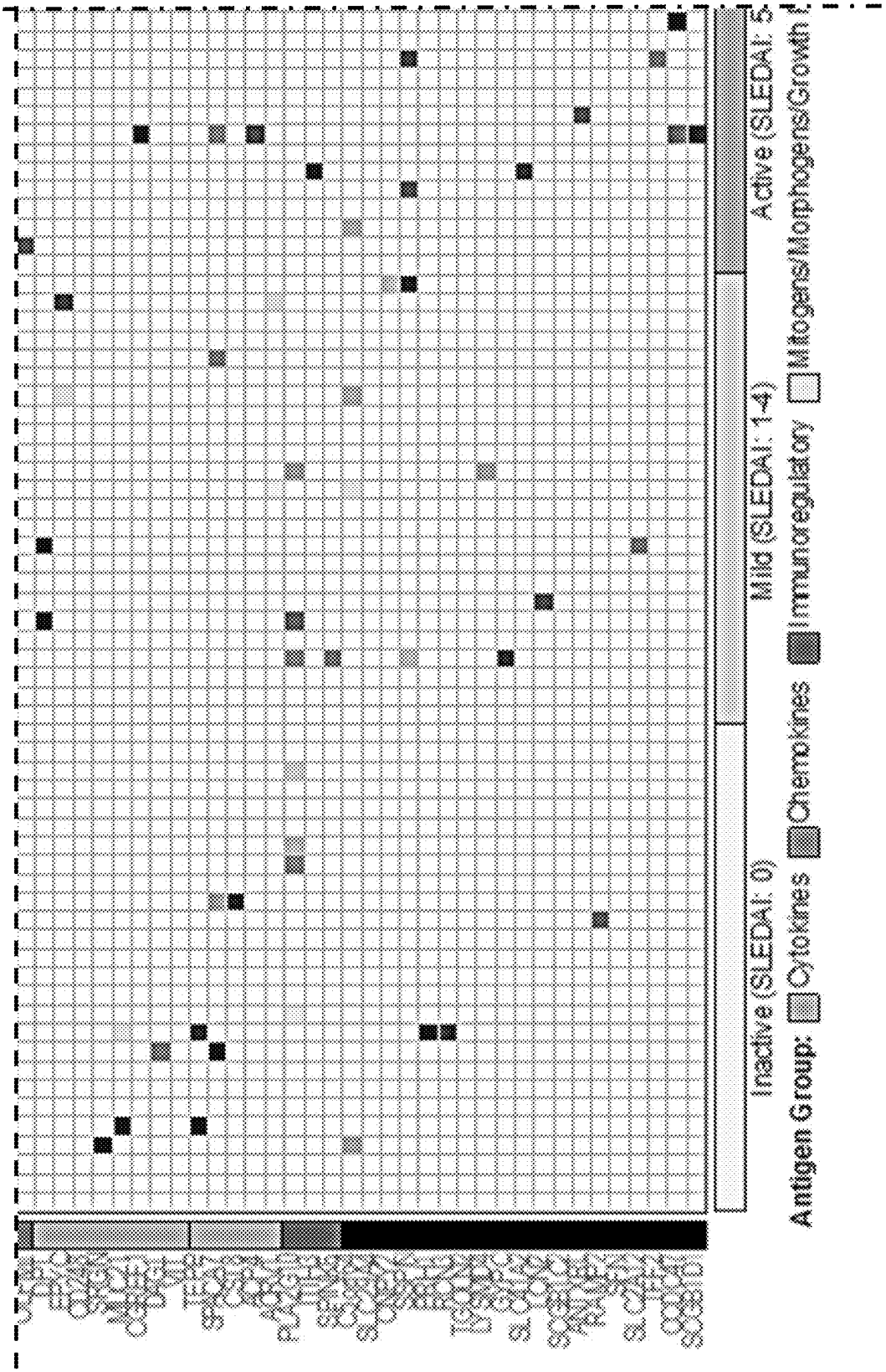


Figure 8 (cont.)

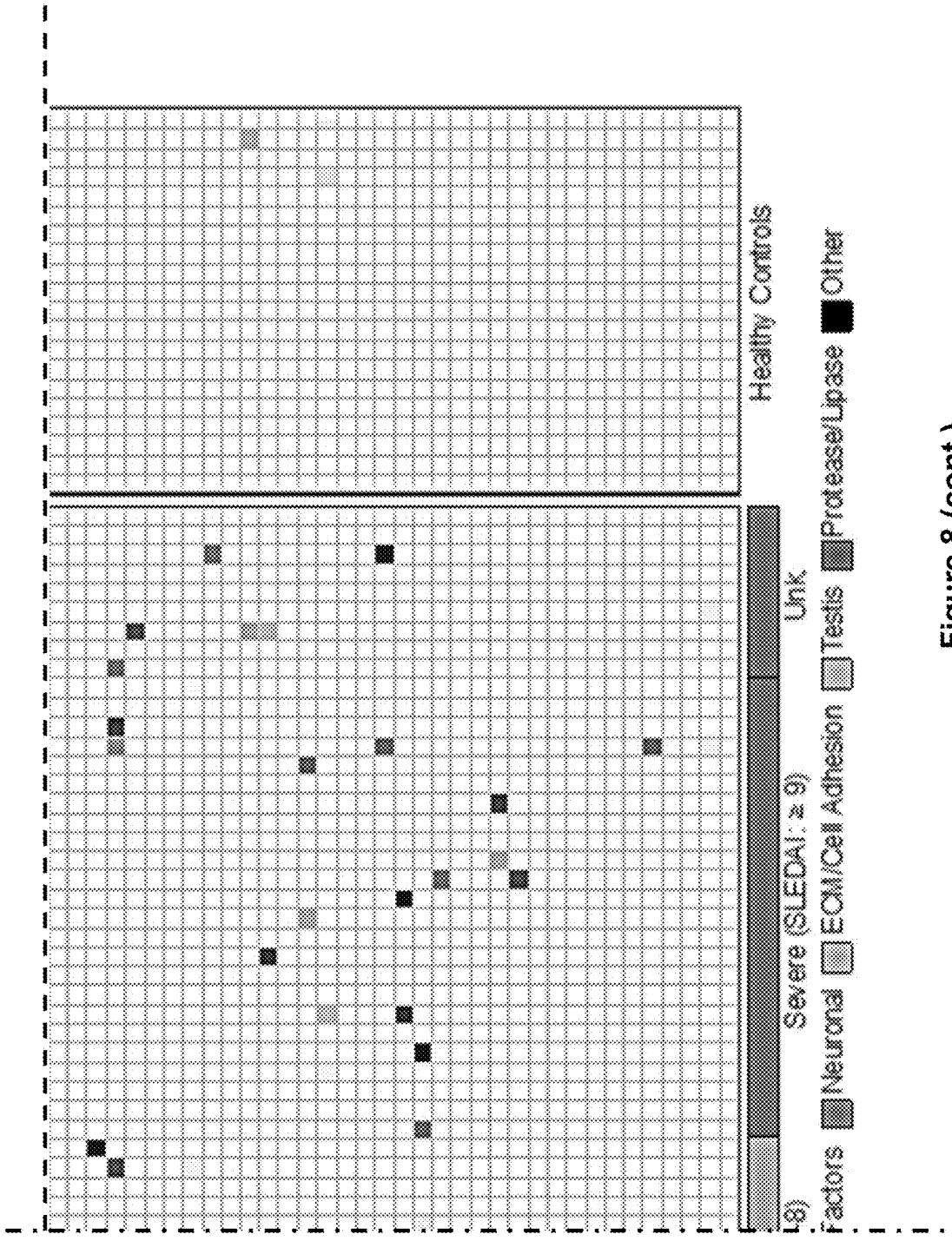


Figure 8 (cont.)

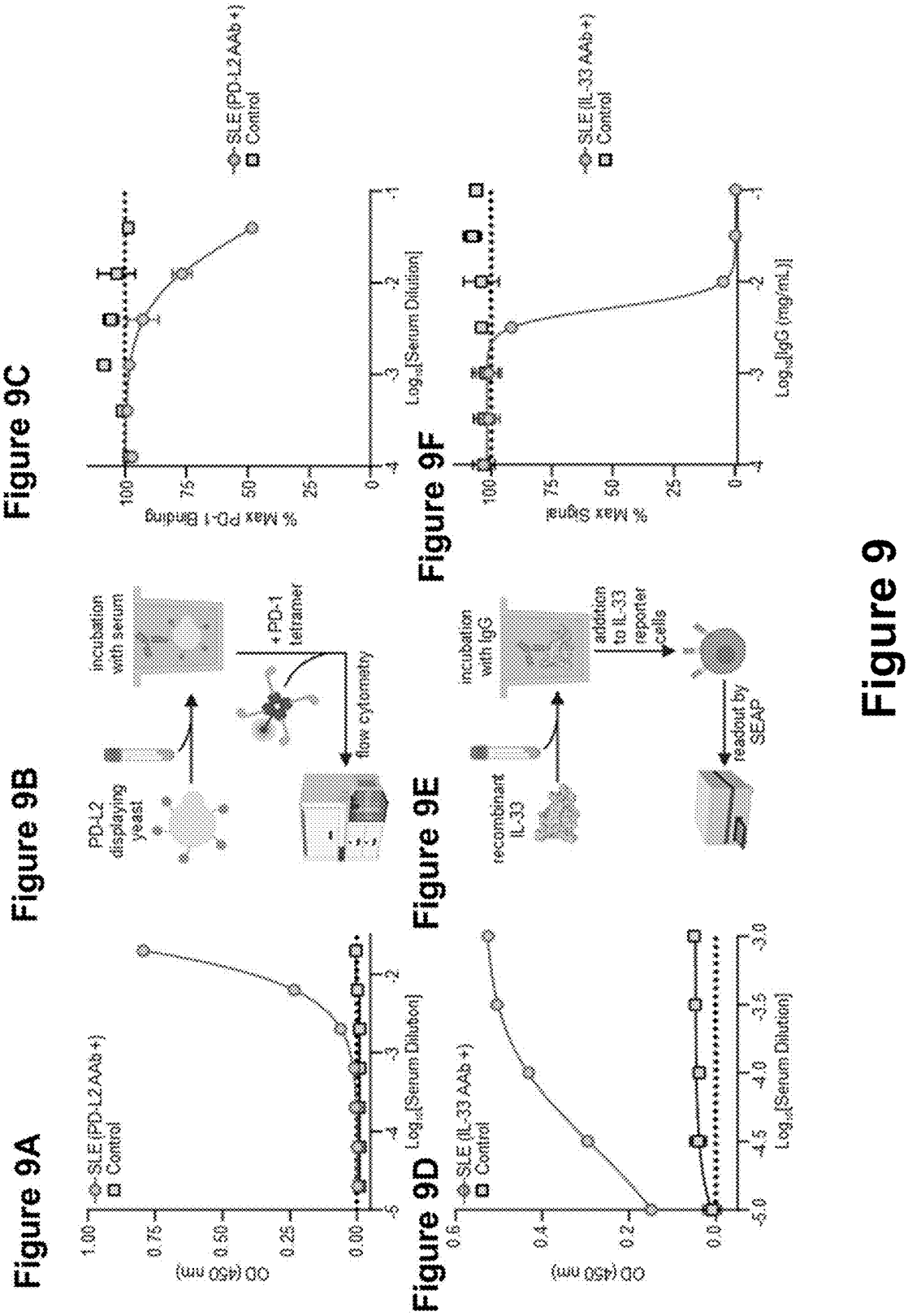


Figure 9A
SLE (PD-L2 AAb +)
Control
OD (450 nm)
Log10(Serum Dilution)
Figure 9B
PD-L2 displaying yeast
incubation with serum
+ PD-1 tetramer
flow cytometry
Figure 9C
SLE (PD-L2 AAb +)
Control
% Max PD-1 Binding
Log10(Serum Dilution)
Figure 9D
SLE (IL-33 AAb +)
Control
OD (450 nm)
Log10(Serum Dilution)
Figure 9E
recombinant IL-33
incubation with IgG
addition to IL-33 reporter cells
readout by SEAP
Figure 9F
SLE (IL-33 AAb +)
Control
% Max Signal
Log10IgG (mg/mL)

Figure 9

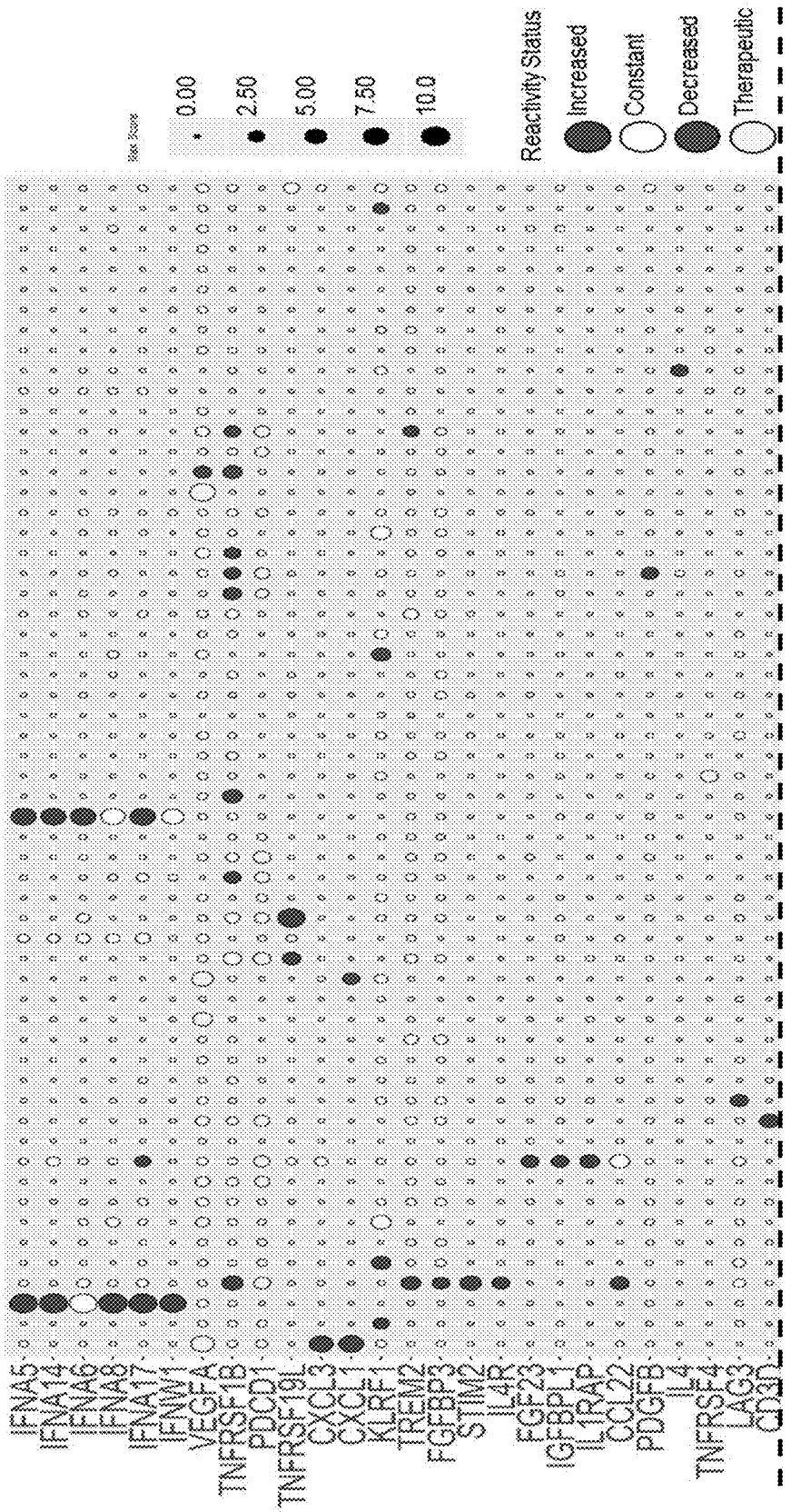

Bar Score
0.00
2.50
5.00
7.50
10.0
Reactivity Status
Increased
Constant
Decreased
Therapeutic
IFNA5
IFNA14
IFNA6
IFNA8
IFNA17
IFNW1
VEGFA
TNFRSF1B
PDCD1
TNFRSF19L
CXCL3
CXCL1
KLRF1
TREM2
FGFBP3
STIM2
IL4R
FGF23
IGFBPL1
IL1RAP
CCL22
PDGFB
IL4
TNFRSF4
LAG3
CD3D

Figure 10

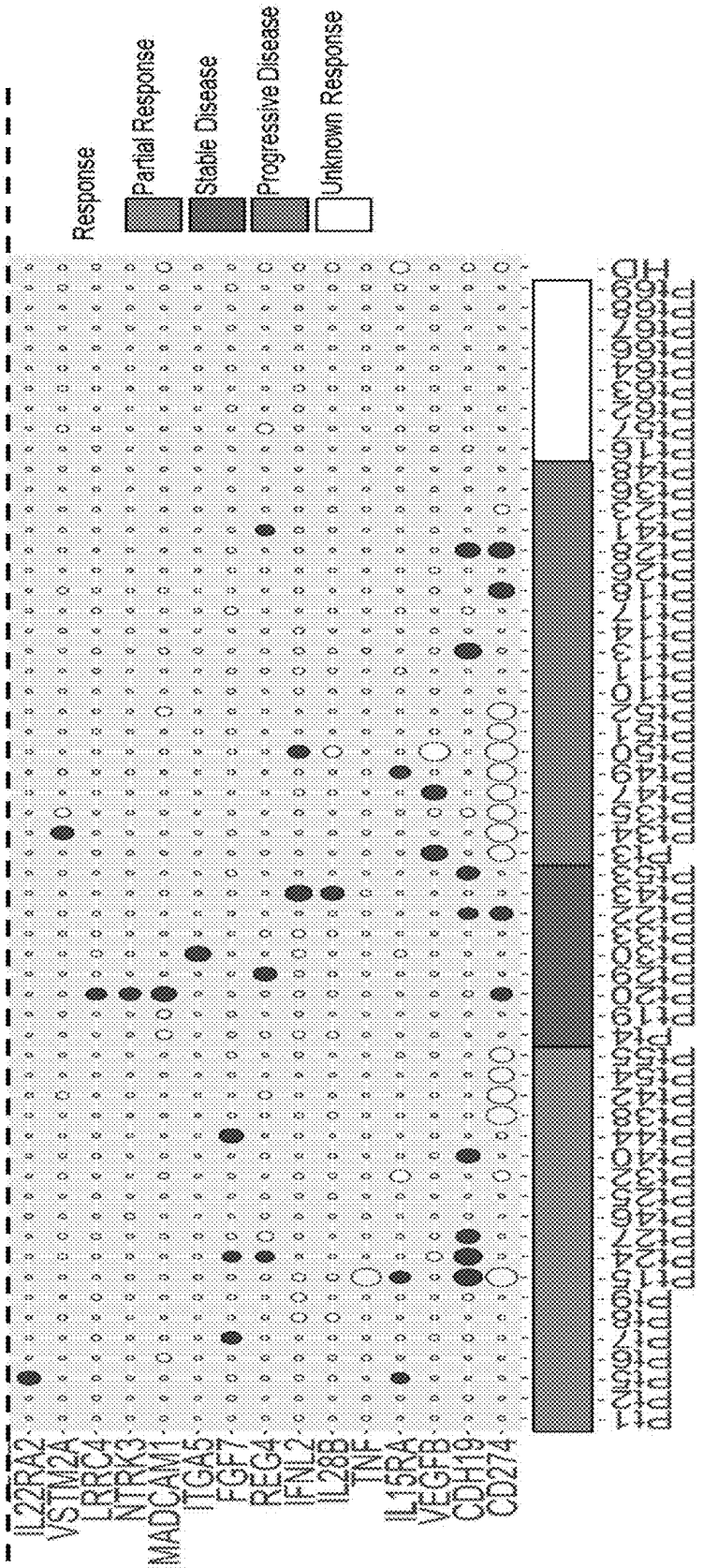


Figure 10 (cont.)

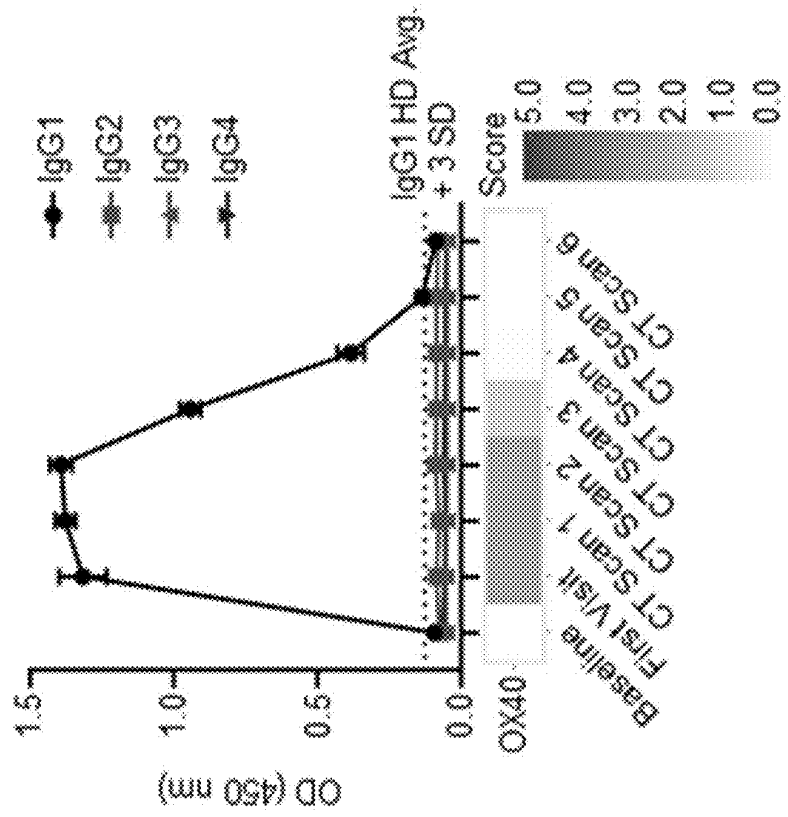

IgG1
IgG2
IgG3
IgG4
IgG1 HD Avg. + 3 SD
Score
5.0
4.0
3.0
2.0
1.0
0.0
OX40
Baseline
First Visit
CT Scan 1
CT Scan 2
CT Scan 3
CT Scan 4
CT Scan 5
CT Scan 6
OD (450 nm)
1.5
1.0
0.5
0.0

Figure 11

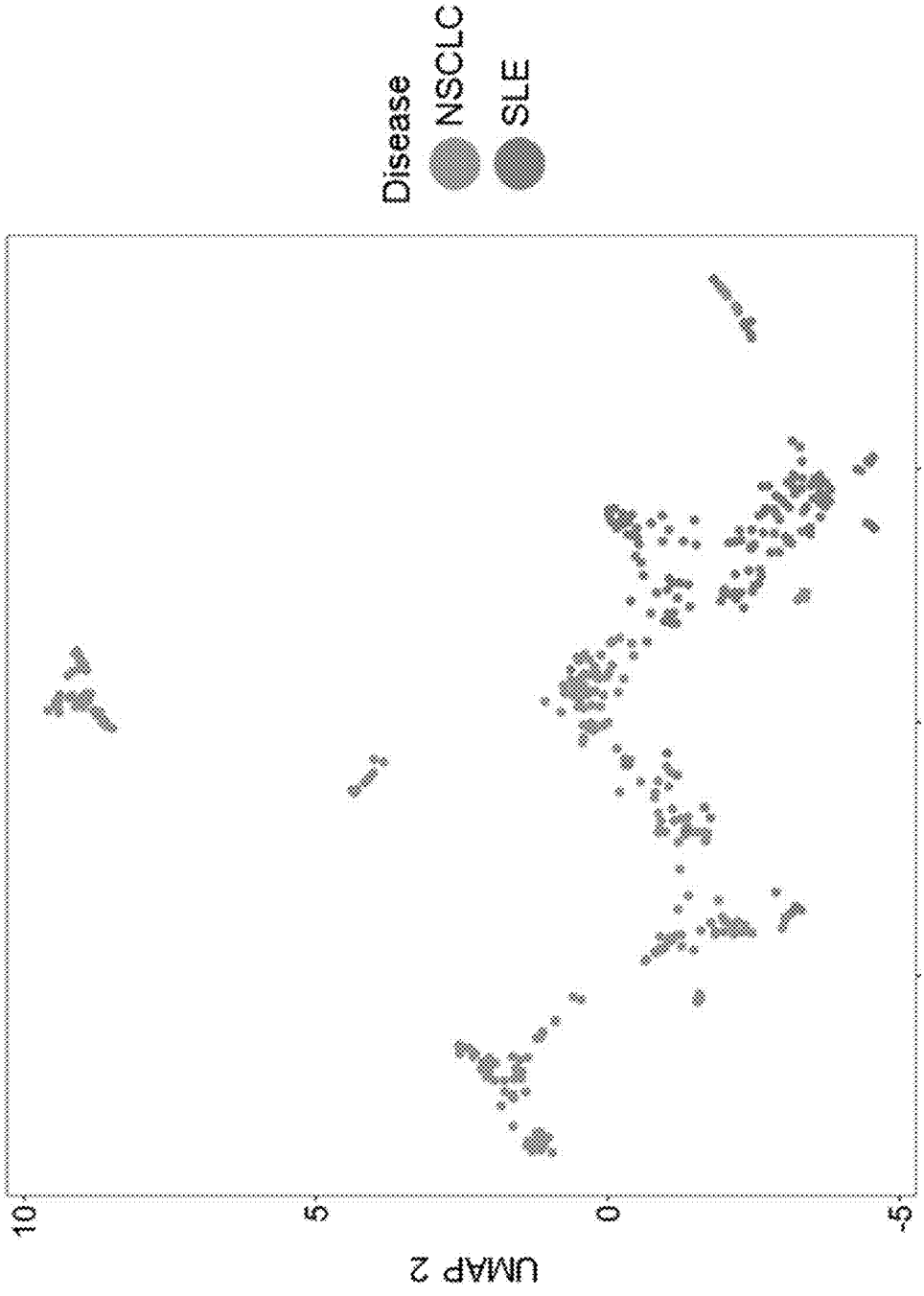


Figure 12

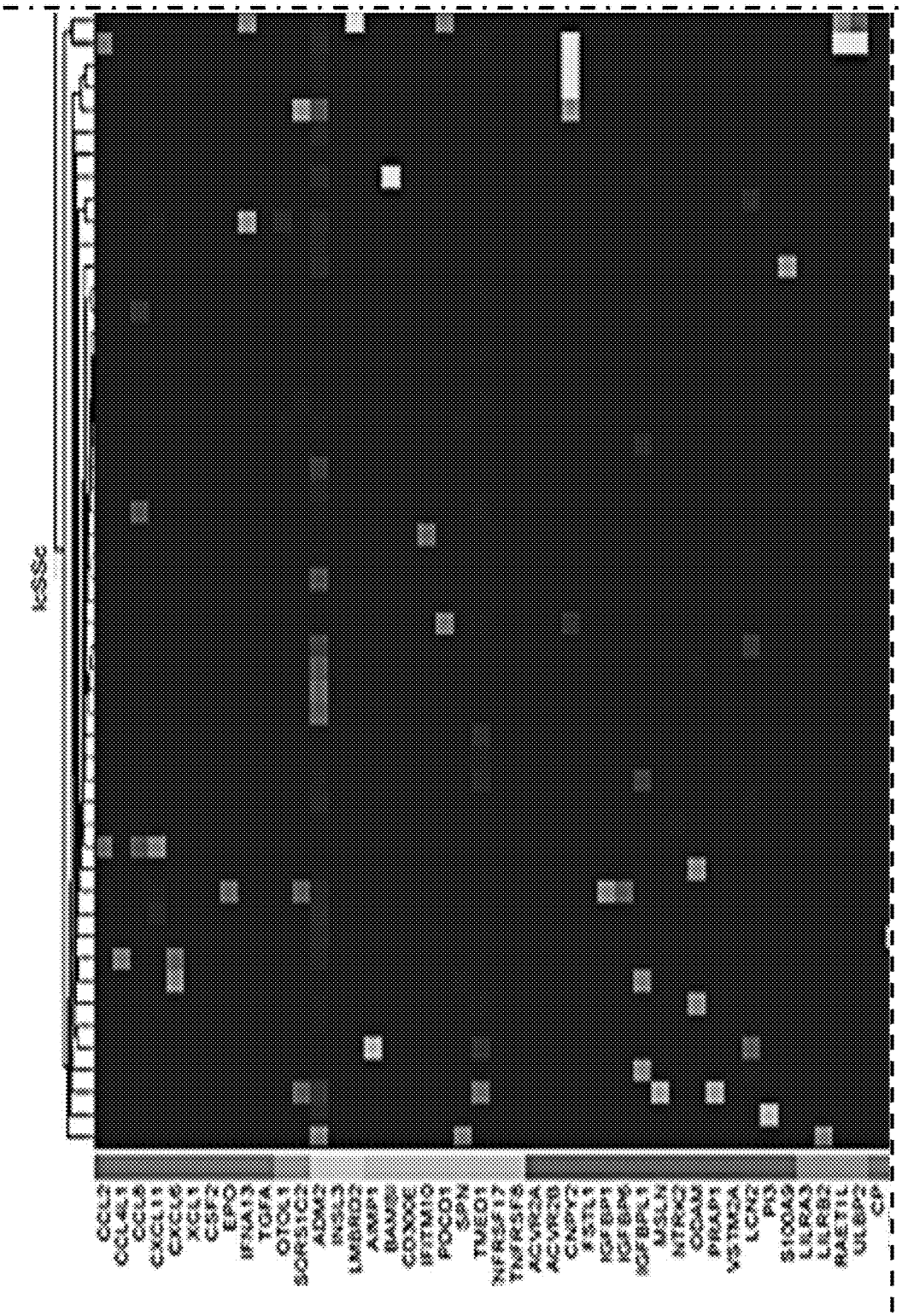


Figure 13

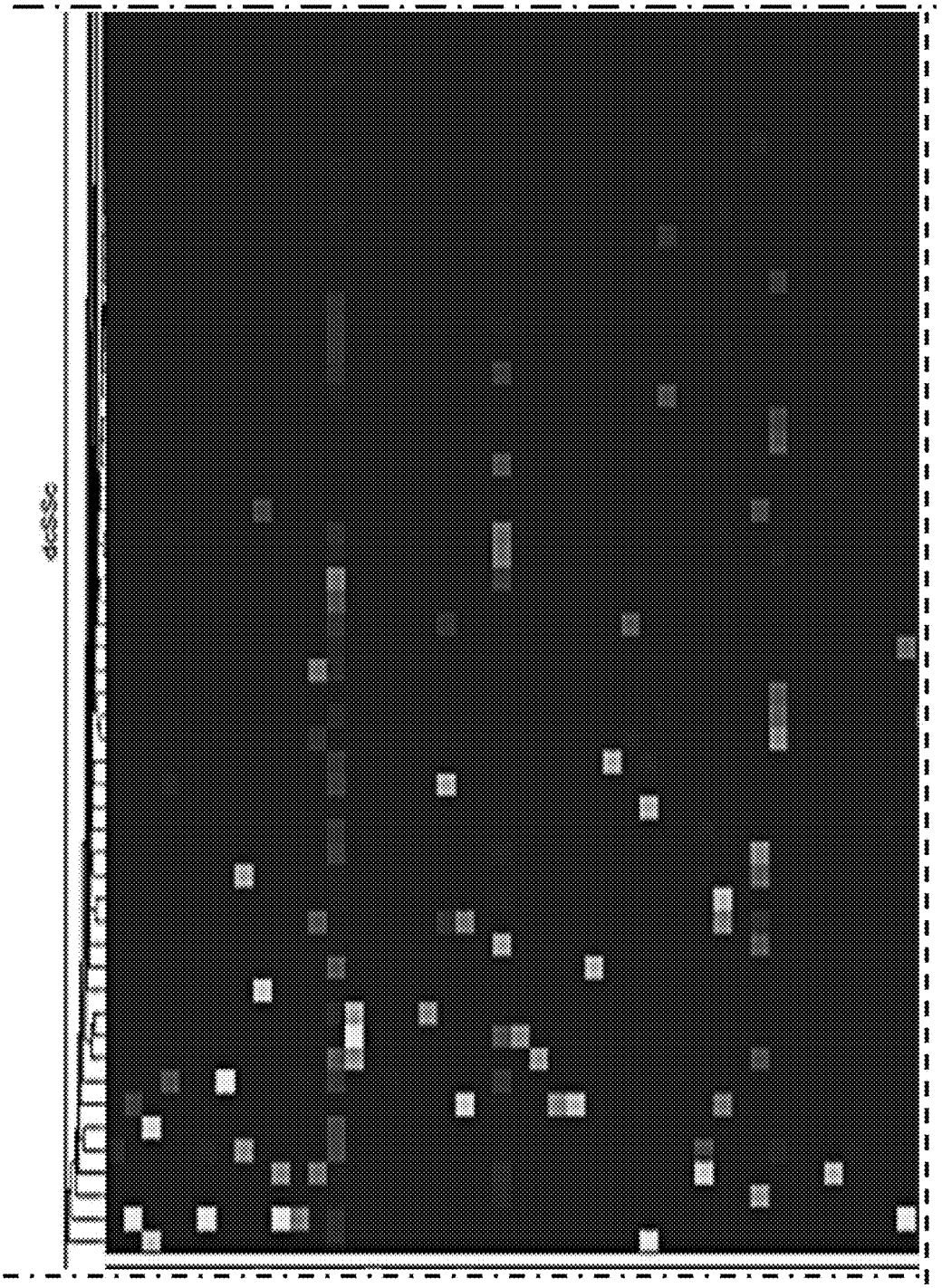


Figure 13 (cont.)

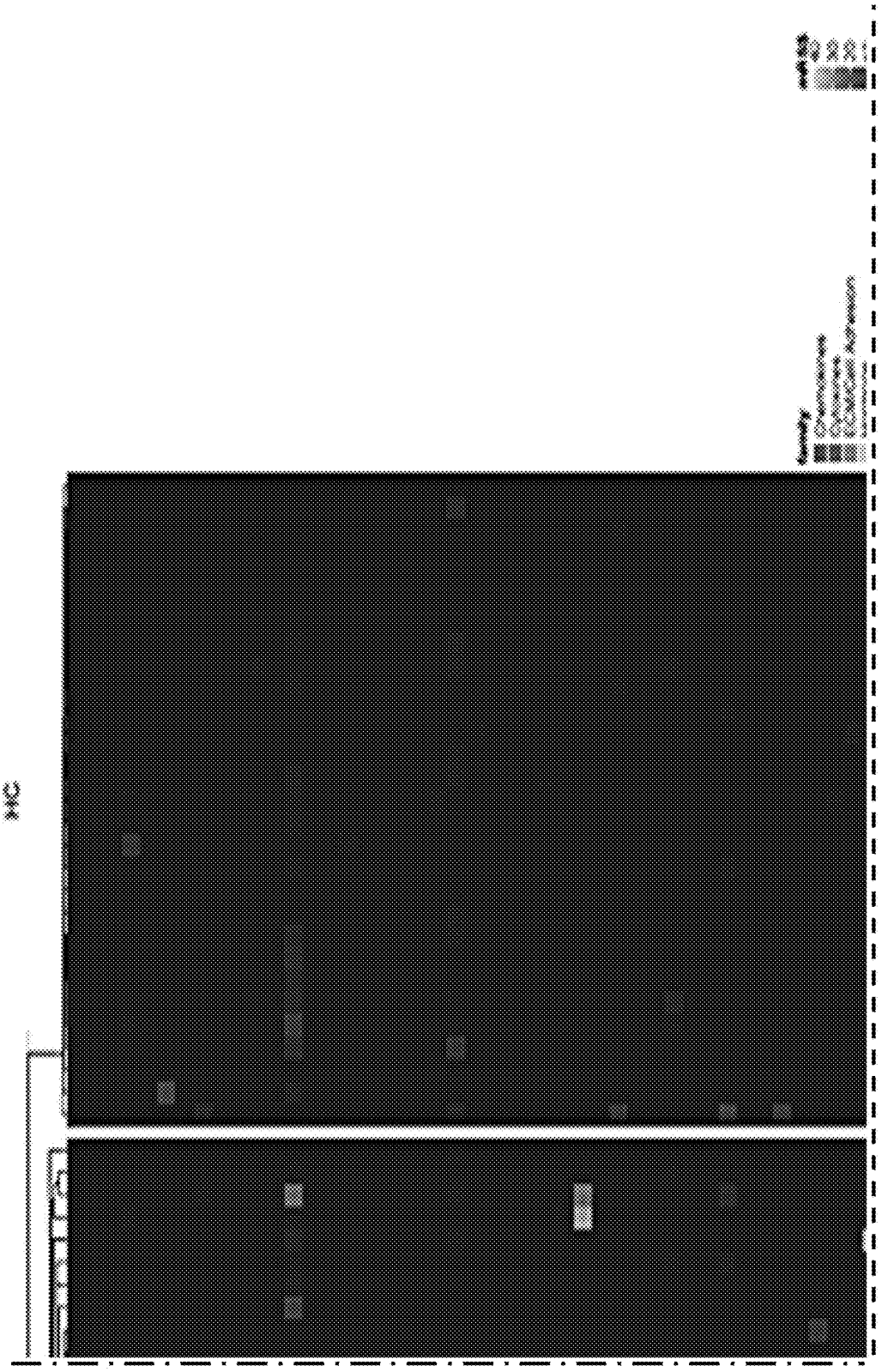


Figure 13 (cont.)

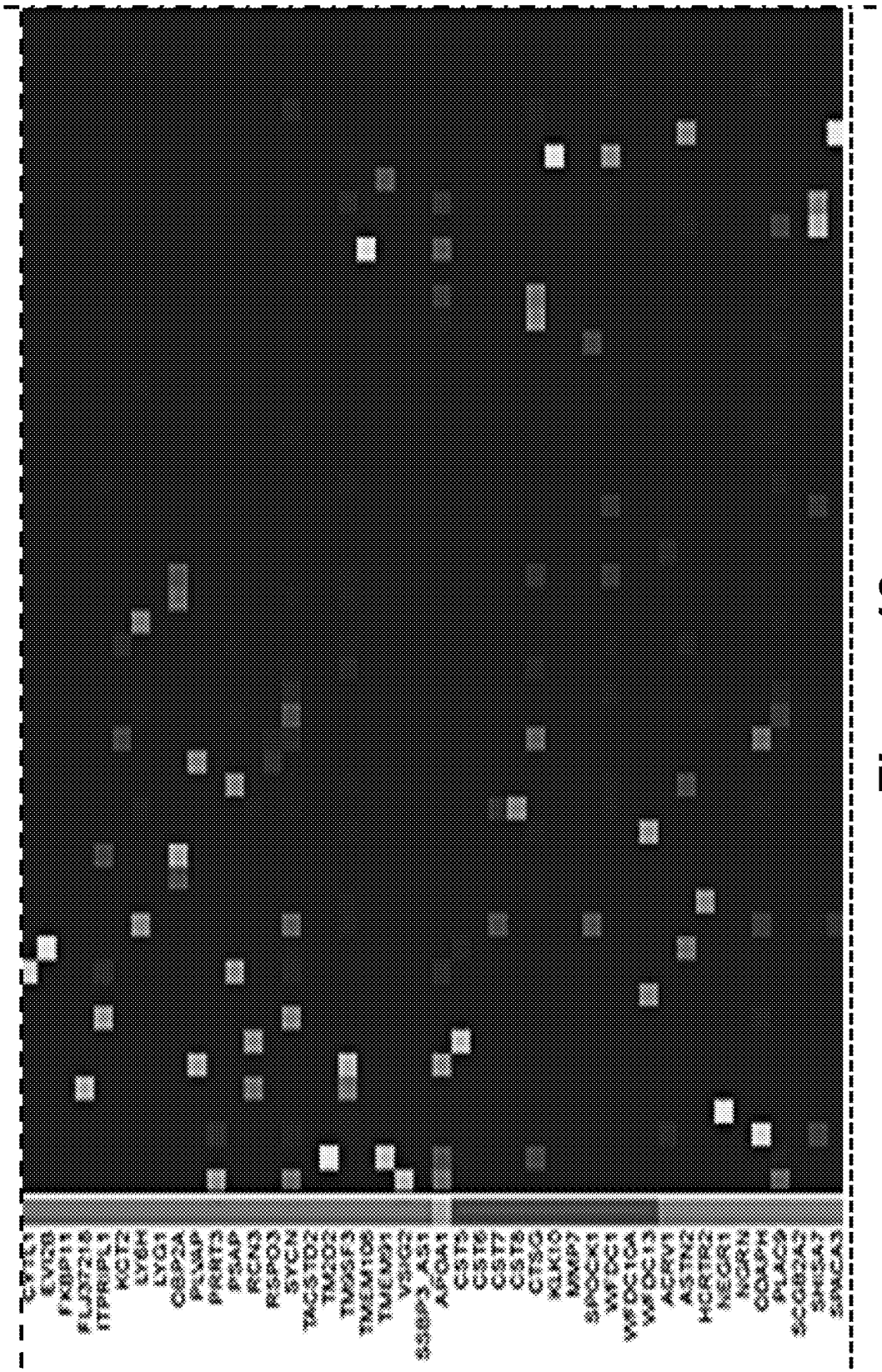


Figure 13

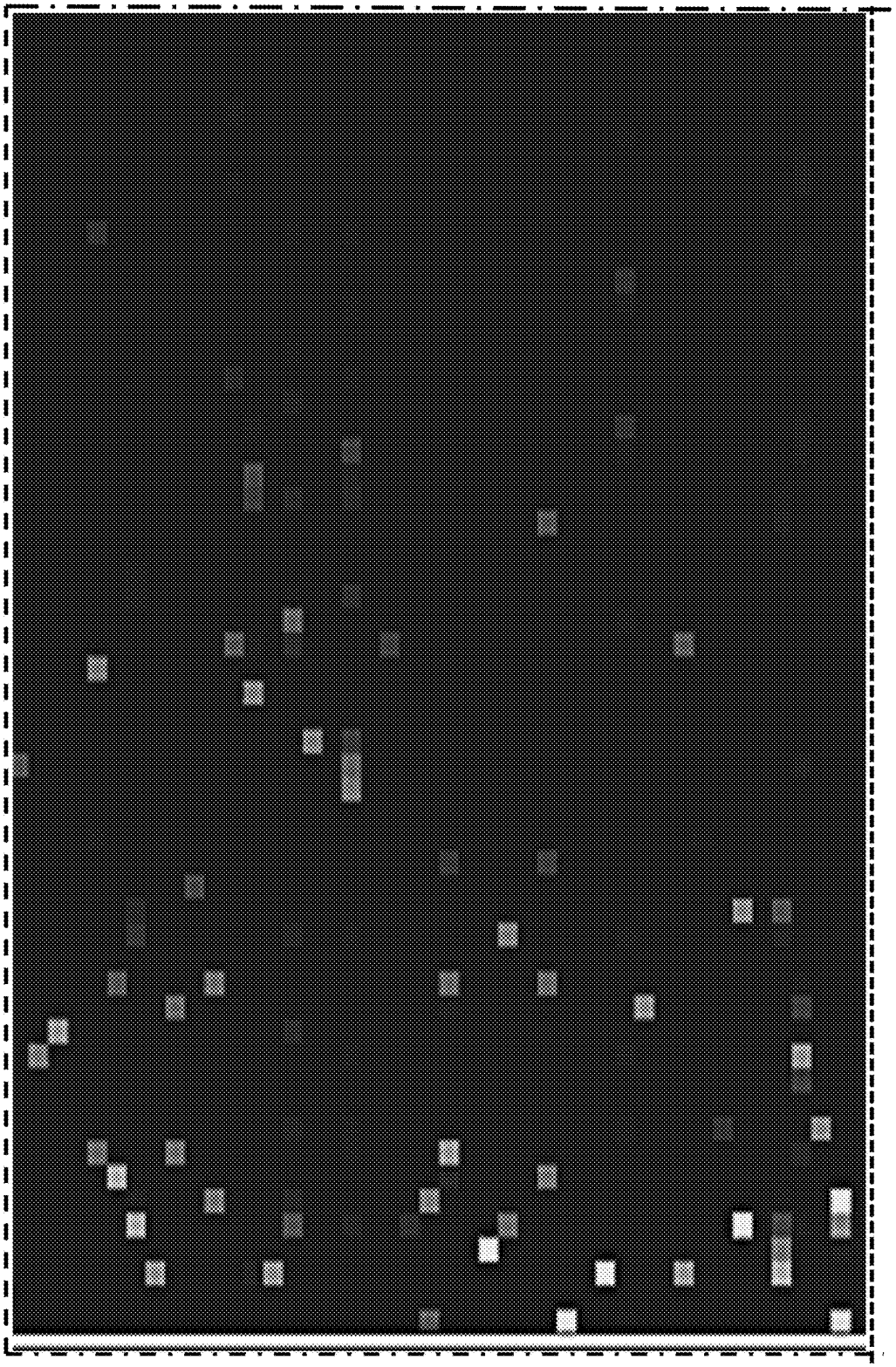


Figure 13 (cont.)

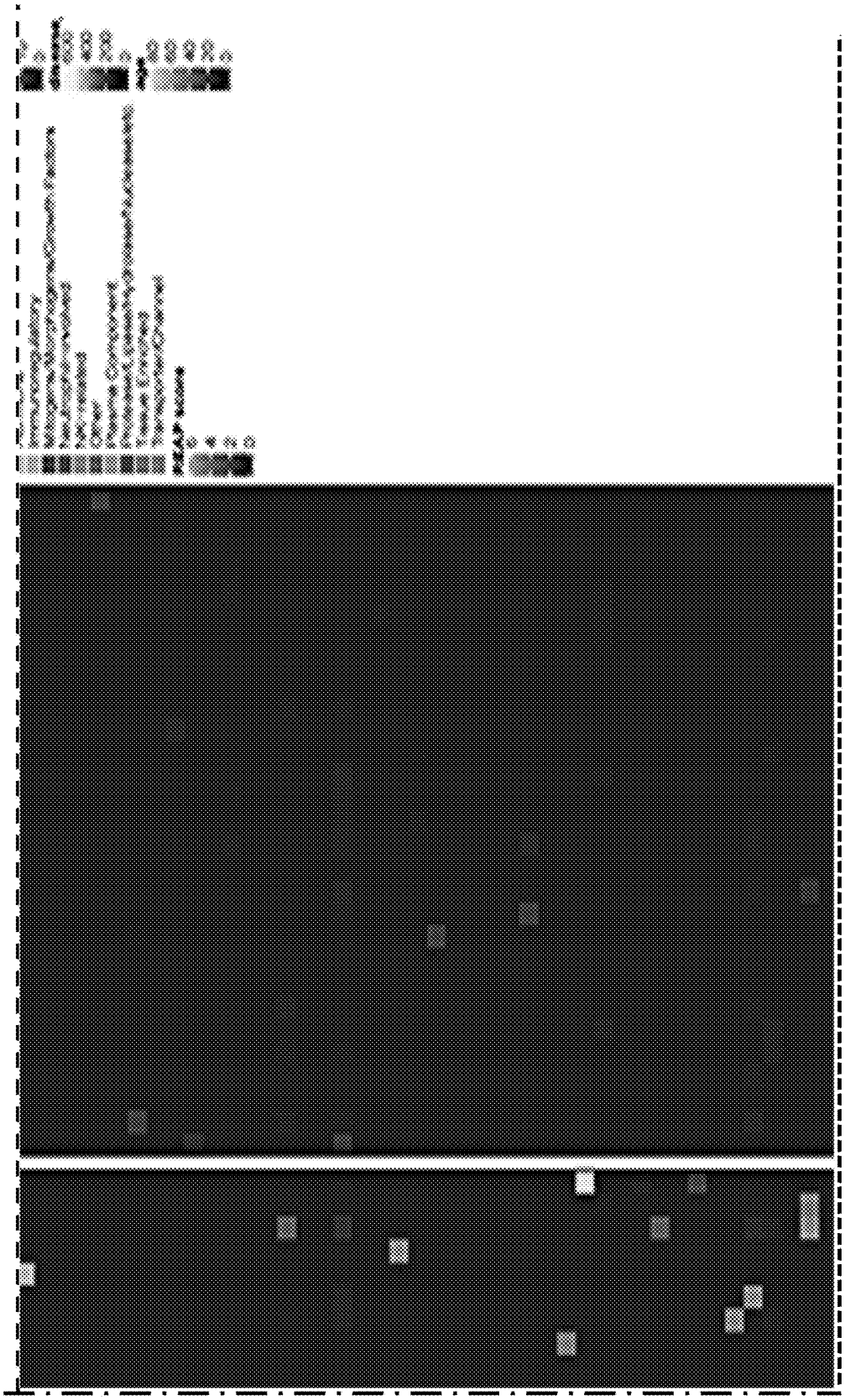


Figure 13 (cont.)

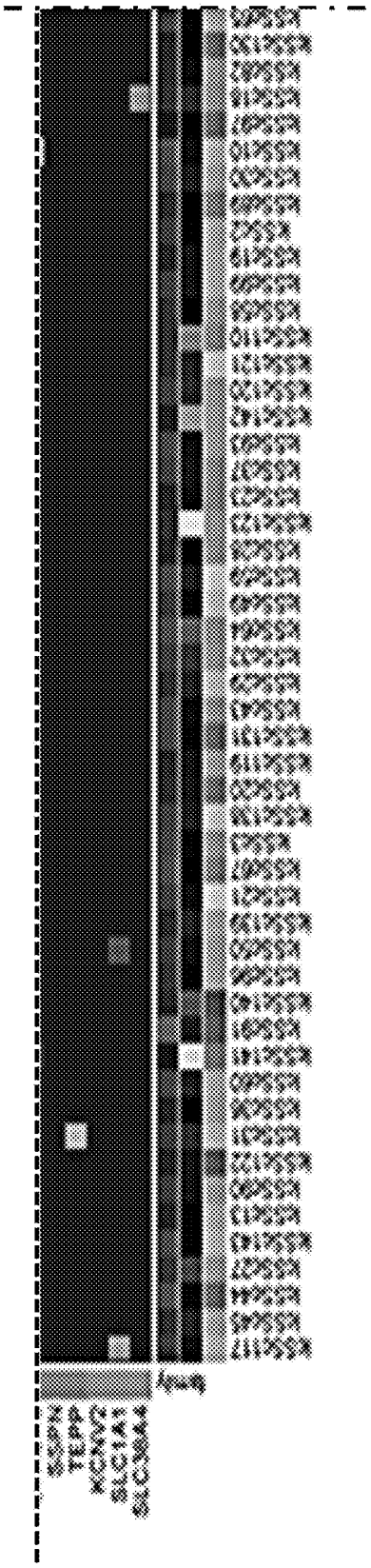


Figure 13 (cont.)

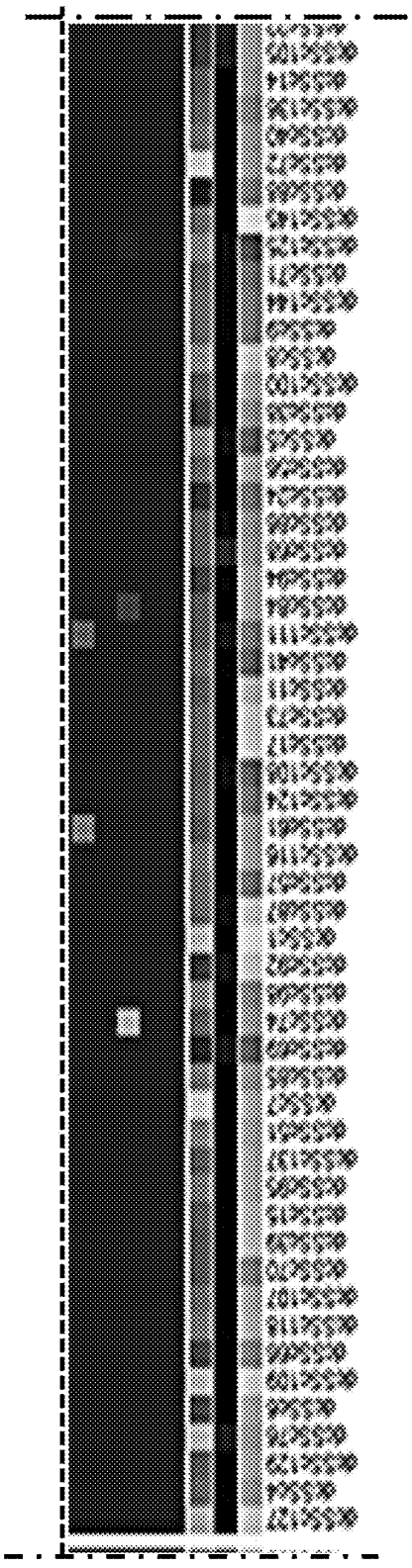


Figure 13 (cont.)

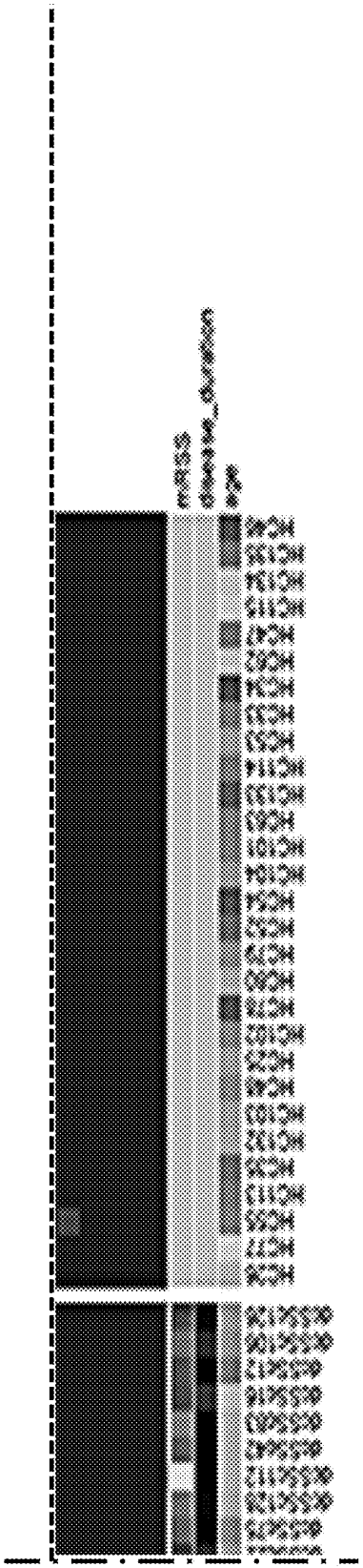


Figure 13 (cont.)

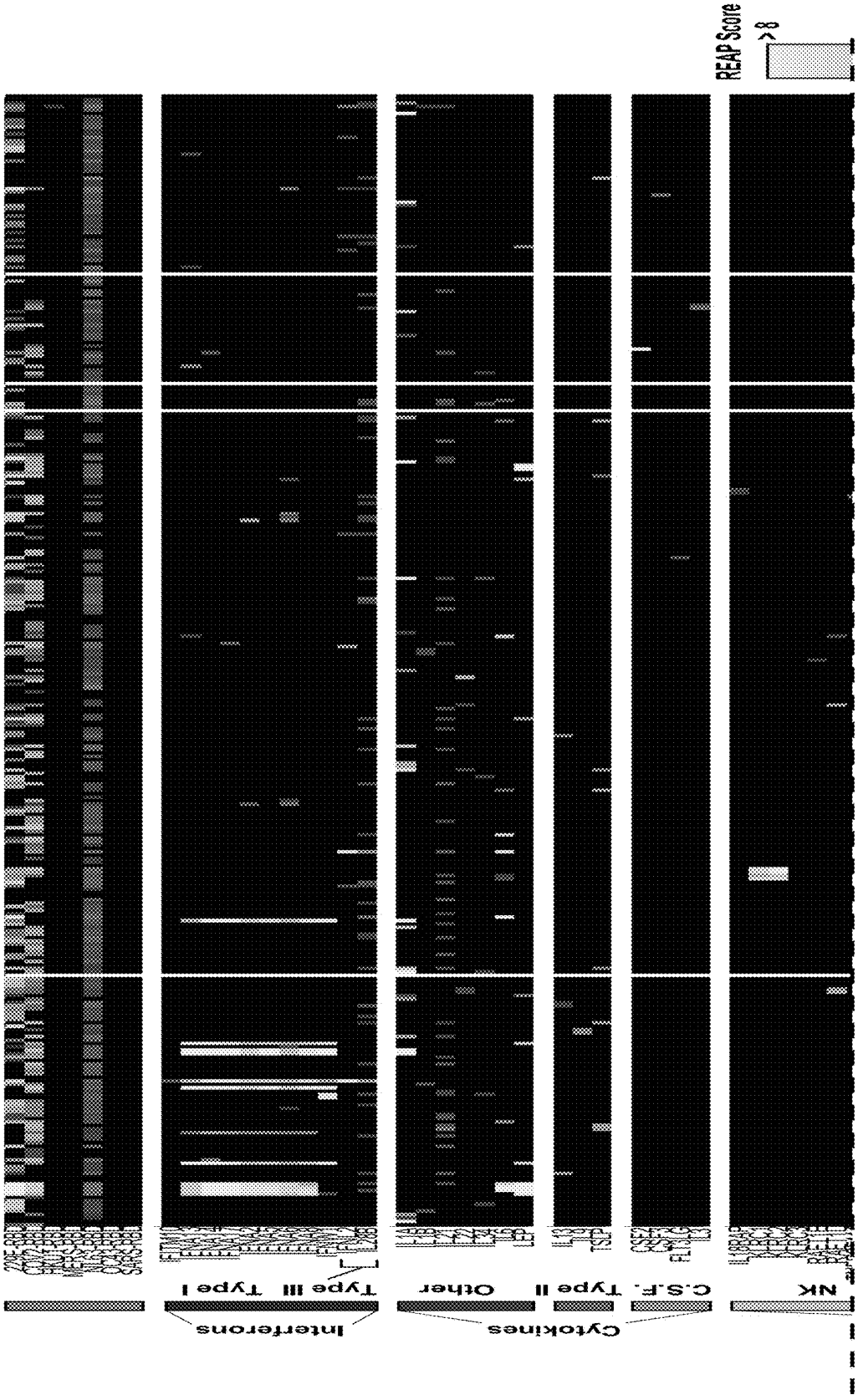

REAP Score
>8
NK
C.S.F.
Type II
Other
Type III
Type I
Interferons
Cytokines

Figure 14

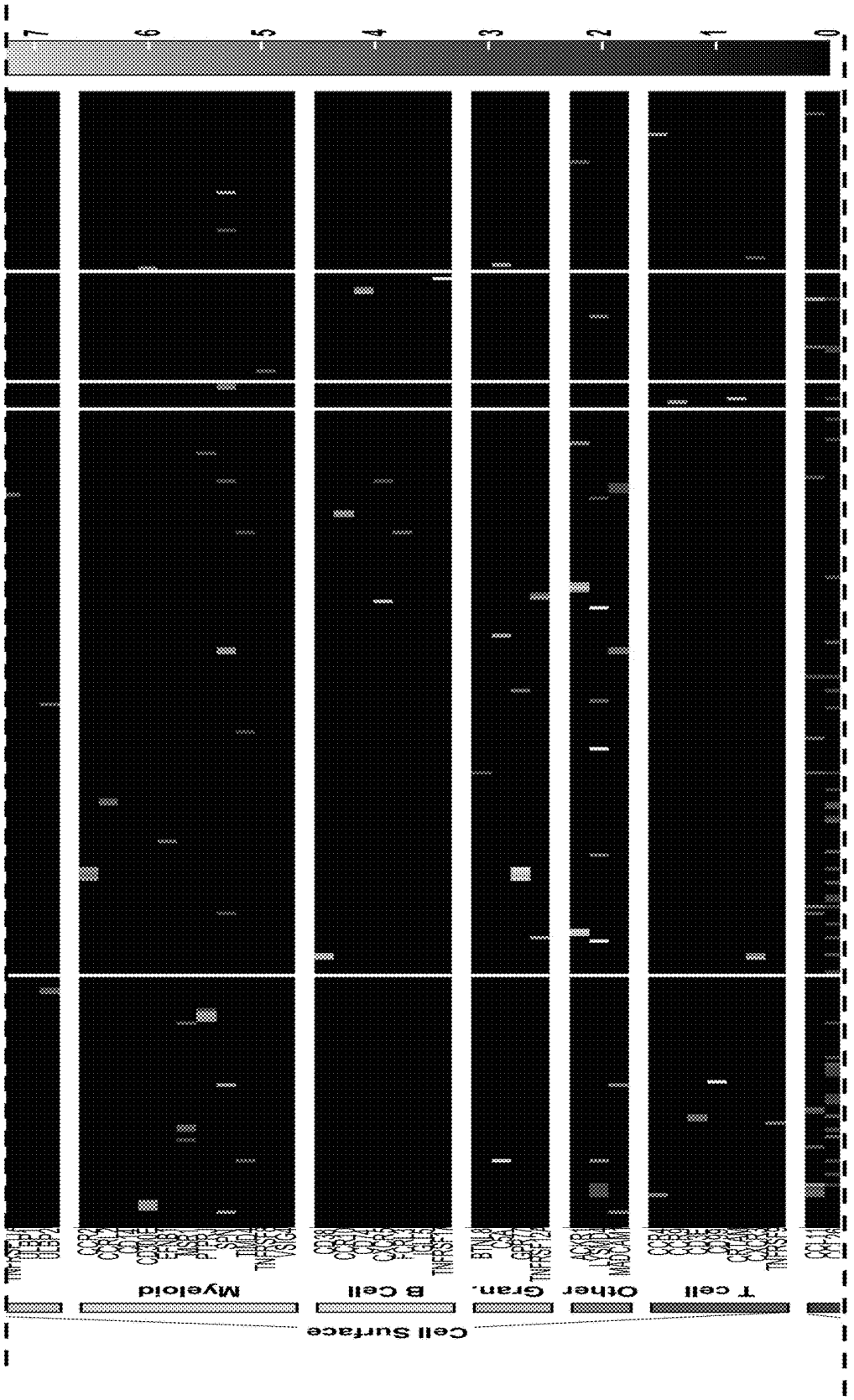


Figure 14 (cont.)

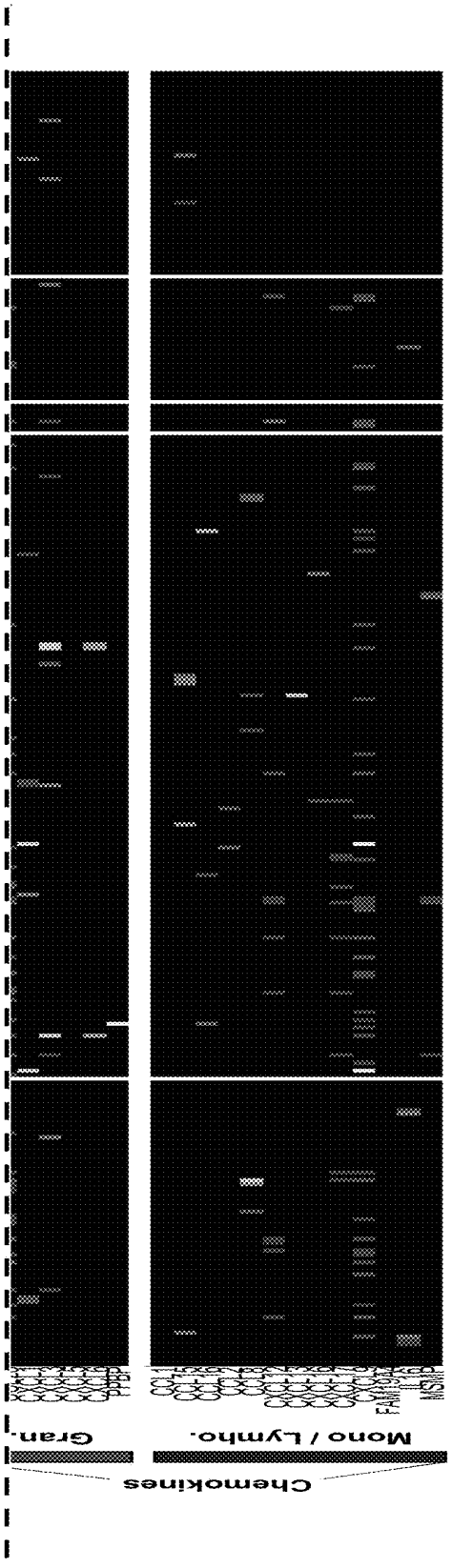


Figure 14 (cont.)

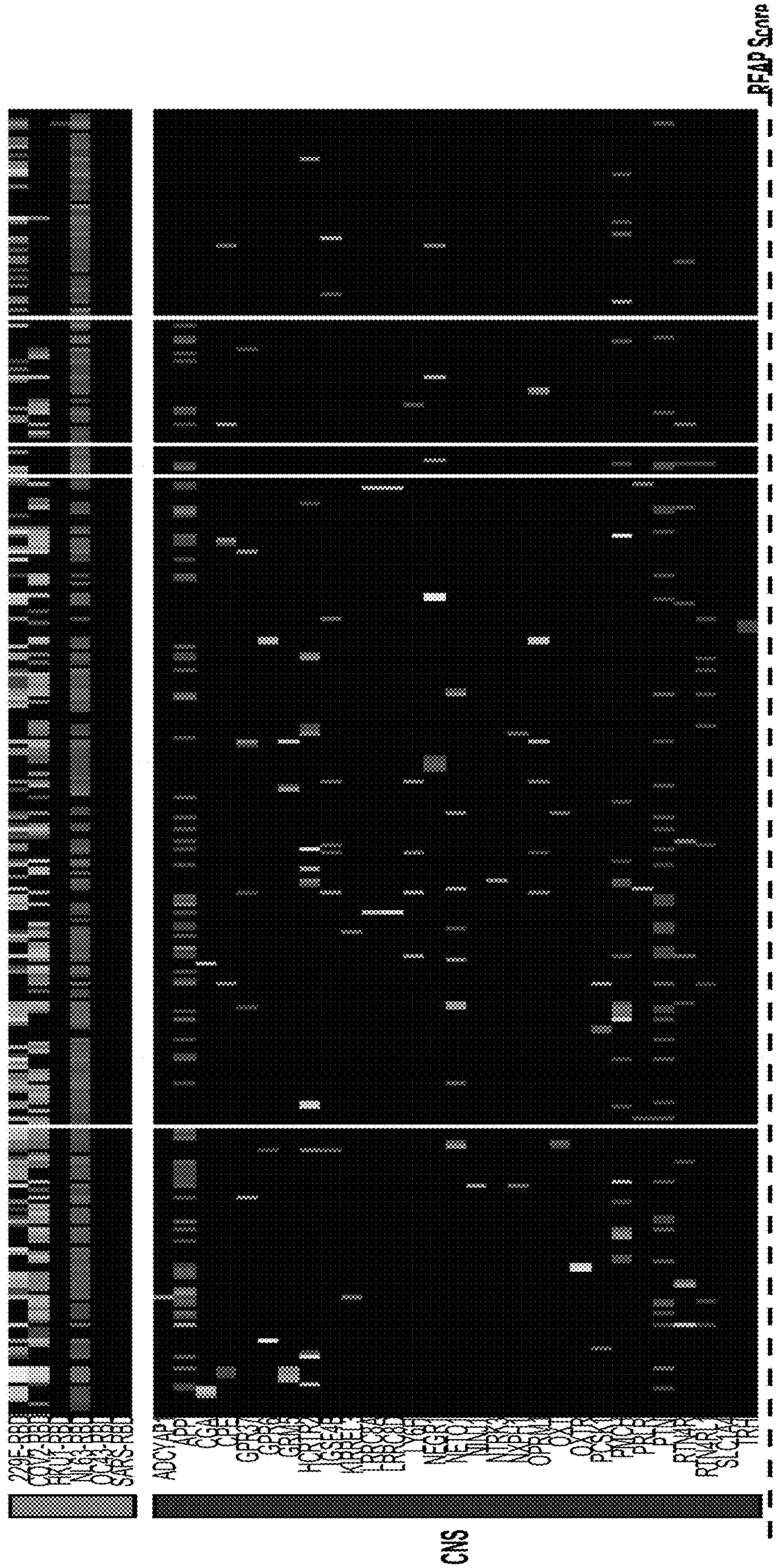


Figure 15

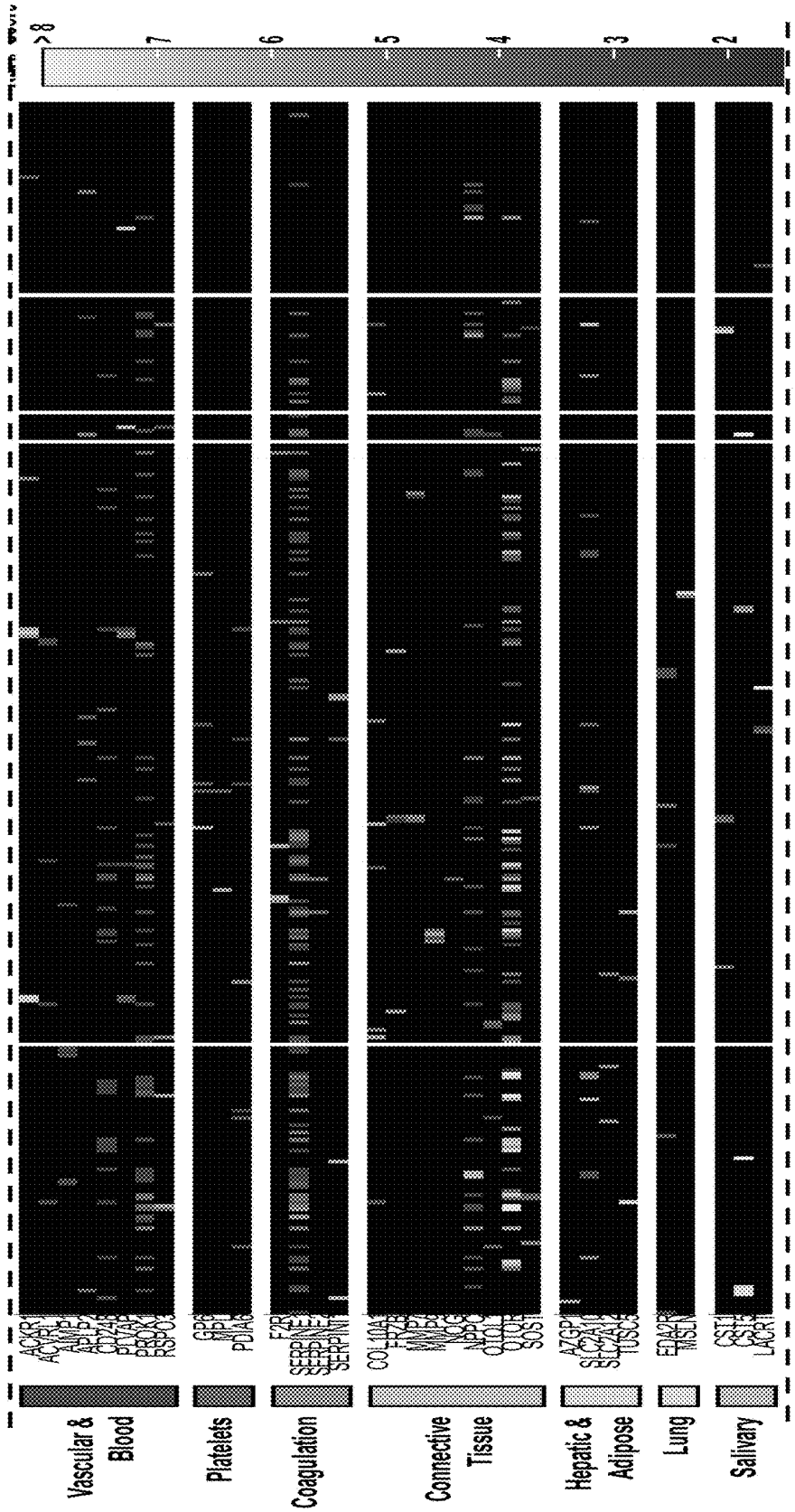


Figure 15 (cont.)

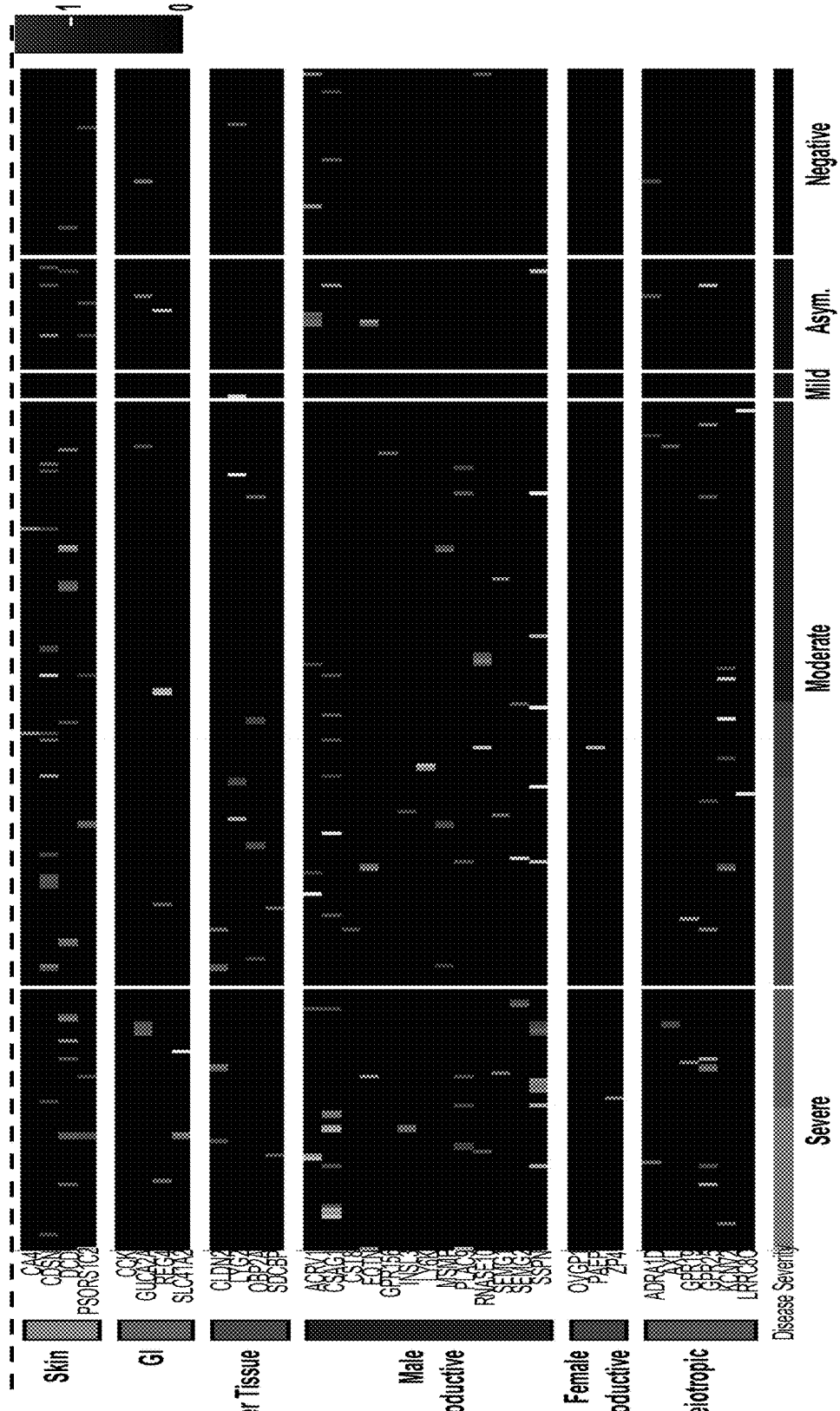


Figure 15 (cont.)

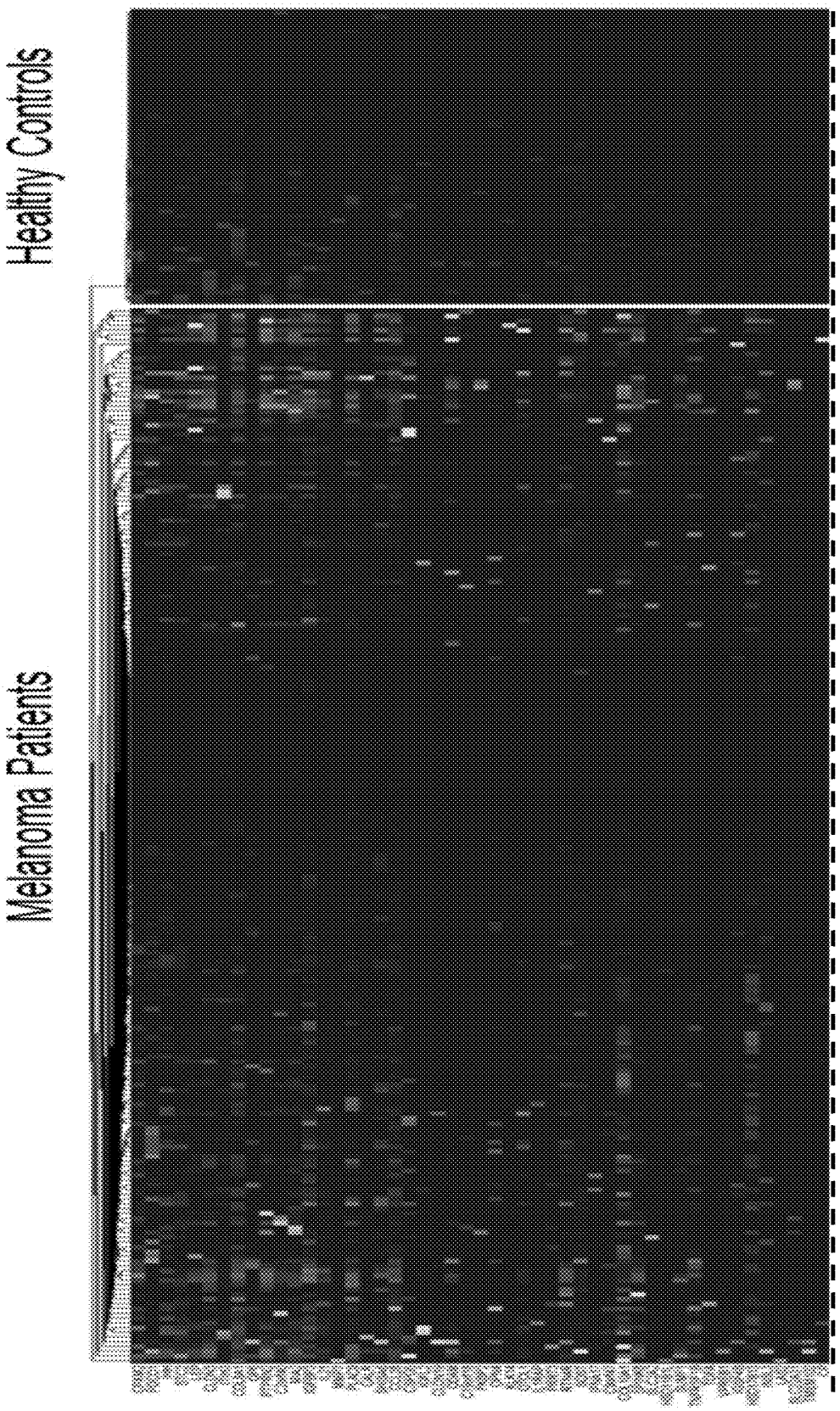


Figure 16

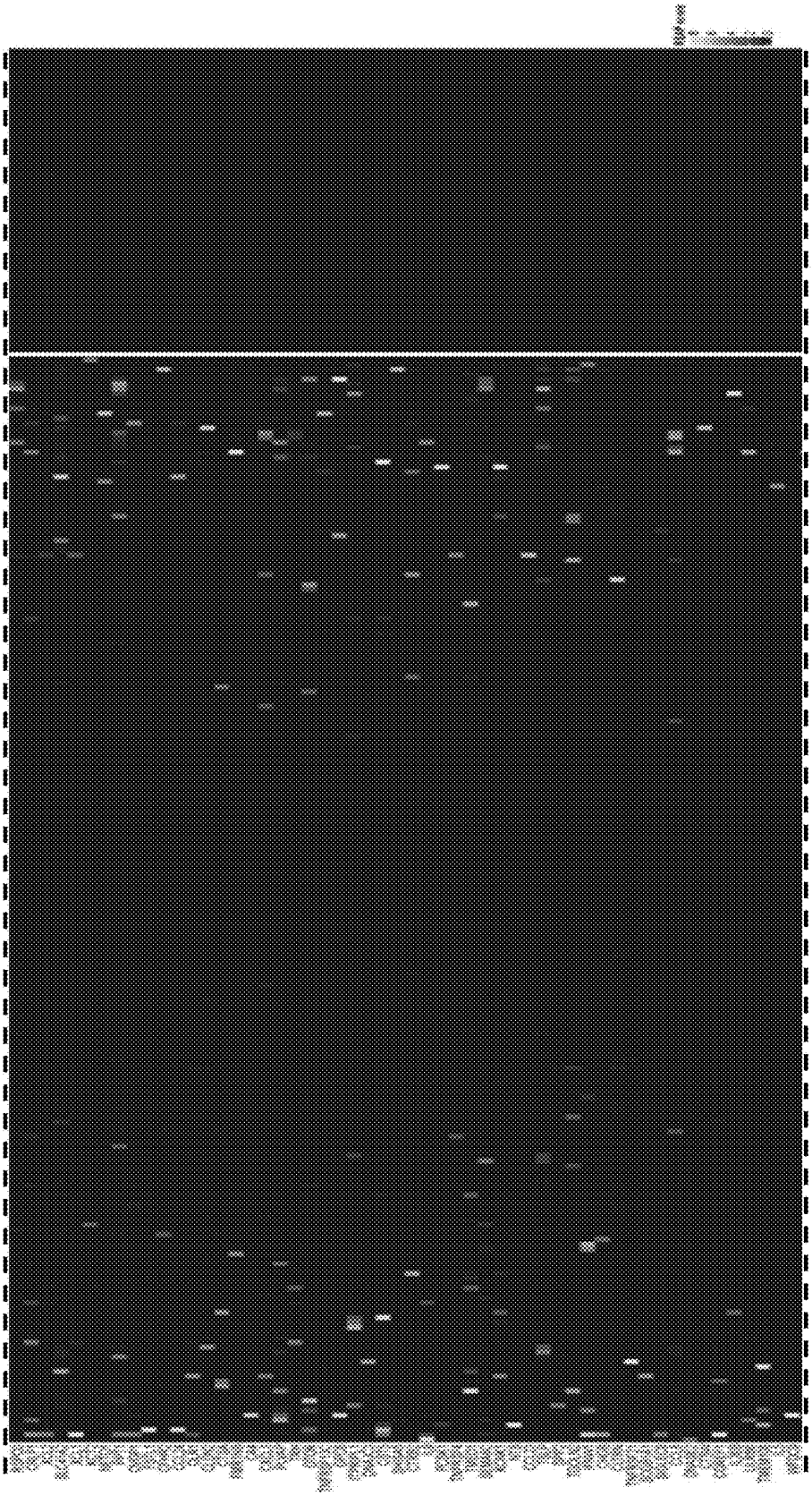


Figure 16 (cont.)

