



US 20220251544A1

(19) **United States**

(12) **Patent Application Publication**
JOHNSTON et al.

(10) **Pub. No.: US 2022/0251544 A1**

(43) **Pub. Date: Aug. 11, 2022**

(54) **METHODS AND COMPOSITIONS FOR IDENTIFYING NEOANTIGENS FOR USE IN TREATING AND PREVENTING CANCER**

(60) Provisional application No. 62/909,748, filed on Oct. 2, 2019.

(71) Applicant: **Arizona Board of Regents on Behalf of Arizona State University**, Scottsdale, AZ (US)

Publication Classification

(51) **Int. Cl.**
C12N 15/10 (2006.01)
G01N 33/574 (2006.01)

(72) Inventors: **Stephen Albert JOHNSTON**, Tempe, AZ (US); **Luhui SHEN**, Tempe, AZ (US)

(52) **U.S. Cl.**
CPC ... *C12N 15/1062* (2013.01); *G01N 33/57484* (2013.01)

(21) Appl. No.: **17/706,469**

(57) **ABSTRACT**

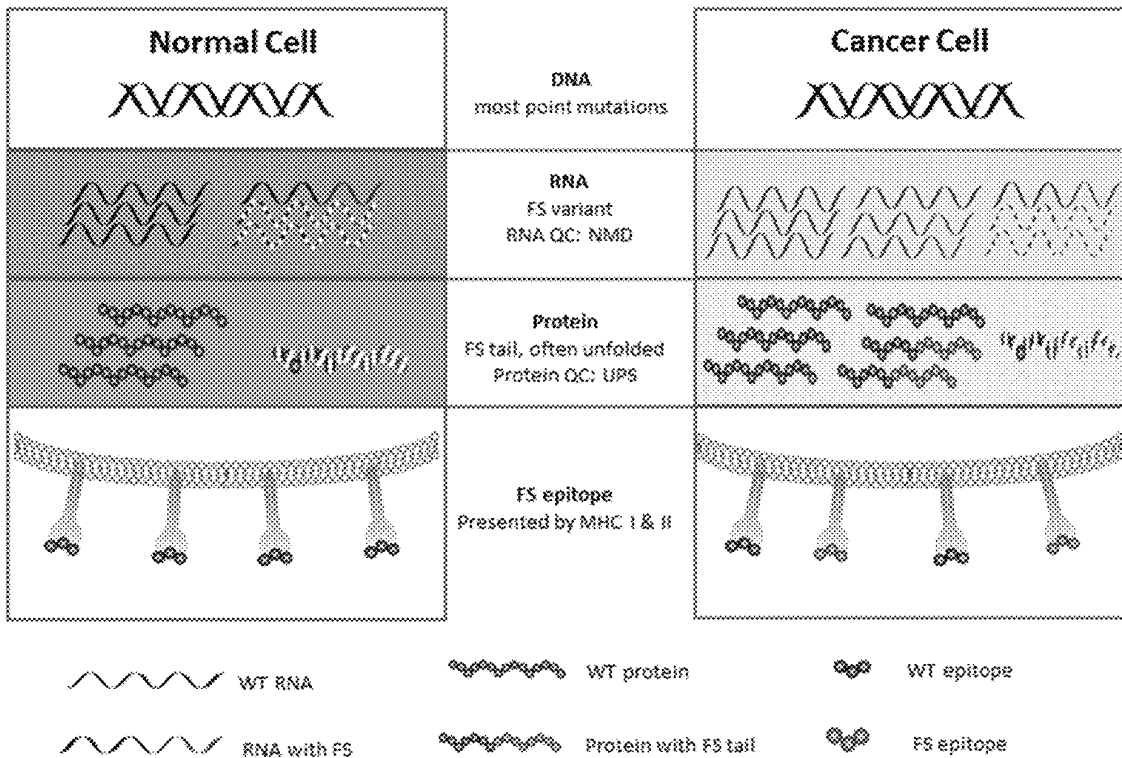
(22) Filed: **Mar. 28, 2022**

Related U.S. Application Data

(63) Continuation of application No. PCT/US2020/053728, filed on Oct. 1, 2020.

Provided herein, are methods of identifying neoantigens for treating and preventing cancer. Also disclosed are methods and compositions for administering identified neoantigens for the treatment and prevention of cancer.

Specification includes a Sequence Listing.



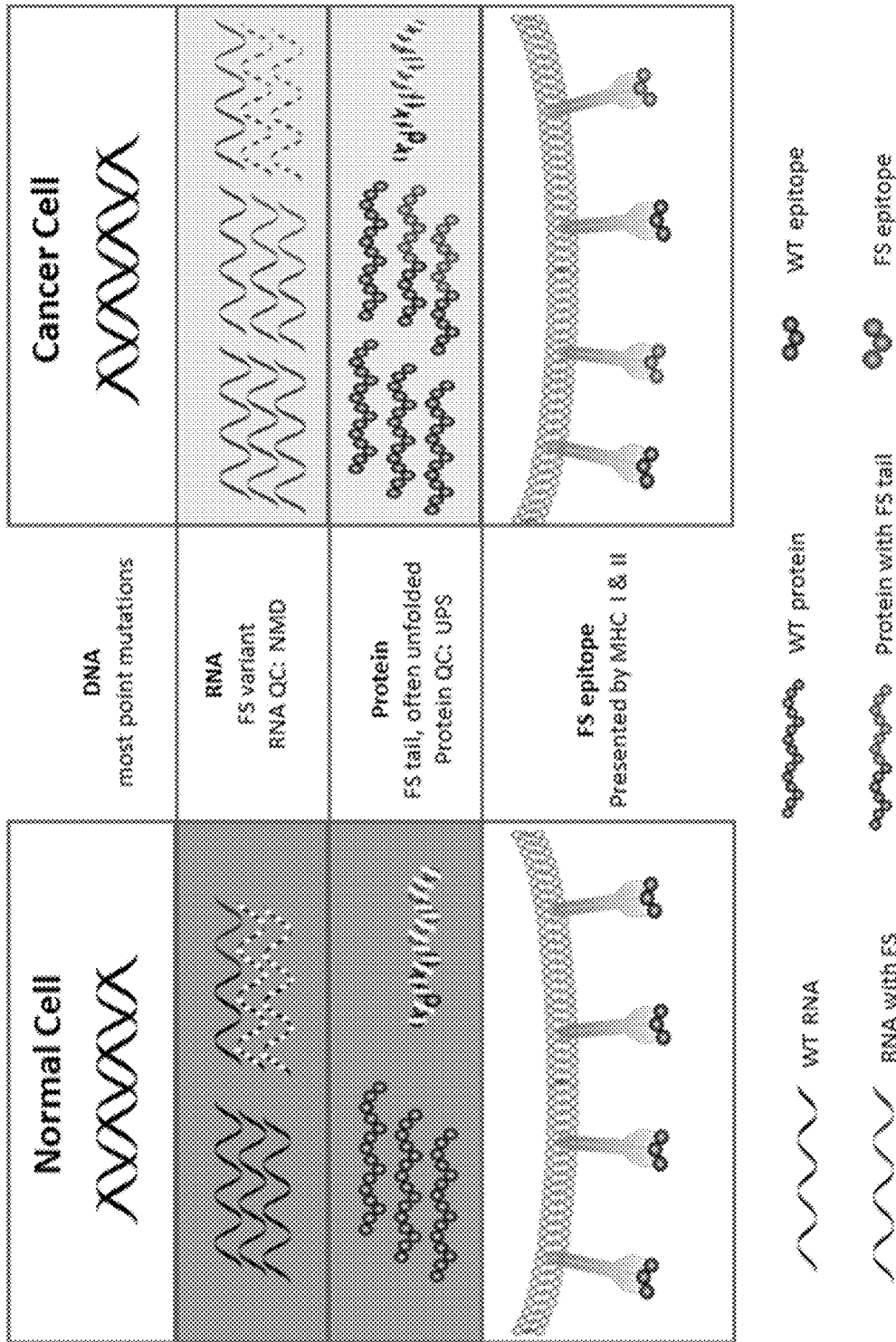


FIG. 1

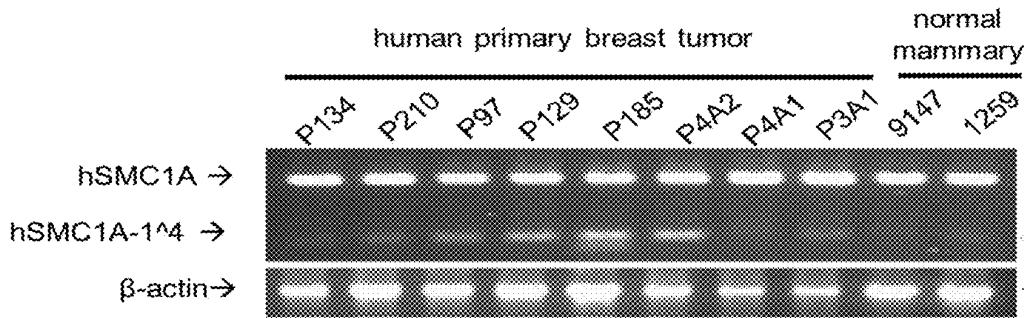
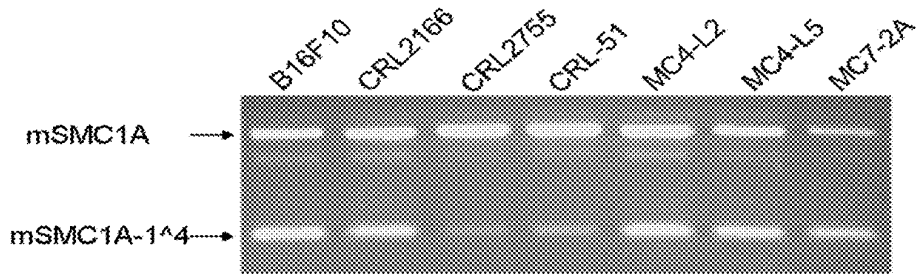


FIG. 2A

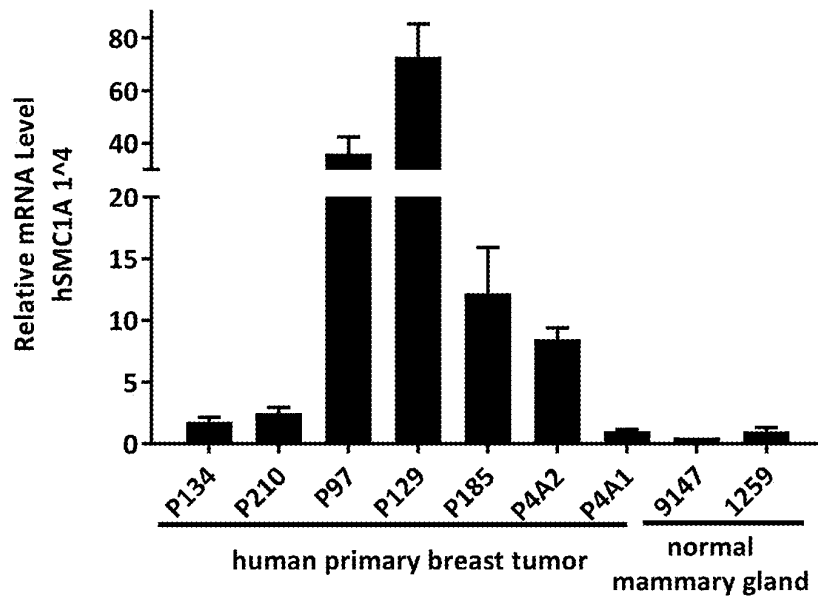


FIG. 2B

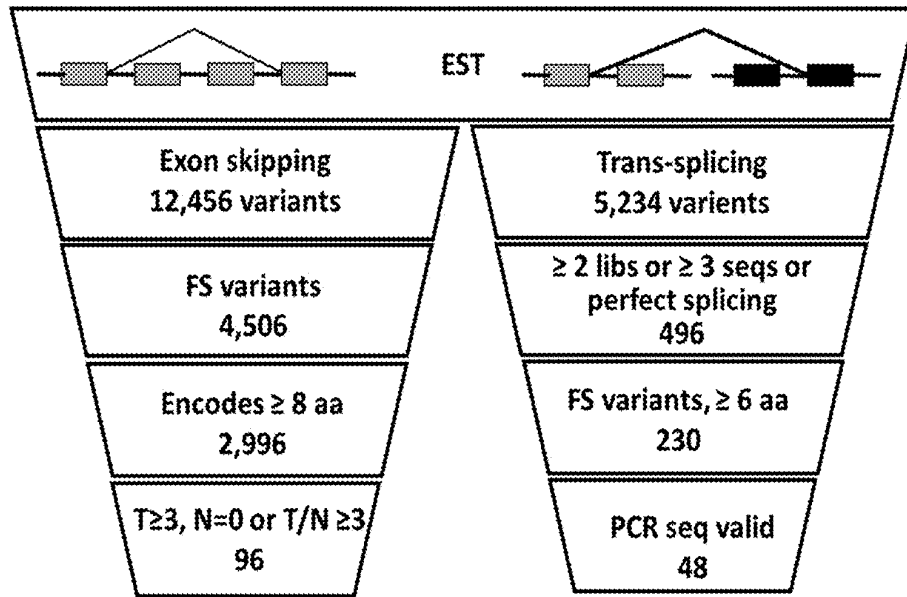


FIG. 2C

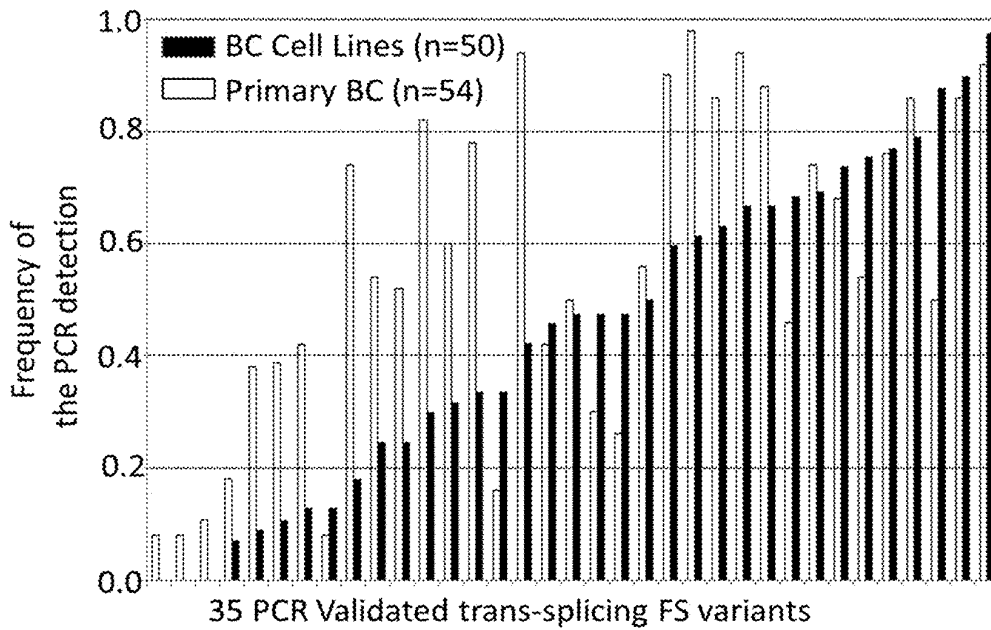


FIG. 2D

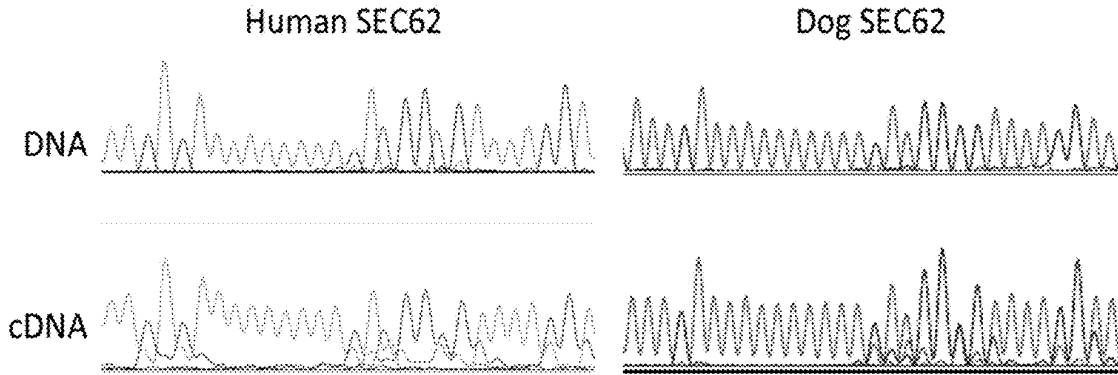


FIG. 2E

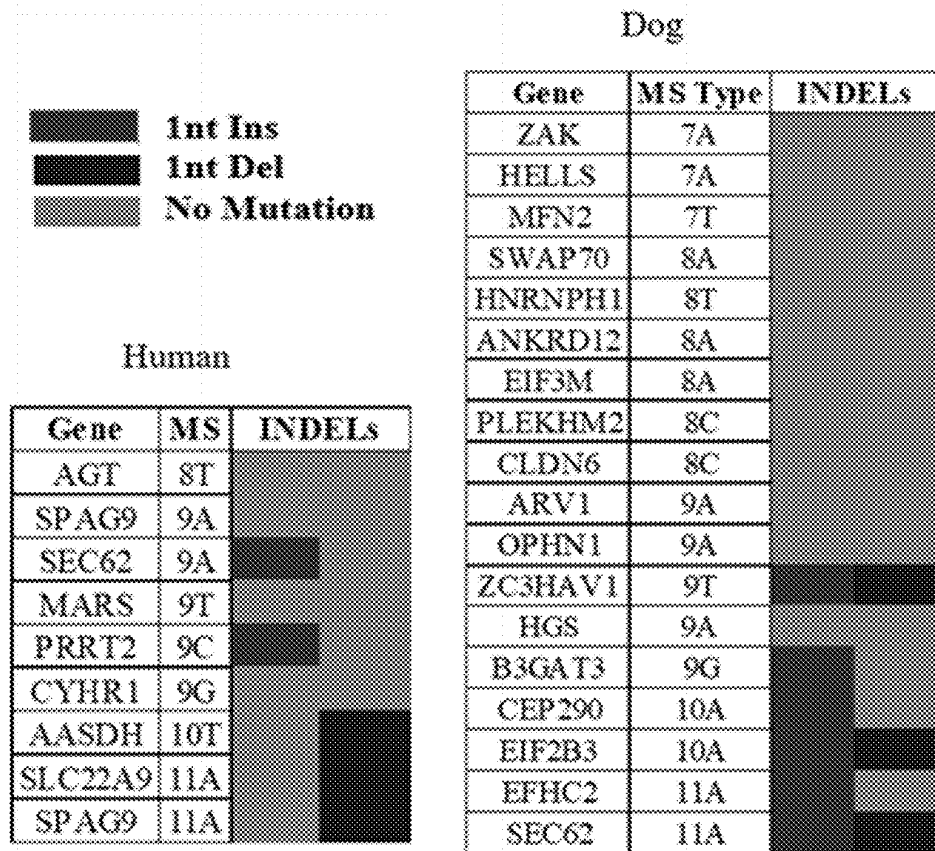


FIG. 2F

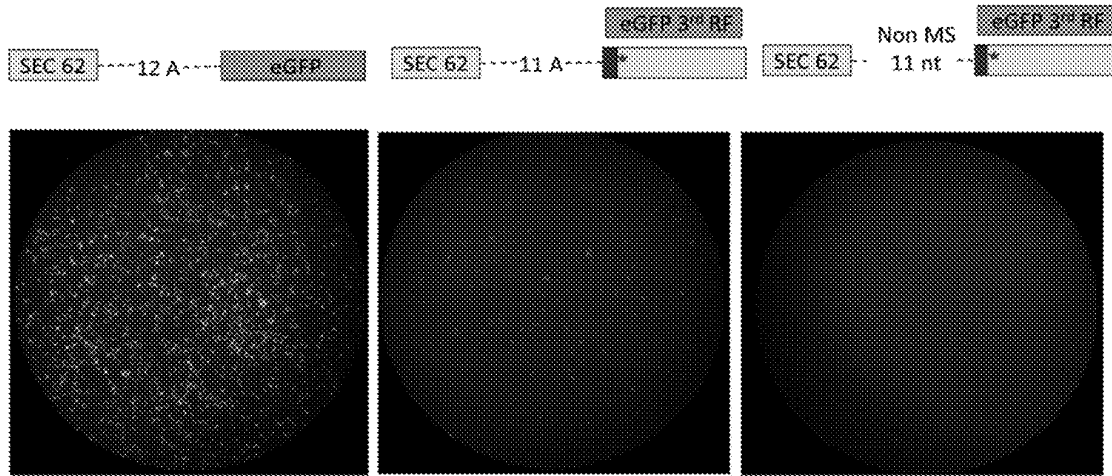


FIG. 2G

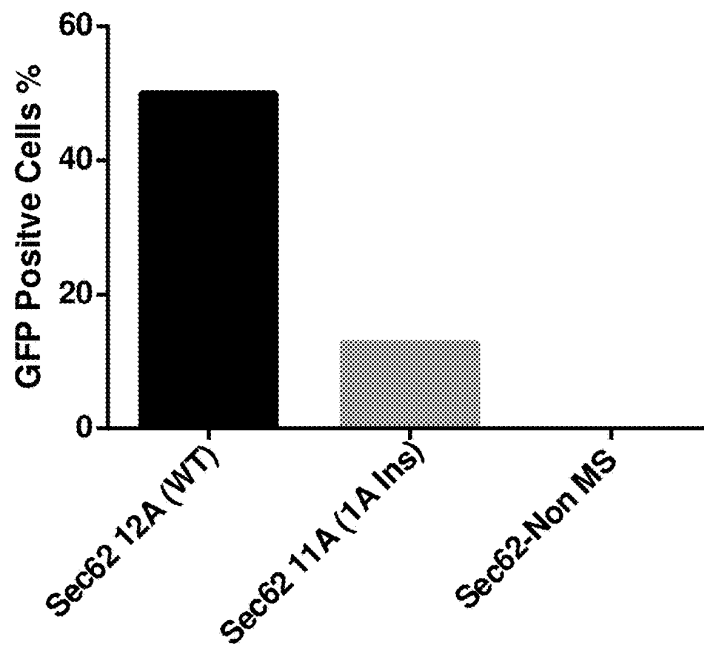


FIG. 2H

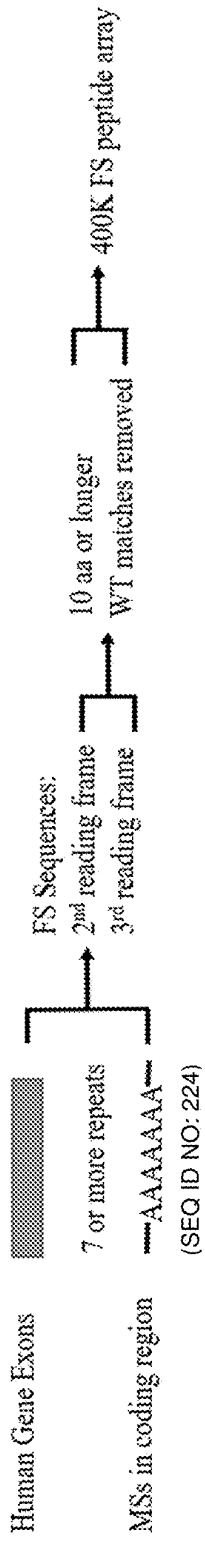


FIG. 3A

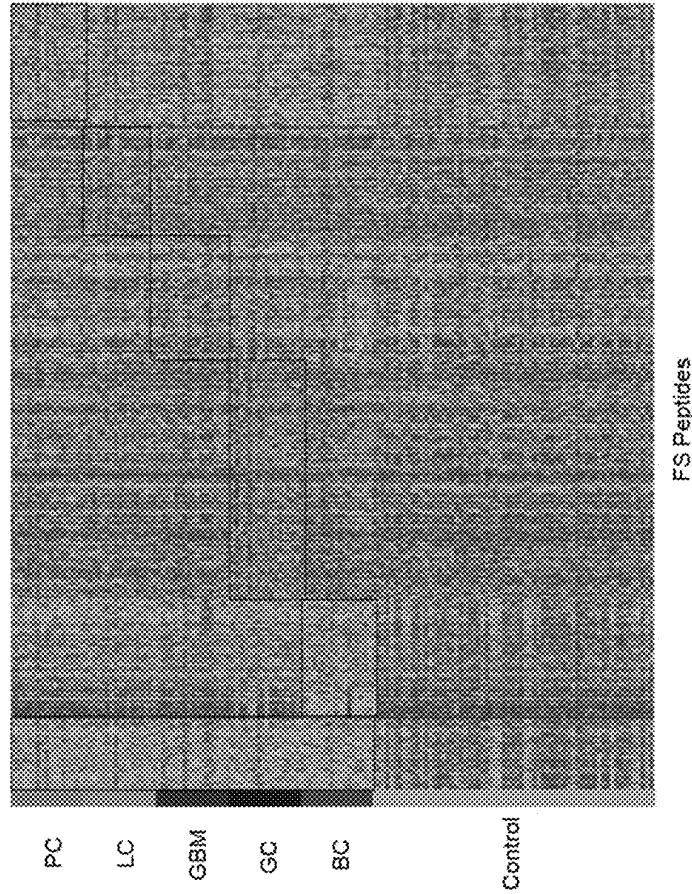


FIG. 3B

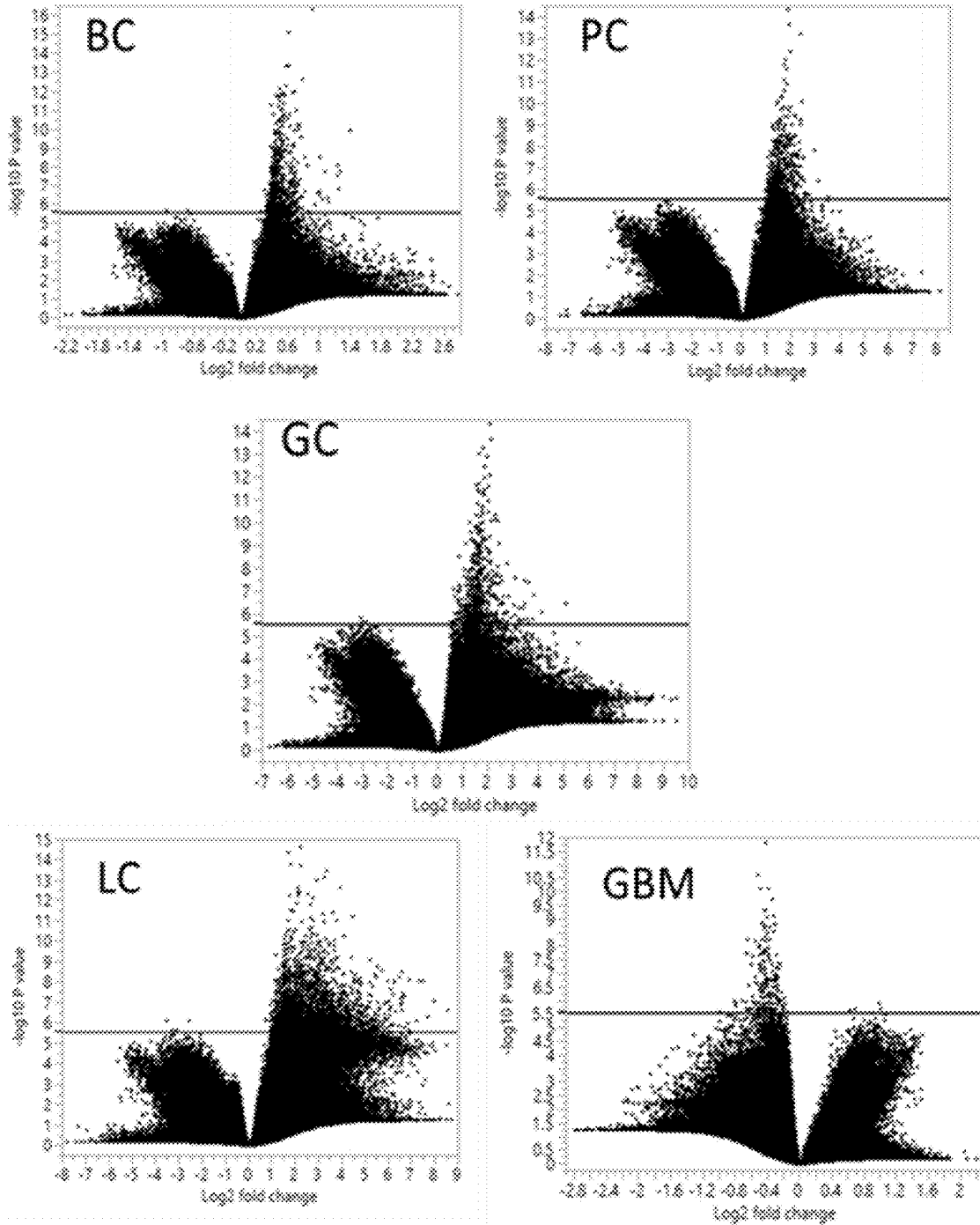