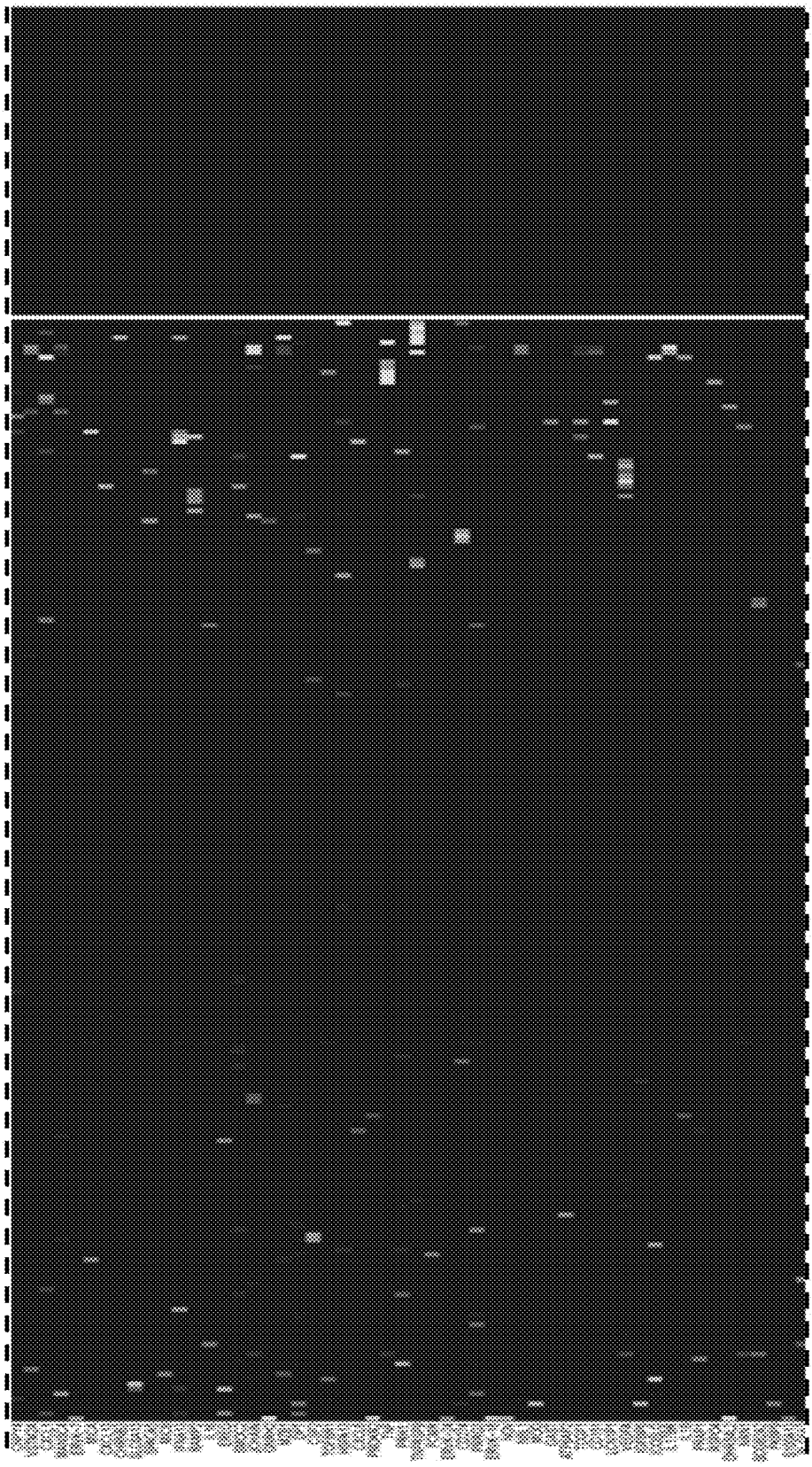


Figure 16 (cont.)

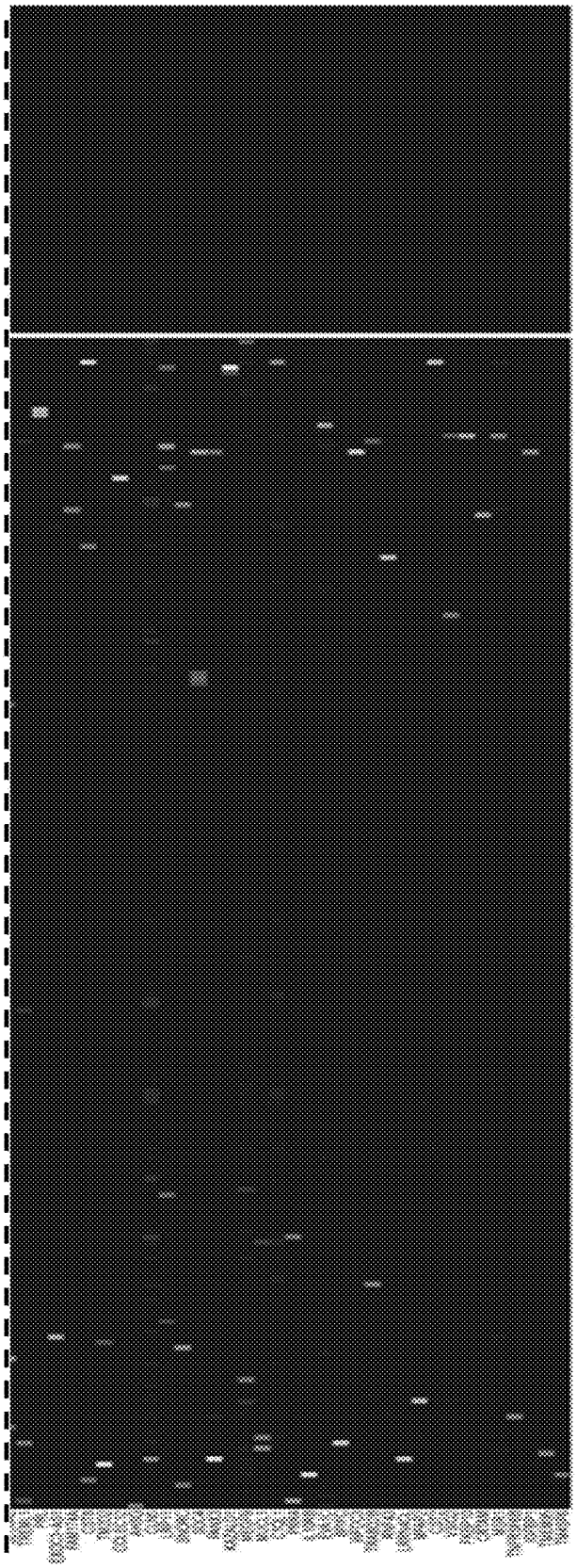


Figure 16 (cont.)

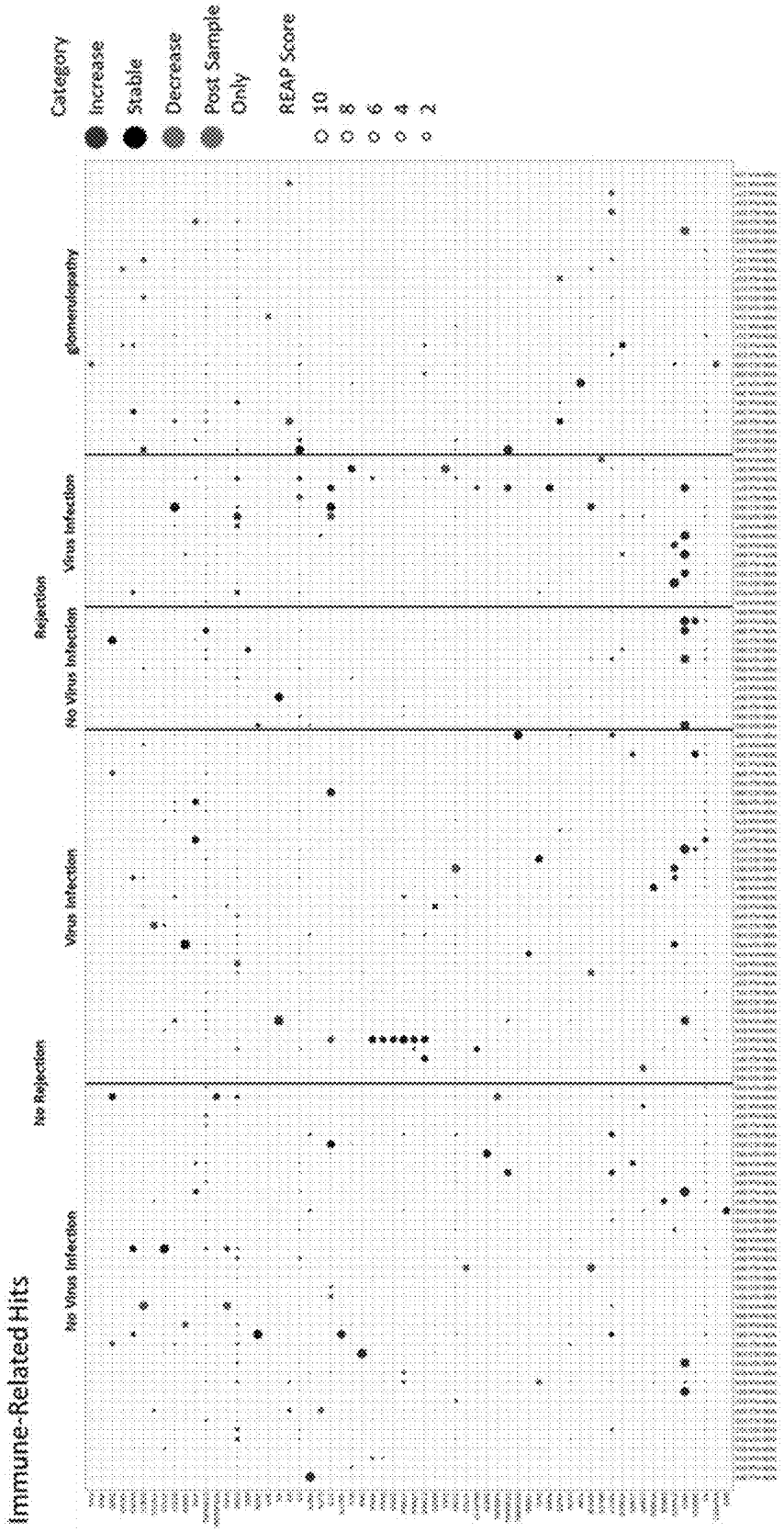

Category
Increase
Stable
Decrease
Post Sample Only
REAP Score
10
8
6
4
2
Immune-Related Hits
No Rejection
Rejection
No Virus Infection
Virus Infection
No Virus Infection
Virus Infection
Nonadherence

Figure 17

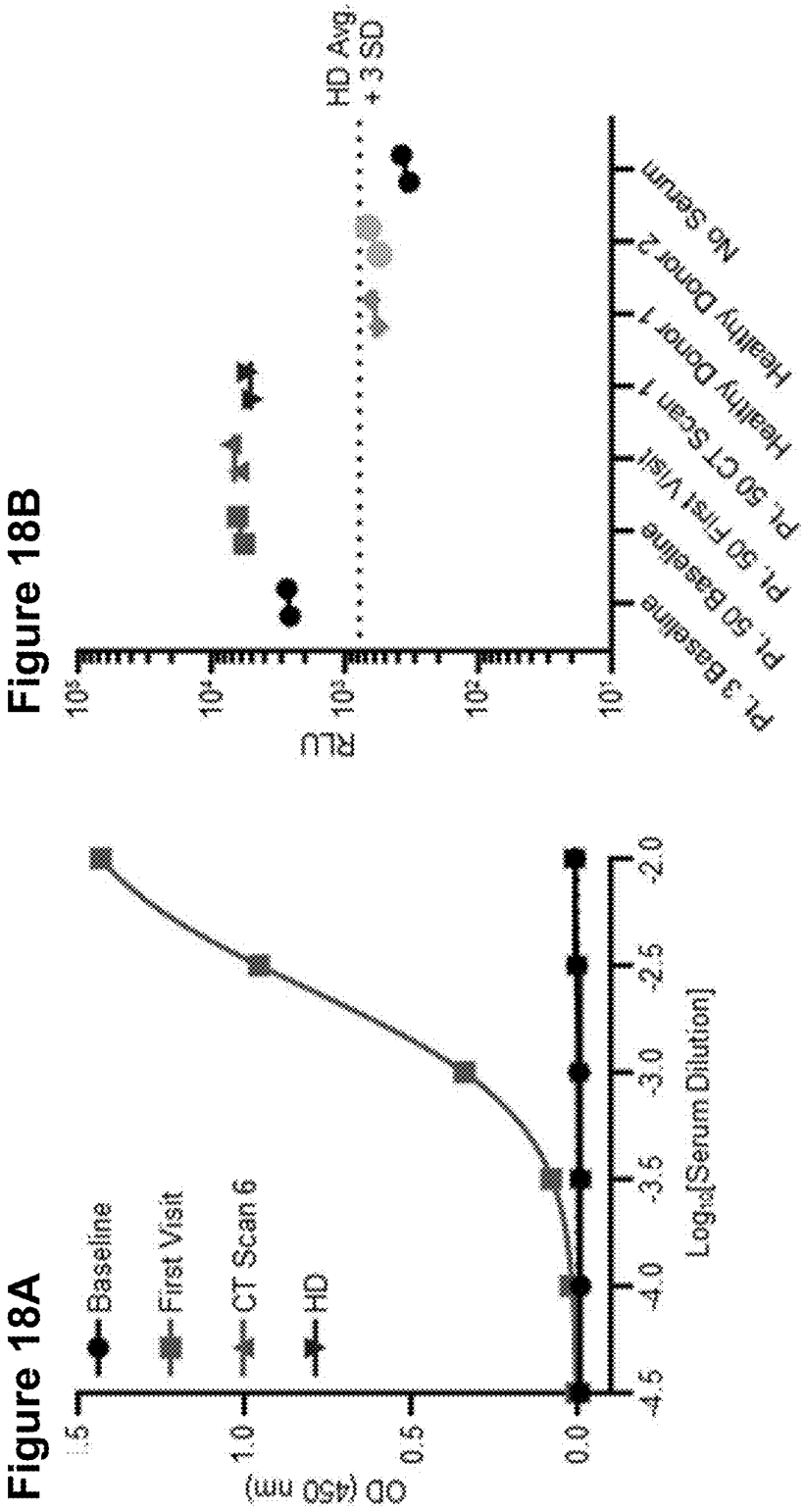


Figure 18A
Baseline
First Visit
CT Scan 6
HD
OD (450 nm)
1.5
1.0
0.5
0.0
-4.5
-4.0
-3.5
-3.0
-2.5
-2.0
Log[Serum Dilution]
Figure 18B
HD Avg. + 3 SD
RLU
10^5
10^4
10^3
10^2
10^1
Pt. 3 Baseline
Pt. 50 Baseline
Pt. 50 First Visit
Pt. 50 CT Scan 1
Healthy Donor 1
Healthy Donor 2
No Serum

Figure 18

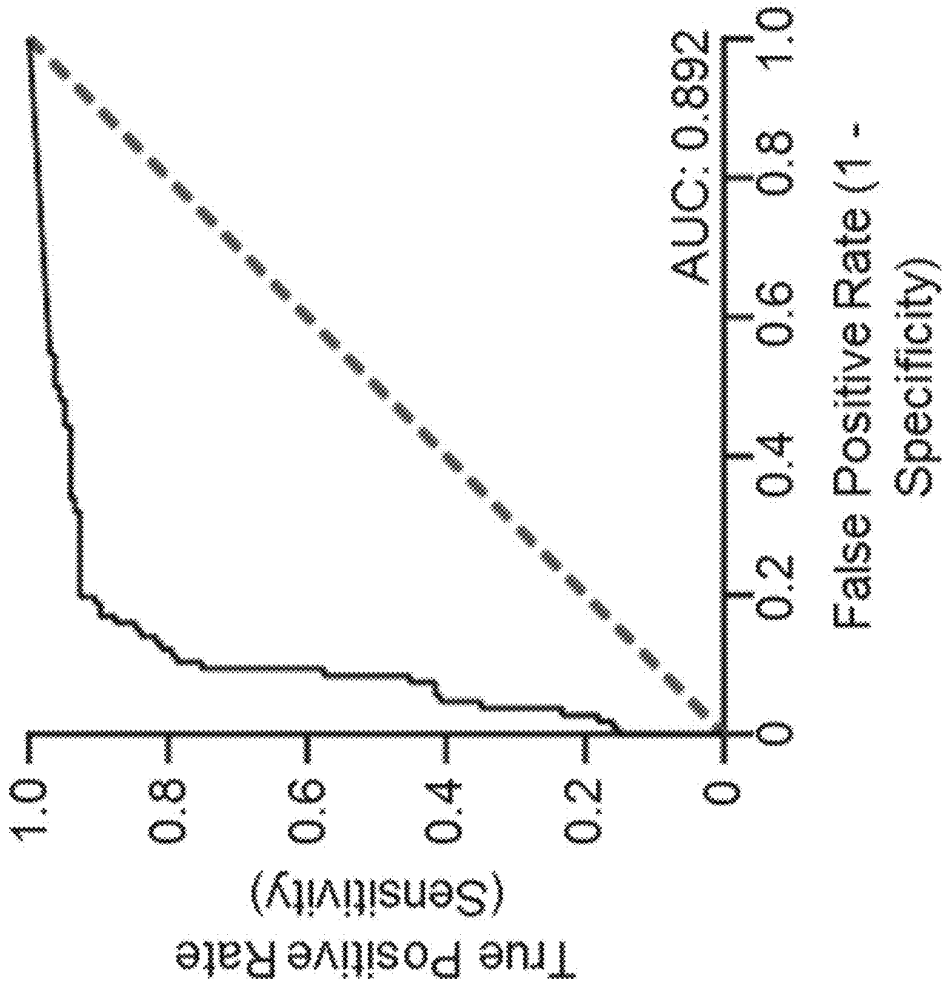

True Positive Rate (Sensitivity)
1.0
0.8
0.6
0.4
0.2
0
0
0.2
0.4
0.6
0.8
1.0
False Positive Rate (1 - Specificity)
AUC: 0.892

Figure 19

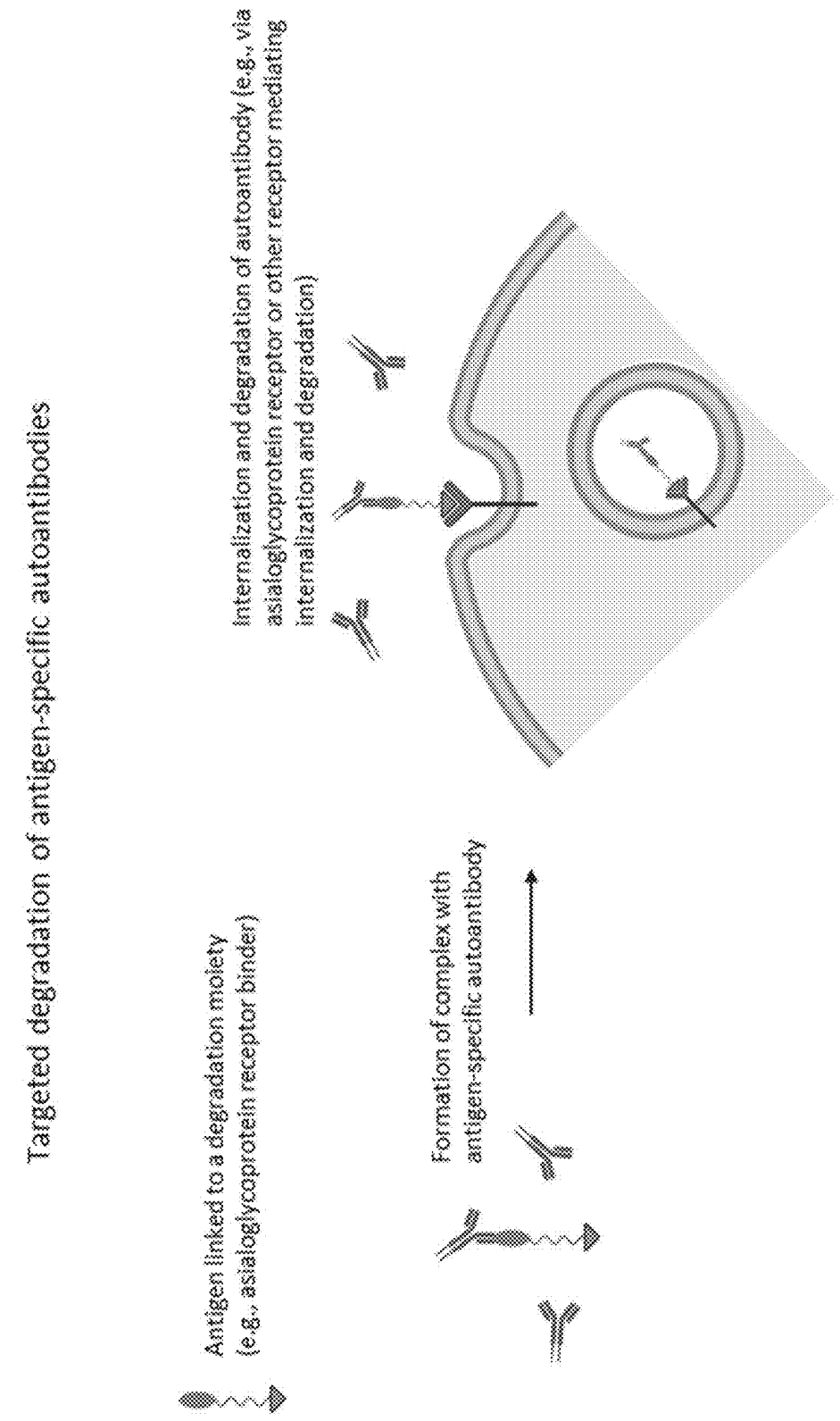

Targeted degradation of antigen-specific autoantibodies
Antigen linked to a degradation moiety (e.g., asialoglycoprotein receptor binder)
Formation of complex with antigen-specific autoantibody
Internalization and degradation of autoantibody (e.g., via asialoglycoprotein receptor or other receptor mediating internalization and degradation)

Figure 20

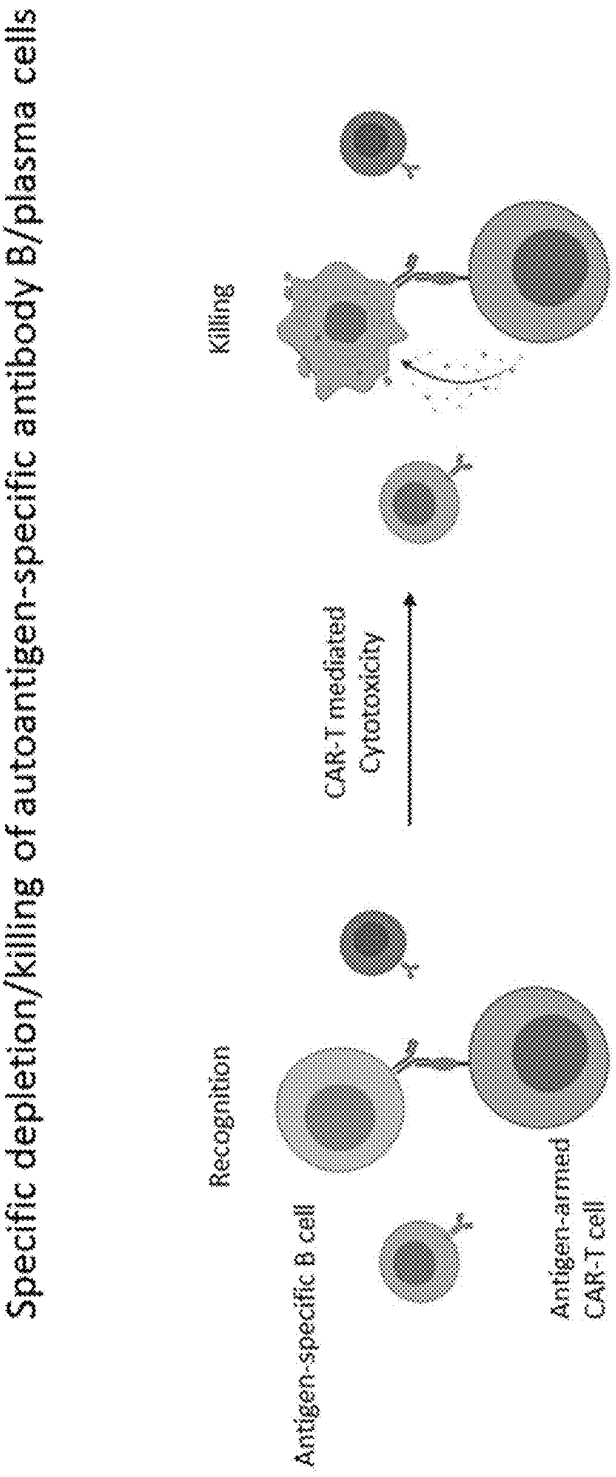

Specific depletion/killing of autoantigen-specific antibody B/plasma cells
Recognition
Killing
CAR-T mediated Cytotoxicity
Antigen-specific B cell
Antigen-armed CAR-T cell

Figure 21

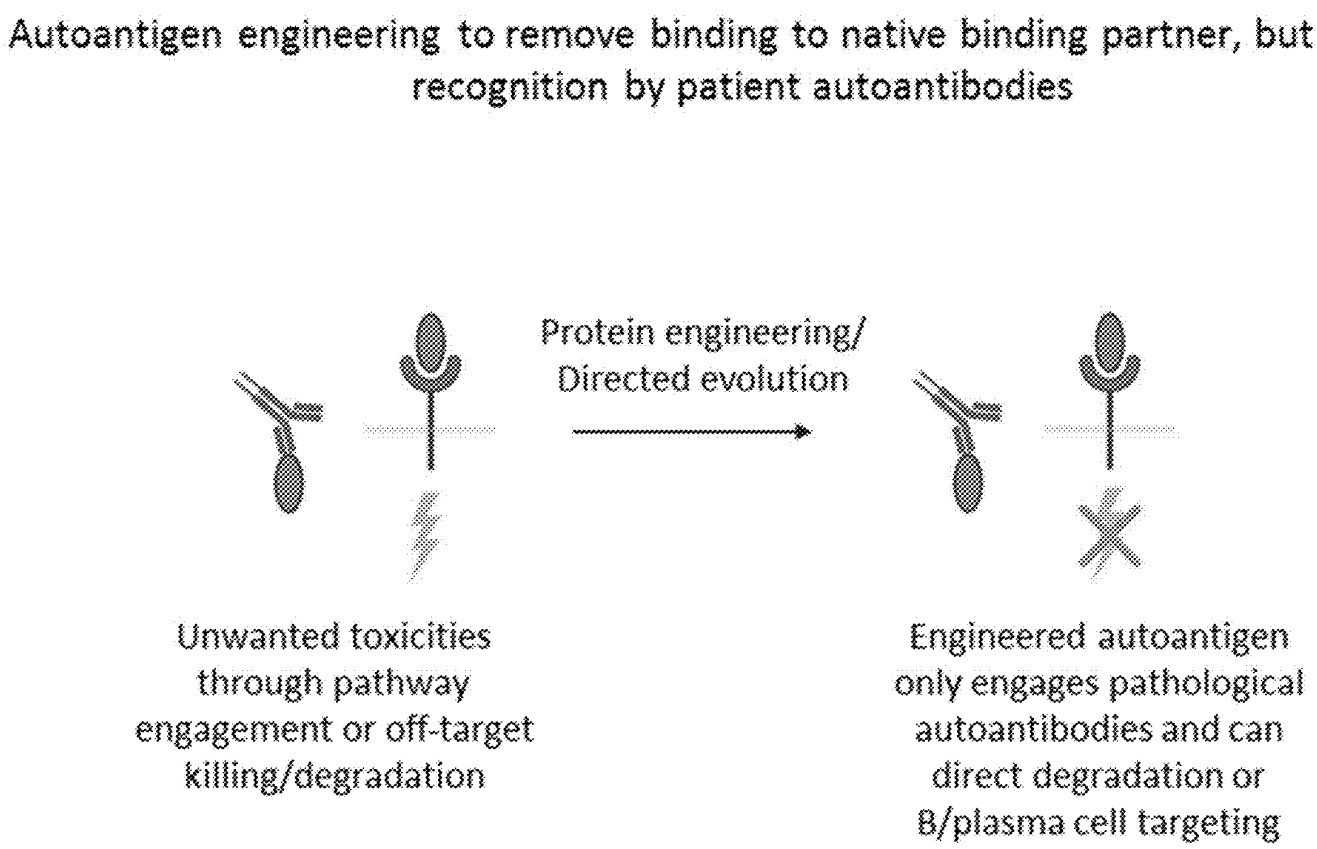

Autoantigen engineering to remove binding to native binding partner, but maintain recognition by patient autoantibodies
Protein engineering/
Directed evolution
Unwanted toxicities through pathway engagement or off-target killing/degradation
Engineered autoantigen only engages pathological autoantibodies and can direct degradation or B/plasma cell targeting

Figure 22

Antigen	Disease	# Candidate Samples Tested	Score Range	# Validated by ELISA or LIPS
IFNA17	APECED	14	6.79 - 8.91	14
IFNA8	APECED	14	5.22 - 7.60	14
IL22	APECED	14	5.02 - 7.60	14
GPHB5	APECED	13	3.03 - 8.53	13
BPIFA2	APECED	6	1.94 - 5.13	6
PNLIP	APECED	6	1.23 - 5.68	6
IFNL2	APECED	3	5.19 - 6.03	3
IL1A	COVID	5	7.36 - 9.03	4
LEP	COVID	6	4.67 - 8.47	4
CST5	COVID	4	5.12 - 8.76	3
IL13	COVID	4	1.67 - 5.73	3
CCL15	COVID	2	4.77 - 5.19	2
CD38	COVID	2	6.33 - 6.60	2
CNPY3	COVID	17	3.45 - 7.86	2
CXCL1	COVID	2	3.89 - 7.17	2
CXCL3	COVID	2	6.78 - 6.98	2
CXCL7	COVID	2	8.09 - 9.43	2
HCRTR2	COVID	5	4.86 - 7.65	2
IFNW1	COVID	5	6.09 - 9.03	2
TSLP	COVID	5	2.02 - 5.83	2
ACKR1	COVID	2	5.05 - 6.92	1
BAMBI	COVID	1	5.06	1
C1QB	COVID	1	4.89	1
CCL16	COVID	2	2.43 - 6.05	1
CNPY4	COVID	5	0.56 - 6.29	1
CSF2	COVID	1	8.53	1
FCMR	COVID	1	4.42	1
SLC2A12	COVID	2	5.22 - 5.40	1
IL18RAP	COVID	1	2.86	1
PDL1	NSCLC	8	5.41 - 9.54	8
IFNA5	NSCLC	8	6.91 - 9.35	8
MADCAM1	NSCLC	3	2.50 - 5.04	3
IL1A	NSCLC	4	1.12 - 2.12	1
VEGFB	SLE	10	1.67 - 8.88	10
IFNA17	SLE	8	1.85 - 10.33	8
IFNA8	SLE	7	1.13 - 8.92	4
FAS	SLE	6	1.73 - 4.95	4
EPYC	SLE	4	4.93 - 9.46	4
CSPG5	SLE	6	1.64 - 5.92	3
IL6	SLE	3	3.60 - 7.82	3
PDL2	SLE	4	2.43 - 9.69	2
IL4	SLE	2	5.78 - 6.09	2
CCL8	SLE	4	4.59 - 6.44	1
IL33	SLE	1	3.88	1
IL18RAP	SLE	1	3.3	1
IL16	SLE	1	4.03	1
LILRB4	SLE	1	3.85	1
ACVR2B	SLE	1	8.56	1
IER3	SLE	1	4.23	1

Figure 23

RAPID EXTRACELLULAR ANTIBODY PROFILING (REAP) FOR THE DISCOVERY AND USE OF SAID ANTIBODIES

CROSS REFERENCE TO RELATED APPLICATIONS

[0001] This application claims priority to U.S. Provisional Application No. 62/992,484, filed Mar. 20, 2020 which is hereby incorporated by reference herein in its entirety.

STATEMENT REGARDING FEDERALLY SPONSORED RESEARCH OR DEVELOPMENT

[0002] This invention was made with government support under CA196530 awarded by National Institutes of Health. The government has certain rights in the invention.

BACKGROUND OF THE INVENTION

[0003] Antibodies are natural products of the immune system that normally mediate host-defense against foreign pathogens. Auto-reactive antibodies that recognize against self-antigens play a major role in numerous facets of normal health and disease. For instance, autoantibodies underlie a wide range of autoimmune diseases, but they also contribute to anti-tumor immune responses against cancer. The precise targets of autoantibodies have been shown in many cases to determine the pathophysiology of disease, in both exacerbating and mitigating mechanisms. In some cases, autoantibodies of particular specificity may be diagnostic. In others, if the autoantibodies are functional and can exert immunomodulatory effects, they can drive disease pathogenesis or attenuate disease severity. Hence, identifying the precise molecular specificities of autoantibodies is critical for understanding the molecular basis for numerous diseases. Furthermore, knowledge of autoantibody reactivities may reveal new therapeutic disease targets, for instance by revealing anti-cancer antibody targets (e.g., endogenous anti-HER2 responses seen in breast cancer and anti-MUC1 in carcinoma) or immunosuppressive targets in autoimmune disease (e.g., endogenous anti-IFN-α in less severe cases of systemic lupus erythematosus). Autoantibodies themselves may represent therapeutic agents, given that they are fully human, recognize a native human antigen, and exert a desired therapeutic activity that can be inferred from clinical outcomes associated with the seroreactivity.

[0004] One major barrier in the identification of autoantibodies is limitations in modern autoantibody discovery methods. On one hand, current autoantibody detection methods that maximize sensitivity are limited in throughput, which forces autoantibody discovery to be done in a deductive process on the basis of well-known protein targets. On the other hand, current high-throughput autoantibody discovery methods that enable unbiased autoantibody detection, such as protein microarray or phage-based peptide display methods, do not effectively detect antibodies against extracellular and secreted proteins (the "exoproteome") due to the conformational nature of these antigens. This is a major limitation because the "exoproteome" contains the very proteins that reside topologically outside the cell and are actually accessible to circulating autoantibodies. As such, extracellular proteins constitute the most likely targets of functional autoantibodies.

[0005] Thus, there is a need in the art for a sensitive and high-throughput detection method of antibodies and targets thereof that can successfully detect autoantibodies against extracellular and secreted proteins. The present invention addresses this need.

BRIEF SUMMARY OF THE INVENTION

[0006] In one embodiment, the invention provides a method of identifying at least one polypeptide which binds to at least one antibody, wherein the method comprises:

[0007] (a) contacting a library of display cells or particles with a sample comprising at least one antibody, wherein the library of display cells comprises a plurality of cells or particles wherein together the plurality of cells or particles comprises nucleic acid molecules for expression of a plurality of extracellular proteins, secreted proteins or a combination thereof,

[0008] wherein each cell or particle of the plurality of cells or particles comprises a barcoded nucleic acid molecule, wherein each nucleic acid molecule comprises

[0009] i) a nucleotide sequence encoding a polypeptide of interest for display on the surface of the cell or particle; and

[0010] ii) a unique nucleotide barcode sequence;

[0011] (b) isolating one or more antibody-bound cell or particle;

[0012] (c) isolating at least one barcoded nucleic acid molecule from at least one cell or particle of step (b); and

[0013] (d) identifying the barcoded nucleic acid molecule, thereby identifying the associated encoded polypeptide as an antigen for binding by at least one antibody in the sample.

[0014] In one embodiment, the method of isolating one or more antibody-bound cell or particle comprises high-throughput magnetic separation.

[0015] In one embodiment, the method further comprises the step of:

[0016] (b') expanding the one or more isolated antibody-bound cell or particle.

[0017] In one embodiment, the method of identifying the barcoded nucleic acid molecule comprises at least one selected from the group consisting of amplifying the barcoded nucleic acid molecule and sequencing the barcoded nucleic acid molecule.

[0018] In one embodiment, the method comprises:

[0019] in step (b), isolating multiple antibody bound cells,

[0020] in step (c), isolating the barcoded nucleic acid molecules from the cells of step (b), and

[0021] in step (d), sequencing the isolated barcoded nucleic acid molecules, and identifying the associated encoded polypeptide as an antigen for binding by the antibody based on an enrichment of the number of reads of the associated barcode in the sequencing data as compared to a threshold level.

[0022] In one embodiment, the threshold level is selected from the group consisting of a predetermined threshold level, a statistically determined threshold, and a threshold level determined using z-scores.

[0023] In one embodiment, the library of display cells or particles comprises a library of barcoded nucleic acid molecules encoding at least one selected from an extracellular domain of a protein, an extracellular protein, and a secreted protein.

[0024] In one embodiment, the library of barcoded nucleic acid molecules comprises a plurality of nucleic acid molecules which together encode the human exoproteome.

[0025] In one embodiment, the library of barcoded nucleic acid molecules comprises at least one nucleic acid molecule encoding at least one polypeptide sequence selected from SEQ ID NO:1-3092.

[0026] In one embodiment, the library of barcoded nucleic acid molecules comprises a plurality of nucleic acid molecules which together encode each of SEQ ID NO:1-3092.

[0027] In one embodiment, the library of barcoded nucleic acid molecules comprises at least one nucleic acid molecule comprising a nucleotide sequence selected from SEQ ID NO:3093-6185.

[0028] In one embodiment, the library of barcoded nucleic acid molecules comprises a plurality of nucleic acid molecules which together comprise each of SEQ ID NO:3093-6185.

[0029] In one embodiment, the sample comprises a biological sample selected from the group consisting of a body fluid, blood, serum, plasma, cerebrospinal fluid, tissue, and any combination thereof.

[0030] In one embodiment, the sample comprises at least one antibody purified from a biological sample selected from the group consisting of a body fluid, blood, serum, plasma, cerebrospinal fluid, tissue, and any combination thereof.

[0031] In one embodiment, the at least one antibody is purified from a biological sample by at least one selected from the group consisting of:

[0032] (a) affinity purification for a specific antibody isotype of interest, and

[0033] (b) contacting the sample with a control cell or particle comprising an empty expression plasmid.

[0034] In one embodiment, the sample is from a subject diagnosed as having a disease or disorder, and whereby the antigen for binding by at least one antibody is a disease-associated antigen.

[0035] In one embodiment, the antibody is an autoantibody.

[0036] In one embodiment, the antibody is associated with an autoimmune disease or disorder, cancer, inflammatory disease or disorder, metabolic disease or disorder, neurodegenerative disease or disorder, organ tissue rejection, organ transplant rejection, or any combination thereof.

[0037] In one embodiment, the invention relates to a method of preventing or treating a disease or disorder in a subject in need thereof; the method comprising administering a therapeutic agent to the subject, wherein the therapeutic agent comprises an agent for modifying the level or reactivity of at least one antibody which interacts with at least one antigen selected from the group consisting of the antigens as set forth in SEQ ID NO:1-3092.

[0038] In one embodiment, the antigen is identified as a target for at least one antibody according to a method comprising:

[0039] (a) contacting a library of display cells or particles with a sample comprising at least one antibody, wherein the library of display cells comprises a plurality of cells or particles wherein together the plurality of cells or particles comprises nucleic acid molecules for expression of a plurality of extracellular proteins, secreted proteins or a combination thereof,

[0040] wherein each cell or particle of the plurality of cells or particles comprises a barcoded nucleic acid molecule, wherein each nucleic acid molecule comprises

[0041] i) a nucleotide sequence encoding a polypeptide of interest for display on the surface of the cell or particle; and

[0042] ii) a unique nucleotide barcode sequence;

[0043] (b) isolating one or more antibody-bound cell or particle;

[0044] (c) isolating at least one barcoded nucleic acid molecule from at least one cell or particle of step (b); and

[0045] (d) identifying the barcoded nucleic acid molecule, thereby identifying the associated encoded polypeptide as an antigen for binding by at least one antibody in the sample

[0046] In one embodiment, the at least one antigen is selected from the group consisting of an antigen as set forth in Table 3, and further wherein the disease or disorder is the disease or disorder associated with the antigen as set forth in Table 3.

[0047] In one embodiment, the therapeutic agent comprises an agent for decreasing the level or reactivity of at least one antibody with at least one disease-associated antigen selected from the group consisting of the antigens as set forth in Table 3.

[0048] In one embodiment, the at least one antigen is selected from the group consisting of an antigen as set forth in Table 6, and further wherein the disease or disorder is the disease or disorder associated with the antigen as set forth in Table 6.

[0049] In one embodiment, the therapeutic agent comprises a therapeutically effective amount of at least agent that reduces or eliminates at least one antibody.

[0050] In one embodiment, the therapeutic agent comprises a composition comprising an antigen selected from the group consisiting of an antigen as set forth in SEQ

[0051] ID NO:1-3092 linked to a domain for endocytosis and degradation.

[0052] In one embodiment, the therapeutic agent comprises a composition comprising an antigen selected from the group consisiting of an antigen as set forth in Table 6 linked to a domain for endocytosis and degradation.

[0053] In one embodiment, the domain for endocytosis and degradation comprises an asialoglycoprotein receptor binding domain.

[0054] In one embodiment, the agent that reduces or eliminates at least one antibody comprises a molecule for targeting and destruction of at least one antibody-expressing cell.

[0055] In one embodiment, the agent comprises a chimeric antigen receptor (CAR) T cell expressing an antigen selected from the group consisting of an antigen as set forth in SEQ ID NO:1-3092, or a fragment thereof.

[0056] In one embodiment, the CAR T cell expresses an antigen selected from the group consisting of an antigen as set forth in Table 6.

[0057] In one embodiment, the therapeutic agent comprises an agent for increasing the level or reactivity of at least one antibody with at least one disease-associated antigen selected from the group consisting of the antigens as set forth in Table 3.

[0058] In one embodiment, the at least one antigen is selected from the group consisting of an antigen as set forth in Table 5, and further wherein the disease or disorder is the disease or disorder associated with the antigen as set forth in Table 5.

[0059] In one embodiment, the therapeutic agent comprises a therapeutically effective amount of at least one antibody, or fragment thereof, wherein the antibody specifically binds to a disease-associated antigen.

[0060] In one embodiment, the disease or disorder is selected from the group consisting of an autoimmune disease or disorder, cancer, inflammatory disease or disorder, metabolic disease or disorder, neurodegenerative disease or disorder, organ tissue rejection, organ transplant rejection, or any combination thereof.

[0061] In one embodiment, the disease or disorder is selected from the group consisting of antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis, autoimmune polyendocrinopathy candidiasis ecto-dermal dystrophy, antiphospholipid antibody syndrome, chronic inflammatory demyelinating polyradiculoneuropathy, cutaneous lupus erythematosus, COVID-19, drug-induced lupus, dermatomyositis, glomerulonephritis, a disease or disorder associated with kidney transplant, malaria, mixed connective tissue disease, myasthenia gravis, malignant melanoma, neuromyelitis optica, non-small cell lung cancer, pediatric autoimmune neuropsychiatric disorders associated with streptococcal infections, systemic lupus erythematosus, sjogren's syndrome, scleroderma, susac syndrome, undifferentiated connective tissue disease, and any combination thereof.

[0062] In one embodiment, the invention relates to a method of diagnosing, assessing the prognosis, or assessing the effectiveness of treatment of a disease or disorder in a subject in need thereof, the method comprising assessing the level or reactivity of at least one antibody which interacts with at least one antigen selected from the group consisting of an antigen as set forth in SEQ ID NO:1-3092.

[0063] In one embodiment, the at least one antigen is selected from the group consisting of an antigen as set forth in Table 3, and further wherein the disease or disorder is the disease or disorder associated with the antigen as set forth in Table 3.

[0064] In one embodiment, the at least one antigen is selected from the group consisting of an antigen as set forth in Table 4, and further wherein the disease or disorder is the disease or disorder associated with the antigen as set forth in Table 4.

[0065] In one embodiment, the disease or disorder is selected from the group consisting of an autoimmune disease or disorder, cancer, inflammatory disease or disorder, metabolic disease or disorder, neurodegenerative disease or disorder, organ tissue rejection, organ transplant rejection, or any combination thereof.

[0066] In one embodiment, the disease or disorder is selected from the group consisting of antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis, autoimmune polyendocrinopathy candidiasis ecto-dermal dystrophy, antiphospholipid antibody syndrome, chronic inflammatory demyelinating polyradiculoneuropathy, cutaneous lupus erythematosus, COVID-19, drug-induced lupus, dermatomyositis, glomerulonephritis, a disease or disorder associated with kidney transplant, malaria, mixed connective tissue disease, myasthenia gravis, malignant melanoma, neuromyelitis optica, non-small cell lung cancer, pediatric autoimmune neuropsychiatric disorders associated with streptococcal infections, systemic lupus erythematosus, sjogren's syndrome, scleroderma, susac syndrome, undifferentiated connective tissue disease, and any combination thereof.

[0067] In one embodiment, the invention relates to a composition comprising an antigen selected from the group consisting of an antigen as set forth in SEQ ID NO:1-3092, or a fragment thereof, linked to a domain for endocytosis, degradation, or a combination thereof.

[0068] In one embodiment, the composition comprises an antigen selected from the group consisting of an antigen as set forth in Table 6 linked to a domain for endocytosis, degradation, or a combination thereof.

[0069] In one embodiment, the domain for endocytosis, degradation, or a combination thereof comprises an asialoglycoprotein receptor binding domain.

[0070] In one embodiment, the invention relates to a composition for targeting and destruction of at least one antibody-expressing cell comprising an antigen selected from the group consisting of an antigen as set forth in SEQ ID NO:1-3092, or a fragment thereof.

[0071] In one embodiment, the agent comprises a chimeric antigen receptor (CAR)

[0072] T cell expressing an antigen as set forth in SEQ ID NO:1-3092, or a fragment thereof. In one embodiment, the CAR T cell expresses an antigen selected from the group consisting of an antigen as set forth in Table 6.

BRIEF DESCRIPTION OF THE DRAWINGS

[0073] The following detailed description of embodiments of the invention will be better understood when read in conjunction with the appended drawings. It should be understood that the invention is not limited to the precise arrangements and instrumentalities of the embodiments shown in the drawings.

[0074] FIG. **1** depicts a REAP schematic. Simplified schematic of REAP. Antibodies are incubated with a genetically-barcoded yeast library displaying members of the exoproteome in 96-well microtiter plates. Antibody bound yeast are enriched by magnetic column-based sorting and enrichment is quantified by next-generation sequencing.

[0075] FIG. **2**A and FIG. **2**B depict exemplary experimental data demonstrating that REAP detects known targets of monoclonal antibodies. A panel of nine monoclonal antibodies were screened using REAP. FIG. **2**A depicts a heatmap of results from REAP screen of nine monoclonal antibodies. Only relevant monoclonal antibody targets (gene names) are displayed. FIG. **2**B depicts a representative sample from the screen. Monoclonal antibody target is highlighted in red and labelled. Background subtraction was performed by subtracting the score of a selection performed with beads and secondary alone. Scores below the average background level are not shown.

[0076] FIG. **3** depicts exemplary experimental data demonstrating a REAP screen of APECED patient samples. Reactivities uncovered in a REAP screen of 77 APECED patients and 20 healthy controls. Heatmap of REAP scores is depicted. Antigen groups were manually categorized.

[0077] FIG. **4** depicts exemplary experimental data demonstrating the concordance of REAP results and clinical anti-GIF autoantibody tests in APECED patients. Violin plot

of GIF REAP scores in APECED samples stratified by intrinsic factor clinical autoantibody test results.

[0078] FIG. **5**A and FIG. **5**B depict exemplary experimental data demonstrating a REAP screen with serial dilutions of APECED 19 sample. REAP screen conducted with half log serial dilutions of APECED 19 IgG. Results are composed of technical duplicates. Only results from known autoantibody targets in APECED are depicted. Results are depicted as (FIG. **5**A) the uncapped score of reactivities at various concentrations of APECED IgG and as (FIG. **5**B) normalized, dose-response curves of reactivities where reactivities are measured by log 2 fold enrichment rather than score. Curves were fit using a sigmoidal 4 parameter logistic curve. Error bars represent standard deviation.

[0079] FIG. **6**A and FIG. **6**B depict exemplary experimental data demonstrating that REAP sensitivity can exceed that of ELISA. REAP (FIG. **6**A) versus ELISA (FIG. **6**B) dose-response curve comparison for APECED 19 autoantibodies against four proteins. Results are the averages of technical duplicates. Curves were fit using a sigmoidal 4 parameter logistic curve. Error bars represent standard deviation.

[0080] FIG. **7** depicts exemplary data demonstrating that REAP exhibits high reproducibility. Box plot of Log 2[fold enrichment] R2 coefficient of determination values between technical replicates of APECED patients screened in FIG. **3**.

[0081] FIG. **8** depicts exemplary data demonstrating a REAP screen of SLE patient samples. Reactivities uncovered in a REAP screen of a cohort of 106 unique SLE patients spanning 155 samples and 20 healthy controls. Heatmap of REAP scores is depicted where each column is a unique patient. For patients with longitudinal samples, the maximum REAP score for each given reactivity is shown. Antigen groups were manually categorized. Patients are ordered from left to right by increasing SLEDAI score. White stars symbolize detection of a therapeutic antibody. Score was artificially capped at 7 to aid visualization.

[0082] FIG. **9**A through FIG. **9**E depict exemplary data demonstrating the biochemical and functional validation of novel SLE autoantibodies. FIG. **9**A depicts an anti-PD-L2 pan-IgG ELISAs conducted with serial dilutions of SLE or control serum. FIG. **9**D depicts an anti-IL-33 pan-IgG ELISAs conducted with serial dilutions of SLE or control serum. FIG. **9**B depicts a schematic and FIG. **9**C depicts results of PD-L2 blocking assay conducted with serial dilutions of serum from a control and the SLE patient in FIG. **9**A. FIG. **9**E depicts a schematic and FIG. **9**F depicts results of IL-33 neutralization assay conducted with serial dilutions of IgG from a control and the SLE patient in FIG. **9**D. All error bars in this figure represent standard deviation.

[0083] FIG. **10** depicts exemplary data demonstrating a REAP screen of immunotherapy-treated NSCLC patients. Reactivities uncovered in a REAP screen of 63 immunotherapy-treated non-small cell lung cancer (NSCLC) patients and 16 healthy donors. Of the 63 patients, longitudinal samples for 57 patients were available. Results are composed of technical duplicates. Longitudinal reactivities for each patient were collapsed and each reactivity was classified as increased, decreased, constant, therapeutic. The maximum reactivity for each protein in the healthy donor group is shown. Only proteins reactivities that developed or regressed in at least one patient are shown. Maximum score is defined as the maximum score of the protein at any time point. Score was not artificially capped. Increased responses are defined as those where the score of the protein increased by 2 or more at any time point after the first screened time point. Decreased responses are defined as those where the maximum score of the protein after the first screened time point was decreased by 2 or more from the initial score. Therapeutic responses are those where the patient was known to be receiving a therapeutic antibody against that protein. Patients are grouped by response to immunotherapy treatment.

[0084] FIG. **11** depicts exemplary data demonstrating that REAP scores can accurately reflect longitudinal changes in autoantibodies. Single point anti-OX40 isotype specific ELISAs conducted with serum from patient 3 at all available time points. REAP reactivity scores are depicted below with score artificially capped at 5. 1:100 serum dilutions were used. Results are averages of technical duplicates.

[0085] FIG. **12** depicts exemplary data demonstrating that unique sample clusters can be identified from REAP data. UMAP analysis of scores from previously described REAP screens of NSCLC, SLE, and UCTD patients. Each dot on the plot represents one patient sample at one time point. UMAP analysis was performed and visualized using a custom R script.

[0086] FIG. **13** depicts a REAP screen of scleroderma patients. Reactivities uncovered in a REAP screen of limited cutaneous systemic sclerosis, diffuse cutaneous systemic sclerosis patients, and healthy controls. Heatmap of REAP scores is depicted where each column is a unique patient. Antigen groups were manually categorized. Patient modified Rodnan skin score (mRSS), disease duration in months, and age in years is displayed below the heatmap.

[0087] FIG. **14** depicts immune-targeting autoantibody reactivities uncovered in COVID-19 patients. Heatmap of REAP scores for autoantibodies against immune-related antigens uncovered in a REAP screen of 194 COVID-19 patients. Antigen groups were manually categorized. Patients were stratified by disease severity. The negative group consists of control samples from uninfected healthcare workers. Abbreviations are as follows: asym: asymptomatic. Score was artificially capped at 7 to aid visualization.

[0088] FIG. **15** depicts tissue-targeting autoantibody reactivities uncovered in COVID-19 patients. Heatmap of REAP scores for autoantibodies against tissue-associated antigens uncovered in a REAP screen of COVID-19 patients. Antigen groups were manually categorized. Patients were stratified by disease severity. The negative group consists of control samples from uninfected healthcare workers. Abbreviations are as follows: asym—asymptomatic. Score was artificially capped at 7 to aid visualization.

[0089] FIG. **16** depicts a REAP screen of immunotherapy-treated melanoma patients. Heatmap of REAP score for autoantibodies identified in a screen of 222 CPI-treated melanoma patients and 62 healthy control samples. Score was artificially capped at 7 to aid visualization.

[0090] FIG. **17** depicts a REAP screen of kidney transplant patients. Heatmap of REAP score for immune-related autoantibodies identified in a screen of 108 kidney transplant patients with pre and post transplantation serum samples. Longitudinal reactivities for each patient were collapsed and each reactivity was classified as increased, decreased, stable. Patients are grouped by rejection and infection status after transplantation.

[0091] FIG. **18** depicts representative ELISA and LIPS validation data. FIG. **18**A depicts an anti-OX40 autoanti-

body enzyme-linked immunosorbent assay (ELISA) titrations of NSCLC patient 3 serum at different time points. Reactivities were considered validated if average optical density (OD) at 1:100 serum dilution was at least 3 healthy donor standard deviations above the average 1:100 healthy donor serum dilution OD. Results are averages of technical duplicates. Error bars represent standard deviation. FIG. **18**B depicts an anti-VEGFB autoantibody single-point luciferase immunoprecipitation systems (LIPS) with various NSCLC patient serum and healthy donor serum. 1:100 serum dilutions were used. Reactivities were considered validated if average relative light units (RLU) was at least 3 healthy donor standard deviations above the average healthy donor RLU.

[0092] FIG. **19** depicts an analysis of the sensitivity and specificity of REAP. An ROC curve based on orthogonal validation data of APECED and SLE screen reactivities is shown. Orthogonal validation was performed with LIPS or ELISA. For ELISA and LIPS, valid reactivities were defined as those 3 standard deviations above the healthy donor average for a given protein in each assay. ROC analysis was performed using 247 test pairs across 25 different proteins.

[0093] FIG. **20** depicts a schematic for targeted degradation of autoantigen-specific antibodies. Autoantigens are conjugated with a degradation moiety (e.g., a binding partner of the asialoglycoprotein receptor or other endocytosis promoting receptor). Once pathogenic autoantibodies bind to their respective autoantigen, they will be removed from circulation by endocytosis and degradation in the lysosome or other intracellular compartment.

[0094] FIG. **21** depicts a schematic for removal of autoantigen-specific B/plasma cells. CAR-T or CAR-NK cells are designed such that instead of an scFv targeting domain, instead, an autoantigen identified via REAP is used to direct CAR activity. Once CAR-T/NK cells bind to autoreactive B cells (that present B cell receptors/immunoglobulin on their plasma membrane), the CAR-T/NK cells will initiate cytotoxic programs that kill the corresponding autoreactive B/plasma cell.

[0095] FIG. **22** depicts schematic for autoantigen engineering to remove unwanted interaction with endogenous binding partners. To avoid unwanted interaction with their native binding partners, autoantigens are engineered to maintain autoantibody binding, but avoid interaction with their native binding partners. For example, a type I interferon engineered with decreasing binding to its receptors IFNAR1 and IFNAR2, but with maintained interaction with anti-interferon autoantibodies. The engineered autoantigens can subsequently be used for targeted autoantibody degradation (FIG. **20**) or targeted B cell removal (FIG. **21**).

[0096] FIG. **23** depicts a summary of validation data. ELISA or LIPS validation data for reactivities identified in REAP.

DETAILED DESCRIPTION

[0097] The present invention relates to methods for the sensitive and high-throughput detection of various antibodies and targets thereof. For example, in one aspect, methods of the present invention identify target extracellular, secreted, and/or transmembrane proteins that specifically bind to various antibodies of interest. In another aspect, the present invention provides methods of preventing or treating diseases or disorders associated with antibodies and/or targets thereof detected via the high-throughput detection methods of the present invention. In various embodiments, the present invention provides methods of diagnosing, assessing prognosis, and assessing the effectiveness of treatments of diseases or disorders associated with antibodies detected via the high-throughput detection methods of the present invention. In another aspect, the present invention provides methods of predicting a response to a therapy. In another aspect, the present invention provides methods of alleviating toxicity of a cancer treatment.

Definitions

[0098] Unless defined otherwise, all technical and scientific terms used herein have the same meaning as commonly understood by one of ordinary skill in the art to which this invention belongs.

[0099] As used herein, each of the following terms has the meaning associated with it in this section.

[0100] The articles "a" and "an" are used herein to refer to one or to more than one (i.e., to at least one) of the grammatical object of the article. By way of example, "an element" means one element or more than one element.

[0101] The term "about" as used herein when referring to a measurable value such as an amount, a temporal duration, and the like, is meant to encompass variations of ±20%, ±10%, ±5%, ±1%, or ±0.1% from the specified value, as such variations are appropriate to perform the disclosed methods.

[0102] The term "antibody," as used herein, refers to an immunoglobulin molecule which is able to specifically bind to a specific epitope of an antigen. Antibodies can be intact immunoglobulins derived from natural sources, or from recombinant sources and can be immunoreactive portions of intact immunoglobulins. The antibodies in the present invention may exist in a variety of forms including, for example, polyclonal antibodies, monoclonal antibodies, intracellular antibodies ("intrabodies"), Fv, Fab, Fab', F(ab)2 and F(ab')2, as well as single chain antibodies (scFv), heavy chain antibodies, such as camelid antibodies, and humanized antibodies (Harlow et al., 1999, Using Antibodies: A Laboratory Manual, Cold Spring Harbor Laboratory Press, NY; Harlow et al., 1989, Antibodies: A Laboratory Manual, Cold Spring Harbor, New York; Houston et al., 1988, Proc. Natl. Acad. Sci. USA 85:5879-5883; Bird et al., 1988, Science 242:423-426).

[0103] The term "antibody fragment" refers to at least one portion of an intact antibody, or recombinant variants thereof, and refers to the antigen binding domain, e.g., an antigenic determining variable region of an intact antibody, that is sufficient to confer recognition and specific binding of the antibody fragment to a target, such as an antigen.

[0104] By the term "synthetic antibody" as used herein, is meant an antibody which is generated using recombinant DNA technology, such as, for example, an antibody expressed by a bacteriophage. The term should also be construed to mean an antibody which has been generated by the synthesis of a DNA molecule encoding the antibody and which DNA molecule expresses an antibody protein, or an amino acid sequence specifying the antibody, wherein the DNA or amino acid sequence has been obtained using synthetic DNA or amino acid sequence technology which is available and well known in the art.

[0105] A "humanized antibody" refers to a type of engineered antibody having its CDRs derived from a non-human donor immunoglobulin, the remaining immunoglobulin-de-

rived parts of the molecule being derived from one (or more) human immunoglobulin(s). In addition, framework support residues may be altered to preserve binding affinity (see, e.g., 1989, Queen et al., Proc. Natl. Acad Sci USA, 86:10029-10032; 1991, Hodgson et al., Bio/Technology, 9:421). A suitable human acceptor antibody may be one selected from a conventional database, e.g., the KABAT database, Los Alamos database, and Swiss Protein database, by homology to the nucleotide and amino acid sequences of the donor antibody. A human antibody characterized by a homology to the framework regions of the donor antibody (on an amino acid basis) may be suitable to provide a heavy chain constant region and/or a heavy chain variable framework region for insertion of the donor CDRs. A suitable acceptor antibody capable of donating light chain constant or variable framework regions may be selected in a similar manner. It should be noted that the acceptor antibody heavy and light chains are not required to originate from the same acceptor antibody. The prior art describes several ways of producing such humanized antibodies (see for example EP-A-0239400 and EP-A-054951).

[0106] A "chimeric antibody" refers to a type of engineered antibody which contains a naturally-occurring variable region (light chain and heavy chains) derived from a donor antibody in association with light and heavy chain constant regions derived from an acceptor antibody.

[0107] The term "donor antibody" refers to an antibody (monoclonal, and/or recombinant) which contributes the amino acid sequences of its variable regions, CDRs, or other functional fragments or analogs thereof to a first immunoglobulin partner, so as to provide the altered immunoglobulin coding region and resulting expressed altered antibody with the antigenic specificity and neutralizing activity characteristic of the donor antibody.

[0108] The term "acceptor antibody" refers to an antibody (monoclonal and/or recombinant) heterologous to the donor antibody, which contributes all (or any portion, but in some embodiments all) of the amino acid sequences encoding its heavy and/or light chain framework regions and/or its heavy and/or light chain constant regions to the first immunoglobulin partner. In certain embodiments a human antibody is the acceptor antibody.

[0109] By the term "recombinant antibody" as used herein, is meant an antibody which is generated using recombinant DNA technology, such as, for example, an antibody expressed by a bacteriophage or yeast cell expression system. The term should also be construed to mean an antibody which has been generated by the synthesis of a DNA molecule encoding the antibody and which DNA molecule expresses an antibody protein, or an amino acid sequence specifying the antibody, wherein the DNA or amino acid sequence has been obtained using recombinant DNA or amino acid sequence technology which is available and well known in the art.

[0110] An "antibody heavy chain," as used herein, refers to the larger of the two types of polypeptide chains present in antibody molecules in their naturally occurring conformations, and which normally determines the class to which the antibody belongs.

[0111] An "antibody light chain," as used herein, refers to the smaller of the two types of polypeptide chains present in antibody molecules in their naturally occurring conformations. Kappa (κ) and lambda (λ) light chains refer to the two major antibody light chain isotypes.

[0112] As used herein, "antigen-binding domain" means that part of the antibody, recombinant molecule, the fusion protein, or the immunoconjugate of the invention which recognizes the target or portions thereof.

[0113] The term "antigen" or "Ag" as used herein is defined as a molecule that provokes an adaptive immune response. This immune response may involve either antibody production, or the activation of specific immunogenically-competent cells, or both. The skilled artisan will understand that any macromolecule, including virtually all proteins or peptides, can serve as an antigen. Furthermore, antigens can be derived from recombinant or genomic DNA or RNA. A skilled artisan will understand that any DNA or RNA, which comprises a nucleotide sequence or a partial nucleotide sequence encoding a protein that elicits an adaptive immune response therefore encodes an "antigen" as that term is used herein. Furthermore, one skilled in the art will understand that an antigen need not be encoded solely by a full-length nucleotide sequence of a gene. It is readily apparent that the present invention includes, but is not limited to, the use of partial nucleotide sequences of more than one gene and that these nucleotide sequences are arranged in various combinations to elicit the desired immune response. Moreover, a skilled artisan will understand that an antigen need not be encoded by a "gene" at all. It is readily apparent that an antigen can be generated synthesized or can be derived from a biological sample. Such a biological sample can include, but is not limited to a tissue sample, tumor sample, cell, biological fluid, body fluid, blood, serum, plasma, tissue, or any combination thereof.

[0114] As used herein, the terms "targeting domain", "targeting moiety", or "targeting group" are used interchangeably and refer to all molecules capable of specifically binding to a particular target molecule and forming a bound complex as described above. Thus, the ligand and its corresponding target molecule form a specific binding pair.

[0115] By the term "specifically binds," as used herein with respect to an antibody, is meant an antibody which recognizes a specific antigen, but does not substantially recognize or bind other molecules in a sample. For example, an antibody that specifically binds to an antigen from one species may also bind to that antigen from one or more other species. But, such cross-species reactivity does not itself alter the classification of an antibody as specific. In another example, an antibody that specifically binds to an antigen may also bind to different allelic forms of the antigen. However, such cross reactivity does not itself alter the classification of an antibody as specific. In some instances, the terms "specific binding" or "specifically binding," can be used in reference to the interaction of an antibody, a protein, or a peptide with a second chemical species, to mean that the interaction is dependent upon the presence of a particular structure (e.g., an antigenic determinant or epitope) on the chemical species; for example, an antibody recognizes and binds to a specific protein structure rather than to proteins generally. If an antibody is specific for epitope "A", the presence of a molecule containing epitope A (or free, unlabeled A), in a reaction containing labeled "A" and the antibody, will reduce the amount of labeled A bound to the antibody.

[0116] The term "transfected" or "transformed" or "transduced" as used herein refers to a process by which exogenous nucleic acid is transferred or introduced into the host

cell. A "transfected" or "transformed" or "transduced" cell is one which has been transfected, transformed or transduced with exogenous nucleic acid. The cell includes the primary subject cell and its progeny.

[0117] The phrase "under transcriptional control" or "operatively linked" as used herein means that the promoter is in the correct location and orientation in relation to a polynucleotide to control the initiation of transcription by RNA polymerase and expression of the polynucleotide.

[0118] The term "operably linked" refers to functional linkage between a regulatory sequence and a heterologous nucleic acid sequence resulting in expression of the latter. For example, a first nucleic acid sequence is operably linked with a second nucleic acid sequence when the first nucleic acid sequence is placed in a functional relationship with the second nucleic acid sequence. For instance, a promoter is operably linked to a coding sequence if the promoter affects the transcription or expression of the coding sequence. Generally, operably linked DNA or RNA sequences are contiguous and, where necessary to join two protein coding regions, in the same reading frame.

[0119] The term "adjuvant" as used herein is defined as any molecule to enhance an antigen-specific adaptive immune response.

[0120] "Immunogen" refers to any substance introduced into the body in order to generate an immune response. That substance can a physical molecule, such as a protein, or can be encoded by a vector, such as DNA, mRNA, or a virus.

[0121] "Immune response," as the term is used herein, means a process involving the activation and/or induction of an effector function in, by way of non-limiting examples, a T cell, B cell, natural killer (NK) cell, and/or an antigen-presenting cell (APC). Thus, an immune response, as would be understood by the skilled artisan, includes, but is not limited to, any detectable antigen-specific activation and/or induction of a helper T cell or cytotoxic T cell activity or response, production of antibodies, antigen presenting cell activity or infiltration, macrophage activity or infiltration, neutrophil activity or infiltration, and the like.

[0122] "Isolated" means altered or removed from the natural state. For example, a nucleic acid or a peptide naturally present in a living animal is not "isolated," but the same nucleic acid or peptide partially or completely separated from the coexisting materials of its natural state is "isolated." An isolated nucleic acid or protein can exist in substantially purified form, or can exist in a non-native environment such as, for example, a host cell.

[0123] As used herein, the terms "peptide," "polypeptide," and "protein" are used interchangeably, and refer to a compound comprised of amino acid residues covalently linked by peptide bonds. A protein or peptide must contain at least two amino acids, and no limitation is placed on the maximum number of amino acids that can comprise a protein's or peptide's sequence. Polypeptides include any peptide or protein comprising two or more amino acids joined to each other by peptide bonds. As used herein, the term refers to both short chains, which also commonly are referred to in the art as peptides, oligopeptides and oligomers, for example, and to longer chains, which generally are referred to in the art as proteins, of which there are many types. "Polypeptides" include, for example, biologically active fragments, substantially homologous polypeptides, oligopeptides, homodimers, heterodimers, variants of polypeptides, modified polypeptides, derivatives, analogs, fusion proteins, among others. The polypeptides include natural peptides, recombinant peptides, synthetic peptides, or a combination thereof.

[0124] A "nucleic acid" refers to a polynucleotide and includes poly-ribonucleotides and poly-deoxyribonucleotides. Nucleic acids according to the present invention may include any polymer or oligomer of pyrimidine and purine bases, preferably cytosine, thymine, and uracil, and adenine and guanine, respectively. (See Albert L. Lehninger, Principles of Biochemistry, at 793-800 (Worth Pub. 1982) which is herein incorporated in its entirety for all purposes). Indeed, the present invention contemplates any deoxyribonucleotide, ribonucleotide or peptide nucleic acid component, and any chemical variants thereof, such as methylated, hydroxymethylated or glucosylated forms of these bases, and the like. The polymers or oligomers may be heterogeneous or homogeneous in composition, and may be isolated from naturally occurring sources or may be artificially or synthetically produced. In addition, the nucleic acids may be DNA or RNA, or a mixture thereof, and may exist permanently or transitionally in single-stranded or double-stranded form, including homoduplex, heteroduplex, and hybrid states.

[0125] The term "DNA" as used herein is defined as deoxyribonucleic acid.

[0126] The term "recombinant DNA" as used herein is defined as DNA produced by joining pieces of DNA from different sources.

[0127] The term "recombinant polypeptide" as used herein is defined as a polypeptide produced by using recombinant DNA methods.

[0128] The term "RNA" as used herein is defined as ribonucleic acid.

[0129] The term "recombinant RNA" as used herein is defined as RNA produced by joining pieces of RNA from different sources.

[0130] As used herein, "conjugated" refers to covalent attachment of one molecule to a second molecule.

[0131] "Variant" as the term is used herein, is a nucleic acid sequence or a peptide sequence that differs in sequence from a reference nucleic acid sequence or peptide sequence respectively, but retains essential biological properties of the reference molecule. Changes in the sequence of a nucleic acid variant may not alter the amino acid sequence of a peptide encoded by the reference nucleic acid, or may result in amino acid substitutions, additions, deletions, fusions and truncations. Changes in the sequence of peptide variants are typically limited or conservative, so that the sequences of the reference peptide and the variant are closely similar overall and, in many regions, identical. A variant and reference peptide can differ in amino acid sequence by one or more substitutions, additions, deletions in any combination. A variant of a nucleic acid or peptide can be a naturally occurring such as an allelic variant, or can be a variant that is not known to occur naturally. Non-naturally occurring variants of nucleic acids and peptides may be made by mutagenesis techniques or by direct synthesis. In various embodiments, the variant sequence is at least 99%, at least 98%, at least 97%, at least 96%, at least 95%, at least 94%, at least 93%, at least 92%, at least 91%, at least 90%, at least 89%, at least 88%, at least 87%, at least 86%, at least 85% identical to the reference sequence.

[0132] As used herein, the term "identical" refers to two or more sequences or subsequences which are the same.

[0133] In addition, the term "substantially identical," as used herein, refers to two or more sequences which have a percentage of sequential units which are the same when compared and aligned for maximum correspondence over a comparison window, or designated region as measured using a comparison algorithm or by manual alignment and visual inspection. By way of example only, two or more sequences may be "substantially identical" if the sequential units are about 60% identical, about 65% identical, about 70% identical, about 75% identical, about 80% identical, about 85% identical, about 90% identical, or about 95% identical over a specified region. Such percentages to describe the "percent identity" of two or more sequences. The identity of a sequence can exist over a region that is at least about 75-100 sequential units in length, over a region that is about 50 sequential units in length, or, where not specified, across the entire sequence. This definition also refers to the complement of a test sequence.

[0134] As used herein, "fragment" is defined as at least a portion of a sequence. For example, in one embodiment, the term "fragment" refers to a portion of the variable region of the immunoglobulin molecule which binds to its target, i.e. the antigen binding region. Some of the constant region of the immunoglobulin may be included.

[0135] In the context of the present invention, the following abbreviations for the commonly occurring nucleosides (nucleobase bound to ribose or deoxyribose sugar via N-glycosidic linkage) are used. "A" refers to adenosine, "C" refers to cytidine, "G" refers to guanosine, "T" refers to thymidine, and "U" refers to uridine.

[0136] The term "polynucleotide" as used herein is defined as a chain of nucleotides. Furthermore, nucleic acids are polymers of nucleotides. Thus, nucleic acids and polynucleotides as used herein are interchangeable. One skilled in the art has the general knowledge that nucleic acids are polynucleotides, which can be hydrolyzed into the monomeric "nucleotides." The monomeric nucleotides can be hydrolyzed into nucleosides. As used herein polynucleotides include, but are not limited to, all nucleic acid sequences which are obtained by any means available in the art, including, without limitation, recombinant means, i.e., the cloning of nucleic acid sequences from a recombinant library or a cell genome, using ordinary cloning technology and PCR™, and the like, and by synthetic means. As used herein, "polynucleotide" includes cDNA, RNA, DNA/RNA hybrid, antisense RNA, ribozyme, genomic DNA, synthetic forms, and mixed polymers, both sense and antisense strands, and may be chemically or biochemically modified to contain non-natural or derivatized, synthetic, or semi-synthetic nucleotide bases. Also, contemplated are alterations of a wild type or synthetic gene, including but not limited to deletion, insertion, substitution of one or more nucleotides, or fusion to other polynucleotide sequences.

[0137] In some instances, the polynucleotide or nucleic acid of the invention is a "nucleoside-modified nucleic acid," which refers to a nucleic acid comprising at least one modified nucleoside. A "modified nucleoside" refers to a nucleoside with a modification. For example, over one hundred different nucleoside modifications have been identified in RNA (Rozenski, et al., 1999, The RNA Modification Database: 1999 update. Nucl Acids Res 27: 196-197).

[0138] Unless otherwise specified, a "nucleotide sequence encoding an amino acid sequence" includes all nucleotide sequences that are degenerate versions of each other and that encode the same amino acid sequence. The phrase nucleotide sequence that encodes a protein or an RNA may also include introns to the extent that the nucleotide sequence encoding the protein may in some version contain an intron (s).

Unless otherwise specified, a "nucleotide sequence encoding an amino acid sequence" includes all nucleotide sequences that are degenerate versions of each other and that encode the same amino acid sequence. Nucleotide sequences that encode proteins and RNA may include introns. In addition, the nucleotide sequence may contain modified nucleosides that are capable of being translated by translational machinery in a cell. Exemplary modified nucleosides are described elsewhere herein. For example, an mRNA where some or all of the uridines have been replaced with pseudouridine, 1-methyl psuedouridine, or another modified nucleoside, such as those described elsewhere herein. In some embodiments, the nucleotide sequence may contain a sequence where some or all cytodines are replaced with methylated cytidine, or another modified nucleoside, such as those described elsewhere herein.

[0139] "Encoding" refers to the inherent property of specific sequences of nucleotides in a polynucleotide, such as a gene, a cDNA, or an mRNA, to serve as templates for synthesis of other polymers and macromolecules in biological processes having either a defined sequence of nucleotides (i.e., rRNA, tRNA and mRNA) or a defined sequence of amino acids and the biological properties resulting therefrom. Thus, a gene encodes a protein if transcription and translation of mRNA corresponding to that gene produces the protein in a cell or other biological system. Both the coding strand, the nucleotide sequence of which is identical to the mRNA sequence and is usually provided in sequence listings, and the non-coding strand, used as the template for transcription of a gene or cDNA, can be referred to as encoding the protein or other product of that gene or cDNA.

[0140] A "vector" is a composition of matter which comprises an isolated nucleic acid and which can be used to deliver the isolated nucleic acid to the interior of a cell. Numerous vectors are known in the art including, but not limited to, linear polynucleotides, polynucleotides associated with ionic or amphiphilic compounds, plasmids, and viruses. Thus, the term "vector" includes an autonomously replicating plasmid or a virus. The term should also be construed to include non-plasmid and non-viral compounds which facilitate transfer of nucleic acid into cells, such as, for example, polylysine compounds, liposomes, and the like. Examples of viral vectors include, but are not limited to, adenoviral vectors, adeno-associated virus vectors, retroviral vectors, and the like.

[0141] The term "expression" as used herein is defined as the transcription and/or translation of a particular nucleotide sequence driven by its promoter.

[0142] "Expression vector" refers to a vector comprising a recombinant polynucleotide comprising expression control sequences operatively linked to a nucleotide sequence to be expressed. An expression vector comprises sufficient cis-acting elements for expression; other elements for expression can be supplied by the host cell or in an in vitro expression system. Expression vectors include all those known in the art, such as cosmids, plasmids (e.g., naked or contained in liposomes) RNA, and viruses (e.g., lentiviruses, retroviruses, adenoviruses, and adeno-associated viruses) that incorporate the recombinant polynucleotide.

[0143] The term "promoter" as used herein is defined as a DNA sequence recognized by the synthetic machinery of the cell, or introduced synthetic machinery, required to initiate the specific transcription of a polynucleotide sequence. By way of one non-limiting example, a promoter that is recognized by bacteriophage RNA polymerase and is used to generate the mRNA by in vitro transcription.

[0144] The terms "patient," "subject," "individual," and the like are used interchangeably herein, and refer to any animal, or cells thereof whether in vitro or in situ, amenable to the methods described herein. In some non-limiting embodiments, the patient, subject or individual is a human. In various embodiments, the subject is a human subject, and may be of any race, sex, and age.

[0145] A "disease" is a state of health of an animal wherein the animal cannot maintain homeostasis, and wherein if the disease is not ameliorated then the animal's health continues to deteriorate. In contrast, a "disorder" in an animal is a state of health in which the animal is able to maintain homeostasis, but in which the animal's state of health is less favorable than it would be in the absence of the disorder. Left untreated, a disorder does not necessarily cause a further decrease in the animal's state of health.

[0146] "Cancer," as used herein, refers to the abnormal growth or division of cells. Generally, the growth and/or life span of a cancer cell exceeds, and is not coordinated with, that of the normal cells and tissues around it. Cancers may be benign, pre-malignant or malignant. Cancer occurs in a variety of cells and tissues, including, but not limited to, the oral cavity (e.g., mouth, tongue, pharynx, etc.), digestive system (e.g., esophagus, stomach, small intestine, colon, rectum, liver, bile duct, gall bladder, pancreas, etc.), respiratory system (e.g., larynx, lung, bronchus, etc.), bones, joints, skin (e.g., basal cell, squamous cell, meningioma, etc.), breast, genital system, (e.g., uterus, ovary, prostate, testis, etc.), urinary system (e.g., bladder, kidney, ureter, etc.), eye, nervous system (e.g., brain, etc.), endocrine system (e.g., thyroid, etc.), soft tissues (e.g., muscle, fat, etc.), and hematopoietic system (e.g., lymphoma, myeloma, leukemia, acute lymphocytic leukemia, chronic lymphocytic leukemia, acute myeloid leukemia, chronic myeloid leukemia, etc.).

[0147] A disease or disorder is "alleviated" if the severity of at least one sign or symptom of the disease or disorder, the frequency with which such a sign or symptom is experienced by a patient, or both, is reduced.

[0148] By the term "modulating," as used herein, is meant mediating a detectable increase or decrease in the level of a response in a subject compared with the level of a response in the subject in the absence of a treatment or compound, and/or compared with the level of a response in an otherwise identical but untreated subject. The term encompasses perturbing and/or affecting a native signal or response thereby mediating a beneficial therapeutic response in a subject, such as, a human.

[0149] The term "inhibit," as used herein, means to suppress or block an activity or function by at least about ten percent relative to a control value. In various embodiments, the activity is suppressed or blocked by at least 50% compared to a comparator value, or by at least 55%, or by at least 60%, or by at least 65%, or by at least 70%, or by at least 75%, or by at least 80%, or by at least 85%, or by at least 90%, or by at least 95%.

[0150] As used herein, the term "diagnosis" refers to the determination of the presence of a disease or disorder. In various embodiments of the present invention, methods for making a diagnosis are provided which permit determination of the presence of a particular disease or disorder.

[0151] To "treat" a disease as the term is used herein, means to reduce the frequency and/or severity of at least one sign or symptom of a disease or disorder experienced by a subject.

[0152] An "effective amount" as used herein, means an amount which provides a therapeutic or prophylactic benefit.

[0153] The term "therapeutic" as used herein means a treatment and/or prophylaxis. A therapeutic effect is obtained by suppression, diminution, remission, prevention, or eradication of at least one sign or symptom of a disease or disorder.

[0154] The term "therapeutically effective amount" refers to the amount of the subject compound that will elicit the biological or medical response of a tissue, system, or subject that is being sought by the researcher, veterinarian, medical doctor or other clinician. The term "therapeutically effective amount" includes that amount of a compound that, when administered, is sufficient to prevent development of, or alleviate to some extent, one or more of the signs or symptoms of the disorder or disease being treated. The therapeutically effective amount will vary depending on the compound, the disease and its severity and the age, weight, etc., of the subject to be treated.

[0155] As used herein, the term "pharmaceutical composition" refers to a mixture of at least one compound of the invention with other chemical components and entities, such as carriers, stabilizers, diluents, dispersing agents, suspending agents, thickening agents, and/or excipients. The pharmaceutical composition facilitates administration of the compound to an organism. Multiple techniques of administering a compound exist in the art including, but not limited to, intravenous, oral, aerosol, parenteral, ophthalmic, pulmonary and topical administration.

[0156] "Pharmaceutically acceptable" refers to those properties and/or substances which are acceptable to the patient from a pharmacological/toxicological point of view and to the manufacturing pharmaceutical chemist from a physical/chemical point of view regarding composition, formulation, stability, patient acceptance and bioavailability. "Pharmaceutically acceptable carrier" refers to a medium that does not interfere with the effectiveness of the biological activity of the active ingredient(s) and is not toxic to the host to which it is administered.