FIG. 3C

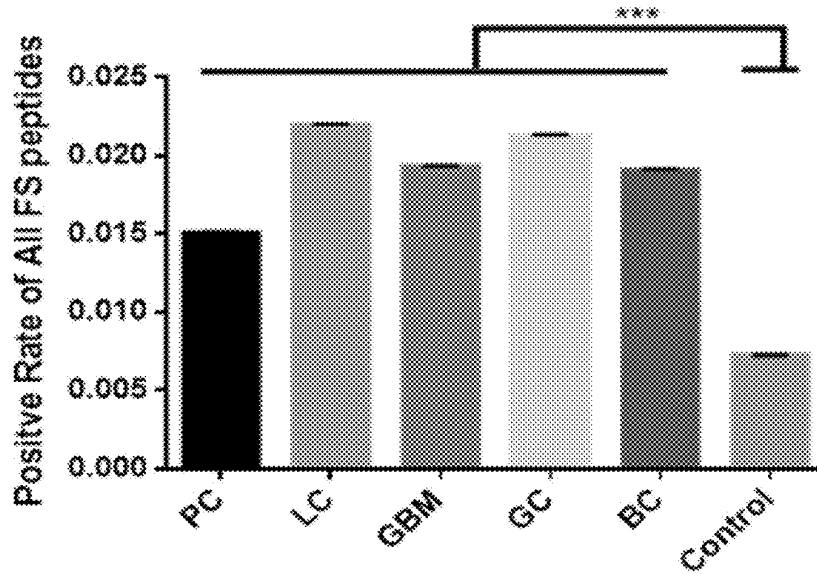


FIG. 3D

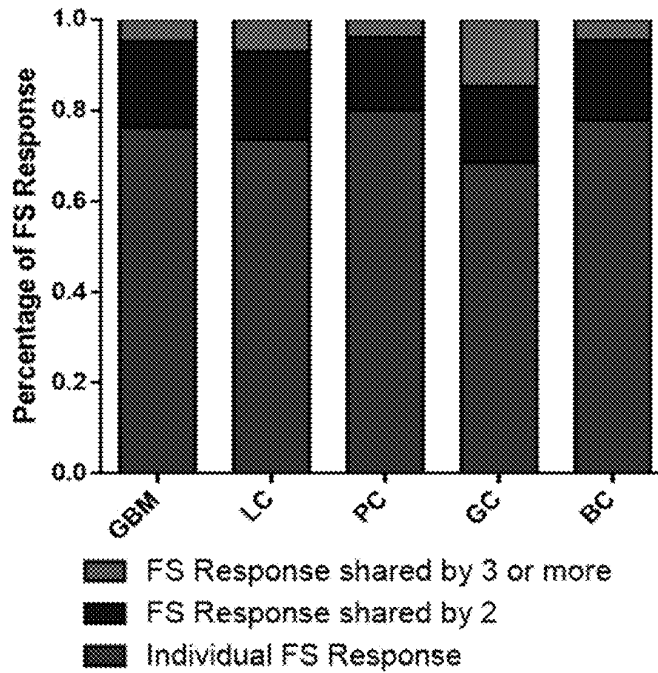


FIG. 3E

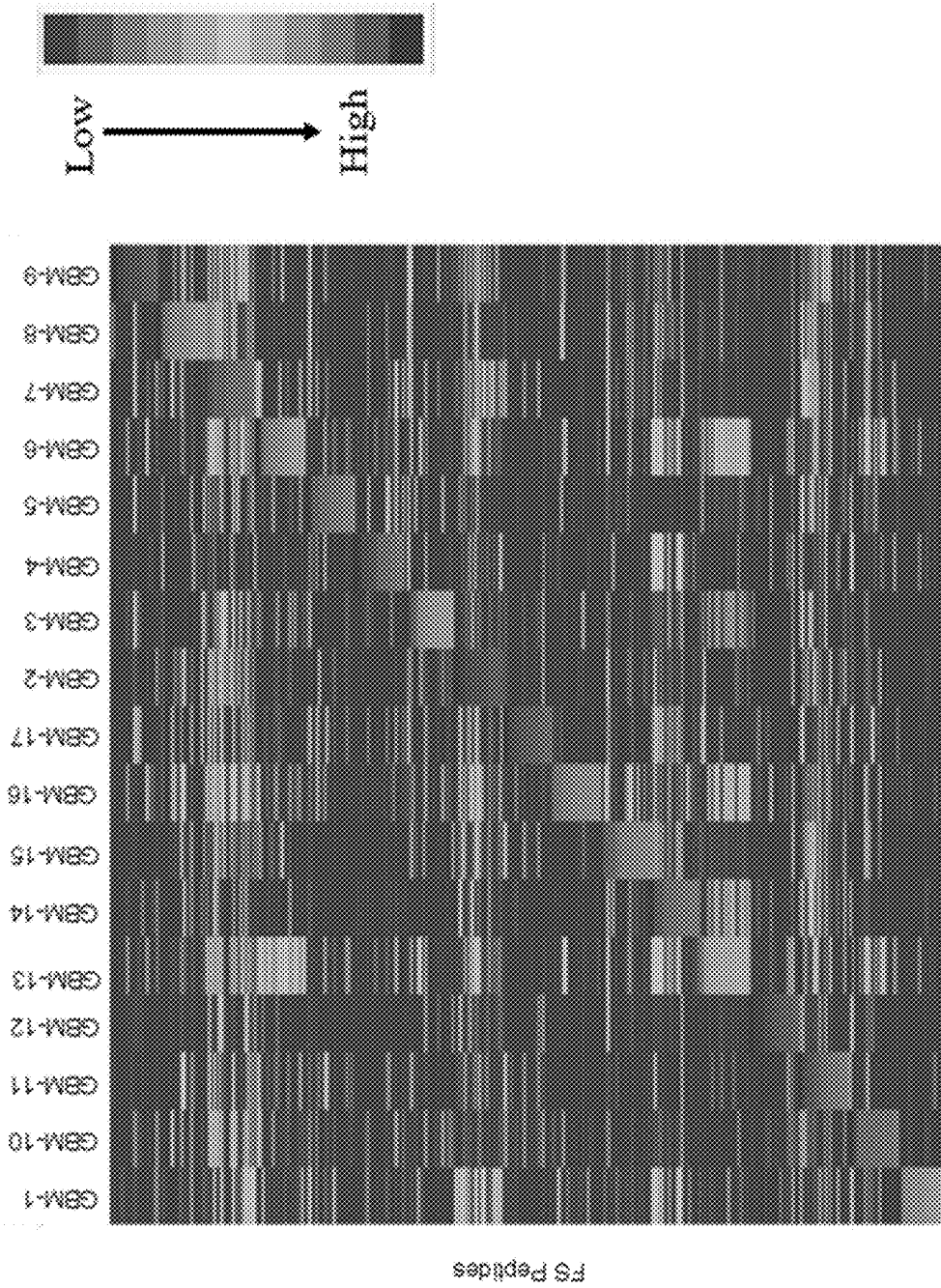


FIG. 3F

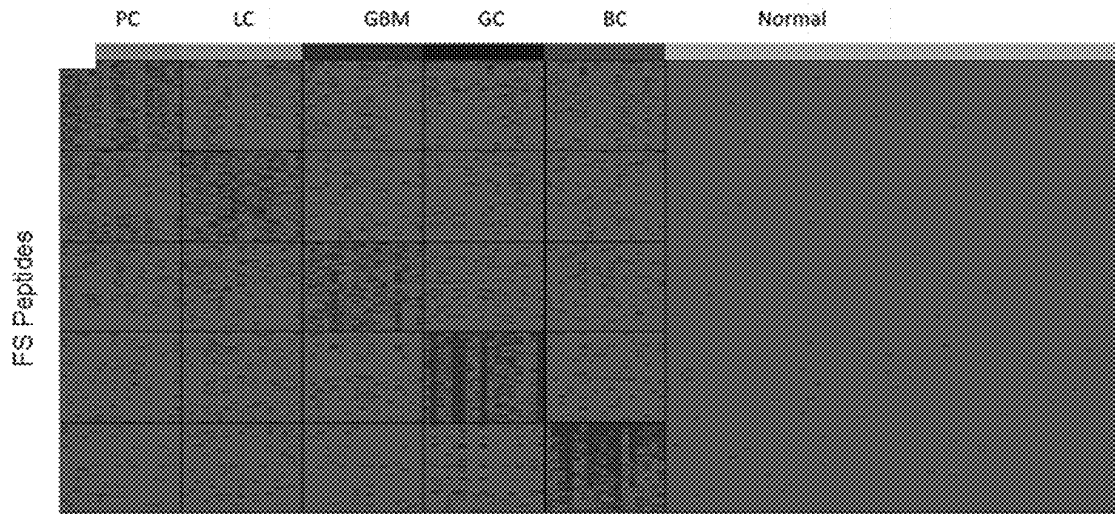


FIG. 3G

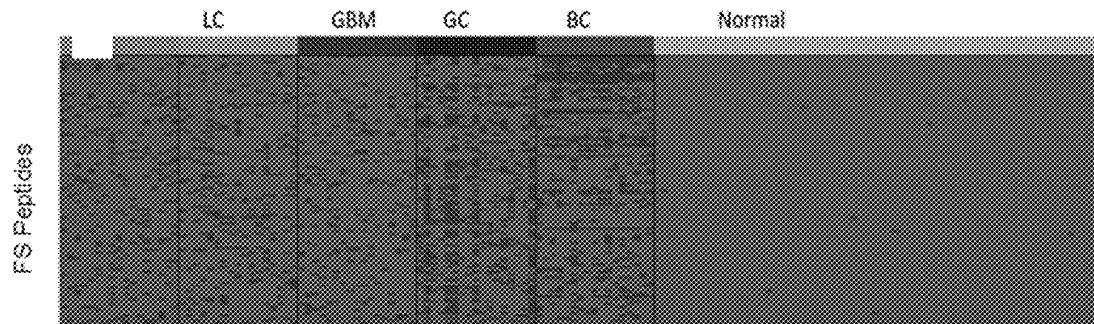


FIG. 3H

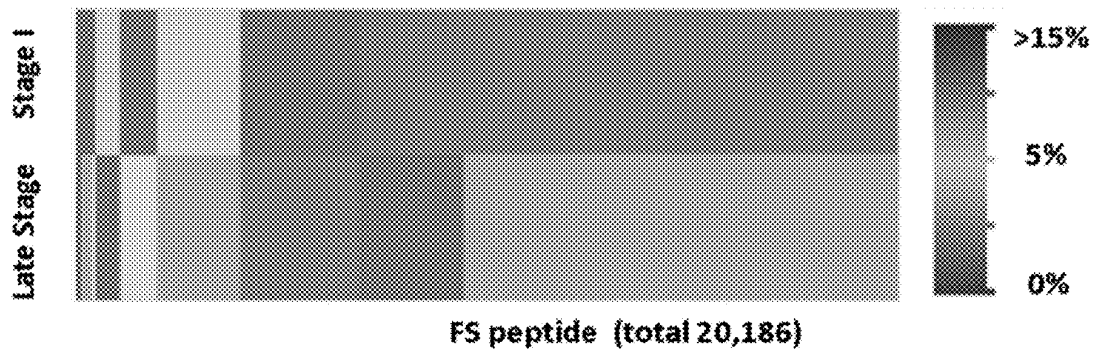


FIG. 3I

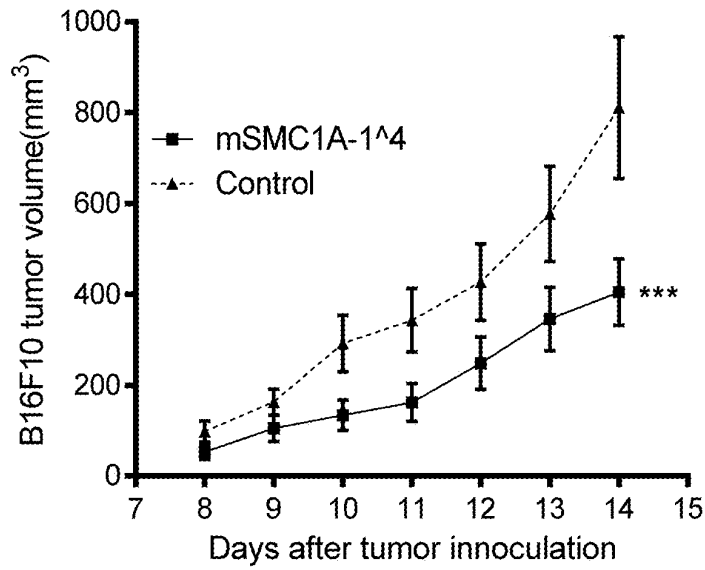


FIG. 4A

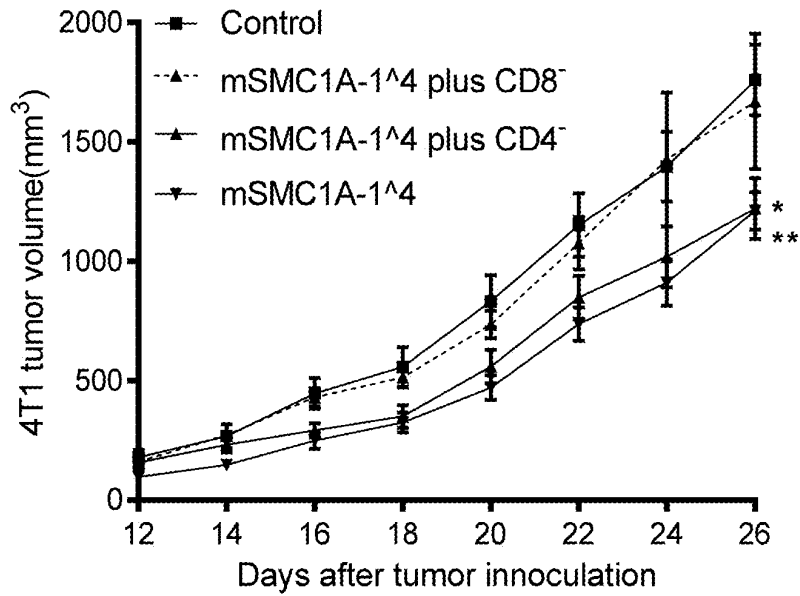


FIG. 4B

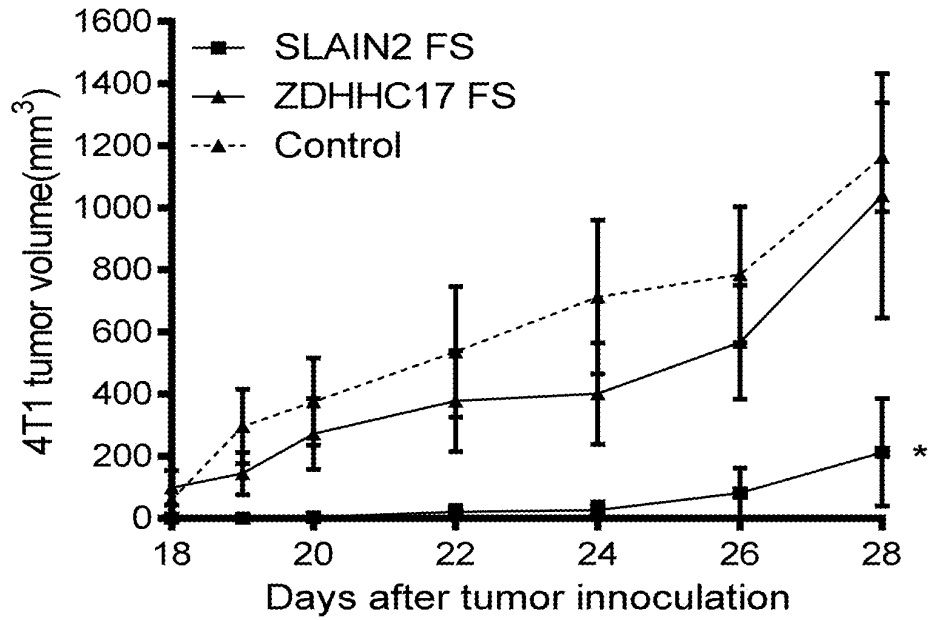


FIG. 4C

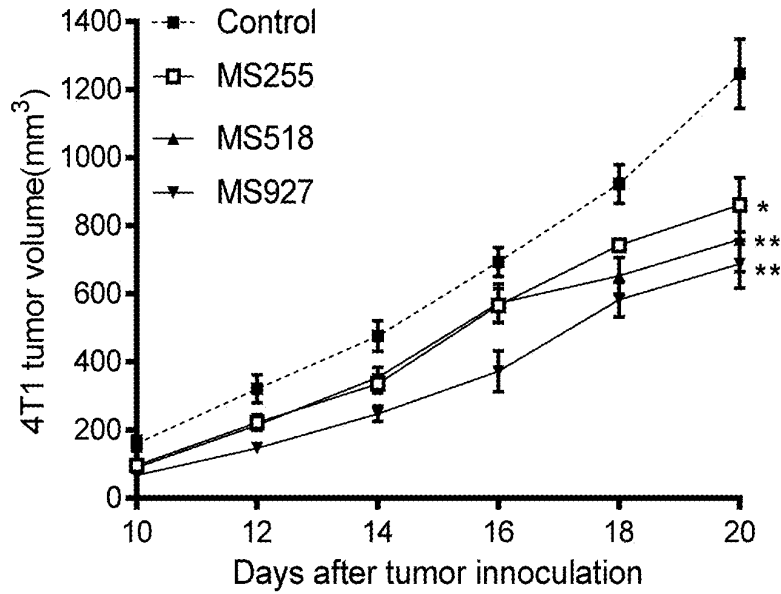


FIG. 4D

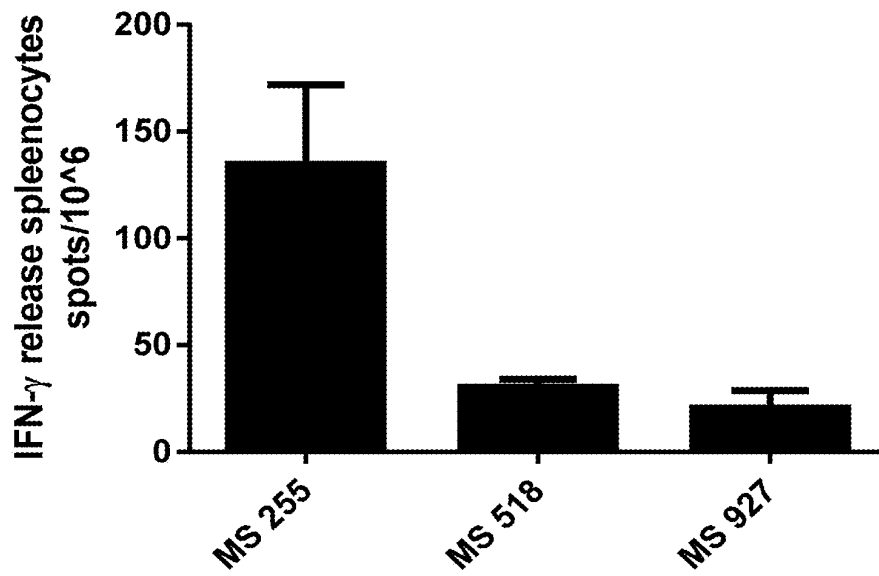


FIG. 4E

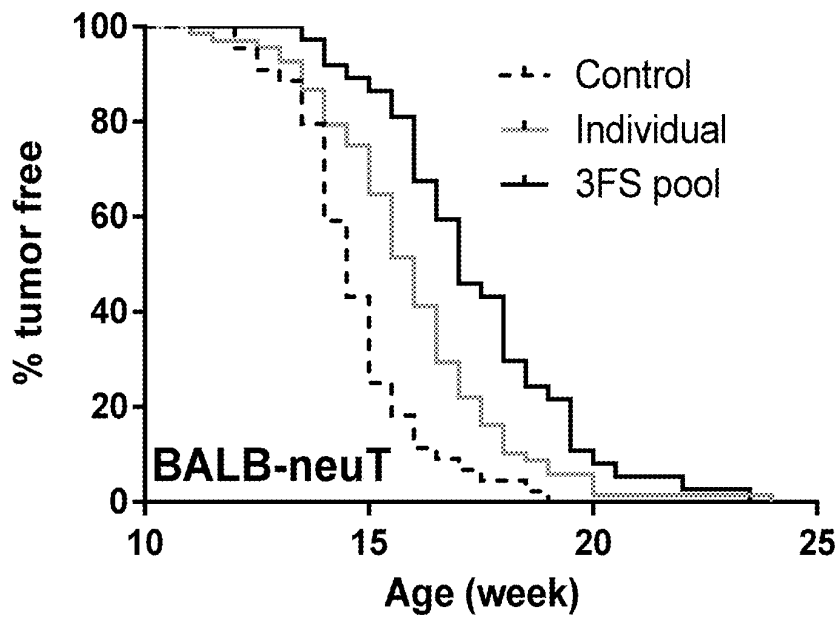


FIG. 4F

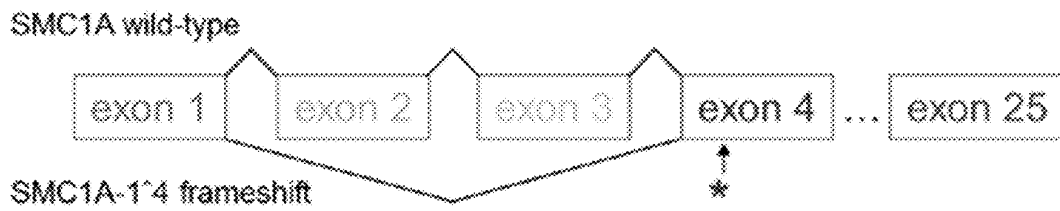


FIG. 5A

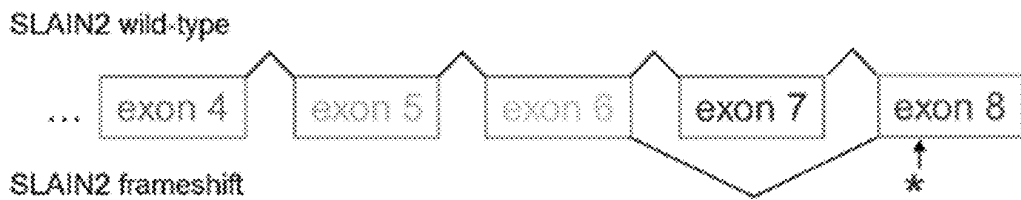


FIG. 5B

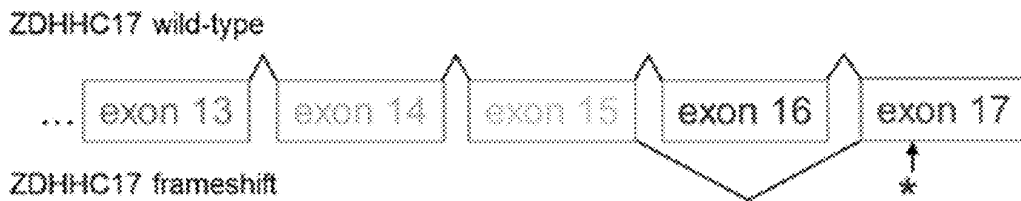


FIG. 5C



FIG. 5D

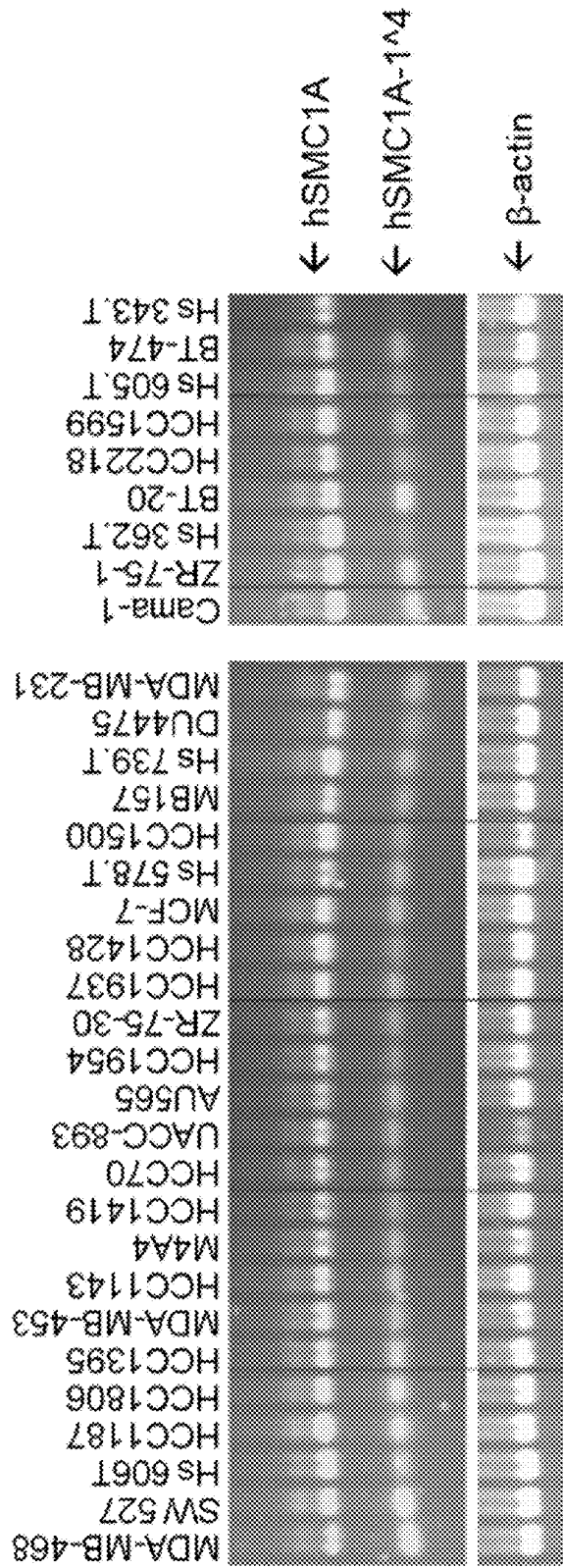


FIG. 5E

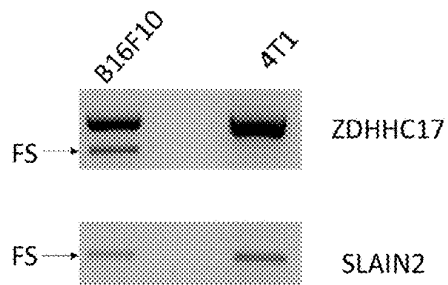


FIG. 5F

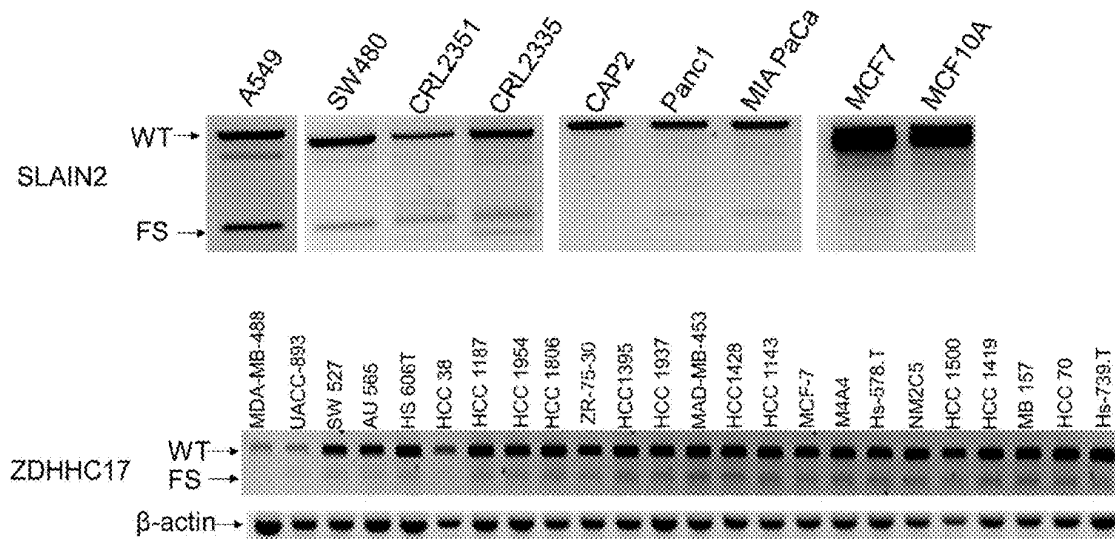


FIG. 5G

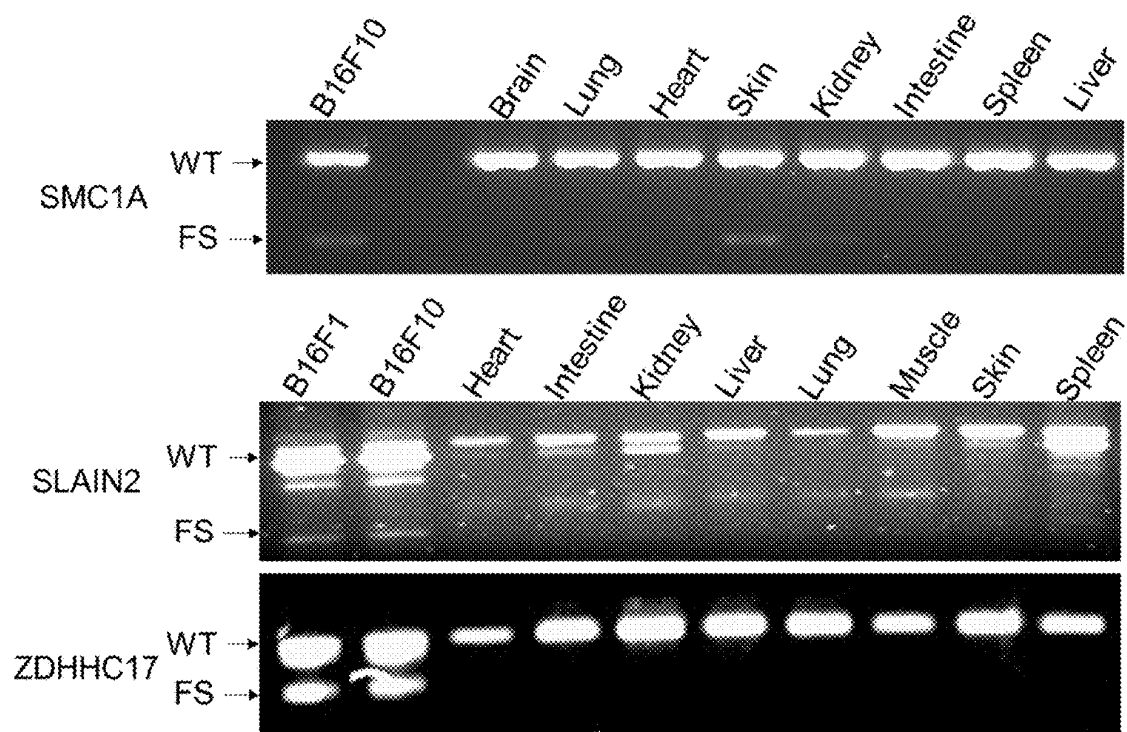


FIG. 5H

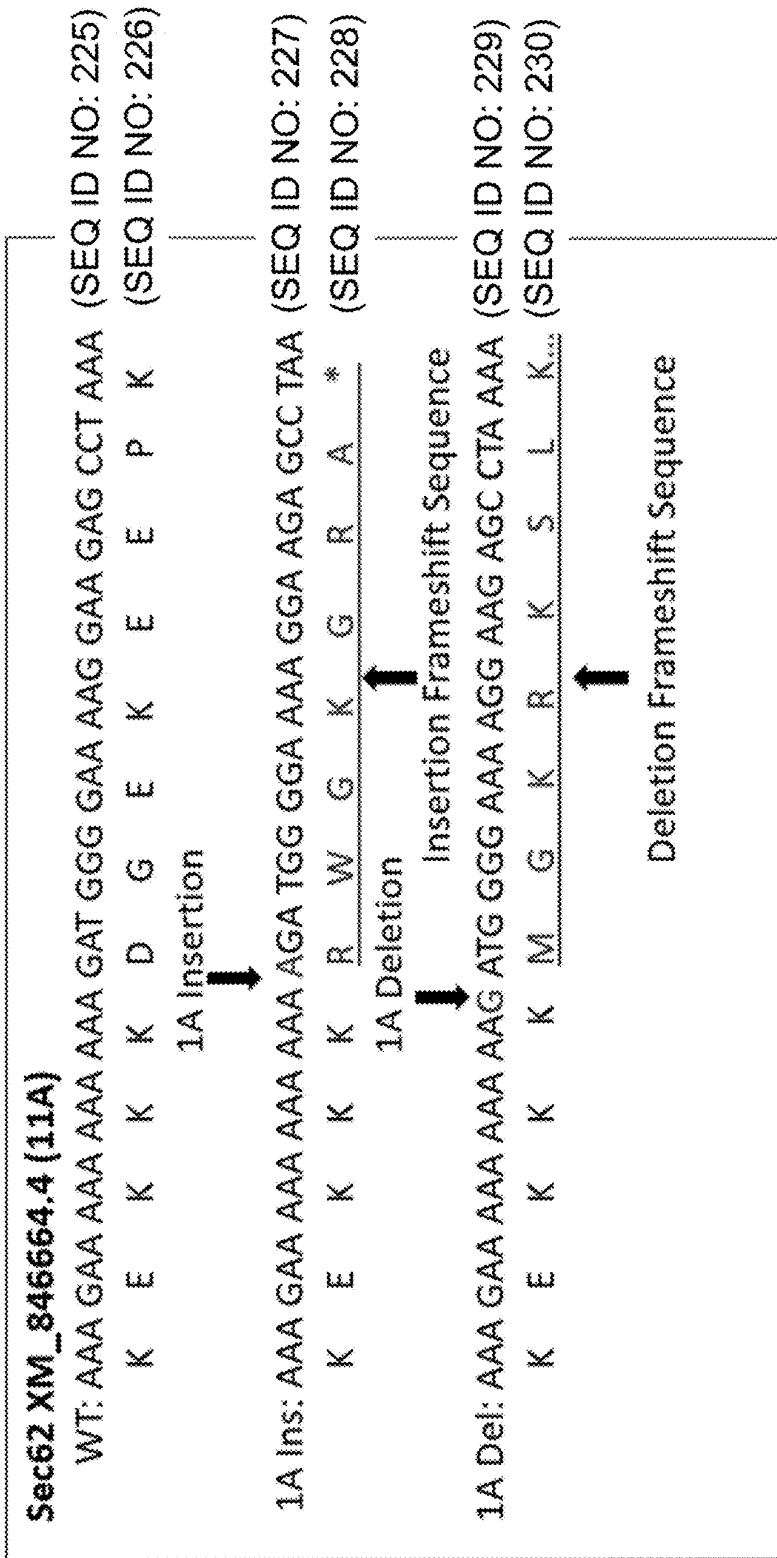


FIG. 6A

Human Exon Junction Frameshift Database

ID	Gene	Frameshift Peptide	SEQ ID NO
NM_001204516.1_Exon1_2nd	KIFAP3	CKGRTPDTSK	231
NM_001243136.1_Exon2_2nd	PELI3	CTTSRRSSP	232
NM_001301138.1_Exon1_2nd	VP539	CTTLSSQCRS	233
NM_001302453.1_Exon1_2nd	CCDC151	CTLRPPVRN	234
NM_001394441.1_Exon2_2nd	MMP8	CNKYLKRSQL	235
NM_001308192.1_Exon2_2nd	CPEB4	CTHWRVHSLT	236
NM_001308351.1_Exon4_2nd	ZNF433	CKKPSGTWPL	237
NM_014350.3_Exon1_2nd	TNFAIP8	CTPKQKNPRK	238
NM_139320.1_Exon3_2nd	CHRFAM7A	CKNIAST5IF	239

Human Exons (RefSeq)