[0157] As used herein, the term "pharmaceutically acceptable carrier" means a pharmaceutically acceptable material, composition or carrier, such as a liquid or solid filler, stabilizer, dispersing agent, suspending agent, diluent, excipient, thickening agent, solvent or encapsulating material, involved in carrying or transporting a compound useful within the invention within or to the patient such that it may perform its intended function. Typically, such constructs are carried or transported from one organ, or portion of the body, to another organ, or portion of the body. Each carrier must be "acceptable" in the sense of being compatible with the other ingredients of the formulation, including the compound useful within the invention, and not injurious to the patient. Some examples of materials that may serve as pharmaceutically acceptable carriers include: sugars, such as lactose, glucose and sucrose; starches, such as corn starch

and potato starch; cellulose, and its derivatives, such as sodium carboxymethyl cellulose, ethyl cellulose and cellulose acetate; powdered tragacanth; malt; gelatin; talc; excipients, such as cocoa butter and suppository waxes; oils, such as peanut oil, cottonseed oil, safflower oil, sesame oil, olive oil, corn oil and soybean oil; glycols, such as propylene glycol; polyols, such as glycerin, sorbitol, mannitol and polyethylene glycol; esters, such as ethyl oleate and ethyl laurate; agar; buffering agents, such as magnesium hydroxide and aluminum hydroxide; surface active agents; alginic acid; pyrogen-free water; isotonic saline; Ringer's solution; ethyl alcohol; phosphate buffer solutions; and other non-toxic compatible substances employed in pharmaceutical formulations. As used herein, "pharmaceutically acceptable carrier" also includes any and all coatings, antibacterial and antifungal agents, and absorption delaying agents, and the like that are compatible with the activity of the compound useful within the invention, and are physiologically acceptable to the patient. Supplementary active compounds may also be incorporated into the compositions. The "pharmaceutically acceptable carrier" may further include a pharmaceutically acceptable salt of the compound useful within the invention. Other additional ingredients that may be included in the pharmaceutical compositions used in the practice of the invention are known in the art and described, for example in Remington's Pharmaceutical Sciences (Genaro, Ed., Mack Publishing Co., 1985, Easton, PA), which is incorporated herein by reference.

[0158] The term "solvate" in accordance with this invention should be understood as meaning any form of the active compound in accordance with the invention in which said compound is bonded by a non-covalent bond to another molecule (normally a polar solvent), including especially hydrates and alcoholates.

[0159] As used herein, an "immunoassay" refers to any binding assay that uses an antibody capable of binding specifically to a target molecule to detect and quantify the target molecule.

[0160] The term "amplification" refers to the operation by which the number of copies of a target nucleotide sequence present in a sample is multiplied.

[0161] The term "next generation sequencing" herein refers to sequencing methods that allow for massively parallel sequencing of clonally amplified molecules and of single nucleic acid molecules. Next generation sequencing is synonymous with "massively parallel sequencing" for most purposes. Non-limiting examples of next generation sequencing include sequencing-by-synthesis using reversible dye terminators, and sequencing-by-ligation.

[0162] Assays for amplification of the known sequence are also disclosed. For example primers for PCR may be designed to amplify regions of the sequence. For RNA, a first reverse transcriptase step may be used to generate double stranded DNA from the single stranded RNA. The array may be designed to detect sequences from an entire genome; or one or more regions of a genome, for example, selected regions of a genome such as those coding for a protein or RNA of interest; or a conserved region from multiple genomes; or multiple genomes, arrays and methods of genetic analysis using arrays is described in Cutler, et al., 2001, Genome Res. 11(11): 1913-1925 and Warrington, et al., 2002, Hum Mutat 19:402-409 and in US Patent Pub No 20030124539, each of which is incorporated herein by reference in its entirety.

[0163] "Instructional material," as that term is used herein, includes a publication, a recording, a diagram, or any other medium of expression which can be used to communicate the usefulness of the nucleic acid, peptide, and/or compound of the invention in the kit for identifying, diagnosing or alleviating or treating the various diseases or disorders recited herein. Optionally, or alternately, the instructional material may describe one or more methods of identifying, diagnosing or alleviating the diseases or disorders in a cell or a tissue of a subject. The instructional material of the kit may, for example, be affixed to a container that contains one or more components of the invention or be shipped together with a container that contains the one or more components of the invention. Alternatively, the instructional material may be shipped separately from the container with the intention that the recipient uses the instructional material and the components cooperatively.

[0164] Ranges: throughout this disclosure, various aspects of the invention can be presented in a range format. It should be understood that the description in range format is merely for convenience and brevity and should not be construed as an inflexible limitation on the scope of the invention. Accordingly, the description of a range should be considered to have specifically disclosed all the possible subranges as well as individual numerical values within that range. For example, description of a range such as from 1 to 6 should be considered to have specifically disclosed subranges such as from 1 to 3, from 1 to 4, from 1 to 5, from 2 to 4, from 2 to 6, from 3 to 6 etc., as well as individual numbers within that range, for example, 1, 2, 2.7, 3, 4, 5, 5.3, and 6. This applies regardless of the breadth of the range.

DESCRIPTION

[0165] The present invention relates to methods of detecting various antibodies and targets thereof. In one aspect, the present invention provides methods of identifying a target extracellular, secreted, and/or transmembrane protein that specifically binds to an antibody of interest. In another aspect, the present invention provides methods of preventing or treating diseases or disorders associated with antibodies and/or a targets thereof identified via the methods of the present invention. In another aspect, the present invention provides methods of diagnosing, assessing prognosis, or assessing the effectiveness of treatments of diseases or disorders associated with antibodies and/or a targets thereof identified via the methods of the present invention. In another aspect, the present invention provides methods of predicting a response to a therapy. In another aspect, the present invention provides methods of alleviating toxicity of a cancer treatment.

Methods of Identifying Antibodies and Targets Thereof

[0166] The present invention relates, in part, to methods of identifying antibodies or binding partners thereof. In one aspect, the method comprises identifying an antigenic polypeptide that specifically binds to an antibody of interest. In one aspect, the method comprises identifying novel antibody-antigen interactions.

[0167] In one embodiment, the invention relates to a screening method for antigen antibody interactions, wherein the method comprises generating a display library of polypeptides that are then screened for interactions with at least one antibody. Therefore, in one embodiment, the invention

relates to a polypeptide display library and methods of use thereof for screening for antigen-antibody interactions.

Display Library

[0168] In various embodiments, the invention relates to methods of screening using a cellular display library. In some embodiments, the cellular display library comprises a plurality of cells, wherein together the plurality of cells displays at least 10, 20, 30, 40, 50, 60, 70, 80, 90, 100, 200, 300, 400, 500, 600, 700, 800, 900, 1000, 2000, 3000, 4000, 5000, 6000, 7000, 8000, 9000, 10,000 or more than 10,000 different polypeptides on the surface of the cells. In one embodiment, the plurality of cells of the display library display proteins or polypeptides of the secretome, representing a plurality of secreted proteins, the exoproteome, representing a plurality of extracellular proteins, or a combination thereof. In one embodiment, the plurality of cells of the display library display a combination of at least 10, 20, 30, 40, 50, 60, 70, 80, 90, 100, 200, 300, 400, 500, 600, 700, 800, 900, 1000, 2000, 3000, 4000, 5000, 6000, or more than 6,000 extracellular and secreted polypeptides or proteins. In one embodiment, together the plurality of cells in the display library, display each of the polypeptide amino acid sequences set forth in SEQ ID NO:1-3092.

[0169] In some embodiments, the polypetides for display are fusion proteins with polypeptides that allow expression and exposure on a cell or particle surface. In one embodiment, nucleic acids encoding the molecules can be cloned into a display vector. The vector is designed to express the fusion molecules and display the encoded antigen on the outer surface of a display cell or partilce containing the vector. For example, antigens can be expressed as fusion proteins with a phage coat protein from the outer surface of the phage. In some embodiments, the polypeptides for display are IgGI Fc fusion molecules. Thereafter, the display cells or particles can be screened for antibody reactivities with the displayed antigens.

[0170] Thus, in various embodiments, the present invention also includes a vector in which a nucleotide sequence encoding a polypeptide for display of the present invention is inserted. The art is replete with suitable vectors that are useful in the present invention.

[0171] In brief summary, the expression of a nucleotide construct is typically achieved by operably linking a nucleic acid sequence comprising a promoter to a nucleic acid sequence encoding an antigen or portions thereof, and incorporating the construct into an expression vector. In one embodiment, the vectors to be used are suitable for replication and, optionally, integration in eukaryotic cells. Typical vectors contain transcription and translation terminators, initiation sequences, and other regulatory sequences useful for regulation of the expression of the desired nucleic acid sequence.

[0172] The recombinant nucleotide sequences encoding an antigen for display of the invention can be cloned into a number of types of vectors. For example, the nucleic acid can be cloned into a vector including, but not limited to a plasmid, a phagemid, a phage derivative, an animal virus, and a cosmid. Vectors of particular interest include expression vectors, replication vectors, probe generation vectors, and sequencing vectors.

[0173] Further, the vector may be provided to a cell in the form of a viral vector. Viral vector technology is well known in the art and is described, for example, in Sambrook et al. (2012, Molecular Cloning: A Laboratory Manual, Cold Spring Harbor Laboratory, New York), and in other virology and molecular biology manuals. Viruses, which are useful as vectors include, but are not limited to, retroviruses, adenoviruses, adeno-associated viruses, herpes viruses, and lentiviruses. In general, a suitable vector contains an origin of replication functional in at least one organism, a promoter sequence, convenient restriction endonuclease sites, and one or more selectable markers, (e.g., WO 01/96584; WO 01/29058; and U.S. Pat. No. 6,326,193).

[0174] A number of viral based systems have been developed for gene transfer into mammalian cells. For example, retroviruses provide a convenient platform for gene delivery systems. A selected gene can be inserted into a vector and packaged in retroviral particles using techniques known in the art. The recombinant virus can then be isolated and delivered to cells of the subject either in vivo or ex vivo. A number of retroviral systems are known in the art. In some embodiments, adenovirus vectors are used. A number of adenovirus vectors are known in the art. In one embodiment, lentivirus vectors are used.

[0175] For example, vectors derived from retroviruses such as the lentivirus are suitable tools to achieve long-term gene transfer since they allow long-term, stable integration of a transgene and its propagation in daughter cells. Lentiviral vectors have the added advantage over vectors derived from onco-retroviruses such as murine leukemia viruses in that they can transduce non-proliferating cells, such as hepatocytes. They also have the added advantage of low immunogenicity. In one embodiment, the composition includes a vector derived from an adeno-associated virus (AAV). Adeno-associated viral (AAV) vectors have become powerful gene delivery tools for the treatment of various disorders. AAV vectors possess a number of features that render them ideally suited for gene therapy, including a lack of pathogenicity, minimal immunogenicity, and the ability to transduce postmitotic cells in a stable and efficient manner. Expression of a particular gene contained within an AAV vector can be specifically targeted to one or more types of cells by choosing the appropriate combination of AAV serotype, promoter, and delivery method

[0176] In certain embodiments, the vector also includes conventional control elements which are operably linked to the encoded antigen sequence in a manner which permits its transcription, translation and/or expression in a cell transfected with the plasmid vector or infected with the virus produced by the invention. As used herein, "operably linked" sequences include both expression control sequences that are contiguous with the reporter molecule and expression control sequences that act in trans or at a distance to control the expression of the reporter molecule. Expression control sequences include appropriate transcription initiation, termination, and enhancer sequences; efficient RNA processing signals such as splicing and polyadenylation (polyA) signals; sequences that stabilize cytoplasmic mRNA; sequences that enhance translation efficiency (i.e., Kozak consensus sequence); sequences that enhance protein stability; and when desired, sequences that enhance secretion of the encoded product. All of the above-described functional elements can be used in any combination to produce a suitable display vector.

[0177] In one embodiment, a display vector comprises an origin of replication capable of initiating DNA synthesis in a suitable host cell. In one embodiment, the origin of

replication is selected based on the type of host cell. For instance, it can be eukaryotic (e.g., yeast) or prokaryotic (e.g., bacterial) or a suitable viral origin of replication may be used.

[0178] In one embodiment, a display vector comprises a selection marker gene to facilitate identification and selection of expressing cells from the population of cells sought to be transfected or infected through viral vectors. In other aspects, the selectable marker may be carried on a separate piece of DNA and used in a co-transfection procedure. Selectable marker genes may be flanked with appropriate regulatory sequences to enable expression in the host cells.

[0179] A selection marker sequence can be used to eliminate host cells in which the display vector has not been properly transfected. A selection marker sequence can be a positive selection marker or negative selection marker. Positive selection markers permit the selection for cells in which the gene product of the marker is expressed. This generally comprises contacting cells with an appropriate agent that, but for the expression of the positive selection marker, kills or otherwise selects against the cells.

[0180] Examples of selection markers also include, but are not limited to, proteins conferring resistance to compounds such as antibiotics, proteins conferring the ability to grow on selected substrates, proteins that produce detectable signals such as luminescence, catalytic RNAs and antisense RNAs. A wide variety of such markers are known and available, including, for example, a Zeocin™ resistance marker, a blasticidin resistance marker, a neomycin resistance (neo) marker (Southern & Berg, J. Mol. Appl. Genet. 1: 327-41 (1982)), a puromycin (puro) resistance marker; a hygromycin resistance (hyg) marker (Te Riele et al., Nature 348:649-651 (1990)), thymidine kinase (tk), hypoxanthine phosphoribosyltransferase (hprt), and the bacterial guanine/xanthine phosphoribosyltransferase (gpt), which permits growth on MAX (mycophenolic acid, adenine, and xanthine) medium. See Song et al., Proc. Nat'l Acad. Sci. U.S.A. 84:6820-6824 (1987). Other selection markers include histidinol-dehydrogenase, chloramphenicol-acetyl transferase (CAT), dihydrofolate reductase (DHFR), β-galactosyltransferase and fluorescent proteins such as GFP.

[0181] Expression of a fluorescent protein can be detected using a fluorescent activated cell sorter (FACS). Expression of 3-galactosyltransferase also can be sorted by FACS, coupled with staining of living cells with a suitable substrate for β-galactosidase. A selection marker also may be a cell-substrate adhesion molecule, such as integrins, which normally are not expressed by the host cell. In one embodiment, the cell selection marker is of mammalian origin, for example, thymidine kinase, aminoglycoside phosphotransferase, asparagine synthetase, adenosine deaminase or metallothionien. In one embodiment, the cell selection marker can be neomycin phosphotransferase, hygromycin phosphotransferase or puromycin phosphotransferase, which confer resistance to G418, hygromycin and puromycin, respectively.

[0182] Suitable prokaryotic and/or bacterial selection markers include proteins providing resistance to antibiotics, such as kanamycin, tetracycline, and ampicillin. In one embodiment, a bacterial selection marker includes a protein capable of conferring selectable traits to both a prokaryotic host cell and a mammalian target cell.

[0183] Negative selection markers permit the selection against cells in which the gene product of the marker is expressed. In some embodiments, the presence of appropriate agents causes cells that express "negative selection markers" to be killed or otherwise selected against. Alternatively, the expression of negative selection markers alone kills or selects against the cells.

[0184] Such negative selection markers include a polypeptide or a polynucleotide that, upon expression in a cell, allows for negative selection of the cell. Illustrative of suitable negative selection markers are (i) herpes simplex virusthymidine kinase (HSV-TK) marker, for negative selection in the presence of any of the nucleoside analogs acyclovir, gancyclovir, and 5-fluoroiodoamino-Uracil (FIAU), (ii) various toxin proteins such as the diphtheria toxin, the tetanus toxin, the cholera toxin and the pertussis toxin, (iii) hypoxanthine-guanine phosphoribosyl transferase (HPRT), for negative selection in the presence of 6-thioguanine, (iv) activators of apoptosis, or programmed cell death, such as the bc12-binding protein (BAX), (v) the cytidine deaminase (codA) gene of *E. coli*, and (vi) phosphotidyl choline phospholipase D. In one embodiment, the negative selection marker requires host genotype modification (e.g. ccdB, tolC, thyA, rpsl and thymidine kinases.)

[0185] In accordance with the present invention, the selection marker usually is selected based on the type of the cell undergoing selection. For instance, it can be eukaryotic (e.g., yeast), prokaryotic (e.g., bacterial) or viral. In such an embodiment, the selection marker sequence is operably linked to a promoter that is suited for that type of cell.

[0186] In one embodiment, the invention provides a plurality of at least 10, 20, 30, 40, 50, 60, 70, 80, 90, 100, 200, 300, 400, 500, 600, 700, 800, 900, 1000, 2000, 3000, 4000, 5000, 6000, 7000, 8000, 9000, 10,000 or more than 10,000 recombinant nucleic acid molecules, wherein together the plurality of recombinant nucleic acid molecules encode at least 10, 20, 30, 40, 50, 60, 70, 80, 90, 100, 200, 300, 400, 500, 600, 700, 800, 900, 1000, 2000, 3000, 4000, 5000, 6000, 7000, 8000, 9000, 10,000 or more than 10,000 different polypeptides for display in a cell display library. In one embodiment, the plurality of cells of the display library display proteins or polypeptides of the secretome, representing a plurality of secreted proteins, the exoproteome, representing a plurality of extracellular proteins, or a combination thereof. In one embodiment, together the plurality of recombinant nucleic acid molecules encodes at least 10, 20, 30, 40, 50, 60, 70, 80, 90, 100, 200, 300, 400, 500, 600, 700, 800, 900, 1000, 2000, 3000, 4000, 5000, 6000, or more than 6,000 extracellular and secreted polypeptides or proteins. In one embodiment, together the plurality of recombinant nucleic acid molecules encodes each of the polypeptide amino acid sequences set forth in SEQ ID NO:1-3092. In one embodiment, together the plurality of recombinant nucleic acid molecules comprises each of the nucleotide sequences set forth in SEQ ID NO:3093-6185.

[0187] In one embodiment, each of the recombinant nucleic acid molecules in the plurality of recombinant nucleic acid molecules encodes a polypeptide sequence for expression on a cell surface, and further comprises a unique nucleotide barcode sequence, which is then associated with the encoded polypeptide sequence. In various embodiments, the unique barcode sequence comprises a nucleotide sequence of at least 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20 or more than 20 nucleotides which is non-redundant within the recombinant nucleotide sequences included in the library.

[0188] In some embodiments, the invention relates to methods of generating a display library for expression of a plurality of extracellular or secreted proteins on the surface of a plurality of cells. In some embodiments, the method comprises obtaining or generating a library of barcoded nucleic acid molecules, wherein each nucleic acid molecule comprises i) a nucleotide sequence encoding a polypeptide for display on the surface of a cell; and ii) a unique nucleotide barcode sequence; and introducing the plurality of recombinant nucleic acid molecules into a system for expression and/or display of the recombinant nucleic acid molecules. Display systems that can be used for expression and/or display of the recombinant nucleic acid library of the invention include, but are not limited to, phage display, mRNA display, ribosome display, yeast display, mammalian cell display, and the like.

[0189] Any method known in the art for introducing nucleic acid sequences into cells can be used to generate the display library of the invention. Exemplary methods of introducing nucleic acid molecules into cells include, but are not limited to, electroporation, cell squeezing, sonoporation, optical transfection, protoplast fusion, impalefection, hydrodynamic delivery, fusion, magnetofection, particle bombardment, nucleofection, heat shock, lipofection, viral transduction, nonviral transfection, lithium acetate/PEG chemical transformation, or any combination thereof.

[0190] In one embodiment, the method comprises generating a library of cells for displaying polypeptides which function as epitopes for antigen binding. Thus, in one embodiment, the method comprises generating a library of cells, wherein the library comprises cells comprising barcode-labeled nucleic acid sequences, wherein the barcode-labeled nucleic acid sequences encode polypeptides which function as epitopes for antigen binding.

Screening Methods

[0191] In some embodiments, the invention provides methods for screening a display library comprising a plurality of proteins or polypeptides of the secretome, representing a plurality of secreted proteins, the exoproteome, representing a plurality of extracellular proteins, or a combination thereof, to identify those proteins or polypeptides which interact with at least one antibody. In one embodiment, the methods comprise contacting the plurality of displayed proteins or polypeptides with a sample comprising at least one antibody.

[0192] In one embodiment, the method comprises the step of contacting a library of display cells with a sample comprising at least one antibody, thus generating one or more antibody-bound cells. In various embodiments, the antibody is a purified antibody. In one embodiment, the antibody is purified from a biological sample. Biological samples may be of any biological tissue or fluid. Frequently the sample will be a "clinical sample" which is a sample derived from a subject. The biological sample may contain any biological material suitable for detecting the desired antibodies or targets thereof, and may comprise cellular and/or non-cellular material obtained from the subject. A biological sample can be obtained by appropriate methods, such as, by way of examples, blood draw, fluid draw, biopsy, or surgical resection. Examples of such samples include but are not limited to serum, blood, lymph, urine, gastrointestinal fluid, cerebrospinal fluid, semen, and samples from biopsies. Samples that are liquid in nature are referred to herein as "bodily fluids." Body samples may be obtained from a subject by a variety of techniques including, for example, by scraping or swabbing an area or by using a needle to aspirate bodily fluids. Methods for collecting various body samples are well known in the art. Frequently, a sample will be a "clinical sample," i.e., a sample derived from a subject. Such samples include, but are not limited to, bodily fluids which may or may not contain cells, e.g., blood (e.g., whole blood, serum or plasma), urine, saliva, cerebrospinal fluid, or fine needle biopsy samples, tissue sample obtained during surgical resection, and archival samples with known diagnosis, treatment and/or outcome history.

[0193] In one embodiment, the method comprises contacting the display cells with at least one antibody purified from a biological sample. In one embodiment, the antibody is purified from a biological sample by affinity purification. In some embodiment, the antibody is purified from a biological sample by affinity purification of the desired antibody isotype (e.g., IgG, IgA, IgE, etc.). In some embodiments, the antibody is purified from a biological sample using any method known in the art for the purification of specific antibodies from a biological sample. For example, in one embodiment, the antibody is purified from a serum by affinity purification. In some embodiments, the antibody is purified by a high-throughput and efficient method for antibody isolation from human serum or plasma. In one embodiment, the method comprises an affinity purification of the desired antibody isotype (IgG, IgA, IgE, etc.) in 96-well microtiter plates.

[0194] In one embodiment, the sample comprising at least one antibody is purified by removing at least one human serum component. In one embodiment, the sample comprising at least one antibody is purified by removing at least one antibody that may bind a display cell and interfere with a downstream selection procedure. For example, in one embodiment, the sample comprising at least one antibody of interest is purified by contacting the sample with at least one control cell or particle comprising an empty display vector, and removing any species that bind to the control cell or particle comprising the empty display vector from the sample.

[0195] In one embodiment, the sample goes through a two-step purification process which involves both a) purification or selection of the specific antibody isotype of interest using an affinity purification for the isotype of interest (e.g., IgG, IgA, IgE, etc.), and b) elimination of human serum components and display cell or particle-reactive antibodies that may bind the display cell or particle and interfere with downstream selection procedures by contacting the purified sample with at least one control cell or particle comprising an empty display vector, and removing any species that bind to the control cell or particle.

[0196] In one embodiment, the biological sample is a healthy, normal or control sample. In some embodiments, a healthy, normal or control sample is a sample from a subject who has not been diagnosed with a disease or disorder. In one embodiment, the biological sample is obtained from a subject having a disease or disorder. Thus, in some embodiments, the biological sample comprises at least one antibody associated with a disease or disorder. Exemplary diseases and disorders include, but are not limited to, an autoimmune disease or disorder, cancer, inflammatory disease or disorder, metabolic disease or disorder, neurodegenerative disease or disorder, organ tissue rejection, organ transplant

rejection, or any combination thereof. In one embodiment, the antibody is an autoantibody.

[0197] In some embodiments, the sample is from a subject who shows good prognosis of a disease or disorder, has reduced symptoms associated with a disease or disorder, or has a mild form of a disease or disorder. In such an embodiment, the methods of the invention serve to identify therapeutic antibodies or antibody-antigen interactions for the treatment of the disease or disorder. In some embodiments, the disease or disorder is selected from antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis, autoimmune polyendocrinopathy candidiasis ecto-dermal dystrophy, antiphospholipid antibody syndrome, chronic inflammatory demyelinating polyradiculoneuropathy, cutaneous lupus erythematosus, COVID-19, drug-induced lupus, dermatomyositis, glomerulonephritis, a disease or disorder associated with kidney transplant, malaria, mixed connective tissue disease, myasthenia gravis, malignant melanoma, neuromyelitis optica, non-small cell lung cancer, pediatric autoimmune neuropsychiatric disorders associated with streptococcal infections, systemic lupus erythematosus, sjogren's syndrome, scleroderma, susac syndrome, undifferentiated connective tissue disease, or any combination thereof, and therefore the antibody is a therapeutic antibody for the treatment of antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis, autoimmune polyendocrinopathy candidiasis ecto-dermal dystrophy, antiphospholipid antibody syndrome, chronic inflammatory demyelinating polyradiculoneuropathy, cutaneous lupus erythematosus, COVID-19, drug-induced lupus, dermatomyositis, glomerulonephritis, a disease or disorder associated with kidney transplant, malaria, mixed connective tissue disease, myasthenia gravis, malignant melanoma, neuromyelitis optica, non-small cell lung cancer, pediatric autoimmune neuropsychiatric disorders associated with streptococcal infections, systemic lupus erythematosus, sjogren's syndrome, scleroderma, susac syndrome, undifferentiated connective tissue disease, or any combination thereof.

[0198] In some embodiments, the sample is from a subject who shows poor prognosis of a disease or disorder, has increased symptoms associated with a disease or disorder, or has a severe form of a disease or disorder. In such an embodiment, the methods of the invention serve to identify antibodies or antibody-antigen interactions that are therapeutic targets for the treatment or prevention of a disease or disorder. In some embodiments, the disease or disorder is selected from antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis, autoimmune polyendocrinopathy candidiasis ecto-dermal dystrophy, antiphospholipid antibody syndrome, chronic inflammatory demyelinating polyradiculoneuropathy, cutaneous lupus erythematosus, COVID-19, drug-induced lupus, dermatomyositis, glomerulonephritis, a disease or disorder associated with kidney transplant, malaria, mixed connective tissue disease, myasthenia gravis, malignant melanoma, neuromyelitis optica, non-small cell lung cancer, pediatric autoimmune neuropsychiatric disorders associated with streptococcal infections, systemic lupus erythematosus, sjogren's syndrome, scleroderma, susac syndrome, undifferentiated connective tissue disease, or any combination thereof, and therefore the antibody is a therapeutic target for the treatment of antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis, autoimmune polyendocrinopathy candidiasis ecto-dermal dystrophy, antiphospholipid antibody syndrome, chronic inflammatory demyelinating polyradiculoneuropathy, cutaneous lupus erythematosus, COVID-19, drug-induced lupus, dermatomyositis, glomerulonephritis, a disease or disorder associated with kidney transplant, malaria, mixed connective tissue disease, myasthenia gravis, malignant melanoma, neuromyelitis optica, non-small cell lung cancer, pediatric autoimmune neuropsychiatric disorders associated with streptococcal infections, systemic lupus erythematosus, sjogren's syndrome, scleroderma, susac syndrome, undifferentiated connective tissue disease, or any combination thereof.

[0199] In one embodiment, the screening method further comprises a step of isolating or purifying one or more antibody-bound display cell of the invention. Any method known in the art for separating or purifying an antibody-bound display cell can be used including, but not limited to, magnetic cell separation, fluorescent cell separation, affinity purification, bead based cell separation, column separation, or any combination thereof.

[0200] In some embodiments, the methods of the invention comprise a step of staining cells. Examples of stains include, but are not limited to: fluorescent dyes, propidium iodine, ethidium homodimer III, thiazole orange, acridine orange, Bismarck brown, carmine, coomassie blue, cresyl violet, crystal violet, DAPI, eosin, ethidium bromide, acid fuchsine, haematoxylin, Hoechst stains, iodine, malachite green, methyl green, methylene blue, neutral red, nile blue, nile red, osmium tetraoxide, rhodamine, safranine, biotin, or any combination thereof.

[0201] In some embodiments, the methods of the invention comprise a step of identifying cells bound to an antibody by contacting the library of cells with a secondary immunoglobulin binding molecule for recognition of a primary antibody isotype of interest. For example, in some embodiments, the secondary immunoglobulin binding molecule is an antibody, nanobody, VHH antibody, monobody, knottin, anticalin, peptide, cyclic peptide, aptamer, designed ankyrin repeat protein (DARPin), or any combination thereof.

[0202] In one embodiment, a cell bound by an antibody of interest is identified using any appropriate sorting or selection method. Exemplary sorting and selection methods include, but are not limited to, biotinylated labeled anti-immunoglobulin antibody, fluorescence activated cell sorting (FACS), fluorescently labeled anti-immunoglobulin antibody, magnetic bead-based selection, magnetic bead conjugated to an anti-immunoglobulin antibody, or any combination thereof.

[0203] In one embodiment, the method comprises isolating at least one antibody-bound cell or particle from a mixture. In one embodiment, the method comprises isolating at least one antibody-bound cell or particle from at least one non-antibody-bound cell or particle. In one embodiment, the isolating at least one antibody-bound cell or particle comprises washing to remove at least one non-specific binder, centrifuging, cell separation, or any combination thereof. In one embodiment, the isolating at least one antibody-bound cell or particle comprises washing to remove at least one non-specific binder, centrifuging, magnetic cell separation, fluorescent cell separation, high-throughput selection process based on 96-well magnetic columns, or any combination thereof. In one embodiment, the magnetic cell separation comprises magnetic columns for capturing cells. In one

embodiment, the magnetic cell separation comprises magnetic columns for capturing antibody-bound cell or particles. In one embodiment, the fluorescent cell separation comprises fluorescence activated cell sorting (FACS). In some embodiments, the high-throughput selection process based on 96-well magnetic columns comprises cell or particle library selections, 96-well magnetic columns, large magnetic columns, FACS, washing, centrifuging, or any combination thereof.

[0204] In one embodiment, the method comprises enriching at least one antibody-bound cell or particle by magnetic column-based sorting. In one embodiment, the method comprises amplifying the barcoded recombinant nucleic acid molecule of the antibody-bound cell or particle. In one embodiment, the enrichment is quantified by sequencing. In one embodiment, the enrichment is quantified by next generation sequencing.

High Throughput Identification of Autoantibody Reactivities

[0205] In one embodiment, the screening methods of the invention include methods of high throughput identification of antigen or autoantigen interactions with antibodies or autoantibodies (reactivities.) In some embodiments the screening methods of the invention include of high throughput identification of antibody or autoantibody reactivities include methods of contacting a sample comprising at least one antibody or autoantibody with a display library of the invention, isolating those cells or particles expressing polypeptides which interact with at least one antibody or autoantibody, and identifying the expressed antigen or autoantigen on at the isolated cells or particles.

[0206] In one embodiment, the screening methods of the invention include a step of isolating and sequencing the barcoded nucleic acid molecules from a plurality of antibody-bound cells or particles. In one embodiment, a polypeptide is identified to be an antigen or autoantigen of at least one antibody in the sample based on detection of an increased or enriched level of the associated encoding nucleotide sequence or associated barcode in sequencing data over an established threshold level. In some embodiments, the threshold level is a predetermined threshold level, a statistically determined threshold, a threshold level determined using z-scores, or an established cut-point.

[0207] In various embodiments of the methods of the invention, the level of the nucleic acid sequence barcode is determined to be increased when the number of associated sequencing reads from Next-gen sequencing data corresponding to the barcode is increased or enriched relative to a reference value or statistically determined cut-off value. In some embodiments, the level of the nucleic acid sequence barcode is determined to be increased when the number of associated sequencing reads Next-gen sequencing data corresponding to the barcode is increased or enriched by at least 0.01 fold, at least 0.05 fold, at least 0.07 fold, at least 0.076 fold, at least 0.1 fold, at least 0.18 fold, at least 0.19 fold, at least 0.3 fold, at least 0.36 fold, at least 0.37 fold, at least 0.38 fold, at least 0.4 fold, at least 0.43 fold, at least 1 fold, at least 1.1 fold, at least 1.2 fold, at least 1.3 fold, at least 1.4 fold, at least 1.5 fold, at least 1.6 fold, at least 1.7 fold, at least 1.8 fold, at least 1.9 fold, at least 2 fold, at least 2.1 fold, at least 2.2 fold, at least 2.3 fold, at least 2.4 fold, at least 2.5 fold, at least 2.6 fold, at least 2.7 fold, at least 2.8 fold, at least 2.9 fold, at least 3 fold, at least 3.5 fold, at least 4 fold, at least 4.5 fold, at least 5 fold, at least 5.5 fold, at least 6 fold, at least 6.5 fold, at least 7 fold, at least 7.5 fold, at least 8 fold, at least 8.5 fold, at least 9 fold, at least 9.5 fold, at least 10 fold, at least 11 fold, at least 12 fold, at least 13 fold, at least 14 fold, at least 15 fold, at least 16 fold, at least 16.3 fold, at least 16.31 fold, at least 20 fold, at least 25 fold, at least 26 fold, at least 26.7 fold, at least 26.72 fold, at least 30 fold, at least 40 fold, at least 50 fold, at least 75 fold, at least 100 fold, at least 192 fold, at least 192.4 fold, at least 192.44 fold, at least 200 fold, at least 250 fold, at least 500 fold, or at least 1000 fold, or at least 10000 fold, when compared with a comparator (e.g., a statistically determined threshold level or pre-determined cut-off).

[0208] In one embodiment, an increased level of a barcode nucleic acid sequence provides an indication that an associated encoded polypeptide serves as a target for antibody binding, or an antigen. In one embodiment, an increased level of a barcode nucleic acid sequence provides an indication that an associated encoded polypeptide serves as a target for autoantibody binding, or an autoantigen. In various embodiments, the associated encoded polypeptide is an extracellular protein, transmembrane protein, secreted protein, or any combination thereof. In one embodiment, the associated encoded polypeptide is selected from those provided in Table 1, or a fragment thereof For example, in some embodiments, the associated encoded polypeptide is BMPR2, BTN1A1, BTNL8, C1QTNF4, C6, CCL11, CCL15, CCL17, CCL2, CCL22, CCL24, CCL4L1, CD207, CD300E, CD3D, CD44, CD74, CD81, CDH19, CNTN5, COLEC12, CSPG5, CX3CL1, CXCL1, CXCL13, CXCL2, CXCL3, EDIL3, EPYC, EREG, FGF10, FGF21, FGF23, FGF7, FGFBP3, FGFRL1, IFNA13, IFNA14, IFNA17, IFNA2, IFNA5, IFNA6, IFNA8, IFNB1, IFNL2, IFNW1, IGF2, IGFBPL1, IGSF4B, IL15RA, IL16, IL17A, IL17F, IL17F, IL18RAP, IL19, IL1A, IL1F9, IL1RAP, IL20RB, IL22, IL22RA2, IL28B, IL29, IL33, IL34, IL4, IL4R, IL5, IL6, IL6R, ITGA5, JCHAIN, LAG3, LGR6, LIF, LRP11, LRRC3B, LRRC4, LRTM2, LY6G6D, LY6H, MADCAM1, MPZL3, MUC21, NGFR, NOTCH2NL, NTRK3, PDCD1LG2, PDGFB, PGLYRP1, REGlA, REG1B, REG4, RTN4RL1, SCARA3, SDC1, SDC4, STIM2, TGFA, TMEM149, TNF, TNFRSF10C, TNFRSF10D, TNFRSF19L, TNFRSF6, TRAILR4, TREM2, TREML1, TSLP, TSPAN2, TYRO3, VEGFB, VSIG4, VSTM2A, or any combination thereof.

[0209] In one embodiment, the method comprises identifying antibody reactivities based on quantitative next generation sequencing data. In one embodiment, the next generation sequencing can determine the total enrichment of antibody target proteins after selection, how many "antibody target protein clones" were enriched, or a combination thereof.

[0210] In one embodiment, the method comprises an incorporation of clonal enrichment into data analysis to eliminate false positive enrichments. In one embodiment, the method comprises an incorporation of clonal enrichment into data analysis to expedite identification of genuine autoantibody reactivities in samples. Thus, in one embodiment, the method comprises quantifying clonal enrichment for identification of antibody reactivities, elimination of non-specific enrichment of antibody target proteins (e.g., polyreactive cell or particle clones), elimination of stochastic variations in library distribution, or any combination

thereof. In one embodiment, the clonal enrichment is a fraction of clones that were enriched above a set cutoff.

[0211] In one embodiment, the methods described herein can utilize next-generation sequencing technologies that allow multiple samples to be sequenced individually as genomic molecules (i.e., singleplex sequencing) or as pooled samples comprising indexed genomic molecules (e.g., multiplex sequencing) on a single sequencing run. These methods can generate up to several hundred million reads of DNA sequences. In various embodiments, the sequences of nucleic acid sequence barcodes can be determined using, for example, the next generation sequencing technologies described herein. In various embodiments, analysis of the massive amount of sequence data obtained using next-generation sequencing can be performed using one or more processors as described herein.

[0212] In some embodiments, the nucleic acid product can be sequenced by next generation sequencing methods. In some embodiments, the next generation sequencing method comprises a method selected from the group consisting of Ion Torrent, Illumina, SOLiD, 454; Massively Parallel Signature Sequencing, solid phase reversible dye terminator sequencing; and DNA nanoball sequencing may be included. In some embodiments, the first and second sequencing primers are compatible with the selected next generation sequencing method.

[0213] In some embodiments, sequencing can be performed by next generation sequencing methods. As used herein, "next generation sequencing" refers to the speeds that were possible with conventional sequencing methods (e.g., Sanger sequencing) by reading thousands of millions of sequencing reactions simultaneously. Means an oligonucleotide sequencing technique that has the ability to sequence oligonucleotides at a greater rate. Non-limiting examples of next generation sequencing methods/platforms include Massively Parallel Signature Sequencing (Lynx Therapeutics); pyrophosphate sequencing/454; 454 Life Sciences/Roche Diagnostics; Solid Phase Reversible Dye Terminator Sequencing (Solexa/illumina): SOLiD technology (Applied Biosystems); ion semiconductor sequencing (ION Torrent.); DNA nanoball sequencing (Complete Genomics); and technologies available from Pacific Biosciences, Intelligen Bio-systems, Oxford Nanopore Technologies, and Helicos Biosciences. In some embodiments, the sequencing primer may comprise a moiety that is compatible with the selected next generation sequencing method.

[0214] Next generation sequencing techniques and related sequencing primer constraints and design parameters are well known in the art (e.g., Shendure et al., 2008, Nature, 26:1135-1145; Mardis, 2007, Trends in Genetics, 24:133-141; Su et al., 2011, Expert. Rev. Mol. Diagn., 11:333-43; Zhang et al., 2011, J. Genet. Genomics, 38:95-109; Nyren P et al. 1993, Anal. Biochem., 208:17175; Bentley et al., 2006, Curr. Opin. Genet. Dev., 16:545-552; Strausberg et al., 2008, Drug Disc. Today, 13:569-577; U.S. Pat. Nos. 7,282,337; 7,279,563; 7,226,720; 7,220,549; 7,169,560; U. S. Patent Application Publication No. 20070070349; U.S. Pat. Nos. 6,818,395; 6,911,345; U.S. Patent Application Publication No. 2006/0252077; No. 2007/0070349).

[0215] Several targeted next generation sequencing methods are described in the literature (for review see e.g., Teer and Mullikin, 2010, Human Mol. Genet. 19:R145-151), all of which can be used in conjunction with the present invention. Many of these methods (described e.g. as genome capture, genome partitioning, genome enrichment etc.) use hybridization techniques and include array-based (e.g., Hodges et al., 2007, Nat. Genet., 39:1522-1527) and liquid based (e.g., Choi et al., 2009, Proc. Natl. Acad. Sci USA, 106:19096-19101) hybridization approaches. Commercial kits for DNA sample preparation are also available: for example, Illumina Inc. (San Diego, California) offers the TruSeq™ DNA Sample Preparation Kit and the Exome Enrichment Kit TruSeq™ Exome Enrichment Kit.

[0216] There are many methods known in the art for the detection, identification, and quantification of specific nucleic acid sequences (e.g., nucleic acid sequence barcodes) and new methods are continually reported. A great majority of the known specific nucleic acid detection, identification, and quantification methods utilize nucleic acid probes in specific hybridization reactions. Preferably, the detection of hybridization to the duplex form is a Southern blot technique. In the Southern blot technique, a nucleic acid sample is separated in an agarose gel based on size (molecular weight) and affixed to a membrane, denatured, and exposed to (admixed with) the labeled nucleic acid probe under hybridizing conditions. If the labeled nucleic acid probe forms a hybrid with the nucleic acid on the blot, the label is bound to the membrane.

[0217] In the Southern blot, the nucleic acid probe is preferably labeled with a tag. That tag can be a radioactive isotope, a fluorescent dye or the other well-known materials. Another type of process for the specific detection of nucleic acids in a biological sample known in the art are the hybridization methods as exemplified by U.S. Pat. Nos. 6,159,693 and 6,270,974, and related patents. To briefly summarize one of those methods, a nucleic acid probe of at least 10 nucleotides, preferably at least 15 nucleotides, more preferably at least 25 nucleotides, having a sequence complementary to a nucleic acid of interest is hybridized in a sample, subjected to depolymerizing conditions, and the sample is treated with an ATP/luciferase system, which will luminesce if the nucleic sequence is present. In quantitative Southern blotting, the level of the nucleic acid of interest can be compared with the level of a second nucleic acid of interest, and/or to one or more comparators nucleic acids (e.g., positive control, negative control, quantity control, etc.).

[0218] Many methods useful for the detection and quantification of nucleic acid takes advantage of the polymerase chain reaction (PCR). The PCR process is well known in the art (U.S. Pat. Nos. 4,683,195, 4,683,202, and 4,800,159). To briefly summarize PCR, nucleic acid primers, complementary to opposite strands of a nucleic acid amplification target sequence, are permitted to anneal to the denatured sample. A DNA polymerase (typically heat stable) extends the DNA duplex from the hybridized primer. The process is repeated to amplify the nucleic acid target. If the nucleic acid primers do not hybridize to the sample, then there is no corresponding amplified PCR product. In this case, the PCR primer acts as a hybridization probe.

[0219] In PCR, the nucleic acid probe can be labeled with a tag as discussed elsewhere herein. Most preferably the detection of the duplex is done using at least one primer directed to the nucleic acid of interest. In yet another embodiment of PCR, the detection of the hybridized duplex comprises electrophoretic gel separation followed by dye-based visualization.

[0220] Typical hybridization and washing stringency conditions depend in part on the size (i.e., number of nucleotides in length) of the oligonucleotide probe, the base composition and monovalent and divalent cation concentrations (Ausubel et al., 1994, eds Current Protocols in Molecular Biology).

[0221] In one embodiment, the process for determining the quantitative and qualitative profile of the nucleic acid of interest according to the present invention is characterized in that the amplifications are real-time amplifications performed using a labeled probe, preferably a labeled hydrolysis-probe, capable of specifically hybridizing in stringent conditions with a segment of the nucleic acid of interest. The labeled probe is capable of emitting a detectable signal every time each amplification cycle occurs, allowing the signal obtained for each cycle to be measured.

[0222] The real-time amplification, such as real-time PCR, is well known in the art, and the various known techniques will be employed in the best way for the implementation of the present process. These techniques are performed using various categories of probes, such as hydrolysis probes, hybridization adjacent probes, or molecular beacons. The techniques employing hydrolysis probes or molecular beacons are based on the use of a fluorescence quencher/reporter system, and the hybridization adjacent probes are based on the use of fluorescence acceptor/donor molecules.

[0223] Hydrolysis probes with a fluorescence quencher/reporter system are available in the market, and are for example commercialized by the Applied Biosystems group (USA). Many fluorescent dyes may be employed, such as FAM dyes (6-carboxy-fluorescein), or any other dye phosphoramidite reagents.

[0224] Among the stringent conditions applied for any one of the hydrolysis-probes of the present invention is the Tm, which is in the range of about 65° C. to 75° C. Preferably, the Tm for any one of the hydrolysis-probes of the present invention is in the range of about 67° C. to about 70° C. Most preferably, the Tm applied for any one of the hydrolysis-probes of the present invention is about 67° C.

[0225] In one aspect, the invention includes a primer that is complementary to a nucleic acid of interest, and more particularly the primer includes 12 or more contiguous nucleotides substantially complementary to the nucleic acid of interest. Preferably, a primer featured in the invention includes a nucleotide sequence sufficiently complementary to hybridize to a nucleic acid sequence of about 12 to 25 nucleotides. More preferably, the primer differs by no more than 1, 2, or 3 nucleotides from the target flanking nucleotide sequence. In another aspect, the length of the primer can vary in length, preferably about 15 to 28 nucleotides in length (e.g., 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, or 27 nucleotides in length).

[0226] In one embodiment, the invention includes detecting one or more barcode-labeled nucleic acid sequences, one or more nucleic acid sequence barcodes, or a combination thereof in the DNA of the antibody-bound cell or particle. Such sequences generally can be measured and detected through a variety of assays, methods and detection systems known to one of skill in the art.

[0227] Various methods include but are not limited to immunoassays, microarray, PCR, RT-PCR, refractive index spectroscopy (RI), ultra-violet spectroscopy (UV), fluorescence analysis, electrochemical analysis, radiochemical analysis, near-infrared spectroscopy (near-IR), infrared (IR) spectroscopy, nuclear magnetic resonance spectroscopy (NMR), light scattering analysis (LS), mass spectrometry, pyrolysis mass spectrometry, nephelometry, dispersive Raman spectroscopy, gas chromatography, liquid chromatography, gas chromatography combined with mass spectrometry, liquid chromatography combined with mass spectrometry, matrix-assisted laser desorption ionization-time of flight (MALDI-TOF) combined with mass spectrometry, ion spray spectroscopy combined with mass spectrometry, capillary electrophoresis, colorimetry and surface plasmon resonance (such as according to systems provided by Biacore Life Sciences). See also PCT Publications WO/2004/056456 and WO/2004/088309. In this regard, the nucleic acid sequence barcodes can be measured using the above-mentioned detection methods, or other methods known to the skilled artisan. Other nucleic acid sequence barcodes can be similarly detected using reagents that are specifically designed or tailored to detect them.

[0228] Different types of antibody targets and their measurements can be combined in the compositions and methods of the present invention. In various embodiments, the nucleic acid sequence encoding one or more antibody target is measured. In various embodiments, the nucleic acid sequence barcode is measured. In exemplary embodiments, the nucleic acid sequence barcode is DNA. In various embodiments, measurements of nucleic acid sequences encoding one or more antibody targets are used in conjunction with measurements of nucleic acid sequence barcodes.

[0229] In various embodiments of the invention, methods of measuring antibody target levels (e.g., the levels of barcode-labeled nucleic acid sequences, levels of nucleic acid sequences encoding one or more antibody targets, levels of the nucleic acid barcodes of the barcode-labeled nucleic acid sequences) include, but are not limited to, an immunochromatography assay, an immunodot assay, a Luminex assay, an ELISA assay, an ELISPOT assay, a protein microarray assay, a ligand-receptor binding assay, displacement of a ligand from a receptor assay, displacement of a ligand from a shared receptor assay, an immunostaining assay, a Western blot assay, a mass spectrophotometry assay, a radioimmunoassay (RIA), a radioimmunodiffusion assay, a liquid chromatography-tandem mass spectrometry assay, an ouchterlony immunodiffusion assay, reverse phase protein microarray, a rocket immunoelectrophoresis assay, an immunohistostaining assay, an immunoprecipitation assay, a complement fixation assay, FACS, an enzyme-substrate binding assay, an enzymatic assay, an enzymatic assay employing a detectable molecule, such as a chromophore, fluorophore, or radioactive substrate, a substrate binding assay employing such a substrate, a substrate displacement assay employing such a substrate, and a protein chip assay (see also, 2007, Van Emon, Immunoassay and Other Bioanalytical Techniques, CRC Press; 2005, Wild, Immunoassay Handbook, Gulf Professional Publishing; 1996, Diamandis and Christopoulos, Immunoassay, Academic Press; 2005, Joos, Microarrays in Clinical Diagnosis, Humana Press; 2005, Hamdan and Righetti, Proteomics Today, John Wiley and Sons; 2007).

[0230] Methods for detecting a nucleic acid sequence (e.g., nucleic acid sequence barcode, such as DNA, nucleic acid sequence encoding one or more antibody targets, and/or a barcode-labeled nucleic acid sequence encoding one or more antibody targets), such as RT-PCR, real time PCR, microarray, branch DNA, NASBA and others, are well known in the art. Using sequence information provided by

the database entries for the nucleic acid sequences, expression of the nucleic acid sequences can be detected (if present) and measured using techniques well known to one of ordinary skill in the art. For example, sequences in sequence database entries or sequences disclosed herein can be used to construct probes for detecting nucleic acid sequence barcodes in, e.g., Northern blot hybridization analyses or methods which specifically, and, preferably, quantitatively amplify specific nucleic acid sequences. As another example, the sequences can be used to construct primers for specifically amplifying the nucleic acid sequence barcodes in, e.g., amplification-based detection methods such as reverse-transcription based polymerase chain reaction (RT-PCR). In addition to Northern blot and RT-PCR, the level of nucleic acid sequence barcodes can also be measured using, for example, other target amplification methods (e.g., TMA, SDA, NASBA), signal amplification methods (e.g., bDNA), nuclease protection assays, in situ hybridization and the like.

[0231] In various embodiments, quantitative hybridization methods, such as Southern analysis, Northern analysis, or in situ hybridizations, can be used (see Current Protocols in Molecular Biology, Ausubel, F. et al., eds., John Wiley & Sons, including all supplements). A "nucleic acid probe," as used herein, can be a DNA probe or an RNA probe. The probe can be, for example, a gene, a gene fragment (e.g., one or more exons), a vector comprising the gene, a probe or primer, etc. For representative examples of use of nucleic acid probes, see, for example, U.S. Pat. Nos. 5,288,611 and 4,851,330. The nucleic acid probe can be, for example, a full-length nucleic acid molecule, or a portion thereof, such as an oligonucleotide of at least 15, 30, 50, 100, 250 or 500 nucleotides in length and sufficient to specifically hybridize under stringent conditions to appropriate target mRNA or cDNA. The hybridization sample is maintained under conditions which are sufficient to allow specific hybridization of the nucleic acid probe to mRNA or cDNA. Specific hybridization can be performed under high stringency conditions or moderate stringency conditions, as appropriate. In a preferred embodiment, the hybridization conditions for specific hybridization are high stringency. Specific hybridization, if present, is then detected using standard methods. If specific hybridization occurs between the nucleic acid probe having a mRNA or cDNA in the test sample, the level of the mRNA or cDNA in the sample can be assessed. More than one nucleic acid probe can also be used concurrently in this method. Specific hybridization of any one of the nucleic acid probes is indicative of the presence of the mRNA or cDNA of interest, as described herein.

[0232] Alternatively, a peptide nucleic acid (PNA) probe can be used instead of a nucleic acid probe in the quantitative hybridization methods described herein. PNA is a DNA mimic having a peptide-like, inorganic backbone, such as N-(2-aminoethyl)glycine units, with an organic base (A, G, C, T or U) attached to the glycine nitrogen via a methylene carbonyl linker (see, for example, 1994, Nielsen et al., Bioconjugate Chemistry 5:1). The PNA probe can be designed to specifically hybridize to a target nucleic acid sequence. Hybridization of the PNA probe to a nucleic acid sequence is used to determine the level of the target nucleic acid in the biological sample.

[0233] In another embodiment, arrays of oligonucleotide probes that are complementary to target nucleic acid sequence barcodes can be used to determine the level of one or more antibody targets. The array of oligonucleotide probes can be used to determine the level of one or more antibody targets alone or the level of the one or more antibody targets in relation to the level of one or more other nucleic acids in the biological sample. Oligonucleotide arrays typically comprise a plurality of different oligonucleotide probes that are coupled to a surface of a substrate in different known locations. These oligonucleotide arrays, also known as "Genechips," have been generally described in the art, for example, U.S. Pat. No. 5,143,854 and PCT patent publication Nos. WO 90/15070 and 92/10092. These arrays can generally be produced using mechanical synthesis methods or light directed synthesis methods which incorporate a combination of photolithographic methods and solid phase oligonucleotide synthesis methods. See Fodor et al., Science, 251:767-777 (1991), Pirrung et al., U.S. Pat. No. 5,143,854 (see also PCT Application No. WO 90/15070) and Fodor et al., PCT Publication No. WO 92/10092 and U.S. Pat. No. 5,424,186. Techniques for the synthesis of these arrays using mechanical synthesis methods are described in, e.g., U.S. Pat. No. 5,384,261.

[0234] After an oligonucleotide array is prepared, a nucleic acid of interest is hybridized with the array and its level is quantified. Hybridization and quantification are generally carried out by methods described herein and also in, e.g., published PCT Application Nos. WO 92/10092 and WO 95/11995, and U.S. Pat. No. 5,424,186. In brief, a target nucleic acid sequence is amplified by well-known amplification techniques, e.g., PCR. Typically, this involves the use of primer sequences that are complementary to the target nucleic acid. Asymmetric PCR techniques may also be used. Amplified target, generally incorporating a label, is then hybridized with the array under appropriate conditions. Upon completion of hybridization and washing of the array, the array is scanned to determine the quantity of hybridized nucleic acid. The hybridization data obtained from the scan is typically in the form of fluorescence intensities as a function of quantity, or relative quantity, of the target nucleic acid in the biological sample. The target nucleic acid can be hybridized to the array in combination with one or more comparators (e.g., positive control, negative control, quantity control, etc.) to improve quantification of the target nucleic acid in the sample.

[0235] The probes and primers according to the invention can be labeled directly or indirectly with a radioactive or nonradioactive compound, by methods well known to those skilled in the art, in order to obtain a detectable and/or quantifiable signal; the labeling of the primers or of the probes according to the invention is carried out with radioactive elements or with nonradioactive molecules. Among the radioactive isotopes used, mention may be made of ^{32}P, ^{33}P, ^{35}S or ^{3}H. The nonradioactive entities are selected from ligands such as biotin, avidin, streptavidin or digoxigenin, haptenes, dyes, and luminescent agents such as radioluminescent, chemoluminescent, bioluminescent, fluorescent or phosphorescent agents.

[0236] Other suitable assays for determining the level of nucleic acid sequence barcode or level of barcode-labeled nucleic acid sequence may include one or more of the following methods, an enzyme assay, an immunoassay, mass spectrometry, chromatography, electrophoresis or an antibody microarray, or any combination thereof. Thus, as would be understood by one skilled in the art, the system and

methods of the invention may include any method known in the art to detect a nucleic acid sequence and/or amino acid sequence in a sample.

[0237] In some embodiments, methods of identifying antibody targets, optionally, utilize methods that focus on cellular components (cellular examination), or methods that focus on examining extracellular components (fluid examination). In one embodiment, a cellular or fluid examination is used to detect or measure a variety of molecules including the nucleic acid barcode, RNA, protein, and a number of molecules that are modified as a result of the protein's function. Exemplary methods focusing on nucleic acids include but are not limited to amplification techniques, such as PCR and RT-PCR (including quantitative variants), and hybridization techniques, such as in situ hybridization, microarrays, and blots. Exemplary methods focusing on amino acid sequences (e.g., proteins) include but are not limited to binding techniques, such as ELISA, immunohistochemistry, microarray, and functional techniques, such as enzymatic assays. For example, in some embodiments, methods of identifying antibody targets, optionally, utilize ELISA, LIPS, or a combination thereof.

Methods of Identifying Antibodies

[0238] In one aspect, the method comprises identifying at least one antibody that specifically binds to an extracellular or secreted protein. Thus, in one embodiment, the method comprises: isolating the antibodies that bound to the display library of the invention; and identifying the sequence of the antibodies that bound to the display library of the invention.

[0239] For example, in various embodiments, the antibody is an anti-BMPR2 antibody, anti-BTN1A1 antibody, anti-BTNL8 antibody, anti-C1QTNF4 antibody, anti-C6 antibody, anti-CCL11 antibody, anti-CCL15 antibody, anti-CCL17 antibody, anti-CCL2 antibody, anti-CCL22 antibody, anti-CCL24 antibody, anti-CCL4L1 antibody, anti-CD207 antibody, anti-CD300E antibody, anti-CD3D antibody, anti-CD44 antibody, anti-CD74 antibody, anti-CD81 antibody, anti-CDH19 antibody, anti-CNTN5 antibody, anti-COLEC12 antibody, anti-CSPG5 antibody, anti-CX3CL1 antibody, anti-CXCL1 antibody, anti-CXCL13 antibody, anti-CXCL2 antibody, anti-CXCL3 antibody, anti-EDIL3 antibody, anti-EPYC antibody, anti-EREG antibody, anti-FGF10 antibody, anti-FGF21 antibody, anti-FGF23 antibody, anti-FGF7 antibody, anti-FGFBP3 antibody, anti-FGFRL1 antibody, anti-IFNA13 antibody, anti-IFNA14 antibody, anti-IFNA17 antibody, anti-IFNA2 antibody, anti-IFNA5 antibody, anti-IFNA6 antibody, anti-IFNA8 antibody, anti-IFNB1 antibody, anti-IFNL2 antibody, anti-IFNW1 antibody, anti-IGF2 antibody, anti-IGFBPL1 antibody, anti-IGSF4B antibody, anti-IL15RA antibody, anti-IL16 antibody, anti-IL17A antibody, anti-IL17F antibody, anti-IL17F antibody, anti-IL18RAP antibody, anti-IL19 antibody, anti-IL1A antibody, anti-IL1F9 antibody, anti-ILIRAP antibody, anti-IL20RB antibody, anti-IL22 antibody, anti-IL22RA2 antibody, anti-IL28B antibody, anti-IL29 antibody, anti-IL33 antibody, anti-IL34 antibody, anti-IL4 antibody, anti-IL4R antibody, anti-IL5 antibody, anti-IL6 antibody, anti-IL6R antibody, anti-ITGA5 antibody, anti-JCHAIN antibody, anti-LAG3 antibody, anti-LGR6 antibody, anti-LIF antibody, anti-LRP11 antibody, anti-LRRC3B antibody, anti-LRRC4 antibody, anti-LRTM2 antibody, anti-LY6G6D antibody, anti-LY6H antibody, anti-MADCAM1 antibody, anti-MPZL3 antibody, anti-MUC21 antibody, anti-NGFR antibody, anti-NOTCH2NL antibody, anti-NTRK3 antibody, anti-PDCD1LG2 antibody, anti-PDGFB antibody, anti-PGLYRP1 antibody, anti-REG1A antibody, anti-REG1B antibody, anti-REG4 antibody, anti-RTN4RL1 antibody, anti-SCARA3 antibody, anti-SDC1 antibody, anti-SDC4 antibody, anti-STIM2 antibody, anti-TGFA antibody, anti-TMEM149 antibody, anti-TNF antibody, anti-TNFRSF10C antibody, anti-TNFRSF10D antibody, anti-TNFRSF19L antibody, anti-TNFRSF6 antibody, anti-TREM2 antibody, anti-TREML1 antibody, anti-TSLP antibody, anti-TSPAN2 antibody, anti-TYRO3 antibody, anti-VEGFB antibody, anti-VSIG4 antibody, anti-VSTM2A antibody, or any combination thereof.

Method of Identifying an Antibody or a Target Thereof Associated with a Disease or Disorder

[0240] The present invention provides, in part, a method of identifying disease associated antigen-antibody interactions. The present invention provides, in part, a method of identifying autoantigens that are targets of disease-associated autoantibodies. In one aspect, the method comprises contacting a display library of the invention with a biological sample from a subject who has been diagnosed as having a disease or disorder. In one embodiment, the disease or disorder is selected from an autoimmune disease or disorder, cancer, inflammatory disease or disorder, metabolic disease or disorder, neurodegenerative disease or disorder, organ tissue rejection, organ transplant rejection, an autoimmune or inflammatory disease or disorder associated with an infectious disease, or any combination thereof. In some embodiments, the disease or disorder is antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis, autoimmune polyendocrinopathy candidiasis ecto-dermal dystrophy, antiphospholipid antibody syndrome, chronic inflammatory demyelinating polyradiculoneuropathy, cutaneous lupus erythematosus, COVID-19, drug-induced lupus, dermatomyositis, glomerulonephritis, a disease or disorder associated with kidney transplant, malaria, mixed connective tissue disease, myasthenia gravis, malignant melanoma, neuromyelitis optica, non-small cell lung cancer, pediatric autoimmune neuropsychiatric disorders associated with streptococcal infections, systemic lupus erythematosus, sjogren's syndrome, scleroderma, susac syndrome, undifferentiated connective tissue disease, or any combination thereof.

[0241] In one embodiment, the antibody is purified from a biological sample obtained from a subject having a disease or disorder.

[0242] In one embodiment, the antigen or autoantigen is identified to be reactive with an antibody or autoantibody associated with a disease or disorder when the level of nucleic acid sequence barcode is statistically different than an expected level based on comparison with a control or a threshold level (e.g., the predetermined threshold level). In one embodiment, the antibody target is identified to be the antibody target associated with the disease or disorder when the level of nucleic acid sequence barcode is higher than the threshold level (e.g., the predetermined threshold level). In some embodiments, the threshold level is obtained from control group samples.

[0243] In various embodiments of the methods of the invention, the level (e.g., activity, amount, concentration, expression, level, etc.) of nucleic acid sequence barcode is determined to be increased or to be higher when the level of nucleic acid sequence barcode is determined to be increased

by at least 0.01 fold, at least 0.05 fold, at least 0.07 fold, at least 0.076 fold, at least 0.1 fold, at least 0.18 fold, at least 0.19 fold, at least 0.3 fold, at least 0.36 fold, at least 0.37 fold, at least 0.38 fold, at least 0.4 fold, at least 0.43 fold, at least 1 fold, at least 1.1 fold, at least 1.2 fold, at least 1.3 fold, at least 1.4 fold, at least 1.5 fold, at least 1.6 fold, at least 1.7 fold, at least 1.8 fold, at least 1.9 fold, at least 2 fold, at least 2.1 fold, at least 2.2 fold, at least 2.3 fold, at least 2.4 fold, at least 2.5 fold, at least 2.6 fold, at least 2.7 fold, at least 2.8 fold, at least 2.9 fold, at least 3 fold, at least 3.5 fold, at least 4 fold, at least 4.5 fold, at least 5 fold, at least 5.5 fold, at least 6 fold, at least 6.5 fold, at least 7 fold, at least 7.5 fold, at least 8 fold, at least 8.5 fold, at least 9 fold, at least 9.5 fold, at least 10 fold, at least 11 fold, at least 12 fold, at least 13 fold, at least 14 fold, at least 15 fold, at least 16 fold, at least 16.3 fold, at least 16.31 fold, at least 20 fold, at least 25 fold, at least 26 fold, at least 26.7 fold, at least 26.72 fold, at least 30 fold, at least 40 fold, at least 50 fold, at least 75 fold, at least 100 fold, at least 192 fold, at least 192.4 fold, at least 192.44 fold, at least 200 fold, at least 250 fold, at least 500 fold, or at least 1000 fold, or at least 10000 fold, when compared with a comparator.

[0244] In one embodiment, an antibody target is identified to be the antibody target associated with a disease or disorder when the expression level of nucleic acid sequence barcode is increased or higher as compared to a comparator (e.g., the predetermined threshold level). For example, in some embodiments, an antibody target is identified to be the antibody target associated with a disease or disorder when the level of nucleic acid sequence barcode is increased by at least 0.01 fold, or at least 0.18 fold. In some embodiments, an antibody target is identified to be the antibody target associated with a disease or disorder when the level of nucleic acid sequence barcode is increased in a range from 0.1 fold to 10,000 fold.

[0245] In one embodiment, the antibody target is identified to be the antibody target associated with the disease or disorder when the level of nucleic acid sequence barcode is lower than the threshold level (e.g., the predetermined threshold level).

[0246] In various embodiments of the methods of the invention, the level (e.g., activity, amount, concentration, expression, level, etc.) of nucleic acid sequence barcode is determined to be decreased or to be lower when the level of nucleic acid sequence barcode is determined to be decreased by at least 0.01 fold, at least 0.05 fold, at least 0.07 fold, at least 0.076 fold, at least 0.1 fold, at least 0.18 fold, at least 0.19 fold, at least 0.3 fold, at least 0.36 fold, at least 0.37 fold, at least 0.38 fold, at least 0.4 fold, at least 0.43 fold, at least 1 fold, at least 1.1 fold, at least 1.2 fold, at least 1.3 fold, at least 1.4 fold, at least 1.5 fold, at least 1.6 fold, at least 1.7 fold, at least 1.8 fold, at least 1.9 fold, at least 2 fold, at least 2.1 fold, at least 2.2 fold, at least 2.3 fold, at least 2.4 fold, at least 2.5 fold, at least 2.6 fold, at least 2.7 fold, at least 2.8 fold, at least 2.9 fold, at least 3 fold, at least 3.5 fold, at least 4 fold, at least 4.5 fold, at least 5 fold, at least 5.5 fold, at least 6 fold, at least 6.5 fold, at least 7 fold, at least 7.5 fold, at least 8 fold, at least 8.5 fold, at least 9 fold, at least 9.5 fold, at least 10 fold, at least 11 fold, at least 12 fold, at least 13 fold, at least 14 fold, at least 15 fold, at least 16 fold, at least 16.3 fold, at least 16.31 fold, at least 20 fold, at least 25 fold, at least 26 fold, at least 26.7 fold, at least 26.72 fold, at least 30 fold, at least 40 fold, at least 50 fold, at least 75 fold, at least 100 fold, at least 192 fold, at least 192.4 fold, at least 192.44 fold, at least 200 fold, at least 250 fold, at least 500 fold, or at least 1000 fold, or at least 10000 fold, when compared with a comparator.

[0247] In one embodiment, an antibody target is identified to be the antibody target associated with a disease or disorder when the expression level of nucleic acid sequence barcode is decreased or lower as compared to a comparator (e.g., the predetermined threshold level). For example, in some embodiments, an antibody target is identified to be the antibody target associated with a disease or disorder when the level of nucleic acid sequence barcode is decreased by at least 0.01 fold, or at least 0.18 fold. In some embodiments, an antibody target is identified to be the antibody target associated with a disease or disorder when the level of nucleic acid sequence barcode is decreased in a range from 0.1 fold to 10,000 fold.

[0248] In one aspect, the present invention provides, in part, a method of identifying an antibody associated with a disease or disorder. Thus, in one embodiment, the antibody is identified to be the antibody associated with the disease or disorder when the level of the target nucleic acid sequence barcode is different than the threshold level (e.g., the predetermined threshold level). In one embodiment, the antibody is identified to be the antibody associated with the disease or disorder when the level of the target nucleic acid sequence barcode is higher than the threshold level (e.g., the predetermined threshold level). In some embodiments, the threshold level is obtained from control group samples.

[0249] In one embodiment, an antibody is identified to be the antibody associated with a disease or disorder when the expression level of the target nucleic acid sequence barcode is increased or higher as compared to a comparator (e.g., the predetermined threshold level). For example, in some embodiments, an antibody is identified to be the antibody associated with a disease or disorder when the level of the target nucleic acid sequence barcode is increased by at least 0.01 fold, or at least 0.18 fold. In some embodiments, an antibody is identified to be the antibody associated with a disease or disorder when the level of nucleic acid sequence barcode is increased in a range from 0.1 fold to 10,000 fold.

[0250] In one embodiment, the antibody is identified to be the antibody associated with the disease or disorder when the level of the target nucleic acid sequence barcode is lower than the threshold level (e.g., the predetermined threshold level).

[0251] In one embodiment, an antibody is identified to be the antibody associated with a disease or disorder when the expression level of the target nucleic acid sequence barcode is decreased or lower as compared to a comparator (e.g., the predetermined threshold level). For example, in some embodiments, an antibody is identified to be the antibody associated with a disease or disorder when the level of nucleic acid sequence barcode is decreased by at least 0.01 fold, or at least 0.18 fold. In some embodiments, an antibody is identified to be the antibody associated with a disease or disorder when the level of nucleic acid sequence barcode is decreased in a range from 0.1 fold to 10,000 fold.

[0252] In some embodiments, the disease or disorder is an autoimmune disease or disorder, cancer, inflammatory disease or disorder, metabolic disease or disorder, neurodegenerative disease or disorder, organ tissue rejection, organ transplant rejection, or any combination thereof. In some embodiments, the disease or disorder is antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis, autoim-

mune polyendocrinopathy candidiasis ecto-dermal dystrophy, antiphospholipid antibody syndrome, chronic inflammatory demyelinating polyradiculoneuropathy, cutaneous lupus erythematosus, COVID-19, drug-induced lupus, dermatomyositis, glomerulonephritis, a disease or disorder associated with kidney transplant, malaria, mixed connective tissue disease, myasthenia gravis, malignant melanoma, neuromyelitis optica, non-small cell lung cancer, pediatric autoimmune neuropsychiatric disorders associated with streptococcal infections, systemic lupus erythematosus, sjogren's syndrome, scleroderma, susac syndrome, undifferentiated connective tissue disease, or any combination thereof.

[0253] In one embodiment, the disease or disorder is a cancer. Examples of cancers include, but are not limited to: acute lymphoblastic; acute myeloid leukemia; adrenocortical carcinoma; adrenocortical carcinoma, childhood; appendix cancer; basal cell carcinoma; bile duct cancer, extrahepatic; bladder cancer; bone cancer; osteosarcoma and malignant fibrous histiocytoma; liposarcoma and anaplastic liposarcoma; brain stem glioma, childhood; brain tumor, adult; brain tumor, brain stem glioma, childhood; brain tumor, central nervous system atypical teratoid/rhabdoid tumor, childhood; central nervous system embryonal tumors; cerebellar astrocytoma; cerebral astrocytotna/malignant glioma; craniopharyngioma; ependymoblastoma; ependymoma; medulloblastoma; medulloepithelioma; pineal parenchymal tumors of intermediate differentiation; supratentorial primitive neuroectodermal tumors and pineoblastoma; visual pathway and hypothalamic glioma; brain and spinal cord tumors; breast cancer; bronchial tumors; Burkitt lymphoma; carcinoid tumor; carcinoid tumor, gastrointestinal; central nervous system atypical teratoid/rhabdoid tumor; central nervous system embryonal tumors; central nervous system lymphoma; cerebellar astrocytoma cerebral astrocytoma/malignant glioma, childhood; cervical cancer; chordoma, childhood; chronic lymphocytic leukemia; chronic myelogenous leukemia; chronic myeloproliferative disorders; colon cancer; colorectal cancer; craniopharyngioma; cutaneous T-cell lymphoma; esophageal cancer; Ewing family of tumors; extragonadal germ cell tumor; extrahepatic bile duct cancer; eye cancer, intraocular melanoma; eye cancer, retinoblastoma; biliary track cancer, cholangiocarcinoma, anal cancer, neuroendocrine tumors, small bowel cancer, gallbladder cancer; gastric (stomach) cancer; gastrointestinal carcinoid tumor; gastrointestinal stromal tumor (gist); germ cell tumor, extracranial; germ cell tumor, extragonadal; germ cell tumor, ovarian; gestational trophoblastic tumor; glioma; glioma, childhood brain stem; glioma, childhood cerebral astrocytoma; glioma, childhood visual pathway and hypothalamic; hairy cell leukemia; head and neck cancer; hepatocellular (liver) cancer; histiocytosis, langerhans cell; Hodgkin lymphoma; hypopharyngeal cancer; hypothalamic and visual pathway glioma; intraocular melanoma; islet cell tumors; kidney (renal cell) cancer; Langerhans cell histiocytosis; laryngeal cancer; leukemia, acute lymphoblastic; leukemia, acute myeloid; leukemia, chronic lymphocytic; leukemia, chronic myelogenous; leukemia, hairy cell; lip and oral cavity cancer; liver cancer; lung cancer, non-small cell; lung cancer, small cell; lymphoma, aids-related; lymphoma, burkitt; lymphoma, cutaneous T-cell; lymphoma, non-Hodgkin lymphoma; lymphoma, primary central nervous system; macroglobulinemia, Waldenstrom; malignant fibrous histiocytoma of bone and osteosarcoma; medulloblastoma; melanoma; melanoma, intraocular (eye); Merkel cell carcinoma; mesothelioma; metastatic squamous neck cancer with occult primary; mouth cancer; multiple endocrine neoplasia syndrome, (childhood); multiple myeloma/plasma cell neoplasm; mycosis; fungoides; myelodysplastic syndromes; myelodysplastic/myeloproliferative diseases; myelogenous leukemia, chronic; myeloid leukemia, adult acute; myeloid leukemia, childhood acute; myeloma, multiple; myeloproliferative disorders, chronic; nasal cavity and paranasal sinus cancer; nasopharyngeal cancer; neuroblastoma; non-small cell lung cancer; oral cancer; oral cavity cancer; oropharyngeal cancer; osteosarcoma and malignant fibrous histiocytoma of bone; ovarian cancer; ovarian epithelial cancer; ovarian germ cell tumor; ovarian low malignant potential tumor; pancreatic cancer, islet cell tumors; papillomatosis; parathyroid cancer; penile cancer; pharyngeal cancer; pheochromocytoma; pineal parenchymal tumors of intermediate differentiation; pineoblastoma and supratentorial primitive neuroectodermal tumors; pituitary tumor; plasma celt neoplasm/multiple myeloma; pleuropulmonary blastoma; primary central nervous system lymphoma; prostate cancer; rectal cancer; renal cell (kidney) cancer; renal pelvis and ureter, transitional cell cancer; respiratory tract carcinoma involving the nut gene on chromosome 15; retinoblastoma; rhabdomyosarcoma; salivary gland cancer; sarcoma, ewing family of tumors; sarcoma, Kaposi; sarcoma, soft tissue; sarcoma, uterine; sezary syndrome; skin cancer (nonmelanoma); skin cancer (melanoma); skin carcinoma, Merkel cell; small cell lung cancer; small intestine cancer; soft tissue sarcoma; squamous cell carcinoma, squamous neck cancer with occult primary, metastatic; stomach (gastric) cancer; supratentorial primitive neuroectodermal tumors; T-cell lymphoma, cutaneous; testicular cancer; throat cancer; thymoma and thymic carcinoma; thyroid cancer; transitional cell cancer of the renal pelvis and ureter; trophoblastic tumor, gestational; urethral cancer; uterine cancer, endometrial; uterine sarcoma; vaginal cancer; vulvar cancer; Waldenstrom macroglobulinemia; Wilms tumor, and any combination thereof.

[0254] Control group samples may either be from a normal subject, samples from subjects with a known diagnosis of a disease or disorder associated with increased level of the antibody or the target thereof, samples from subjects with a known diagnosis of a disease or disorder associated with decreased level of the antibody or the target thereof, or any combination thereof. As described below, comparison of the expression patterns of the sample to be tested with those of the comparators can be used to assess the risk of developing a disease or disorder associated with decreased antibody level, increased level of the antibody or the target thereof, or any combination thereof in the subject. In some instances, the control groups are only for the purposes of establishing initial cutoffs or thresholds for the assays of the invention. Therefore, in some instances, the systems and methods of the invention can evaluate a treatment of a disease or disorder associated with decreased level of the antibody or target thereof, increased level of the antibody or target thereof, or any combination thereof without the need to compare with a control group.

Method of Diagnosing a Disease or Disorder

[0255] The present invention further relates, in part, to a method of diagnosing a disease or disorder associated with

at least one antibody or target thereof (e.g., an antibody level, antibody target level, antibody activity, or antibody target activity) in a subject in need thereof.

[0256] In one aspect, the present invention provides a method of diagnosing a disease or disorder in a subject, the method comprising assessing the presence of at least one antibody in the subject, wherein the at least one antibody is identified to be associated with the disease or disorder according to the method described above. In one aspect, the present invention provides a method of diagnosing a disease or disorder in a subject, the method comprising assessing the level or activity of at least one antibody in the subject, wherein the at least one antibody is identified to be associated with the disease or disorder according to the method described above.

[0257] In one embodiment, the subject is diagnosed with a disease or disorder when the level or activity of at least one antibody is different than the threshold level (e.g., the predetermined threshold level). In one embodiment, the subject is diagnosed with a disease or disorder when the level or activity of at least one antibody is higher than the threshold level (e.g., the predetermined threshold level). In some embodiments, the threshold level is obtained from control group samples. In one embodiment, the threshold is 0.

[0258] In one embodiment, the subject is diagnosed with a disease or disorder by detecting an altered or increased level of an antibody that binds to at least one antibody target associated with the disease or disorder, relative to a control level. In some embodiments, the control level is a level of a particular marker (i.e., an antibody that binds to at least one antibody target associated with the disease or disorder) in a subject or population known not to have the disease.

[0259] In various embodiments of the methods of the invention, the level (e.g., activity, amount, concentration, expression, level, etc.) of antibody is determined to be increased or to be higher when the level of antibody is determined to be more than 0.

[0260] In various embodiments of the methods of the invention, the level (e.g., activity, amount, concentration, expression, level, etc.) of antibody is determined to be increased or to be higher when the level of antibody is determined to be increased by at least 0.01 fold, at least 0.05 fold, at least 0.07 fold, at least 0.076 fold, at least 0.1 fold, at least 0.18 fold, at least 0.19 fold, at least 0.3 fold, at least 0.36 fold, at least 0.37 fold, at least 0.38 fold, at least 0.4 fold, at least 0.43 fold, at least 1 fold, at least 1.1 fold, at least 1.2 fold, at least 1.3 fold, at least 1.4 fold, at least 1.5 fold, at least 1.6 fold, at least 1.7 fold, at least 1.8 fold, at least 1.9 fold, at least 2 fold, at least 2.1 fold, at least 2.2 fold, at least 2.3 fold, at least 2.4 fold, at least 2.5 fold, at least 2.6 fold, at least 2.7 fold, at least 2.8 fold, at least 2.9 fold, at least 3 fold, at least 3.5 fold, at least 4 fold, at least 4.5 fold, at least 5 fold, at least 5.5 fold, at least 6 fold, at least 6.5 fold, at least 7 fold, at least 7.5 fold, at least 8 fold, at least 8.5 fold, at least 9 fold, at least 9.5 fold, at least 10 fold, at least 11 fold, at least 12 fold, at least 13 fold, at least 14 fold, at least 15 fold, at least 16 fold, at least 16.3 fold, at least 16.31 fold, at least 20 fold, at least 25 fold, at least 26 fold, at least 26.7 fold, at least 26.72 fold, at least 30 fold, at least 40 fold, at least 50 fold, at least 75 fold, at least 100 fold, at least 192 fold, at least 192.4 fold, at least 192.44 fold, at least 200 fold, at least 250 fold, at least 500 fold, or at least 1000 fold, or at least 10000 fold, when compared with a comparator (e.g., the level of antibody in control group samples).

[0261] In one embodiment, the subject is diagnosed with a disease or disorder when the level or activity of at least one antibody associated with the disease or disorder is increased or higher as compared to a comparator (e.g., the predetermined threshold level). For example, in some embodiments, the subject is diagnosed with a disease or disorder when at least one antibody associated with the disease or disorder is present in the subject (i.e., the level or activity of at least one antibody associated with the disease or disorder is more than 0). In some embodiments, the subject is diagnosed with a disease or disorder when the level or activity of at least one antibody associated with the disease or disorder is increased by at least 0.01 fold, or at least 0.18 fold. In some embodiments, the subject is diagnosed with a disease or disorder when the level or activity of at least one antibody associated with the disease or disorder is increased in a range from 0.1 fold to 10,000 fold.

[0262] For example, in some embodiments, the subject is diagnosed with ANCA-associated vasculitis by detecting an altered or increased level of an antibody that binds to EDIL3, LY6H, TREM2, or any combination thereof, relative to a control level.

[0263] In some embodiments, the subject is diagnosed with autoimmune polyendocrinopathy candidiasis ecto-dermal dystrophy by detecting an altered or increased level of an antibody that binds to FGF10, LRRC3B, VSTM2A, IL22, IL17F, IL17A, IL5, IL22RA2, IFNL2, IGSF4B, IL28B, IFNA13, IFNA14, IFNA17, IFNA2, IFNA5, IFNA6, IFNA8, or any combination thereof, relative to a control level.

[0264] In some embodiments, the subject is diagnosed with antiphospholipid antibody syndrome by detecting an altered or increased level of an antibody that binds to IFNA13, IFNA14, IFNA17, IFNA2, IFNA5, IFNA6, IFNA8, IL6R, or any combination thereof, relative to a control level.

[0265] In some embodiments, the subject is diagnosed with chronic inflammatory demyelinating polyradiculoneuropathy by detecting an altered or increased level of an antibody that binds to CXCL1, CXCL2, CXCL3, PDGFB, TMEM149, CD74, CXCL13, or any combination thereof, relative to a control level.

[0266] In some embodiments, the subject is diagnosed with cutaneous lupus erythematosus by detecting an altered or increased level of an antibody that binds to CCL11, CCL24, CD300E, IFNL2, TMEM149, TYRO3, VEGFB, or any combination thereof, relative to a control level.

[0267] In some embodiments, the subject is diagnosed with drug-induced lupus by detecting an altered or increased level of an antibody that binds to CXCL1, TNF, TSLP, or any combination thereof, relative to a control level.

[0268] In some embodiments, the subject is diagnosed with dermatomyositis by detecting an altered or increased level of an antibody that binds to CD81, relative to a control level.

[0269] In some embodiments, the subject is diagnosed with glomerulonephritis by detecting an altered or increased level of an antibody that binds to C1QTNF4, CCL17, CCL4L1, CXCL2, CXCL3, EDIL3, EPYC, IFNL2, IL34, PDGFB, RTN4RL1, TMEM149, TREM2, TSLP, or any combination thereof, relative to a control level.

[0270] In some embodiments, the subject is diagnosed with mixed connective tissue disease by detecting an altered or increased level of an antibody that binds to BTNL8, CXCL3, EPYC, JCHAIN, SDC4, TSPAN2, VEGFB, or any combination thereof, relative to a control level.

[0271] In some embodiments, the subject is diagnosed with myasthenia gravis by detecting an altered or increased level of an antibody that binds to CXCL2, PDGFB, REG4, CCL22, CCL2, or any combination thereof, relative to a control level.

[0272] In some embodiments, the subject is diagnosed with neuromyelitis optica by detecting an altered or increased level of an antibody that binds to CXCL2, CXCL3, IGFBPL1, CCL22, IL1F9, LY6G6D, or any combination thereof, relative to a control level.

[0273] In some embodiments, the subject is diagnosed with non-small cell lung cancer by detecting an altered or increased level of an antibody that binds to CCL17, CCL24, CXCL1, CXCL3, EDIL3, IFNA13, IFNA14, IFNA17, IFNA2, IFNA5, IFNA6, IFNA8, IFNL2, IFNW1, IL28B, IL34, MADCAM1, PDGFB, REG1A, SDC1, BTN1A1, C6, CD207, CD3D, CDH19, COLEC12, EREG, FGF23, FGF7, FGFBP3, IGFBPL1, IL15RA, IL17F, IL1RAP, IL22RA2, IL4, IL4R, ITGA5, LAG3, LRRC4, MPZL3, NOTCH2NL, NTRK3, REG4, SCARA3, STIM2, TNFRSF10C, TNFRSF19L, TREML1, or any combination thereof, relative to a control level.

[0274] In some embodiments, the subject is diagnosed with pediatric autoimmune neuropsychiatric disorders associated with streptococcal infections by detecting an altered or increased level of an antibody that binds to LRP 11, relative to a control level.

[0275] In some embodiments, the subject is diagnosed with sarcoidosis by detecting an altered or increased level of an antibody that binds to CX3CL1, EPYC, PGLYRP1, or any combination thereof, relative to a control level.