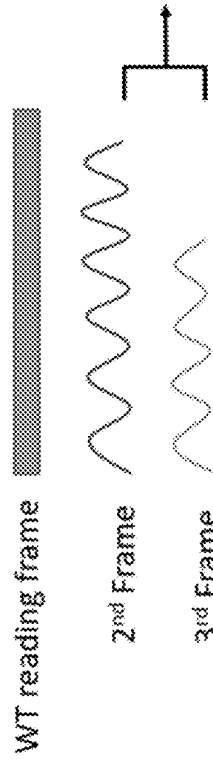


FIG. 6B

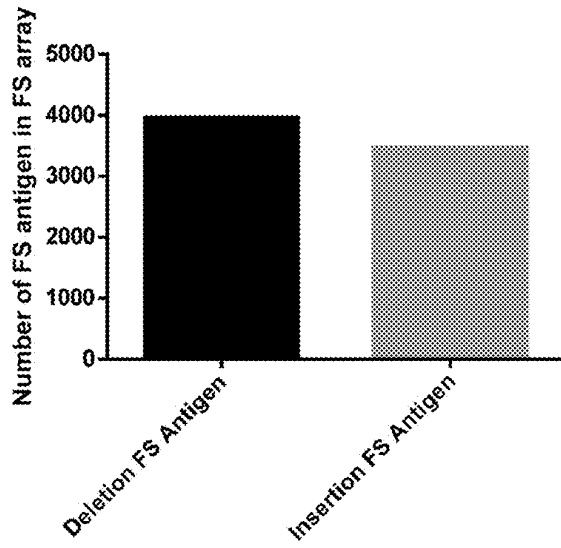


FIG. 6C

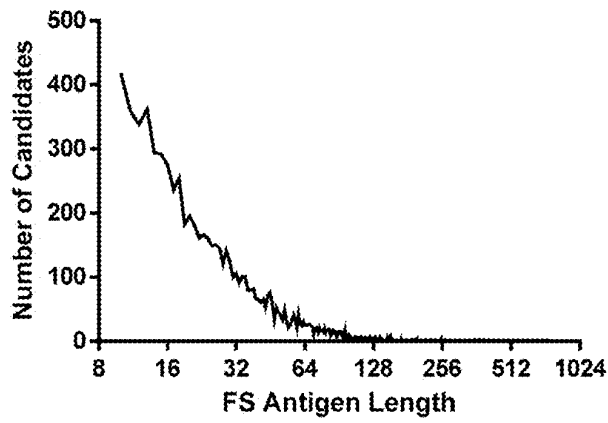


FIG. 6D

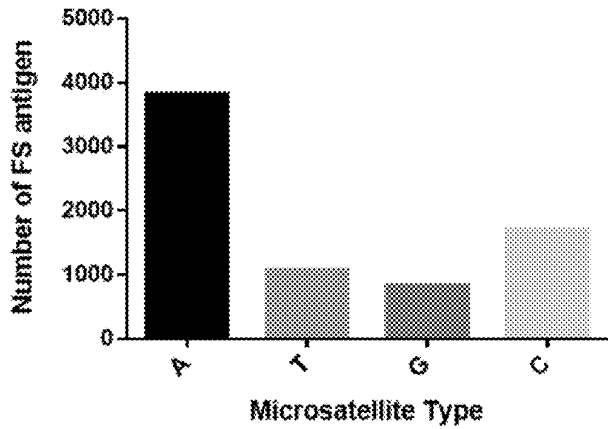


FIG. 6E

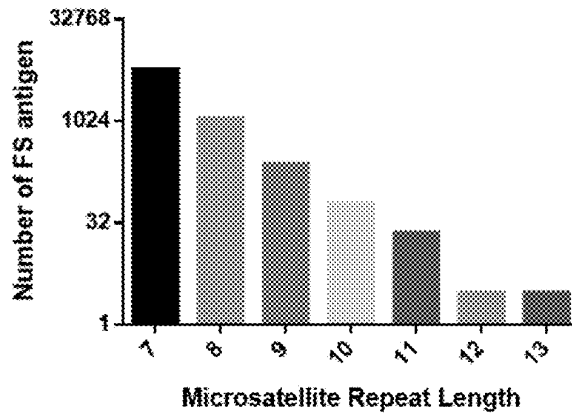


FIG. 6F

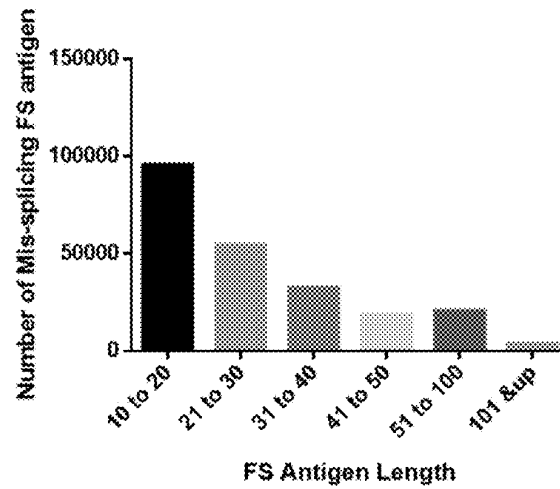


FIG. 6G

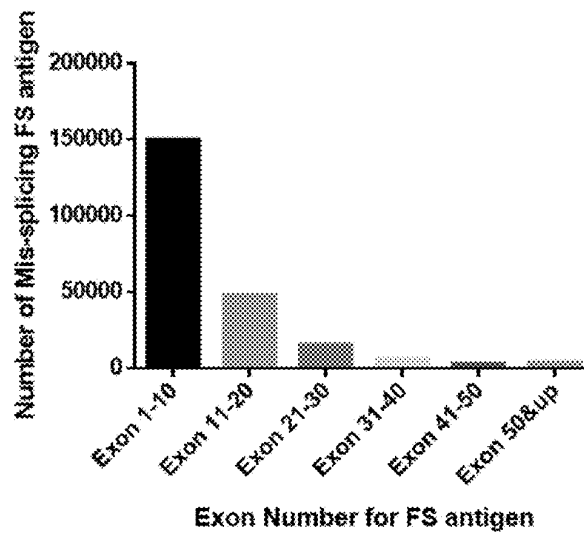


FIG. 6H

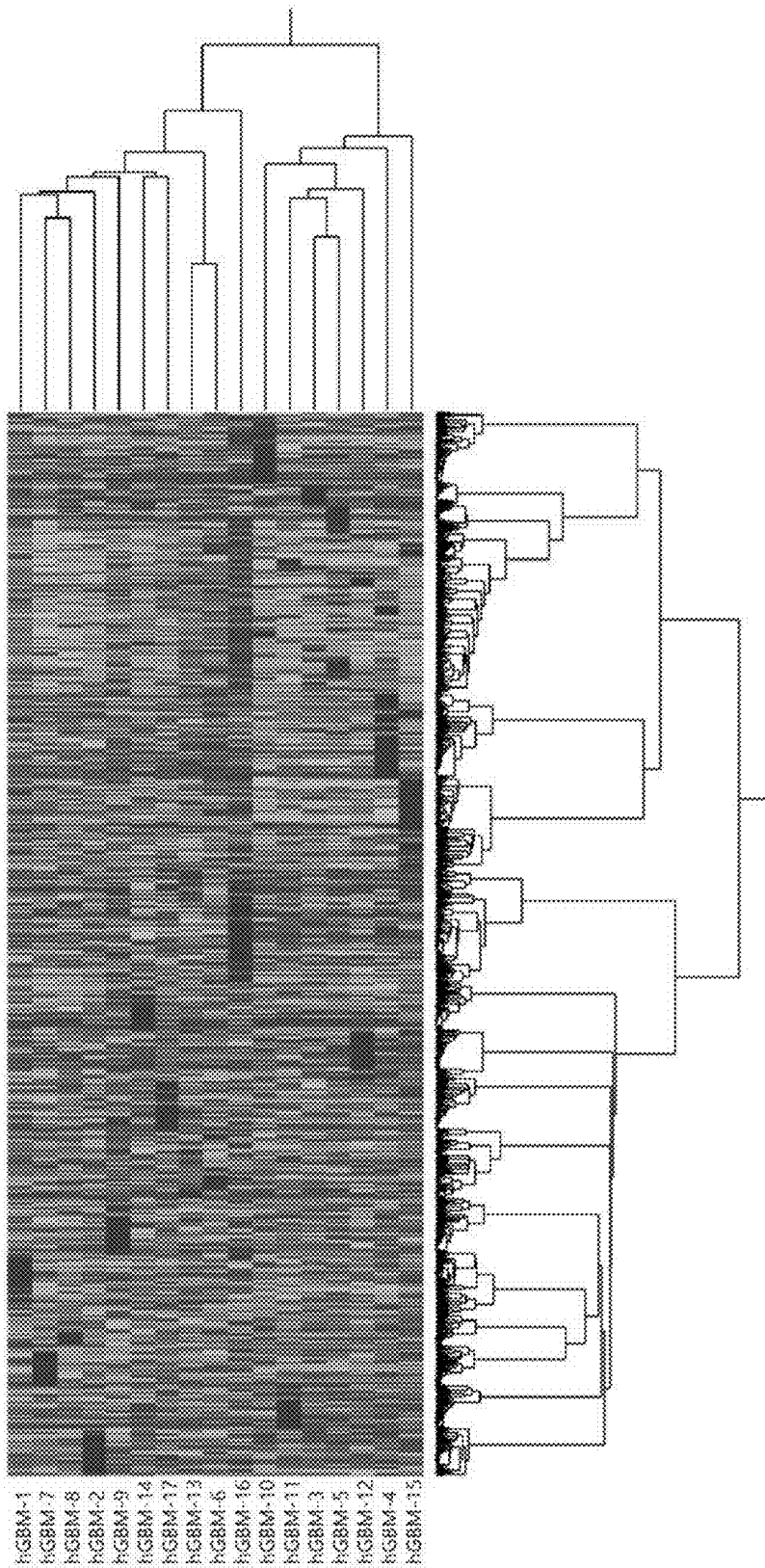


FIG. 7A

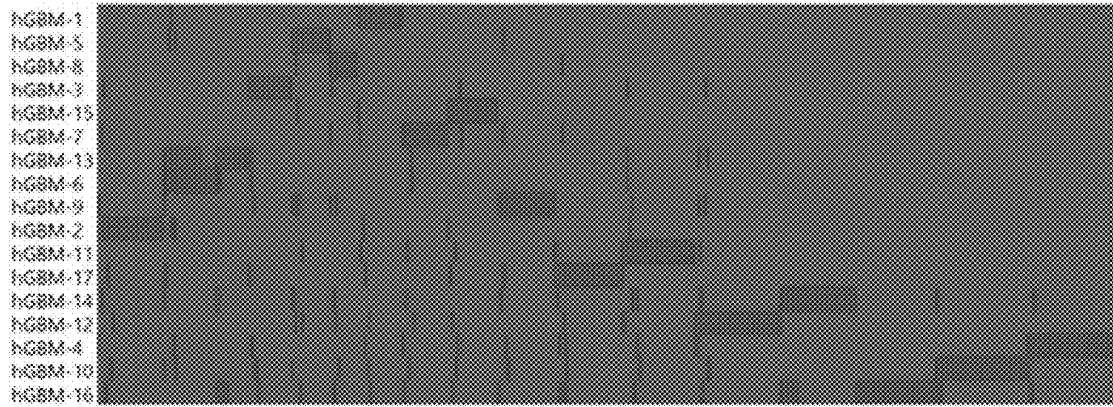


FIG. 7B

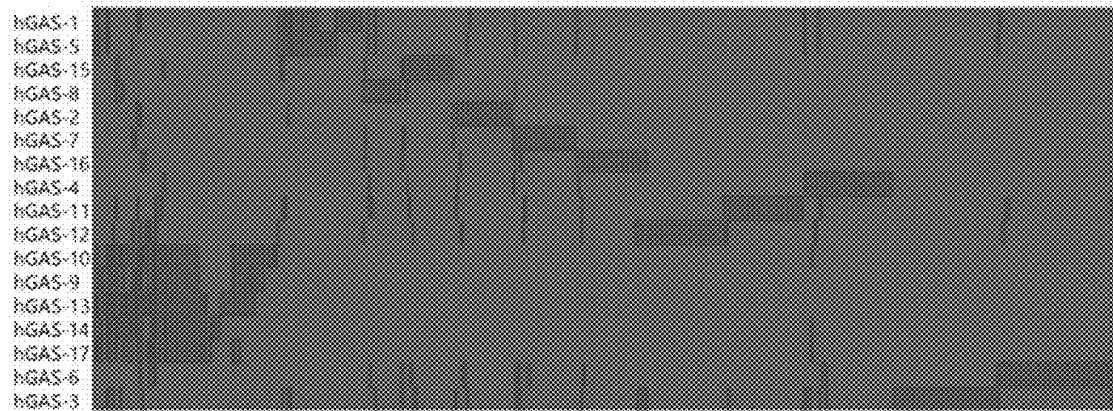


FIG. 7C

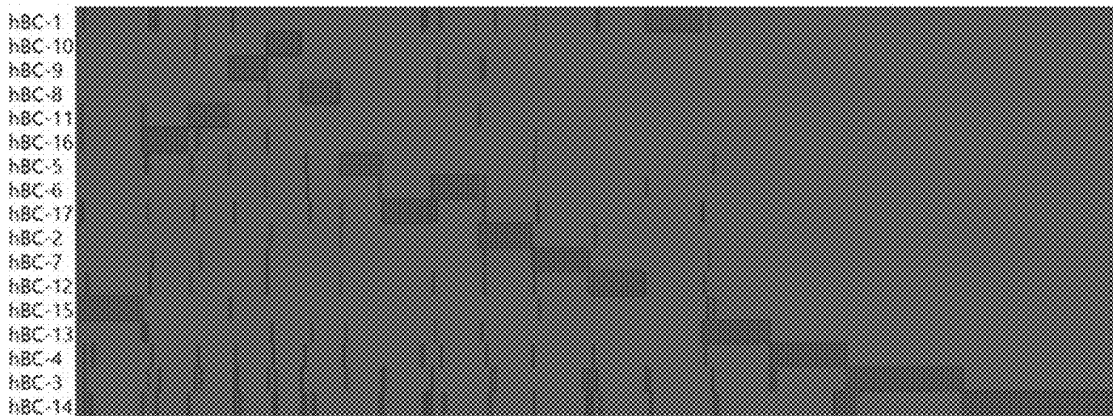


FIG. 7D

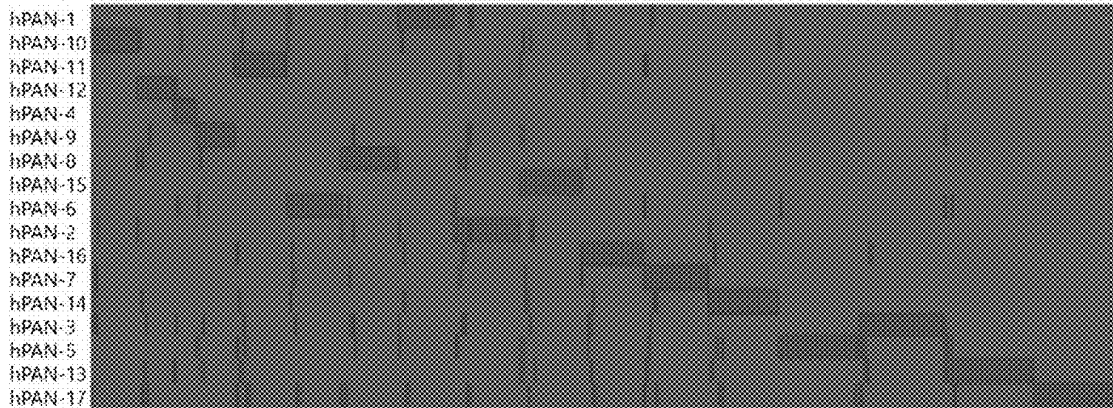


FIG. 7E