[0276] In some embodiments, the subject is diagnosed with systemic lupus erythematosus by detecting an altered or increased level of an antibody that binds to BMPR2, BTNL8, C1QTNF4, CCL11, CCL15, CCL17, CCL24, CCL4L1, CD300E, CD44, CSPG5, CX3CL1, CXCL1, CXCL2, CXCL3, EDIL3, EPYC, FGF21, FGFRL1, IFNA13, IFNA14, IFNA17, IFNA2, IFNA5, IFNA6, IFNA8, IFNB1, IFNL2, IFNW1, IGF2, IGSF4B, IL16, IL18RAP, IL19, IL1A, IL20RB, IL28B, IL29, L33, IL34, IL6, IL6R, JCHAIN, LGR6, LIF, LRTM2, LY6H, MADCAM1, MUC21, NGFR, PDCD1LG2, PDGFB, PGLYRP1, REG1A, REG1B, RTN4RL1, SDC1, SDC4, TGFA, TMEM149, TNF, TNFRSF10D, TNFRSF6, TREM2, TSLP, TSPAN2, TYRO3, VEGFB, or any combination thereof, relative to a control level.

[0277] In some embodiments, the subject is diagnosed with sjogren's syndrome by detecting an altered or increased level of an antibody that binds to CXCL1, CXCL3, PDCD1LG2, or any combination thereof, relative to a control level.

[0278] In some embodiments, the subject is diagnosed with susac syndrome by detecting an altered or increased level of an antibody that binds to CCL24, SDC4, TREML1, VSIG4, or any combination thereof, relative to a control level.

[0279] In some embodiments, the subject is diagnosed with undifferentiated connective tissue disease by detecting an altered or increased level of an antibody that binds to CNTN5, TNF, or any combination thereof, relative to a control level.

[0280] In one aspect, the present invention provides a method of diagnosing a disease or disorder in a subject, the method comprising assessing the presence of at least one antibody or autoantibody in a biological sample from the subject, wherein the at least one antibody or autoantibody is identified to be associated with the disease or disorder according to the methods described elsewhere herein. In one aspect, the present invention provides a method of diagnosing a disease or disorder in a subject, the method comprising detecting the binding of at least one autoantibody with at least one autoantigen as set forth in Table 3, and diagnosing the subject as having or at risk of having the associated disease or disorder as set forth in Table 3. In one aspect, the present invention provides a method of diagnosing a disease or disorder in a subject, the method comprising assessing detecting the binding of at least one autoantibody with at least one autoantigen as set forth in Table 4, and diagnosing the subject as having or at risk of having the associated disease or disorder as set forth in Table 4.

[0281] In one aspect, the present invention provides a method of evaluating the effectiveness of a treatment for a disease or disorder in a subject, the method comprising assessing the presence of at least one antibody or autoantibody in a biological sample from the subject, wherein the at least one antibody or autoantibody is identified to be associated with the disease or disorder according to the methods described elsewhere herein. In one aspect, the present invention provides a method of evaluating the effectiveness of a treatment for a disease or disorder in a subject, the method comprising detecting the binding of at least one autoantibody with at least one autoantigen as set forth in Table 3, in a subject pre administration of a treatment regimen, post administration of a treatment regimen, or both pre- and post-administration of a treatment regimen. For example, in one embodiment, the treatment regimen comprises administration of an antibody, and the method of the invention is used to evaluate the effectiveness of the treatment regimen by detecting the presence of or an increased level of antibody reactivity with a target antigen following treatment. In one embodiment, the treatment regimen comprises administering a therapeutic agent to reduce or eliminate one or more autoantibodies, and the method of the invention is used to evaluate the effectiveness of the treatment regimen by detecting the absence of or a reduced level of antibody reactivity with a target antigen following treatment.

[0282] In one embodiment, the subject is diagnosed with a disease or disorder when the level or activity of at least one antibody target associated with the disease or disorder is different than the threshold level. In one embodiment, the subject is diagnosed with a disease or disorder when the level or activity (e.g., activity, amount, concentration, expression, level, etc.) of at least one antibody target associated with the disease or disorder is higher than the threshold level. In some embodiments, the threshold level is obtained from control group samples.

[0283] In one embodiment, the subject is diagnosed with a disease or disorder by detecting an altered or increased level of an antibody target associated with the disease or disorder, relative to a control level. In some embodiments, the control level is a level of a particular marker (i.e., an antibody that binds to at least one antibody target associated

with the disease or disorder) in a subject or population known not to have the disease. In various embodiments of the methods of the invention, the level (e.g., activity, amount, concentration, expression, level, etc.) of antibody target is determined to be increased or to be higher when the level of antibody target is determined to be increased by at least 0.01 fold, at least 0.05 fold, at least 0.07 fold, at least 0.076 fold, at least 0.1 fold, at least 0.18 fold, at least 0.19 fold, at least 0.3 fold, at least 0.36 fold, at least 0.37 fold, at least 0.38 fold, at least 0.4 fold, at least 0.43 fold, at least 1 fold, at least 1.1 fold, at least 1.2 fold, at least 1.3 fold, at least 1.4 fold, at least 1.5 fold, at least 1.6 fold, at least 1.7 fold, at least 1.8 fold, at least 1.9 fold, at least 2 fold, at least 2.1 fold, at least 2.2 fold, at least 2.3 fold, at least 2.4 fold, at least 2.5 fold, at least 2.6 fold, at least 2.7 fold, at least 2.8 fold, at least 2.9 fold, at least 3 fold, at least 3.5 fold, at least 4 fold, at least 4.5 fold, at least 5 fold, at least 5.5 fold, at least 6 fold, at least 6.5 fold, at least 7 fold, at least 7.5 fold, at least 8 fold, at least 8.5 fold, at least 9 fold, at least 9.5 fold, at least 10 fold, at least 11 fold, at least 12 fold, at least 13 fold, at least 14 fold, at least 15 fold, at least 16 fold, at least 16.3 fold, at least 16.31 fold, at least 20 fold, at least 25 fold, at least 26 fold, at least 26.7 fold, at least 26.72 fold, at least 30 fold, at least 40 fold, at least 50 fold, at least 75 fold, at least 100 fold, at least 192 fold, at least 192.4 fold, at least 192.44 fold, at least 200 fold, at least 250 fold, at least 500 fold, or at least 1000 fold, or at least 10000 fold, when compared with a comparator (e.g., the level of antibody target in control group samples).

[0284] In one embodiment, the subject is diagnosed with a disease or disorder when the level or activity of at least one antibody target associated with the disease or disorder is increased or higher as compared to a comparator (e.g., the predetermined threshold level). For example, in some embodiments, the subject is diagnosed with a disease or disorder when at least one antibody target associated with the disease or disorder is present in the subject (i.e., the level or activity of at least one antibody target associated with the disease or disorder is more than 0). In some embodiments, the subject is diagnosed with a disease or disorder when the level or activity of at least one antibody target associated with the disease or disorder is increased by at least 0.01 fold, or at least 0.18 fold. In some embodiments, the subject is diagnosed with a disease or disorder when the level or activity of at least one antibody target associated with the disease or disorder is increased in a range from 0.1 fold to 10,000 fold.

Method of Preventing or Treating a Disease or Disorder

[0285] The present invention further relates, in part, to methods of preventing or treating a diseases or disorders associated with at least one antibody or target thereof (e.g., an antibody level, antibody target level, antibody activity, or antibody target activity) in a subject in need thereof. In one aspect, the method comprises administering a treatment to the subject comprising eliminating or modifying the level (e.g., activity, amount, concentration, expression, level, etc.) of at least one antibody target that is identified to be the antibody target associated with the disease or disorder according to the method of the present invention.

[0286] In one aspect, the present invention relates to a method of preventing or treating a disease or disorder associated with at least one antibody target in a subject in need thereof. In one embodiment, the method comprises administering a treatment to reduce the level (e.g., activity, amount, concentration, expression, level, etc.) of the antibody target identified to be associated with the disease or disorder according to the method of the present invention in the subject. In one embodiment, the treatment comprises inhibiting at least one antibody target associated with the disease or disorder. In one embodiment, the treatment comprises administering a therapeutically effective amount of an inhibitor of at least one antibody target associated with the disease or disorder. For example, in some embodiments, the inhibitor of the antibody target is an antibody, nucleic acid, peptide, small molecule, antagonist, aptamer, peptidomemetic, or a combination thereof.

[0287] In one aspect, the present invention relates to a method of preventing or treating a disease or disorder associated with an increased level of at least one antibody target in a subject in need thereof. In one embodiment, the method comprises administering a treatment to reduce the level (e.g., activity, amount, concentration, expression, level, etc.) of the antibody target identified to be associated with the disease or disorder according to the method of the present invention in the subject. In one embodiment, the treatment comprises inhibiting at least one antibody target associated with the disease or disorder. In one embodiment, the treatment comprises administering a therapeutically effective amount of an inhibitor of at least one antibody target associated with the disease or disorder. For example, in some embodiments, the inhibitor of the antibody target is an antibody For example, in some embodiments, the inhibitor of the antibody target is an antibody, nucleic acid, peptide, small molecule, antagonist, aptamer, peptidomemetic, or a combination thereof.

[0288] In one aspect, the present invention relates to a method of preventing or treating a disease or disorder associated with a decreased level of at least one antibody target in a subject in need thereof. In one embodiment, the method comprises administering a treatment to increase the level (e.g., activity, amount, concentration, expression, level, etc.) of the antibody target identified to be associated with the disease or disorder according to the method of the present invention in the subject. In one embodiment, the treatment comprises activating at least one antibody target associated with the disease or disorder. For example, in some embodiments, the treatment comprises increasing the level or activity of at least one antibody target associated with the disease or disorder by administering a therapeutically effective amount of at least one antibody target associated with the disease or disorder or a fragment thereof, nucleic acid sequences encoding the antibody target associated with the disease or disorder or a fragment thereof, inhibitor of the antibody that specifically binds to the antibody target, therapeutic agent, or a combination thereof. In some embodiments, the inhibitor of the antibody that specifically binds to the antibody target is an antibody, therapeutic agent, or a combination thereof.

[0289] The present invention also relates, in part, to methods of preventing or treating a disease or disorder associated with at least one antibody (e.g., antibody level or activity) in a subject in need thereof. In one aspect, the method comprises administering a treatment to the subject comprising modifying the level (e.g., activity, amount, concentration, expression, level, etc.) of at least one antibody that binds to an antigen associated with the disease or disorder according to the method of the present invention.

[0290] In one aspect, the present invention relates to a method of preventing or treating a disease or disorder associated with at least one antibody in a subject in need thereof. In one embodiment, the method comprises administering a treatment to reduce the level (e.g., activity, amount, concentration, expression, level, etc.) of the antibody identified to be associated with the disease or disorder according to the method of the present invention in the subject. In one embodiment, the treatment comprises inhibiting at least one antibody associated with the disease or disorder. In one embodiment, the treatment comprises administering a therapeutically effective amount of an inhibitor of at least one antibody associated with the disease or disorder. For example, in some embodiments, the inhibitor of the antibody is a composition comprising an antigen identified according to the methods of the invention, or a fragment thereof, that specifically binds to the antibody associated with the disease or disorder. In some embodiments, the composition comprising the antigen further comprises a therapeutic agent, a nucleic acid, a peptide, an antibody, a small molecule, or a combination thereof.

[0291] In one aspect, the present invention relates to a method of preventing or treating a disease or disorder associated with at least one antibody in a subject in need thereof. In one embodiment, the method comprises administering a therapeutic agent for decreasing the level (e.g., activity, amount, concentration, expression, level, etc.) of at least one antibody identified to be associated with the disease or disorder according to the method of the present invention in the subject. In one embodiment, the method comprises administering a therapeutic agent for inhibiting the reactivity of at least one antibody with at least one antigen identified to be associated with the disease or disorder according to the method of the present invention in the subject. In one embodiment, the method comprises inhibiting the reactivitiy of at least of antibody with at least one antigen for the treatment of the associated disease as set forth in Table 3. In one embodiment, the method comprises modulating the reactivitiy of at least of antibody with at least one antigen for the treatment of the associated disease as set forth in Table 3.

[0292] Exemplary therapeutic autoantigens whose reactivities with autoantibodies can be increased for the treatment of diseases and disorders include, but are not limited to, those autoantigens identified in Table 5, and associated diseases. Therefore, in one embodiment, the methods of the invention include methods of admininstering an autoantibody directed to autoantigen as set forth in Table 5, or a fragment thereof.

[0293] Exemplary autoantigens whose reactivities with autoantibodies can be inhibited or decreased for the treatment of diseases and disorders include, but are not limited to, those autoantigens identified in Table 6, and associated diseases. Therefore, in one embodiment, the methods of the invention include methods of admininstering an agent to decrease the level or activity of an autoantibody directed to autoantigen as set forth in Table 6, or a fragment thereof.

[0294] In one embodiment, the methods of the invention include methods of administering a fusion molecule comprising an antigen identified according to the methods of the invention fused to a domain to support degradation of an antibody. Exemplary domains to promote internalization and degradation of autoantibodies include, but are not limited to, an asialoglycoprotein receptor binding domain. In such an embodiment, binding of the autoantibody to the fusion antigen would result in targeted degradation of the bound autoantibody. Therefore, in some embodiments, the invention relates to fusion molecules comprising the antigens as set forth in Table 3 fused to a molecule for endocytosis and degradation, and their use for treating the associated disease or disorder as set forth in Table 3. In some embodiments, the invention relates to fusion molecules comprising the antigens as set forth in Table 6 fused to a molecule for endocytosis and degradation, and their use for treating the associated disease or disorder as set forth in Table 6.

[0295] In one embodiment, the methods of the invention include methods of directing T cells to B cells expressing autoantibodies. For example, in one embodiment, the invention provides compositions comprising engineered T cells expressing an autoantigen identified according to the methods of the invention, and their use to target auto-antigen expressing B cells for depletion or killing. Therefore, in various embodiments, the invention includes engineered T cells, including but not limited to, CAR-T cells and CAAR-T cells, expressing an antigen as set forth in Table 3, and the use thereof for the treatment of the associated disease or disorder as set forth in Table 3. Therefore, in various embodiments, the invention includes engineered T cells, including but not limited to, CAR-T cells and CAAR-T cells, expressing an antigen as set forth in Table 6, and the use thereof for the treatment of the associated disease or disorder as set forth in Table 6.

[0296] In some embodiments, the method of preventing or treating COVID-19 comprises administering a treatment to the subject for decreasing the level or activity of at least one autoantibody directed to IFITM10, IFNA13, IFNA14, IFNA17, IFNA2, IFNA5, IFNA6, IFNA8, IFNW1, KLRC1, KLRC2, KLRC3, CCR2, CD38, C5A, CCR4, CD3E, TNFRSF9, ADCYAP1, CGA, HCTR2, AZGP1, SCC41A2 or LAIR1 or any combination thereof. In some embodiments, the method of preventing or treating COVID-19 comprises administering a composition comprising at least one of IFITM10, IFNA13, IFNA14, IFNA17, IFNA2, IFNA5, IFNA6, IFNA8, IFNW1, KLRC1, KLRC2, KLRC3, CCR2, CD38, C5A, CCR4, CD3E, TNFRSF9, ADCYAP1, CGA, HCTR2, AZGP1, SCC41A2 and LAIR1, and further comprising a domain for degradation of an autoantibody directed to at least one of IFITM10, IFNA13, IFNA14, IFNA17, IFNA2, IFNA5, IFNA6, IFNA8, IFNW1, KLRC1, KLRC2, KLRC3, CCR2, CD38, C5A, CCR4, CD3E, TNFRSF9, ADCYAP1, CGA, HCTR2, AZGP1, SCC41A2 and LAIR1. In one embodiment, the method of preventing or treating COVID-19 comprises administering a composition comprising a CAR T cell expressing at least one of IFITM10, IFNA13, IFNA14, IFNA17, IFNA2, IFNA5, IFNA6, IFNA8, IFNW1, KLRC1, KLRC2, KLRC3, CCR2, CD38, C5A, CCR4, CD3E, TNFRSF9, ADCYAP1, CGA, HCTR2, AZGP1, SCC41A2 and LAIR1.

[0297] In some embodiments, the method of preventing or treating a disease or disorder associated with kidney transplant comprises administering a treatment to the subject for decreasing the level or activity of at least one autoantibody directed to IL4, EXOC3-AS1, IFNA13, CD99L2, OSTN, SYCN, LYG2, BTN1A1, or any combination thereof. In some embodiments, the method of preventing or treating a disease or disorder associated with kidney transplant comprises administering a composition comprising at least one of IL4, EXOC3-AS1, IFNA13, CD99L2, OSTN, SYCN,

LYG2, and BTN1A1, and further comprising a domain for degradation of an autoantibody directed to at least one of IL4, EXOC3-AS1, IFNA13, CD99L2, OSTN, SYCN, LYG2, and BTN1A1. In one embodiment, the method of preventing or treating a disease or disorder associated with kidney transplant comprises administering a composition comprising a CAR T cell expressing at least one of IL4, EXOC3-AS1, IFNA13, CD99L2, OSTN, SYCN, LYG2, and BTN1A1.

[0298] In some embodiments, the method of preventing or treating malignant melanoma comprises administering a treatment to the subject for decreasing the level or activity of at least one autoantibody directed to IFNA13, OBP2B, TMEM108, CELA1, OTOL1, ATP4B, ICOSLG, REG1A, CCL24, TMEM91, LALBA, ITPRIPL1, LCN2, BTN1A1, OS9, FGF17 or any combination thereof. In some embodiments, the method of preventing or treating malignant melanoma comprises administering a composition comprising at least one of IFNA13, OBP2B, TMEM108, CELA1, OTOL1, ATP4B, ICOSLG, REG1A, CCL24, TMEM91, LALBA, ITPRIPL1, LCN2, BTN1A1, OS9, and FGF17, and further comprising a domain for degradation of an autoantibody directed to at least one of IFNA13, OBP2B, TMEM108, CELA1, OTOL1, ATP4B, ICOSLG, REG1A, CCL24, TMEM91, LALBA, ITPRIPL1, LCN2, BTN1A1, OS9, and FGF17. In one embodiment, the method of preventing or treating malignant melanoma comprises administering a composition comprising a CAR T cell expressing at least one of IFNA13, OBP2B, TMEM108, CELA1, OTOL1, ATP4B, ICOSLG, REG1A, CCL24, TMEM91, LALBA, ITPRIPL1, LCN2, BTN1A1, OS9, FGF17.

[0299] In some embodiments, the method of preventing or treating non-small cell lung cancer comprises administering a treatment to the subject for decreasing the level or activity of at least one autoantibody directed to IFNL2, VSTM2A, PDGFB or any combination thereof. In some embodiments, the method of preventing or treating non-small cell lung cancer comprises administering a composition comprising at least one of IFNL2, VSTM2A, and PDGFB, and further comprising a domain for degradation of an autoantibody directed to at least one of IFNL2, VSTM2A, and PDGFB. In one embodiment, the method of preventing or treating non-small cell lung cancer comprises administering a composition comprising a CAR T cell expressing at least one of IFNL2, VSTM2A, and PDGFB.

[0300] In some embodiments, the method of preventing or treating systemic lupus erythematosus comprises administering a treatment to the subject for decreasing the level or activity of at least one autoantibody directed to TMEM102, CCL8, CCL4L1, ACVR2B, FGF21, IGFBP2, RGMB, ACVR1B, ACRV1, SCGB1D1, TFF2, SFN, ANTXRL, SLC41A2, CD248 or any combination thereof. In some embodiments, the method of preventing or treating systemic lupus erythematosus comprises administering a composition comprising at least one of TMEM102, CCL8, CCL4L1, ACVR2B, FGF21, IGFBP2, RGMB, ACVR1B, ACRV1, SCGB1D1, TFF2, SFN, ANTXRL, SLC41A2, and CD248, and further comprising a domain for degradation of an autoantibody directed to at least one of TMEM102, CCL8, CCL4L1, ACVR2B, FGF21, IGFBP2, RGMB, ACVR1B, ACRV1, SCGB1D1, TFF2, SFN, ANTXRL, SLC41A2, and CD248. In one embodiment, the method of preventing or treating systemic lupus erythematosus comprises administering a composition comprising a CAR T cell expressing at least one of TMEM102, CCL8, CCL4L1, ACVR2B, FGF21, IGFBP2, RGMB, ACVR1B, ACRV1, SCGB1D1, TFF2, SFN, ANTXRL, SLC41A2, and CD248.

[0301] In one aspect, the present invention relates to a method of preventing or treating a disease or disorder associated with insufficient level of at least one antibody in a subject in need thereof. In one embodiment, the method comprises administering a treatment for decreasing the level (e.g., activity, amount, concentration, expression, level, etc.) of an antigen identified to be associated with the disease or disorder according to the method of the present invention in the subject. In one embodiment, the treatment comprises administering at least one antibody specific for binding to the antigen. For example, in some embodiments, the treatment comprises decreasing the level or activity of at least one autoantigen associated with a disease or disorder by administering a therapeutically effective amount of at least one antibody, or a fragment thereof, specific for binding to the antigen, a nucleic acid sequence encoding the antibody, or a fragment thereof, a therapeutic agent, nucleic acid, peptide, small molecule, antagonist, aptamer, peptidomemetic, or a combination thereof, or a combination thereof.

[0302] For example, in some embodiments, the method of preventing or treating autoimmune polyendocrinopathy candidiasis ecto-dermal dystrophy comprises administering a treatment to the subject for modulating the level or activity of IL22RA2, or administering an antibody that binds to IL22RA2.

[0303] In some embodiments, the method of preventing or treating cutaneous lupus erythematosus comprises administering a treatment to the subject for modulating the level or activity of CD300E, TYRO3, or any combination thereof, or administering an antibody that binds to CD300E, TYRO3, or any combination thereof.

[0304] In some embodiments, the method of preventing or treating COVID-19 comprises administering a treatment to the subject for modulating the level or activity of IL13, IL18RAP, TNFRSF8, CCR10, CD74, TNFRSF17, CCR9, CRTAM, C6, or any combination thereof, or administering an antibody that binds to IL13, IL18RAP, TNFRSF8, CCR10, CD74, TNFRSF17, CCR9, CRTAM, C6, or any combination thereof.

[0305] In some embodiments, the method of preventing or treating dermatomyositis comprises administering a treatment to the subject for modulating the level or activity of CD81, or administering an antibody that binds to CD81.

[0306] In some embodiments, the method of preventing or treating glomerulonephritis comprises administering a treatment to the subject for modulating the level or activity of IL34, or administering an antibody that binds to IL34.

[0307] In some embodiments, the method of preventing or treating a disease or disorder associated with kidney transplant comprises administering a treatment to the subject for modulating the level or activity of IGFBP1, IL15RA, NXPH1, CST5, C6, or any combination thereof, or administering an antibody that binds to IGFBP1, IL15RA, NXPH1, CST5, C6, or any combination thereof.

[0308] In some embodiments, the method of preventing or treating myasthenia gravis comprises administering a treatment to the subject for modulating the level or activity of CCL22, CCL2, or any combination thereof, or administering an antibody that binds to CCL22, CCL2, or any combination thereof.

[0309] In some embodiments, the method of preventing or treating malignant melanoma comprises administering a treatment to the subject for modulating the level or activity of PSORS1C2, LHFPL1, PTPRR, ZG16B, IGF1, IFLL1, LRIT3, VEGFB, or any combination thereof, or administering an antibody that binds to PSORS1C2, LHFPL1, PTPRR, ZG16B, IGF1, IFLL1, LRIT3, VEGFB, or any combination thereof.

[0310] In some embodiments, the method of preventing or treating neuromyelitis opticas comprises administering a treatment to the subject for modulating the level or activity of CCL22, IL1F9, or any combination thereof, or administering an antibody that binds to CCL22, IL1F9, or any combination thereof.

[0311] In some embodiments, the method of preventing or treating non-small cell lung cancer comprises administering a treatment to the subject for modulating the level or activity of CCL22, FGF23, FGF7, EREG, CXCL1, CXCL2, CXCL3, VEGFB, IL1A, LAG3, IFNA13, IFNA14, IFNA17, IFNA2, IFNA5, IFNA6, IFNA8, IFNL2, IFNW1, IL34, IL22RA2, IGFBPL1 or any combination thereof, or an administering antibody that binds to CCL22, FGF23, FGF7, EREG, CXCL1, CXCL2, CXCL3, VEGFB, IL1A, LAG3, IFNA13, IFNA14, IFNA17, IFNA2, IFNA5, IFNA6, IFNA8, IFNL2, IFNW1, IL34, IL22RA2, IGFBPL1 or any combination thereof.

[0312] In some embodiments, the method of preventing or treating systemic lupus erythematosus comprises administering a treatment to the subject for modulating the level or activity of PDCD1LG2, LIF, IFNA13, IFNA14, IFNA17, IFNA2, IFNA5, IFNA6, IFNA8, IFNB1, IFNL2, IFNW1, IL6, IL6R, IL33, IL34, IL16, IL19, IL20RB, IL18RAP, MADCAM1, TNF, TRAILR4, TYRO3, CD44, CD300E, FGF21, CXCL1, CXCL2, CXCL3, VEGFB, IL1A, LILRB2, LILRB4 or any combination thereof, or administering an antibody that binds to PDCD1LG2, LIF, IFNA13, IFNA14, IFNA17, IFNA2, IFNA5, IFNA6, IFNA8, IFNB1, IFNL2, IFNW1, IL6, TL6R, IL33, IL34, IL16, IL19, IL20RB, IL18RAP, MADCAM1, TNF, TRAILR4, TYRO3, CD44, CD300E, FGF21, CXCL1, CXCL2, CXCL3, VEGFB, IL1A, LILRB2, LILRB4 or any combination thereof.

[0313] In some embodiments, the method of preventing or treating sjogren's syndrome comprises administering a treatment to the subject for modulating the level or activity of PDCD1LG2, or administering an antibody that binds to PDCD1LG2.

[0314] In one embodiment, the invention relates to the use of therapeutic agent to modulate the reactivity of at least one autoantibody with at least one autoantigen of the invention. Examples of therapeutic agents include, but are not limited to, one or more drugs, metabolites, metabolic inhibitors, proteins, amino acids, peptides, antibodies, medical imaging agents, therapeutic moieties, one or more non-therapeutic moieties or a combination to target cancer or atherosclerosis, selected from folic acid, peptides, proteins, aptamers, antibodies, siRNA, poorly water soluble drugs, anti-cancer drugs, antibiotics, analgesics, vaccines, anticonvulsants; anti-diabetic agents, antifungal agents, antineoplastic agents, anti-parkinsonian agents, anti-rheumatic agents, appetite suppressants, biological response modifiers, cardiovascular agents, central nervous system stimulants, contraceptive agents, dietary supplements, vitamins, minerals, lipids, saccharides, metals, amino acids (and precursors), nucleic acids and precursors, contrast agents, diagnostic agents, dopamine receptor agonists, erectile dysfunction agents, fertility agents, gastrointestinal agents, hormones, immunomodulators, antihypercalcemia agents, mast cell stabilizers, muscle relaxants, nutritional agents, ophthalmic agents, osteoporosis agents, psychotherapeutic agents, parasympathomimetic agents, parasympatholytic agents, respiratory agents, sedative hypnotic agents, skin and mucous membrane agents, smoking cessation agents, steroids, sympatholytic agents, urinary tract agents, uterine relaxants, vaginal agents, vasodilator, anti-hypertensive, hyperthyroids, anti-hyperthyroids, anti-asthmatics and vertigo agents, anti-tumor agents, including cytotoxic/antineoplastic agents and anti-angiogenic agents, or any combination thereof.

[0315] Cytotoxic/anti-neoplastic agents are defined as agents which attack and kill cancer cells. Some cytotoxic/anti-neoplastic agents are alkylating agents, which alkylate the genetic material in tumor cells, e.g., cis-platin, cyclophosphamide, nitrogen mustard, trimethylene thiophosphoramide, carmustine, busulfan, chlorambucil, belustine, uracil mustard, chlomaphazin, and dacabazine. Other cytotoxic/anti-neoplastic agents are antimetabolites for tumor cells, e.g., cytosine arabinoside, fluorouracil, methotrexate, mercaptopuirine, azathioprime, and procarbazine. Other cytotoxic/anti-neoplastic agents are antibiotics, e.g., doxorubicin, bleomycin, dactinomycin, daunorubicin, mithramycin, mitomycin, mytomycin C, and daunomycin. There are numerous liposomal formulations commercially available for these compounds. Still other cytotoxic/anti-neoplastic agents are mitotic inhibitors (*vinca* alkaloids). These include vincristine, vinblastine and etoposide. Miscellaneous cytotoxic/anti-neoplastic agents include taxol and its derivatives, L-asparaginase, anti-tumor antibodies, dacarbazine, azacytidine, amsacrine, melphalan, VM-26, ifosfamide, mitoxantrone, and vindesine.

[0316] Anti-angiogenic agents are well known to those of skill in the art. Suitable anti-angiogenic agents for use in the methods of the present disclosure include anti-VEGF antibodies, including humanized and chimeric antibodies, anti-VEGF aptamers and antisense oligonucleotides. Other known inhibitors of angiogenesis include angiostatin, endostatin, interferons, interleukin 1 (including alpha and beta) interleukin 12, retinoic acid, and tissue inhibitors of metalloproteinase-1 and -2. (TIMP-1 and -2). Small molecules, including topoisomerases such as razoxane, a topoisomerase II inhibitor with anti-angiogenic activity, can also be used.

[0317] Other anti-cancer agents that can be used in combination with the disclosed compounds include, but are not limited to: acivicin; aclarubicin; acodazole hydrochloride; acronine; adozelesin; aldesleukin; altretamine; ambomycin; ametantrone acetate; aminoglutethimide; amsacrine; anastrozole; anthramycin; asparaginase; asperlin; azacitidine; azetepa; azotomycin; batimastat; benzodepa; bicalutamide; bisantrene hydrochloride; bisnafide dimesylate; bizelesin; bleomycin sulfate; brequinar sodium; bropirimine; busulfan; cactinomycin; calusterone; caracemide; carbetimer; carboplatin; carmustine; carubicin hydrochloride; carzelesin; cedefingol; chlorambucil; cirolemycin; cisplatin; cladribine; crisnatol mesylate; cyclophosphamide; cytarabine; dacarbazine; dactinomycin; daunorubicin hydrochloride; decitabine; dexormaplatin; dezaguanine; dezaguanine mesylate; diaziquone; docetaxel; doxorubicin; doxorubicin hydrochlo-

ride; droloxifene; droloxifene citrate; dromostanolone propionate; duazomycin; edatrexate; eflornithine hydrochloride; elsamitrucin; enloplatin; enpromate; epipropidine; epirubicin hydrochloride; erbulozole; esorubicin hydrochloride; estramustine; estramustine phosphate sodium; etanidazole; etoposide; etoposide phosphate; etoprine; fadrozole hydrochloride; fazarabine; fenretinide; floxuridine; fludarabine phosphate; fluorouracil; fluorocitabine; fosquidone; fostriecin sodium; gemcitabine; gemcitabine hydrochloride; hydroxyurea; idarubicin hydrochloride; ifosfamide; ilmofosine; interleukin II (including recombinant interleukin II, or rIL2), interferon alfa-2a; interferon alfa-2b; interferon alfa-n1; interferon alfa-n3; interferon beta-I a; interferon gamma-I b; iproplatin; irinotecan hydrochloride; lanreotide acetate; letrozole; leuprolide acetate; liarozole hydrochloride; lometrexol sodium; lomustine; losoxantrone hydrochloride; masoprocol; maytansine; mechlorethamine hydrochloride; megestrol acetate; melengestrol acetate; melphalan; menogaril; mercaptopurine; methotrexate; methotrexate sodium; metoprine; meturedepa; mitindomide; mitocarcin; mitocromin; mitogillin; mitomalcin; mitomycin; mitosper; mitotane; mitoxantrone hydrochloride; mycophenolic acid; nocodazole; nogalamycin; ormaplatin; oxisuran; paclitaxel; pegaspargase; peliomycin; pentamustine; peplomycin sulfate; perfosfamide; pipobroman; piposulfan; piroxantrone hydrochloride; plicamycin; plomestane; porfimer sodium; porfiromycin; prednimustine; procarbazine hydrochloride; puromycin; puromycin hydrochloride; pyrazofurin; riboprine; rogletimide; safingol; safingol hydrochloride; semustine; simtrazene; sparfosate sodium; sparsomycin; spirogermanium hydrochloride; spiromustine; spiroplatin; streptonigrin; streptozocin; sulofenur; talisomycin; tecogalan sodium; tegafur; teloxantrone hydrochloride; temoporfin; teniposide; teroxirone; testolactone; thiamiprine; thioguanine; thiotepa; tiazofurin; tirapazamine; toremifene citrate; trestolone acetate; triciribine phosphate; trimetrexate; trimetrexate glucuronate; triptorelin; tubulozole hydrochloride; uracil mustard; uredepa; vapreotide; verteporfin; vinblastine sulfate; vincristine sulfate; vindesine; vindesine sulfate; vinepidine sulfate; vinglycinate sulfate; vinleurosine sulfate; vinorelbine tartrate; vinrosidine sulfate; vinzolidine sulfate; vorozole; zeniplatin; zinostatin; zorubicin hydrochloride. Other anti-cancer drugs include, but are not limited to: 20-epi-1,25 dihydroxyvitamin D3; 5-ethynyluracil; abiraterone; aclarubicin; acylfulvene; adecypenol; adozelesin; aldesleukin; ALL-TK antagonists; altretamine; ambamustine; amidox; amifostine; aminolevulinic acid; amrubicin; amsacrine; anagrelide; anastrozole; andrographolide; angiogenesis inhibitors; antagonist D; antagonist G; antarelix; anti-dorsalizing morphogenetic protein-1; antiandrogen, prostatic carcinoma; antiestrogen; antineoplaston; antisense oligonucleotides; aphidicolin glycinate; apoptosis gene modulators; apoptosis regulators; apurinic acid; ara-CDP-DL-PTBA; arginine deaminase; asulacrine; atamestane; atrimustine; axinastatin 1; axinastatin 2; axinastatin 3; azasetron; azatoxin; azatyrosine; baccatin III derivatives; balanol; batimastat; BCR/ABL antagonists; benzochlorins; benzoylstaurosporine; beta lactam derivatives; beta-alethine; betaclamycin B; betulinic acid; bFGF inhibitor; bicalutamide; bisantrene; bisaziridinylspermine; bisnafide; bistratene A; bizelesin; breflate; bropirimine; budotitane; buthionine sulfoximine; calcipotriol; calphostin C; camptothecin derivatives; canarypox IL-2; capecitabine; carboxamide-amino-triazole; carboxyamidotriazole; CaRest M3; CARN 700; cartilage derived inhibitor; carzelesin; casein kinase inhibitors (ICOS); castanospermine; cecropin B; cetrorelix; chlorins; chloroquinoxaline sulfonamide; cicaprost; cis-porphyrin; cladribine; clomifene analogues; clotrimazole; collismycin A; collismycin B; combretastatin A4; combretastatin analogue; conagenin; crambescidin 816; crisnatol; cryptophycin 8; cryptophycin A derivatives; curacin A; cyclopentanthraquinones; cycloplatam; cypemycin; cytarabine ocfosfate; cytolytic factor; cytostatin; daclixmab; decitabine; dehydrodidemnin B; deslorelin; dexamethasone; dexifosfamide; dexrazoxane; dexverapamil; diaziquone; didemnin B; didox; diethylnorspermine; dihydro-5-azacytidine; dihydrotaxol, 9-; dioxamycin; diphenyl spiromustine; docetaxel; docosanol; dolasetron; doxifluridine; droloxifene; dronabinol; duocarmycin SA; ebselen; ecomustine; edelfosine; edrecolomab; eflornithine; elemene; emitefur; epirubicin; epristeride; estramustine analogue; estrogen agonists; estrogen antagonists; etanidazole; etoposide phosphate; exemestane; fadrozole; fazarabine; fenretinide; filgrastim; finasteride; flavopiridol; flezelastine; fluasterone; fludarabine; fluorodaunorunicin hydrochloride; forfenimex; formestane; fostriecin; fotemustine; gadolinium texaphyrin; gallium nitrate; galocitabine; ganirelix; gelatinase inhibitors; gemcitabine; glutathione inhibitors; hepsulfam; heregulin; hexamethylene bisacetamide; hypericin; ibandronic acid; idarubicin; idoxifene; idramantone; ilmofosine; ilomastat; imidazoacridones; imiquimod; immunostimulant peptides; insulin-like growth factor-1 receptor inhibitor; interferon agonists; interferons; interleukins; iobenguane; idodoxorubicin; ipomeanol, 4-; iroplact; irsogladine; isobengazole; isohomohalicondrin B; itasetron; jasplakinolide; kahalalide F; lamellarin-N triacetate; lanreotide; leinamycin; lenograstim; lentinan sulfate; leptolstatin; letrozole; leukemia inhibiting factor; leukocyte alpha interferon; leuprolide+estrogen+progesterone; leuprorelin; levamisole; liarozole; linear polyamine analogue; lipophilic disaccharide peptide; lipophilic platinum compounds; lissoclinamide 7; lobaplatin; lombricine; lometrexol; lonidamine; losoxantrone; lovastatin; loxoribine; lurtotecan; lutetium texaphyrin; lysofylline; lytic peptides; maitansine; mannostatin A; marimastat; masoprocol; maspin; matrilysin inhibitors; matrix metalloproteinase inhibitors; menogaril; merbarone; meterelin; methioninase; metoclopramide; MIF inhibitor; mifepristone; miltefosine; mirimostim; mismatched double stranded RNA; mitoguazone; mitolactol; mitomycin analogues; mitonafide; mitotoxin fibroblast growth factor-saporin; mitoxantrone; mofarotene; molgramostim; monoclonal antibody, human chorionic gonadotrophin; monophosphoryl lipid A+myobacterium cell wall sk; mopidamol; multiple drug resistance gene inhibitor; multiple tumor suppressor 1-based therapy; mustard anticancer agent; mycaperoxide B; mycobacterial cell wall extract; myriaporone; N-acetyldinaline; N-substituted benzamides; nafarelin; nagrestip; naloxone+pentazocine; napavin; naphterpin; nartograstim; nedaplatin; nemorubicin; neridronic acid; neutral endopeptidase; nilutamide; nisamycin; nitric oxide modulators; nitroxide antioxidant; nitrullyn; 06-benzylguanine; octreotide; okicenone; oligonucleotides; onapristone; ondansetron; ondansetron; oracin; oral cytokine inducer; ormaplatin; osaterone; oxaliplatin; oxaunomycin; paclitaxel; paclitaxel analogues; paclitaxel derivatives; palauamine; palmitoylrhizoxin; pamidronic acid; panaxytriol; panomifene; parabactin; pazelliptine; pegaspargase; peldesine; pentosan polysulfate sodium; pentostatin; pentro-

zole; perflubron; perfosfamide; perillyl alcohol; phenazinomycin; phenylacetate; phosphatase inhibitors; picibanil; pilocarpine hydrochloride; pirarubicin; piritrexim; placetin A; placetin B; plasminogen activator inhibitor; platinum complex; platinum compounds; platinum-triamine complex; porfimer sodium; porfiromycin; prednisone; propyl bis-acridone; prostaglandin J2; proteasome inhibitors; protein A-based immune modulator; protein kinase C inhibitor; protein kinase C inhibitors, microalgal; protein tyrosine phosphatase inhibitors; purine nucleoside phosphorylase inhibitors; purpurins; pyrazoloacridine; pyridoxylated hemoglobin polyoxyethylene conjugate; raf antagonists; raltitrexed; ramosetron; ras farnesyl protein transferase inhibitors; ras inhibitors; ras-GAP inhibitor; retelliptine demethylated; rhenium Re 186 etidronate; rhizoxin; ribozymes; RII retinamide; rogletimide; rohitukine; romurtide; roquinimex; rubiginone B1; ruboxyl; safingol; saintopin; SarCNU; sarcophytol A; sargramostim; Sdi 1 mimetics; semustine; senescence derived inhibitor 1; sense oligonucleotides; signal transduction inhibitors; signal transduction modulators; single chain antigen binding protein; sizofuran; sobuzoxane; sodium borocaptate; sodium phenylacetate; solverol; somatomedin binding protein; sonermin; sparfosic acid; spicamycin D; spiromustine; splenopentin; spongistatin 1; squalamine; stem cell inhibitor; stem-cell division inhibitors; stipiamide; stromelysin inhibitors; sulfinosine; superactive vasoactive intestinal peptide antagonist; suradista; suramin; swainsonine; synthetic glycosaminoglycans; tallimustine; tamoxifen methiodide; tauromustine; tazarotene; tecogalan sodium; tegafur; tellurapyrylium; telomerase inhibitors; temoporfin; temozolomide; teniposide; tetrachlorodecaoxide; tetrazomine; thaliblastine; thiocoraline; thrombopoietin; thrombopoietin mimetic; thymalfasin; thymopoietin receptor agonist; thymotrinan; thyroid stimulating hormone; tin ethyl etiopurpurin; tirapazamine; titanocene bichloride; topsentin; toremifene; totipotent stem cell factor; translation inhibitors; tretinoin; triacetyluridine; triciribine; trimetrexate; triptorelin; tropisetron; turosteride; tyrosine kinase inhibitors; tyrphostins; UBC inhibitors; ubenimex; urogenital sinus-derived growth inhibitory factor; urokinase receptor antagonists; vapreotide; variolin B; vector system, erythrocyte gene therapy; velaresol; veramine; verdins; verteporfin; vinorelbine; vinxaltine; vitaxin; vorozole; zanoterone; zeniplatin; zilascorb; and zinostatin stimalamer. In one embodiment, the anti-cancer drug is 5-fluorouracil, taxol, or leucovorin.

[0318] In some embodiments, the anti-cancer agent may be a prodrug form of an anti-cancer agent. As used herein, the term "prodrug form" and its derivatives is used to refer to a drug that has been chemically modified to add and/or remove one or more substituents in such a manner that, upon introduction of the prodrug form into a subject, such a modification may be reversed by naturally occurring processes, thus reproducing the drug. The use of a prodrug form of an anti-cancer agent in the compositions, among other things, may increase the concentration of the anti-cancer agent in the compositions of the present disclosure. In certain embodiments, an anti-cancer agent may be chemically modified with an alkyl or acyl group or some form of lipid. The selection of such a chemical modification, including the substituent(s) to add and/or remove to create the prodrug, may depend upon a number of factors including, but not limited to, the particular drug and the desired properties of the prodrug. One of ordinary skill in the art, with the benefit of this disclosure, will recognize suitable chemical modifications.

[0319] In one embodiment, the treatment comprises administering a therapeutically effective amount of at least one agent for modulating the reactivity of at least one antibody with at least one antigen.

[0320] In some embodiments, the treatment comprises decreasing or eliminating the level of at least one antibody associated with the disease or disorder by administering a therapeutically effective amount of an inhibitor of at least one antibody associated with the disease or disorder. For example, in one embodiment, the inhibitor of the antibody comprises an autoantigen identified using the methods of the invention.

[0321] Any drug or any combination of drugs disclosed herein may be administered to a subject to treat the disease or disorder. The drugs herein can be formulated in any number of ways, often according to various known formulations in the art or as disclosed or referenced herein.

[0322] In various embodiments, any drug or any combination of drugs disclosed herein is not administered to a subject to treat a disease. In these embodiments, the practitioner may refrain from administering the drug or any combination of drugs, may recommend that the subject not be administered the drug or any combination of drugs or may prevent the subject from being administered the drug or any combination of drugs.

[0323] In various embodiments, one or more additional drugs may be optionally administered in addition to those that are recommended or have been administered. An additional drug will typically not be any drug that is not recommended or that should be avoided.

[0324] In one aspect, the present invention also provides a method of alleviating toxicity of the treatment. In one embodiment, the method of alleviating toxicity of the treatment alleviates the toxicity of a cancer treatment. For example, in one embodiment, the method of alleviating toxicity of the treatment alleviates the toxicity of an immune-modifying checkpoint blockage therapies.

Method of Assessing the Prognosis, Assessing the Effectiveness, or Alleviating the Toxicity of Treatment of a Disease or Disorder

[0325] The present invention further relates, in part, to a method of assessing the prognosis or assessing the effectiveness of treatment of a disease or disorder associated with at least one antibody or target thereof (e.g., an antibody level, antibody target level, antibody activity, or antibody target activity) in a subject in need thereof.

[0326] In one aspect, the present invention provides a method of assessing the prognosis or assessing the effectiveness of treatment of a disease or disorder in a subject, the method comprising assessing the presence of at least one antibody target in the subject, wherein the at least one antibody target is identified to be associated with the disease or disorder according to the method described above. In one aspect, the present invention provides a method of assessing the prognosis or assessing the effectiveness of treatment of a disease or disorder in a subject, the method comprising assessing the level or activity of at least one antibody target in the subject, wherein the at least one antibody target is identified to be associated with the disease or disorder according to the method described above.

[0327] In one embodiment, the method of assessing the prognosis or assessing the effectiveness of treatment of a disease or disorder comprises comparing the level of at least one antibody target, that is identified to be associated with the disease or disorder according to the method described above, to the threshold level. In some embodiments, the threshold level is obtained from control group samples.

[0328] The present invention further relates, in part, to a method of assessing the prognosis or assessing the effectiveness of treatment of a disease or disorder associated with at least one antibody in a subject in need thereof. In one aspect, the present invention provides a method of assessing the prognosis or assessing the effectiveness of treatment of a disease or disorder in a subject, the method comprising assessing the presence of at least one antibody in the subject, wherein the at least one antibody is identified to be associated with the disease or disorder according to the method described above. In one aspect, the present invention provides a method of assessing the prognosis or assessing the effectiveness of treatment of a disease or disorder in a subject, the method comprising assessing the level or activity of at least one antibody in the subject, wherein the at least one antibody is identified to be associated with the disease or disorder according to the method described above.

[0329] In one embodiment, the method of assessing the prognosis or assessing the effectiveness of treatment of a disease or disorder comprises comparing the level of at least one antibody, that is identified to be associated with the disease or disorder according to the method described above, to the threshold level. In some embodiments, the threshold level is obtained from control group samples. In one embodiment, the threshold is 0.

[0330] In another aspect, the present invention provides a method of predicting a response to the treatment.

[0331] Information obtained from the methods of the invention described herein can be used alone, or in combination with other information (e.g., age, family history, disease status, disease history, vital signs, blood chemistry, PSA level, Gleason score, primary tumor staging, lymph node staging, metastasis staging, expression of other gene signatures relevant to outcomes of a disease or disorder, such as autoimmune disease or disorder, cancer, inflammatory disease or disorder, metabolic disease or disorder, neurodegenerative disease or disorder, organ tissue rejection, organ transplant rejection, or any combination thereof, etc.) from the subject or from the biological sample obtained from the subject.

Compositions

[0332] The present invention also provides various compositions comprising the antibodies or targets thereof identified by methods of the present invention. In one embodiment, the compositions modulate a reactivity between an autoantibody and at least one antigen. In one embodiment, the antigen is an antigen set forth in Table 1.

[0333] In some embodiments, the composition of the invention increases the reactivity of at least one antigen of the invention with an antibody. In some embodiments, the composition of the invention comprises at least one autoantibody directed to at least one antigen set forth in Table 1.

[0334] In some embodiments, the composition of the invention decreases the reactivity of at least one antigen of the invention with an antibody. In one embodiment, the invention provides compositions comprising at least one antigen of the invention linked to at least one domain for endocytosis, degradation, or a combination thereof. In one embodiment, the invention provides a composition comprising an antigen selected from the antigens set forth in Table 3, or a fragment thereof, linked to a domain for endocytosis, degradation, or a combination thereof. In one embodiment, the invention provides a composition comprising an antigen selected from the antigens set forth in Table 6, or a fragment thereof, linked to a domain for endocytosis, degradation, or a combination thereof.

[0335] In one embodiment, the invention provides a composition comprising a nucleic acid molecule encoding an antigen selected from the antigens set forth in Table 3, or a fragment thereof, linked to a domain for endocytosis, degradation, or a combination thereof. In one embodiment, the invention provides a composition comprising a nucleic acid molecule encoding an antigen selected from the antigens set forth in Table 6, or a fragment thereof, linked to a domain for endocytosis, degradation, or a combination thereof.

[0336] In one embodiment, the invention provides compositions comprising a cell or particle expressing at least one antigen of the invention, for example, a CAR T-cell expressing at least one antigen of the invention as described elsewhere herein.

[0337] In various aspects, the composition comprises: one or more antibodies or targets thereof of the present invention and one or more stabilizers. In various embodiments, the stabilizer to compound weight ratio is less than 50%. In one embodiment, the stabilizer comprises a biocompatible polymer. Examples of stabilizers include, but are not limited to, biocompatible polymer, a biodegradable polymer, a multifunctional linker, starch, modified starch, and starch derivatives, gums, including but not limited to polymers, polypeptides, albumin, amino acids, thiols, amines, carboxylic acid and combinations or derivatives thereof, citric acid, xanthan gum, alginic acid, other alginates, benitoniite, veegum, agar, guar, locust bean gum, gum arabic, quince psyllium, flax seed, okra gum, arabinoglactin, pectin, tragacanth, scleroglucan, dextran, amylose, amylopectin, dextrin, etc., crosslinked polyvinylpyrrolidone, ion-exchange resins, potassium polymethacrylate, carrageenan (and derivatives), gum karaya and biosynthetic gum, polycarbonates (linear polyesters of carbonic acid); microporous materials (bisphenol, a microporous poly(vinylchloride), micro-porous polyamides, microporous modacrylic copolymers, microporous styrene-acrylic and its copolymers); porous polysulfones, halogenated poly(vinylidene), polychloroethers, acetal polymers, polyesters prepared by esterification of a dicarboxylic acid or anhydride with an alkylene polyol, poly(alkylene-sulfides), phenolics, polyesters, asymmetric porous polymers, cross-linked olefin polymers, hydrophilic microporous homopolymers, copolymers or interpolymers having a reduced bulk density, and other similar materials, poly (urethane), cross-linked chain-extended poly(urethane), poly(imides), poly(benzimidazoles), collodion, regenerated proteins, semi-solid cross-linked poly(vinylpyrrolidone), monomeric, dimeric, oligomeric or long-chain, copolymers, block polymers, block co-polymers, polymers, PEG, dextran, modified dextran, polyvinylalcohol, polyvinylpyrollidone, polyacrylates, polymethacrylates, polyanhydrides, polypeptides, albumin, alginates, amino acids, thiols, amines, carboxylic acids, or combinations thereof.

[0338] The compositions may be formulated in a pharmaceutically acceptable excipient, such as wetting agents,

buffers, disintegrants, binders, fillers, flavoring agents and liquid carrier media such as sterile water, water/ethanol etc. The compositions should be suitable for administration either by topical administration or injection or inhalation or catheterization or instillation or transdermal introduction into any of the various body cavities including the alimentary canal, the vagina, the rectum, the bladder, the ureter, the urethra, the mouth, etc. For oral administration, the pH of the composition is preferably in the acid range (e.g., 2 to 7) and buffers or pH adjusting agents may be used. The contrast media may be formulated in conventional pharmaceutical administration forms, such as tablets, capsules, powders, solutions, dispersion, syrups, suppositories etc.

[0339] The compositions of the invention can be formulated and administered to a subject, as now described. The invention encompasses the preparation and use of pharmaceutical compositions comprising the compositions of the invention useful for the delivery of a therapeutic agent to a cell. The invention also encompasses the preparation and use of pharmaceutical compositions comprising the compositions of the invention useful for the treatment of a disease or disorder. The invention also encompasses the preparation and use of pharmaceutical compositions comprising the compositions of the invention useful for improved cell penetration.

[0340] Such a pharmaceutical composition may consist of the active ingredient alone, in a form suitable for administration to a subject, or the pharmaceutical composition may comprise the active ingredient and one or more pharmaceutically acceptable carriers, one or more additional ingredients, or some combination of these. The active ingredient may be present in the pharmaceutical composition in the form of a physiologically acceptable ester or salt, such as in combination with a physiologically acceptable cation or anion, as is well known in the art.

[0341] In various embodiments, the pharmaceutical compositions useful in the methods of the invention may be administered, by way of example, systemically, parenterally, or topically, such as, in oral formulations, inhaled formulations, including solid or aerosol, and by topical or other similar formulations. In addition to the appropriate therapeutic composition, such pharmaceutical compositions may contain pharmaceutically acceptable carriers and other ingredients known to enhance and facilitate drug administration. Other possible formulations, such as nanoparticles, liposomes, resealed erythrocytes, and immunologically based systems may also be used to administer an appropriate modulator thereof, according to the methods of the invention.

[0342] The formulations of the pharmaceutical compositions described herein may be prepared by any method known or hereafter developed in the art of pharmacology. In general, such preparatory methods include the step of bringing the active ingredient into association with a carrier or one or more other accessory ingredients, and then, if necessary or desirable, shaping or packaging the product into a desired single- or multi-dose unit.

[0343] Pharmaceutical compositions that are useful in the methods of the invention may be prepared, packaged, or sold in formulations suitable for oral, rectal, vaginal, parenteral, topical, pulmonary, intranasal, buccal, intravenous, ophthalmic, intrathecal and other known routes of administration. Other contemplated formulations include projected nanoparticles, liposomal preparations, resealed erythrocytes containing the active ingredient, and immunologically-based formulations.

[0344] A pharmaceutical composition of the invention may be prepared, packaged, or sold in bulk, as a single unit dose, or as a plurality of single unit doses. As used herein, a "unit dose" is discrete amount of the pharmaceutical composition comprising a predetermined amount of the active ingredient. The amount of the active ingredient is generally equal to the dosage of the active ingredient which would be administered to a subject or a convenient fraction of such a dosage such as, for example, one-half or one-third of such a dosage.

[0345] The relative amounts of the active ingredient, the pharmaceutically acceptable carrier, and any additional ingredients in a pharmaceutical composition of the invention will vary, depending upon the identity, size, and condition of the subject treated and further depending upon the route by which the composition is to be administered. By way of example, the composition may comprise between 0.1% and 100% (w/w) active ingredient. In various embodiments, the composition comprises at least about 1%, at least about 2%, at least about 3%, at least about 4%, at least about 5%, at least about 6%, at least about 7%, at least about 8%, at least about 9%, at least about 10%, at least about 11%, at least about 12%, at least about 13%, at least about 14%, at least about 15%, at least about 16%, at least about 17%, at least about 18%, at least about 19%, at least about 20%, at least about 21%, at least about 22%, at least about 23%, at least about 24%, at least about 25%, at least about 26%, at least about 27%, at least about 28%, at least about 29%, at least about 30%, at least about 31%, at least about 32%, at least about 33%, at least about 34%, at least about 35%, at least about 36%, at least about 37%, at least about 38%, at least about 39%, at least about 40%, at least about 41%, at least about 42%, at least about 43%, at least about 44%, at least about 45%, at least about 46%, at least about 47%, at least about 48%, at least about 49%, at least about 50%, at least about 51%, at least about 52%, at least about 53%, at least about 54%, at least about 55%, at least about 56%, at least about 57%, at least about 58%, at least about 59%, at least about 60%, at least about 61%, at least about 62%, at least about 63%, at least about 64%, at least about 65%, at least about 66%, at least about 67%, at least about 68%, at least about 69%, at least about 70%, at least about 71%, at least about 72%, at least about 73%, at least about 74%, at least about 75%, at least about 76%, at least about 77%, at least about 78%, at least about 79%, at least about 80%, at least about 81%, at least about 82%, at least about 83%, at least about 84%, at least about 85%, at least about 86%, at least about 87%, at least about 88%, at least about 89%, at least about 90%, at least about 91%, at least about 92%, at least about 93%, at least about 94%, at least about 95%, at least about 96%, at least about 97%, at least about 98%, at least about 99%, or at least about 100% (w/w) active ingredient.

[0346] In addition to the active ingredient, a pharmaceutical composition of the invention may further comprise one or more additional pharmaceutically active agents.

[0347] Controlled- or sustained-release formulations of a pharmaceutical composition of the invention may be made using conventional technology.

[0348] A formulation of a pharmaceutical composition of the invention suitable for oral administration may be prepared, packaged, or sold in the form of a discrete solid dose

unit including, but not limited to, a tablet, a hard or soft capsule, a cachet, a troche, or a lozenge, each containing a predetermined amount of the active ingredient. Other formulations suitable for oral administration include, but are not limited to, a powdered or granular formulation, an aqueous or oily suspension, an aqueous or oily solution, or an emulsion.

[0349] A tablet comprising the active ingredient may, for example, be made by compressing or molding the active ingredient, optionally with one or more additional ingredients. Compressed tablets may be prepared by compressing, in a suitable device, the active ingredient in a free-flowing form such as a powder or granular preparation, optionally mixed with one or more of a binder, a lubricant, an excipient, a surface active agent, and a dispersing agent. Molded tablets may be made by molding, in a suitable device, a mixture of the active ingredient, a pharmaceutically acceptable carrier, and at least sufficient liquid to moisten the mixture. Pharmaceutically acceptable excipients used in the manufacture of tablets include, but are not limited to, inert diluents, granulating and disintegrating agents, binding agents, and lubricating agents. Known dispersing agents include, but are not limited to, potato starch and sodium starch glycolate. Known surface active agents include, but are not limited to, sodium lauryl sulphate. Known diluents include, but are not limited to, calcium carbonate, sodium carbonate, lactose, microcrystalline cellulose, calcium phosphate, calcium hydrogen phosphate, and sodium phosphate. Known granulating and disintegrating agents include, but are not limited to, corn starch and alginic acid. Known binding agents include, but are not limited to, gelatin, acacia, pre-gelatinized maize starch, polyvinylpyrrolidone, and hydroxypropyl methylcellulose. Known lubricating agents include, but are not limited to, magnesium stearate, stearic acid, silica, and talc.

[0350] Tablets may be non-coated or they may be coated using known methods to achieve delayed disintegration in the gastrointestinal tract of a subject, thereby providing sustained release and absorption of the active ingredient. By way of example, a material such as glyceryl monostearate or glyceryl distearate may be used to coat tablets. Further by way of example, tablets may be coated using methods described in U.S. Pat. Nos. 4,256,108; 4,160,452; and U.S. Pat. No. 4,265,874 to form osmotically-controlled release tablets. Tablets may further comprise a sweetening agent, a flavoring agent, a coloring agent, a preservative, or some combination of these in order to provide pharmaceutically elegant and palatable preparation.

[0351] Hard capsules comprising the active ingredient may be made using a physiologically degradable composition, such as gelatin. Such hard capsules comprise the active ingredient, and may further comprise additional ingredients including, for example, an inert solid diluent such as calcium carbonate, calcium phosphate, or kaolin.

[0352] Soft gelatin capsules comprising the active ingredient may be made using a physiologically degradable composition, such as gelatin. Such soft capsules comprise the active ingredient, which may be mixed with water or an oil medium such as peanut oil, liquid paraffin, or olive oil.

[0353] Liquid formulations of a pharmaceutical composition of the invention which are suitable for oral administration may be prepared, packaged, and sold either in liquid form or in the form of a dry product intended for reconstitution with water or another suitable vehicle prior to use.

[0354] Liquid suspensions may be prepared using conventional methods to achieve suspension of the active ingredient in an aqueous or oily vehicle. Aqueous vehicles include, for example, water and isotonic saline. Oily vehicles include, for example, almond oil, oily esters, ethyl alcohol, vegetable oils such as *arachis*, olive, sesame, or coconut oil, fractionated vegetable oils, and mineral oils such as liquid paraffin. Liquid suspensions may further comprise one or more additional ingredients including, but not limited to, suspending agents, dispersing or wetting agents, emulsifying agents, demulcents, preservatives, buffers, salts, flavorings, coloring agents, and sweetening agents. Oily suspensions may further comprise a thickening agent.

[0355] Known suspending agents include, but are not limited to, sorbitol syrup, hydrogenated edible fats, sodium alginate, polyvinylpyrrolidone, gum tragacanth, gum acacia, and cellulose derivatives such as sodium carboxymethylcellulose, methylcellulose, and hydroxypropylmethylcellulose. Known dispersing or wetting agents include, but are not limited to, naturally-occurring phosphatides such as lecithin, condensation products of an alkylene oxide with a fatty acid, with a long chain aliphatic alcohol, with a partial ester derived from a fatty acid and a hexitol, or with a partial ester derived from a fatty acid and a hexitol anhydride (e.g. polyoxyethylene stearate, heptadecaethyleneoxycetanol, polyoxyethylene sorbitol monooleate, and polyoxyethylene sorbitan monooleate, respectively). Known emulsifying agents include, but are not limited to, lecithin and acacia. Known preservatives include, but are not limited to, methyl, ethyl, or n-propyl-para-hydroxybenzoates, ascorbic acid, and sorbic acid. Known sweetening agents include, for example, glycerol, propylene glycol, sorbitol, sucrose, and saccharin. Known thickening agents for oily suspensions include, for example, beeswax, hard paraffin, and cetyl alcohol.

[0356] Liquid solutions of the active ingredient in aqueous or oily solvents may be prepared in substantially the same manner as liquid suspensions, the primary difference being that the active ingredient is dissolved, rather than suspended in the solvent. Liquid solutions of the pharmaceutical composition of the invention may comprise each of the components described with regard to liquid suspensions, it being understood that suspending agents will not necessarily aid dissolution of the active ingredient in the solvent. Aqueous solvents include, for example, water and isotonic saline. Oily solvents include, for example, almond oil, oily esters, ethyl alcohol, vegetable oils such as *arachis*, olive, sesame, or coconut oil, fractionated vegetable oils, and mineral oils such as liquid paraffin.

[0357] Powdered and granular formulations of a pharmaceutical preparation of the invention may be prepared using known methods. Such formulations may be administered directly to a subject, used, for example, to form tablets, to fill capsules, or to prepare an aqueous or oily suspension or solution by addition of an aqueous or oily vehicle thereto. Each of these formulations may further comprise one or more of dispersing or wetting agent, a suspending agent, and a preservative. Additional excipients, such as fillers and sweetening, flavoring, or coloring agents, may also be included in these formulations.

[0358] A pharmaceutical composition of the invention may also be prepared, packaged, or sold in the form of oil-in-water emulsion or a water-in-oil emulsion. The oily phase may be a vegetable oil such as olive or *arachis* oil, a

mineral oil such as liquid paraffin, or a combination of these. Such compositions may further comprise one or more emulsifying agents such as naturally occurring gums such as gum acacia or gum tragacanth, naturally-occurring phosphatides such as soybean or lecithin phosphatide, esters or partial esters derived from combinations of fatty acids and hexitol anhydrides such as sorbitan monooleate, and condensation products of such partial esters with ethylene oxide such as polyoxyethylene sorbitan monooleate. These emulsions may also contain additional ingredients including, for example, sweetening or flavoring agents.

[0359] Methods for impregnating or coating a material with a chemical composition are known in the art, and include, but are not limited to methods of depositing or binding a chemical composition onto a surface, methods of incorporating a chemical composition into the structure of a material during the synthesis of the material (i.e., such as with a physiologically degradable material), and methods of absorbing an aqueous or oily solution or suspension into an absorbent material, with or without subsequent drying.

[0360] Parenteral administration of a pharmaceutical composition includes any route of administration characterized by physical breaching of a tissue of an individual and administration of the pharmaceutical composition through the breach in the tissue. Parental administration can be local, regional or systemic. Parenteral administration thus includes, but is not limited to, administration of a pharmaceutical composition by injection of the composition, by application of the composition through a surgical incision, by application of the composition through a tissue-penetrating non-surgical wound, and the like. In particular, parenteral administration is contemplated to include, but is not limited to, intravenous, intraocular, intravitreal, subcutaneous, intraperitoneal, intramuscular, intradermal, intrasternal injection, and intratumoral.

[0361] Formulations of a pharmaceutical composition suitable for parenteral administration comprise the active ingredient combined with a pharmaceutically acceptable carrier, such as sterile water or sterile isotonic saline. Such formulations may be prepared, packaged, or sold in a form suitable for bolus administration or for continuous administration. Injectable formulations may be prepared, packaged, or sold in unit dosage form, such as in ampules or in multi-dose containers containing a preservative. Formulations for parenteral administration include, but are not limited to, suspensions, solutions, emulsions in oily or aqueous vehicles, pastes, and implantable sustained-release or biodegradable formulations. Such formulations may further comprise one or more additional ingredients including, but not limited to, suspending, stabilizing, or dispersing agents. In one embodiment of a formulation for parenteral administration, the active ingredient is provided in dry (i.e., powder or granular) form for reconstitution with a suitable vehicle (e.g., sterile pyrogen-free water) prior to parenteral administration of the reconstituted composition.

[0362] The pharmaceutical compositions may be prepared, packaged, or sold in the form of a sterile injectable aqueous or oily suspension or solution. This suspension or solution may be formulated according to the known art, and may comprise, in addition to the active ingredient, additional ingredients such as the dispersing agents, wetting agents, or suspending agents described herein. Such sterile injectable formulations may be prepared using a non-toxic parenterally-acceptable diluent or solvent, such as water or 1,3-butane diol, for example. Other acceptable diluents and solvents include, but are not limited to, Ringer's solution, isotonic sodium chloride solution, and fixed oils such as synthetic mono-or di-glycerides. Other parentally-administrable formulations which are useful include those which comprise the active ingredient in microcrystalline form, in a liposomal preparation, or as a component of a biodegradable polymer systems. Compositions for sustained release or implantation may comprise pharmaceutically acceptable polymeric or hydrophobic materials such as an emulsion, an ion exchange resin, a sparingly soluble polymer, or a sparingly soluble salt.

[0363] Formulations suitable for topical administration include, but are not limited to, liquid or semi-liquid preparations such as liniments, lotions, oil-in-water or water-in-oil emulsions such as creams, ointments or pastes, and solutions or suspensions. Topically-administrable formulations may, for example, comprise from about 1% to about 10% (w/w) active ingredient, although the concentration of the active ingredient may be as high as the solubility limit of the active ingredient in the solvent Formulations for topical administration may further comprise one or more of the additional ingredients described herein.

[0364] A pharmaceutical composition of the invention may be prepared, packaged, or sold in a formulation suitable for pulmonary administration via the buccal cavity. Such a formulation may comprise dry particles which comprise the active ingredient and which have a diameter in the range from about 0.5 to about 7 nanometers, and preferably from about 1 to about 6 nanometers. Such compositions are conveniently in the form of dry powders for administration using a device comprising a dry powder reservoir to which a stream of propellant may be directed to disperse the powder or using a self-propelling solvent/powder-dispensing container such as a device comprising the active ingredient dissolved or suspended in a low-boiling propellant in a sealed container. Preferably, such powders comprise particles wherein at least 98% of the particles by weight have a diameter greater than 0.5 nanometers and at least 95% of the particles by number have a diameter less than 7 nanometers. More preferably, at least 95% of the particles by weight have a diameter greater than 1 nanometer and at least 90% of the particles by number have a diameter less than 6 nanometers. In some embodiments, dry powder compositions include a solid fine powder diluent such as sugar and are conveniently provided in a unit dose form.

[0365] Low boiling propellants generally include liquid propellants having a boiling point of below 65° F. at atmospheric pressure. Generally, the propellant may constitute 50 to 99.9% (w/w) of the composition, and the active ingredient may constitute 0.1 to 20% (w/w) of the composition. The propellant may further comprise additional ingredients such as a liquid non-ionic or solid anionic surfactant or a solid diluent (in some embodiments having a particle size of the same order as particles comprising the active ingredient).

[0366] Pharmaceutical compositions of the invention formulated for pulmonary delivery may also provide the active ingredient in the form of droplets of a solution or suspension. Such formulations may be prepared, packaged, or sold as aqueous or dilute alcoholic solutions or suspensions, optionally sterile, comprising the active ingredient, and may conveniently be administered using any nebulization or atomization device. Such formulations may further comprise

one or more additional ingredients including, but not limited to, a flavoring agent such as saccharin sodium, a volatile oil, a buffering agent, a surface active agent, or a preservative such as methylhydroxybenzoate. The droplets provided by this route of administration preferably have an average diameter in the range from about 0.1 to about 200 nanometers.

[0367] The formulations described herein as being useful for pulmonary delivery are also useful for intranasal delivery of a pharmaceutical composition of the invention.

[0368] Another formulation suitable for intranasal administration is a coarse powder comprising the active ingredient and having an average particle from about 0.2 to 500 micrometers.

[0369] Such a formulation is administered in the manner in which snuff is taken i.e. by rapid inhalation through the nasal passage from a container of the powder held close to the nares. Formulations suitable for nasal administration may, for example, comprise from about as little as 0.1% (w/w) and as much as 100% (w/w) of the active ingredient, and may further comprise one or more of the additional ingredients described herein.

[0370] A pharmaceutical composition of the invention may be prepared, packaged, or sold in a formulation suitable for buccal administration. Such formulations may, for example, be in the form of tablets or lozenges made using conventional methods, and may, for example, contain 0.1 to 20% (w/w) active ingredient, the balance comprising an orally dissolvable or degradable composition and, optionally, one or more of the additional ingredients described herein. Alternately, formulations suitable for buccal administration may comprise a powder or an aerosolized or atomized solution or suspension comprising the active ingredient. Such powdered, aerosolized, or aerosolized formulations, when dispersed, preferably have an average particle or droplet size in the range from about 0.1 nanomaters to about 2000 micrometers, and may further comprise one or more of the additional ingredients described herein.

[0371] A pharmaceutical composition of the invention may be prepared, packaged, or sold in a formulation suitable for ophthalmic administration. Such formulations may, for example, be in the form of eye drops including, for example, a 0.1-1.0% (w/w) solution or suspension of the active ingredient in an aqueous or oily liquid carrier. Such drops may further comprise buffering agents, salts, or one or more other of the additional ingredients described herein. Other opthalmically-administrable formulations which are useful include those which comprise the active ingredient in microcrystalline form or in a liposomal preparation.

[0372] As used herein, "additional ingredients" include, but are not limited to, one or more of the following: excipients; surface active agents; dispersing agents; inert diluents; granulating and disintegrating agents; binding agents; lubricating agents; sweetening agents; flavoring agents; coloring agents; preservatives; physiologically degradable compositions such as gelatin; aqueous vehicles and solvents; oily vehicles and solvents; suspending agents; dispersing or wetting agents; emulsifying agents, demulcents; buffers; salts; thickening agents; fillers; emulsifying agents; antioxidants; antibiotics; antifungal agents; stabilizing agents; and pharmaceutically acceptable polymeric or hydrophobic materials. Other "additional ingredients" which may be included in the pharmaceutical compositions of the invention are known in the art and described, for example in Genaro, ed., 1985, Remington's Pharmaceutical Sciences, Mack Publishing Co., Easton, Pa.

[0373] Administration of the compounds of the present invention or the compositions thereof may be continuous or intermittent, depending, for example, upon the recipient's physiological condition, whether the purpose of the administration is therapeutic or prophylactic, and other factors known to skilled practitioners. The administration of the agents of the invention may be essentially continuous over a preselected period of time or may be in a series of spaced doses. Both local and systemic administration is contemplated. The amount administered will vary depending on various factors including, but not limited to, the composition chosen, the particular disease, the weight, the physical condition, and the age of the mammal, and whether prevention or treatment is to be achieved. Such factors can be readily determined by the clinician employing animal models or other test systems which are well known to the art.

[0374] One or more suitable unit dosage forms having the therapeutic agent(s) of the invention, which, as discussed below, may optionally be formulated for sustained release (for example using microencapsulation, see WO 94/07529, and U.S. Pat. No. 4,962,091 the disclosures of which are incorporated by reference herein), can be administered by a variety of routes including parenteral, including by intravenous and intramuscular routes, as well as by direct injection into the diseased tissue. For example, the therapeutic agent may be directly injected into the muscle. The formulations may, where appropriate, be conveniently presented in discrete unit dosage forms and may be prepared by any of the methods well known to pharmacy. Such methods may include the step of bringing into association the therapeutic agent with liquid carriers, solid matrices, semi-solid carriers, finely divided solid carriers or combinations thereof, and then, if necessary, introducing or shaping the product into the desired delivery system.

[0375] When the therapeutic agents of the invention are prepared for administration, they are preferably combined with a pharmaceutically acceptable carrier, diluent or excipient to form a pharmaceutical formulation, or unit dosage form. The total active ingredients in such formulations include from 0.1 to 99.9% by weight of the formulation. A "pharmaceutically acceptable" is a carrier, diluent, excipient, and/or salt that is compatible with the other ingredients of the formulation, and not deleterious to the recipient thereof. The active ingredient for administration may be present as a powder or as granules; as a solution, a suspension or an emulsion.

[0376] Pharmaceutical formulations containing the therapeutic agents of the invention can be prepared by procedures known in the art using well known and readily available ingredients. The therapeutic agents of the invention can also be formulated as solutions appropriate for parenteral administration, for instance by intramuscular, subcutaneous or intravenous routes.

[0377] The pharmaceutical formulations of the therapeutic agents of the invention can also take the form of an aqueous or anhydrous solution or dispersion, or alternatively the form of an emulsion or suspension.

[0378] Thus, the therapeutic agent may be formulated for parenteral administration (e.g., by injection, for example, bolus injection or continuous infusion) and may be presented in unit dose form in ampules, pre-filled syringes, small volume infusion containers or in multi-dose containers

with an added preservative. The active ingredients may take such forms as suspensions, solutions, or emulsions in oily or aqueous vehicles, and may contain formulatory agents such as suspending, stabilizing and/or dispersing agents. Alternatively, the active ingredients may be in powder form, obtained by aseptic isolation of sterile solid or by lyophilization from solution, for constitution with a suitable vehicle, e.g., sterile, pyrogen-free water, before use.

[0379] It will be appreciated that the unit content of active ingredient or ingredients contained in an individual aerosol dose of each dosage form need not in itself constitute an effective amount for treating the particular indication or disease since the necessary effective amount can be reached by administration of a plurality of dosage units. Moreover, the effective amount may be achieved using less than the dose in the dosage form, either individually, or in a series of administrations.

[0380] The pharmaceutical formulations of the present invention may include, as optional ingredients, pharmaceutically acceptable carriers, diluents, solubilizing or emulsifying agents, and salts of the type that are well-known in the art. Specific non-limiting examples of the carriers and/or diluents that are useful in the pharmaceutical formulations of the present invention include water and physiologically acceptable buffered saline solutions, such as phosphate buffered saline solutions pH 7.0-8.0.

[0381] In general, water, suitable oil, saline, aqueous dextrose (glucose), and related sugar solutions and glycols such as propylene glycol or polyethylene glycols are suitable carriers for parenteral solutions. Solutions for parenteral administration contain the active ingredient, suitable stabilizing agents and, if necessary, buffer substances. Antioxidizing agents such as sodium bisulfate, sodium sulfite or ascorbic acid, either alone or combined, are suitable stabilizing agents. Also used are citric acid and its salts and sodium Ethylenediaminetetraacetic acid (EDTA). In addition, parenteral solutions can contain preservatives such as benzalkonium chloride, methyl- or propyl-paraben and chlorobutanol. Suitable pharmaceutical carriers are described in Remington's Pharmaceutical Sciences, a standard reference text in this field.

[0382] The active ingredients of the invention may be formulated to be suspended in a pharmaceutically acceptable composition suitable for use in mammals and in particular, in humans. Such formulations include the use of adjuvants such as muramyl dipeptide derivatives (MDP) or analogs that are described in U.S. Pat. Nos. 4,082,735; 4,082,736; 4,101,536; 4,185,089; 4,235,771; and 4,406,890. Other adjuvants, which are useful, include alum (Pierce Chemical Co.), lipid A, trehalose dimycolate and dimethyldioctadecylammonium bromide (DDA), Freund's adjuvant, and IL-12. Other components may include a polyoxypropylene-polyoxyethylene block polymer (Pluronic®), a non-ionic surfactant, and a metabolizable oil such as squalene (U.S. Pat. No. 4,606,918).

[0383] Additionally, standard pharmaceutical methods can be employed to control the duration of action. These are well known in the art and include control release preparations and can include appropriate macromolecules, for example polymers, polyesters, polyamino acids, polyvinyl, pyrolidone, ethylenevinylacetate, methyl cellulose, carboxymethyl cellulose or protamine sulfate. The concentration of macromolecules as well as the methods of incorporation can be adjusted in order to control release. Additionally, the agent can be incorporated into particles of polymeric materials such as polyesters, polyamino acids, hydrogels, poly (lactic acid) or ethylenevinylacetate copolymers. In addition to being incorporated, these agents can also be used to trap the compound in microcapsules.

[0384] Accordingly, the composition of the present invention may be delivered via various routes and to various sites in a mammal body to achieve a particular effect (see, e.g., Rosenfeld et al., 1991; Rosenfeld et al., 1991a; Jaffe et al., supra; Berkner, supra). One skilled in the art will recognize that although more than one route can be used for administration, a particular route can provide a more immediate and more effective reaction than another route. In one embodiment, the composition described above is administered to the subject by subretinal injection. In other embodiments, the composition is administered by intravitreal injection. Other forms of administration that may be useful in the methods described herein include, but are not limited to, direct delivery to a desired organ (e.g., the eye), oral, inhalation, intranasal, intratracheal, intravenous, intramuscular, subcutaneous, intradermal, and other parental routes of administration. Additionally, routes of administration may be combined, if desired. In another embodiments, route of administration is subretinal injection or intravitreal injection.

[0385] The active ingredients of the present invention can be provided in unit dosage form wherein each dosage unit, e.g., a teaspoonful, tablet, solution, or suppository, contains a predetermined amount of the composition, alone or in appropriate combination with other active agents. The term "unit dosage form" as used herein refers to physically discrete units suitable as unitary dosages for human and mammal subjects, each unit containing a predetermined quantity of the compositions of the present invention, alone or in combination with other active agents, calculated in an amount sufficient to produce the desired effect, in association with a pharmaceutically acceptable diluent, carrier, or vehicle, where appropriate. The specifications for the unit dosage forms of the present invention depend on the particular effect to be achieved and the particular pharmacodynamics associated with the composition in the particular host.

[0386] The pharmaceutical compositions useful for practicing the invention may be administered to deliver a dose of at least about 1 ng/kg, at least about 5 ng/kg, at least about 10 ng/kg, at least about 25 ng/kg, at least about 50 ng/kg, at least about 100 ng/kg, at least about 500 ng/kg, at least about 1 μg/kg, at least about 5 μg/kg, at least about 10 μg/kg, at least about 25 μg/kg, at least about 50 μg/kg, at least about 100 μg/kg, at least about 500 μg/kg, at least about 1 mg/kg, at least about 5 mg/kg, at least about 10 mg/kg, at least about 25 mg/kg, at least about 50 mg/kg, at least about 100 mg/kg, at least about 200 mg/kg, at least about 300 mg/kg, at least about 400 mg/kg, and at least about 500 mg/kg of body weight of the subject.

[0387] In some embodiments, the pharmaceutical compositions useful for practicing the invention may be administered to deliver a dose of no more than about 1 ng/kg, no more than about 5 ng/kg, no more than about 10 ng/kg, no more than about 25 ng/kg, no more than about 50 ng/kg, no more than about 100 ng/kg, no more than about 500 ng/kg, no more than about 1 μg/kg, no more than about 5 μg/kg, no more than about 10 μg/kg, no more than about 25 μg/kg, no more than about 50 μg/kg, no more than about 100 μg/kg, no

more than about 500 μg/kg, no more than about 1 mg/kg, no more than about 5 mg/kg, no more than about 10 mg/kg, no more than about 25 mg/kg, no more than about 50 mg/kg, no more than about 100 mg/kg, no more than about 200 mg/kg, no more than about 300 mg/kg, no more than about 400 mg/kg, and no more than about 500 mg/kg of body weight of the subject. Also contemplated are dosage ranges between any of the doses disclosed herein.

[0388] Typically, dosages which may be administered in a method of the invention to a subject, in some embodiments a human, range in amount from 0.5 μg to about 100 g per kilogram of body weight of the subject. While the precise dosage administered will vary depending upon any number of factors, including but not limited to, the type of subject and type of disease state being treated, the age of the subject and the route of administration. In some embodiments, the dosage of the compound will vary from about 1 μg to about 10 mg per kilogram of body weight of the subject. In other embodiments, the dosage will vary from about 3 μg to about 1 mg per kilogram of body weight of the subject.

[0389] The compositions may be administered to a subject as frequently as several times daily, or it may be administered less frequently, such as once a day, twice a day, thrice a day, once a week, twice a week, thrice a week, once every two weeks, twice every two weeks, thrice every two weeks, once a month, twice a month, thrice a month, or even less frequently, such as once every several months or even once or a few times a year or less. The frequency of the dose will be readily apparent to the skilled artisan and will depend upon any number of factors, such as, but not limited to, the type and severity of the disease being treated, the type and age of the subject, etc. The formulations of the pharmaceutical compositions may be prepared by any method known or hereafter developed in the art of pharmacology. In general, such preparatory methods include the step of bringing the active ingredient into association with a carrier or one or more other accessory ingredients, and then, if necessary or desirable, shaping or packaging the product into a desired single- or multi-dose unit.

[0390] Individuals to which administration of the pharmaceutical compositions of the invention is contemplated include, but are not limited to, humans and other primates, mammals including commercially relevant mammals such as non-human primates, cattle, pigs, horses, sheep, cats, and dogs.

[0391] These compositions described herein are by no means all-inclusive, and further modifications to suit the specific application will be apparent to the ordinary skilled artisan. Moreover, the effective amount of the compositions can be further approximated through analogy to compounds known to exert the desired effect.

Kits

[0392] The present invention also pertains to kits useful in the methods of the invention. Such kits comprise various combinations of components useful in any of the methods described elsewhere herein, including for example, materials for identifying at least one antibody target, quantitatively analyzing at least one antibody or a target thereof (e.g., quantitatively analyzing a nucleic acid sequence barcode), materials for diagnosing or assessing the prognosis of a disease or disorder associated with the antibody or target thereof, materials for preventing or treating a disease or disorder associated with the antibody or target thereof, materials for alleviating toxicity of the treatment, and instructional material. For example, in one embodiment, the kit comprises components useful for the identification of a desired antibody target in a biological sample. In another embodiment, the kit comprises components useful for the quantification of a desired antibody or a desired antibody target (e.g., quantification of a desired nucleic acid sequence barcode). In a further embodiment, the kit comprises components useful for diagnosing or assessing the prognosis of a disease or disorder associated with the antibody or target thereof In a further embodiment, the kit comprises components useful for preventing or treating a disease or disorder associated with the antibody or target thereof. In a further embodiment, the kit comprises components useful for alleviating toxicity of the treatment.

[0393] In a further embodiment, the kit comprises the components of an assay for monitoring the effectiveness of a treatment administered to a subject in need thereof, containing instructional material and the components for determining whether the level of an antibody or a target thereof of the invention in a biological sample obtained from the subject is modulated during or after administration of the treatment. In various embodiments, to determine whether the level of an antibody or a target thereof of the invention is modulated in a biological sample obtained from the subject, the level of the antibody or the target thereof is compared with the level of at least one comparator contained in the kit, such as a positive control, a negative control, a historical control, a historical norm, or the level of another reference molecule in the biological sample. In certain embodiments, the ratio of the antibody or the target thereof and a reference molecule is determined to aid in the monitoring of the treatment.

EXPERIMENTAL EXAMPLES

[0394] The invention is further described in detail by reference to the following experimental examples. These examples are provided for purposes of illustration only, and are not intended to be limiting unless otherwise specified. Thus, the invention should in no way be construed as being limited to the following examples, but rather should be construed to encompass any and all variations which become evident as a result of the teaching provided herein.

[0395] Without further description, it is believed that one of ordinary skill in the art can, using the preceding description and the following illustrative examples, make and utilize the present invention and practice the claimed methods. The following working examples therefore are not to be construed as limiting in any way the remainder of the disclosure.

Example 1: Rapid Extracellular Antibody Profiling (READ)

[0396] Current high-throughput autoantibody discovery techniques have limited sensitivity towards extracellular and secreted proteins largely due to the biochemical challenges associated with producing these proteins in a high-throughput manner. In this regard, yeast cell surface display offers several important advantages over other common systems. Unlike in vitro translation or peptide-array-based approaches, yeast cell surface display can express full-length proteins in folded three-dimensional conformations, allowing for the identification of non-linear binding

epitopes. Compared to phage or bacterial expression systems, yeast cell produced extracellular proteins in a eukaryotic cell system that included ER chaperones, glycosylation machinery, and disulfide "proofreading." While mammalian systems may offer even superior quality control owing to more native glycosylation machinery and chaperones, a yeast cell surface display library is far more economical to maintain and expand. These advantages combine to make a yeast-displayed exoproteome library a robust solution that can maximize the sensitivity and throughput of extracellular autoantibody discovery.

[0397] The present study generated, characterized, and applied a high-quality yeast-display based platform to identify extracellular proteins that are targets of autoantibodies. The system was benchmarked using a well-characterized autoimmune syndrome with pathognomonic autoantibody targets and showed that it has high sensitivity and specificity. The method was additionally applied to a cohort of immunotherapy-treated NSCLC patients and another cohort of patients with SLE, UCTD, and sarcoidosis. In both cohorts several novel autoantibody reactivities were identified and validated.

[0398] REAP as a Novel Autoantibody Discovery Platform

[0399] In order to leverage the power of yeast cell surface display systems for autoantibody discovery, a yeast-displayed "exoproteome" library of approximately 1400 human extracellular or secreted proteins, where each protein in the library was paired with unique DNA barcodes, was used. Using this library, REAP, a platform that allowed for sensitive high throughput identification of autoantibody reactivities against extracellular proteins, was developed. In it, purified patient antibodies were incubated with the library. Autoantibodies, if present, bound to yeast cell clones displaying their target antigen. These autoantibody-coated yeast cells were enriched by magnetic bead-based selection and enrichment was quantified through next generation sequencing of the unique DNA barcodes (FIG. **1**).

[0400] In developing REAP, a number of novel methodologies had to be established. These include advances in antigen library preparation as well as advances in methodology for preparation of patient biological samples, high-throughput selection, and downstream data analysis. First, a necessary component of REAP was the defined linkage between a genetically encoded barcode that may be read out by next-generation sequencing and an associated gene. While multiple barcodes may be associated with the same gene, no barcode may be associated with multiple genes for the REAP assay to function. Additionally, REAP required a library composed of native, properly-folded proteins comprising individual extracellular domains ("ectodomains"). Therefore, approaches, such as peptide tiling, shotgun DNA cloning, or whole-cDNA cloning approaches, which have previously been used to generate libraries for autoantibody screening, did not offer the same specificity or coverage as the curated library since they did not present the full, properly folded tertiary structure of the secreted or ectodomain antigen. As such, these technologies cannot readily detect antibodies recognizing discontinuous, three-dimensional epitopes. These difficulties were overcome and generated a curated library of full-length ectodomains that were individually cloned, normalized during a pooling step, and confidently associated with multiple unique genetic barcodes.

[0401] Second, a high-throughput and efficient method for antibody isolation from human serum or plasma were developed. This method involved affinity purification of the desired antibody isotype (IgG, IgA, IgE, etc.) in 96-well microtiter plates. This allowed for the isolation of antibodies from hundreds of patient samples in a day. Importantly, after the antibodies were isolated, they were incubated with empty vector yeast. Since yeast cell contained conserved epitopes that may be targeted by endogenous anti-*saccharomyces* antibodies and proteins, such as complement/MBL, this step removed human serum components and yeast-reactive antibodies that may bind yeast cell and interfere with downstream selection procedures. Ultimately, the antibody isolation method allowed to rapidly process patient samples while generating antibody inputs that lead to minimal background in the REAP selection process.

[0402] Third, a novel high-throughput selection process based on 96-well magnetic columns were developed. Traditionally, yeast cell library selections for directed evolution purposes have been conducted with either large magnetic columns designed for capturing cells or fluorescence activated cell sorting (FACS). While this process was effective, it was entirely low-throughput. Using these large magnetic columns, only a few dozen selections can be performed at a time. Use of FACS was similarly limiting, as one FACS machine can only sort one sample at a time at a maximum speed of ~17 minutes per 100 million cells. In order to achieve the desired level of throughput, 96-well magnetic columns designed for analytical scale isolations of proteins and nucleic acids were repurposed. Through optimization, a standard protocol for use of these columns that involved washing to remove non-specific binders as well as centrifugation for maximum elution efficiency was developed. Using this novel selection method, the entire selection process for 96 samples consisting of 100 million cells per sample can be completed in ~40 minutes, while comparable sorting using FACS would take ~27 hours.

[0403] Finally, a custom scoring algorithm was developed to identify genuine autoantibody reactivities based on quantitative next generation sequencing data. The data analysis method relied on the fact that each protein in the library was displayed on multiple yeast cell clones and each clone carried a unique DNA barcode. In other words, each protein in the library consisted of multiple "protein clones". Through next generation sequencing, not only can the total enrichment of a protein after selection be determined, but also how many "protein clones" were enriched. This allows for quantifying "clonal enrichment", which was defined as the fraction of clones that were enriched above a set cutoff. Incorporation of clonal enrichment in REAP data analysis was essential for identification of true reactivities because it allowed for the elimination of non-specific enrichment of proteins due to polyreactive "sticky" yeast cell clones or stochastic variations in library distribution. These factors may result in enrichment of a single protein clone, but it was extremely unlikely that they would result in enrichment of all of the "protein clones" for a protein. On the other hand, genuine enrichment of a protein due to the presence of autoantibodies targeting it would result in enrichment of many if not all protein clones. Thus, incorporation of clonal enrichment into data analysis allowed for elimination of false positive enrichments, expediting identification of genuine autoantibody reactivities in samples.

[0404] REAP Allows for Specific and Sensitive High-Throughput Autoantibody Discovery

[0405] To validate that this method can accurately detect antibody targets, REAP was performed on a panel of 9 commercial monoclonal antibodies with known targets (FIG. **2**). All antibody targets in this panel were detect accurately and specifically. Next, the assay was benchmarked using samples from patients with autoimmune-polyendocrinopathy-candidiasis-ectodermal dystrophy (APECED), an autoimmune disease characterized by near universal presence of high titer autoantibodies against type 1 interferons and IL22 and rarer autoantibodies against other cytokines. IgG was purified from the serum of twelve APECED patients along with 16 healthy donor samples and conducted REAP on them. This REAP screen revealed that all APECED samples exhibited robust enrichment of type 1 interferons (IFNA & IFNW1) and 1L22 and several exhibited enrichment of other known autoantibody targets in APECED such as IL17, IL5, and IL28 at frequencies comparable to previously described autoantibody distributions in the APECED patient population (FIG. **3**). Little to no enrichment of these proteins was seen in the 20 healthy donor samples. Autoantibodies were identified against gastric intrinsic factor (GIF), lipocalin-1 (LCN1), IL-5, IL-6, protein disulfide-isomerase-like protein of the testis (PDILT), and BPI fold containing family member 1 and 2 (BPIFA1/2), which have been previously described in APECED. With respect to GIF reactivities, the results seen with REAP demonstrated strong concordance with clinical anti-GIF ELISA results from the same patients (FIG. **4**). To quantify the sensitivity of the assay, REAP screens were conducted using serial dilutions of antibody from an APECED patient (FIG. **5**) and compared the results to that of enzyme-linked immunosorbent assays (ELISAs), the "gold-standard" assay for autoantibody detection (FIG. **6**). For the four protein targets tested, REAP exhibited higher sensitivity than ELISA, as seen by the left-shifted dose response curves in the REAP assay. To investigate the reproducibility of REAP, log 2[fold enrichment] was compared between technical (intra-assay) replicates across all APECED patient samples and strong positive correlations were found between replicates (median R2=0.914; FIG. **7**). Together, these data show that REAP is a sensitive and specific assay for high-throughput autoantibody identification from patient serum.

[0406] REAP Identifies Novel Autoantibodies in a Wide Variety of Disease Contexts

[0407] Using REAP, a cohort of patients with systemic lupus erythematosus (SLE) was screened (FIG. **8**). THe screen identified autoantibody reactivities that are known to be present in SLE patients, such as those against TNF, IL6, and type I interferons. Importantly, many previously undescribed autoantibody reactivities were identified against proteins with a wide range of biological functions. For example, autoantibody reactivities were identified targeting cytokines (e.g., IL4, IL33), chemokines (e.g., CXCL3, CCL8), growth factors (e.g., VEGFB, FGF21), immunoregulatory proteins (e.g., PD-L2, B7H4), and extracellular matrix proteins (e.g., EPYC, CD248).

[0408] Two notable autoantibody reactivities uncovered in SLE patients were those against PD-L2 and IL-33. These were biochemically validated using ELISAs and the function of these autoantibodies was characterized. As the primary biological function of PD-L2 is mediated by its binding to its receptor PD-1, it was tested whether autoantibodies against PD-L2 could block this interaction. Serum samples from an SLE patient with anti-PD-L2 autoantibodies were present at titers >1:100 and inhibited the interaction between PD-L2 and PD-1 in a dose-dependent manner, while serum from a control patient without anti-PD-L2 autoantibodies did not (FIG. **9**A-**9**C). To test the functional effects of anti-IL-33 autoantibodies, a HEK-Blue IL-33 reporter cell line was used, which produces secreted alkaline phosphatase downstream of an NFκB promoter that is activated by the IL-33 pathway. Bulk IgG (isolated via protein G) from the SLE patient harboring anti-IL-33 autoantibodies potently neutralized IL-33 signaling with an IC50 less than 0.01 mg/mL, while IgG from a control patient without anti-IL-33 autoantibodies had no neutralizing effect (FIG. **9**D-**9**F). These findings underscore the ability of REAP to discover novel autoantibodies with functional biological effects.

[0409] In addition, a longitudinal cohort of 63 non-small cell lung cancer (NSCLC) patients treated primarily with anti-PD-L1 and anti-PD-1 checkpoint inhibition along with a variety of other antibody immunotherapies (FIG. **10**) was screened. From this screen, novel autoantibody reactivities against proteins that have not yet been described in the context of cancer and that could potentially have disease-modifying effects were identified. These include autoantibodies targeting chemokines (e.g., CXCL1/2/3), type 1 interferons, growth factors (e.g., VEGFB), and adhesion receptors (e.g., MADCAM1).

[0410] Using REAP, many of the therapeutic antibodies administered to these patients were accurately detected, which served as internal positive controls. The assay was able to detect therapeutic antibody presence with high sensitivity. In one patient, patient 9, bevacizumab (anti-VEGFA therapeutic antibody) was detected 6 months after their last dose. The assay was also able to accurately detect longitudinal changes in therapeutic antibody titer. For example, REAP score accurately reflected changes in therapeutic anti-OX40 antibody titers in one patient, as measured by ELISA (FIG. **11**).

[0411] Combining these data with the SLE REAP data, the heterogeneity in REAP data was analyzed between different diseases by performing UMAP analysis on the NSCLC, SLE, and UCTD patient data (FIG. **12**). While some NSCLC and SLE patients clustered together, some subsets of patients formed distinct disease-specific clusters.

[0412] A cohort of patients was screened with systemic sclerosis, a chronic autoimmune rheumatic disorder (FIG. **13**). Similar to the screen of SLE patients, numerous novel autoantibody reactivities targeting proteins involved in a wide variety of biological functions were found. Of note, many reactivities against NK cell related proteins (LILRA3, LILRB2, RAETIL, ULBP2) were identified and multiple patients had autoantibody reactivities against PD-1, an immune checkpoint receptor that plays an important role in inhibiting immune responses.

[0413] Finally, a longitudinal cohort of 194 COVID-19 patients were screened. It was found that autoantibodies in COVID-19 patients targeted proteins involved in diverse immunological functions such as acute phase response, type II immunity, leukocyte trafficking, interferon responses, and lymphocyte function/activation (FIG. **14**). Cytokine autoantibody targets included type 1 and type 3 interferons, IL-1α/β, IL-6, IL-21, IL-22, GM-CSF (CSF2), IL-18Rβ

(IL18RAP), and Leptin (LEP). Chemokine autoantibody targets included CXCL1, CXCL7 (PPBP), CCL2, CCL15, CCL16, and the chemokine decoy receptor ACKR1 (Duffy blood group antigen). Immunomodulatory cell surface autoantibody targets included NKG2D ligands (e.g., RAET1E/L, ULBP1/2), NK cell receptors NKG2A/C/E (e.g., KLRC1/2/3), B cell expressed proteins (e.g., CD38, FCMR, FCRL3, CXCR5), T cell expressed proteins (e.g., CD3E, CXCR3, CCR4), and myeloid expressed proteins (e.g., CCR2, CD300E).

[0414] In addition to immune-targeting autoantibodies, a high prevalence of tissue-associated autoantibodies in COVID-19 patients (FIG. **15**) was observed. A list of tissue associated antigens with significant differences in REAP signals was manually curated between uninfected controls and symptomatic patients, and a heatmap organized by COVID-19 disease severity was generated. Broadly, a high frequency of autoantibodies were found directed against vascular cell types (e.g., endothelial adhesion molecule PLVAP, regulator of angiogenesis RSPO3); against coagulation factors (e.g., coagulation factor II receptor F2R, SERPINEl and 2) and platelets (e.g., glycoprotein VI GP6); and against connective tissue and extracellular matrix targets (e.g., suspected regulator of cartilage maintenance OTOR, matrix metalloproteinases MMP7 and MMP9). In addition, REAP hits were observed against various organ systems including lung (e.g., ectodysplasin A2 Receptor EDA2R and mesothelin MSLN), the CNS compartment (e.g., orexin receptor HCRTR2, metabotropic glutamate receptor GRM5, neuronal injury marker NINJ1), skin (e.g., dermcidin DCD), gastrointestinal tract (e.g., regenerating family member 4 REG4, guanylate cyclase activator 2A GUCA2A), and other tissues.

[0415] To explore the correlation of autoantibodies with disease progression/adverse events in cancer patients treated with immunotherapy, 1,454 longitudinal samples were screened from 222 CPI-treated melanoma patients (FIG. **16**). Anti-CTLA4/PD1/PDL1 drugs were detected in most treated patients. Beyond these "controls", more than 400 hits with significant REAP scores were observed across the samples. Many hits like ICOSLG, IL6, TNFa, and IL1A are present in multiple patients and these antibodies could have a modulation role in drug response and immune-related adverse events.

[0416] The broad autoantibody reactivity is also observed in kidney transplant patients (FIG. **17**). 108 patients with pre and post transplantation serum samples were screened. Around 320 autoantibodies and 70/320 are immune-related hits were detected. Patients treated with Belatacept (CTLA-4 Fc) were accurately captured, with high CD80 scores. Patients are grouped by rejection and infection status after transplantation. Some hits like IFITM10, IL4, EXOC3-AS1 are highly associated with post-transplantation rejection while anti-IGFBP1 shows a potential protective role. Anti-IFNa family/CD99L2/OSTN/SYCN/LYG2/BTN1A1 autoantibodies are enriched in the infection group, suggesting a protective role of these proteins in virus infection. Anti-NXPH1/CST5 autoantibodies are observed in the non-infection group, indicates the potential immune-inhibitory role of these proteins. The existence of these autoantibodies is an opportunity to modulate patients' responses with kidney transplantation.

[0417] Custom Scoring Algorithm has High Sensitivity and Specificity

[0418] To validate the autoantibody reactivities that were discovered, two parallel and orthogonal assays were used. Luciferase Immunoprecipitation Systems (LIPS) offers a highly sensitive, higher-throughput validation process, but relies on luciferase fusions that may interfere with protein folding or lead to higher noise and variability between proteins. ELISA requires larger amounts of purified recombinant protein but is a "gold-standard" assay that is widely used. In both assays, valid autoantibody reactivities were defined as those with signals 3 standard deviations above the average healthy donor signal. Representative ELISA and LIPS validation plots can be seen in FIG. **18**A and FIG. **18**B. Using orthogonal validation data from APECED and SLE patients (247 test pairs across 25 different proteins), a receiver operating characteristic analysis was conducted and it was found that using the current scoring algorithm, REAP could distinguish autoantibody reactivities with an area under the curve of 0.892 (FIG. **19**). A list of all REAP reactivities that have been orthogonally validated is provided in FIG. **23**.

[0419] Pathogenic Autoantibodies Identified by REAP could be Specifically Targeted for Degradation in Clinical Settings

[0420] Autoantibodies that are identified in REAP screens and are further demonstrated to have pathogenic effects could be targeted for degradation in clinical settings using existing therapeutic modalities. For example, pathogenic autoantibodies could be removed from circulation in patients through the use of recombinant biologics in the form of autoantigens conjugated to endocytosis-promoting protein tags. Upon injection of these autoantigen conjugates into circulation, pathogenic autoantibodies will bind to their respective autoantigen, be trafficked to endosomal pathways, and ultimately be degraded intracellularly (FIG. **20**). Chimeric autoantigen receptor (CAAR) T cells, a recently developed drug modality, could also be used to eliminate the B cells responsible for pathogenic autoantibody production. CAAR T cells display autoantigens on their cell surfaces that are connected to intracellular T cell activation domains. Inside a patient, CAAR T cells can bind to the B cell receptors of autoreactive B cells and initiate cytotoxic pathways that lead to lysis of the target autoreactive B cell (FIG. **21**). In some cases, when autoantigens are proteins that have potentially harmful physiological effects when administered systemically and in large quantities (e.g., cytokines, chemokines, growth factors) or have native binding partners that are widely expressed, autoantigens could be engineered so that they do not interact with their native partner (FIG. **22**). For example, if depletion of anti-IFNα autoantibodies was clinically indicated, IFNα could be engineered so that it does not bind to IFNAR1/2 and this engineered protein could be used as the autoantigen in the previously described therapeutic modalities.

[0421] The materials and methods employed in this experiment are now described.

[0422] Library Design:

[0423] An initial library of 3093 human extracellular proteins was assembled based on protein domains, immunological functions, and yeast-display compatibility. The extracellular portion of each protein was identified by manual inspection of topological domains annotated in the SwissProt database (January 2018). For proteins with uncertain topology, full sequences were run through SignalP 4, Topcons, and GPTPred to identify most likely topologies.

For proteins with multiple extracellular portions, in general the longest individual region was chosen for initial amplification. cDNAs for chosen proteins were purchased from GE Dharmacon or DNASU. The protein sequences were further modified to match isoforms available in purchased cDNAs. An inventory of antigens included in the library are compiled in Table 1.

TABLE 1

Representative list of DNA and protein sequences amplified for the initial and expanded libraries.

Seq. Id. No. (protein)	Seq. Id. No. (DNA)	Uniprot ID	Gene Symbol
1	3093	P04217	A1BG
2	3094	P01023	A2M
3	3095	Q7Z7G0	ABI3BP
4	3096	P16112	ACAN
5	3097	Q9BYF1	ACE2
6	3098	O75078	ADAM11
7	3099	O43184	ADAM12
8	3100	Q13444	ADAM15
9	3101	Q9Y3Q7	ADAM18
10	3102	Q9H013	ADAM19
11	3103	Q99965	ADAM2
12	3104	O43506	ADAM20
13	3105	Q9UKJ8	ADAM21
14	3106	Q9P0K1	ADAM22
15	3107	O75077	ADAM23
16	3108	QOUKQ2	ADAM28
17	3109	Q9UKF5	ADAM29
18	3110	Q9UKF2	ADAM30
19	3111	Q8TC27	ADAM32
20	3112	Q9BZ11	ADAM33
21	3113	P78325	ADAM8
22	3114	Q13443	ADAM9
23	3115	P82987	ADAMTSL3
24	3116	Q9UHX3	ADGRE2
25	3117	Q9BY15	ADGRE3
26	3118	Q86SQ3	ADGRE4P
27	3119	P48960	ADGRE5
28	3120	P35318	ADM
29	3121	Q7Z4H4	ADM2
30	3122	Q15109	AGER
31	3123	O00468	AGRN
32	3124	Q13740	ALCAM
33	3125	Q86YT9	AMICA1
34	3126	Q86WK6	AMIGO1
35	3127	Q86SJ2	AMIGO2
36	3128	Q86WK7	AMIGO3
37	3129	Q15389	ANGPT1
38	3130	O15123	ANGPT2
39	3131	Q9Y264	ANGPT4
40	3132	Q9UKU9	ANGPTL2
41	3133	Q9Y5C1	ANGPTL3
42	3134	Q9BY76	ANGPTL4
43	3135	Q9H6X2	ANTXR1
44	3136	P58335	ANTXR2
45	3137	A6NF34	ANTXRL
46	3138	P15514	AREG
47	3139	Q9H6B4	ASAM
48	3140	P07306	ASGR1
49	3141	P07307	ASGR2
50	3142	Q9BXN1	ASPN
51	3143	O14525	ASTN1
52	3144	O75129	ASTN2
53	3145	Q6UW56	ATRAID
54	3146	O75882	ATRN
55	3147	Q5VV63	ATRNL1
56	3148	P30530	AXL
57	3149	P25311	AZGP1
58	3150	P61769	B2M
59	3151	P50895	BCAM
60	3152	Q96GW7	BCAN
61	3153	P21810	BGN

TABLE 1-continued

Representative list of DNA and protein sequences amplified for the initial and expanded libraries.

Seq. Id. No. (protein)	Seq. Id. No. (DNA)	Uniprot ID	Gene Symbol
62	3154	P13497	BMP1
63	3155	O95393	BMP10
64	3156	O95972	BMP15
65	3157	P12643	BMP2
66	3158	P12645	BMP3
67	3159	P12644	BMP4
68	3160	P22003	BMP5
69	3161	P18075	BMP7
70	3162	Q7Z5Y6	BMP8A
71	3163	P34820	BMP8B
72	3164	P36894	BMPR1A
73	3165	O00238	BMPR1B
74	3166	Q13873	BMPR2
75	3167	Q9BWV1	BOC
76	3168	P35613	BSG
77	3169	Q075Z2	BSPH1
78	3170	P35070	BTC
79	3171	Q7Z6A9	BTLA
80	3172	Q13410	BTN1A1
81	3173	Q7KYR7	BTN2A1
82	3174	Q8WVV5	BTN2A2
83	3175	Q96KV6	BTN2A3P
84	3176	O00481	BTN3A1
85	3177	P78410	BTN3A2
86	3178	O00478	BTN3A3
87	3179	A8MVZ5	BTNL10
88	3180	Q9UIR0	BTNL2
89	3181	Q6UXE8	BTNL3
90	3182	Q6UX41	BTNL8
91	3183	Q6UXG8	BTNL9
92	3184	O95971	BY55
93	3185	Q9H7M9	C10orf54
94	3186	Q5VYX0	C10orf59
95	3187	Q6UX52	C17orf99
96	3188	Q969H8	C19orf10
97	3189	F2Z333	C1orf233
98	3190	Q71H61	C1orf32
99	3191	O75973	C1QL1
100	3192	Q7Z5L3	C1QL2
101	3193	Q9NPY3	C1QR1
102	3194	Q9BXJ5	C1QTNF2
103	3195	Q9BXJ3	C1QTNF4
104	3196	Q9BXJ0	C1QTNF5
105	3197	P00736	C1R
106	3198	P09871	C1S
107	3199	P01024	C3
108	3200	P0C0L4	C4A
109	3201	P01031	C5
110	3202	P13671	C6
111	3203	O95866	C6orf25
112	3204	P10643	C7
113	3205	P07357	C8A
114	3206	P07358	C8B
115	3207	P02748	C9
116	3208	Q9BY67	CADM1
117	3209	Q8N3J6	CADM2
118	3210	Q6UXH8	CCBE1
119	3211	P22362	CCL1
120	3212	P51671	CCL11
121	3213	Q99616	CCL13
122	3214	Q16627	CCL14
123	3215	Q16663	CCL15
124	3216	O15467	CCL16
125	3217	Q92583	CCL17
126	3218	P55774	CCL18
127	3219	Q99731	CCL19
128	3220	P13500	CCL2
129	3221	P78556	CCL20
130	3222	O00585	CCL21
131	3223	O00626	CCL22
132	3224	P55773	CCL23

TABLE 1-continued

Representative list of DNA and protein sequences amplified for the initial and expanded libraries.

Seq. Id. No. (protein)	Seq. Id. No. (DNA)	Uniprot ID	Gene Symbol
133	3225	O00175	CCL24
134	3226	O15444	CCL25
135	3227	Q9Y258	CCL26
136	3228	Q9Y4X3	CCL27
137	3229	Q9NRJ3	CCL28
138	3230	P10147	CCL3
139	3231	P16619	CCL3L3
140	3232	P13236	CCL4
141	3233	Q8NHW4	CCL4L1
142	3234	P13501	CCL5
143	3235	P80098	CCL7
144	3236	P80075	CCL8
145	3237	P08571	CD14
146	3238	P48509	CD151
147	3239	Q86VB7	CD163
148	3240	Q9NR16	CD163L1
149	3241	Q99467	CD180
150	3242	P15391	CD19
151	3243	P06126	CD1A
152	3244	P29016	CD1B
153	3245	P29017	CD1C
154	3246	P15813	CD1D
155	3247	P15812	CD1E
156	3248	P06729	CD2
157	3249	P41217	CD200
158	3250	Q8TD46	CD200R1
159	3251	Q6Q8B3	CD200R1L
160	3252	Q9UJ71	CD207
161	3253	Q9NNX6	CD209
162	3254	P20273	CD22
163	3255	Q15762	CD226
164	3256	Q9BZW8	CD244
165	3257	Q9HCU0	CD248
166	3258	Q9NZQ7	CD274
167	3259	Q5ZPR3	CD276
168	3260	P10747	CD28
169	3261	Q9UGN4	CD300A
170	3262	Q08708	CD300C
171	3263	Q496F6	CD300E
172	3264	A8K4G0	CD300LB
173	3265	Q6UXZ3	CD300LD
174	3266	Q8TDQ1	CD300LF
175	3267	Q6UXG3	CD300LG
176	3268	Q8IX05	CD302
177	3269	Q9NPF0	CD320
178	3270	P20138	CD33
179	3271	P28906	CD34
180	3272	P16671	CD36
181	3273	P11049	CD37
182	3274	P28907	CD38
183	3275	P04234	CD3D
184	3276	P07766	CD3E
185	3277	P09693	CD3G
186	3278	P01730	CD4
187	3279	P29965	CD40LG
188	3280	P16070	CD44
189	3281	Q08722	CD47
190	3282	P09326	CD48
191	3283	P06127	CD5
192	3284	P19397	CD53
193	3285	P08174	CD55
194	3286	P19256	CD58
195	3287	P13987	CD59
196	3288	P30203	CD6
197	3289	P08962	CD63
198	3290	Q07108	CD69
199	3291	P09564	CD7
200	3292	P32970	CD70
201	3293	P21854	CD72
202	3294	P04233	CD74
203	3295	P11912	CD79A

TABLE 1-continued

Representative list of DNA and protein sequences amplified for the initial and expanded libraries.

Seq. Id. No. (protein)	Seq. Id. No. (DNA)	Uniprot ID	Gene Symbol
204	3296	P40259	CD79B
205	3297	P33681	CD80
206	3298	P60033	CD81
207	3299	P27701	CD82
208	3300	Q01151	CD83
209	3301	Q9UIB8	CD84
210	3302	P42081	CD86
211	3303	P01732	CD8A
212	3304	P10966	CD8B
213	3305	A6NJW9	CD8B2
214	3306	P21926	CD9
215	3307	P40200	CD96
216	3308	P14209	CD99
217	3309	P12830	CDH1
218	3310	Q9Y6N8	CDH10
219	3311	P55287	CDH11
220	3312	P55289	CDH12
221	3313	P55290	CDH13
222	3314	P55291	CDH15
223	3315	O75309	CDH16
224	3316	Q12864	CDH17
225	3317	Q13634	CDH18
226	3318	Q9H159	CDH19
227	3319	P19022	CDH2
228	3320	Q9HBT6	CDH20
229	3321	Q9UJ99	CDH22
230	3322	Q9H251	CDH23
231	3323	Q86UP0	CDH24
232	3324	Q8IXH8	CDH26
233	3325	P22223	CDH3
234	3326	P55283	CDH4
235	3327	P33151	CDH5
236	3328	P55285	CDH6
237	3329	Q9ULB5	CDH7
238	3330	P55286	CDH8
239	3331	Q9ULB4	CDH9
240	3332	Q4KMG0	CDON
241	3333	O43827	CDT6
242	3334	P13688	CEACAM1
243	3335	Q2WEN9	CEACAM16
244	3336	A8MTB9	CEACAM18
245	3337	Q7Z692	CEACAM19
246	3338	Q6UY09	CEACAM20
247	3339	Q3KPI0	CEACAM21
248	3340	P40198	CEACAM3
249	3341	O75871	CEACAM4
250	3342	P06731	CEACAM5
251	3343	P40199	CEACAM6
252	3344	Q14002	CEACAM7
253	3345	P31997	CEACAM8
254	3346	P0CG37	CFC1
255	3347	P0CG36	CFC1B
256	3348	P00746	CFD
257	3349	P08603	CFH
258	3350	Q92496	CFHR4
259	3351	P05156	CFI
260	3352	O15335	CHAD
261	3353	Q6NUI6	CHADL
262	3354	O00533	CHL1
263	3355	Q9H9P2	CHODL
264	3356	O75339	CILP
265	3357	Q8IUL8	CILP2
266	3358	QOUQC9	CLCA2
267	3359	Q14CN2	CLCA4
268	3360	Q8WXI8	CLEC-6
269	3361	Q8IUN9	CLEC10A
270	3362	Q9Y240	CLEC11A
271	3363	Q5QGZ9	CLEC12A
272	3364	Q2HXU8	CLEC12B
273	3365	Q86T13	CLEC14A
274	3366	Q6ZS10	CLEC17A

TABLE 1-continued

Representative list of DNA and protein sequences amplified for the initial and expanded libraries.

Seq. Id. No. (protein)	Seq. Id. No. (DNA)	Uniprot ID	Gene Symbol
275	3367	Q6UXF7	CLEC18A
276	3368	A5D8T8	CLEC18A
277	3369	Q6UXS0	CLEC19A
278	3370	Q8NC01	CLEC1A
279	3371	Q9P126	CLEC1B
280	3372	Q92478	CLEC2B
281	3373	Q9UHP7	CLEC2D
282	3374	O75596	CLEC3A
283	3375	Q9UMR7	CLEC4A
284	3376	Q8WTT0	CLEC4C
285	3377	Q9ULY5	CLEC4E
286	3378	Q8N1N0	CLEC4F
287	3379	Q6UXB4	CLEC4G
288	3380	Q9H2X3	CLEC4M
289	3381	Q9NY25	CLEC5A
290	3382	Q6EIG7	CLEC6A
291	3383	Q9BXN2	CLEC7A
292	3384	Q6UXN8	CLEC9A
293	3385	Q8IZS7	CLECL1
294	3386	P26992	CNTFR
295	3387	Q12860	CNTN1
296	3388	Q02246	CNTN2
297	3389	Q9P232	CNTN3
298	3390	Q8IWV2	CNTN4
299	3391	O94779	CNTN5
300	3392	Q9UQ52	CNTN6
301	3393	P78357	CNTNAP1
302	3394	Q9UHC6	CNTNAP2
303	3395	Q9BZ76	CNTNAP3
304	3396	Q9C0A0	CNTNAP4
305	3397	Q8WYK1	CNTNAP5
306	3398	Q05707	COL14A1
307	3399	Q9P218	COL20A1
308	3400	Q9Y6Z7	COLEC10
309	3401	Q9BWP8	COLEC11
310	3402	Q5KU26	COLEC12
311	3403	P49747	COMP
312	3404	Q8IZJ3	CPAMD8
313	3405	P22792	CPN2
314	3406	P82279	CRB1
315	3407	Q96HD1	CRELD1
316	3408	Q6UXH1	CRELD2
317	3409	O75462	CRLF1
318	3410	Q9HC73	CRLF2
319	3411	Q9NQ79	CRTAC1
320	3412	O95727	CRTAM
321	3413	P07333	CSF1R
322	3414	P04141	CSF2
323	3415	P15509	CSF2RA
324	3416	P32927	CSF2RB
325	3417	P09919	CSF3
326	3418	Q99062	CSF3R
327	3419	O95196	CSPG5
328	3420	P16410	CTLA4
329	3421	P78423	CX3CL1
330	3422	P78310	CXADR
331	3423	P09341	CXCL1
332	3424	P02778	CXCL10
333	3425	O14625	CXCL11
334	3426	P48061	CXCL12
335	3427	O43927	CXCL13
336	3428	O95715	CXCL14
337	3429	Q9H2A7	CXCL16
338	3430	Q6UXB2	CXCL17
339	3431	P19875	CXCL2
340	3432	P19876	CXCL3
341	3433	P42830	CXCL5
342	3434	P80162	CXCL6
343	3435	Q07325	CXCL9
344	3436	Q14118	DAG1
345	3437	Q8N907	DAND5

TABLE 1-continued

Representative list of DNA and protein sequences amplified for the initial and expanded libraries.

Seq. Id. No. (protein)	Seq. Id. No. (DNA)	Uniprot ID	Gene Symbol
346	3438	P07585	DCN
347	3439	Q5T197	DCST1
348	3440	Q9H295	DCSTAMP
349	3441	P59665	DEFA1
350	3442	B2R9L8	Delta
351	3443	P98153	DGCR2
352	3444	Q68D85	DKFZp686O24166
353	3445	P80370	DLK1
354	3446	Q6UY11	DLK2
355	3447	O00548	DLL1
356	3448	Q9NYJ7	DLL3
357	3449	Q9NR61	DLL4
358	3450	Q8NFT8	DNER
359	3451	Q02487	DSC2
360	3452	Q14574	DSC3
361	3453	Q14126	DSG2
362	3454	P32926	DSG3
363	3455	Q86SJ6	DSG4
364	3456	Q14213	EBI3
365	3457	O94769	ECM2
366	3458	Q92838	EDA
367	3459	Q9HAV5	EDA2R
368	3460	Q9UNE0	EDAR
369	3461	O43854	EDIL3
370	3462	Q12805	EFEMP1
371	3463	O95967	EFEMP2
372	3464	P20827	EFNA1
373	3465	O43921	EFNA2
374	3466	P52797	EFNA3
375	3467	P52803	EFNA5
376	3468	P98172	EFNB1
377	3469	P52799	EFNB2
378	3470	Q15768	EFNB3
379	3471	P01133	EGF
380	3472	O75095	EGFL3
381	3473	Q8IUX8	EGFL6
382	3474	Q9UHF1	EGFL7
383	3475	Q63HQ2	EGFLAM
384	3476	P00533	EGFR
385	3477	P0C7U0	ELFN1
386	3478	Q5R3F8	ELFN2
387	3479	Q96BH3	ELSPBP1
388	3480	Q9HBW9	ELTD1
389	3481	Q6PCB8	EMB
390	3482	Q9ULC0	EMCN
391	3483	Q14246	EMR1
392	3484	P22413	ENPP1
393	3485	P49961	ENTPD1
394	3486	O75355	ENTPD3
395	3487	Q6UW88	EPGN
396	3488	P21709	EPHA1
397	3489	Q5JZY3	EPHA10
398	3490	P29317	EPHA2
399	3491	P29320	EPHA3
400	3492	P54764	EPHA4
401	3493	P54756	EPHA5
402	3494	Q9UF33	EPHA6
403	3495	Q15375	EPHA7
404	3496	P29322	EPHA8
405	3497	P54762	EPHB1
406	3498	P29323	EPHB2
407	3499	P54753	EPHB3
408	3500	P54760	EPHB4
409	3501	O15197	EPHB6
410	3502	P01588	EPO
411	3503	P19235	EPOR
412	3504	Q99645	EPYC
413	3505	P04626	ERBB2
414	3506	P21860	ERBB3
415	3507	Q15303	ERBB4
416	3508	O14944	EREG

TABLE 1-continued

Representative list of DNA and protein sequences amplified for the initial and expanded libraries.

Seq. Id. No. (protein)	Seq. Id. No. (DNA)	Uniprot ID	Gene Symbol
417	3509	Q96PL5	ERMAP
418	3510	Q96AP7	ESAM
419	3511	Q5T1H1	EYS
420	3512	P00742	F10
421	3513	Q9Y624	F11R
422	3514	P00748	F12
423	3515	P00488	F13A1
424	3516	P13726	F3
425	3517	P08709	F7
426	3518	P00740	F9
427	3519	Q4G0M1	FAM132B
428	3520	Q5VUB5	FAM171A1
429	3521	A6NFU0	FAM187A
430	3522	Q17R55	FAM187B
431	3523	Q8IXL6	FAM20C
432	3524	Q9NYQ8	FAT2
433	3525	P23142	FBLN1
434	3526	P98095	FBLN2
435	3527	Q9UBX5	FBLN5
436	3528	Q53RD9	FBLN7
437	3529	P35556	FBN2
438	3530	Q75N90	FBN3
439	3531	Q8WWV6	FCAMR
440	3532	P24071	FCAR
441	3533	P12319	FCER1A
442	3534	P06734	FCER2
443	3535	P12314	FCGR1A
444	3536	Q92637	FCGR1B
445	3537	P12318	FCGR2A
446	3538	P31994	FCGR2B
447	3539	P31994	FCGR2C
448	3540	P31995	FCGR2C
449	3541	P08637	FCGR3A
450	3542	P08637	FCGR3A
451	3543	P55899	FCGRT
452	3544	O60667	FCMR
453	3545	Q96LA6	FCRL1
454	3546	Q96LA5	FCRL2
455	3547	Q96P31	FCRL3
456	3548	Q96PJ5	FCRL4
457	3549	Q96RD9	FCRL5
458	3550	Q6DN72	FCRL6
459	3551	Q6BAA4	FCRLB
460	3552	Q7L513	FCRLM1
461	3553	P05230	FGF1
462	3554	O15520	FGF10
463	3555	O43320	FGF16
464	3556	O60258	FGF17
465	3557	O76093	FGF18
466	3558	O95750	FGF19
467	3559	Q9NP95	FGF20
468	3560	Q9NSA1	FGF21
469	3561	Q9GZV9	FGF23
470	3562	P11487	FGF3
471	3563	P12034	FGF5
472	3564	P10767	FGF6
473	3565	P21781	FGF7
474	3566	P31371	FGF9
475	3567	Q14512	FGFBP1
476	3568	Q8TAT2	FGFBP3
477	3569	P11362	FGFR1
478	3570	P21802	FGFR2
479	3571	P22607	FGFR3
480	3572	P22455	FGFR4
481	3573	Q8N441	FGFRL1
482	3574	O43915	FIGF
483	3575	Q6NSJ5	FLJ23420
484	3576	Q9NZU1	FLRT1
485	3577	O43155	FLRT2
486	3578	Q9NZU0	FLRT3
487	3579	P17948	FLT1

TABLE 1-continued

Representative list of DNA and protein sequences amplified for the initial and expanded libraries.

Seq. Id. No. (protein)	Seq. Id. No. (DNA)	Uniprot ID	Gene Symbol
488	3580	P36888	FLT3
489	3581	Q06828	FMOD
490	3582	P02751	FN1
491	3583	Q9H6D8	FNDC4
492	3584	Q8NAU1	FNDC5
493	3585	Q5VTL7	FNDC7
494	3586	Q5H8C1	FREM1
495	3587	P23945	FSHR
496	3588	Q6MZW2	FSTL4
497	3589	Q8N475	FSTL5
498	3590	P05161	G1P2
499	3591	Q14393	GAS6
500	3592	P55107	GDF10
501	3593	O95390	GDF11
502	3594	Q99988	GDF15
503	3595	Q9UK05	GDF2
504	3596	Q9NR23	GDF3
505	3597	P43026	GDF5
506	3598	Q6KF10	GDF6
507	3599	O14793	GDF8
508	3600	O60383	GDF9
509	3601	P39905	GDNF
510	3602	P56159	GFRA1
511	3603	O00451	GFRA2
512	3604	O60609	GFRA3
513	3605	Q9GZZ7	GFRA4
514	3606	P10912	GHR
515	3607	Q9Y5U5	GITR
516	3608	Q99445	GML
517	3609	P22749	GNLY
518	3610	P07359	GP1BA
519	3611	P13224	GP1BB
520	3612	P55259	GP2
521	3613	P40197	GP5
522	3614	Q9HCN6	GP6
523	3615	P14770	GP9
524	3616	Q99795	GPA33
525	3617	P06744	GPI
526	3618	Q8IV16	GPIHBP1
527	3619	Q14956	GPNMB
528	3620	P08236	GUSB
529	3621	Q14520	HABP2
530	3622	P81172	HAMP
531	3623	P10915	HAPLN1
532	3624	Q9GZV7	HAPLN2
533	3625	Q96S86	HAPLN3
534	3626	Q86UW8	HAPLN4
535	3627	Q96D42	HAVCR1
536	3628	Q8TDQ0	HAVCR2
537	3629	Q99075	HBEGF
538	3630	Q14CZ8	HEPACAM
539	3631	A8MVW5	HEPACAM2
540	3632	Q30201	HFE
541	3633	P14210	HGF
542	3634	Q04756	HGFAC
543	3635	Q96QV1	HHIP
544	3636	Q9UM44	HHLA2
545	3637	P01893	HLA
546	3638	P01889	HLA
547	3639	P01891	HLA
548	3640	P01892	HLA
549	3641	P30685	HLA
550	3642	P04439	HLA-A
551	3643	P01889	HLA-B
552	3644	P10321	HLA-C
553	3645	P28067	HLA-DMA
554	3646	P28068	HLA-DMB
555	3647	P06340	HLA-DOA
556	3648	P13765	HLA-DOB
557	3649	P20036	HLA-DPA1
558	3650	P04440	HLA-DPB1

TABLE 1-continued

Representative list of DNA and protein sequences amplified for the initial and expanded libraries.

Seq. Id. No. (protein)	Seq. Id. No. (DNA)	Uniprot ID	Gene Symbol
559	3651	P01909	HLA-DQA1
560	3652	P01920	HLA-DQB1
561	3653	P01903	HLA-DRA
562	3654	P01911	HLA-DRB1
563	3655	P13747	HLA-E
564	3656	P30511	HLA-F
565	3657	P17693	HLA-G
566	3658	P09429	HMGB1
567	3659	P26583	HMGB2
568	3660	Q12794	HYAL1
569	3661	Q12891	HYAL2
570	3662	O43820	HYAL3
571	3663	P05362	ICAM1
572	3664	P13598	ICAM2
573	3665	P32942	ICAM3
574	3666	Q14773	ICAM4
575	3667	Q9UMF0	ICAM5
576	3668	Q9Y6W8	ICOS
577	3669	O75144	ICOSLG
578	3670	A6NMD0	IFITM10
579	3671	P01566	IFNA10
580	3672	P01562	IFNA13
581	3673	P01570	IFNA14
582	3674	P05015	IFNA16
583	3675	P01571	IFNA17
584	3676	P01571	IFNA17
585	3677	P01563	IFNA2
586	3678	P01568	IFNA21
587	3679	P01567	IFNA4
588	3680	P01569	IFNA5
589	3681	P05013	IFNA6
590	3682	P32881	IFNA8
591	3683	P17181	IFNAR1
592	3684	P48551	IFNAR2
593	3685	P01574	IFNB1
594	3686	Q86WN2	IFNE
595	3687	P01579	IFNG
596	3688	P15260	IFNGR1
597	3689	P38484	IFNGR2
598	3690	Q9P0W0	IFNK
599	3691	Q8IZJ0	IFNL2
600	3692	P05000	IFNW1
601	3693	Q8IVU1	IGDCC3
	3694	P08069	IGF1R
602	3695	P01344	IGF2
603	3696	P11717	IGF2R
604	3697	P35858	IGFALS
605	3698	Q16270	IGFBP7
606	3699	Q8WX77	IGFBPL1
607	3700	Q6UW32	IGFL1
608	3701	Q6UWQ7	IGFL2
609	3702	Q6UXB1	IGFL3
610	3703	A6NJ69	IGIP
611	3704	P15814	IGLL1
612	3705	B9A064	IGLL5
613	3706	A6NGN9	IGLON5
614	3707	Q8N6C5	IGSF1
615	3708	Q6WRI0	IGSF10
616	3709	Q5DX21	IGSF11
617	3710	Q96ID5	IGSF21
618	3711	O75054	IGSF3
619	3712	Q8N126	IGSF4B
620	3713	Q8NFZ8	IGSF4C
621	3714	Q9NSI5	IGSF5
622	3715	O95976	IGSF6
623	3716	Q969P0	IGSF8
624	3717	Q9P212	IGSF9
625	3718	P22301	IL10
626	3719	Q13651	IL10RA
627	3720	Q08334	IL10RB
628	3721	P20809	IL11

TABLE 1-continued

Representative list of DNA and protein sequences amplified for the initial and expanded libraries.

Seq. Id. No. (protein)	Seq. Id. No. (DNA)	Uniprot ID	Gene Symbol
629	3722	Q14626	IL11RA
630	3723	P29459	IL12A
631	3724	P29460	IL12B
632	3725	P42701	IL12RB1
633	3726	Q99665	IL12RB2
634	3727	P35225	IL13
635	3728	P78552	IL13RA1
636	3729	Q14627	IL13RA2
637	3730	P40933	IL15
638	3731	Q13261	IL15RA
639	3732	Q14005	IL16
640	3733	Q16552	IL17A
641	3734	Q9UHF5	IL17B
642	3735	Q9NRM6	IL17BR
643	3736	Q9P0M4	IL17C
644	3737	Q8TAD2	IL17D
645	3738	Q96PD4	IL17F
646	3739	Q96F46	IL17RA
647	3740	Q8NAC3	IL17RC
648	3741	Q8NFM7	IL17RD
649	3742	Q8NFR9	IL17RE
650	3743	Q14116	IL18
651	3744	O95998	IL18BP
652	3745	Q13478	IL18R1
653	3746	O95256	IL18RAP
654	3747	Q9UHD0	IL19
655	3748	P01583	IL1A
656	3749	P01584	IL1B
657	3750	Q8WWZ1	IL1F10
658	3751	Q9UBH0	IL1F5
659	3752	Q9UHA7	ILIF6
660	3753	Q9NZH6	IL1F7
661	3754	Q9NZH8	IL1F9
662	3755	P14778	ILIR1
663	3756	P27930	ILIR2
664	3757	Q9NPH3	IL1RAP
665	3758	Q9NZN1	IL1RAPL1
666	3759	Q9NP60	IL1RAPL2
667	3760	Q01638	IL1RL1
668	3761	Q9HB29	IL1RL2
669	3762	P18510	IL1RN
670	3763	P60568	IL2
671	3764	Q9NYY1	IL20
672	3765	Q9UHF4	IL20RA
673	3766	Q6UXL0	IL20RB
674	3767	Q9HBE4	IL21
675	3768	Q9HBE5	IL21R
676	3769	Q9GZX6	IL22
677	3770	Q8N6P7	IL22RA1
678	3771	Q969J5	IL22RA2
679	3772	Q9NPF7	IL23A
680	3773	Q5VWK5	IL23R
681	3774	Q13007	IL24
682	3775	Q9H293	IL25
683	3776	Q9NPH9	IL26
684	3777	Q8NEV9	IL27
685	3778	Q6UWB1	IL27RA
686	3779	Q8IZI9	IL28B
687	3780	Q8IU57	IL28RA
688	3781	Q8IU54	IL29
689	3782	P01589	IL2RA
690	3783	P14784	IL2RB
691	3784	P31785	IL2RG
692	3785	P08700	IL3
693	3786	Q6EBC2	IL31
694	3787	Q8NI17	IL31RA
695	3788	P24001	IL32
696	3789	O95760	IL33
697	3790	Q6ZMJ4	IL34
698	3791	Q9NZH7	IL36B
699	3792	P26951	IL3RA

TABLE 1-continued

Representative list of DNA and protein sequences amplified for the initial and expanded libraries.

Seq. Id. No. (protein)	Seq. Id. No. (DNA)	Uniprot ID	Gene Symbol
700	3793	P05112	IL4
701	3794	P24394	IL4R
702	3795	P05113	IL5
703	3796	Q01344	IL5RA
704	3797	P05231	IL6
705	3798	P08887	IL6R
706	3799	P40189	IL6ST
707	3800	P13232	IL7
708	3801	P16871	IL7R
709	3802	P10145	IL8
710	3803	P25025	IL8RB
711	3804	P15248	IL9
712	3805	Q01113	IL9R
713	3806	Q86SU0	ILDR1
714	3807	Q9BZV3	IMPG2
715	3808	K9M1U5	INFL4
716	3809	P01308	INS
717	3810	P51460	INSL3
718	3811	Q9Y5Q6	INSL5
719	3812	Q9Y581	INSL6
720	3813	P06213	INSR
721	3814	O14498	ISLR
722	3815	Q6UXK2	ISLR2
723	3816	P56199	ITGA1
724	3817	P17301	ITGA2
725	3818	P08514	ITGA2B
726	3819	P26006	ITGA3
727	3820	P13612	ITGA4
728	3821	P08648	ITGA5
729	3822	P23229	ITGA6
730	3823	Q13683	ITGA7
731	3824	P53708	ITGA8
732	3825	Q13797	ITGA9
733	3826	P38570	ITGAE
734	3827	P20701	ITGAL
735	3828	P11215	ITGAM
736	3829	P06756	ITGAV
737	3830	P20702	ITGAX
738	3831	P05556	ITGB1
739	3832	P05107	ITGB2
740	3833	P05106	ITGB3
741	3834	P18084	ITGB5
742	3835	P18564	ITGB6
743	3836	P26010	ITGB7
744	3837	P26012	ITGB8
745	3838	O95965	ITGBL1
746	3839	Q8IYV9	IZUMO
747	3840	P78504	JAG1
748	3841	Q9Y219	JAG2
749	3842	P57087	JAM2
750	3843	Q9BX67	JAM3
751	3844	P01591	JCHAIN
752	3845	P23352	KAL1
753	3846	Q96I82	KAZALD1
754	3847	Q6UW63	KDELC1
755	3848	Q7ZAH8	KDELC2
756	3849	P35968	KDR
757	3850	O60938	KERA
758	3851	Q5VV43	KIAA0319
759	3852	Q8IZA0	KIAA0319L
760	3853	P43626	KIR2DL2
761	3854	P43627	KIR2DL3
762	3855	P43628	KIR2DL3
763	3856	Q99706	KIR2DL4
764	3857	Q8NHK3	KIR2DL5B
765	3858	Q8N109	KIR2DL5B
766	3859	P43631	KIR2DS2
767	3860	Q14952	KIR2DS3
768	3861	Q14954	KIR2DS4
769	3862	P43632	KIR2DS4
770	3863	Q14953	KIR2DS5

TABLE 1-continued

Representative list of DNA and protein sequences amplified for the initial and expanded libraries.

Seq. Id. No. (protein)	Seq. Id. No. (DNA)	Uniprot ID	Gene Symbol
771	3864	P43629	KIR3DL1
772	3865	P43630	KIR3DL2
773	3866	Q8N743	KIR3DL3
774	3867	A8MWS1	KIR3DP1
775	3868	Q14943	KIR3DS1
776	3869	Q9H7L2	KIR3DX1
777	3870	Q96I84	KIRREL
778	3871	Q6UWL6	KIRREL2
779	3872	Q8IZU9	KIRREL3
780	3873	P10721	KIT
781	3874	P21583	KITLG
782	3875	Q12918	KLRB1
783	3876	P26715	KLRC1
784	3877	P26717	KLRC2
785	3878	Q07444	KLRC3
786	3879	Q13241	KLRD1
787	3880	Q9NZS2	KLRF1
788	3881	D3W0D1	KLRF2
789	3882	Q96E93	KLRG1
790	3883	P26718	KLRK1
791	3884	Q9BYJ0	KSP37
792	3885	P32004	LICAM
793	3886	P18627	LAG3
794	3887	Q6GTX8	LAIR1
795	3888	Q6ISS4	LAIR2
796	3889	P25391	LAMA1
797	3890	Q16787	LAMA3
798	3891	P07942	LAMB1
799	3892	Q13751	LAMB3
800	3893	A4D0S4	LAMB4
801	3894	P11047	LAMC1
802	3895	Q13753	LAMC2
803	3896	Q6UX15	LAYN
804	3897	P01130	LDLR
805	3898	P48357	LEPR
806	3899	O95970	LGI1
807	3900	Q8N0V4	LGI2
808	3901	Q8N145	LGI3
809	3902	Q8N135	LGI4
810	3903	Q9BXB1	LGR4
811	3904	O75473	LGR5
812	3905	Q9HBX8	LGR6
813	3906	Q8WXD0	LGR8
814	3907	P22888	LHCGR
815	3908	P15018	LIF
816	3909	P42702	LIFR
817	3910	O75019	LILRA1
818	3911	Q8N149	LILRA2
819	3912	Q8N6C8	LILRA3
820	3913	P59901	LILRA4
821	3914	A6NI73	LILRA5
822	3915	Q8NHL6	LILRB1
823	3916	Q8N423	LILRB2
824	3917	O75022	LILRB3
825	3918	Q8NHJ6	LILRB4
826	3919	O75023	LILRB5
827	3920	Q6PI73	LILRB6
828	3921	Q96FE5	LINGO1
829	3922	Q7L985	LINGO2
830	3923	P0C6S8	LINGO3
831	3924	Q6UY18	LINGO4
832	3925	Q8NCF0	LOC348174
833	3926	P28300	LOX
834	3927	Q08397	LOXL1
835	3928	Q96II8	LRCH3
836	3929	Q9P244	LRFN1
837	3930	Q9ULH4	LRFN2
838	3931	Q9BTN0	LRFN3
839	3932	Q6PJG9	LRFN4
840	3933	Q96NI6	LRFN5
841	3934	P02750	LRG1

TABLE 1-continued

Representative list of DNA and protein sequences amplified for the initial and expanded libraries.

Seq. Id. No. (protein)	Seq. Id. No. (DNA)	Uniprot ID	Gene Symbol
842	3935	Q96JA1	LRIG1
843	3936	O94898	LRIG2
844	3937	Q6UXM1	LRIG3
845	3938	A6NDA9	LRIT2
846	3939	Q3SXY7	LRIT3
847	3940	Q86VZ4	LRP11
848	3941	O75096	LRP4
849	3942	O75197	LRP5
850	3943	O75581	LRP6
851	3944	Q14114	LRP8
852	3945	Q8TF66	LRRC15
853	3946	Q8N6Y2	LRRC17
854	3947	Q9H756	LRRC19
855	3948	Q9P2V4	LRRC21
856	3949	Q50LG9	LRRC24
857	3950	Q8N386	LRRC25
858	3951	Q2I0M4	LRRC26
859	3952	Q9BY71	LRRC3
860	3953	Q14392	LRRC32
861	3954	A6NMS7	LRRC37A
862	3955	O60309	LRRC37A3
863	3956	Q96QE4	LRRC37B
864	3957	Q5VT99	LRRC38
865	3958	Q96PB8	LRRC3B
866	3959	A6NJW4	LRRC3C
867	3960	Q9HBW1	LRRC4
868	3961	Q9NT99	LRRC4B
869	3962	Q9HCJ2	LRRC4C
870	3963	Q8N7C0	LRRC52
871	3964	Q6ZSA7	LRRC55
872	3965	Q7Z2Q7	LRRC70
873	3966	Q8IWT6	LRRC8A
874	3967	Q6P9F7	LRRC8B
875	3968	Q8TDW0	LRRC8C
876	3969	Q7L1W4	LRRC8D
877	3970	Q6UXK5	LRRN1
878	3971	Q9H3W5	LRRN3
879	3972	Q8WUT4	LRRN4
880	3973	Q8ND94	LRRN4CL
881	3974	O75325	LRRN5
882	3975	Q86UE6	LRRTM1
883	3976	O43300	LRRTM2
884	3977	Q86VH5	LRRTM3
885	3978	Q86VH4	LRRTM4
886	3979	Q9HBL6	LRTM1
887	3980	Q8N967	LRTM2
888	3981	Q13449	LSAMP
889	3982	Q86X29	LSR
890	3983	P01374	LTA
891	3984	Q06643	LTB
892	3985	Q14766	LTBP1
893	3986	P36941	LTBR
894	3987	P02788	LTF
895	3988	P29376	LTK
896	3989	P51884	LUM
897	3990	Q14210	LY6D
898	3991	Q16553	LY6E
899	3992	Q8NDX9	LY6G5B
900	3993	Q5SRR4	LY6G5C
901	3994	O95867	LY6G6C
902	3995	O95868	LY6G6D
903	3996	Q5SQ64	LY6G6F
904	3997	O94772	LY6H
905	3998	Q17RY6	LY6K
906	3999	H3BQJ8	Ly6L
907	4000	O60449	LY75
908	4001	Q9HBG7	LY9
909	4002	Q9BZG9	LYNX1
910	4003	Q8N2G4	LYPD1
911	4004	Q6UXB3	LYPD2
912	4005	O95274	LYPD3

TABLE 1-continued

Representative list of DNA and protein sequences amplified for the initial and expanded libraries.

Seq. Id. No. (protein)	Seq. Id. No. (DNA)	Uniprot ID	Gene Symbol
913	4006	Q6UWN0	LYPD4
914	4007	Q6UWN5	LYPD5
915	4008	Q86Y78	LYPD6
916	4009	Q8NI32	LYPD6B
917	4010	Q6UX82	LYPD8
918	4011	Q13477	MADCAM1
919	4012	P20916	MAG
920	4013	O00462	MANBA
921	4014	P48740	MASP1
922	4015	P21941	MATN1
923	4016	O00339	MATN2
924	4017	O15232	MATN3
925	4018	O95460	MATN4
926	4019	P11226	MBL2
927	4020	P43121	MCAM
928	4021	P15529	MCP
929	4022	Q8NFP4	MDGA1
930	4023	Q7Z553	MDGA2
931	4024	Q96KG7	MEGF10
932	4025	A6BM72	MEGF11
933	4026	Q9H1U4	MEGF9
934	4027	Q16819	MEP1A
935	4028	Q16820	MEP1B
936	4029	Q12866	MERTK
937	4030	P08581	MET
938	4031	P55082	MFAP3
939	4032	O75121	MFAP3L
940	4033	Q08431	MFGE8
941	4034	P08582	MFI2
942	4035	Q29983	MICA
943	4036	Q29980	MICB
944	4037	P14174	MIF
945	4038	Q7Z6M3	MILR1
946	4039	P51511	MMP15
947	4040	P51512	MMP16
948	4041	Q9ULZ9	MMP17
949	4042	P08253	MMP2
950	4043	Q9Y5R2	MMP24
951	4044	Q9H239	MMP28
952	4045	P14780	MMP9
953	4046	Q13201	MMRN1
954	4047	Q16653	MOG
955	4048	P40238	MPL
956	4049	P25189	MPZ
957	4050	O95297	MPZL1
958	4051	O60487	MPZL2
959	4052	Q6UWV2	MPZL3
960	4053	Q95460	MR1
961	4054	P22897	MRC1
962	4055	Q9UBG0	MRC2
963	4056	P21757	MSR1
964	4057	P26927	MST1
965	4058	P15941	MUC1
966	4059	Q9H3R2	MUC13
967	4060	Q685J3	MUC17
968	4061	Q8N307	MUC20
969	4062	Q5SSG8	MUC21
970	4063	P98088	MUC5AC
971	4064	O15146	MUSK
972	4065	Q9BRK3	MXRA8
973	4066	Q9UK23	NAGPA
974	4067	P13591	NCAM1
975	4068	O15394	NCAM2
976	4069	O14594	NCAN
977	4070	O76036	NCR1
978	4071	O95944	NCR2
979	4072	O14931	NCR3
980	4073	Q8TB73	NDNF
981	4074	Q7Z3B1	NEGR1
982	4075	Q92832	NELL1
983	4076	Q99435	NELL2

TABLE 1-continued

Representative list of DNA and protein sequences amplified for the initial and expanded libraries.

Seq. Id. No. (protein)	Seq. Id. No. (DNA)	Uniprot ID	Gene Symbol
984	4077	Q92859	NEO1
985	4078	Q8NET5	NFAM1
986	4079	O94856	NFASC
987	4080	P01138	NGFB
988	4081	P08138	NGFR
989	4082	P14543	NID1
990	4083	Q14112	NID2
991	4084	Q8NFZ3	NLGN4Y
992	4085	Q8NFZ3	NLGN4Y
993	4086	Q96P20	NLRP3
994	4087	Q8TDY8	NOPE
995	4088	Q04721	NOTCH2
996	4089	Q7Z3S9	NOTCH2NL
997	4090	Q99466	NOTCH4
998	4091	O60500	NPHS1
999	4092	Q6UXI9	NPNT
1000	4093	Q9Y639	NPTN
1001	4094	Q92823	NRCAM
1002	4095	Q02297	NRG1
1003	4096	Q02297	NRGI
1004	4097	O14511	NRG2
1005	4098	P56975	NRG3
1006	4099	Q8WWG1	NRG4
1007	4100	O14786	NRP1
1008	4101	O60462	NRP2
1009	4102	Q86YC3	NRROS
1010	4103	P58400	NRXN1
1011	4104	Q9HDB5	NRXN3
1012	4105	P21589	NT5E
1013	4106	P20783	NTF3
1014	4107	P34130	NTF5
1015	4108	Q9P121	NTM
1016	4109	O95631	NTN1
1017	4110	O00634	NTN3
1018	4111	Q9HB63	NTN4
1019	4112	Q8WTR8	NTN5
1020	4113	Q9Y212	NTNG1
1021	4114	Q96CW9	NTNG2
1022	4115	P04629	NTRK1
1023	4116	Q16620	NTRK2
1024	4117	Q16288	NTRK3
1025	4118	Q8N323	NXPE1
1026	4119	Q969Y0	NXPE3
1027	4120	Q6UWF7	NXPE4
1028	4121	Q9GZU5	NYX
1029	4122	P20774	OGN
1030	4123	Q8WWZ8	OIT3
1031	4124	P78380	OLR1
1032	4125	Q99983	OMD
1033	4126	P23515	OMG
1034	4127	Q14982	OPCML
1035	4128	Q9UBM4	OPTC
1036	4129	Q8IYS5	OSCAR
1037	4130	Q99650	OSMR
1038	4131	Q6UXH9	PAMR1
1039	4132	Q06141	PAP
1040	4133	O95428	PAPLN
1041	4134	Q13219	PAPPA
1042	4135	Q8WXA2	PATE1
1043	4136	Q6UY27	PATE2
1044	4137	B3GLJ2	PATE3
1045	4138	P0C8F1	PATE4
1046	4139	Q9P2E7	PCDH10
1047	4140	Q9NPG4	PCDH12
1048	4141	Q8N6Y1	PCDH20
1049	4142	Q9HC56	PCDH9
1050	4143	Q9Y5H5	PCDHA9
1051	4144	Q9Y5F3	PCDHB1
1052	4145	Q9Y5F2	PCDHB11
1053	4146	Q9UN66	PCDHB13
1054	4147	Q9Y5E8	PCDHB15

TABLE 1-continued

Representative list of DNA and protein sequences amplified for the initial and expanded libraries.

Seq. Id. No. (protein)	Seq. Id. No. (DNA)	Uniprot ID	Gene Symbol
1055	4148	Q9NRJ7	PCDHB16
1056	4149	Q9Y5E6	PCDHB3
1057	4150	Q9Y5E4	PCDHB5
1058	4151	Q9Y5E3	PCDHB6
1059	4152	Q9Y5E2	PCDHB7
1060	4153	Q9Y5E1	PCDHB9
1061	4154	Q9Y5G9	PCDHGA4
1062	4155	Q9Y5G1	PCDHGB3
1063	4156	Q9Y5F9	PCDHGB6
1064	4157	Q9UN70	PCDHGC3
1065	4158	Q9UHG2	PCSK1N
1066	4159	Q8NBP7	PCSK9
1067	4160	Q15116	PDCD1
1068	4161	Q9BQ51	PDCD1LG2
1069	4162	P04085	PDGFA
1070	4163	P01127	PDGFB
1071	4164	Q9NRA1	PDGFC
1072	4165	Q9GZP0	PDGFD
1073	4166	P16234	PDGFRA
1074	4167	P09619	PDGFRB
1075	4168	Q15198	PDGFRL
1076	4169	P16284	PECAM1
1077	4170	P02776	PF4
1078	4171	P49763	PGF
1079	4172	O75594	PGLYRP1
1080	4173	P01833	PIGR
1081	4174	Q96FE7	PIK3IP1
1082	4175	Q9UKJ1	PILRA
1083	4176	Q9UKJ0	PILRB
1084	4177	A6NC86	PINLYP
1085	4178	P12273	PIP
1086	4179	Q504Y2	PKDCC
1087	4180	P00750	PLAT
1088	4181	P00749	PLAU
1089	4182	Q03405	PLAUR
1090	4183	Q9HCM2	PLXNA4
1091	4184	Q7Z5L7	PODN
1092	4185	Q6PEZ8	PODNL1
1093	4186	P02775	PPBP
1094	4187	Q99944	PPT2
1095	4188	P51888	PRELP
1096	4189	P14222	PRF1
1097	4190	P13727	PRG2
1098	4191	Q9Y2Y8	PRG3
1099	4192	P16471	PRLR
1100	4193	P04070	PROC
1101	4194	Q9UNN8	PROCR
1102	4195	P07225	PROS1
1103	4196	P22891	PROZ
1104	4197	Q2VWP7	PRTG
1105	4198	Q8N6Q3	PRV1
1106	4199	O43653	PSCA
1107	4200	Q9UQ74	PSG1
1108	4201	P11464	PSG1
1109	4202	Q9UQ72	PSG2
1110	4203	P11465	PSG2
1111	4204	Q16557	PSG4
1112	4205	Q00888	PSG4
1113	4206	Q15238	PSG5
1114	4207	Q00889	PSG6
1115	4208	Q13046	PSG8
1116	4209	Q00887	PSG9
1117	4210	O60542	PSPN
1118	4211	P23219	PTGS1
1119	4212	P35354	PTGS2
1120	4213	Q13308	PTK7
1121	4214	Q9H106	PTPNS1L2
1122	4215	P23467	PTPRB
1123	4216	P08575	PTPRC
1124	4217	P23468	PTPRD
1125	4218	P10586	PTPRF

TABLE 1-continued

Representative list of DNA and protein sequences amplified for the initial and expanded libraries.

Seq. Id. No. (protein)	Seq. Id. No. (DNA)	Uniprot ID	Gene Symbol
1126	4219	P23470	PTPRG
1127	4220	Q9HD43	PTPRH
1128	4221	Q12913	PTPRJ
1129	4222	Q15262	PTPRK
1130	4223	Q16849	PTPRN
1131	4224	Q16827	PTPRO
1132	4225	Q15256	PTPRR
1133	4226	Q13332	PTPRS
1134	4227	P26022	PTX3
1135	4228	P15151	PVR
1136	4229	Q15223	PVRL1
1137	4230	Q92692	PVRL2
1138	4231	Q9NQS3	PVRL3
1139	4232	Q96NY8	PVRL4
1140	4233	P20742	PZP
1141	4234	P05451	REG1A
1142	4235	P48304	REG1B
1143	4236	Q6UW15	REG3G
1144	4237	Q9BYZ8	REG4
1145	4238	Q9HCK4	ROBO2
1146	4239	Q8WZ75	ROBO4
1147	4240	Q01973	ROR1
1148	4241	Q01974	ROR2
1149	4242	P08922	ROS1
1150	4243	Q9BZR6	RTN4R
1151	4244	Q86UN2	RTN4RL1
1152	4245	Q86UN3	RTN4RL2
1153	4246	Q9HBX9	RXFP1
1154	4247	Q6AZY7	SCARA3
1155	4248	Q14162	SCARF1
1156	4249	Q96GP6	SCARF2
1157	4250	Q07699	SCN1B
1158	4251	O60939	SCN2B
1159	4252	Q9NY72	SCN3B
1160	4253	Q8IWT1	SCN4B
1161	4254	Q8IWY4	SCUBE1
1162	4255	Q9NQ36	SCUBE2
1163	4256	Q8IX30	SCUBE3
1164	4257	P18827	SDC1
1165	4258	P34741	SDC2
1166	4259	P31431	SDC4
1167	4260	Q58EX2	SDK2
1168	4261	Q8WVN6	SECTM1
1169	4262	P16581	SELE
1170	4263	P14151	SELL
1171	4264	P16109	SELP
1172	4265	Q14563	SEMA3A
1173	4266	Q13214	SEMA3B
1174	4267	Q99985	SEMA3C
1175	4268	O95025	SEMA3D
1176	4269	O15041	SEMA3E
1177	4270	Q13275	SEMA3F
1178	4271	Q9NS98	SEMA3G
1179	4272	Q9H3S1	SEMA4A
1180	4273	Q9NPR2	SEMA4B
1181	4274	Q9C0C4	SEMA4C
1182	4275	Q92854	SEMA4D
1183	4276	O95754	SEMA4F
1184	4277	Q9NTN9	SEMA4G
1185	4278	Q9P283	SEMA5B
1186	4279	Q9H2E6	SEMA6A
1187	4280	Q9H3T3	SEMA6B
1188	4281	Q9H3T2	SEMA6C
1189	4282	O75326	SEMA7A
1190	4283	Q8IWL2	SFTPA1
1191	4284	Q8IWL1	SFTPA2
1192	4285	P35247	SFTPD
1193	4286	Q6IA17	SIGIRR
1194	4287	Q96LC7	SIGLEC10
1195	4288	Q96RL6	SIGLEC11
1196	4289	Q96PQ1	SIGLEC12

TABLE 1-continued

Representative list of DNA and protein sequences amplified for the initial and expanded libraries.

Seq. Id. No. (protein)	Seq. Id. No. (DNA)	Uniprot ID	Gene Symbol
1197	4290	Q08ET2	SIGLEC14
1198	4291	Q6ZMC9	SIGLEC15
1199	4292	A6NMB1	SIGLEC16
1200	4293	O15389	SIGLEC5
1201	4294	O43699	SIGLEC6
1202	4295	Q9Y286	SIGLEC7
1203	4296	Q9NYZ4	SIGLEC8
1204	4297	Q9Y336	SIGLEC9
1205	4298	P78324	SIRPA
1206	4299	O00241	SIRPB1
1207	4300	Q5JXA9	SIRPB2
1208	4301	Q9P1W8	SIRPG
1209	4302	Q13291	SLAMF1
1210	4303	Q96DU3	SLAMF6
1211	4304	Q9NQ25	SLAMF7
1212	4305	Q9P0V8	SLAMF8
1213	4306	Q96A28	SLAMF9
1214	4307	O94813	SLIT2
1215	4308	O75094	SLIT3
1216	4309	Q96PX8	SLITRK1
1217	4310	Q9H156	SLITRK2
1218	4311	O94933	SLITRK3
1219	4312	Q8IW52	SLITRK4
1220	4313	O94991	SLITRK5
1221	4314	Q9H5Y7	SLITRK6
1222	4315	P55000	SLURP1
1223	4316	Q8TER0	SNED1
1224	4317	Q8TDM5	SPACA4
1225	4318	W5XKT8	SPACA6P
1226	4319	O43278	SPINT1
1227	4320	P78539	SRPX
1228	4321	O60687	SRPX2
1229	4322	Q8WTU2	SSC4D
1230	4323	Q13586	STIM1
1231	4324	Q9P246	STIM2
1232	4325	Q6UWL2	SUSD1
1233	4326	Q9UGT4	SUSD2
1234	4327	Q5VX71	SUSD4
1235	4328	Q86UU9	TAC4
1236	4329	B6A8C7	TARM1
1237	4330	P13385	TDGF1
1238	4331	Q02763	TEK
1239	4332	Q9UKZ4	TENM1
1240	4333	Q9BY14	TEX101
1241	4334	P02787	TF
1242	4335	Q9UP52	TFR2
1243	4336	P02786	TFRC
1244	4337	P01135	TGFA
1245	4338	P01137	TGFB1
1246	4339	P61812	TGFB2
1247	4340	P10600	TGFB3
1248	4341	Q15582	TGFBI
1249	4342	P36897	TGFBR1
1250	4343	P37173	TGFBR2
1251	4344	Q03167	TGFBR3
1252	4345	P07204	THBD
1253	4346	P07996	THBS1
1254	4347	P35442	THBS2
1255	4348	P49746	THBS3
1256	4349	P35443	THBS4
1257	4350	P04216	THY1
1258	4351	P35590	TIE1
1259	4352	Q495A1	TIGIT
1260	4353	Q96H15	TIMD4
1261	4354	O43897	TLL1
1262	4355	Q9Y6L7	TLL2
1263	4356	Q15399	TLR1
1264	4357	Q9BXR5	TLR10
1265	4358	O60603	TLR2
1266	4359	O15455	TLR3
1267	4360	O00206	TLR4

TABLE 1-continued

Representative list of DNA and protein sequences amplified for the initial and expanded libraries.

Seq. Id. No. (protein)	Seq. Id. No. (DNA)	Uniprot ID	Gene Symbol
1268	4361	O60602	TLR5
1269	4362	Q9Y2C9	TLR6
1270	4363	Q9NYK1	TLR7
1271	4364	Q9NR97	TLR8
1272	4365	Q9NR96	TLR9
1273	4366	O43657	TM4SF6
1274	4367	Q8IYR6	TMEFF1
1275	4368	Q9UIK5	TMEFF2
1276	4369	Q8N3G9	TMEM130
1277	4370	Q9H665	TMEM149
1278	4371	Q86YD3	TMEM25
1279	4372	Q9HCN3	TMEM8
1280	4373	Q6P7N7	TMEM81
1281	4374	A6NDV4	TMEM8B
1282	4375	Q6UXZ0	TMIGD1
1283	4376	Q96BF3	TMIGD2
1284	4377	P05452	TNA
1285	4378	P01375	TNF
1286	4379	O00220	TNFRSF10A
1287	4380	O14763	TNFRSF10B
1288	4381	O14798	TNFRSF10C
1289	4382	Q9UBN6	TNFRSF10D
1290	4383	Q9Y6Q6	TNFRSF11A
1291	4384	O00300	TNFRSF11B
1292	4385	Q9NP84	TNFRSF12A
1293	4386	O14836	TNFRSF13B
1294	4387	Q96RJ3	TNFRSF13C
1295	4388	Q92956	TNFRSF14
1296	4389	Q02223	TNFRSF17
1297	4390	Q9NS68	TNFRSF19
1298	4391	Q969Z4	TNFRSF19L
1299	4392	P19438	TNFRSF1A
1300	4393	P20333	TNFRSF1B
1301	4394	O75509	TNFRSF21
1302	4395	Q93038	TNFRSF25
1303	4396	P43489	TNFRSF4
1304	4397	P25942	TNFRSF5
1305	4398	P25445	TNFRSF6
1306	4399	O95407	TNFRSF6B
1307	4400	P26842	TNFRSF7
1308	4401	P28908	TNFRSF8
1309	4402	Q07011	TNFRSF9
1310	4403	P50591	TNFSF10
1311	4404	O14788	TNFSF11
1312	4405	O43508	TNFSF12
1313	4406	O75888	TNFSF13
1314	4407	Q9Y275	TNFSF13B
1315	4408	O43557	TNFSF14
1316	4409	O95150	TNFSF15
1317	4410	Q9UNG2	TNFSF18
1318	4411	P23510	TNFSF4
1319	4412	P48023	TNFSF6
1320	4413	P32971	TNFSF8
1321	4414	P41273	TNFSF9
1322	4415	Q9UQP3	TNN
1323	4416	Q92752	TNR
1324	4417	P22105	TNXB
1325	4418	Q13641	TPBG
1326	4419	P0DKB5	TPBGL
1327	4420	P07202	TPO
1328	4421	Q86V40	TRABD2A
1329	4422	Q9NP99	TREM1
1330	4423	Q9NZC2	TREM2
1331	4424	Q86YW5	TREML1
1332	4425	Q5T2D2	TREML2
1333	4426	Q6UXN2	TREML4
1334	4427	Q7L0X0	TRIL
1335	4428	P16473	TSHR
1336	4429	Q8WUA8	TSKU
1337	4430	Q969D9	TSLP
1338	4431	O60635	TSPAN1

TABLE 1-continued

Representative list of DNA and protein sequences amplified for the initial and expanded libraries.

Seq. Id. No. (protein)	Seq. Id. No. (DNA)	Uniprot ID	Gene Symbol
1339	4432	O95859	TSPAN12
1340	4433	O95857	TSPAN13
1341	4434	O95858	TSPAN15
1342	4435	Q96FV3	TSPAN17
1343	4436	Q96SJ8	TSPAN18
1344	4437	O60636	TSPAN2
1345	4438	O60637	TSPAN3
1346	4439	Q12999	TSPAN31
1347	4440	Q86UF1	TSPAN33
1348	4441	O14817	TSPAN4
1349	4442	P62079	TSPAN5
1350	4443	P41732	TSPAN7
1351	4444	P19075	TSPAN8
1352	4445	O75954	TSPAN9
1353	4446	Q06418	TYRO3
1354	4447	O43914	TYROBP
1355	4448	P07911	UMOD
1356	4449	Q6ZN44	UNC5A
1357	4450	Q8IZJ1	UNC5B
1358	4451	O95185	UNC5C
1359	4452	Q6UXZ4	UNC5D
1360	4453	O00322	UPK1A
1361	4454	O75841	UPK1B
1362	4455	Q6EMK4	VASN
1363	4456	P19320	VCAM1
1364	4457	P15692	VEGFA
1365	4458	P49765	VEGFB
1366	4459	P49767	VEGFC
1367	4460	P98155	VLDLR
1368	4461	Q86XK7	VSIG1
1369	4462	Q8N0Z9	VSIG10
1370	4463	Q96IQ7	VSIG2
1371	4464	Q9Y279	VSIG4
1372	4465	Q5VU13	VSIG8
1373	4466	Q6UX27	VSTM1
1374	4467	Q8TAG5	VSTM2A
1375	4468	A6NLU5	VSTM2B
1376	4469	Q96N03	VSTM2L
1377	4470	Q8IW00	VSTM4
1378	4471	A8MXK1	VSTM5
1379	4472	Q7Z7D3	VTCN1
1380	4473	Q6PCB0	VWA1
1381	4474	Q5GFL6	VWA2
1382	4475	Q96DN2	VWCE
1383	4476	Q96NZ8	WFIKKN1
1384	4477	Q8TEU8	WFIKKN2
1385	4478	Q9Y5W5	WIF1
1386	4479	P47992	XCL1
1387	4480	Q9UBD3	XCL2
1388	4481	Q9BS86	ZPBP
1389	4482	Q6X784	ZPBP2
1390	4483	Q96GS6	ABHD17A
1391	4484	Q5VST6	ABHD17B
1392	4485	Q0P651	ABHD18
1393	4486	Q9C0K3	ACTR3C
1394	4487	O15204	ADAMDEC1
1395	4488	Q6ZMM2	ADAMTSL5
1396	4489	Q9UKB5	AJAP1
1397	4490	Q6UX46	ALKAL2
1398	4491	P03971	AMH
1399	4492	Q9BXJ7	AMN
1400	4493	P04746	AMY2A
1401	4494	P19961	AMY2B
1402	4495	O95841	ANGPTL1
1403	4496	Q86XS5	ANGPTL5
1404	4497	Q8NI99	ANGPTL6
1405	4498	Q6UXH0	ANGPTL8
1406	4499	A6NMY6	ANXA2P2
1407	4500	P28039	AOAH
1408	4501	Q8NCL9	APCDD1L
1409	4502	P06727	APOA4

TABLE 1-continued

Representative list of DNA and protein sequences amplified for the initial and expanded libraries.

Seq. Id. No. (protein)	Seq. Id. No. (DNA)	Uniprot ID	Gene Symbol
1410	4503	P15848	ARSB
1411	4504	Q5T4W7	ARTN
1412	4505	Q16515	ASIC2
1413	4506	Q86Y30	BAGE2
1414	4507	Q86Y29	BAGE3
1415	4508	P23560	BDNF
1416	4509	P22004	BMP6
1417	4510	Q9BQP9	BPIFA3
1418	4511	Q86YQ2	BPIFA4P
1419	4512	Q8NFQ6	BPIFC
1420	4513	A6NE02	BTBD17
1421	4514	Q8N8P7	C11orf44
1422	4515	C9JXX5	C11orf94
1423	4516	Q9H972	C14orf93
1424	4517	A6NNL5	C15orf61
1425	4518	Q96HA4	C1orf159
1426	4519	P02745	C1QA
1427	4520	P02746	C1QB
1428	4521	P02747	C1QC
1429	4522	Q5VWW1	C1QL3
1430	4523	Q5T7M4	C1QTNF12
1431	4524	Q9NYP8	C21orf62
1432	4525	C9J442	C22orf46
1433	4526	Q8N8R5	C2orf69
1434	4527	Q7Z4R8	C6orf120
1435	4528	Q5VTT2	C9orf135
1436	4529	Q6ZRZ4	C9orf47
1437	4530	P23280	CA6
1438	4531	Q9NYX4	CALY
1439	4532	Q8IUK8	CBLN2
1440	4533	Q6UW01	CBLN3
1441	4534	P0C854	CECR9
1442	4535	Q8N7Q2	CELF2-AS1
1443	4536	Q9UKY3	CES1P1
1444	4537	Q5XG92	CES4A
1445	4538	Q6NT32	CES5A
1446	4539	P01215	CGA
1447	4540	A6NKQ9	CGB1
1448	4541	Q6NT52	CGB2
1449	4542	P0DN86	CGB3
1450	4543	P0DN87	CGB7
1451	4544	Q9BZP6	CHIA
1452	4545	P02708	CHRNA1
1453	4546	Q15822	CHRNA2
1454	4547	Q04844	CHRNE
1455	4548	P07510	CHRNG
1456	4549	Q9Y6N3	CLCA3P
1457	4550	Q6UVW9	CLEC2A
1458	4551	Q6UWE3	CLPSL2
1459	4552	Q9HBJ8	CLTRN
1460	4553	Q15846	CLUL1
1461	4554	O43405	COCH
1462	4555	Q96A83	COL26A1
1463	4556	Q2VPA4	CR1L
1464	4557	P54107	CRISP1
1465	4558	O76096	CST7
1466	4559	Q5W188	CST9LP1
1467	4560	Q5H943	CT83
1468	4561	Q16619	CTF1
1469	4562	Q9UBX1	CTSF
1470	4563	P25774	CTSS
1471	4564	P56202	CTSW
1472	4565	O60888	CUTA
1473	4566	A0A087X1C5	CYP2D7
1474	4567	P81605	DCD
1475	4568	Q9BYW3	DEFB126
1476	4569	Q7Z7B8	DEFB128
1477	4570	Q6IED9	DGAT2L7P
1478	4571	Q6UWP2	DHRS11
1479	4572	Q6UX07	DHRS13
1480	4573	Q6PKH6	DHRS4L2

TABLE 1-continued

Representative list of DNA and protein sequences amplified for the initial and expanded libraries.