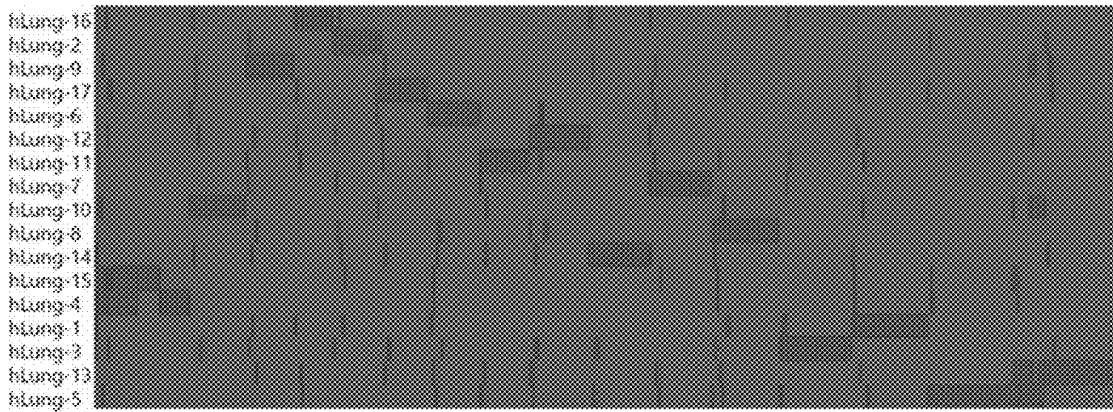


FIG. 7F

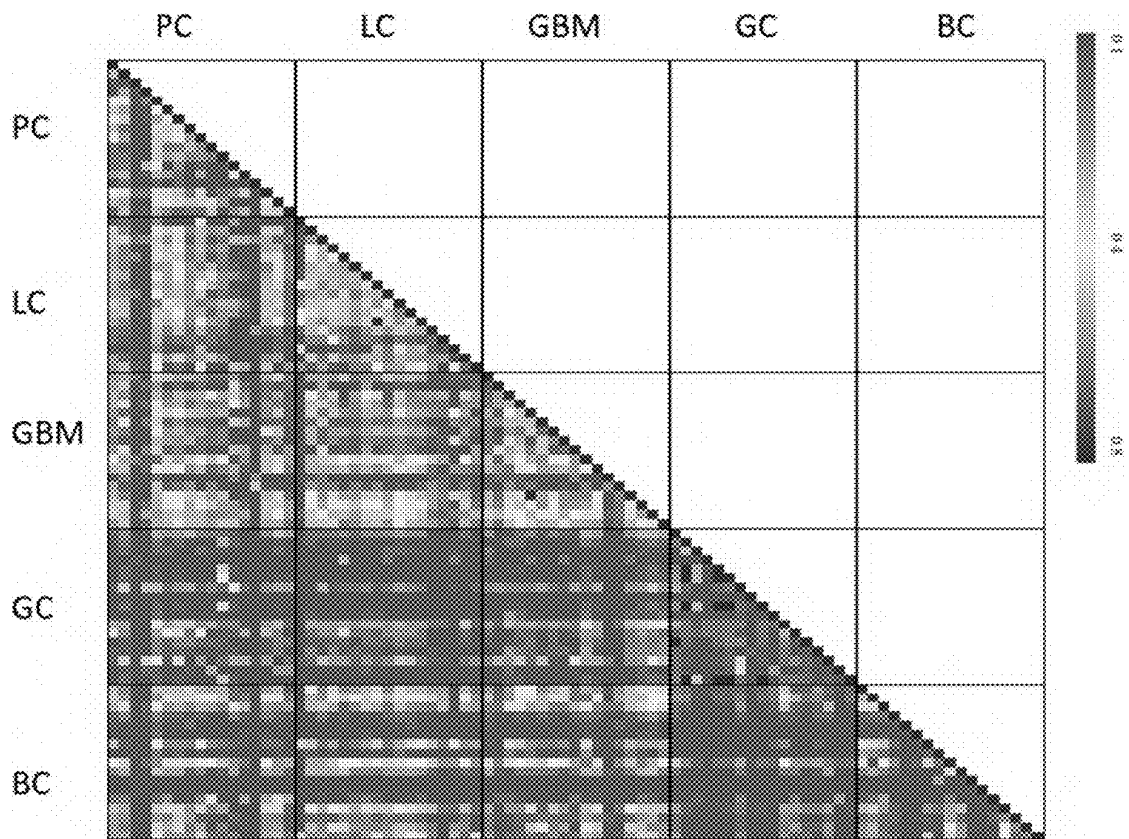


FIG. 7G

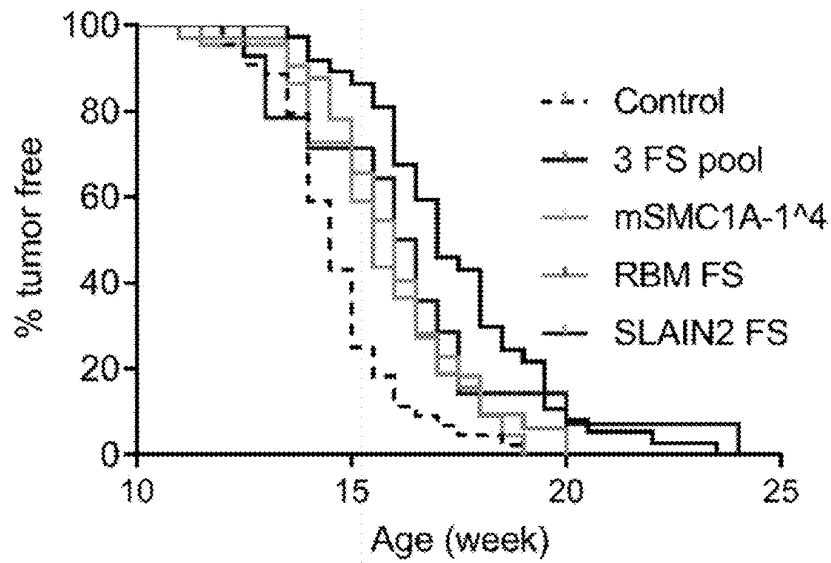


FIG. 8

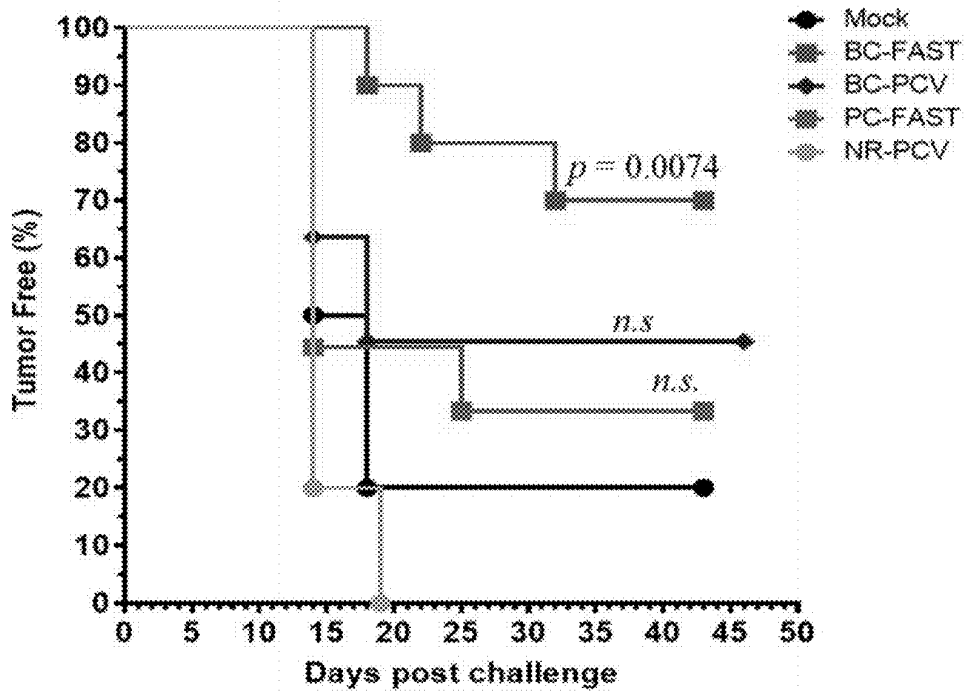


FIG. 9

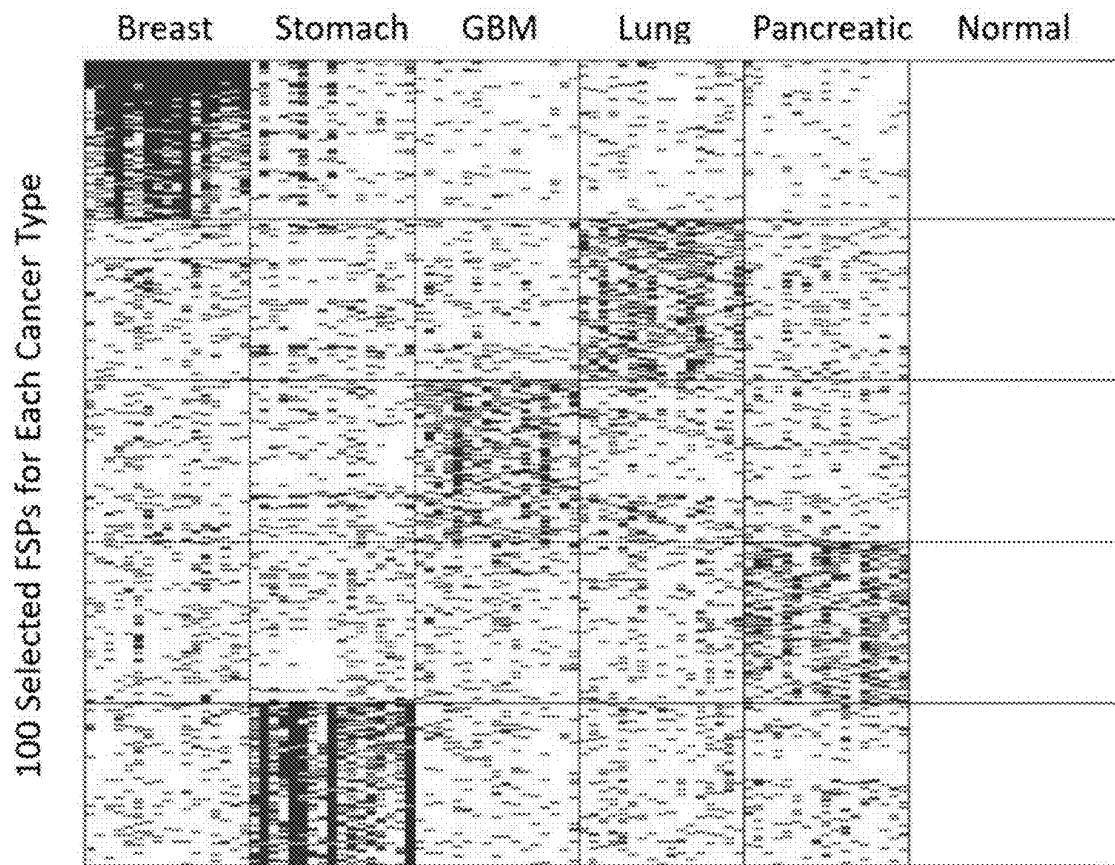


FIG. 10

METHODS AND COMPOSITIONS FOR IDENTIFYING NEOANTIGENS FOR USE IN TREATING AND PREVENTING CANCER

INCORPORATION BY REFERENCE TO ANY PRIORITY APPLICATIONS

[0001] Any and all applications for which a foreign or domestic priority claim is identified in the Application Data Sheet as filed with the present application are hereby incorporated by reference under 37 CFR 1.57.