Seq. Id. No. (protein)	Seq. Id. No. (DNA)	Uniprot ID	Gene Symbol
1481	4574	Q9BPW9	DHRS9
1482	4575	Q9H7Y0	DIPK2B
1483	4576	Q9H4A9	DPEP2
1484	4577	Q8NBI3	DRAXIN
1485	4578	Q8N1N2	DYNAP
1486	4579	P52798	EFNA4
1487	4580	O94919	ENDOD1
1488	4581	P21128	ENDOU
1489	4582	Q5NDL2	EOGT
1490	4583	P60507	ERVFC1
1491	4584	M5A8F1	ERVH48-1
1492	4585	O42043	ERVK-18
1493	4586	P61566	ERVK-24
1494	4587	P61567	ERVK-7
1495	4588	Q9NX77	ERVK13-1
1496	4589	B6SEH8	ERVV-1
1497	4590	B6SEH9	ERVV-2
1498	4591	P22794	EVI2A
1499	4592	Q8N2X6	EXOC3-AS1
1500	4593	A1KXE4	FAM168B
1501	4594	Q7Z5A7	FAM19A5
1502	4595	A6NFZ4	FAM24A
1503	4596	P98173	FAM3A
1504	4597	Q15485	FCN2
1505	4598	Q9UGM5	FETUB
1506	4599	Q9HCT0	FGF22
1507	4600	P08620	FGF4
1508	4601	P55075	FGF8
1509	4602	A5D6W6	FITM1
1510	4603	Q86VR8	FJX1
1511	4604	Q71RG6	FP248
1512	4605	O95633	FSTL3
1513	4606	Q14332	FZD2
1514	4607	P14867	GABRA1
1515	4608	P47869	GABRA2
1516	4609	P78334	GABRE
1517	4610	Q99928	GABRG3
1518	4611	A8MPY1	GABRR3
1519	4612	P54826	GAS1
1520	4613	Q9UFP1	GASKIA
1521	4614	P27539	GDF1
1522	4615	Q7Z4P5	GDF7
1523	4616	Q8N9F7	GDPD1
1524	4617	Q7L5L3	GDPD3
1525	4618	Q3B7J2	GFOD2
1526	4619	Q6UXV0	GFRAL
1527	4620	A6NGU5	GGT3P
1528	4621	Q8N2G8	GHDC
1529	4622	P0CG01	GKN3P
1530	4623	Q6ZMI3	GLDN
1531	4624	Q5JXX5	GLRA4
1532	4625	Q96MS3	GLT1D1
1533	4626	Q86YW7	GPHB5
1534	4627	Q9NPR9	GPR108
1535	4628	Q6UXU4	GSG1L
1536	4629	A8MUP6	GSG1L2
1537	4630	Q8N7I0	GVQW1
1538	4631	Q9BXW7	HDHD5
1539	4632	C9JL84	HHLA1
1540	4633	A8MTL9	HMSD
1541	4634	P22626	HNRNPA2B1
1542	4635	P00738	HP
1543	4636	P00739	HPR
1544	4637	P02790	HPX
1545	4638	Q7Z5J1	HSD11B1L
1546	4639	Q70Z44	HTR3D
1547	4640	Q92743	HTRA1
1548	4641	P22304	IDS
1549	4642	P05019	IGF1
1550	4643	Q6B9Z1	IGFL4
1551	4644	Q14623	IHH

TABLE 1-continued

Representative list of DNA and protein sequences amplified for the initial and expanded libraries.

Seq. Id. No. (protein)	Seq. Id. No. (DNA)	Uniprot ID	Gene Symbol
1552	4645	P09529	INHBB
1553	4646	B1AKI9	ISM1
1554	4647	Q8IWB1	ITPRIP
1555	4648	Q6GPH6	ITPRIPL1
1556	4649	Q6PHW0	IYD
1557	4650	A6ND01	IZUMO1R
1558	4651	Q6UXV1	IZUMO2
1559	4652	Q5VZ72	IZUMO3
1560	4653	P17658	KCNA6
1561	4654	Q8WWG9	KCNE4
1562	4655	Q16558	KCNMB1
1563	4656	Q9UBX7	KLK11
1564	4657	Q9UKR0	KLK12
1565	4658	O60259	KLK8
1566	4659	Q8NCW0	KREMEN2
1567	4660	Q8IYD9	LAS2
1568	4661	P04180	LCAT
1569	4662	P31025	LCN1
1570	4663	Q6JVE6	LCN10
1571	4664	Q6JVE5	LCN12
1572	4665	Q5VSP4	LCN1P1
1573	4666	Q5SZI1	LDLRAD2
1574	4667	Q86YD5	LDLRAD3
1575	4668	Q6P5S2	LEG1
1576	4669	P01229	LHB
1577	4670	Q7Z4B0	LINC00305
1578	4671	Q9UJ94	LINC00527
1579	4672	Q5VYY2	LIPM
1580	4673	Q5VXI9	LIPN
1581	4674	Q96L11	LLCFC1
1582	4675	Q16609	LPAL2
1583	4676	A6NCL2	LRCOL1
1584	4677	Q5XG99	LYSMD4
1585	4678	A6NHS7	MANSC4
1586	4679	Q9BUN1	MENT
1587	4680	Q9UJH8	METRN
1588	4681	Q641Q3	METRNL
1589	4682	Q5JXM2	METTL24
1590	4683	Q6UX53	METTL7B
1591	4684	Q9BY79	MFRP
1592	4685	P08493	MGP
1593	4686	P24347	MMP11
1594	4687	Q8N119	MMP21
1595	4688	Q9NPA2	MMP25
1596	4689	A6NHM9	MOXD2P
1597	4690	Q1L6U9	MSMP
1598	4691	Q3MIW9	MUCL3
1599	4692	Q02083	NAAA
1600	4693	P41271	NBL1
1601	4694	Q8TDF5	NETO1
1602	4695	Q9NPE2	NGRN
1603	4696	Q0D2K0	NIPAL4
1604	4697	Q6P988	NOTUM
1605	4698	Q9HBY0	NOX3
1606	4699	A6NHN6	NPIPB15
1607	4700	O75200	NPIPB7
1608	4701	P16860	NPPB
1609	4702	P17342	NPR3
1610	4703	Q9NPD7	NRN1
1611	4704	Q99748	NRTN
1612	4705	Q02818	NUCB1
1613	4706	P80303	NUCB2
1614	4707	P00973	OAS1
1615	4708	Q9NY56	OBP2A
1616	4709	Q02509	OC90
1617	4710	A1E959	ODAM
1618	4711	Q17RF5	ODAPH
1619	4712	A8MZH6	OOSP1
1620	4713	Q86WS3	OOSP2
1621	4714	A6NHN0	OTOL1
1622	4715	Q8NHW6	OTOS

TABLE 1-continued

Representative list of DNA and protein sequences amplified for the initial and expanded libraries.

Seq. Id. No. (protein)	Seq. Id. No. (DNA)	Uniprot ID	Gene Symbol
1623	4716	Q7RTZ1	OVCH2
1624	4717	Q9UBL9	P2RX2
1625	4718	Q8NBM8	PCYOX1L
1626	4719	Q15084	PDIA6
1627	4720	Q96S96	PEBP4
1628	4721	P0DJD8	PGA3
1629	4722	P20142	PGC
1630	4723	Q96PD5	PGLYRP2
1631	4724	Q96LB8	PGLYRP4
1632	4725	Q6UXB8	PI16
1633	4726	Q8NCC3	PLA2G15
1634	4727	Q5R387	PLA2G2C
1635	4728	Q6P4A8	PLBD1
1636	4729	Q8NHP8	PLBD2
1637	4730	Q6UQ28	PLET1
1638	4731	Q15195	PLGLA
1639	4732	Q02325	PLGLB1
1640	4733	Q6GTS8	PM20D1
1641	4734	P54315	PNLIPRP1
1642	4735	Q86SH4	PRNT
1643	4736	Q99946	PRRT1
1644	4737	O95084	PRSS23
1645	4738	Q9BQR3	PRSS27
1646	4739	P35030	PRSS3
1647	4740	Q8NHM4	PRSS3P2
1648	4741	Q7RTY9	PRSS41
1649	4742	E7EML9	PRSS44
1650	4743	A8MTI9	PRSS47
1651	4744	Q6UWB4	PRSS55
1652	4745	Q8IYP2	PRSS58
1653	4746	Q6NUJ1	PSAPL1
1654	4747	Q9UIG4	PSORS1C2
1655	4748	P01270	PTH
1656	4749	Q96A99	PTX4
1657	4750	Q6H3X3	RAET1G
1658	4751	Q5VY80	RAET1L
1659	4752	Q5W5W9	RESP18
1660	4753	Q86XS8	RNF130
1661	4754	Q8N7C7	RNF148
1662	4755	Q9H6Y7	RNF167
1663	4756	Q96EX2	RNFT2
1664	4757	Q6UXX9	RSPO2
1665	4758	P80511	S100A12
1666	4759	Q6ZMJ2	SCARA5
1667	4760	Q8TD33	SCGB1C1
1668	4761	O75056	SDC3
1669	4762	P0C7V7	SEC11B
1670	4763	P04279	SEMG1
1671	4764	Q6UXR4	SERPINA13P
1672	4765	P20848	SERPINA2
1673	4766	P36952	SERPINB5
1674	4767	P01008	SERPINC1
1675	4768	A8MV23	SERPINE3
1676	4769	Q99574	SERPINI1
1677	4770	P0C7M3	SFTA3
1678	4771	Q13326	SGCG
1679	4772	Q96LD1	SGCZ
1680	4773	Q8N114	SHISA5
1681	4774	Q6ZSJ9	SHISA6
1682	4775	A6NL88	SHISA7
1683	4776	B8ZZ34	SHISA8
1684	4777	B4DS77	SHISA9
1685	4778	Q5TFQ8	SIRPB1
1686	4779	Q63ZE4	SLC22A10
1687	4780	Q9Y226	SLC22A13
1688	4781	O15244	SLC22A2
1689	4782	A6NK97	SLC22A20P
1690	4783	Q6T423	SLC22A25
1691	4784	A6NKX4	SLC22A31
1692	4785	P11168	SLC2A2
1693	4786	Q8N130	SLC34A3

TABLE 1-continued

Representative list of DNA and protein sequences amplified for the initial and expanded libraries.

Seq. Id. No. (protein)	Seq. Id. No. (DNA)	Uniprot ID	Gene Symbol
1694	4787	Q969I6	SLC38A4
1695	4788	A6NLE4	SMIM23
1696	4789	Q92485	SMPDL3B
1697	4790	Q2M3V2	SOWAHA
1698	4791	Q96QH8	SPACA5
1699	4792	Q96KW9	SPACA7
1700	4793	Q6PDA7	SPAG11A
1701	4794	Q08648	SPAG11B
1702	4795	P09486	SPARC
1703	4796	P0C7L1	SPINK8
1704	4797	Q6UDR6	SPINT4
1705	4798	Q9BUD6	SPON2
1706	4799	Q13103	SPP2
1707	4800	Q7Z2R9	SSBP3-AS1
1708	4801	A6NDD5	SYNDIG1L
1709	4802	H3BTG2	TEX46
1710	4803	P10646	TFPI
1711	4804	H3BV60	TGFBR3L
1712	4805	Q8WUY1	THEM6
1713	4806	Q86YJ6	THNSL2
1714	4807	P40225	THPO
1715	4808	Q9NS93	TM7SF3
1716	4809	Q9HD45	TM9SF3
1717	4810	Q4V9L6	TMEM119
1718	4811	Q9BXJ8	TMEM120A
1719	4812	Q8N614	TMEM156
1720	4813	Q8WZ71	TMEM158
1721	4814	Q8NBL3	TMEM178A
1722	4815	H3BS89	TMEM178B
1723	4816	Q9H813	TMEM206
1724	4817	Q86XT9	TMEM219
1725	4818	A6NFC5	TMEM235
1726	4819	Q9P0T7	TMEM9
1727	4820	Q6ZNR0	TMEM91
1728	4821	Q8N816	TMEM99
1729	4822	Q6ZWK6	TMPRSS11F
1730	4823	Q9H1E5	TMX4
1731	4824	Q9H2S6	TNMD
1732	4825	Q8N2E6	TOR2A
1733	4826	Q8NBR0	TP53I13
1734	4827	Q15661	TPSAB1
1735	4828	Q9BZJ3	TPSD1
1736	4829	A6NFA1	TRABD2B
1737	4830	O00294	TULP1
1738	4831	O75386	TULP3
1739	4832	P10599	TXN
1740	4833	Q8WVF2	UCMA
1741	4834	Q9Y4X1	UGT2A1
1742	4835	P36537	UGT2B10
1743	4836	Q9BY64	UGT2B28
1744	4837	Q16880	UGT8
1745	4838	Q9BZM4	ULBP3
1746	4839	Q6UY13	UNQ5830/ PRO19650/ PRO19816
1747	4840	Q6UXV3	UNQ6126/ PRO20091
1748	4841	Q6UXQ8	UNQ6190/ PRO20217
1749	4842	Q6UXR6	UNQ6494/ PRO21346
1750	4843	Q6UXU0	UNQ9165/ PRO28630
1751	4844	Q9N2K0	ENH3
1752	4845	Q9N2J8	ENH1
1753	4846	Q8N1Y9	FLJ37218
1754	4847	Q6ZRU5	FLJ46089
1755	4848	Q8N9W7	FLJ36131
1756	4849	A6NDX4	ENSP00000320207
1757	4850	A8MUN3	ENSP00000381830
1758	4851	Q8TAT8	LOC644613

TABLE 1-continued

Representative list of DNA and protein sequences amplified for the initial and expanded libraries.

Seq. Id. No. (protein)	Seq. Id. No. (DNA)	Uniprot ID	Gene Symbol
1759	4852	B0FP48	UPK3BL1
1760	4853	Q86V25	VASH2
1761	4854	Q9NY84	VNN3
1762	4855	Q8IUB5	WFDC13
1763	4856	Q8IUA0	WFDC8
1764	4857	O95388	WISP1
1765	4858	P56703	WNT3
1766	4859	Q9Y6F9	WNT6
1767	4860	Q9H1J5	WNT8A
1768	4861	O14905	WNT9B
1769	4862	P21754	ZP3
1770	4863	Q12836	ZP4
1771	4864	A1L453	PRSS38
1772	4865	A2RUU4	CLPSL1
1773	4866	A4D0V7	CPED1
1774	4867	A4D1T9	PRSS37
1775	4868	A5X5Y0	HTR3E
1776	4869	A6NNS2	DHRS7C
1777	4870	A8K7I4	CLCA1
1778	4871	A8MVS5	HIDE1
1779	4872	B2RNN3	C1QTNF9B
1780	4873	B2RUY7	VWC2L
1781	4874	C9JUS6	ADM5
1782	4875	O00115	DNASE2
1783	4876	O00144	FZD9
1784	4877	O00180	KCNK1
1785	4878	O00182	LGALS9
1786	4879	O00253	AGRP
1787	4880	O00292	LEFTY2
1788	4881	O00295	TULP2
1789	4882	O00515	LAD1
1790	4883	O00560	SDCBP
1791	4884	O00584	RNASET2
1792	4885	O00590	ACKR2
1793	4886	O00591	GABRP
1794	4887	O00592	PODXL
1795	4888	O00602	FCN1
1796	4889	O00622	CYR61
1797	4890	O00744	WNT10B
1798	4891	O00748	CES2
1799	4892	O00754	MAN2B1
1800	4893	O00755	WNT7A
1801	4894	O14493	CLDN4
1802	4895	O14638	ENPP3
1803	4896	O14656	TOR1A
1804	4897	O14657	TOR1B
1805	4898	O14668	PRRG1
1806	4899	O14756	HSD17B6
1807	4900	O14764	GABRD
1808	4901	O14773	TPP1
1809	4902	O14791	APOL1
1810	4903	O14792	HS3ST1
1811	4904	O14904	WNT9A
1812	4905	O14958	CASQ2
1813	4906	O14960	LECT2
1814	4907	O15120	AGPAT2
1815	4908	O15245	SLC22A1
1816	4909	O15321	TM9SF1
1817	4910	O15393	TMPRSS2
1818	4911	O15431	SLC31A1
1819	4912	O15460	P4HA2
1820	4913	O15496	PLA2G10
1821	4914	O15537	RS1
1822	4915	O15547	P2RX6
1823	4916	O15551	CLDN3
1824	4917	O43240	KLK10
1825	4918	O43280	TREH
1826	4919	O43291	SPINT2
1827	4920	O43323	DHH
1828	4921	O43493	TGOLN2
1829	4922	O43555	GNRH2

TABLE 1-continued

Representative list of DNA and protein sequences amplified for the initial and expanded libraries.

Seq. Id. No. (protein)	Seq. Id. No. (DNA)	Uniprot ID	Gene Symbol
1830	4923	O43556	SGCE
1831	4924	O43570	CA12
1832	4925	O43614	HCRTR2
1833	4926	O43692	PI15
1834	4927	O43852	CALU
1835	4928	O43866	CD5L
1836	4929	O43908	KLRC4
1837	4930	O60218	AKR1B10
1838	4931	O60235	TMPRSS11D
1839	4932	O60565	GREM1
1840	4933	O60568	PLOD3
1841	4934	O60575	SPINK4
1842	4935	O60656	UGT1A9
1843	4936	O60676	CST8
1844	4937	O60844	ZG16
1845	4938	O60882	MMP20
1846	4939	O60894	RAMP1
1847	4940	O60895	RAMP2
1848	4941	O60896	RAMP3
1849	4942	O60911	CTSV
1850	4943	O75084	FZD7
1851	4944	O75106	AOC2
1852	4945	O75185	ATP2C2
1853	4946	O75310	UGT2B11
1854	4947	O75311	GLRA3
1855	4948	O75356	ENTPD5
1856	4949	O75398	DEAF1
1857	4950	O75487	GPC4
1858	4951	O75493	CA11
1859	4952	O75503	CLN5
1860	4953	O75508	CLDN11
1861	4954	O75556	SCGB2A1
1862	4955	O75610	LEFTY1
1863	4956	O75629	CREG1
1864	4957	O75636	FCN3
1865	4958	O75711	SCRG1
1866	4959	O75715	GPX5
1867	4960	O75718	CRTAP
1868	4961	O75787	ATP6AP2
1869	4962	O75795	UGT2B17
1870	4963	O75830	SERPINI2
1871	4964	O75951	LYZL6
1872	4965	O76038	SCGN
1873	4966	O76061	STC2
1874	4967	O76076	WISP2
1875	4968	O76082	SLC22A5
1876	4969	O76095	JTB
1877	4970	O94907	DKK1
1878	4971	O94956	SLCO2B1
1879	4972	O94985	CLSTN1
1880	4973	O95156	NXPH2
1881	4974	O95157	NXPH3
1882	4975	O95158	NXPH4
1883	4976	O95264	HTR3B
1884	4977	O95302	FKBP9
1885	4978	O95389	WISP3
1886	4979	O95436	SLC34A2
1887	4980	O95445	APOM
1888	4981	O95471	CLDN7
1889	4982	O95484	CLDN9
1890	4983	O95497	VNN1
1891	4984	O95498	VNN2
1892	4985	O95500	CLDN14
1893	4986	O95502	NPTXR
1894	4987	O95528	SLC2A10
1895	4988	O95622	ADCY5
1896	4989	O95711	LY86
1897	4990	O95813	CER1
1898	4991	O95832	CLDN1
1899	4992	O95881	TXNDC12
1900	4993	O95897	OLFM2

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Representative list of DNA and protein sequences amplified for the initial and expanded libraries.

Seq. Id. No. (protein)	Seq. Id. No. (DNA)	Uniprot ID	Gene Symbol
1901	4994	O95925	EPPIN
1902	4995	O95968	SCGB1D1
1903	4996	O95969	SCGB1D2
1904	4997	O95994	AGR2
1905	4998	O96005	CLPTM1
1906	4999	O96009	NAPSA
1907	5000	O96014	WNT11
1908	5001	P00450	CP
1909	5002	P00709	LALBA
1910	5003	P00734	F2
1911	5004	P00751	CFB
1912	5005	P00797	REN
1913	5006	P00995	SPINK1
1914	5007	P01009	SERPINA1
1915	5008	P01011	SERPINA3
1916	5009	P01019	AGT
1917	5010	P01033	TIMP1
1918	5011	P01034	CST3
1919	5012	P01036	CST4
1920	5013	P01037	CST1
1921	5014	P01148	GNRH1
1922	5015	P01178	OXT
1923	5016	P01185	AVP
1924	5017	P01189	POMC
1925	5018	P01222	TSHB
1926	5019	P01225	FSHB
1927	5020	P01236	PRL
1928	5021	P01241	GH1
1929	5022	P01275	GCG
1930	5023	P01350	GAST
1931	5024	P02647	APOA1
1932	5025	P02649	APOE
1933	5026	P02652	APOA2
1934	5027	P02654	APOC1
1935	5028	P02655	APOC2
1936	5029	P02656	APOC3
1937	5030	P02675	FGB
1938	5031	P02679	FGG
1939	5032	P02724	GYPA
1940	5033	P02741	CRP
1941	5034	P02743	APCS
1942	5035	P02749	APOH
1943	5036	P02753	RBP4
1944	5037	P02760	AMBP
1945	5038	P02763	ORM1
1946	5039	P02765	AHSG
1947	5040	P02766	TTR
1948	5041	P02768	ALB
1949	5042	P02771	AFP
1950	5043	P02774	GC
1951	5044	P02810	PRH1;
1952	5045	P02814	SMR3B
1953	5046	P02818	BGLAP
1954	5047	P03950	ANG
1955	5048	P03951	F11
1956	5049	P03952	KLKB1
1957	5050	P03956	MMP1
1958	5051	P03973	SLP1
1959	5052	P04001	OPN1MW
1960	5053	P04003	C4BPA
1961	5054	P04004	VTN
1962	5055	P04054	PLA2G1B
1963	5056	P04062	GBA
1964	5057	P04066	FUCA1
1965	5058	P04083	ANXA1
1966	5059	P04090	RLN2
1967	5060	P04118	CLPS
1968	5061	P04155	TFF1
1969	5062	P04156	PRNP
1970	5063	P04196	HRG
1971	5064	P04278	SHBG

TABLE 1-continued

Representative list of DNA and protein sequences amplified for the initial and expanded libraries.

Seq. Id. No. (protein)	Seq. Id. No. (DNA)	Uniprot ID	Gene Symbol
1972	5065	P04628	WNT1
1973	5066	P04745	AMY1A
1974	5067	P04808	RLN1
1975	5068	P04920	SLC4A2
1976	5069	P04921	GYPC
1977	5070	P05023	ATP1A1
1978	5071	P05026	ATP1B1
1979	5072	P05060	CHGB
1980	5073	P05067	APP
1981	5074	P05090	APOD
1982	5075	P05109	S100A8
1983	5076	P05111	INHA
1984	5077	P05120	SERPINB2
1985	5078	P05121	SERPINE1
1986	5079	P05154	SERPINA5
1987	5080	P05155	SERPING1
1988	5081	P05160	F13B
1989	5082	P05164	MPO
1990	5083	P05186	ALPL
1991	5084	P05187	ALPP
1992	5085	P05408	SCG5
1993	5086	P05543	SERPINA7
1994	5087	P05546	SERPIND1
1995	5088	P05814	CSN2
1996	5089	P05981	HPN
1997	5090	P06133	UGT2B4
1998	5091	P06276	BCHE
1999	5092	P06280	GLA
2000	5093	P06307	CCK
2001	5094	P06396	GSN
2002	5095	P06681	C2
2003	5096	P06702	S100A9
2004	5097	P06858	LPL
2005	5098	P06865	HEXA
2006	5099	P06870	KLK1
2007	5100	P07093	SERPINE2
2008	5101	P07098	LIPF
2009	5102	P07237	P4HB
2010	5103	P07288	KLK3
2011	5104	P07339	CTSD
2012	5105	P07355	ANXA2
2013	5106	P07360	C8G
2014	5107	P07477	PRSS1
2015	5108	P07478	PRSS2
2016	5109	P07498	CSN3
2017	5110	P07602	PSAP
2018	5111	P07686	HEXB
2019	5112	P07711	CTSL
2020	5113	P07949	RET
2021	5114	P07988	SFTPB
2022	5115	P07998	RNASE1
2023	5116	P08118	MSMB
2024	5117	P08185	SERPINA6
2025	5118	P08217	CELA2A
2026	5119	P08218	CELA2B
2027	5120	P08246	ELANE
2028	5121	P08254	MMP3
2029	5122	P08294	SOD3
2030	5123	P08311	CTSG
2031	5124	P08473	MME
2032	5125	P08476	INHBA
2033	5126	P08572	COL4A2
2034	5127	P08697	SERPINF2
2035	5128	P08833	IGFBP1
2036	5129	P08861	CELA3B
2037	5130	P08910	ABHD2
2038	5131	P09093	CELA3A
2039	5132	P09228	CST2
2040	5133	P09237	MMP7
2041	5134	P09238	MMP10
2042	5135	P09382	LGALS1

TABLE 1-continued

Representative list of DNA and protein sequences amplified for the initial and expanded libraries.

Seq. Id. No. (protein)	Seq. Id. No. (DNA)	Uniprot ID	Gene Symbol
2043	5136	P09466	PAEP
2044	5137	P09544	WNT2
2045	5138	P09668	CTSH
2046	5139	P09758	TACSTD2
2047	5140	P09923	ALPI
2048	5141	P09958	FURIN
2049	5142	P0C862	C1QTNF9
2050	5143	P0DJD7	PGA4
2051	5144	P0DJD9	PGA5
2052	5145	P0DJI8	SAA1
2053	5146	P0DJI9	SAA2
2054	5147	P0DML2	CSH
2055	5148	P0DML3	CSH2
2056	5149	P0DMR2	SCGB1C2
2057	5150	P10124	SRGN
2058	5151	P10144	GZMB
2059	5152	P10153	RNASE2
2060	5153	P10253	GAA
2061	5154	P10323	ACR
2062	5155	P10451	SPP1
2063	5156	P10619	CTSA
2064	5157	P10645	CHGA
2065	5158	P10696	ALPPL2
2066	5159	P10720	PF4V1
2067	5160	P10909	CLU
2068	5161	P11021	HSPA5
2069	5162	P11150	LIPC
2070	5163	P11230	CHRNB1
2071	5164	P11597	CETP
2072	5165	P11684	SCGB1A1
2073	5166	P12018	VPREB1
2074	5167	P12110	COL6A2
2075	5168	P12259	F5
2076	5169	P12272	PTHLH
2077	5170	P12544	GZMA
2078	5171	P12724	RNASE3
2079	5172	P12872	MLN
2080	5173	P13284	IFI30
2081	5174	P13521	SCG2
2082	5175	P13637	ATP1A3
2083	5176	P13667	PDIA4
2084	5177	P13674	P4HA1
2085	5178	P13686	ACP5
2086	5179	P13725	OSM
2087	5180	P13762	HLA-DRB4
2088	5181	P13866	SLC5A1
2089	5182	P14091	CTSE
2090	5183	P14207	FOLR2
2091	5184	P14384	CPM
2092	5185	P14415	ATP1B2
2093	5186	P14555	PLA2G2A
2094	5187	P14625	HSP90B1
2095	5188	P14735	IDE
2096	5189	P15085	CPA1
2097	5190	P15086	CPB1
2098	5191	P15088	CPA3
2099	5192	P15169	CPN1
2100	5193	P15289	ARSA
2101	5194	P15309	ACPP
2102	5195	P15328	FOLR1
2103	5196	P15586	GNS
2104	5197	P16035	TIMP2
2105	5198	P16150	SPN
2106	5199	P16233	PNLIP
2107	5200	P16278	GLB1
2108	5201	P16422	EPCAM
2109	5202	P16444	DPEP1
2110	5203	P16519	PCSK2
2111	5204	P16562	CRISP2
2112	5205	P16662	UGT2B7
2113	5206	P16870	CPE

TABLE 1-continued

Representative list of DNA and protein sequences amplified for the initial and expanded libraries.

Seq. Id. No. (protein)	Seq. Id. No. (DNA)	Uniprot ID	Gene Symbol
2114	5207	P17050	NAGA
2115	5208	P17213	BPI
2116	5209	P17787	CHRNB2
2117	5210	P17813	ENG
2118	5211	P17900	GM2A
2119	5212	P17931	LGALS3
2120	5213	P17936	IGFBP3
2121	5214	P18065	IGFBP2
2122	5215	P18433	PTPRA
2123	5216	P18505	GABRB1
2124	5217	P18507	GABRG2
2125	5218	P18509	ADCYAP1
2126	5219	P19224	UGT1A6
2127	5220	P19440	GGT1
2128	5221	P19652	ORM2
2129	5222	P19883	FST
2130	5223	P19957	PI3
2131	5224	P20023	CR2
2132	5225	P20061	TCN1
2133	5226	P20062	TCN2
2134	5227	P20151	KLK2
2135	5228	P20160	AZU1
2136	5229	P20231	TPSB2
2137	5230	P20382	PMCH
2138	5231	P20396	TRH
2139	5232	P20718	GZMH
2140	5233	P20851	C4BPB
2141	5234	P20933	AGA
2142	5235	P21246	PTN
2143	5236	P21741	MDK
2144	5237	P21815	IBSP
2145	5238	P21964	COMT
2146	5239	P22309	UGT1A1
2147	5240	P22310	UGT1A4
2148	5241	P22692	IGFBP4
2149	5242	P22748	CA4
2150	5243	P22894	MMP8
2151	5244	P23141	CES1
2152	5245	P23276	KEL
2153	5246	P23284	PPIB
2154	5247	P23327	HRC
2155	5248	P23415	GLRA1
2156	5249	P23416	GLRA2
2157	5250	P23435	CBLN1
2158	5251	P23582	NPPC
2159	5252	P23946	CMA1
2160	5253	P23975	SLC6A2
2161	5254	P24046	GABRR1
2162	5255	P24158	PRTN3
2163	5256	P24387	CRHBP
2164	5257	P24592	IGFBP6
2165	5258	P24593	IGFBP5
2166	5259	P24855	DNASE1
2167	5260	P25092	GUCY2C
2168	5261	P26436	ACRV1
2169	5262	P26885	FKBP2
2170	5263	P27037	ACVR2A
2171	5264	P27169	PON1
2172	5265	P27352	GIF
2173	5266	P27658	COL8A1
2174	5267	P27797	CALR
2175	5268	P27918	CFP
2176	5269	P28325	CST5
2177	5270	P28472	GABRB3
2178	5271	P28476	GABRR2
2179	5272	P28799	GRN
2180	5273	P29120	PCSK1
2181	5274	P29279	CTGF
2182	5275	P29622	SERPINA4
2183	5276	P29973	CNGA1
2184	5277	P30040	ERP29

TABLE 1-continued

Representative list of DNA and protein sequences amplified for the initial and expanded libraries.

Seq. Id. No. (protein)	Seq. Id. No. (DNA)	Uniprot ID	Gene Symbol
2185	5278	P30101	PDIA3
2186	5279	P30531	SLC6A1
2187	5280	P30532	CHRNA5
2188	5281	P30533	LRPAP1
2189	5282	P30926	CHRNB4
2190	5283	P30990	NTS
2191	5284	P31151	S100A7
2192	5285	P31415	CASQ1
2193	5286	P31644	GABRA5
2194	5287	P31947	SFN
2195	5288	P32297	CHRNA3
2196	5289	P32455	GBP1
2197	5290	P34059	GALNS
2198	5291	P34096	RNASE4
2199	5292	P34810	CD68
2200	5293	P34903	GABRA3
2201	5294	P34910	EVI2B
2202	5295	P34925	RYK
2203	5296	P35052	GPC1
2204	5297	P35503	UGT1A3
2205	5298	P35542	SAA4
2206	5299	P35625	TIMP3
2207	5300	P36222	CHI3L1
2208	5301	P36269	GGT5
2209	5302	P36896	ACVR1B
2210	5303	P36955	SERPINF1
2211	5304	P36980	CFHR2
2212	5305	P37023	ACVRL1
2213	5306	P37840	SNCA
2214	5307	P38567	SPAM1
2215	5308	P38571	LIPA
2216	5309	P39086	GRIK1
2217	5310	P39877	PLA2G5
2218	5311	P39900	MMP12
2219	5312	P40313	CTRL
2220	5313	P41159	LEP
2221	5314	P41221	WNT5A
2222	5315	P41222	PTGDS
2223	5316	P41439	FOLR3
2224	5317	P42127	ASIP
2225	5318	P42261	GRIA1
2226	5319	P42263	GRIA3
2227	5320	P42658	DPP6
2228	5321	P42785	PRCP
2229	5322	P42892	ECE1
2230	5323	P43005	SLC1A1
2231	5324	P43007	SLC1A4
2232	5325	P43234	CTSO
2233	5326	P43235	CTSK
2234	5327	P43251	BTD
2235	5328	P43490	NAMPT
2236	5329	P43652	AFM
2237	5330	P43681	CHRNA4
2238	5331	P45452	MMP13
2239	5332	P45844	ABCG1
2240	5333	P46059	SLC15A1
2241	5334	P46098	HTR3A
2242	5335	P46695	IER3
2243	5336	P47710	CSN1S1
2244	5337	P47870	GABRB2
2245	5338	P47929	LGALS7
2246	5339	P47972	NPTX2
2247	5340	P48029	SLC6A8
2248	5341	P48052	CPA2
2249	5342	P48060	GLIPR1
2250	5343	P48065	SLC6A12
2251	5344	P48066	SLC6A11
2252	5345	P48067	SLC6A9
2253	5346	P48167	GLRB
2254	5347	P48169	GABRA4
2255	5348	P48307	TFPI2

TABLE 1-continued

Representative list of DNA and protein sequences amplified for the initial and expanded libraries.

Seq. Id. No. (protein)	Seq. Id. No. (DNA)	Uniprot ID	Gene Symbol
2256	5349	P48723	HSPA13
2257	5350	P48745	NOV
2258	5351	P48995	TRPC1
2259	5352	P49184	DNASE1L1
2260	5353	P49662	CASP4
2261	5354	P49771	FLT3LG
2262	5355	P49862	KLK7
2263	5356	P49863	GZMK
2264	5357	P50281	MMP14
2265	5358	P50443	SLC26A2
2266	5359	P50454	SERPINH1
2267	5360	P50897	PPT1
2268	5361	P51124	GZMM
2269	5362	P51164	ATP4B
2270	5363	P51168	SCNN1B
2271	5364	P51170	SCNN1G
2272	5365	P51575	P2RX1
2273	5366	P51654	GPC3
2274	5367	P51674	GPM6A
2275	5368	P51686	CCR9
2276	5369	P51688	SGSH
2277	5370	P51689	ARSD
2278	5371	P51690	ARSE
2279	5372	P51693	APLP1
2280	5373	P51811	XK
2281	5374	P51841	GUCY2F
2282	5375	P52823	STC1
2283	5376	P52961	ART1
2284	5377	P53634	CTSC
2285	5378	P53801	PTTG1IP
2286	5379	P54108	CRISP3
2287	5380	P54317	PNLIPRP2
2288	5381	P54709	ATP1B3
2289	5382	P54793	ARSF
2290	5383	P54803	GALC
2291	5384	P54855	UGT2B15
2292	5385	P55001	MFAP2
2293	5386	P55056	APOC4
2294	5387	P55058	PLTP
2295	5388	P55083	MFAP4
2296	5389	P55103	INHBC
2297	5390	P55145	MANF
2298	5391	P55808	XG
2299	5392	P56373	P2RX3
2300	5393	P56704	WNT3A
2301	5394	P56705	WNT4
2302	5395	P56706	WNT7B
2303	5396	P56748	CLDN8
2304	5397	P56749	CLDN12
2305	5398	P56750	CLDN17
2306	5399	P56817	BACE1
2307	5400	P56851	EDDM3B
2308	5401	P56856	CLDN18
2309	5402	P56880	CLDN20
2310	5403	P56937	HSD17B7
2311	5404	P57727	TMPRSS3
2312	5405	P57739	CLDN2
2313	5406	P58062	SPINK7
2314	5407	P58166	INHBE
2315	5408	P58294	PROK1
2316	5409	P58417	NXPH1
2317	5410	P58499	FAM3B
2318	5411	P58658	EVA1C
2319	5412	P59666	DEFA3
2320	5413	P59826	BPIFB3
2321	5414	P60153	RNASE9
2322	5415	P60508	ERVFRD-1
2323	5416	P60827	C1QTNF8
2324	5417	P60985	KRTDAP
2325	5418	P61366	OSTN
2326	5419	P61626	LYZ

TABLE 1-continued

Representative list of DNA and protein sequences amplified for the initial and expanded libraries.

Seq. Id. No. (protein)	Seq. Id. No. (DNA)	Uniprot ID	Gene Symbol
2327	5420	P61916	NPC2
2328	5421	P62502	LCN6
2329	5422	P62937	PPIA
2330	5423	P67809	YBX1
2331	5424	P78333	GPC5
2332	5425	P78348	ASIC1
2333	5426	P78369	CLDN10
2334	5427	P78562	PHEX
2335	5428	P79483	HLA-DRB3
2336	5429	P80108	GPLD1
2337	5430	P80188	LCN2
2338	5431	P83105	HTRA4
2339	5432	P83110	HTRA3
2340	5433	P98066	TNFAIP6
2341	5434	Q00604	NDP
2342	5435	Q01459	CTBS
2343	5436	Q01523	DEFA5
2344	5437	Q02383	SEMG2
2345	5438	Q02413	DSG1
2346	5439	Q02747	GUCA2A
2347	5440	Q02809	PLOD1
2348	5441	Q02846	GUCY2D
2349	5442	Q02985	CFHR3
2350	5443	Q03403	TFF2
2351	5444	Q03591	CFHR1
2352	5445	Q03692	COL10A1
2353	5446	Q04771	ACVR1
2354	5447	Q04900	CD164
2355	5448	Q05901	CHRNB3
2356	5449	Q05996	ZP2
2357	5450	Q06033	ITIH3
2358	5451	Q06481	APLP2
2359	5452	Q06495	SLC34A1
2360	5453	Q07001	CHRND
2361	5454	Q07021	C1QBP
2362	5455	Q07075	ENPEP
2363	5456	Q07507	DPT
2364	5457	Q07837	SLC3A1
2365	5458	Q08345	DDR1
2366	5459	Q08380	LGALS3BP
2367	5460	Q08554	DSC1
2368	5461	Q08629	SPOCK1
2369	5462	Q08830	FGL1
2370	5463	Q0P5P2	C17orf67
2371	5464	Q0VAF6	SYCN
2372	5465	Q10588	BST1
2373	5466	Q10589	BST2
2374	5467	Q12841	FSTL1
2375	5468	Q12884	FAP
2376	5469	Q12889	OVGP1
2377	5470	Q12904	AIMP1
2378	5471	Q13003	GRIK3
2379	5472	Q13087	PDIA2
2380	5473	Q13093	PLA2G7
2381	5474	Q13145	BAMBI
2382	5475	Q13162	PRDX4
2383	5476	Q13217	DNAJC3
2384	5477	Q13231	CHIT1
2385	5478	Q13253	NOG
2386	5479	Q13296	SCGB2A2
2387	5480	Q13316	DMP1
2388	5481	Q13361	MFAP5
2389	5482	Q13421	MSLN
2390	5483	Q13438	OS9
2391	5484	Q13445	TMED1
2392	5485	Q13467	FZD5
2393	5486	Q13507	TRPC3
2394	5487	Q13508	ART3
2395	5488	Q13530	SERINC3
2396	5489	Q13563	PKD2
2397	5490	Q13609	DNASE1L3

TABLE 1-continued

Representative list of DNA and protein sequences amplified for the initial and expanded libraries.

Seq. Id. No. (protein)	Seq. Id. No. (DNA)	Uniprot ID	Gene Symbol
2398	5491	Q13705	ACVR2B
2399	5492	Q13790	APOF
2400	5493	Q13822	ENPP2
2401	5494	Q14050	COL9A3
2402	5495	Q14242	SELPLG
2403	5496	Q14257	RCN2
2404	5497	Q14314	FGL2
2405	5498	Q14406	CSHL1
2406	5499	Q14507	EDDM3A
2407	5500	Q14508	WFDC2
2408	5501	Q14515	SPARCL1
2409	5502	Q14696	MESD
2410	5503	Q14714	SSPN
2411	5504	Q14832	GRM3
2412	5505	Q14993	COL19A1
2413	5506	Q14C87	TMEM132D
2414	5507	Q15043	SLC39A14
2415	5508	Q15046	KARS
2416	5509	Q15063	POSTN
2417	5510	Q15113	PCOLCE
2418	5511	Q15165	PON2
2419	5512	Q15166	PON3
2420	5513	Q15293	RCN1
2421	5514	Q15465	SHH
2422	5515	Q15517	CDSN
2423	5516	Q15726	KISS1
2424	5517	Q15758	SLC1A5
2425	5518	Q15782	CHI3L2
2426	5519	Q15818	NPTX1
2427	5520	Q15825	CHRNA6
2428	5521	Q15828	CST6
2429	5522	Q15848	ADIPOQ
2430	5523	Q15884	FAM189A2
2431	5524	Q15904	ATP6AP1
2432	5525	Q16281	CNGA3
2433	5526	Q16378	PRR4
2434	5527	Q16445	GABRA6
2435	5528	Q16549	PCSK7
2436	5529	Q16568	CARTPT
2437	5530	Q16570	ACKR1
2438	5531	Q16585	SGCB
2439	5532	Q16586	SGCA
2440	5533	Q16610	ECM1
2441	5534	Q16651	PRSS8
2442	5535	Q16671	AMHR2
2443	5536	Q16674	MIA
2444	5537	Q16769	QPCT
2445	5538	Q16790	CA9
2446	5539	Q16832	DDR2
2447	5540	Q16853	AOC3
2448	5541	Q17R60	IMPG1
2449	5542	Q17RR3	PNLIPRP3
2450	5543	Q19T08	ECSCR
2451	5544	Q1HG43	DUOXA1
2452	5545	Q1HG44	DUOXA2
2453	5546	Q1W4C9	SPINK13
2454	5547	Q1ZYL8	IZUMO4
2455	5548	Q24JP5	TMEM132A
2456	5549	Q2I0M5	RSPO4
2457	5550	Q2M2E5	C5orf64
2458	5551	Q2M385	MPEG1
2459	5552	Q2M3T9	HYAL4
2460	5553	Q2MKA7	RSPO1
2461	5554	Q2MV58	TCTN1
2462	5555	Q2TAL6	VWC2
2463	5556	Q30154	HLA-DRB5
2464	5557	Q30KP8	DEFB136
2465	5558	Q30KP9	DEFB135
2466	5559	Q30KQ4	DEFB116
2467	5560	Q30KQ5	DEFB115
2468	5561	Q30KQ7	DEFB113

TABLE 1-continued

Representative list of DNA and protein sequences amplified for the initial and expanded libraries.

Seq. Id. No. (protein)	Seq. Id. No. (DNA)	Uniprot ID	Gene Symbol
2469	5562	Q30KQ8	DEFB112
2470	5563	Q32M45	ANO4
2471	5564	Q3KNT9	TMEM95
2472	5565	Q3SXP7	SHISAL1
2473	5566	Q3SY77	UGT3A2
2474	5567	Q401N2	ZACN
2475	5568	Q496H8	NRN1L
2476	5569	Q496J9	SV2C
2477	5570	Q49AH0	CDNF
2478	5571	Q4G0G5	SCGB2B2
2479	5572	Q4KMQ2	ANO6
2480	5573	Q4U2R8	SLC22A6
2481	5574	Q4W5P6	TMEM155
2482	5575	Q504Y0	SLC39A12
2483	5576	Q53EL9	SEZ6
2484	5577	Q53H76	PLA1A
2485	5578	Q53RT3	ASPRV1
2486	5579	Q5DT21	SPINK9
2487	5580	Q5EBL8	PDZD11
2488	5581	Q5FWE3	PRRT3
2489	5582	Q5FYB0	ARSJ
2490	5583	Q5FYB1	ARSI
2491	5584	Q5GAN3	RNASE13
2492	5585	Q5GAN4	RNASE12
2493	5586	Q5GAN6	RNASE10
2494	5587	Q5J5C9	DEFB121
2495	5588	Q5JS37	NHLRC3
2496	5589	Q5JTB6	PLAC9
2497	5590	Q5MY95	ENTPD8
2498	5591	Q5PT55	SLC10A5
2499	5592	Q5T742	C10orf25
2500	5593	Q5TF21	SOGA3
2501	5594	Q5UCC4	EMC10
2502	5595	Q5VXJ0	LIPK
2503	5596	Q5VXM1	CDCP2
2504	5597	Q5W186	CST9
2505	5598	Q68BL8	OLFML2B
2506	5599	Q68DH5	LMBRD2
2507	5600	Q68DV7	RNF43
2508	5601	Q695T7	SLC6A19
2509	5602	Q6E0U4	DMKN
2510	5603	Q6FHJ7	SFRP4
2511	5604	Q6GPI1	CTRB2
2512	5605	Q6H9L7	ISM2
2513	5606	Q6HA08	ASTL
2514	5607	Q6IE38	SPINK14
2515	5608	Q6ISU1	PTCRA
2516	5609	Q6J4K2	SLC8B1
2517	5610	Q6MZM9	PRR27
2518	5611	Q6NSJ0	MYORG
2519	5612	Q6NSX1	CCDC70
2520	5613	Q6NUM9	RETSAT
2521	5614	Q6NUS6	TCTN3
2522	5615	Q6NUS8	UGT3A1
2523	5616	Q6NVV3	NIPAL1
2524	5617	Q6NW40	RGMB
2525	5618	Q6P093	AADACL2
2526	5619	Q6P4Q7	CNNM4
2527	5620	Q6P5W5	SLC39A4
2528	5621	Q6P995	FAM171B
2529	5622	Q6P9G4	TMEM154
2530	5623	Q6PB30	CSAG1
2531	5624	Q6PL45	BRICD5
2532	5625	Q6Q788	APOA5
2533	5626	Q6SPF0	SAMD1
2534	5627	Q6URK8	TEPP
2535	5628	Q6UW10	SFTA2
2536	5629	Q6UW49	SPESP1
2537	5630	Q6UWF9	FAM180A
2538	5631	Q6UWH4	FAM198B
2539	5632	Q6UWI2	PARM1

TABLE 1-continued

Representative list of DNA and protein sequences amplified for the initial and expanded libraries.

Seq. Id. No. (protein)	Seq. Id. No. (DNA)	Uniprot ID	Gene Symbol
2540	5633	Q6UWI4	SHISA2
2541	5634	Q6UWJ1	TMCO3
2542	5635	Q6UWJ8	CD164L2
2543	5636	Q6UWM5	GLIPR1L1
2544	5637	Q6UWM7	LCTL
2545	5638	Q6UWM9	UGT2A3
2546	5639	Q6UWN8	SPINK6
2547	5640	Q6UWQ5	LYZL1
2548	5641	Q6UWR7	ENPP6
2549	5642	Q6UWU4	C6orf89
2550	5643	Q6UWV6	ENPP7
2551	5644	Q6UWW0	LCN15
2552	5645	Q6UWW8	CES3
2553	5646	Q6UWY0	ARSK
2554	5647	Q6UWY2	PRSS57
2555	5648	Q6UWY5	OLFML1
2556	5649	Q6UX06	OLFM4
2557	5650	Q6UX34	SNORC
2558	5651	Q6UX39	AMTN
2559	5652	Q6UX71	PLXDC2
2560	5653	Q6UXA7	C6orf15
2561	5654	Q6UXF1	TMEM108
2562	5655	Q6UXI7	VIT
2563	5656	Q6UXQ4	C2orf66
2564	5657	Q6UXT8	ALKAL1
2565	5658	Q6UXT9	ABHD15
2566	5659	Q6UXX5	ITIH6
2567	5660	Q6WN34	CHRDL2
2568	5661	Q6X4U4	SOSTDC1
2569	5662	Q6XE38	SCGB1D4
2570	5663	Q6XZB0	LIPI
2571	5664	Q6ZMH5	SLC39A5
2572	5665	Q6ZMR5	TMPRSS11A
2573	5666	Q6ZNF0	ACP7
2574	5667	Q6ZP80	TMEM182
2575	5668	Q6ZQN7	SLCO4C1
2576	5669	Q6ZTQ4	CDHR3
2577	5670	Q75V66	ANO5
2578	5671	Q76B58	BRINP3
2579	5672	Q7L0J3	SV2A
2580	5673	Q7L1I2	SV2B
2581	5674	Q7L8A9	VASH1
2582	5675	Q7RTT9	SLC29A4
2583	5676	Q7RTW8	OTOA
2584	5677	Q7RTX0	TAS1R3
2585	5678	Q7RTY5	PRSS48
2586	5679	Q7RTY7	OVCH1
2587	5680	Q7Z304	MAMDC2
2588	5681	Q7Z3D4	LYSMD3
2589	5682	Q7Z3S7	CACNA2D4
2590	5683	Q7Z404	TMC4
2591	5684	Q7Z410	TMPRSS9
2592	5685	Q7Z4F1	LRP10
2593	5686	Q7Z4W2	LYZL2
2594	5687	Q7Z5A4	PRSS42
2595	5688	Q7Z5A8	FAM19A3
2596	5689	Q7Z5A9	FAM19A1
2597	5690	Q7Z5L0	VMO1
2598	5691	Q7Z5M5	TMC3
2599	5692	Q7Z5P4	HSD17B13
2600	5693	Q7Z7B7	DEFB132
2601	5694	Q86SG7	LYG2
2602	5695	Q86SI9	C5orf38
2603	5696	Q86T26	TMPRSS11B
2604	5697	Q86TE4	LUZP2
2605	5698	Q86TW2	ADCK1
2606	5699	Q86TY3	C14orf37
2607	5700	Q86U17	SERPINA11
2608	5701	Q86UD1	OAF
2609	5702	Q86UL3	GPAT4
2610	5703	Q86W47	KCNMB4

TABLE 1-continued

Representative list of DNA and protein sequences amplified for the initial and expanded libraries.

Seq. Id. No. (protein)	Seq. Id. No. (DNA)	Uniprot ID	Gene Symbol
2611	5704	Q86WD7	SERPINA9
2612	5705	Q86WI0	LHFPL1
2613	5706	Q86WS5	TMPRSS12
2614	5707	Q86XP6	GKN2
2615	5708	Q86YB8	ERO1B
2616	5709	Q86YL7	PDPN
2617	5710	Q86Z14	KLB
2618	5711	Q86Z23	CIQL4
2619	5712	Q8IU80	TMPRSS6
2620	5713	Q8IU99	CALHM1
2621	5714	Q8IUB2	WFDC3
2622	5715	Q8IUH2	CREG2
2623	5716	Q8IUK5	PLXDC1
2624	5717	Q8IVL6	P3H3
2625	5718	Q8IVL8	CPO
2626	5719	Q8IVM8	SLC22A9
2627	5720	Q8IVN8	SBSPON
2628	5721	Q8IW75	SERPINA12
2629	5722	Q8IW92	GLB1L2
2630	5723	Q8IWF2	FOXRED2
2631	5724	Q8IWU5	SULF2
2632	5725	Q8IWU6	SULF1
2633	5726	Q8IX19	MCEMP1
2634	5727	Q8IXA5	SPACA3
2635	5728	Q8IXB1	DNAJC10
2636	5729	Q8IXB3	TUSC5
2637	5730	Q8IYJ0	PIANP
2638	5731	Q8IYK4	COLGALT2
2639	5732	Q8IYS2	KIAA2013
2640	5733	Q8IZS8	CACNA2D3
2641	5734	Q8J025	APCDD1
2642	5735	Q8N0W4	NLGN4X
2643	5736	Q8N0W7	FMR1NB
2644	5737	Q8N129	CNPY4
2645	5738	Q8N131	TMEM123
2646	5739	Q8N158	GPC2
2647	5740	Q8N1C3	GABRG1
2648	5741	Q8N1E2	LYG1
2649	5742	Q8N2K0	ABHD12
2650	5743	Q8N2Q7	NLGN1
2651	5744	Q8N302	AGGF1
2652	5745	Q8N387	MUC15
2653	5746	Q8N3H0	FAM19A2
2654	5747	Q8N3Z0	PRSS35
2655	5748	Q8N436	CPXM2
2656	5749	Q8N474	SFRP1
2657	5750	Q8N4F0	BPIFB2
2658	5751	Q8N4T0	CPA6
2659	5752	Q8N539	FIBCD1
2660	5753	Q8N5I4	DHRSX
2661	5754	Q8N5W8	FAM24B
2662	5755	Q8N608	DPP10
2663	5756	Q8N695	SLC5A8
2664	5757	Q8N6F1	CLDN19
2665	5758	Q8N766	EMC1
2666	5759	Q8N807	PDILT
2667	5760	Q8N9M5	TMEM102
2668	5761	Q8NA29	MFSD2A
2669	5762	Q8NA58	PNLDC1
2670	5763	Q8NB37	GATD1
2671	5764	Q8NBJ9	SIDT2
2672	5765	Q8NBK3	SUMF1
2673	5766	Q8NBL1	POGLUT1
2674	5767	Q8NBQ5	HSD17B11
2675	5768	Q8NC42	RNF149
2676	5769	Q8NC54	KCT2
2677	5770	Q8NC67	NETO2
2678	5771	Q8NCS7	SLC44A5
2679	5772	Q8NCW5	NAXE
2680	5773	Q8NDZ4	C3orf58
2681	5774	Q8NE79	BVES

TABLE 1-continued

Representative list of DNA and protein sequences amplified for the initial and expanded libraries.

Seq. Id. No. (protein)	Seq. Id. No. (DNA)	Uniprot ID	Gene Symbol
2682	5775	Q8NEA5	C19orf18
2683	5776	Q8NEB7	ACRBP
2684	5777	Q8NER1	TRPV1
2685	5778	Q8NER5	ACVR1C
2686	5779	Q8NET1	DEFB108B
2687	5780	Q8NEX5	WFDC9
2688	5781	Q8NEX6	WFDC11
2689	5782	Q8NF86	PRSS33
2690	5783	Q8NFJ6	PROKR2
2691	5784	Q8NFQ5	BPIFB6
2692	5785	Q8NFU4	FDCSP
2693	5786	Q8NFZ6	VN1R2
2694	5787	Q8NI22	MCFD2
2695	5788	Q8TAA1	RNASE11
2696	5789	Q8TAF8	LHFPL5
2697	5790	Q8TAL6	FIBIN
2698	5791	Q8TAV5	C11orf45
2699	5792	Q8TAX7	MUC7
2700	5793	Q8TB22	SPATA20
2701	5794	Q8TB96	ITFG1
2702	5795	Q8TBP5	FAM174A
2703	5796	Q8TCC7	SLC22A8
2704	5797	Q8TCP9	FAM200A
2705	5798	Q8TCW7	ZPLD1
2706	5799	Q8TCW9	PROKR1
2707	5800	Q8TCZ2	CD99L2
2708	5801	Q8TD06	AGR3
2709	5802	Q8TD07	RAET1E
2710	5803	Q8TD20	SLC2A12
2711	5804	Q8TDE3	RNASE8
2712	5805	Q8TDL5	BPIFB1
2713	5806	Q8TDN2	KCNV2
2714	5807	Q8TE23	TAS1R2
2715	5808	Q8TE56	ADAMTS17
2716	5809	Q8TE57	ADAMTS16
2717	5810	Q8TE58	ADAMTS15
2718	5811	Q8TE60	ADAMTS18
2719	5812	Q8TEB7	RNF128
2720	5813	Q8TEB9	RHBDD1
2721	5814	Q8WTR4	GDPD5
2722	5815	Q8WTV0	SCARB1
2723	5816	Q8WU39	MZB1
2724	5817	Q8WUF8	FAM172A
2725	5818	Q8WUJ1	CYB5D2
2726	5819	Q8WUM4	PDCD6IP
2727	5820	Q8WUM9	SLC20A1
2728	5821	Q8WWA0	ITLN1
2729	5822	Q8WWF1	C1orf54
2730	5823	Q8WWQ2	HPSE2
2731	5824	Q8WWU7	ITLN2
2732	5825	Q8WWY7	WFDC12
2733	5826	Q8WWY8	LIPH
2734	5827	Q8WX39	LCN9
2735	5828	Q8WXA8	HTR3C
2736	5829	Q8WXD2	SCG3
2737	5830	Q8WXQ8	CPA5
2738	5831	Q8WXS8	ADAMTS14
2739	5832	Q8WXW3	PIBF1
2740	5833	Q8WZ59	TMEM190
2741	5834	Q8WZ79	DNASE2B
2742	5835	Q92484	SMPDL3A
2743	5836	Q92520	FAM3C
2744	5837	Q92537	SUSD6
2745	5838	Q92542	NCSTN
2746	5839	Q92563	SPOCK2
2747	5840	Q92629	SGCD
2748	5841	Q92765	FRZB
2749	5842	Q92781	RDH5
2750	5843	Q92820	GGH
2751	5844	Q92874	DNASE1L2
2752	5845	Q92876	KLK6

TABLE 1-continued

Representative list of DNA and protein sequences amplified for the initial and expanded libraries.

Seq. Id. No. (protein)	Seq. Id. No. (DNA)	Uniprot ID	Gene Symbol
2753	5846	Q92911	SLC5A5
2754	5847	Q92932	PTPRN2
2755	5848	Q92959	SLCO2A1
2756	5849	Q92982	NINJ1
2757	5850	Q93070	ART4
2758	5851	Q93086	P2RX5
2759	5852	Q93091	RNASE6
2760	5853	Q93098	WNT8B
2761	5854	Q96A33	CCDC47
2762	5855	Q96A84	EMID1
2763	5856	Q96AY3	FKBP10
2764	5857	Q96B33	CLDN23
2765	5858	Q96B86	RGMA
2766	5859	Q96BD0	SLCO4A1
2767	5860	Q96BQ1	FAM3D
2768	5861	Q96CG8	CTHRC1
2769	5862	Q96D15	RCN3
2770	5863	Q96DA0	ZG16B
2771	5864	Q96DB9	FXYD5
2772	5865	Q96DD7	SHISA4
2773	5866	Q96DN0	ERP27
2774	5867	Q96DR5	BPIFA2
2775	5868	Q96DR8	MUCL1
2776	5869	Q96DX4	RSPRY1
2777	5870	Q96DZ1	ERLEC1
2778	5871	Q96EE4	CCDC126
2779	5872	Q96EG1	ARSG
2780	5873	Q96EP9	SLC10A4
2781	5874	Q96F05	C11orf24
2782	5875	Q96FT7	ASIC4
2783	5876	Q96GC9	VMP1
2784	5877	Q96GX1	TCTN2
2785	5878	Q96HE7	ERO1A
2786	5879	Q96HF1	SFRP2
2787	5880	Q96HH4	TMEM169
2788	5881	Q96HP4	OXNAD1
2789	5882	Q96HV5	TMEM41A
2790	5883	Q96HY6	DDRGK1
2791	5884	Q96IY4	CPB2
2792	5885	Q96J42	TXNDC15
2793	5886	Q96JB6	LOXL4
2794	5887	Q96JW4	SLC41A2
2795	5888	Q96K78	ADGRG7
2796	5889	Q96KA5	CLPTM1L
2797	5890	Q96KN2	CNDP1
2798	5891	Q96KX0	LYZL4
2799	5892	Q96L08	SUSD3
2800	5893	Q96L12	CALR3
2801	5894	Q96L15	ART5
2802	5895	Q96LB9	PGLYRP3
2803	5896	Q96LR4	FAM19A4
2804	5897	Q96LT7	C9orf72
2805	5898	Q96MK3	FAM20A
2806	5899	Q96MU5	C17orf77
2807	5900	Q96NZ9	PRAP1
2808	5901	Q96P44	COL21A1
2809	5902	Q96PB7	OLFM3
2810	5903	Q96PC5	MIA2
2811	5904	Q96PD2	DCBLD2
2812	5905	Q96PH1	NOX5
2813	5906	Q96PL1	SCGB3A2
2814	5907	Q96PL2	TECTB
2815	5908	Q96PS8	AQP10
2816	5909	Q96PZ7	CSMD1
2817	5910	Q96QD8	SLC38A2
2818	5911	Q96QE2	SLC2A13
2819	5912	Q96QR1	SCGB3A1
2820	5913	Q96QZ0	PANX3
2821	5914	Q96RQ9	IL4I1
2822	5915	Q96S42	NODAL
2823	5916	Q96S66	CLCC1

TABLE 1-continued

Representative list of DNA and protein sequences amplified for the initial and expanded libraries.

Seq. Id. No. (protein)	Seq. Id. No. (DNA)	Uniprot ID	Gene Symbol
2824	5917	Q96SL4	GPX7
2825	5918	Q96T91	GPHA2
2826	5919	Q99217	AMELX
2827	5920	Q99218	AMELY
2828	5921	Q99470	SDF2
2829	5922	Q99519	NEU1
2830	5923	Q99523	SORT1
2831	5924	Q99538	LGMN
2832	5925	Q99542	MMP19
2833	5926	Q99571	P2RX4
2834	5927	Q99572	P2RX7
2835	5928	Q99584	S100A13
2836	5929	Q99674	CGREF1
2837	5930	Q99727	TIMP4
2838	5931	Q99784	OLFM1
2839	5932	Q99835	SMO
2840	5933	Q99884	SLC6A7
2841	5934	Q99895	CTRC
2842	5935	Q99943	AGPAT1
2843	5936	Q99954	SMR3A
2844	5937	Q99969	RARRES2
2845	5938	Q99972	MYOC
2846	5939	Q9BPW4	APOL4
2847	5940	Q9BQ08	RETNLB
2848	5941	Q9BQ16	SPOCK3
2849	5942	Q9BQB4	SOST
2850	5943	Q9BQI4	CCDC3
2851	5944	Q9BQS7	HEPH
2852	5945	Q9BQT9	CLSTN3
2853	5946	Q9BQY6	WFDC6
2854	5947	Q9BRK5	SDF4
2855	5948	Q9BRN9	TM2D3
2856	5949	Q9BRR6	ADPGK
2857	5950	Q9BS26	ERP44
2858	5951	Q9BSA4	TTYH2
2859	5952	Q9BSG0	PRADC1
2860	5953	Q9BSG5	RTBDN
2861	5954	Q9BSJ5	C17orf80
2862	5955	Q9BSN7	TMEM204
2863	5956	Q9BT09	CNPY3
2864	5957	Q9BT56	SPX
2865	5958	Q9BTY2	FUCA2
2866	5959	Q9BU40	CHRDL1
2867	5960	Q9BUR5	APOO
2868	5961	Q9BV94	EDEM2
2869	5962	Q9BWS9	CHID1
2870	5963	Q9BX73	TM2D2
2871	5964	Q9BX74	TM2D1
2872	5965	Q9BX93	PLA2G12B
2873	5966	Q9BX97	PLVAP
2874	5967	Q9BXI9	C1QTNF6
2875	5968	Q9BXJ1	C1QTNF1
2876	5969	Q9BXJ2	C1QTNF7
2877	5970	Q9BXJ4	C1QTNF3
2878	5971	Q9BXR6	CFHR5
2879	5972	Q9BXS4	TMEM59
2880	5973	Q9BXY4	RSPO3
2881	5974	Q9BYE2	TMPRSS13
2882	5975	Q9BYE9	CDHR2
2883	5976	Q9BZD6	PRRG4
2884	5977	Q9BZD7	PRRG3
2885	5978	Q9BZG2	ACP4
2886	5979	Q9BZM1	PLA2G12A
2887	5980	Q9BZM2	PLA2G2F
2888	5981	Q9BZM5	ULBP2
2889	5982	Q9BZM6	ULBP1
2890	5983	Q9C0B6	BRINP2
2891	5984	Q9C0H2	TTYH3
2892	5985	Q9C0K1	SLC39A8
2893	5986	Q9GZM7	TINAGL1
2894	5987	Q9GZN4	PRSS22

TABLE 1-continued

Representative list of DNA and protein sequences amplified for the initial and expanded libraries.

Seq. Id. No. (protein)	Seq. Id. No. (DNA)	Uniprot ID	Gene Symbol
2895	5988	Q9GZT5	WNT10A
2896	5989	Q9GZX9	TWSG1
2897	5990	Q9GZZ6	CHRNA10
2898	5991	Q9GZZ8	LACRT
2899	5992	Q9H015	SLC22A4
2900	5993	Q9H0B8	CRISPLD2
2901	5994	Q9H0U3	MAGT1
2902	5995	Q9H0X4	FAM234A
2903	5996	Q9H112	CST11
2904	5997	Q9H114	CSTL1
2905	5998	Q9H173	SIL1
2906	5999	Q9H1A3	METTL9
2907	6000	Q9H1E1	RNASE7
2908	6001	Q9H1F0	WFDC10A
2909	6002	Q9H1J7	WNT5B
2910	6003	Q9H1M3	DEFB129
2911	6004	Q9H1Z8	C2orf40
2912	6005	Q9H221	ABCG8
2913	6006	Q9H2J7	SLC6A15
2914	6007	Q9H2R5	KLK15
2915	6008	Q9H2U9	ADAM7
2916	6009	Q9H306	MMP27
2917	6010	Q9H336	CRISPLD1
2918	6011	Q9H3G5	CPVL
2919	6012	Q9H3N1	TMX1
2920	6013	Q9H3S3	TMPRSS5
2921	6014	Q9H3U7	SMOC2
2922	6015	Q9H3Y0	R3HDML
2923	6016	Q9H461	FZD8
2924	6017	Q9H497	TOR3A
2925	6018	Q9H4A4	RNPEP
2926	6019	Q9H4B8	DPEP3
2927	6020	Q9H4D0	CLSTN2
2928	6021	Q9H4F8	SMOC1
2929	6022	Q9H4G1	CST9L
2930	6023	Q9H5V8	CDCP1
2931	6024	Q9H6B9	EPHX3
2932	6025	Q9H6E4	CCDC134
2933	6026	Q9H741	C12orf49
2934	6027	Q9H772	GREM2
2935	6028	Q9H7B7	C7orf69
2936	6029	Q9H8H3	METTL7A
2937	6030	Q9H8J5	MANSC1
2938	6031	Q9H9K5	ERVMER34-1
2939	6032	Q9HAT2	SIAE
2940	6033	Q9HAW8	UGT1A10
2941	6034	Q9HAW9	UGT1A8
2942	6035	Q9HB40	SCPEP1
2943	6036	Q9HBJ0	PLAC1
2944	6037	Q9HBL7	PLGRKT
2945	6038	Q9HBV2	SPACA1
2946	6039	Q9HC23	PROK2
2947	6040	Q9HC57	WFDC1
2948	6041	Q9HC58	SLC24A3
2949	6042	Q9HCB6	SPON1
2950	6043	Q9HCC8	GDPD2
2951	6044	Q9HCN8	SDF2L1
2952	6045	Q9HCX4	TRPC7
2953	6046	Q9HD89	RETN
2954	6047	Q9HDC9	APMAP
2955	6048	Q9NNX1	TUFT1
2956	6049	Q9NP55	BPIFA1
2957	6050	Q9NP70	AMBN
2958	6051	Q9NP91	SLC6A20
2959	6052	Q9NPA0	EMC7
2960	6053	Q9NPA1	KCNMB3
2961	6054	Q9NPD5	SLCO1B3
2962	6055	Q9NPH5	NOX4
2963	6056	Q9NPH6	OBP2B
2964	6057	Q9NQ30	ESM1
2965	6058	Q9NQ34	TMEM9B

TABLE 1-continued

Representative list of DNA and protein sequences amplified for the initial and expanded libraries.

Seq. Id. No. (protein)	Seq. Id. No. (DNA)	Uniprot ID	Gene Symbol
2966	6059	Q9NQ38	SPINK5
2967	6060	Q9NQ40	SLC52A3
2968	6061	Q9NQ60	EQTN
2969	6062	Q9NQ76	MEPE
2970	6063	Q9NQ90	ANO2
2971	6064	Q9NQE7	PRSS16
2972	6065	Q9NQX5	NPDC1
2973	6066	Q9NRC9	OTOR
2974	6067	Q9NRE1	MMP26
2975	6068	Q9NRM1	ENAM
2976	6069	Q9NRN5	OLFML3
2977	6070	Q9NRR1	CYTL1
2978	6071	Q9NRS4	TMPRSS4
2979	6072	Q9NS71	GKN1
2980	6073	Q9NSA0	SLC22A11
2981	6074	Q9NSD5	SLC6A13
2982	6075	Q9NT22	EMILIN3
2983	6076	Q9NTU7	CBLN4
2984	6077	Q9NU53	GINM1
2985	6078	Q9NUN5	LMBRD1
2986	6079	Q9NW15	ANO10
2987	6080	Q9NWH7	SPATA6
2988	6081	Q9NWM8	FKBP14
2989	6082	Q9NX61	TMEM161A
2990	6083	Q9NXC2	GFOD1
2991	6084	Q9NY37	ASIC5
2992	6085	Q9NY91	SLC5A4
2993	6086	Q9NYL4	FKBP11
2994	6087	Q9NZ20	PLA2G3
2995	6088	Q9NZ53	PODXL2
2996	6089	Q9NZ94	NLGN3
2997	6090	Q9NZG7	NINJ2
2998	6091	Q9NZK5	ADA2
2999	6092	Q9NZK7	PLA2G2E
3000	6093	Q9NZP8	C1RL
3001	6094	Q9NZQ8	TRPM5
3002	6095	Q9P0G3	KLK14
3003	6096	Q9P0L9	PKD2L1
3004	6097	Q9P2E8	MARCHF4
3005	6098	Q9P2K2	TXNDC16
3006	6099	Q9UBC7	GALP
3007	6100	Q9UBD9	CLCF1
3008	6101	Q9UBN1	CACNG4
3009	6102	Q9UBN4	TRPC4
3010	6103	Q9UBP4	DKK3
3011	6104	Q9UBR2	CTSZ
3012	6105	Q9UBS3	DNAJB9
3013	6106	Q9UBS4	DNAJB11
3014	6107	Q9UBT3	DKK4
3015	6108	Q9UBU2	DKK2
3016	6109	Q9UBV4	WNT16
3017	6110	Q9UEW3	MARCO
3018	6111	Q9UGM1	CHRNA9
3019	6112	Q9UHC3	ASIC3
3020	6113	Q9UHG3	PCYOX1
3021	6114	Q9UHI8	ADAMTS1
3022	6115	Q9UHL4	DPP7
3023	6116	Q9UHM6	OPN4
3024	6117	Q9UI38	PRSS50
3025	6118	Q9UI42	CPA4
3026	6119	Q9UIG8	SLCO3A1
3027	6120	Q9UJ14	GGT7
3028	6121	Q9UJA9	ENPP5
3029	6122	Q9UJJ9	GNPTG
3030	6123	Q9UJQ1	LAMP5
3031	6124	Q9UJW2	TINAG
3032	6125	Q9UK28	TMEM59L
3033	6126	Q9UK55	SERPINA10
3034	6127	Q9UK85	DKKL1
3035	6128	Q9UKI3	VPREB3
3036	6129	Q9UKQ9	KLK9

TABLE 1-continued

Representative list of DNA and protein sequences amplified for the initial and expanded libraries.

Seq. Id. No. (protein)	Seq. Id. No. (DNA)	Uniprot ID	Gene Symbol
3037	6130	Q9UKR3	KLK13
3038	6131	Q9UKU6	TRHDE
3039	6132	Q9UKY0	PRND
3040	6133	Q9UKZ9	PCOLCE2
3041	6134	Q9UL01	DSE
3042	6135	Q9UL52	TMPRSS11E
3043	6136	Q9UL62	TRPC5
3044	6137	Q9ULV1	FZD4
3045	6138	Q9ULW2	FZD10
3046	6139	Q9ULX7	CA14
3047	6140	Q9UM22	EPDR1
3048	6141	Q9UMR5	PPT2
3049	6142	Q9UMX5	NENF
3050	6143	Q9UN76	SLC6A14
3051	6144	Q9UN88	GABRQ
3052	6145	Q9UNI1	CELA1
3053	6146	Q9UNK4	PLA2G2D
3054	6147	Q9UNQ0	ABCG2
3055	6148	Q9UNW1	MINPP1
3056	6149	Q9UQF0	ERVW-1
3057	6150	Q9UQQ1	NAALADL1
3058	6151	Q9Y215	COLQ
3059	6152	Q9Y251	HPSE
3060	6153	Q9Y267	SLC22A14
3061	6154	Q9Y2B0	CNPY2
3062	6155	Q9Y2B1	RXYLT1
3063	6156	Q9Y2E5	MAN2B2
3064	6157	Q9Y2G5	POFUT2
3065	6158	Q9Y2G8	DNAJC16
3066	6159	Q9Y320	TMX2
3067	6160	Q9Y337	KLK5
3068	6161	Q9Y345	SLC6A5
3069	6162	Q9Y394	DHRS7
3070	6163	Q9Y4K0	LOXL2
3071	6164	Q9Y561	LRP12
3072	6165	Q9Y5I7	CLDN16
3073	6166	Q9Y5K2	KLK4
3074	6167	Q9Y5L3	ENTPD2
3075	6168	Q9Y5S8	NOX1
3076	6169	Q9Y5X9	LIPG
3077	6170	Q9Y5Y6	ST14
3078	6171	Q9Y5Y7	LYVE1
3079	6172	Q9Y5Z0	BACE2
3080	6173	Q9Y625	GPC6
3081	6174	Q9Y646	CPQ
3082	6175	Q9Y680	FKBP7
3083	6176	Q9Y691	KCNMB2
3084	6177	Q9Y693	LHFPL6
3085	6178	Q9Y6C5	PTCH2
3086	6179	Q9Y6I9	TEX264
3087	6180	Q9Y6L6	SLCO1B1
3088	6181	Q9Y6M0	PRSS21
3089	6182	Q9Y6M7	SLC4A7
3090	6183	Q9Y6U7	RNF215
3091	6184	Q9Y6X5	ENPP4
3092	6185	Q9Y6Y9	LY96

[0424] Library Construction:

[0425] A two-step PCR process was used to amplify cDNAs for cloning into a barcoded yeast-display vector. cDNAs were amplified with gene-specific primers, with the forward primer containing a 5' sequence (CTGTTAT-TGCTAGCGTTTTAGCA (SEQ ID NO: 6186)) and the reverse primer containing a 5' sequence (GC-CACCAGAAGCGGCCGC (SEQ ID NO: 6187)) for template addition in the second step of PCR. PCR reactions were conducted using 1 μL pooled cDNA, gene-specific primers, and the following PCR settings: 98° C. denatur-

ation, 58° C. annealing, 72° C. extension, 35 rounds of amplification. 1 μL of PCR product was used for direct amplification by common primers Aga2FOR and 159REV, and the following PCR settings: 98° C. denaturation, 58° C. annealing, 72° C. extension, 35 rounds of amplification. PCR product was purified using magnetic PCR purification beads (AvanBio). 90 μL beads were added to the PCR product and supernatant was removed. Beads were washed twice with 200 μL 70% ethanol and resuspended in 50 μL water to elute PCR products from the beads. Beads were removed from purified PCR products. The 15 bp barcode fragment was constructed by overlap PCR. 4 primers (bc1, bc2, bc3, bc4) were mixed in equimolar ratios and used as template for a PCR reaction using the following PCR settings: 98° C. denaturation, 55° C. annealing, 72° C. extension, 35 rounds of amplification. Purified product was reamplified with the first and fourth primer using identical PCR conditions. PCR products were run on 2% agarose gels and purified by gel extraction (Qiagen). Purified barcode and gene products were combined with linearized yeast-display vector (pDD003 digested with EcoRI and BamHI) and electroporated into JAR300 yeast cell using a 96-well electroporater (BTX Harvard Apparatus) using the following electroporation conditions: Square wave, 500 V, 5 ms pulse, 2 mm gap. Yeast cell were immediately recovered into 1 mL liquid synthetic dextrose medium lacking uracil (SDO-Ura) in 96-well deepwell blocks and grown overnight at 30° C. Yeast cell were passaged once by 1:10 dilution in SDO-Ura, then frozen as glycerol stocks. To construct the final library, 2.5 μL of all wells except 32 containing genes previously identified as incompatible with high-quality yeast cell display were pooled and counted. A limited dilution of 56,000 clones was sub-sampled and expanded in SDO-Ura. Expression was induced by passaging into synthetic galactose medium lacking uracil (SGO-Ura) at a 1:10 dilution and growing at 30° C. overnight. 10^8 yeast cell were pelleted and resuspend in 1 mL PBE (PBS with 0.5% BSA and 0.5 mM EDTA) containing 1:100 anti-FLAG PE antibody (BioLegend). Yeast cell were stained at 4° C. for 75 minutes, then washed twice with 1 mL PBE and sorted for FLAG display on a Sony SH800Z cell sorter. Sorted cells were expanded in SDO-Ura supplemented with 35 μg/mL chloramphenicol, expanded, and frozen as the final library.

(SEQ ID NO: 6188)
bc1-TTGTTAATATACCTCTATACTTTAACGTCAAGGAGAAAAAACCCCG

GATC

(SEQ ID NO: 6189)
bc2-CTGCATCCTTTAGTGAGGGTTGAANNNNNNNNNNNNNNNTTCGATC

CGGGGTTTTTTCTCCTTG

(SEQ ID NO: 6190)
bc3-TTCAACCCTCACTAAAGGATGCAGTTACTTCGCTGTTTTTCAATAT

TTTCTGTTATTGC

(SEQ ID NO: 6191)
bc4-TGCTAAAACGCTAGCAATAACAGAAAATATTGAAAAACAGCG

[0426] Barcode Identification:

[0427] Barcode-gene pairings were identified using a custom Tn5-based sequence approach. Tn5 transposase was purified as previously described, using the on-column assembly method for loading oligos. DNA was extracted from the yeast library using Zymoprep-96 Yeast Plasmid Miniprep kits or Zymoprep Yeast Plasmid Miniprep II kits (Zymo Research) according to standard manufacturer protocols. 5 μL of purified plasmid DNA was digested with Tn5 in a 20 μL total reaction as previously described. 2 μL of digested DNA was amplified using primers index1 and index2, using the following PCR settings: 98° C. denaturation, 56° C. annealing, 72° C. extension, 25 rounds of amplification. The product was run on a 2% gel and purified by gel extraction (Qiagen). Purified product was amplified using primers index3 and index4, using the following PCR settings: 98° C. denaturation, 60° C. annealing, 72° C. extension, 25 rounds of amplification. In parallel, the barcode region alone was amplified using primers index1 and index5, using the following PCR settings: 98° C. denaturation, 56° C. annealing, 72° C. extension, 25 rounds of amplification. The product was run on a 2% gel and purified by gel extraction (Qiagen). Purified product was amplified using primers index3 and index6, using the following PCR settings: 98° C. denaturation, 60° C. annealing, 72° C. extension, 20 rounds of amplification. Both barcode and digested fragment products were run on a 2% gel and purified by gel extraction (Qiagen). NGS library was sequenced using an Illumina MiSeq and Illumina v3 MiSeq Reagent Kits with 150 base pair single-end sequencing according to standard manufacturer protocols. Gene-barcode pairings were identified using custom code. Briefly, from each read, the barcode sequence was extracted based on the identification of the flanking constant vector backbone sequences, and the first 25 bp of sequence immediately following the constant vector backbone-derived signal peptide were extracted and mapped to a gene identity based on the first 25 bp of all amplified cDNA constructs. The number of times each barcode was paired with an identified gene was calculated. Barcode-gene pairings that were identified more than twice, with an overall observed barcode frequency of greater than 0.0002% were compiled. For barcodes with multiple gene pairings matching the above criteria, the best-fit gene was manually identified by inspection of all barcode-gene pairing frequencies and, in general, identification of the most abundant gene pairing. In the final library, 2,688 genes were confidently mapped to 35,835 barcodes.

[0428] Rapid Extracellular Antigen Profiling.

[0429] Antibody Purification and Yeast Cell Adsorption

[0430] 20 μL protein G magnetic resin (Lytic Solutions) was washed twice with 100 μL sterile PBS, resuspended in 50 μL PBS, and added to 50 μL serum or plasma. Serum-resin mixture was incubated for three hours at 4° C. with shaking. Resin was washed five times with 200 μL PBS, resuspended in 90 μL 100 mM glycine pH 2.7, and incubated for five minutes at room temperature. Supernatant was extracted and added to 10 μL sterile 1M Tris pH 8.0 (purified IgG). Empty vector (pDD003) yeast cell were expanded in SDO-Ura at 30° C. One day later, yeast cell were induced by 1:10 dilution in SGO-Ura for 24 hours. 10^8 induced yeast cell were washed twice with 200 μL PBE (PBS with 0.5% BSA and 0.5 mM EDTA), resuspended with 100 μL purified IgG, and incubated for three hours at 4° C. with shaking. Yeast-IgG mixtures were placed into 96 well 0.45 um filter plates (Thomas Scientific) and yeast-depleted IgG was eluted into sterile 96 well plates by centrifugation at 3000 g for 3 minutes.

[0431] Antibody Yeast Library Selections.

[0432] Transformed yeast were expanded in SDO-Ura at 30° C. One day later, at an optical density (OD) below 8, yeast were induced by resuspension at an OD of 1 in SGO-Ura supplemented with ten percent SDO-Ura and culturing at 30° C. for 20 hours. Prior to selection, 400 μL pre-selection library was set aside to allow for comparison to post-selection libraries. 10^8 induced yeast were washed twice with 200 μL PBE and added to wells of a sterile 96-well v-bottom microtiter plate. Yeast were resuspended in 100 μL PBE containing appropriate antibody concentration and incubated with shaking for 1 hour at 4° C. Unless otherwise indicated, 10 μg antibody per well was used for human serum or plasma derived antibodies and 1 μg antibody was used for monoclonal antibodies. Yeast were washed twice with 200 μL PBE, resuspended in 100 μL PBE with a 1:100 dilution of biotin anti-human IgG Fc antibody (clone HP6017, BioLegend) for human serum or plasma derived antibodies or a 1:25 dilution of biotin goat anti-rat or anti-mouse IgG antibody (A16088, Thermo Fisher Scientific; A18869, Thermo Fisher Scientific) for monoclonal antibodies. Yeast-antibody mixtures were incubated with shaking for 30 minutes at 4° C. Yeast were washed twice with 200 μL PBE, resuspended in 100 μL PBE with a 1:20 dilution of Streptavidin MicroBeads (Miltenyi Biotec), and incubated with shaking for 30 minutes at 4° C. Yeast were then pelleted and kept on ice. Multi-96 Columns (Miltenyi Biotec) were placed into a MultiMACS M96 Separator (Miltenyi Biotec) and the separator was placed into positive selection mode. All following steps were carried out at room temperature. Columns were equilibrated with 400 μL 70% ethanol followed by 700 μL degassed PBE. Yeast were resuspended in 200 μL degassed PBE and placed into the columns. After the mixture had completely passed through, columns were washed three times with 700 μL degassed PBE. To elute the selected yeast, columns were removed from the separator and placed over 96-well deep well plates. 700 μL degassed PBE was added to each well of the column and the column and deep well plate were spun at 50 g for 30 seconds. This process was repeated 3 times. Selected yeast were pelleted, and recovered in 1 mL SDO-Ura at 30° C.

[0433] Recombinant Protein Yeast Library Selections.

[0434] All pre-selection and yeast induction steps were performed identically as those of the antibody yeast library selections. 10^8 induced yeast were washed twice with 200 μL PBE and added to wells of a sterile 96-well v-bottom microtiter plate. Yeast were resuspended in 100 μL PBE containing 75 μL clarified protein expression supernatant and incubated with shaking for 1 hour at 4° C. Yeast were washed twice with 200 μL PBE, resuspended in 100 μL PBE with 5 μL MACS Protein G MicroBeads (Miltenyi Biotec), and incubated with shaking for 30 minutes at 4° C. Selection of yeast using the MultiMACS M96 Separator and subsequent steps were performed identically as those of the antibody yeast library selections.

[0435] Next Generation Sequencing Library Preparation and Sequencing.

[0436] DNA was extracted from yeast libraries using Zymoprep-96 Yeast Plasmid Miniprep kits or Zymoprep Yeast Plasmid Miniprep II kits (Zymo Research) according to standard manufacturer protocols. A first round of PCR was used to amplify a DNA sequence containing the protein display barcode on the yeast plasmid. PCR reactions were conducted using 1 μL plasmid DNA, 159_DIF2 and 159_DIR2 primers (sequences listed below), and the following PCR settings: 98° C. denaturation, 58° C. annealing, 72° C. extension, 25 rounds of amplification. PCR product was purified using magnetic PCR purification beads (AvanBio). 45 μL beads were added to the PCR product and supernatant was removed. Beads were washed twice with 100 μL 70% ethanol and resuspended in 25 μL water to elute PCR products from the beads. Beads were removed from purified PCR products. A second round of PCR was conducted using 1 μL purified PCR product, Nextera i5 and i7 dual-index library primers (Illumina), and the following PCR settings: 98° C. denaturation, 58° C. annealing, 72° C. extension, 25 rounds of amplification. PCR products were pooled and run on a 1% agarose gel. The band corresponding to 257 base pairs was cut out and DNA (NGS library) was extracted using a QIAquick Gel Extraction Kit (Qiagen) according to standard manufacturer protocols. NGS library was sequenced using an Illumina MiSeq and Illumina v3 MiSeq Reagent Kits with 75 base pair single-end sequencing or using an Illumina NovaSeq 6000 and Illumina NovaSeq S4 200 cycle kit with 101 base pair paired-end sequencing according to standard manufacturer protocols. A minimum of 50,000 reads per sample was collected and the pre-selection library was sampled at ten times greater depth than other samples.

(SEQ ID NO: 6192)
159_DIF2-TCGTCGGCAGCGTCAGATGTGTATAAGAGACAGNNNNNNNN

NNGAGAAAAAACCCCGGATCG

(SEQ ID NO: 6193)
159_DIR2-GTCTCGTGGGCTCGGAGATGTGTATAAGAGACAGNNNNNNN

NNNACGCTAGCAATAACAGAAAATATTG

[0437] Data Analysis.

[0438] REAP scores were calculated as follows. First, barcode counts were extracted from raw NGS data using custom codes and counts from technical replicates were summed. Next, aggregate and clonal enrichment was calculated using edgeR[62] and custom codes. For aggregate enrichment, barcode counts across all unique barcodes associated with a given protein were summed, library sizes across samples were normalized using default edgeR parameters, common and tagwise dispersion were estimated using default edgeR parameters, and exact tests comparing each sample to the pre-selection library were performed using default edgeR parameters. Aggregate enrichment is thus the log 2 fold change values from these exact tests with zeroes in the place of negative fold changes. Log 2 fold change values for clonal enrichment were calculated in an identical manner, but barcode counts across all unique barcodes associated with a given protein were not summed. Clonal enrichment for a given reactivity was defined as the fraction of clones out of total clones that were enriched (log 2 fold change ≥2). Aggregate (E_a) and clonal enrichment (E_c) for a given protein, a scaling factor (β_u) based on the number of unique yeast clones (yeast that have a unique DNA barcode) displaying a given protein, and a scaling factor (β_f) based on the overall frequency of yeast in the library displaying a given protein were used as inputs to calculate the REAP score, which is defined as follows.

$$\text{REAP score} = E_a * (E_c)^2 * \beta_u * \beta_f$$

[0439] β_u and β_f are logarithmic scaling factors that progressively penalize the REAP score of proteins with low numbers of unique barcodes or low frequencies in the library. β_u is applied to proteins with ≤5 unique yeast clones in the library and β_f is applied to proteins with a frequency ≤0.0001 in the library. β_f was implemented to mitigate spurious enrichment signals from low frequency proteins, which could occur due to sequencing errors or stochasticity in the selection process. β_u was implemented because the clonal enrichment metric is less valid for proteins with low numbers of unique yeast clones, decreasing confidence in the validity of the reactivity. β_u and β_f are defined as follows where x_u is the number of unique yeast clones for a given protein and x_f is the log 10 transformed frequency of a given protein in the library.

$$\beta_u = \frac{\ln(x_u + 0.5)}{1.705}$$

$$\beta_f = \frac{\ln(x_f + 7.1)}{1.16}$$

[0440] Recombinant Protein Production.

[0441] REAP Recombinant Protein Production.

[0442] Proteins were produced as human IgG1 Fc fusions to enable binding of secondary antibody and magnetic beads to the produced proteins during the REAP process. Sequences encoding the extracellular portions of proteins-of-interests that were present in the yeast display library were cloned by Gibson assembly into a modified pD2610-v12 plasmid (ATUM). Modifications include addition of an H7 signal sequence followed by a $(GGGGS)_3$ linker and a truncated human IgG1 Fc (N297A). Protein-of-interest sequences were inserted directly downstream of the H7 leader sequence. Protein was produced by transfection into Expi293 cells (Thermo Fisher Scientific) in 96-well plate format. One day prior to transfection, cells were seeded at a density of 2 million cells per mL in Expi293 Expression Medium (Thermo Fisher Scientific). In a 96-well plate, 0.5 μg plasmid DNA was diluted added to 25 μL Opti-MEM (Thermo Fisher Scientific) and mixed gently. In a separate 96-well plate, 1.35 μL ExpiFectamine was added to 25 μL Opti-MEM and mixed gently. The ExpiFectamine-Opti-MEM mixture was added to the diluted DNA, mixed gently, and incubated for 20 minutes at room temperature. Expi293 cells were diluted to a density of 2.8 million cells per mL and 500 L of cells were added to each well of a 96-well deep well plate. 50 μL of the DNA-ExpiFectamine-Opti-MEM mixture was added to each well. The plate was sealed with Breathe-Easier sealing film (Diversified Biotech) and incubated in a humidified tissue culture incubator (37° C., 8% CO_2) with shaking at 1,200 rpm so that cells were kept in suspension. 18-20 hours post-transfection, 25 μL enhancer 2 and 2.5 μL enhancer 1 (Thermo Fisher Scientific) were added to each well. 4 days post-transfection, media was clarified by centrifugation at 3000-4000 g for 5 minutes. Clarified media was used for recombinant protein REAP.

[0443] ELISA Protein Production.

[0444] Sequences encoding the extracellular portions of proteins-of-interests that were present in the yeast display library were cloned by Gibson assembly into pEZT_Dlux, a modified pEZT-BM vector. The pEZT-BM vector was a gift from Ryan Hibbs (Addgene plasmid #74099). Modifications included insertion of an H7 Leader Sequence followed by an AviTag (Avidity), HRV 3C site, protein C epitope, and an 8×his tag. Protein-of-interest sequences were inserted directly downstream of the H7 leader sequence. Protein was produced by transfection into Expi293 cells (Thermo Fisher Scientific) according to standard manufacturer protocols. Transfected cells were maintained according to manufacturer protocols. 4 days post-transfection, media was clarified by centrifugation at 300 g for 5 minutes. Protein was purified from clarified media by nickel-nitrilotriacetic acid (Ni-NTA) chromatography and desalted into HEPES buffered saline+100 mM sodium chloride, pH 7.5. Protein purity was verified by SDS-PAGE.

[0445] Biotinylated Protein Production.

[0446] Sequences encoding the extracellular portions of proteins-of-interests were cloned into pEZT_Dlux as described above. Protein was expressed and purified as described above minus desalting. Enzymatic biotinylation with BirA ligase was performed and protein was purified by size-exclusion fast protein liquid chromatography using a NGC Quest 10 Chromatography System (Bio-Rad).

[0447] LIPS Protein Production.

[0448] Sequences encoding Lucia luciferase (InvivoGen) fused by a GGSG linker to the N-terminus of the protein-of-interest extracellular portion (as defined above) were cloned by Gibson assembly into pEZT-BM. Protein was produced by transfection into Expi293 cells (Thermo Fisher Scientific) according to standard manufacturer protocols. Transfected cells were maintained according to manufacturer protocols. 3 days post-transfection, media was clarified by centrifugation at 300 g for 5 minutes. Clarified media was used in luciferase immunoprecipitation systems assays.

[0449] Enzyme-Linked Immunosorbent Assays (ELISAs).

[0450] 200 or 400 ng of purchased or independently produced recombinant protein in 100 μL of PBS pH 7.0 was added to 96-well flat bottom Immulon 2HB plates (Thermo Fisher Scientific) and placed at 4° C. overnight. Plates were washed once with 225 μL ELISA wash buffer (PBS+0.05% Tween 20) and 150 μL ELISA blocking buffer (PBS+2% Human Serum Albumin) was added to the well. Plates were incubated with shaking for 2 hours at room temperature. ELISA blocking buffer was removed from the wells and appropriate dilutions of sample serum in 100 μL ELISA blocking buffer were added to each well. Plates were incubated with shaking for 2 hours at room temperature. Plates were washed 6 times with 225 μL ELISA wash buffer and 1:5000 goat anti-human IgG HRP (Millipore Sigma) or anti-human IgG isotype specific HRP (Southern Biotech; IgG1: clone HP6001, IgG2: clone 31-7-4, IgG3: clone HP6050, IgG4: clone HP6025) in 100 μL ELISA blocking buffer was added to the wells. Plates were incubated with shaking for 1 hour at room temperature. Plates were washed 6 times with 225 μL ELISA wash buffer. 50 μL TMB substrate (BD Biosciences) was added to the wells and plates were incubated for 15 minutes (pan-IgG ELISAs) or 20 minutes (isotype specific IgG ELISAs) in the dark at room temperature. 50 μL 1 M sulfuric acid was added to the wells and absorbance at 450 nm was measured in a Synergy HTX Multi-Mode Microplate Reader (BioTek).

[0451] Luciferase Immunoprecipitation Systems (LIPS) Assays.

[0452] Pierce Protein A/G Ultralink Resin (5 μL; Thermo Fisher Scientific) and 1 μL sample serum in 100 μL Buffer A (50 mM Tris, 150 mM NaCl, 0.1% Triton X-100, pH 7.5) was added to 96-well opaque Multiscreen HTS 96 HV 0.45

um filter plates (Millipore Sigma). Plates were incubated with shaking at 300 rpm for 1 hour at room temperature. Supernatant in wells was removed by centrifugation at 2000 g for 1 minute. Luciferase fusion protein (10^6 RLU) was added to the wells in 100 μL Buffer A. Plates were incubated with shaking at 300 rpm for 1 hour at room temperature. Using a vacuum manifold, wells were washed 8 times with 100 μL Buffer A followed by 2 washes with 100 μL PBS. Remaining supernatant in wells was removed by centrifugation at 2000 g for 1 minute. Plates were dark adapted for 5 minutes. An autoinjector equipped Synergy HTX Multi-Mode Microplate Reader (BioTek) was primed with QUANTI-Luc Gold (InvivoGen). Plates were read using the following per well steps: 50 μL QUANTI-Luc Gold injection, 4 second delay with shaking, read luminescence with an integration time of 0.1 seconds and a read height of 1 mm.

[0453] PD-L2 Blocking Assay.

[0454] A single clone of PD-L2 displaying yeast was isolated from the library and expanded in SDO-Ura at 30° C. Yeast were induced by 1:10 dilution into SGO-Ura and culturing at 30° C. for 24 hours. 105 induced PD-L1 yeast were washed twice with 200 μL PBE and added to wells of a 96-well v-bottom microtiter plate. Yeast were resuspended in 25 μL PBE containing serial dilutions of sample serum and incubated with shaking for 1 hour at 4° C. PD-1 tetramers were prepared by incubating a 5:1 ratio of biotinylated PD-1 and PE streptavidin (BioLegend) for 10 minutes on ice in the dark. Yeast were washed twice with 200 μL PBE, resuspended in 25 μL PBE containing 10 nM previously prepared PD-1 tetramers, and incubated with shaking for 1 hour at 4° C. Yeast were washed twice with 200 μL PBE and resuspended in 75 μL PBE. PE fluorescent intensity was quantified by flow cytometry using a Sony SA3800 Spectral Cell Analyzer. Percent max binding was calculated based on fluorescent PD-1 tetramer binding in the absence of any serum.

[0455] IL-33 Neutralization Assay.

[0456] IL-33 Reporter Cell Line Construction.

[0457] The full-length coding sequence for ST2 was cloned by Gibson assembly into the lentiviral transfer plasmid pL-SFFV.Reporter.RFP657.PAC, a kind gift from Benjamin Ebert (Addgene plasmid #61395). REK-293FT cells were seeded into a 6-well plate in 2 mL growth media (DMEM with 10% (v/v) FBS, 100 units/mL penicillin, and 0.1 mg/mL streptomycin) and were incubated at 37° C., 5% CO2. Once cells achieved 70-80% confluence approximately one day later, cells were transfected using TransIT-LT1 (Mirus Bio) in Opti-MEM media (Life Technologies). TransIT-LTI Reagent was pre-warmed to room temperature and vortexed gently. For each well, 0.88 ug lentiviral transfer plasmid along with 0.66 ug pSPAX2 (Addgene plasmid #12260) and 0.44 ug pMD2.G (Addgene plasmid #12259), kind gifts from Didier Trono, were added to 250 μL Opti-MEM media and mixed gently. TransIT-LT1 reagent (6 μl) was added to the DNA mixture, mixed gently, and incubated at room temperature for 15-20 minutes. The mixture was added dropwise to different areas of the well Plates were incubated at 37° C., 5% CO2; 48 hrs later, the virus-containing media was collected and filtered with a 0.45 μm low protein-binding filter. H1EK-BIlue IL-18 cells (InvivoGen) were seeded into a 6-well plate in 1 mL growth media (DMEM with 10% (v/v) FBS, 100 units/mL penicillin, and 0.1 mg/mL streptomycin) and 1 mL virus-containing media. Cells were incubated at 37° C., 5% CO2 for two days before the media was changed.

[0458] Reporter Cell Stimulation and Reading.

[0459] Purified IgG titrations and 2 nM IL-33 were mixed in 50 μL assay media (DMEM with 10% (v/v) FBS, 100 units/mL penicillin, and 0.1 mg/mL streptomycin) and incubated with shaking for 1 hour at room temperature. Approximately 50,000 IL-33 reporter cells in 50 μl assay media were added to wells of a sterile tissue culture grade flat-bottom 96-well plate. IgG-IL-33 mixtures were added to respective wells (1 nM IL-33 final concentration). Plates were incubated at 37° C. 5% CO2 for 20 hours, then 20 μL media from each well was added to 180 μL room temperature QUANTI-Blue Solution (InvivoGen) in a separate flat-bottom 96-well plate and incubated at 37° C. for 3 hours. Absorbance at 655 nm was measured in a Synergy HTX Multi-Mode Microplate Reader (BioTek). Percent max signal was calculated based on signal generated by IL-33 in the absence of any serum.

[0460] ROC Analysis of REAP Score Performance.

[0461] Orthogonal validation data for the receiver operator curve (ROC) analysis was obtained by ELISA, LIPS, or clinical autoantibody tests. For ELISA and LIPS, valid reactivities were defined as those 3 standard deviations above the healthy donor average for a given protein in each assay. ROC analysis was performed using 247 test pairs across 25 different proteins.

[0462] Statistical Analysis.

[0463] Statistical details of experiments can be found in the figure legends. All error bars in figures indicate standard deviation. Data analysis was performed using R, Python, Excel, and GraphPad Prism.

[0464] In summary, autoantibodies targeting extracellular proteins are known to mediate autoimmune diseases and paraneoplastic syndromes in cancer. However, discovery of new autoantibodies against extracellular (transmembrane and secreted) proteins in high throughput remained difficult due to a lack of methods for screening the thousands of extracellular proteins in the human proteome. The autoantibodies can mediate new forms of autoimmune disease, predict response to therapy, or mediate toxicity or responses in cancer in response to immune-modifying checkpoint blockade therapies.

[0465] The essence of the invention is the discovery of extracellular antibody targets using a yeast-displayed library of proteins and next-generation sequencing, which enabled high-throughput interrogation of natively folded proteins by total human serum. Moreover, yeast cell display is a technique well-suited to display of human extracellular proteins, and amenable to high-throughput screening due to the ease of handling yeast. This allowed unbiased assessment of autoantibody repertoires in any human patient or healthy population at a previously unattainable scale and cost. Furthermore, it was accomplished by (Step I) using a yeast-displayed library of extracellular antigens as a substrate to interrogate whole sero-reactivities, (Step II) optimizing an antibody isolation protocol, (Step III) staining and selecting conditions for yeast cell selection with total serum antibodies, and (Step IV) next-generation sequencing pipelines to identify the antigen targets. Consequently, this technique enabled screening against thousands of candidate antigens simultaneously

[0466] More specifically, (Step I) standard methods were used to identify and amplify the ectodomains of human extracellular proteins, and individually transformed them into standard yeast-display strains for fusion to cell-wall associated proteins in yeast. A random nucleotide barcode was additionally incorporated into the display vector to enable tracking of proteins by next-generation sequencing. These individual strains were then pooled to create a single library encompassing all proteins of interest.

[0467] (Step II) Antibodies were isolated from human serum by affinity purification. For example, antibodies were purified with Protein A or Protein G, using either magnetic or agarose beads, and via standard methods. If other isotypes of antibody besides IgG were desired, appropriate affinity purification methods were used in place of Protein A or Protein G. After antibody purification, yeast-reactive antibodies present in human serum were removed by incubation with parental yeast cell strains and filtration. The final elution was suitable for yeast cell staining and selection.

[0468] (Step III) Yeast cell were stained with a normalized concentration of purified, non-yeast-reactive antibody from 1-10 μg per reaction. Stained yeast cell were identified with any appropriate secondary antibody recognizing immunoglobulins of the isotype used, such as a biotinylated or fluorescently labeled anti-immunoglobulin antibody. Stained yeast cell were then selected via magnetic separation using standard methods and appropriate magnetic reagents or by FACS. Stained yeast cell were also directly selected with appropriate anti-immunoglobulin magnetic particles. Selected yeast cell were expanded following selection and their DNA isolated via standard methods.

[0469] (Step IV) Yeast cell DNA was amplified and prepared for next-generation sequencing by standard methods appropriate from the next-generation sequencing method of interest (e.g. Illumina sequencing-by-synthesis). The frequencies of each protein were measured in the initial library and in all samples following selection, by tabulating the frequencies of all barcodes corresponding to an individual protein. An enrichment score was calculated based on the total enrichment of each protein in each sample and the fraction of associated barcodes that enrich. Different thresholds were applied to this enrichment score depending on the desired level of sensitivity or specificity. Proteins with scores above a particular threshold were predicted as candidate autoantigens.

[0470] Accordingly, the primary novel feature of the present invention is, in part, the design of the display library to improve display success and quality of results over previous methods, such as shotgun cDNA library preparations. A high-quality curation of the library greatly improved the specificity and sensitivity by removing out-of-frame or truncated protein products. Additional novelty comes, in part, from the next-generation sequencing approach and analytical methods, which increased confidence in the predicted candidate autoantigens. Finally, the optimized method for staining and selection was more amenable to high-throughput screening of hundreds of serum samples due to applicability to 96-well formats.

[0471] As described above, the herein described technique used a more advanced library with higher display success rates that can cover the full complement of well-folded ectodomains in the human proteome. It was additionally scalable, sensitive, and amenable to high-throughput screening and even automation. Compared to the gold-standard approaches, such as protein arrays, it was found that known and novel autoantibody responses can be detected that were previously undectable. As the technique was amenable to high-throughput screening approaches and requires small samples volumes, it can rapidly query large patient cohorts for a small fraction of the cost of previous methods, such as protein arrays.

Diagnostic or Prognostic Antibodies

[0472]

TABLE 2

List of Diseases or Disorders and the Corresponding Abbreviations

Abbreviation	Full Name
AAV	ANCA-Associated vasculitis
APECED	Autoimmune Polyendocrinopathy Candidiasis Ecto-Dermal Dystrophy
APS	Antiphospholipid Antibody Syndome
CIDP	Chronic Inflammatory Demyelinating Polyradiculoneuropathy
COVID-19	Coronavirus Disease 2019
DIL	Drug-Induced Lupus
DM	Dermatomyositis
KT	Kidney Transplant
Malaria	Malaria
MG	Myasthenia Gravis
MM	Malignant Melanoma
NMO	Neuromyelitis Optica
NSCLC	Non-Small Cell Lung Cancer
PANDAS	Pediatric Autoimmune Neuropsychiatric Disorders Associated with Streptococcal Infections
SLE	Systemic Lupus Erythematosus
SS	Sjogren's Syndrome
SSC	Scleroderma
SUSAC	Susac Syndrome

TABLE 3

List of Autoantigens and the Corresponding Diseases or Disorders

Disease	Target
AAV	EDIL3
AAV	LY6H
AAV	TREM2
APECED	ACRV1
APECED	ADM2
APECED	AFP
APECED	APOA4
APECED	APOO
APECED	BPIFA1
APECED	BPIFA2
APECED	BTN1A1
APECED	C5orf64
APECED	CASQ1
APECED	CCDC47
APECED	CCL11
APECED	CCL15
APECED	CCL17
APECED	CCL18
APECED	CCL7
APECED	CCL8
APECED	CDSN
APECED	CELA2B
APECED	CLCC1
APECED	CLPS
APECED	CLSTN1
APECED	CLU
APECED	CNPY2

TABLE 3-continued

List of Autoantigens and the Corresponding Diseases or Disorders

Disease	Target
APECED	CNPY3
APECED	CP
APECED	CSHL1
APECED	CSN2
APECED	CSPG5
APECED	CST4
APECED	CST5
APECED	CST6
APECED	CTSG
APECED	DEFA5
APECED	DKK1
APECED	DRAXIN
APECED	ECSCR
APECED	EPHA4
APECED	EREG
APECED	FAM19A4
APECED	FAM3A
APECED	FGF1
APECED	FGFR2
APECED	FKBP14
APECED	GFRAL
APECED	GIF
APECED	GPHB5
APECED	HCRTR2
APECED	HSPA13
APECED	IBSP
APECED	IFNA13
APECED	IFNA14
APECED	IFNA17
APECED	IFNA2
APECED	IFNA5
APECED	IFNA6
APECED	IFNA8
APECED	IFNL2
APECED	IFNW1
APECED	IGF1
APECED	IGFBP1
APECED	IGSF4B
APECED	IL17A
APECED	IL17F
APECED	IL22
APECED	IL22RA2
APECED	IL28B
APECED	IL5
APECED	IL6
APECED	KAL1
APECED	KLK2
APECED	LAIR2
APECED	LCN1
APECED	LEG1
APECED	LIPF
APECED	LRIT3
APECED	LRRC3B
APECED	LY6H
APECED	MMP1
APECED	MMP7
APECED	MPZL3
APECED	MSMP
APECED	MSR1
APECED	OBP2A
APECED	ODAPH
APECED	OPN4
APECED	OTOL1
APECED	OTOR
APECED	PANX3
APECED	PAP
APECED	PDGFB
APECED	PDILT
APECED	PGC
APECED	PLA2G10
APECED	PLA2G2E
APECED	PLAC9
APECED	PLVAP

TABLE 3-continued

List of Autoantigens and the Corresponding Diseases or Disorders

Disease	Target
APECED	PMCH
APECED	PNLIP
APECED	PNLIPRP1
APECED	PNLIPRP2
APECED	PPT1
APECED	PRG3
APECED	PRLR
APECED	PRRG1
APECED	PRRG3
APECED	PRRT1
APECED	PRRT3
APECED	PSAP
APECED	PTPRN2
APECED	PTPRR
APECED	RAMP2
APECED	REG1A
APECED	REG3G
APECED	REG4
APECED	RNASE8
APECED	RTBDN
APECED	SERPINE1
APECED	SLC2A10
APECED	SLC41A2
APECED	SMR3A
APECED	SOSTDC1
APECED	SPACA7
APECED	SPAG11B
APECED	SPINK1
APECED	SPINK4
APECED	SPINK8
APECED	SRGN
APECED	SYCN
APECED	TEPP
APECED	TEX264
APECED	TFF2
APECED	TGFA
APECED	TM4SF6
APECED	TM9SF3
APECED	TMEM119
APECED	TMEM149
APECED	TNFRSF12A
APECED	TSLP
APECED	TXNDC12
APECED	VSTM2A
APS	IL6R
APS	IFNA13
APS	IFNA14
APS	IFNA17
APS	IFNA2
APS	IFNA5
APS	IFNA6
APS	IFNA8
APS	IL6R
CIDP	CXCL1
CIDP	CXCL2
CIDP	CXCL3
CIDP	PDGFB
CIDP	TMEM149
CIDP	CD74
CIDP	CXCL13
COVID-19	APOO
COVID-19	OPRL1
COVID-19	IFNA14
COVID-19	MIA2
COVID-19	FKBP2
COVID-19	GPR1
COVID-19	IL29
COVID-19	PTPRR
COVID-19	RCN2
COVID-19	IFNA13
COVID-19	IFNW1
COVID-19	IL1A
COVID-19	TSPAN9

TABLE 3-continued

List of Autoantigens and the Corresponding Diseases or Disorders

Disease	Target
COVID-19	SHISA7
COVID-19	IFNA17
COVID-19	LEP
COVID-19	CALU
COVID-19	SSPN
COVID-19	LPAL2
COVID-19	OBP2B
COVID-19	CST5
COVID-19	IL6
COVID-19	CCDC47
COVID-19	ACRV1
COVID-19	PGA3
COVID-19	LRRC8C
COVID-19	PMCH
COVID-19	GPR6
COVID-19	CSF2
COVID-19	RCN3
COVID-19	LYSMD4
COVID-19	CD99
COVID-19	IFNA5
COVID-19	IFNL2
COVID-19	CXCL9
COVID-19	SLC41A2
COVID-19	EPYC
COVID-19	DUOXA1
COVID-19	LACRT
COVID-19	CNPY2
COVID-19	KLK8
COVID-19	MZB1
COVID-19	LYG2
COVID-19	MUCL3
COVID-19	LALBA
COVID-19	ZG16B
COVID-19	ODAM
COVID-19	PILRA
COVID-19	HRC
COVID-19	PPBP
COVID-19	CSPG5
COVID-19	PTPRN2
COVID-19	CST4
COVID-19	FAM168B
COVID-19	TNFRSF17
COVID-19	OTOS
COVID-19	SPINK9
COVID-19	KLRC2
COVID-19	IFNA8
COVID-19	TMEM119
COVID-19	CSAG1
COVID-19	OTOR
COVID-19	KCT2
COVID-19	PGA4
COVID-19	SPINK4
COVID-19	FCGR2A
COVID-19	CNPY3
COVID-19	NEGR1
COVID-19	ERP27
COVID-19	AGRP
COVID-19	PRR27
COVID-19	MCFD2
COVID-19	IGFBP6
COVID-19	IFNA2
COVID-19	LGALS3
COVID-19	SPOCK1
COVID-19	KCNV2
COVID-19	HCRTR2
COVID-19	LECT2
COVID-19	PLA2G2E
COVID-19	FAM19A3
COVID-19	SPACA7
COVID-19	NENF
COVID-19	IL6R
COVID-19	SPX
COVID-19	IGFBP1

TABLE 3-continued

List of Autoantigens and the Corresponding Diseases or Disorders

Disease	Target
COVID-19	SRGN
COVID-19	LAIR2
COVID-19	CPXM2
COVID-19	CCL17
COVID-19	TUSC5
COVID-19	LOC644613
COVID-19	TNFRSF21
COVID-19	GPR77
COVID-19	C2orf40
COVID-19	C5A
COVID-19	IFNA6
COVID-19	SPP1
COVID-19	SERPINA3
COVID-19	OXTR
COVID-19	KLRC1
COVID-19	SEMG2
COVID-19	APOH
COVID-19	PRRG1
COVID-19	BTC
COVID-19	MSLN
COVID-19	FAM19A2
COVID-19	CXCL1
COVID-19	PRSS55
COVID-19	SLCO2B1
COVID-19	BTN1A1
COVID-19	COV2-RBD
COVID-19	OS9
COVID-19	PGLYRP1
COVID-19	DKK3
COVID-19	TOR1B
COVID-19	CST1
COVID-19	LRRC8D
COVID-19	ACKR1
COVID-19	COL8A1
COVID-19	CXCL3
COVID-19	ODAPH
COVID-19	PIANP
COVID-19	PSORS1C2
COVID-19	RNASE10
COVID-19	CXCR7
COVID-19	PLVAP
COVID-19	CDSN
COVID-19	SDF2L1
COVID-19	TFF2
COVID-19	HSPA13
COVID-19	CXCR5
COVID-19	C5orf64
COVID-19	EPO
COVID-19	GNLY
COVID-19	OPRM1
COVID-19	TGFA
COVID-19	SLC2A10
COVID-19	CXCL13
COVID-19	CD99L2
COVID-19	AGER
COVID-19	CGA
COVID-19	CRTAM
COVID-19	SLC1A1
COVID-19	CDH19
COVID-19	GPR25
COVID-19	CCL8
COVID-19	SERPINI1
COVID-19	SPINK8
COVID-19	SLPI
COVID-19	HRH3
COVID-19	TMEM149
COVID-19	CD38
COVID-19	REG4
COVID-19	IGFBP5
COVID-19	FKBP7
COVID-19	GRM5
COVID-19	CXCR3
COVID-19	PTHLH

TABLE 3-continued

List of Autoantigens and the Corresponding Diseases or Disorders

Disease	Target
COVID-19	LY6K
COVID-19	PLAC9
COVID-19	LPL
COVID-19	CCKAR
COVID-19	RTN4R
COVID-19	GYPA
COVID-19	TMED1
COVID-19	DRAXIN
COVID-19	CCL13
COVID-19	LRRC8A
COVID-19	ANGPTL4
COVID-19	NPPC
COVID-19	IL22
COVID-19	CCL21
COVID-19	RCN1
COVID-19	CD74
COVID-19	FGF17
COVID-19	PAEP
COVID-19	CNPY4
COVID-19	APOC3
COVID-19	SPINK1
COVID-19	AZGP1
COVID-19	STC2
COVID-19	S1PR4
COVID-19	IBSP
COVID-19	CEACAM18
COVID-19	SLC38A4
COVID-19	CSN2
COVID-19	VSIG2
COVID-19	ENSP00000381830
COVID-19	CSHL1
COVID-19	CASQ1
COVID-19	XG
COVID-19	ENDOU
COVID-19	RAET1L
COVID-19	COL10A1
COVID-19	PTH
COVID-19	SLC15A1
COVID-19	SLC6A2
COVID-19	PRRT1
COVID-19	CLCC1
COVID-19	F2R
COVID-19	JTB
COVID-19	TGOLN2
COVID-19	CCL16
COVID-19	MIA
COVID-19	TNF
COVID-19	TMEM91
COVID-19	RTBDN
COVID-19	MPL
COVID-19	RSPO1
COVID-19	RSPO3
COVID-19	PRSS3
COVID-19	GPR17
COVID-19	CCR9
COVID-19	GP6
COVID-19	PRH1;
COVID-19	EQTN
COVID-19	RNF43
COVID-19	SPN
COVID-19	IGSF4B
COVID-19	CFD
COVID-19	SPACA5
COVID-19	CHGA
COVID-19	UNQ6190/PRO20217
COVID-19	APOA1
COVID-19	PRG3
COVID-19	SLC2A2
COVID-19	CCL11
COVID-19	TSLP
COVID-19	SMOC2
COVID-19	HTR5
COVID-19	PRAP1

TABLE 3-continued

List of Autoantigens and the Corresponding Diseases or Disorders

Disease	Target
COVID-19	LY6H
COVID-19	IMPG1
COVID-19	TNFRSF12A
COVID-19	SSTR2
COVID-19	IGFBP3
COVID-19	PRLR
COVID-19	PRR4
COVID-19	IL13
COVID-19	HCTR1
COVID-19	IGF1
COVID-19	CD300E
COVID-19	LINC00305
COVID-19	SPESP1
COVID-19	FRZB
COVID-19	IL28B
COVID-19	MMP9
COVID-19	GAST
COVID-19	FGF1
COVID-19	IL15RA
COVID-19	CCR10
COVID-19	VEGFB
COVID-19	SERPINE1
COVID-19	EXOC3-AS1
COVID-19	PRRT3
COVID-19	NETO1
COVID-19	VSTM2B
COVID-19	CCR4
COVID-19	APP
COVID-19	AMTN
COVID-19	CXCL6
COVID-19	NINJ1
COVID-19	KLK9
COVID-19	SDF4
COVID-19	CPE
COVID-19	AMELX
COVID-19	DCD
COVID-19	ANTXRL
COVID-19	CCR2
COVID-19	PCSK1
COVID-19	QRFP
COVID-19	RGMB
COVID-19	NPY2R
COVID-19	IGFBP7
COVID-19	SLC2A12
COVID-19	PPT1
COVID-19	CCL7
COVID-19	JCHAIN
COVID-19	ADCYAP1
COVID-19	PDZD11
COVID-19	CP
COVID-19	MANF
COVID-19	GZMA
COVID-19	TXNDC12
COVID-19	PGC
COVID-19	ACVR1
COVID-19	WFDC13
COVID-19	SFRP4
COVID-19	REG1A
COVID-19	GPR37
COVID-19	NOPE
COVID-19	C1lorf94
COVID-19	SCARA5
COVID-19	GPR19
COVID-19	EMC7
COVID-19	CCL15
COVID-19	CA4
COVID-19	RNASE8
COVID-19	MLN
COVID-19	UNQ9165/PRO28630
COVID-19	NTRK3
COVID-19	TREML1
COVID-19	CDH15
COVID-19	SMR3A

TABLE 3-continued

List of Autoantigens and the Corresponding Diseases or Disorders

Disease	Target
COVID-19	DKK1
COVID-19	OXER1
COVID-19	FAM24B
COVID-19	CRLF1
COVID-19	PDIA6
COVID-19	PLA2G12B
COVID-19	FGF7
COVID-19	ZP4
COVID-19	BAMBI
COVID-19	GKN2
COVID-19	IGFBPL1
COVID-19	MMP7
COVID-19	MANSC4
COVID-19	APOA4
COVID-19	SUSD6
COVID-19	CELA1
COVID-19	IGLL1
COVID-19	IL9
COVID-19	MADCAM1
COVID-19	NPBW1
COVID-19	HAVCR1
COVID-19	ITPRIPL1
COVID-19	SOST
COVID-19	LHFPL1
COVID-19	SDC3
COVID-19	SEMG1
COVID-19	C1QB
COVID-19	ASIP
COVID-19	CCL18
COVID-19	LHFPL5
COVID-19	IGFL2
COVID-19	FGFRL1
COVID-19	EFNB2
COVID-19	C2orf66
COVID-19	MFAP3
COVID-19	C6orf15
COVID-19	OPN4
COVID-19	NOV
COVID-19	GNS
COVID-19	FKBP14
COVID-19	CELA2B
COVID-19	C9
COVID-19	VWC2L
COVID-19	BMPR2
COVID-19	CSH2
COVID-19	IL1RAP
COVID-19	C1QTNF2
COVID-19	SLC10A4
COVID-19	IL16
COVID-19	LRIT3
COVID-19	GRN
COVID-19	NIPAL4
COVID-19	GNRH1
COVID-19	ATP4B
COVID-19	APLP2
COVID-19	TMEM123
COVID-19	IL3
COVID-19	PDGFA
COVID-19	EVI2B
COVID-19	NGFR
COVID-19	PROK1
COVID-19	SOSTDC1
COVID-19	FLJ36131
COVID-19	EREG
COVID-19	TNFRSF9
COVID-19	LYG1
COVID-19	SLCO4C1
COVID-19	GUCA2A
COVID-19	FAM19A5
COVID-19	IL21
COVID-19	FCMR
COVID-19	CADM2
COVID-19	CSF3

TABLE 3-continued

List of Autoantigens and the Corresponding Diseases or Disorders

Disease	Target
COVID-19	CA11
COVID-19	NTRK2
COVID-19	CRELD2
COVID-19	GPR120
COVID-19	C9orf135
COVID-19	SLC1A5
COVID-19	SYCN
COVID-19	COL9A3
COVID-19	ADRA1D
COVID-19	GLB1
COVID-19	SV2C
COVID-19	DKFZp686O24166
COVID-19	PRSS3P2
COVID-19	KIRREL3
COVID-19	VSTM2A
COVID-19	GCG
COVID-19	SERPINE2
COVID-19	EDA2R
COVID-19	CPAMD8
COVID-19	SCN3B
COVID-19	OXT
COVID-19	CD3E
COVID-19	INSL3
COVID-19	CALY
COVID-19	GHSR
COVID-19	SCGB1D1
COVID-19	C6
COVID-19	CLDN2
COVID-19	MUC7
COVID-19	KISS1
COVID-19	ULBP2
COVID-19	CLDN7
COVID-19	IGFBP2
COVID-19	EFNB3
COVID-19	NXPH1
COVID-19	GHRHR
COVID-19	LILRA4
COVID-19	OTOL1
COVID-19	EFNB1
COVID-19	FGFBP3
COVID-19	GPR63
COVID-19	PRRG4
COVID-19	MUCL1
COVID-19	XCL1
COVID-19	TMEM120A
COVID-19	TMEM108
COVID-19	IL1F5
COVID-19	MSMP
COVID-19	CXCL12
COVID-19	GNPTG
COVID-19	SDC4
COVID-19	FZD9
COVID-19	CCL4L1
COVID-19	GPRC6A
COVID-19	GPR156
COVID-19	ITIH3
COVID-19	RAMP2
COVID-19	TNFRSF11A
COVID-19	DKK2
COVID-19	SPINK13
COVID-19	SDCBP
COVID-19	CD8B2
COVID-19	CTSG
COVID-19	CST2
COVID-19	EDDM3B
COVID-19	CLTRN
COVID-19	PLA2G10
COVID-19	DCN
COVID-19	DAG1
COVID-19	CXCL16
COVID-19	CCRL2
COVID-19	DEFB108B
COVID-19	MRGPRF

TABLE 3-continued

List of Autoantigens and the Corresponding Diseases or Disorders

Disease	Target
COVID-19	FCRL3
COVID-19	NPS
COVID-19	OBP2A
COVID-19	ACKR2
COVID-19	GRM2
COVID-19	FAM174A
COVID-19	MSR1
COVID-19	NOG
COVID-19	TMEM102
COVID-19	LAIR1
COVID-19	IL22RA2
COVID-19	SPACA3
COVID-19	WIF1
COVID-19	F13B
COVID-19	LRTM1
COVID-19	ERVH48-1
COVID-19	CCL2
COVID-19	TFF1
COVID-19	ADM2
COVID-19	IFITM10
COVID-19	HSD11B1L
COVID-19	AXL
COVID-19	FMR1NB
COVID-19	C6orf25
COVID-19	OPN3
COVID-19	MUC13
COVID-19	CCL28
COVID-19	CCL26
COVID-19	PTN
COVID-19	SLC39A8
COVID-19	FGF21
COVID-19	TIMD4
COVID-19	NPTX2
COVID-19	IL17RD
COVID-19	PAPLN
COVID-19	TMEM219
COVID-19	CYB5D2
COVID-19	IL1B
COVID-19	FSTL1
COVID-19	PTPRJ
COVID-19	NPY1R
COVID-19	CLDN18
COVID-19	FLT3LG
COVID-19	C17orf99
COVID-19	SLC6A5
COVID-19	AIMP1
COVID-19	TNFRSF8
COVID-19	CD248
COVID-19	TM9SF3
COVID-19	FCGR2C
COVID-19	MPZL3
COVID-19	OSTN
COVID-19	SPARCL1
COVID-19	TMPRSS11D
COVID-19	KLK7
COVID-19	GDPD3
COVID-19	IL34
COVID-19	BTNL8
COVID-19	ASTL
COVID-19	CLDN19
COVID-19	SCG5
COVID-19	PSAP
COVID-19	PRRG3
COVID-19	PLA2G12A
COVID-19	LCN1
COVID-19	LRRTM2
COVID-19	FAM3D
COVID-19	PTGS2
COVID-19	FCRLB
COVID-19	CST8
COVID-19	ANGPTL5
COVID-19	OPRK1
COVID-19	APOD

TABLE 3-continued

List of Autoantigens and the Corresponding Diseases or Disorders

Disease	Target
COVID-19	ADM
COVID-19	CLU
COVID-19	PANX3
COVID-19	SLC52A3
COVID-19	VASN
COVID-19	CMKLR1
COVID-19	BGLAP
COVID-19	IL4
COVID-19	IL18BP
COVID-19	ACVRL1
COVID-19	FLRT3
COVID-19	FAM234A
COVID-19	CPVL
COVID-19	GPR3
COVID-19	LMBRD2
COVID-19	TMEM169
COVID-19	LRRC8B
COVID-19	INSL6
COVID-19	PDCD1
COVID-19	EMC10
COVID-19	IL18RAP
COVID-19	NRN1
COVID-19	TRABD2A
COVID-19	SSBP3-AS1
COVID-19	IL17C
COVID-19	LGALS1
COVID-19	MDK
COVID-19	WFDC1
COVID-19	NRN1L
COVID-19	TNFRSF1B
COVID-19	HNRNPA2B1
COVID-19	DKKL1
COVID-19	NTSR1
COVID-19	IL32
COVID-19	FAM24A
COVID-19	SGCA
COVID-19	IL1RN
COVID-19	LY6D
COVID-19	HSD17B7
COVID-19	SCG3
COVID-19	TNFRSF4
COVID-19	CCL22
COVID-19	XK
COVID-19	RETN
COVID-19	GALP
COVID-19	FGL2
COVID-19	PDGFB
COVID-19	CTF1
COVID-19	C8G
COVID-19	EBI3
COVID-19	EDIL3
COVID-19	TRABD2B
COVID-19	GP5
COVID-19	CLEC2B
COVID-19	SEMA6C
COVID-19	CLDN9
COVID-19	CSN3
COVID-19	TRH
COVID-19	CCL25
COVID-19	APOE
COVID-19	IER3
COVID-19	DHRS7C
COVID-19	C19orf18
COVID-19	MCHR1
COVID-19	CHRDL2
COVID-19	FGF18
COVID-19	PINLYP
COVID-19	MFAP2
COVID-19	C11orf44
COVID-19	CXCL17
COVID-19	ART1
COVID-19	LILRB4
COVID-19	DUOXA2

TABLE 3-continued

List of Autoantigens and the Corresponding Diseases or Disorders

Disease	Target
COVID-19	CSN1S1
COVID-19	PEBP4
COVID-19	RTN4RL1
COVID-19	SCGB2A2
COVID-19	TGFBR3L
COVID-19	UCMA
COVID-19	RAET1E
COVID-19	PKD2L1
COVID-19	ACVR1B
COVID-19	AVPR1A
COVID-19	HEPACAM2
COVID-19	P4HB
COVID-19	AJAP1
COVID-19	MOG
COVID-19	EPHA4
COVID-19	BAGE3
COVID-19	CPA6
COVID-19	FSTL3
COVID-19	ARTN
COVID-19	LRRN4
COVID-19	BRINP3
COVID-19	EPOR
COVID-19	NRG1
COVID-19	MEGF9
COVID-19	MFSD2A
COVID-19	SERPINA13P
COVID-19	CLDN10
COVID-19	SCG2
COVID-19	ENDOD1
COVID-19	TMEFF1
COVID-19	F12
COVID-19	NUCB1
COVID-19	CEACAM19
COVID-19	B2M
COVID-19	FETUB
COVID-19	UNQ5830/PRO19650/PRO19816
COVID-19	DNASE1L2
COVID-19	CLEC-6
COVID-19	IL20RB
COVID-19	CHRNA9
COVID-19	APOC2
COVID-19	SLC1A4
COVID-19	MC5R
COVID-19	COLQ
COVID-19	IMPG2
COVID-19	VTCN1
COVID-19	DEFB126
COVID-19	TMEM41A
COVID-19	SDC1
COVID-19	IL15
COVID-19	BPIFA3
COVID-19	LTBR
COVID-19	CELA3B
COVID-19	MPEG1
COVID-19	ADAMTS16
COVID-19	S1PR3
COVID-19	GPR37L1
COVID-19	LAS2
COVID-19	SNCA
COVID-19	SLC6A11
COVID-19	LYPD6B
COVID-19	FLJ46089
COVID-19	CXCL11
COVID-19	FAM3A
COVID-19	NINJ2
COVID-19	HBEGF
COVID-19	C9orf47
COVID-19	CST6
COVID-19	CRTAC1
COVID-19	CD14
COVID-19	LAG3
COVID-19	LILRB2
COVID-19	SLC22A31

TABLE 3-continued

List of Autoantigens and the Corresponding Diseases or Disorders

Disease	Target
COVID-19	HS3ST1
COVID-19	GIF
COVID-19	NLGN4X
COVID-19	NOTCH2NL
COVID-19	MFGE8
COVID-19	RXFP3
COVID-19	LCAT
COVID-19	TRPC3
COVID-19	MARCO
COVID-19	IGLL5
COVID-19	GKN1
COVID-19	CST7
COVID-19	FMOD
DIL	CXCL1
DIL	TNF
DIL	TSLP
DM	CD81
MG	CXCL2
MG	PDGFB
MC	REG4
MG	CCL22
MG	CCL2
MM	PLA2G2E
MM	SPX
MM	KCNK1
MM	TNFRSF21
MM	CLDN19
MM	MMP7
MM	NGRN
MM	PSORS1C2
MM	FGFBP3
MM	VEGFB
MM	LOC644613
MM	C9
MM	COLEC12
MM	SLC38A4
MM	SOST
MM	SLC41A2
MM	MOG
MM	DNASE2
MM	FMR1NB
MM	ODAPH
MM	LY6H
MM	OPN4
MM	PRRT3
MM	CCL18
MM	TMEM41A
MM	APOC3
MM	LGALS1
MM	SSPN
MM	IL21
MM	ACRV1
MM	TFF2
MM	AGER
MM	DKK1
MM	CST9L
MM	EPHA5
MM	PDIA6
MM	DHRS4L2
MM	MZB1
MM	EVI2B
MM	C19orf18
MM	SPOCK1
MM	SCN3B
MM	CCL11
MM	HCRTR2
MM	MFSD2A
MM	IFNA17
MM	LILRB1
MM	SHISA5
MM	GNRH2
MM	COL8A1
MM	TGFA

TABLE 3-continued

List of Autoantigens and the Corresponding Diseases or Disorders

Disease	Target
MM	ACP5
MM	SMR3A
MM	PSAPL1
MM	ZG16B
MM	GYPA
MM	IGLL5
MM	CCL22
MM	MANSC4
MM	DNAJC3
MM	TNFRSF8
MM	ARTN
MM	NEGR1
MM	CHRNA9
MM	APOO
MM	UNQ6190/PRO20217
MM	CST6
MM	CD164L2
MM	ASTN2
MM	KAL1
MM	TRPC3
MM	IGFBP6
MM	MLN
MM	IL15RA
MM	PPT1
MM	FGF1
MM	PRRG3
MM	IFNA5
MM	C9orf47
MM	FAM3A
MM	LCN12
MM	IFNL2
MM	SECTM1
MM	PMCH
MM	BMPR2
MM	FAM19A5
MM	PNLIPRP1
MM	IL13RA1
MM	LCN2
MM	LAIR2
MM	ERVK13-1
MM	SLPI
MM	OPTC
MM	SPN
MM	CXCL17
MM	CASQ1
MM	TMEM108
MM	MCFD2
MM	IL19
MM	SLC6A5
MM	POMC
MM	ACVRL1
MM	IL5
MM	PRL
MM	OVGP1
MM	LCN15
MM	ITPRIPL1
MM	TMEM91
MM	FCGR2C
MM	CHGA
MM	TIMD4
MM	RBP4
MM	LYG2
MM	OBP2A
MM	KIR3DL3
MM	PTHLH
MM	CCL8
MM	AMELX
MM	CST4
MM	GNLY
MM	KCNMB3
MM	IFNW1
MM	WFDC9
MM	CLDN2

TABLE 3-continued

List of Autoantigens and the Corresponding Diseases or Disorders

Disease	Target
MM	KCT2
MM	CPXM2
MM	BCAM
MM	RAMP2
MM	ERVK-7
MM	NHLRC3
MM	OS9
MM	DKK2
MM	IL2RA
MM	SPINK8
MM	SYNDIG1L
MM	SPINK9
MM	DPT
MM	AXL
MM	SPINK1
MM	BTN1A1
MM	SLC2A2
MM	SLC24A3
MM	DRAXIN
MM	ERVK-24
MM	TNFRSF4
MM	CST5
MM	IER3
MM	SLC22A25
MM	CLCC1
MM	TNFRSF1B
MM	FP248
MM	LYSMD4
MM	AGRP
MM	ADAMTS16
MM	DEFB126
MM	ECM1
MM	IL16
MM	INSL6
MM	XCL2
MM	ENDOU
MM	CST8
MM	UGT2A1
MM	FAM174A
MM	RCN1
MM	UGT1A1
MM	RTN4RL1
MM	C11orf94
MM	FAM187B
MM	APOE
MM	BTC
MM	LHFPL1
MM	PRLR
MM	FGFRL1
MM	CCL15
MM	MPZL3
MM	PPBP
MM	PDCD1
MM	SPINK4
MM	RTBDN
MM	CD99L2
MM	PGA4
MM	HSPA13
MM	CNTN2
MM	TMED1
MM	IL1B
MM	WFDC12
MM	SDF2L1
MM	IL1F9
MM	IGFBP5
MM	TNFRSF12A
MM	MICB
MM	S100A13
MM	RNASE8
MM	FAM19A2
MM	IMPG1
MM	SERPINE1
MM	CTSA

TABLE 3-continued

List of Autoantigens and the Corresponding Diseases or Disorders

Disease	Target
MM	NPPC
MM	PLA2G1B
MM	OBP2B
MM	CCL16
MM	IL13
MM	EREG
MM	KLK8
MM	IL6
MM	TNF
MM	C1QTNF2
MM	KLK14
MM	PTPRR
MM	ADM2
MM	CCL24
MM	NCR3
MM	NETO1
MM	C5orf64
MM	GP6
MM	MIA2
MM	FGF17
MM	TREML4
MM	SOSTDC1
MM	COL9A3
MM	FCER1A
MM	ENSP00000320207
MM	IGFBP3
MM	C6orf15
MM	PROK1
MM	SLC22A31
MM	CD151
MM	EPYC
MM	PROKR2
MM	FKBP9
MM	IL34
MM	MMP1
MM	LAMC1
MM	SRGN
MM	ERVK-18
MM	IGSF4B
MM	CALY
MM	FKBP14
MM	RCN2
MM	IL17BR
MM	CALR
MM	CLDN3
MM	GPC6
MM	OTOL1
MM	MANF
MM	STC2
MM	CSAG1
MM	TNFRSF9
MM	TMEM161A
MM	PRH1;
MM	TRH
MM	CXCL1
MM	FSTL1
MM	TDGF1
MM	PRSS3
MM	PGA3
MM	VSTM2A
MM	IGFL2
MM	CRTAC1
MM	F13B
MM	CTRB2
MM	UNQ9165/PRO28630
MM	GNRH1
MM	SERPINA3
MM	APP
MM	IGFBP2
MM	ITIH3
MM	TM9SF3
MM	CNPY2
MM	IL29

TABLE 3-continued

List of Autoantigens and the Corresponding Diseases or Disorders

Disease	Target
MM	OTOR
MM	TM2D2
MM	CSN3
MM	APOH
MM	SEMA6A
MM	CD14
MM	MUC7
MM	LAS2
MM	C2orf40
MM	TNFRSF5
MM	FGFR2
MM	CXCL3
MM	ADM
MM	IL1RAP
MM	CSPG5
MM	RARRES2
MM	MIA
MM	FKBP2
MM	JCHAIN
MM	NINJ1
MM	RCN3
MM	ZP4
MM	MDK
MM	LCN1P1
MM	SIGLEC9
MM	COL10A1
MM	SPACA7
MM	SPAG11B
MM	XG
MM	CLDN18
MM	CCL17
MM	SHISA7
MM	TMEM149
MM	NBL1
MM	GAST
MM	OXT
MM	SEMA6C
MM	CCL28
MM	LRIT3
MM	CHRNB3
MM	CCDC47
MM	SLC2A10
MM	LECT2
MM	CRLF1
MM	PSAP
MM	TMEM119
MM	SPACA5
MM	CALU
MM	MUCL3
MM	LILRB2
MM	ODAM
MM	CLU
MM	CD40LG
MM	CFHR1
MM	CHGB
MM	IL7
MM	XCL1
MM	CPVL
MM	SYCN
MM	SLC39A8
MM	DCD
MM	PLA2G10
MM	IL36B
MM	SLC6A2
MM	FAM24B
MM	LEP
MM	IL9
MM	PTN
MM	CCL26
MM	AHSG
MM	RNASE10
MM	CD274
MM	KCNV2

TABLE 3-continued

List of Autoantigens and the Corresponding Diseases or Disorders

Disease	Target
MM	FAM3C
MM	LY6G6D
MM	SPINK13
MM	ASIP
MM	LGALS3
MM	CTSW
MM	FCAMR
MM	CD320
MM	PRRG4
MM	CA4
MM	LILRB6
MM	APLP2
MM	BMPR1A
MM	APOA4
MM	TXNDC12
MM	OLR1
MM	CXCL6
MM	CXCL9
MM	OTOS
MM	XK
MM	PRG3
MM	ANGPTL4
MM	CCL23
MM	PRRT1
MM	ATP4B
MM	IL17C
MM	CSF2
MM	CCL13
MM	HSD11B1L
MM	MICA
MM	IGF1
MM	MSMP
MM	TGOLN2
MM	ERP27
MM	PTPRN2
MM	KLRK1
MM	LRP11
MM	PIANP
MM	LIF
MM	S100A8
MM	CSN2
MM	EVAIC
MM	IFNA6
MM	PCSK1
MM	LILRB4
MM	QPCT
MM	SNORC
MM	SHISA6
MM	PRR27
MM	KLRF1
MM	CTSG
MM	PDIA3
MM	CNPY4
MM	RSPO4
MM	REG1A
MM	PEBP4
MM	CRTAP
MM	TGFBR1
MM	VSTM2B
MM	CP
MM	VPREB1
MM	CD44
MM	IGFBP7
MM	FGF7
MM	ENSP00000381830
MM	SEMG1
MM	IL1A
MM	EPO
MM	CDH19
MM	IL32
MM	SUMF1
MM	ANTXRL
MM	LHFPL5

TABLE 3-continued

List of Autoantigens and the Corresponding Diseases or Disorders

Disease	Target
MM	CCL21
MM	PLVAP
MM	CELA1
MM	ICOSLG
MM	FGF23
MM	SLC6A11
MM	CLDN1
MM	SFTPB
MM	NTS
MM	REG4
MM	IGLL1
MM	CSF3
MM	CNPY3
MM	NOPE
MM	TXN
MM	CDSN
MM	KLK7
MM	TNFRSF13C
MM	RAET1L
MM	FAM19A3
MM	LALBA
MM	RTN4R
MM	CFD
MM	PGLYRP1
MM	CRELD2
MM	AMTN
MM	CCL7
MM	TMEM102
MM	TNFRSF10B
MM	C2orf66
MM	HAVCR1
MM	FAM234A
MM	NOV
MM	RSPO3
MM	IFNA13
MM	CTLA4
MM	PLAC9
MM	UGT2B28
MM	IL28B
MM	TOR1B
MM	INSL3
MM	APOA1
MM	CFHR2
MM	FCGR2A
MM	IGF2
MM	AMBN
MM	ASIC5
MM	NTRK2
MM	HNRNPA2B1
MM	PRELP
MM	CILP2
MM	EPHA4
MM	KAZALD1
MM	FAM168B
MM	CD248
MM	COL14A1
MM	VTN
MM	CELA3A
MM	PTPRD
MM	CELA3B
MM	DKK3
MM	CREG2
MM	ANGPTL5
MM	MUCL1
MM	SLC15A1
MM	GREM2
MM	WFDC3
MM	PRR4
MM	VSIG4
MM	FAM19A4
MM	CST7
MM	TEX46
MM	TFF1

TABLE 3-continued

List of Autoantigens and the Corresponding Diseases or Disorders

Disease	Target
MM	FCMR
MM	CST1
MM	CGREF1
MM	AIMP1
MM	IL4
MM	SERPINI1
MM	PRAP1
MM	PGC
MM	GZMA
MM	CXCL11
MM	SDC4
MM	CXCL5
MM	PANX3
MM	CCL20
MM	BPIFC
MM	TGFBR3L
MM	SNCA
MM	IL22RA2
MM	ARSJ
MM	SFRP4
MM	TREML1
MM	LYPD6B
MM	CCL1
MM	HRC
MM	CLTRN
MM	FZD4
MM	LRRC8C
MM	GH1
MM	IHH
MM	IL10RB
MM	IGFBP1
MM	IGDCC3
MM	VEGFA
MM	SPOCK2
MM	FGF16
MM	SLC39A14
MM	BST2
MM	SCG2
MM	MFAP2
MM	CT83
MM	TMEM95
MM	ABHD12
MM	CLN5
MM	SCGB1A1
MM	HSD17B13
MM	SPACA3
MM	BTNL8
MM	SLC22A9
MM	SLC2A13
MM	MPO
MM	TTYH2
MM	TMEM169
MM	CD72
MM	TRABD2B
MM	SCG5
MM	SERPINI2
MM	SPP2
MM	S100A7
MM	KRTDAP
MM	CST2
MM	CREG1
MM	TSPAN2
MM	NRN1
MM	VSIG2
MM	MEGF9
MM	RNF43
MM	CLDN8
MM	ENH1
MM	SMOC1
MM	LRRN4CL
MM	PDGFA
MM	PLA2G12B
MM	PTTG1IP

TABLE 3-continued

List of Autoantigens and the Corresponding Diseases or Disorders

Disease	Target
MM	FAM24A
MM	FKBP10
MM	SLC6A13
MM	SLC10A4
MM	GFRA2
MM	SLURP1
MM	OLFM1
MM	BTLA
MM	ATP6AP2
MM	SCGB2A2
MM	PILRB
MM	SLC22A4
MM	EXOC3-AS1
MM	ART1
MM	MUC5AC
MM	CHAD
MM	DKKL1
MM	SLC8B1
MM	TSLP
MM	SCGB1C2
MM	PDGFB
MM	C1QL1
MM	TM4SF6
MM	FRZB
MM	TMEFF1
MM	IL17B
MM	DAG1
MM	COLQ
MM	PLAT
MM	TNFRSF6B
MM	CLDN4
MM	TREM2
MM	SUSD6
MM	VSTM2L
MM	NFASC
MM	COMT
MM	MSR1
MM	LSR
MM	CER1
MM	AZU1
MM	CCK
MM	PLA2G2A
MM	SMOC2
MM	CXCL13
MM	CRTAM
MM	GKN1
MM	NRXN3
MM	DHRS7C
MM	CHRDL2
MM	HTR3D
MM	TRPC4
NMO	CXCL2
NMO	CXCL3
NMO	IGFBPL1
NMO	CCL22
NMO	IL1F9
NMO	LY6G6D
NSCLC	CCL17
NSCLC	CCL24
NSCLC	CXCL1
NSCLC	CXCL3
NSCLC	EDIL3
NSCLC	IFNA13
NSCLC	IFNA14
NSCLC	IFNA17
NSCLC	IFNA2
NSCLC	IFNA5
NSCLC	IFNA6
NSCLC	IFNA8
NSCLC	IFNL2
NSCLC	IFNW1
NSCLC	IL28B
NSCLC	IL34

TABLE 3-continued

List of Autoantigens and the Corresponding Diseases or Disorders

Disease	Target
NSCLC	MADCAM1
NSCLC	PDGFB
NSCLC	REG1A
NSCLC	SDC1
NSCLC	BTN1A1
NSCLC	C6
NSCLC	CD207
NSCLC	CD3D
NSCLC	CDH19
NSCLC	COLEC12
NSCLC	EREG
NSCLC	FGF23
NSCLC	FGF7
NSCLC	FGFBP3
NSCLC	IGFBPL1
NSCLC	IL15RA
NSCLC	IL17F
NSCLC	IL1RAP
NSCLC	IL22RA2
NSCLC	IL4
NSCLC	IL4R
NSCLC	ITGA5
NSCLC	LAG3
NSCLC	LRRC4
NSCLC	MPZL3
NSCLC	NOTCH2NL
NSCLC	NTRK3
NSCLC	REG4
NSCLC	SCARA3
NSCLC	STIM2
NSCLC	TNFRSF10C
NSCLC	TNFRSF19L
NSCLC	TREML1
PANDAS	LRP11
Sarcoidosis	CX3CL1
Sarcoidosis	EPYC
Sarcoidosis	PGLYRP1
SLE	CXCL3
SLE	IFNA17
SLE	CXCL1
SLE	LOC644613
SLE	IFNA6
SLE	SV2C
SLE	TMEM102
SLE	PDCD1LG2
SLE	SLC29A4
SLE	IL1A
SLE	C5orf64
SLE	IFNW1
SLE	SCGB1D1
SLE	EPYC
SLE	CNPY2
SLE	CCL4L1
SLE	SPINK9
SLE	TNF
SLE	KIRREL3
SLE	IFNA8
SLE	IFNA14
SLE	VEGFB
SLE	TMEM108
SLE	IFNA5
SLE	ACVR2B
SLE	OBP2B
SLE	MCFD2
SLE	DPT
SLE	SPACA7
SLE	IFNA13
SLE	FKBP14
SLE	LACRT
SLE	IL6
SLE	FAM19A3
SLE	IFNL2
SLE	ERP27

TABLE 3-continued

List of Autoantigens and the Corresponding Diseases or Disorders

Disease	Target
SLE	TMEM149
SLE	PRH1;
SLE	ZG16B
SLE	IFNA2
SLE	RAET1E
SLE	CCDC47
SLE	MUC21
SLE	CCL22
SLE	CGREF1
SLE	TEPP
SLE	FAM19A2
SLE	SPOCK1
SLE	SRGN
SLE	SHISA7
SLE	CCL17
SLE	RNASE10
SLE	FGF21
SLE	APOA4
SLE	NGFR
SLE	KCNV2
SLE	AGER
SLE	FGFRL1
SLE	LGR6
SLE	CCL8
SLE	CD44
SLE	ITIH3
SLE	CST8
SLE	SSPN
SLE	CELA1
SLE	IL4
SLE	RCN3
SLE	PRRG4
SLE	MFAP5
SLE	CSPG5
SLE	VTCN1
SLE	PLA2G2E
SLE	LY6H
SLE	GYPC
SLE	SLC41A2
SLE	DRAXIN
SLE	CSHL1
SLE	LAIR2
SLE	IGFBP2
SLE	CD248
SLE	RGMB
SLE	TGOLN2
SLE	CSAG1
SLE	ACP4
SLE	CALU
SLE	BTNL8
SLE	SOSTDC1
SLE	LYSMD4
SLE	LCN2
SLE	SCGB1C2
SLE	CST4
SLE	IGF1
SLE	PRRT1
SLE	CHRNA5
SLE	ANTXRL
SLE	TNFRSF6
SLE	CD300LG
SLE	SERPINE1
SLE	OLFM1
SLE	PLA2G10
SLE	CD300E
SLE	CDH19
SLE	RAMP2
SLE	ATP4B
SLE	PTPRR
SLE	SFN
SLE	HCRTR2
SLE	ACRV1
SLE	FAM3A

TABLE 3-continued

List of Autoantigens and the Corresponding Diseases or Disorders

Disease	Target
SLE	ACVR1B
SLE	FGF23
SLE	IL15RA
SLE	IGFBP7
SLE	LHFPL1
SLE	IL28B
SLE	VIT
SLE	IER3
SLE	C2orf40
SLE	PLVAP
SLE	LECT2
SLE	DAG1
SLE	SPINK6
SLE	SLC2A12
SLE	IGLL1
SLE	TFF2
SLE	ASIP
SLE	IL16
SLE	EDIL3
SLE	CCL13
SLE	RCN1
SLE	CSH2
SLE	IL33
SLE	LILRB4
SLE	SPESP1
SLE	PDGFB
SLE	PTHLH
SLE	C9orf47
SLE	CHRDL2
SLE	ART3
SLE	CPVL
SLE	CCL15
SSC	SERPINE1
SSC	LEP
SSC	LECT2
SSC	OTOR
SSC	CASQ1
SSC	CST6
SSC	INSL3
SSC	SPACA3
SSC	AMTN
SSC	ZG16B
SSC	LOC644613
SSC	PGA4
SSC	LYSMD4
SSC	SRGN
SSC	CDH19
SSC	SHISA7
SSC	FAM19A3
SSC	HAVCR1
SSC	BAMBI
SSC	MSMP
SSC	SPACA7
SSC	PTHLH
SSC	PLA2G12B
SSC	CXCL3
SSC	CST4
SSC	DKK3
SSC	PIANP
SSC	PRG3
SSC	BTC
SSC	CCL17
SSC	XCL1
SSC	LMBRD2
SSC	LALBA
SSC	TGFA
SSC	IL29
SSC	EVI2B
SSC	SLPI
SSC	CLCC1
SSC	RNASE10
SSC	FGFBP3
SSC	FAM168B

TABLE 3-continued

List of Autoantigens and the Corresponding Diseases or Disorders

Disease	Target
SSC	PGLYRP1
SSC	ANGPTL4
SSC	CLU
SSC	AGER
SSC	TMEM108
SSC	C1QTNF2
SSC	TMEM119
SSC	CCL8
SSC	ODAPH
SSC	CNPY3
SSC	MZB1
SSC	CYTL1
SSC	PRH1
SSC	SLC2A10
SSC	PRRG1
SSC	CSPG5
SSC	DRAXIN
SSC	PRR27
SSC	DKK1
SSC	NTRK2
SSC	IFNA13
SSC	PDCD1
SSC	FAM19A2
SSC	IFNW1
SSC	RCN1
SSC	CFD
SSC	CRELD2
SSC	CCL18
SSC	CD14
SSC	BTN1A1
SSC	PTPRR
SSC	TMEM91
SSC	VSIG2
SSC	CCL13
SSC	C2orf40
SSC	VEGFB
SSC	REG4
SSC	TXNDC12
SSC	ACVR2B
SSC	ODAM
SSC	CST5
SSC	PI3
SSC	TMEM149
SSC	TEPP
SSC	KCNV2
SSC	PLA2G2E
SSC	AIMP1
SSC	IGFBP5
SSC	ASIP
SSC	PGC
SSC	TM9SF3
SSC	AMELX
SSC	CSN2
SSC	CPXM2
SSC	PRSS3
SSC	FAM3A
SSC	LILRA3
SSC	CSAG1
SSC	RTBDN
SSC	CELA1
SSC	ANTXRL
SSC	PLA2G10
SSC	KCT2
SSC	APOH
SSC	NENF
SSC	NPPC
SSC	LY6H
SSC	FGF1
SSC	SLC1A1
SSC	IFNL2
SSC	HSPA13
SSC	C6orf15
SSC	FLJ37218

TABLE 3-continued

List of Autoantigens and the Corresponding Diseases or Disorders

Disease	Target
SSC	CCL7
SSC	APOA4
SSC	FSTL1
SSC	IGFBP1
SSC	FCGR2A
SSC	SMR3A
SSC	IFITM10
SSC	MSLN
SSC	PRAP1
SSC	EPO
SSC	PLVAP
SSC	PROK1
SSC	TSLP
SSC	MIA
SSC	APP
SSC	OBP2A
SSC	RTN4RL1
SSC	PRRT3
SSC	APOA1
SSC	FGF7
SSC	TMED1
SSC	LGALS3
SSC	JCHAIN
SSC	PRRG3
SSC	IGF1
SSC	ACRV1
SSC	SLC38A4
SSC	FKBP11
SSC	ITPRIPL1
SSC	PLAC9
SSC	TFF2
SSC	WFDC13
SSC	LCN1
SSC	LYG1
SSC	LAIR2
SSC	TNFRSF8
SSC	SOSTDC1
SSC	VSTM2A
SSC	IGFBP7
SSC	PSORS1C2
SSC	FGF23
SSC	RSPO3
SSC	S100A9
SSC	CXCL9
SSC	TGOLN2
SSC	ACP5
SSC	MANF
SSC	AMBN
SSC	PSAPL1
SSC	WFDC10A
SSC	PPT1
SSC	MANSC4
SSC	CD248
SSC	NGRN
SSC	PSAP
SSC	LILRB2
SSC	SCGB2A2
SSC	IGFBPL1
SSC	SV2C
SSC	CXCL6
SSC	CD300E
SSC	RCN3
SSC	IGFBP3
SSC	RTN4R
SSC	PRRT1
SSC	ACVR2A
SSC	LCN2
SSC	HCRTR2
SSC	CELA3A
SSC	ADM2
SSC	LRIT3
SSC	MIA2
SSC	TNFRSF17

TABLE 3-continued

List of Autoantigens and the Corresponding Diseases or Disorders

Disease	Target
SSC	SPN
SSC	SLC6A5
SSC	WFDC1
SSC	LILRB4
SSC	CTSG
SSC	CXCL11
SSC	KLK7
SSC	CST8
SSC	NOPE
SSC	GAST
SSC	ASTN2
SSC	MCFD2
SSC	CCL22
SSC	OTOL1
SSC	SYCN
SSC	CCL2
SSC	SOST
SSC	PTN
SSC	TACSTD2
SSC	IL21
SSC	IGLL1
SSC	MMP7
SSC	APLP2
SSC	SSBP3__AS1
SSC	CST7
SSC	SSPN
SSC	HS3ST1
SSC	GP6
SSC	RNASE8
SSC	ACVR1B
SSC	PDIA3
SSC	IL15RA
SSC	PTPRN2
SSC	IL28B
SSC	PMCH
SSC	PVRL2
SSC	WIF1
SSC	EREG
SSC	EDIL3
SSC	CDSN
SSC	REG1A
SSC	PTH
SSC	LHFPL1
SSC	TRABD2B
SSC	TIGIT
SSC	KISS1
SSC	CXCL17
SSC	SPOCK2
SSC	CTF1
SSC	CD55
SSC	DEFB108B
SSC	IL17C
SSC	GPHB5
SSC	PRLR
SSC	NLGN4Y
SSC	SPACA5
SSC	FGF17
SSC	C9
SSC	CHRDL2
SSC	PF4V1
SSC	RAMP2
SSC	CCL26
SSC	CD151
SSC	TRPC5
SSC	MMP1
SSC	PRRG4
SSC	ART3
SSC	HEPACAM2
SSC	SDF2L1
SSC	IGFBP2
SSC	AXL
SSC	SCN3B
SSC	EPHA5

TABLE 3-continued

List of Autoantigens and the Corresponding Diseases or Disorders

Disease	Target
SSC	IL1RAP
SSC	ATP6AP2
SSC	CCL20
SSC	GNRH1
SSC	SEMG1
SSC	APOE
SSC	FGFRL1
SSC	IBSP
SSC	TEX264
SSC	CCBE1
SSC	BCAM
SSC	LRRC8C
SSC	DKK2
SSC	EPHA4
SSC	SFRP4
SSC	SYNDIG1L
SSC	FAM19A5
SSC	LYG2
SSC	FAM3C
SSC	TUSC5
SSC	MDK
SSC	FGF16
SSC	MFGE8
SSC	PRELP
SSC	COL10A1
SSC	IGF2
SSC	CSN3
SSC	CLDN18
SSC	PDIA6
SSC	CHAD
SSC	TNFRSF21
SSC	C6orf120
SSC	COL9A3
SSC	PDGFB
SSC	TOR1B
SSC	LHFPL5
SSC	UNQ9165_PRO28630
SSC	CCL15
SSC	BMPR1A
SSC	FGFR2
SSC	DGAT2L7P
SSC	SERPINA13P
SSC	FCAMR
SSC	XCL2
SSC	TMEM9B
SSC	RNF167
SSC	LCN15
SSC	TREML1
SSC	FGF21
SSC	SLC22A31
SSC	IL20RB
SSC	CCL11
SSC	STC2
SSC	FKBP14
SUSAC	CCL24
SUSAC	SDC4
SUSAC	TREML1
SUSAC	VSIG4
Malaria	LCN15
Malaria	IL21
Malaria	LEP
Malaria	FKBP7
Malaria	CCL11
Malaria	BMPR2
Malaria	SCGB2A2
Malaria	GZMK
Malaria	MSMP
Malaria	DCD
Malaria	SPARC
Malaria	COL9A3
Malaria	FLRT3
Malaria	TNFRSF10B
Malaria	FZD4

TABLE 3-continued

List of Autoantigens and the Corresponding Diseases or Disorders

Disease	Target
Malaria	TSPAN13
Malaria	HTRA3
Malaria	PCSK1
Malaria	LYPD6B
Malaria	CPE
Malaria	GFRAL
Malaria	TGOLN2
Malaria	PRLR
Malaria	TNFRSF21
Malaria	TSPAN2
Malaria	AMTN
Malaria	F12
Malaria	SLC1A1
Malaria	MPZL3
Malaria	F13B
Malaria	C6orf120
Malaria	PRAP1
Malaria	IGFBP6
Malaria	FGL2
Malaria	SPX
Malaria	GPC6
Malaria	INSL3
Malaria	CYTL1
Malaria	TM4SF6
Malaria	SGCA
Malaria	C9orf135
Malaria	CD300A
Malaria	CTF1
Malaria	OPN4
Malaria	SLC22A31
Malaria	ZP4
Malaria	IL21R
Malaria	ADM
Malaria	AXL
Malaria	EPHA5
Malaria	IL17A
Malaria	PTH
Malaria	TNFRSF17
Malaria	SHISA6
Malaria	FGF17
Malaria	GNRH1
Malaria	SDF2L1
Malaria	CNPY4
Malaria	SLC6A9
Malaria	NPR3
Malaria	SIGLEC10
Malaria	IL13
Malaria	SFTPA2
Malaria	GDPD3
Malaria	CD164L2
Malaria	KLK2
Malaria	ENSP00000381830
Malaria	AKR1B10
Malaria	KLK3
Malaria	FCER1A
Malaria	SNORC
Malaria	CSHL1
Malaria	CSH2
Malaria	CSN3
Malaria	SLC1A4
Malaria	HEPACAM2
Malaria	INS
Malaria	GP6
Malaria	RNASE8
Malaria	SLAMF9
Malaria	DPT
Malaria	MINPP1
Malaria	FGFR3
Malaria	C2orf66
Malaria	IMPG1
Malaria	NENF
Malaria	DKK3
Malaria	NOV

TABLE 3-continued

List of Autoantigens and the Corresponding Diseases or Disorders

Disease	Target
Malaria	SERPINI2
Malaria	IFNA6
Malaria	COLEC12
Malaria	CALR
Malaria	PRRG1
Malaria	GSN
Malaria	SLC10A4
Malaria	CD99
Malaria	FSTL1
Malaria	IL16
Malaria	TRH
Malaria	SLC6A14
Malaria	GLB1
Malaria	CCL20
Malaria	ARTN
Malaria	SPP2
Malaria	LINC00305
Malaria	LAS2
Malaria	S100A13
Malaria	MZB1
Malaria	RETN
Malaria	FAM172A
Malaria	CD99L2
Malaria	CD151
Malaria	SDF4
Malaria	CEACAM19
Malaria	CHGB
Malaria	SLC8B1
Malaria	CDNF
Malaria	BCAM
Malaria	TSPAN9
Malaria	ENDOD1
Malaria	EMC10
Malaria	OS9
Malaria	TMEM169
Malaria	IL22
Malaria	NBL1
Malaria	IL1RN
Malaria	SMOC2
Malaria	PRRG3
Malaria	LRIT3
Malaria	KCT2
Malaria	XG
Malaria	IGF1
Malaria	GAST
Malaria	CGREF1
Malaria	RAMP2
Malaria	PRRG4
Malaria	CDSN
Malaria	C11orf94
Malaria	OTOL1
Malaria	IBSP
Malaria	LGALS3
Malaria	LYSMD4
Malaria	SYCN
Malaria	JCHAIN
Malaria	CST8
Malaria	PRRT1
Malaria	CCL15
Malaria	SSPN
Malaria	APOO
Malaria	CST5
Malaria	SPINK1
Malaria	HCRTR2
Malaria	PRRT3
Malaria	PSORS1C2
Malaria	RTBDN
Malaria	ACRV1
Malaria	FKBP14
Malaria	SPINK4
Malaria	IGFBP1
Malaria	PLA2G2E
Malaria	OBP2A

TABLE 3-continued

List of Autoantigens and the Corresponding Diseases or Disorders

Disease	Target
Malaria	CCL8
Malaria	VEGFB
Malaria	TGFA
Malaria	COL10A1
Malaria	IFNW1
Malaria	RNASE10
Malaria	PRH1;
Malaria	CDH19
Malaria	CPXM2
Malaria	CSPG5
Malaria	RCN3
Malaria	IFNA13
Malaria	IGFBP2
Malaria	PLA2G10
Malaria	SRGN
Malaria	EPYC
Malaria	CXCL1
Malaria	CNPY2
Malaria	MCFD2
Malaria	ANGPTL4
Malaria	SPACA7
Malaria	SLC2A10
Malaria	RTN4R
Malaria	CXCL3
Malaria	CCDC47
Malaria	CST4
Malaria	CELA1
Malaria	LALBA
Malaria	PTPRR
Malaria	OBP2B
Malaria	TXNDC12
Malaria	PTN
Malaria	ZG16B
Malaria	PRSS3
Malaria	CNPY3
Malaria	PTHLH
Malaria	PGLYRP1
Malaria	KLK7
Malaria	CCL13
Malaria	FAM19A3
Malaria	KLK8
Malaria	SERPINA3
Malaria	HCTR1
Malaria	DRD5
Malaria	GPR37L1
Malaria	BDKBR1
Malaria	NPY2R
Malaria	SCTR
Malaria	ADCYAP1R1
Malaria	GPR19
Malaria	S1PR3
Malaria	NMBR
Malaria	CCR4
Malaria	GPR17
Malaria	CNR1
Malaria	OPRK1
Malaria	CYSLTR2
Malaria	P2RY10
Malaria	HTR1B
Malaria	OPRM1
Malaria	RXFP3
Malaria	OXER1
Malaria	CXCR3
Malaria	HTR2B
Malaria	GPR1
Malaria	NPBW1
Malaria	VSTM2A
Malaria	LY6G6D
Malaria	SLC41A2
Malaria	MOG
Malaria	RNASE9
Malaria	IGLL5
Malaria	CHGA

TABLE 3-continued

List of Autoantigens and the Corresponding Diseases or Disorders

Disease	Target
Malaria	TREML1
Malaria	GHRHR
Malaria	XK
Malaria	KITLG
Malaria	WFDC10A
Malaria	TMEM108
Malaria	OTOR
Malaria	GPR63
Malaria	PLGRKT
Malaria	CTSG
Malaria	SLC6A5
Malaria	CSAG1
Malaria	FZD9
Malaria	CMKLR1
Malaria	FKBP2
Malaria	ITIH3
Malaria	LILRA4
Malaria	TNFRSF12A
Malaria	CXCL13
Malaria	PPT1
Malaria	CXCL17
Malaria	ODAM
Malaria	IL1RAP
Malaria	SLC38A4
Malaria	ACKR1
Malaria	CADM2
Malaria	PAPLN
Malaria	GPR37
Malaria	SLC38A2
Malaria	TMEM59
Malaria	RAET1L
Malaria	SPINK8
Malaria	TRABD2B
Malaria	FGF23
Malaria	TMEM91
Malaria	SV2C
Malaria	REG1A
KT	SPOCK1
KT	CD99L2
KT	ACRV1
KT	SPINK4
KT	MCFD2
KT	CD80
KT	IL2RA
KT	LOC644613
KT	AGRP
KT	SHISA7
KT	RCN2
KT	ACKR1
KT	IFNG
KT	SCGB3A1
KT	CCL16
KT	IL29
KT	OBP2B
KT	CXCL3
KT	CCDC47
KT	SSPN
KT	EPYC
KT	SPACA3
KT	MRGPRF
KT	KLK8
KT	MUCL3
KT	IL9
KT	IFNL2
KT	IGFBP1
KT	CALU
KT	MZB1
KT	CCL22
KT	TNFRSF21
KT	SPACA7
KT	LYG2
KT	TNFRSF5
KT	ANGPTL4

TABLE 3-continued

List of Autoantigens and the Corresponding Diseases or Disorders

Disease	Target
KT	ENDOU
KT	PTPRR
KT	CSPG5
KT	SPINK9
KT	IL7
KT	FLJ37218
KT	DKK3
KT	ZG16B
KT	SERPINE1
KT	SLPI
KT	CD274
KT	FAM19A2
KT	VSIG2
KT	CD40LG
KT	EDDM3B
KT	HCRTR2
KT	FGFR2
KT	EXOC3-AS1
KT	IGFBP2
KT	SERPINA3
KT	CXCL1
KT	OTOR
KT	TSPAN9
KT	CNPY3
KT	PRR27
KT	RCN3
KT	CNPY2
KT	BTC
KT	ADRB3
KT	IGFBP5
KT	NPY1R
KT	TMEM102
KT	LALBA
KT	CXCL2
KT	CCL13
KT	OTOL1
KT	IL1A
KT	APOO
KT	LGALS3
KT	LECT2
KT	CDH19
KT	RTN4R
KT	RETN
KT	CSF2
KT	APOH
KT	MICA
KT	GPR6
KT	IL4
KT	CRLF1
KT	LAIR2
KT	NPY2R
KT	LYSMD4
KT	DCD
KT	TXNDC12
KT	GP6
KT	NOV
KT	DRAXIN
KT	CCR10
KT	PILRA
KT	GPR1
KT	OPRL1
KT	FAM168B
KT	PRLR
KT	CFD
KT	IBSP
KT	PTPRN2
KT	ERP27
KT	BTN1A1
KT	PDCD1
KT	SV2C
KT	CSN2
KT	NINJ1
KT	TMEM91

TABLE 3-continued

List of Autoantigens and the Corresponding Diseases or Disorders

Disease	Target
KT	SLC1A1
KT	ADCYAP1
KT	SEMG2
KT	APOA1
KT	MPO
KT	VEGFB
KT	IL34
KT	IFNA17
KT	S100A13
KT	AVPR1A
KT	CCL17
KT	AMTN
KT	IL17RD
KT	DKK1
KT	PSORS1C2
KT	SSTR2
KT	SYCN
KT	GPR37
KT	ANTXRL
KT	AGER
KT	PGLYRP1
KT	WFDC12
KT	IMPG1
KT	GNRH1
KT	SLC2A12
KT	FKBP2
KT	ULBP1
KT	TMEM119
KT	PRSS3
KT	MIA2
KT	SLC2A2
KT	C5orf64
KT	TFPI2
KT	PCSK1
KT	PRH1;
KT	IGFBP7
KT	UNQ6190/PRO20217
KT	CELA1
KT	OSTN
KT	RARRES2
KT	AZGP1
KT	TGFA
KT	IL6
KT	FMR1NB
KT	REG1B
KT	CXCL12
KT	IL28B
KT	JCHAIN
KT	CES3
KT	FAM19A3
KT	FAM174A
KT	CCL4L1
KT	PLA2G2E
KT	COL10A1
KT	ITPRIPL1
KT	PPBP
KT	MANF
KT	TMEM149
KT	PRRG4
KT	GFRA2
KT	CA11
KT	TLR1
KT	CCL21
KT	REG4
KT	PRG3
KT	IFNA13
KT	SLC22A25
KT	CCL7
KT	ATP6AP2
KT	BRICD5
KT	GAST
KT	KAL1
KT	TMEM108

TABLE 3-continued

List of Autoantigens and the Corresponding Diseases or Disorders

Disease	Target
KT	IL16
KT	GPR182
KT	TNFRSF6
KT	TSLP
KT	APOA4
KT	SIRPA
KT	FCER1A
KT	PLBD2
KT	KCNV2
KT	NXPH1
KT	BCAM
KT	IFNA6
KT	SPESP1
KT	NENF
KT	PLA2G10
KT	VSTM2A
KT	GPR19
KT	NOG
KT	CD300E
KT	CST5
KT	MMP7
KT	HAVCR1
KT	CST4
KT	THBD
KT	MLN
KT	TRABD2A
KT	ATP4B
KT	PIANP
KT	GNLY
KT	CCKAR
KT	GPR63
KT	ICAM2
KT	LYPD6B
KT	TMEM120A
KT	DHRS4L2
KT	OTOS
KT	RCN1
KT	B2M
KT	CCL24
KT	IFNA2
KT	IFNA14
KT	BMPR2
KT	SRGN
KT	FCGR2A
KT	ITIH3
KT	CPXM2
KT	ACP5
KT	KAZALD1
KT	MIA
KT	FGF1
KT	LRRC4B
KT	CCL26
KT	C2orf40
KT	PLVAP
KT	SOSTDC1
KT	CGREF1
KT	TNFRSF12A
KT	CLCC1
KT	SMR3A
KT	LY6G6D
KT	CCL18
KT	CCL2
KT	RTN4RL2
KT	C10orf54
KT	FAM24B
KT	FGF23
KT	RSPO3
KT	GPR156
KT	TGOLN2
KT	XG
KT	UNQ9165/PRO28630
KT	FKBP14
KT	GPRC6A

TABLE 3-continued

List of Autoantigens and the Corresponding Diseases or Disorders

Disease	Target
KT	C6orf15
KT	CREG2
KT	PTHLH
KT	ASIP
KT	GPR25
KT	GPR17
KT	HCTR1
KT	SLC38A4
KT	SLC8B1
KT	IL15RA
KT	SLC2A10
KT	NPBW1
KT	PAEP
KT	DKK2
KT	CADM2
KT	CCL15
KT	CXCR3
KT	ADRA1D
KT	IFNA5
KT	KIRREL3
KT	BMPR1A
KT	TNFRSF17
KT	MFSD2A
KT	C12orf49
KT	FCGR2C
KT	COL9A3
KT	SPINK7
KT	WFDC1
KT	ADM
KT	SOST
KT	RXFP3
KT	TM4SF6
KT	IGFBP3
KT	NETO1
KT	FGF7
KT	LPA4
KT	SPINK1
KT	TMED1
KT	ADM2
KT	RAET1L
KT	S1PR4
KT	C2orf66
KT	CST6
KT	SERPINI1
KT	IFITM10
KT	SEMG1
KT	SCG3
KT	SCG5
KT	IL17BR
KT	ANGPTL5
KT	CSAG1
KT	REG1A
KT	IGFBP6
KT	GPR83
KT	INSL3
KT	PRRG1
KT	CD248
KT	EFNB3
KT	IL21
KT	NOPE
KT	APOC3
KT	NPPC
KT	JTB
KT	SELL
KT	UNC5B
KT	WFDC13
KT	APLP2
KT	LYPD1
KT	C17orf99
KT	MADCAM1
KT	FZD9
KT	CST1
KT	IL32

TABLE 3-continued

List of Autoantigens and the Corresponding Diseases or Disorders

Disease	Target
KT	PGA3
KT	ADAMTS16
KT	PSAPL1
KT	IL1F5
KT	P4HB
KT	CXCL11
KT	SLC20A1
KT	SPX
KT	SLC10A4
KT	TMEM41A
KT	LRFN2
KT	ULBP2
KT	LAG3
KT	EPCAM
KT	OSM
KT	SLC39A8
KT	FGFRL1
KT	GPR22
KT	CP
KT	AMELX
KT	MUCL1
KT	FSTL1
KT	GZMM
KT	GSN
KT	SLC6A5
KT	LCN1
KT	PRL
KT	CXCL9
KT	229E-S1
KT	F13B
KT	CPVL
KT	TFF2
KT	SPINK13
KT	SNORC
KT	STC2
KT	LIFR
KT	OS9
KT	HRC
KT	SMOC2
KT	FGFBP3
KT	CRTAP
KT	SGCB
KT	TOR1B
KT	C6
KT	GALP
KT	SDC1
KT	PDGFA
KT	OXTR
KT	KLK7
KT	RNASE8
KT	CYTL1
KT	SPINK8
KT	HRH3
KT	CALY
KT	LCN15
KT	APP
KT	TRPC3
KT	AVP
KT	RNF167
KT	GPR77
KT	IGF1
KT	CXCR5
KT	PGA4
KT	CLDN9
KT	OXER1
KT	CTSG
KT	FGF17
KT	GPR3
KT	COV2-S1
KT	EDIL3
KT	AZU1
KT	NPTX2
KT	LRRC8C

TABLE 3-continued

List of Autoantigens and the Corresponding Diseases or Disorders

Disease	Target
KT	DEFB126
KT	CXCR1
KT	PMCH
KT	CCL11
KT	MOG
KT	TNFRSF6B
KT	PDGFB
KT	TFF1
KT	BTNL8
KT	CHGA
KT	NTRK2
KT	PTN
KT	ACKR2
KT	SERPINE2
KT	C9
KT	MCP
KT	CMKLR1
KT	C6orf25
KT	OBP2A
KT	SLC22A8
KT	NGFR
KT	CT83
KT	CCL8
KT	IL6R
KT	PLGRKT
KT	ART1
KT	CXCL13
KT	HNRNPA2B1
KT	CD14
KT	LHFPL6
KT	FAM20A
KT	NOTCH2NL
KT	ISM2
KT	MUC7
KT	LGALS1
KT	PLAC9
KT	FAM187B
KT	FGF19
KT	FAM3D
KT	ODAPH
KT	KCNK1
KT	LRIT3
KT	RTN4RL1
KT	SLC22A4
KT	FAM19A4
KT	PRRT3
KT	F2R
KT	F12
KT	PKD2L1
KT	OPRM1
KT	VSTM2B
KT	KLRF1
KT	MC5R
KT	CCL1
KT	EREG
KT	PLA2G15
KT	CLDN4
KT	LHFPL1
KT	CDSN
KT	APOE
KT	TNF
KT	OPRK1
KT	PDIA6
KT	NTNG2
KT	TRH
KT	FAM24A
KT	OPN4
KT	TIMP1
KT	CD99
KT	CSN3
KT	AIMP1
KT	XK
KT	SLC6A11

TABLE 3-continued

List of Autoantigens and the Corresponding Diseases or Disorders

Disease	Target
KT	IGFBPL1
KT	HAPLN2
KT	ALPI
KT	FCMR
KT	CSHL1
KT	PRAP1
KT	COL26A1
KT	APLP1
KT	RAMP2
KT	LYPD2
KT	TMEM219
KT	CASQ1
KT	NAPSA
KT	COL8A1
KT	FRZB
KT	DEFB116
KT	DLL3
KT	KCNMB4
KT	S100A8
KT	COMT
KT	ANGPT4
KT	C1QL1
KT	GRM5
KT	KLRK1
KT	VTCN1
KT	MARCO
KT	RNASE10
KT	FCN2
KT	IL13
KT	WFDC8
KT	CCL20
KT	CD300A
KT	IL1RN
KT	GGH
KT	IL8RB
KT	WNT5A
KT	MDK
KT	CELA3B
KT	PSAP
KT	IL25
KT	SELE
KT	ACVRL1
KT	PAPLN
KT	DEAF1
KT	CDNF
KT	SDF2L1
KT	PRR4
KT	SHBG
KT	IFNA8
KT	FAM3A
KT	SPP2
KT	C1QTNF2
KT	TMPRSS2
KT	CXCL17
KT	PRRT1
KT	EDAR
KT	LIPF
KT	TREM2
KT	FZD7
KT	FCRL6
KT	CLCF1
KT	FAM20C
KT	TNFSF9
KT	LRRN4
KT	CELA3A
KT	LCN12
KT	CHODL
KT	CLEC-6
KT	RNF149
KT	SYNDIG1L
KT	ISLR2
KT	EPOR
KT	ASTN2

TABLE 3-continued

List of Autoantigens and the Corresponding Diseases or Disorders

Disease	Target
KT	LGI4
KT	INHBE
KT	NRG1
KT	FAM19A5
KT	EGFR
KT	CLDN12
KT	CD74
KT	PRSS55
KT	PLA2G2C
KT	CFP
KT	LCAT
KT	BPIFA1
KT	CNNM4
KT	THBS3
KT	CRELD2
KT	C9orf47
KT	MANSC4
KT	METTL24
KT	NPY4R
KT	SLCO1B1
KT	ALPPL2
KT	TMPRSS3
KT	SPACA4
KT	CDH9
KT	GYPA
KT	GLRA1
KT	CX3CL1
KT	OLR1
KT	EFNA5
KT	PRSS22
KT	LRRC21
KT	IER3
KT	PROK1
KT	TREM1
KT	IL6ST
KT	DNASE1L1
KT	MMP17
KT	PRSS23
KT	NPNT
KT	IL1B
KT	MMP9
KT	CA14
KT	NXPH4
KT	GABRR3

Example 3: Diagnostic or Prognostic Autoantigens

[0473]

TABLE 4

List of Diagnostic or Prognostic Autoantigens and their Corresponding Diseases or Disorders

Disease	Target
AAV	EDIL3
AAV	LY6H
AAV	TREM2
APECED	IFNA6
APECED	IFNW1
APECED	IFNA17
APECED	IFNA14
APECED	LCN1
APECED	GPHB5
APECED	IFNA13
APECED	IFNA8
APECED	IL22RA2
APECED	PRRT3
APECED	IL22

TABLE 4-continued

List of Diagnostic or Prognostic Autoantigens and their Corresponding Diseases or Disorders

Disease	Target
APECED	C5orf64
APECED	CP
APECED	IFNA5
APECED	LEG1
APECED	PNLIPRP2
APECED	IL17A
APECED	PRG3
APECED	IL17F
APECED	IFNA2
APECED	IL5
APECED	SLC2A10
APECED	GIF
APECED	PNLIPRP1
APECED	BPIFA1
APECED	PDILT
APECED	IFNL2
APECED	PDGFB
APECED	CST5
APECED	PNLIP
APECED	IGSF4B
APECED	TGFA
APECED	BPIFA2
APECED	HSPA13
APECED	ODAPH
APECED	SPINK4
APECED	IGFBP1
APECED	IL6
APECED	CLCC1
APECED	BTN1A1
APECED	EREG
APECED	FAM19A4
APECED	PTPRR
APECED	CST6
APECED	RAMP2
APECED	IL28B
APECED	TSLP
APECED	SPAG11B
APECED	CNPY3
APECED	FAM3A
APECED	SLC41A2
APECED	FKBP14
APECED	AFP
APECED	TM4SF6
APECED	REG1A
APECED	PANX3
APECED	PRRG3
APECED	RNASE8
APECED	SMR3A
APECED	SPINK1
APECED	PSAP
APECED	SERPINE1
APECED	CST4
APECED	PRRG1
APECED	KLK2
APECED	HCRTR2
APECED	LAIR2
APECED	OTOR
APECED	TFF2
APECED	MSR1
APECED	CCL7
APECED	ADM2
APECED	OPN4
APECED	PAP
APECED	MMP1
APECED	REG4
APECED	PMCH
APECED	CLPS
APECED	OBP2A
APECED	ACRV1
APECED	DEFA5
APECED	ECSCR
APECED	LRIT3

TABLE 4-continued

List of Diagnostic or Prognostic Autoantigens and their Corresponding Diseases or Disorders

Disease	Target
APECED	PLA2G10
APECED	TM9SF3
APS	IL6R
APS	IFNA13
APS	IFNA14
APS	IFNA17
APS	IFNA2
APS	IFNA5
APS	IFNA6
APS	IFNA8
APS	IL6R
CIDP	CXCL1
CIDP	CXCL2
CIDP	CXCL3
CIDP	PDGFB
CIDP	TMEM149
CIDP	CD74
CIDP	CXCL13
COVID-19	APOO
COVID-19	OPRL1
COVID-19	IFNA14
COVID-19	MIA2
COVID-19	FKBP2
COVID-19	GPR1
COVID-19	IL29
COVID-19	PTPRR
COVID-19	RCN2
COVID-19	IFNA13
COVID-19	IFNW1
COVID-19	IL1A
COVID-19	TSPAN9
COVID-19	SHISA7
COVID-19	IFNA17
COVID-19	LEP
COVID-19	CALU
COVID-19	SSPN
COVID-19	LPAL2
COVID-19	OBP2B
COVID-19	CST5
COVID-19	IL6
COVID-19	CCDC47
COVID-19	ACRV1
COVID-19	PGA3
COVID-19	LRRC8C
COVID-19	PMCH
COVID-19	GPR6
COVID-19	CSF2
COVID-19	RCN3
COVID-19	LYSMD4
COVID-19	CD99
COVID-19	IFNA5
COVID-19	IFNL2
COVID-19	CXCL9
COVID-19	SLC41A2
COVID-19	EPYC
COVID-19	DUOXA1
COVID-19	LACRT
COVID-19	CNPY2
COVID-19	KLK8
COVID-19	MZB1
COVID-19	LYG2
COVID-19	MUCL3
COVID-19	LALBA
COVID-19	ZG16B
COVID-19	ODAM
COVID-19	PILRA
COVID-19	HRC
COVID-19	PPBP
COVID-19	CSPG5
COVID-19	PTPRN2
COVID-19	CST4
COVID-19	FAM168B

TABLE 4-continued

List of Diagnostic or Prognostic Autoantigens and their Corresponding Diseases or Disorders

Disease	Target
COVID-19	TNFRSF17
COVID-19	OTOS
COVID-19	SPINK9
COVID-19	KLRC2
COVID-19	IFNA8
COVID-19	TMEM119
COVID-19	CSAG1
COVID-19	OTOR
COVID-19	KCT2
COVID-19	PGA4
COVID-19	SPINK4
COVID-19	FCGR2A
COVID-19	CNPY3
COVID-19	NEGR1
COVID-19	ERP27
COVID-19	AGRP
COVID-19	PRR27
COVID-19	MCFD2
COVID-19	IGFBP6
COVID-19	IFNA2
COVID-19	LGALS3
COVID-19	SPOCK1
COVID-19	KCNV2
COVID-19	HCRTR2
COVID-19	LECT2
COVID-19	PLA2G2E
COVID-19	FAM19A3
COVID-19	SPACA7
COVID-19	NENF
COVID-19	IL6R
COVID-19	SPX
COVID-19	IGFBP1
COVID-19	SRGN
COVID-19	LAIR2
COVID-19	CPXM2
COVID-19	CCL17
COVID-19	TUSC5
COVID-19	LOC644613
COVID-19	TNFRSF21
COVID-19	GPR77
COVID-19	C2orf40
COVID-19	C5A
COVID-19	IFNA6
COVID-19	SPP1
COVID-19	SERPINA3
COVID-19	OXTR
COVID-19	KLRC1
COVID-19	SEMG2
COVID-19	APOH
COVID-19	PRRG1
COVID-19	BTC
COVID-19	MSLN
COVID-19	FAM19A2
COVID-19	CXCL1
COVID-19	PRSS55
COVID-19	SLCO2B1
COVID-19	BTN1A1
COVID-19	COV2-RBD
COVID-19	OS9
COVID-19	PGLYRP1
COVID-19	DKK3
COVID-19	TOR1B
COVID-19	CST1
COVID-19	LRRC8D
COVID-19	ACKR1
COVID-19	COL8A1
COVID-19	CXCL3
COVID-19	ODAPH
COVID-19	PIANP
COVID-19	PSORS1C2
COVID-19	RNASE10
COVID-19	CXCR7

TABLE 4-continued

List of Diagnostic or Prognostic Autoantigens and their Corresponding Diseases or Disorders

Disease	Target
COVID-19	PLVAP
COVID-19	CDSN
COVID-19	SDF2L1
COVID-19	TFF2
COVID-19	HSPA13
COVID-19	CXCR5
COVID-19	C5orf64
COVID-19	EPO
COVID-19	GNLY
COVID-19	OPRM1
COVID-19	TGFA
COVID-19	SLC2A10
COVID-19	CXCL13
COVID-19	CD99L2
COVID-19	AGER
COVID-19	CGA
COVID-19	CRTAM
COVID-19	SLC1A1
COVID-19	CDH19
COVID-19	GPR25
COVID-19	CCL8
COVID-19	SERPINI1
COVID-19	SPINK8
COVID-19	SLPI
COVID-19	HRH3
COVID-19	TMEM149
COVID-19	CD38
COVID-19	REG4
COVID-19	IGFBP5
COVID-19	FKBP7
COVID-19	GRM5
COVID-19	CXCR3
COVID-19	PTHLH
COVID-19	LY6K
COVID-19	PLAC9
COVID-19	LPL
COVID-19	CCKAR
COVID-19	RTN4R
COVID-19	GYPA
COVID-19	TMED1
COVID-19	DRAXIN
COVID-19	CCL13
COVID-19	LRRC8A
COVID-19	ANGPTL4
COVID-19	NPPC
COVID-19	IL22
COVID-19	CCL21
COVID-19	RCN1
COVID-19	CD74
COVID-19	FGF17
COVID-19	PAEP
COVID-19	CNPY4
COVID-19	APOC3
COVID-19	SPINK1
COVID-19	AZGP1
COVID-19	STC2
COVID-19	S1PR4
COVID-19	IBSP
COVID-19	CEACAM18
COVID-19	SLC38A4
COVID-19	CSN2
COVID-19	VSIG2
COVID-19	ENSP00000381830
COVID-19	CSHL1
COVID-19	CASQ1
COVID-19	XG
COVID-19	ENDOU
COVID-19	RAET1L
COVID-19	COL10A1
COVID-19	PTH
COVID-19	SLC15A1
COVID-19	SLC6A2

TABLE 4-continued

List of Diagnostic or Prognostic Autoantigens and their Corresponding Diseases or Disorders

Disease	Target
COVID-19	PRRT1
COVID-19	CLCC1
COVID-19	F2R
COVID-19	JTB
COVID-19	TGOLN2
COVID-19	CCL16
COVID-19	MIA
COVID-19	TNF
COVID-19	TMEM91
COVID-19	RTBDN
COVID-19	MPL
COVID-19	RSPO1
COVID-19	RSPO3
COVID-19	PRSS3
COVID-19	GPR17
COVID-19	CCR9
COVID-19	GP6
COVID-19	PRH1;
COVID-19	EQTN
COVID-19	RNF43
COVID-19	SPN
COVID-19	IGSF4B
COVID-19	CFD
COVID-19	SPACA5
COVID-19	CHGA
COVID-19	UNQ6190/PRO20217
COVID-19	APOA1
COVID-19	PRG3
COVID-19	SLC2A2
COVID-19	CCL11
COVID-19	TSLP
COVID-19	SMOC2
COVID-19	HTR5
COVID-19	PRAP1
COVID-19	LY6H
COVID-19	IMPG1
COVID-19	TNFRSF12A
COVID-19	SSTR2
COVID-19	IGFBP3
COVID-19	PRLR
COVID-19	PRR4
COVID-19	IL13
COVID-19	HCTR1
COVID-19	IGF1
COVID-19	CD300E
COVID-19	LINC00305
COVID-19	SPESP1
COVID-19	FRZB
COVID-19	IL28B
COVID-19	MMP9
COVID-19	GAST
COVID-19	FGF1
COVID-19	IL15RA
COVID-19	CCR10
COVID-19	VEGFB
COVID-19	SERPINE1
COVID-19	EXOC3-AS1
COVID-19	PRRT3
COVID-19	NETO1
COVID-19	VSTM2B
COVID-19	CCR4
COVID-19	APP
COVID-19	AMTN
COVID-19	CXCL6
COVID-19	NINJ1
COVID-19	KLK9
COVID-19	SDF4
COVID-19	CPE
COVID-19	AMELX
COVID-19	DCD
COVID-19	ANTXRL
COVID-19	CCR2

TABLE 4-continued

List of Diagnostic or Prognostic Autoantigens and their Corresponding Diseases or Disorders

Disease	Target
COVID-19	PCSK1
COVID-19	QRFP
COVID-19	RGMB
COVID-19	NPY2R
COVID-19	IGFBP7
COVID-19	SLC2A12
COVID-19	PPT1
COVID-19	CCL7
COVID-19	JCHAIN
COVID-19	ADCYAP1
COVID-19	PDZD11
COVID-19	CP
COVID-19	MANF
COVID-19	GZMA
COVID-19	TXNDC12
COVID-19	PGC
COVID-19	ACVR1
COVID-19	WFDC13
COVID-19	SFRP4
COVID-19	REG1A
COVID-19	GPR37
COVID-19	NOPE
COVID-19	C11orf94
COVID-19	SCARA5
COVID-19	GPR19
COVID-19	EMC7
COVID-19	CCL15
COVID-19	CA4
COVID-19	RNASE8
COVID-19	MLN
COVID-19	UNQ9165/PRO28630
COVID-19	NTRK3
COVID-19	TREML1
COVID-19	CDH15
COVID-19	SMR3A
COVID-19	DKK1
COVID-19	OXER1
COVID-19	FAM24B
COVID-19	CRLF1
COVID-19	PDIA6
COVID-19	PLA2G12B
COVID-19	FGF7
COVID-19	ZP4
COVID-19	BAMBI
COVID-19	GKN2
COVID-19	IGFBPL1
COVID-19	MMP7
COVID-19	MANSC4
COVID-19	APOA4
COVID-19	SUSD6
COVID-19	CELA1
COVID-19	IGLL1
COVID-19	IL9
COVID-19	MADCAM1
COVID-19	NPBW1
COVID-19	HAVCR1
COVID-19	ITPRIPL1
COVID-19	SOST
COVID-19	LHFPL1
COVID-19	SDC3
COVID-19	SEMG1
COVID-19	C1QB
COVID-19	ASIP
COVID-19	CCL18
COVID-19	LHFPL5
COVID-19	IGFL2
COVID-19	FGFRL1
COVID-19	EFNB2
COVID-19	C2orf66
COVID-19	MFAP3
COVID-19	C6orf15
COVID-19	OPN4

TABLE 4-continued

List of Diagnostic or Prognostic Autoantigens and their Corresponding Diseases or Disorders

Disease	Target
COVID-19	NOV
COVID-19	GNS
COVID-19	FKBP14
COVID-19	CELA2B
COVID-19	C9
COVID-19	VWC2L
COVID-19	BMPR2
COVID-19	CSH2
COVID-19	IL1RAP
COVID-19	C1QTNF2
COVID-19	SLC10A4
COVID-19	IL16
COVID-19	LRIT3
COVID-19	GRN
COVID-19	NIPAL4
COVID-19	GNRH1
COVID-19	ATP4B
COVID-19	APLP2
COVID-19	TMEM123
COVID-19	IL3
COVID-19	PDGFA
COVID-19	EVI2B
COVID-19	NGFR
COVID-19	PROK1
COVID-19	SOSTDC1
COVID-19	FLJ36131
COVID-19	EREG
COVID-19	TNFRSF9
COVID-19	LYG1
COVID-19	SLCO4C1
COVID-19	GUCA2A
COVID-19	FAM19A5
COVID-19	IL21
COVID-19	FCMR
COVID-19	CADM2
COVID-19	CSF3
COVID-19	CA11
COVID-19	NTRK2
COVID-19	CRELD2
COVID-19	GPR120
COVID-19	C9orf135
COVID-19	SLC1A5
COVID-19	SYCN
COVID-19	COL9A3
COVID-19	ADRA1D
COVID-19	GLB1
COVID-19	SV2C
COVID-19	DKFZp686O24166
COVID-19	PRSS3P2
COVID-19	KIRREL3
COVID-19	VSTM2A
COVID-19	GCG
COVID-19	SERPINE2
COVID-19	EDA2R
COVID-19	CPAMD8
COVID-19	SCN3B
COVID-19	OXT
COVID-19	CD3E
COVID-19	INSL3
COVID-19	CALY
COVID-19	GHSR
COVID-19	SCGB1D1
COVID-19	C6
COVID-19	CLDN2
COVID-19	MUC7
COVID-19	KISS1
COVID-19	ULBP2
COVID-19	CLDN7
COVID-19	IGFBP2
COVID-19	EFNB3
COVID-19	NXPH1
COVID-19	GHRHR

TABLE 4-continued

List of Diagnostic or Prognostic Autoantigens and their Corresponding Diseases or Disorders

Disease	Target
COVID-19	LILRA4
COVID-19	OTOL1
COVID-19	EFNB1
COVID-19	FGFBP3
COVID-19	GPR63
COVID-19	PRRG4
COVID-19	MUCL1
COVID-19	XCL1
COVID-19	TMEM120A
COVID-19	TMEM108
COVID-19	IL1F5
COVID-19	MSMP
COVID-19	CXCL12
COVID-19	GNPTG
COVID-19	SDC4
COVID-19	FZD9
COVID-19	CCL4L1
COVID-19	GPRC6A
COVID-19	GPR156
COVID-19	ITIH3
COVID-19	RAMP2
COVID-19	TNFRSF11A
COVID-19	DKK2
COVID-19	SPINK13
COVID-19	SDCBP
COVID-19	CD8B2
COVID-19	CTSG
COVID-19	CST2
COVID-19	EDDM3B
COVID-19	CLTRN
COVID-19	PLA2G10
COVID-19	DCN
COVID-19	DAG1
COVID-19	CXCL16
COVID-19	CCRL2
COVID-19	DEFB108B
COVID-19	MRGPRF
COVID-19	FCRL3
COVID-19	NPS
COVID-19	OBP2A
COVID-19	ACKR2
COVID-19	GRM2
COVID-19	FAM174A
COVID-19	MSR1
COVID-19	NOG
COVID-19	TMEM102
COVID-19	LAIR1
COVID-19	IL22RA2
COVID-19	SPACA3
COVID-19	WIF1
COVID-19	F13B
COVID-19	LRTM1
COVID-19	ERVH48-1
COVID-19	CCL2
COVID-19	TFF1
COVID-19	ADM2
COVID-19	IFITM10
COVID-19	HSD11BIL
COVID-19	AXL
COVID-19	FMR1NB
COVID-19	C6orf25
COVID-19	OPN3
COVID-19	MUC13
COVID-19	CCL28
COVID-19	CCL26
COVID-19	PTN
COVID-19	SLC39A8
COVID-19	FGF21
COVID-19	TIMD4
COVID-19	NPTX2
COVID-19	IL17RD
COVID-19	PAPLN

TABLE 4-continued

List of Diagnostic or Prognostic Autoantigens and their Corresponding Diseases or Disorders

Disease	Target
COVID-19	TMEM219
COVID-19	CYB5D2
COVID-19	IL1B
COVID-19	FSTL1
COVID-19	PTPRJ
COVID-19	NPY1R
COVID-19	CLDN18
COVID-19	FLT3LG
COVID-19	C17orf99
COVID-19	SLC6A5
COVID-19	AIMP1
COVID-19	TNFRSF8
COVID-19	CD248
COVID-19	TM9SF3
COVID-19	FCGR2C
COVID-19	MPZL3
COVID-19	OSTN
COVID-19	SPARCL1
COVID-19	TMPRSS11D
COVID-19	KLK7
COVID-19	GDPD3
COVID-19	IL34
COVID-19	BTNL8
COVID-19	ASTL
COVID-19	CLDN19
COVID-19	SCG5
COVID-19	PSAP
COVID-19	PRRG3
COVID-19	PLA2G12A
COVID-19	LCN1
COVID-19	LRRTM2
COVID-19	FAM3D
COVID-19	PTGS2
COVID-19	FCRLB
COVID-19	CST8
COVID-19	ANGPTL5
COVID-19	OPRK1
COVID-19	APOD
COVID-19	ADM
COVID-19	CLU
COVID-19	PANX3
COVID-19	SLC52A3
DIL	CXCL1
DIL	TNF
DIL	TSLP
DM	CD81
KT	CD99L2
KT	CD80
KT	TNFRSF21
KT	TMEM102
KT	MICA
KT	PILRA
KT	AGER
KT	ULBP1
KT	JCHAIN
KT	TLR1
KT	TNFRSF6
KT	SIRPA
KT	FCER1A
KT	CD300E
KT	B2M
KT	C10orf54
KT	GPR17
KT	IL15RA
KT	TMED1
KT	S1PR4
KT	IFITM10
KT	IL17BR
KT	EFNB3
KT	C6
KT	GPR77
KT	IL2RA

TABLE 4-continued

List of Diagnostic or Prognostic Autoantigens and their Corresponding Diseases or Disorders

Disease	Target
KT	IFNG
KT	IL9
KT	IFNL2
KT	MZB1
KT	IL1A
KT	CSF2
KT	IL4
KT	CRLF1
KT	IL34
KT	IFNA17
KT	IL17RD
KT	TGFA
KT	IL6
KT	IL28B
KT	PRG3
KT	IFNA13
KT	IL16
KT	TSLP
KT	IFNA6
KT	IFNA2
KT	IFNA14
KT	TNFRSF12A
KT	CCL15
KT	IFNA5
KT	TNFRSF17
KT	IL21
KT	C17orf99
KT	IL1F5
KT	OSM
KT	GZMM
KT	LIFR
KT	ACKR1
KT	CCL16
KT	CXCL3
KT	CCL22
KT	CXCL1
KT	CCR10
KT	GPR1
KT	CXCL12
KT	CCL4L1
KT	PPBP
KT	CCL26
KT	CCL2
KT	CXCR3
KT	CXCL9
KT	TFF2
KT	CXCR5
KT	ANGPTL4
KT	ADRB3
KT	RETN
KT	PRLR
KT	ADCYAP1
KT	AVPR1A
KT	GNRH1
KT	GAST
KT	THBD
KT	CCKAR
KT	C2orf40
KT	PTHLH
KT	NPBW1
KT	RXFP3
KT	ADM2
KT	INSL3
KT	ADM
KT	NPPC
KT	SPX
KT	STC2
KT	OXTR
KT	AVP
KT	SLC1A1
KT	SLC2A2
KT	SLC22A25

TABLE 4-continued

List of Diagnostic or Prognostic Autoantigens and their Corresponding Diseases or Disorders

Disease	Target
KT	KCNV2
KT	HCTR1
KT	SLC38A4
KT	SLC8B1
KT	SLC2A10
KT	MFSD2A
KT	SLC20A1
KT	SLC10A4
KT	SLC6A5
KT	GALP
KT	EPYC
KT	OTOL1
KT	CDH19
KT	IBSP
KT	AMTN
KT	PSORS1C2
KT	IMPG1
KT	COL10A1
KT	BCAM
KT	ICAM2
KT	SRGN
KT	CPXM2
KT	CGREF1
KT	CADM2
KT	COL9A3
KT	CD248
KT	SELL
KT	MADCAM1
KT	EPCAM
KT	CRTAP
KT	SGCB
KT	SDC1
KT	LYG2
KT	LGALS3
KT	DCD
KT	BTN1A1
KT	MPO
KT	PGLYRP1
KT	WFDC12
KT	AZU1
KT	IGFBP1
KT	DKK3
KT	FGFR2
KT	IGFBP2
KT	CNPY2
KT	NOV
KT	VEGFB
KT	TMEM119
KT	FAM19A3
KT	MANF
KT	TMEM149
KT	NENF
KT	VSTM2A
KT	BMPR2
KT	FGF1
KT	FGF23
KT	RSPO3
KT	BMPR1A
KT	TM4SF6
KT	IGFBP3
KT	FGF7
KT	IGFBP6
KT	FZD9
KT	FGFRL1
KT	AMELX
KT	FSTL1
KT	SNORC
KT	SMOC2
KT	FGFBP3
KT	PDGFA
KT	CYTL1
KT	IGF1

TABLE 4-continued

List of Diagnostic or Prognostic Autoantigens and their Corresponding Diseases or Disorders

Disease	Target
KT	FGF17
KT	EDIL3
KT	CNPY3
KT	MCFD2
KT	CCDC47
KT	RCN3
KT	RCN1
KT	TGOLN2
KT	C12orf49
KT	OS9
KT	SHISA7
KT	MRGPRF
KT	CSPG5
KT	HCRTR2
KT	OTOR
KT	SV2C
KT	PRRG4
KT	GFRA2
KT	TMEM108
KT	LRRC4B
KT	UNC5B
KT	LYPD1
KT	LRFN2
KT	SCGB3A1
KT	OBP2B
KT	FLJ37218
KT	VSIG2
KT	EDDM3B
KT	EXOC3-AS1
KT	NPY1R
KT	APOO
KT	GPR6
KT	LYSMD4
KT	OPRL1
KT	PTPRN2
KT	ERP27
KT	NINJ1
KT	TMEM91
KT	S100A13
KT	SSTR2
KT	SYCN
KT	ANTXRL
KT	SLC2A12
KT	MIA2
KT	C5orf64
KT	REG1B
KT	FAM174A
KT	ITPRIPL1
KT	REG4
KT	BRICD5
KT	GPR182
KT	NXPH1
KT	NOG
KT	MLN
KT	GPR63
KT	TMEM120A
KT	ACP5
KT	KAZALD1
KT	MIA
KT	PLVAP
KT	SMR3A
KT	RTN4RL2
KT	FAM24B
KT	UNQ9165/PRO28630
KT	GPRC6A
KT	ASIP
KT	GPR25
KT	ADRA1D
KT	KIRREL3
KT	SOST
KT	LPA4
KT	SCG3

TABLE 4-continued

List of Diagnostic or Prognostic Autoantigens and their Corresponding Diseases or Disorders

Disease	Target
KT	SCG5
KT	REG1A
KT	GPR83
KT	PRRG1
KT	JTB
KT	CST1
KT	PSAPL1
KT	GPR22
KT	CP
KT	GSN
KT	LCN1
KT	PRL
KT	HRC
KT	LCN15
KT	OXER1
KT	NPTX2
KT	APOA1
KT	APOA4
KT	APOC3
KT	F13B
KT	SPOCK1
KT	SPINK4
KT	KLK8
KT	PTPRR
KT	SERPINE1
KT	LALBA
KT	TXNDC12
KT	FKBP2
KT	PRSS3
KT	TFPI2
KT	PCSK1
KT	CELA1
KT	AZGP1
KT	CES3
KT	PLA2G2E
KT	ATP6AP2
KT	PLBD2
KT	PLA2G10
KT	CST5
KT	MMP7
KT	CST4
KT	TRABD2A
KT	DHRS4L2
KT	ITIH3
KT	FKBP14
KT	SPINK7
KT	WFDC1
KT	SPINK1
KT	CST6
KT	SERPINI1
KT	WFDC13
KT	P4HB
KT	TOR1B
KT	KLK7
KT	RNASE8
KT	SPINK8
KT	RNF167
KT	CTSG
KT	ACRV1
KT	SPACA7
KT	SSPN
KT	SPACA3
KT	ZG16B
KT	TSPAN9
KT	RTN4R
KT	NPY2R
KT	GP6
KT	FAM168B
KT	CSN2
KT	SEMG2
KT	GPR37
KT	PRH1;

TABLE 4-continued

List of Diagnostic or Prognostic Autoantigens and their Corresponding Diseases or Disorders

Disease	Target
KT	OSTN
KT	FMR1NB
KT	CA11
KT	SPESP1
KT	GPR19
KT	LYPD6B
KT	CLCC1
KT	LY6G6D
KT	GPR156
KT	XG
KT	NETO1
KT	C2orf66
KT	SEMG1
KT	ANGPTL5
KT	CSAG1
KT	MUCL1
KT	HRH3
KT	APP
KT	229E-RBD
KT	NL63-RBD
KT	COV2-RBD
KT	229E-S1
KT	COV2-S1
KT	LOC644613
KT	AGRP
KT	RCN2
KT	IL29
KT	MUCL3
KT	CALU
KT	ENDOU
KT	SPINK9
KT	SLPI
KT	FAM19A2
KT	SERPINA3
KT	PRR27
KT	BTC
KT	IGFBP5
KT	CXCL2
KT	CCL13
KT	LECT2
KT	APOH
KT	LAIR2
KT	DRAXIN
KT	CFD
KT	CCL17
KT	DKK1
KT	IGFBP7
KT	UNQ6190/PRO20217
KT	RARRES2
KT	CCL21
KT	CCL7
KT	KAL1
KT	HAVCR1
KT	ATP4B
KT	PIANP
KT	GNLY
KT	OTOS
KT	CCL24
KT	FCGR2A
KT	SOSTDC1
KT	CCL18
KT	C6orf15
KT	CREG2
KT	DKK2
KT	NOPE
KT	APLP2
KT	IL32
KT	PGA3
KT	ADAMTS16
KT	CXCL11
KT	TMEM41A
KT	LAG3

TABLE 4-continued

List of Diagnostic or Prognostic Autoantigens and their Corresponding Diseases or Disorders

Disease	Target
KT	SLC39A8
KT	CPVL
KT	SPINK13
KT	CALY
KT	TRPC3
KT	PGA4
KT	CLDN9
KT	GPR3
Malaria	SPINK8
Malaria	OBP2B
Malaria	GPR1
Malaria	MCFD2
Malaria	SDF2L1
Malaria	FKBP2
Malaria	EPYC
Malaria	PTPRR
Malaria	LGALS3
Malaria	CD99L2
Malaria	HCRTR2
Malaria	TM4SF6
Malaria	CGREF1
Malaria	SSPN
Malaria	FZD4
Malaria	SPINK4
Malaria	GPR17
Malaria	SRGN
Malaria	PRRG1
Malaria	SLC1A4
Malaria	CCDC47
Malaria	ODAM
Malaria	MZB1
Malaria	CSPG5
Malaria	ACKR1
Malaria	C9orf135
Malaria	ZG16B
Malaria	KCT2
Malaria	ANGPTL4
Malaria	KLK8
Malaria	DPT
Malaria	CD164L2
Malaria	LY6G6D
Malaria	COL10A1
Malaria	FAM19A3
Malaria	RCN3
Malaria	KLK3
Malaria	COLEC12
Malaria	DKK3
Malaria	COL9A3
Malaria	CSAG1
Malaria	CNPY4
Malaria	BCAM
Malaria	ADM
Malaria	ACRV1
Malaria	SLC38A2
Malaria	NBL1
Malaria	TGFA
Malaria	CYTL1
Malaria	SPACA7
Malaria	CALR
Malaria	SMOC2
Malaria	CSHL1
Malaria	DCD
Malaria	IMPG1
Malaria	IL1RN
Malaria	RAMP2
Malaria	IGFBP6
Malaria	TNFRSF17
Malaria	SPX
Malaria	SERPINA3
Malaria	NPY2R
Malaria	GPR19
Malaria	FKBP7

TABLE 4-continued

List of Diagnostic or Prognostic Autoantigens and their Corresponding Diseases or Disorders

Disease	Target
Malaria	CXCL3
Malaria	NOV
Malaria	CXCR3
Malaria	CCL15
Malaria	RTBDN
Malaria	HEPACAM2
Malaria	CST4
Malaria	LEP
Malaria	SNORC
Malaria	CHGA
Malaria	SLC22A31
Malaria	CCL13
Malaria	OTOL1
Malaria	C11orf94
Malaria	RETN
Malaria	PLA2G2E
Malaria	PRRG3
Malaria	APOO
Malaria	PGLYRP1
Malaria	PRAP1
Malaria	GAST
Malaria	TMEM91
Malaria	HTR2B
Malaria	SCTR
Malaria	CNPY2
Malaria	ZP4
Malaria	CD151
Malaria	SLC6A9
Malaria	TMEM59
Malaria	SERPINI2
Malaria	CYSLTR2
Malaria	SLC8B1
Malaria	TRABD2B
Malaria	IGF1
Malaria	S1PR3
Malaria	IBSP
Malaria	JCHAIN
Malaria	CSH2
Malaria	IL16
Malaria	CELA1
Malaria	NENF
Malaria	SGCA
Malaria	LINC00305
Malaria	CXCL1
Malaria	CNPY3
Malaria	229E-RBD
Malaria	LAS2
Malaria	LYSMD4
Malaria	PTHLH
Malaria	SLC10A4
Malaria	RNASE10
Malaria	KLK2
Malaria	RAET1L
Malaria	HCTR1
Malaria	SLC41A2
Malaria	AXL
Malaria	CCL20
Malaria	PRSS3
Malaria	GPC6
Malaria	TGOLN2
Malaria	LRIT3
Malaria	EMC10
Malaria	AMTN
Malaria	PSORS1C2
Malaria	NPBW1
Malaria	S100A13
Malaria	PCSK1
Malaria	PTH
Malaria	INS
Malaria	CDNF
Malaria	SLC2A10
Malaria	TXNDC12

TABLE 4-continued

List of Diagnostic or Prognostic Autoantigens and their Corresponding Diseases or Disorders

Disease	Target
Malaria	ITIH3
Malaria	LILRA4
Malaria	IL1RAP
Malaria	XG
Malaria	IL17A
Malaria	CST5
Malaria	CPE
Malaria	NL63-RBD
Malaria	GNRH1
Malaria	CADM2
Malaria	IL21R
Malaria	TSPAN13
Malaria	OS9
Malaria	P2RY10
Malaria	SPARC
Malaria	PLA2G10
Malaria	FKBP14
Malaria	RXFP3
Malaria	VEGFB
Malaria	VSTM2A
Malaria	ENSP00000381830
Malaria	IFNA13
Malaria	LYPD6B
Malaria	TREML1
Malaria	GDPD3
Malaria	SLC38A4
Malaria	OPRK1
Malaria	SV2C
Malaria	CPXM2
Malaria	IGFBP2
Malaria	TMEM169
Malaria	CD300A
Malaria	GZMK
Malaria	ADCYAP1R1
Malaria	LALBA
Malaria	PRH1;
Malaria	IFNW1
Malaria	PTN
Malaria	OPN4
Malaria	FLRT3
Malaria	TRH
Malaria	FGF23
Malaria	NPR3
Malaria	MPZL3
Malaria	TMEM108
Malaria	TNFRSF10B
Malaria	SIGLEC10
Malaria	GLB1
Malaria	PRRT1
Malaria	OPRM1
Malaria	AKR1B10
Malaria	KITLG
Malaria	OTOR
Malaria	CNR1
Malaria	MINPP1
Malaria	SDF4
Malaria	GP6
Malaria	GPR63
Malaria	RNASE8
Malaria	BDKBR1
Malaria	CDH19
Malaria	CCR4
Malaria	SLC6A5
Malaria	IL22
Malaria	SHISA6
Malaria	FZD9
Malaria	GSN
Malaria	FCER1A
Malaria	IFNA6
Malaria	KLK7
Malaria	CTF1
Malaria	NMBR

TABLE 4-continued

List of Diagnostic or Prognostic Autoantigens and their Corresponding Diseases or Disorders

Disease	Target
Malaria	C2orf66
Malaria	TNFRSF12A
Malaria	INSL3
Malaria	DRD5
Malaria	SFTPA2
Malaria	GPR37
Malaria	IL13
Malaria	GFRAL
Malaria	MOG
Malaria	TSPAN2
Malaria	IGFBP1
Malaria	SPINK1
Malaria	PLGRKT
Malaria	PAPLN
Malaria	SCGB2A2
Malaria	LCN15
Malaria	SLC6A14
Malaria	RNASE9
MG	CXCL2
MG	PDGFB
MG	REG4
MG	CCL22
MG	CCL2
MM	CTLA4
MM	RCN2
MM	IL36B
MM	TNF
MM	CP
MM	CALU
MM	KLK8
MM	SSPN
MM	IL1A
MM	TNFRSF9
MM	SERPINA3
MM	CDH19
MM	OBP2B
MM	FGFBP3
MM	NEGR1
MM	XCL1
MM	CST5
MM	CNPY2
MM	SRGN
MM	SPINK9
MM	TM2D2
MM	HSPA13
MM	AXL
MM	FSTL1
MM	MCFD2
MM	ZG16B
MM	LEP
MM	TMEM108
MM	MUCL3
MM	IL17BR
MM	ODAPH
MM	CNPY3
MM	FAM168B
MM	FAM19A3
MM	IGFL2
MM	DPT
MM	CCDC47
MM	CXCL1
MM	COL10A1
MM	SPINK4
MM	WFDC9
MM	CSPG5
MM	ENDOU
MM	VEGFB
MM	SPINK8
MM	GNLY
MM	CRELD2
MM	ERP27
MM	RCN3

TABLE 4-continued

List of Diagnostic or Prognostic Autoantigens and their Corresponding Diseases or Disorders

Disease	Target
MM	TMEM119
MM	LOC644613
MM	AGRP
MM	PIANP
MM	FAM19A2
MM	IL9
MM	GNRH2
MM	LECT2
MM	GNRH1
MM	CCL17
MM	IL29
MM	KAZALD1
MM	CST4
MM	KCNK1
MM	PANX3
MM	FKBP14
MM	PGA3
MM	IGFBP2
MM	PGLYRP1
MM	NTS
MM	OTOL1
MM	SOST
MM	SHISA7
MM	CCL13
MM	CGREF1
MM	PRR27
MM	IFNL2
MM	DHRS4L2
MM	LYG2
MM	OTOS
MM	UNQ6190/PRO20217
MM	GPC6
MM	TNFRSF21
MM	PSORS1C2
MM	IFNA13
MM	JCHAIN
MM	ACP5
MM	TXNDC12
MM	C5orf64
MM	CLCC1
MM	IL10RB
MM	FMR1NB
MM	SLPI
MM	HRC
MM	CCL22
MM	CASQ1
MM	CELA1
MM	LCN1P1
MM	ODAM
MM	TMED1
MM	REG1A
MM	MZB1
MM	ACRV1
MM	IGLL1
MM	HCRTR2
MM	CST8
MM	PLA2G2E
MM	BTN1A1
MM	CLDN19
MM	CSAG1
MM	REG4
MM	VEGFA
MM	COLEC12
MM	LYSMD4
MM	CCL24
MM	C1QTNF2
MM	PCSK1
MM	PGA4
MM	ITIH3
MM	ICOSLG
MM	SDF2L1
MM	LALBA

TABLE 4-continued

List of Diagnostic or Prognostic Autoantigens and their Corresponding Diseases or Disorders

Disease	Target
MM	PTPRN2
MM	FGFRL1
MM	SERPINE1
MM	CSN2
MM	BTC
MM	ANGPTL4
MM	C2orf40
MM	FCGR2A
MM	FGF1
MM	IGSF4B
MM	CLTRN
MM	ERVK-18
MM	BPIFC
MM	LAIR2
MM	IFNW1
MM	APOC3
MM	CCL21
MM	WFDC3
MM	CD274
MM	PTHLH
MM	PROKR2
MM	LRRN4CL
MM	CA4
MM	TMEM102
MM	SLC41A2
MM	MIA2
MM	CDSN
MM	SLC6A13
MM	CLDN2
MM	RNF43
MM	CALR
MM	PSAP
MM	AMELX
MM	RTBDN
MM	MICA
MM	HAVCR1
MM	PDCD1
MM	C9orf47
MM	DRAXIN
MM	OTOR
MM	CCL18
MM	PRSS3
MM	IL6
MM	C6orf15
MM	NETO1
MM	TMEM149
MM	AMTN
MM	KLK14
MM	RAMP2
MM	SHISA6
MM	TNFRSF12A
MM	FAM3A
MM	PLA2G10
MM	MFAP2
MM	PMCH
MM	CCL23
MM	PRL
MM	LCN2
MM	MOG
MM	ITPRIPL1
MM	CST2
MM	APOO
MM	CFD
MM	CTSW
MM	GP6
MM	NOV
MM	MMP7
MM	CXCL13
MM	EREG
MM	NPPC
MM	IGFBP6
MM	PRLR

TABLE 4-continued

List of Diagnostic or Prognostic Autoantigens and their Corresponding Diseases or Disorders

Disease	Target
MM	EXOC3-AS1
MM	MIA
MM	OPN4
MM	KCNV2
MM	IL1F9
MM	INSL3
MM	CXCL6
MM	SMR3A
MM	CFHR2
MM	SHISA5
MM	SLC2A2
MM	PRH1;
MM	CHRNB3
MM	TNFRSF13C
MM	RCN1
MM	CCL15
MM	TMEM91
MM	RNASE10
MM	PTPRR
MM	IL15RA
MM	CD151
MM	SLC2A10
MM	ERVK-7
MM	PLVAP
MM	FKBP10
MM	CCL28
MM	ANTXRL
MM	CTRB2
MM	FGF17
MM	APP
MM	PNLIPRP1
MM	LILRB6
MM	ATP4B
MM	IGFBP5
MM	LGALS3
MM	IFNA17
MM	LRIT3
MM	CCL8
MM	CTSA
MM	PRR4
MM	DNAJC3
MM	LCN15
MM	TGOLN2
MM	TSLP
MM	TGFA
MM	APOA1
MM	CCL7
MM	EVA1C
MM	SDC4
MM	CSF2
MM	IL28B
MM	ENSP00000381830
MM	PPT1
MM	CRTAM
MM	SPN
MM	DCD
MM	LAS2
MM	CHGB
MM	DKK1
MM	IL34
MM	ERVK-24
MM	IL1B
MM	LRP11
MM	AIMP1
MM	RSPO4
MM	APOA4
MM	PROK1
MM	RSPO3
MM	FKBP2
MM	SCGB1A1
MM	TM9SF3
MM	MANSC4

TABLE 4-continued

List of Diagnostic or Prognostic Autoantigens and their Corresponding Diseases or Disorders

Disease	Target
MM	CST6
MM	SPACA7
MM	SPACA5
MM	DEFB126
MM	SLC6A2
MM	EPHA5
MM	ASIP
MM	CD14
MM	CRLF1
MM	SNORC
MM	PRG3
MM	RNASE8
MM	IGF1
MM	MUCL1
MM	CLN5
MM	STC2
MM	SOSTDC1
MM	MMP1
MM	VSTM2A
MM	PRRT1
MM	CELA3A
MM	PRRG4
MM	C1QL1
MM	CXCL17
MM	IGFBP1
MM	SLC22A31
MM	LHFPL5
MM	SLC6A5
MM	VPREB1
MM	FGF7
MM	OLR1
MM	AGER
MM	PRRT3
MM	ATP6AP2
MM	APOH
MM	CCL11
MM	S100A13
MM	CPXM2
MM	CD248
MM	FAM24B
MM	TDGF1
MM	XG
MM	TNFRSF6B
MM	KLK7
MM	PGC
MM	IGFBP3
MM	IFNA6
MM	SUMF1
MM	FAM19A4
MM	AHSG
MM	SMOC2
MM	AMBN
MM	IL5
MM	OVGP1
MM	CCL26
MM	EPYC
MM	FAM19A5
MM	MSR1
MM	IER3
MM	OS9
MM	XCL2
MM	TRABD2B
MM	ADM2
MM	CXCL3
MM	MICB
MM	PDIA3
MM	TMEM95
MM	TM4SF6
MM	RTN4R
MM	FKBP9
MM	LHFPL1
MM	TFF2

TABLE 4-continued

List of Diagnostic or Prognostic Autoantigens and their Corresponding Diseases or Disorders

Disease	Target
MM	TNFRSF1B
MM	SPOCK1
MM	GAST
MM	FAM174A
MM	CNPY4
MM	C19orf18
MM	TREML1
MM	CLU
MM	KAL1
MM	NBL1
MM	TGFBR1
MM	MANF
MM	MUC7
MM	KCT2
MM	PRRG3
MM	FGF23
MM	CTSG
MM	IL1RAP
MM	SCGB2A2
MM	LY6H
MM	IHH
MM	NRN1
MM	PTN
MM	PRAP1
MM	FCMR
MM	APLP2
MM	IL21
MM	TNFRSF4
MM	VSIG2
MM	SIGLEC9
MM	TRH
MM	SPP2
MM	SPINK13
MM	SEMA6C
MM	MEGF9
MM	IL32
MM	IL16
MM	PLAC9
MM	UNQ9165/PRO28630
MM	DNASE2
MM	IGFBP7
MM	COL8A1
MM	HSD11B1L
MM	CLDN3
MM	HSD17B13
MM	OBP2A
NMO	CXCL2
NMO	CXCL3
NMO	IGFBPL1
NMO	CCL22
NMO	IL1F9
NMO	LY6G6D
NSCLC	CCL17
NSCLC	CCL24
NSCLC	CXCL1
NSCLC	CXCL3
NSCLC	EDIL3
NSCLC	IFNA13
NSCLC	IFNA14
NSCLC	IFNA17
NSCLC	IFNA2
NSCLC	IFNA5
NSCLC	IFNA6
NSCLC	IFNA8
NSCLC	IFNL2
NSCLC	IFNW1
NSCLC	IL28B
NSCLC	IL34
NSCLC	MADCAM1
NSCLC	PDGFB
NSCLC	REG1A
NSCLC	SDC1

TABLE 4-continued

List of Diagnostic or Prognostic Autoantigens and their Corresponding Diseases or Disorders

Disease	Target
NSCLC	BTN1A1
NSCLC	C6
NSCLC	CD207
NSCLC	CD3D
NSCLC	CDH19
NSCLC	COLEC12
NSCLC	EREG
NSCLC	FGF23
NSCLC	FGF7
NSCLC	FGFBP3
NSCLC	IGFBPL1
NSCLC	IL15RA
NSCLC	IL17F
NSCLC	IL1RAP
NSCLC	IL22RA2
NSCLC	IL4
NSCLC	IL4R
NSCLC	ITGA5
NSCLC	LAG3
NSCLC	LRRC4
NSCLC	MPZL3
NSCLC	NOTCH2NL
NSCLC	NTRK3
NSCLC	REG4
NSCLC	SCARA3
NSCLC	STIM2
NSCLC	TNFRSF10C
NSCLC	TNFRSF19L
NSCLC	TREML1
PANDAS	LRP11
Sarcoidosis	CX3CL1
Sarcoidosis	EPYC
Sarcoidosis	PGLYRP1
SLE	CXCL3
SLE	IFNA17
SLE	CXCL1
SLE	LOC644613
SLE	IFNA6
SLE	SV2C
SLE	TMEM102
SLE	PDCD1LG2
SLE	SLC29A4
SLE	IL1A
SLE	C5orf64
SLE	IFNW1
SLE	SCGB1D1
SLE	EPYC
SLE	CNPY2
SLE	CCL4L1
SLE	SPINK9
SLE	TNF
SLE	KIRREL3
SLE	IFNA8
SLE	IFNA14
SLE	VEGFB
SLE	TMEM108
SLE	IFNA5
SLE	ACVR2B
SLE	OBP2B
SLE	MCFD2
SLE	DPT
SLE	SPACA7
SLE	IFNA13
SLE	FKBP14
SLE	LACRT
SLE	IL6
SLE	FAM19A3
SLE	IFNL2
SLE	ERP27
SLE	TMEM149
SLE	PRH1;
SLE	ZG16B

TABLE 4-continued

List of Diagnostic or Prognostic Autoantigens and their Corresponding Diseases or Disorders

Disease	Target
SLE	IFNA2
SLE	RAET1E
SLE	CCDC47
SLE	MUC21
SLE	CCL22
SLE	CGREF1
SLE	TEPP
SLE	FAM19A2
SLE	SPOCK1
SLE	SRGN
SLE	SHISA7
SLE	CCL17
SLE	RNASE10
SLE	FGF21
SLE	APOA4
SLE	NGFR
SLE	KCNV2
SLE	AGER
SLE	FGFRL1
SLE	LGR6
SLE	CCL8
SLE	CD44
SLE	ITIH3
SLE	CST8
SLE	SSPN
SLE	CELA1
SLE	IL4
SLE	RCN3
SLE	PRRG4
SLE	MFAP5
SLE	CSPG5
SLE	VTCN1
SLE	PLA2G2E
SLE	LY6H
SLE	GYPC
SLE	SLC41A2
SLE	DRAXIN
SLE	CSHL1
SLE	LAIR2
SLE	IGFBP2
SLE	CD248
SLE	RGMB
SLE	TGOLN2
SLE	CSAG1
SLE	ACP4
SLE	CALU
SLE	BTNL8
SLE	SOSTDC1
SLE	LYSMD4
SLE	LCN2
SLE	SCGB1C2
SLE	CST4
SLE	IGF1
SLE	PRRT1
SLE	CHRNA5
SLE	ANTXRL
SLE	TNFRSF6
SLE	CD300LG
SLE	SERPINE1
SLE	OLFM1
SLE	PLA2G10
SLE	CD300E
SLE	CDH19
SLE	RAMP2
SLE	ATP4B
SLE	PTPRR
SLE	SFN
SLE	HCRTR2
SLE	ACRV1
SLE	FAM3A
SLE	ACVR1B
SLE	FGF23

TABLE 4-continued

List of Diagnostic or Prognostic Autoantigens and their Corresponding Diseases or Disorders

Disease	Target
SLE	IL15RA
SLE	IGFBP7
SLE	LHFPL1
SLE	IL28B
SLE	VIT
SLE	IER3
SLE	C2orf40
SLE	PLVAP
SLE	LECT2
SLE	DAG1
SLE	SPINK6
SLE	SLC2A12
SLE	IGLL1
SLE	TFF2
SLE	ASIP
SLE	IL16
SLE	EDIL3
SLE	CCL13
SLE	RCN1
SLE	CSH2
SLE	IL33
SLE	LILRB4
SLE	SPESP1
SLE	PDGFB
SLE	PTHLH
SLE	C9orf47
SLE	CHRDL2
SLE	ART3
SLE	CPVL
SLE	CCL15
SLE	CFD
SLE	MFSD2A
SLE	RTN4RL1
SLE	ADM2
SLE	APOO
SLE	CTSG
SLE	PMCH
SLE	DKK2
SLE	CARTPT
SLE	BTC
SLE	IL18RAP
SLE	LRIT3
SLE	LHFPL5
SLE	SPN
SLE	FAM19A5
SLE	IL6R
SLE	SDC1
SLE	IL20RB
SLE	CXCL9
SLE	RNASE8
SLE	LILRB2
SLE	CDSN
SS	CXCL1
SS	CXCL3
SS	PDCD1LG2
SSC	KLK10
SSC	RCN2
SSC	IGFBP6
SSC	SERPINA3
SSC	SPOCK1
SSC	SPINK9
SSC	AGRP
SSC	CCL21
SSC	CSF2
SSC	CALU
SSC	ENDOU
SSC	CXCL1
SSC	NEGR1
SSC	C5orf64
SSC	CCDC47
SSC	IL1A
SSC	EPYC

TABLE 4-continued

List of Diagnostic or Prognostic Autoantigens and their Corresponding Diseases or Disorders

Disease	Target
SSC	GNLY
SSC	PGA3
SSC	UNQ6190_PRO20217
SSC	CCL4L1
SSC	OBP2B
SSC	KLK8
SSC	OTOS
SSC	CNPY2
SSC	ERP27
SSC	CP
SSC	MUCL3
SSC	RAET1L
SSC	ULBP2
SSC	TM2D2
SSC	SLC2A2
SSC	IL6
SSC	SERPINE1
SSC	LEP
SSC	LECT2
SSC	OTOR
SSC	CASQ1
SSC	CST6
SSC	INSL3
SSC	SPACA3
SSC	AMTN
SSC	ZG16B
SSC	LOC644613
SSC	PGA4
SSC	LYSMD4
SSC	SRGN
SSC	CDH19
SSC	SHISA7
SSC	FAM19A3
SSC	HAVCR1
SSC	BAMBI
SSC	MSMP
SSC	SPACA7
SSC	PTHLH
SSC	PLA2G12B
SSC	CXCL3
SSC	CST4
SSC	DKK3
SSC	PIANP
SSC	PRG3
SSC	BTC
SSC	CCL17
SSC	XCL1
SSC	LMBRD2
SSC	LALBA
SSC	TGFA
SSC	IL29
SSC	EVI2B
SSC	SLPI
SSC	CLCC1
SSC	RNASE10
SSC	FGFBP3
SSC	FAM168B
SSC	PGLYRP1
SSC	ANGPTL4
SSC	CLU
SSC	AGER
SSC	TMEM108
SSC	C1QTNF2
SSC	TMEM119
SSC	CCL8
SSC	ODAPH
SSC	CNPY3
SSC	MZB1
SSC	CYTL1
SSC	PRH1
SSC	SLC2A10
SSC	PRRG1

TABLE 4-continued

List of Diagnostic or Prognostic Autoantigens and their Corresponding Diseases or Disorders

Disease	Target
SSC	CSPG5
SSC	DRAXIN
SSC	PRR27
SSC	DKK1
SSC	NTRK2
SSC	IFNA13
SSC	PDCD1
SSC	FAM19A2
SSC	IFNW1
SSC	RCN1
SSC	CFD
SSC	CRELD2
SSC	CCL18
SSC	CD14
SSC	BTN1A1
SSC	PTPRR
SSC	TMEM91
SSC	VSIG2
SSC	CCL13
SSC	C2orf40
SSC	VEGFB
SSC	REG4
SSC	TXNDC12
SSC	ACVR2B
SSC	ODAM
SSC	CST5
SSC	PI3
SSC	TMEM149
SSC	TEPP
SSC	KCNV2
SSC	PLA2G2E
SSC	AIMP1
SSC	IGFBP5
SSC	ASIP
SSC	PGC
SSC	TM9SF3
SSC	AMELX
SSC	CSN2
SSC	CPXM2
SSC	PRSS3
SSC	FAM3A
SSC	LILRA3
SSC	CSAG1
SSC	RTBDN
SSC	CELA1
SSC	ANTXRL
SSC	PLA2G10
SSC	KCT2
SSC	APOH
SSC	NENF
SSC	NPPC
SSC	LY6H
SSC	FGF1
SSC	SLC1A1
SSC	IFNL2
SSC	HSPA13
SSC	C6orf15
SSC	FLJ37218
SSC	CCL7
SSC	APOA4
SSC	FSTL1
SSC	IGFBP1
SSC	FCGR2A
SSC	SMR3A
SSC	IFITM10
SSC	MSLN
SSC	PRAP1
SSC	EPO
SSC	PLVAP
SSC	PROK1
SSC	TSLP
SSC	MIA

TABLE 4-continued

List of Diagnostic or Prognostic Autoantigens and their Corresponding Diseases or Disorders

Disease	Target
SSC	APP
SSC	OBP2A
SSC	RTN4RL1
SSC	PRRT3
SSC	APOA1
SSC	FGF7
SSC	TMED1
SSC	LGALS3
SSC	JCHAIN
SSC	PRRG3
SSC	IGF1
SSC	ACRV1
SSC	SLC38A4
SSC	FKBP11
SSC	ITPRIPL1
SSC	PLAC9
SSC	TFF2
SSC	WFDC13
SSC	LCN1
SSC	LYG1
SSC	LAIR2
SSC	TNFRSF8
SSC	SOSTDC1
SSC	VSTM2A
SSC	IGFBP7
SSC	PSORS1C2
SSC	FGF23
SSC	RSPO3
SSC	S100A9
SSC	CXCL9
SSC	TGOLN2
SSC	ACP5
SSC	MANF
SSC	AMBN
SSC	PSAPL1
SSC	WFDC10A
SSC	PPT1
SSC	MANSC4
SSC	CD248
SSC	NGRN
SSC	PSAP
SSC	LILRB2
SSC	SCGB2A2
SSC	IGFBPL1
SSC	SV2C
SSC	CXCL6
SSC	CD300E
SSC	RCN3
SSC	IGFBP3
SSC	RTN4R
SSC	PRRT1
SSC	ACVR2A
SSC	LCN2
SSC	HCRTR2
SSC	CELA3A
SSC	ADM2
SSC	LRIT3
SSC	MIA2
SSC	TNFRSF17
SSC	SPN
SSC	SLC6A5
SSC	WFDC1
SSC	LILRB4
SSC	CTSG
SSC	CXCL11
SSC	KLK7
SSC	CST8
SSC	NOPE
SSC	GAST
SSC	ASTN2
SSC	MCFD2
SSC	CCL22

TABLE 4-continued

List of Diagnostic or Prognostic Autoantigens and their Corresponding Diseases or Disorders

Disease	Target
SSC	OTOL1
SSC	SYCN
SSC	CCL2
SSC	SOST
SSC	PTN
SSC	TACSTD2
SSC	IL21
SSC	IGLL1
SSC	MMP7
SSC	APLP2
SSC	SSBP3_AS1
SSC	CST7
SSC	SSPN
SUSAC	CCL24
SUSAC	SDC4
SUSAC	TREML1
SUSAC	VSIG4

TABLE 5

Therapeutic Autoantigens and Corresponding Disease or Disorder

Disease	Target
APECED	IL22RA2
CLE	TYRO3
CLE	CD300E
COVID-19	IL13
COVID-19	IL18RAP
COVID-19	TNFRSF8
COVID-19	CCR10
COVID-19	CD74
COVID-19	TNFRSF17
COVID-19	CCR9
COVID-19	CRTAM
COVID-19	C6
DM	CD81
GN	IL34
KT	IGFBP1
KT	IL15RA
KT	NXPH1
KT	CST5
KT	C6
MG	CCL22
MG	CCL2
MM	PSORS1C2
MM	LHFPL1
MM	PTPRR
MM	ZG16B
MM	IGF1
MM	IGLL1
MM	LRIT3
MM	VEGFB
NSCLC	CCL22
NMO	CCL22
NMO	IL1F9
NSCLC	FGF23
NSCLC	FGF7
NSCLC	EREG
NSCLC	CXCL1
NSCLC	CXCL2
NSCLC	CXCL3
NSCLC	VEGFB
NSCLC	IL1A
NSCLC	LAG3
NSCLC	IFNA13
NSCLC	IFNA14
NSCLC	IFNA17
NSCLC	IFNA2

TABLE 5-continued

Therapeutic Autoantigens and Corresponding Disease or Disorder

Disease	Target
NSCLC	IFNA5
NSCLC	IFNA6
NSCLC	IFNA8
NSCLC	IFNW1
NSCLC	IL34
NSCLC	IL22RA2
SLE	PDCD1LG2
SLE	LIF
SLE	IFNA13
SLE	IFNA14
SLE	IFNA17
SLE	IFNA2
SLE	IFNA5
SLE	IFNA6
SLE	IFNA8
SLE	IFNB1
SLE	IFNL2
SLE	IFNW1
SLE	IL6
SLE	IL6R
SLE	IL33
SLE	IL34
SLE	IL16
SLE	IL19
SLE	IL20RB
SLE	IL18RAP
SLE	MADCAM1
SLE	TNF
SLE	TRAILR4
SLE	TYRO3
SLE	CD44
SLE	CD300E
SLE	CXCL1
SLE	CXCL2
SLE	CXCL3
SLE	VEGFB
SLE	IL1A
SLE	LILRB2
SLE	LILRB4
SS	PDCD1LG2
NSCLC	IGFBPL1

TABLE 6

Autoantigen Specific Therapies

Disease	Target
COVID-19	IFITM10
COVID-19	IFNA13
COVID-19	IFNA14
COVID-19	IFNA17
COVID-19	IFNA2
COVID-19	IFNA5
COVID-19	IFNA6
COVID-19	IFNA8
COVID-19	IFNW1
COVID-19	KLRC1
COVID-19	KLRC2
COVID-19	KLRC3
COVID-19	CCR2
COVID-19	CD38
COVID-19	C5A
COVID-19	CCR4
COVID-19	CD3E
COVID-19	TNFRSF9
COVID-19	ADCYAP1
COVID-19	CGA
COVID-19	HCTR2
COVID-19	AZGP1

TABLE 6-continued

Autoantigen Specific Therapies

Disease	Target
COVID-19	SLC41A2
COVID-19	LAIR1
KT	IFITM10
KT	IL4
KT	EXOC3-AS1
KT	IFNA13
KT	CD99L2
KT	OSTN
KT	SYCN
KT	LYG2
KT	BTN1A1
MM	IFNA13
MM	OBP2B
MM	TMEM108
MM	CELA1
MM	OTOL1
MM	ATP4B
MM	ICOSLG
MM	REG1A
MM	CCL24
MM	TMEM91
MM	LALBA
MM	ITPRIPL1
MM	LCN2
MM	BTN1A1
MM	OS9
MM	FGF17
NSCLC	IFNL2
NSCLC	VSTM2A

TABLE 6-continued

Autoantigen Specific Therapies

Disease	Target
NSCLC	PDGFB
SLE	TMEM102
SLE	CCL8
SLE	CCL4L1
SLE	ACVR2B
SLE	FGF21
SLE	IGFBP2
SLE	RGMB
SLE	ACVR1B
SLE	ACRV1
SLE	SCGB1D1
SLE	TFF2
SLE	SFN
SLE	ANTXRL
SLE	SLC41A2
SLE	CD248

[0474] The disclosures of each and every patent, patent application, and publication cited herein are hereby incorporated herein by reference in their entirety. While this invention has been disclosed with reference to specific embodiments, it is apparent that other embodiments and variations of this invention may be devised by others skilled in the art without departing from the true spirit and scope of the invention. The appended claims are intended to be construed to include all such embodiments and equivalent variations.

SEQUENCE LISTING

The patent application contains a lengthy sequence listing. A copy of the sequence listing is available in electronic form from the USPTO web site (https://seqdata.uspto.gov/?pageRequest=docDetail&DocID=US20230357754A1). An electronic copy of the sequence listing will also be available from the USPTO upon request and payment of the fee set forth in 37 CFR 1.19(b)(3).

What is claimed is:

1. A method of identifying at least one polypeptide which binds to at least one antibody, wherein the method comprises:

(a) contacting a library of display cells or particles with a sample comprising at least one antibody, wherein the library of display cells comprises a plurality of cells or particles wherein together the plurality of cells or particles comprises nucleic acid molecules for expression of a plurality of extracellular proteins, secreted proteins or a combination thereof;

wherein each cell or particle of the plurality of cells or particles comprises a barcoded nucleic acid molecule, wherein each nucleic acid molecule comprises

i) a nucleotide sequence encoding a polypeptide of interest for display on the surface of the cell or particle; and

ii) a unique nucleotide barcode sequence;

(b) isolating one or more antibody-bound cell or particle;

(c) isolating at least one barcoded nucleic acid molecule from at least one cell or particle of step (b); and

(d) identifying the barcoded nucleic acid molecule, thereby identifying the associated encoded polypeptide as an antigen for binding by at least one antibody in the sample.

2. The method of claim **1**, wherein the method of isolating one or more antibody-bound cell or particle comprises high-throughput magnetic separation.

3. The method of claim **1**, wherein the method further comprises the step of:

(b') expanding the one or more isolated antibody-bound cell or particle.

4. The method of claim **1**, wherein the method of identifying the barcoded nucleic acid molecule comprises at least one selected from the group consisting of amplifying the barcoded nucleic acid molecule and sequencing the barcoded nucleic acid molecule.

5. The method of claim **1**, comprising:

in step (b), isolating multiple antibody bound cells,

in step (c), isolating the barcoded nucleic acid molecules from the cells of step (b), and

in step (d), sequencing the isolated barcoded nucleic acid molecules, and identifying the associated encoded polypeptide as an antigen for binding by the antibody based on an enrichment of the number of reads of the associated barcode in the sequencing data as compared to a threshold level.

6. The method of claim **3**, wherein the threshold level is selected from the group consisting of a predetermined threshold level, a statistically determined threshold, and a threshold level determined using z-scores.

7. The method of claim **1**, wherein the library of display cells or particles comprises a library of barcoded nucleic acid molecules encoding at least one selected from an extracellular domain of a protein, an extracellular protein, and a secreted protein.

8. The method of claim **7**, wherein the library of barcoded nucleic acid molecules comprises a plurality of nucleic acid molecules which together encode the human exoproteome.

9. The method of claim **7**, wherein the library of barcoded nucleic acid molecules comprises at least one nucleic acid molecule encoding at least one polypeptide sequence selected from SEQ ID NO:1-3092.

10. The method of claim **7**, wherein the library of barcoded nucleic acid molecules comprises a plurality of nucleic acid molecules which together encode each of SEQ ID NO:1-3092.

11. The method of claim **7**, wherein the library of barcoded nucleic acid molecules comprises at least one nucleic acid molecule comprising a nucleotide sequence selected from SEQ ID NO:3093-6185.

12. The method of claim **7**, wherein the library of barcoded nucleic acid molecules comprises a plurality of nucleic acid molecules which together comprise each of SEQ ID NO:3093-6185.

13. The method of claim **1**, wherein the sample comprises a biological sample selected from the group consisting of a body fluid, blood, serum, plasma, cerebrospinal fluid, tissue, and any combination thereof.

14. The method of claim **1**, wherein the sample comprises at least one antibody purified from a biological sample selected from the group consisting of a body fluid, blood, serum, plasma, cerebrospinal fluid, tissue, and any combination thereof.

15. The method of claim **14**, wherein at least one antibody is purified from a biological sample by at least one selected from the group consisting of:

(a) affinity purification for a specific antibody isotype of interest, and

(b) contacting the sample with a control cell or particle comprising an empty expression plasmid.

16. The method of claim **1**, wherein the sample is from a subject diagnosed as having a disease or disorder, and whereby the antigen for binding by at least one antibody is a disease-associated antigen.

17. The method of claim **1**, wherein the antibody is an autoantibody.

18. The method of claim **1**, wherein the antibody is associated with an autoimmune disease or disorder, cancer, inflammatory disease or disorder, metabolic disease or disorder, neurodegenerative disease or disorder, organ tissue rejection, organ transplant rejection, or any combination thereof.

19. A method of preventing or treating a disease or disorder in a subject in need thereof; the method comprising administering a therapeutic agent to the subject, wherein the therapeutic agent comprises an agent for modifying the level or reactivity of at least one antibody which interacts with at least one antigen selected from the group consisting of the antigens as set forth in SEQ ID NO:1-3092.

20. The method of claim **19**, wherein the antigen is identified as a target for at least one antibody according to the method of claim **1**.

21. The method of claim **19**, wherein the at least one antigen is selected from the group consisting of an antigen as set forth in Table 3, and further wherein the disease or disorder is the disease or disorder associated with the antigen as set forth in Table 3.

22. The method of claim **21**, wherein the therapeutic agent comprises an agent for decreasing the level or reactivity of at least one antibody with at least one disease-associated antigen selected from the group consisting of the antigens as set forth in Table 3.

23. The method of claim **19**, wherein the at least one antigen is selected from the group consisting of an antigen as set forth in Table 6, and further wherein the disease or disorder is the disease or disorder associated with the antigen as set forth in Table 6.

23. The method of claim **19**, wherein the therapeutic agent comprises a therapeutically effective amount of at least agent that reduces or eliminates at least one antibody.

24. The method of claim **23**, wherein the therapeutic agent comprises a composition comprising an antigen selected from the group consisting of an antigen as set forth in SEQ ID NO:1-3092 linked to a domain for endocytosis and degradation.

25. The method of claim **23**, wherein the therapeutic agent comprises a composition comprising an antigen selected from the group consisting of an antigen as set forth in Table 6 linked to a domain for endocytosis and degradation.

26. The method of claim **24**, wherein the domain for endocytosis and degradation comprises an asialoglycoprotein receptor binding domain.

27. The method of claim **23**, wherein the agent that reduces or eliminates at least one antibody comprises a molecule for targeting and destruction of at least one antibody-expressing cell.

28. The method of claim **27**, wherein the agent comprises a chimeric antigen receptor (CAR) T cell expressing an antigen selected from the group consisting of an antigen as set forth in SEQ ID NO:1-3092, or a fragment thereof.

29. The method of claim **28**, wherein the CAR T cell expresses an antigen selected from the group consisting of an antigen as set forth in Table 6.

30. The method of claim **19**, wherein the therapeutic agent comprises an agent for increasing the level or reactivity of at least one antibody with at least one disease-associated antigen selected from the group consisting of the antigens as set forth in Table 3.

31. The method of claim **30**, wherein the at least one antigen is selected from the group consisting of an antigen as set forth in Table 5, and further wherein the disease or disorder is the disease or disorder associated with the antigen as set forth in Table 5.

32. The method of claim **30**, wherein the therapeutic agent comprises a therapeutically effective amount of at least one antibody, or fragment thereof, wherein the antibody specifically binds to a disease-associated antigen.

33. The method of claim **19**, wherein the disease or disorder is selected from the group consisting of an autoimmune disease or disorder, cancer, inflammatory disease or disorder, metabolic disease or disorder, neurodegenerative disease or disorder, organ tissue rejection, organ transplant rejection, or any combination thereof.

34. The method of claim **19**, wherein the disease or disorder is selected from the group consisting of antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis, autoimmune polyendocrinopathy candidiasis ecto-dermal dystrophy, antiphospholipid antibody syndrome, chronic inflammatory demyelinating polyradiculoneuropathy, cutaneous lupus erythematosus, COVID-19, drug-induced lupus, dermatomyositis, glomerulonephritis, a disease or disorder associated with kidney transplant, malaria, mixed connective tissue disease, myasthenia gravis, malignant melanoma, neuromyelitis optica, non-small cell lung cancer, pediatric autoimmune neuropsychiatric disorders associated with streptococcal infections, systemic lupus erythematosus, sjogren's syndrome, scleroderma, susac syndrome, undifferentiated connective tissue disease, and any combination thereof.

35. A method of diagnosing, assessing the prognosis, or assessing the effectiveness of treatment of a disease or disorder in a subject in need thereof; the method comprising assessing the level or reactivity of at least one antibody which interacts with at least one antigen selected from the group consisting of an antigen as set forth in SEQ ID NO:1-3092.

36. The method of claim **35**, wherein the at least one antigen is selected from the group consisting of an antigen as set forth in Table 3, and further wherein the disease or disorder is the disease or disorder associated with the antigen as set forth in Table 3.

37. The method of claim **35**, wherein the at least one antigen is selected from the group consisting of an antigen as set forth in Table 4, and further wherein the disease or disorder is the disease or disorder associated with the antigen as set forth in Table 4.

38. The method of claim **35**, wherein the disease or disorder is selected from the group consisting of an autoimmune disease or disorder, cancer, inflammatory disease or disorder, metabolic disease or disorder, neurodegenerative disease or disorder, organ tissue rejection, organ transplant rejection, or any combination thereof.

39. The method of claim **35**, wherein the disease or disorder is selected from the group consisting of antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis, autoimmune polyendocrinopathy candidiasis ecto-dermal dystrophy, antiphospholipid antibody syndrome, chronic inflammatory demyelinating polyradiculoneuropathy, cutaneous lupus erythematosus, COVID-19, drug-induced lupus, dermatomyositis, glomerulonephritis, a disease or disorder associated with kidney transplant, malaria, mixed connective tissue disease, myasthenia gravis, malignant melanoma, neuromyelitis optica, non-small cell lung cancer, pediatric autoimmune neuropsychiatric disorders associated with streptococcal infections, systemic lupus erythematosus, sjogren's syndrome, scleroderma, susac syndrome, undifferentiated connective tissue disease, and any combination thereof.

40. A composition comprising an antigen selected from the group consisting of an antigen as set forth in SEQ ID NO:1-3092, or a fragment thereof, linked to a domain for endocytosis, degradation, or a combination thereof.

41. The composition of claim **40**, wherein the composition comprises an antigen selected from the group consisting of an antigen as set forth in Table 6 linked to a domain for endocytosis, degradation, or a combination thereof.

42. The composition of claim **40**, wherein the domain for endocytosis, degradation, or a combination thereof comprises an asialoglycoprotein receptor binding domain.

43. A composition for targeting and destruction of at least one antibody-expressing cell comprising an antigen selected from the group consisting of an antigen as set forth in SEQ ID NO:1-3092, or a fragment thereof.

44. The composition of claim **43**, wherein the agent comprises a chimeric antigen receptor (CAR) T cell expressing an antigen as set forth in SEQ ID NO:1-3092, or a fragment thereof.

45. The composition of claim **44**, wherein the CAR T cell expresses an antigen selected from the group consisting of an antigen as set forth in Table 6.

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