[0002] The present application is a continuation of PCT application PCT/US2020/053728, filed Oct. 1, 2020, which claims the benefit of U.S. Provisional patent application Ser. No. 62/909,748 entitled "Methods and Compositions for Identifying Neoantigens for Use in Treating and Preventing Cancer," filed Oct. 2, 2019, which are incorporated herein by reference in its entirety.

STATEMENT AS TO FEDERALLY SPONSORED RESEARCH

[0003] This invention was made with the support of the United States government under Contract number CDRMP W81XWH-07-1-0549 by the Department of Defense.

REFERENCE TO SEQUENCE LISTING

[0004] The present application is being filed along with a sequence listing in electronic format. The sequence listing is provided as a file entitled SequenceListingCALV007C1, created Apr. 28, 2022 which is 147 KB in size. The information in the electronic format of the sequence listing is incorporated herein by reference in its entirety.

BACKGROUND

[0005] Checkpoint inhibitor immunotherapeutics are revolutionizing cancer therapy. However, even in the most responsive cancers a substantial portion (50%-80%) of the patients have poor to no positive response (1-5). The evidence to date is that whether a patient has an effective response to the treatment depends on the nature of the immune response they have established against the tumor. More specifically, the level and quality of the immune response to neoantigens in the cancer seems to be most important.

SUMMARY

[0006] Provided herein, in certain aspects, are peptide arrays comprising a plurality of frameshift variant peptides. In some cases, the plurality of frameshift variant peptides comprise peptides encoded by genes having a variant in a microsatellite (MS) in a coding region of the gene. Alternatively or in combination, the plurality of frameshift variant peptides comprise peptides encoded by an mRNA having a splicing error. In some embodiments, the plurality of frameshift variant peptides comprise two or more pooled frameshift peptides. In some cases, the plurality of frameshift variant peptides comprise one or more peptides provided in any one of Tables 1 or 7. In some embodiments, the plurality of frameshift variant peptides are fixed on a substrate. In some embodiments, the substrate comprises glass, composite, resin, or combination thereof. In some embodiments, the peptide array is configured to detect binding by at least one of fluorescence, luminescence, calorimetry,

chromatography, radioactivity, Bio-Layer Interferometry, and surface plasmon resonance. In some embodiments, the peptide array comprises at least about 25000, about 50000, about 75000, about 100000, about 125000, about 150000, about 175000, about 200000, about 225000, about 250000, about 275000, about 300000, about 325000, about 350000, about 375000, or about 400000 frameshift variant peptides.

[0007] In additional aspects, there are provided methods of measuring an immune response to a neoantigen peptide in a subject. In some cases, the method comprises: (a) contacting a biological sample obtained from a subject to a peptide array comprising a plurality of frameshift variant peptides. In some cases, the plurality of frameshift variant peptides comprise peptides encoded by genes having a variant in a microsatellite (MS) in a coding region of the gene. Alternatively or in combination, the plurality of frameshift variant peptides comprise peptides encoded by an mRNA having a splicing error. In some cases, the method further comprises detecting binding of the biological sample to at least one peptide in the peptide array. In some embodiments, the plurality of frameshift variant peptides comprise two or more pooled frameshift peptides. In some embodiments, the plurality of frameshift variant peptides comprise one or more peptides provided in any one of Tables 1 or 7. In some embodiments, the plurality of frameshift variant peptides are fixed on a substrate. In some embodiments, the substrate comprises glass, composite, resin, or combination thereof. In some embodiments, the peptide array is configured to detect binding by at least one of fluorescence, luminescence, calorimetry, chromatography, radioactivity, Bio-Layer Interferometry, and surface plasmon resonance. In some embodiments, the peptide array comprises at least about 25000, about 50000, about 75000, about 100000, about 125000, about 150000, about 175000, about 200000, about 225000, about 250000, about 275000, about 300000, about 325000, about 350000, about 375000, or about 400000 frameshift variant peptides. In some embodiments, the biological sample comprises blood, serum, plasma, cerebrospinal fluid, saliva, urine, or combinations thereof. In some embodiments, the biological sample comprises an antibody. In some embodiments, the subject is a mammal. In some embodiments, the subject is a human, a dog, a cat, a mouse, a rat, a rabbit, a horse, a cow, or a pig. In some embodiments, the subject is suspected of having a cancer. In some embodiments, the cancer is selected from the group consisting of Acute lymphoblastic leukemia, Acute monocytic leukemia, Acute myeloid leukemia, Acute promyelocytic leukemia, Adenocarcinoma, Adult T-cell leukemia, Astrocytoma, Bladder cancer, Bone Cancer, Brain Tumor, Breast Cancer, Burkitt's lymphoma, Carcinoma, Cervical Cancer, Chronic Lymphocytic Leukemia, Chronic myelogenous leukemia, Colon Cancer, Colorectal cancer, Endometrial cancer, Glioblastoma multiforme, Glioma, Hepatocellular carcinoma, Hodgkin's lymphoma, Inflammatory breast cancer, Kidney Cancer, Leukemia, Lung cancer, Lymphoma, Malignant Mesothelioma, Medulloblastoma, Melanoma, Multiple myeloma, Neuroblastoma, Non-Hodgkin Lymphoma, Non-Small Cell Lung Cancer, Ovarian Cancer, Pancreatic Cancer, Pituitary tumor, Prostate cancer, Retinoblastoma, Skin Cancer, Small Cell Lung Cancer, Squamous cell carcinoma, Stomach cancer, T-cell leukemia, T-cell lymphoma, Thyroid cancer, and Wilms' tumor.

[0008] In further aspects, there are provided methods of detecting a cancer in a subject. In some embodiments, the

method comprises: (a) contacting a biological sample obtained from a subject to a peptide array comprising a plurality of frameshift variant peptides. In some embodiments, the plurality of frameshift variant peptides comprise peptides encoded by genes having a variant in a microsatellite (MS) in a coding region of the gene. Alternatively or in combination, the plurality of frameshift variant peptides comprise peptides encoded by an mRNA having a splicing error. In some embodiments, the method further comprises detecting binding of the biological sample to at least one peptide in the peptide array. In some embodiments, the plurality of frameshift variant peptides comprise one or more peptides provided in any one of Tables 1 or 7. In some embodiments, the plurality of frameshift variant peptides comprise two or more pooled frameshift peptides. In some embodiments, the plurality of frameshift variant peptides are fixed on a substrate. In some embodiments, the substrate comprises glass, composite, resin, or combination thereof. In some embodiments, the peptide array is configured to detect binding by at least one of fluorescence, luminescence, calorimetry, chromatography, radioactivity, Bio-Layer Interferometry, and surface plasmon resonance. In some embodiments, the peptide array comprises at least about 25000, about 50000, about 75000, about 100000, about 125000, about 150000, about 175000, about 200000, about 225000, about 250000, about 275000, about 300000, about 325000, about 350000, about 375000, or about 400000 frameshift variant peptides. In some embodiments, the biological sample comprises blood, serum, plasma, cerebrospinal fluid, saliva, urine, or combinations thereof. In some embodiments, the biological sample comprises an antibody. In some embodiments, the subject is a mammal. In some embodiments, the subject is a human, a dog, a cat, a mouse, a rat, a rabbit, a horse, a cow, or a pig. In some embodiments, the subject is suspected of having a cancer. In some embodiments, the cancer is selected from the group consisting of Acute lymphoblastic leukemia, Acute monocytic leukemia, Acute myeloid leukemia, Acute promyelocytic leukemia, Adenocarcinoma, Adult T-cell leukemia, Astrocytoma, Bladder cancer, Bone Cancer, Brain Tumor, Breast Cancer, Burkitt's lymphoma, Carcinoma, Cervical Cancer, Chronic Lymphocytic Leukemia, Chronic myelogenous leukemia, Colon Cancer, Colorectal cancer, Endometrial cancer, Glioblastoma multiforme, Glioma, Hepatocellular carcinoma, Hodgkin's lymphoma, Inflammatory breast cancer, Kidney Cancer, Leukemia, Lung cancer, Lymphoma, Malignant Mesothelioma, Medulloblastoma, Melanoma, Multiple myeloma, Neuroblastoma, Non-Hodgkin Lymphoma, Non-Small Cell Lung Cancer, Ovarian Cancer, Pancreatic Cancer, Pituitary tumor, Prostate cancer, Retinoblastoma, Skin Cancer, Small Cell Lung Cancer, Squamous cell carcinoma, Stomach cancer, T-cell leukemia, T-cell lymphoma, Thyroid cancer, and Wilms' tumor.

[0009] In further aspects, there are provided compositions comprising a plurality of frameshift variant peptides. In some cases, the plurality of frameshift variant peptides comprise peptides encoded by genes having a variant in a microsatellite (MS) in a coding region of the gene. Alternatively or in combination, wherein the plurality of frameshift variant peptides comprise peptides encoded by an mRNA having a splicing error. In some embodiments, the plurality of frameshift variant peptides comprise one or more peptides provided in any one of Tables 1 or 7. In some embodiments, the plurality of frameshift variant peptides

comprise two or more pooled frameshift peptides. In some embodiments, the composition further comprises an adjuvant. In some embodiments, the adjuvant is selected from the group consisting of ABM2, AS01B, AS02, AS02A, Adjuver, Adjuvax, Algammulin, Alum, Aluminum phosphate, Aluminum potassium sulfate, *Bordetella pertussis*, Calcitriol, Chitosan, Cholera toxin, CpG, Dibutyl phthalate, Dimethyldioctadecylammonium bromide (DDA), Freund's adjuvant, Freund's complete, Freund's incomplete (IFA), GM-CSF, GMDP, Gamma Inulin, Glycerol, HBSS (Hank's Balanced Salt Solution), IL-12, IL-2, Imiquimod, Interferon-Gamma, ISCOM, Lipid Core Peptide (LCP), Lipofectin, Lipopolysaccharide (LPS), Liposomes, MF59, MLP+TDM, Monophosphoryl lipid A, Montanide IMS-1313, Montanide ISA 206, Montanide ISA 720, Montanide ISA-51, Montanide ISA-50, nor-MDP, Oil-in-water emulsion, P1005 (non-ionic copolymer), Pam3Cys (lipoprotein), Pertussis toxin, Poloxamer, QS21, RaLPS, Ribi, Saponin, Seppic ISA 720, Soybean Oil, Squalene, Syntex Adjuvant Formulation (SAF), Synthetic polynucleotides (poly IC/poly AU), TiterMax Tomatine, Vaxfectin, XtendIII, and Zymo-san.

[0010] In additional aspects, there are provided methods of treating or preventing cancer in a subject comprising administering a composition comprising any one of the frameshift variant peptides provided herein. In some embodiments, the subject is a mammal. In some embodiments, the subject is a human, a dog, a cat, a mouse, a rat, a rabbit, a horse, a cow, or a pig. In some embodiments, the cancer is selected from the group consisting of Acute lymphoblastic leukemia, Acute monocytic leukemia, Acute myeloid leukemia, Acute promyelocytic leukemia, Adenocarcinoma, Adult T-cell leukemia, Astrocytoma, Bladder cancer, Bone Cancer, Brain Tumor, Breast Cancer, Burkitt's lymphoma, Carcinoma, Cervical Cancer, Chronic Lymphocytic Leukemia, Chronic myelogenous leukemia, Colon Cancer, Colorectal cancer, Endometrial cancer, Glioblastoma multiforme, Glioma, Hepatocellular carcinoma, Hodgkin's lymphoma, Inflammatory breast cancer, Kidney Cancer, Leukemia, Lung cancer, Lymphoma, Malignant Mesothelioma, Medulloblastoma, Melanoma, Multiple myeloma, Neuroblastoma, Non-Hodgkin Lymphoma, Non-Small Cell Lung Cancer, Ovarian Cancer, Pancreatic Cancer, Pituitary tumor, Prostate cancer, Retinoblastoma, Skin Cancer, Small Cell Lung Cancer, Squamous cell carcinoma, Stomach cancer, T-cell leukemia, T-cell lymphoma, Thyroid cancer, and Wilms' tumor.

INCORPORATION BY REFERENCE

[0011] All publications, patents, and patent applications mentioned in this specification are herein incorporated by reference to the same extent as if each individual publication, patent, or patent application was specifically and individually indicated to be incorporated by reference.

BRIEF DESCRIPTION OF THE DRAWINGS

[0012] The novel features of the disclosure are set forth with particularity in the appended claims. A better understanding of the features and advantages of the present disclosure will be obtained by reference to the following detailed description that sets forth illustrative embodiments, in which the principles of the disclosure are utilized, and the accompanying drawings of which:

[0013] FIG. 1: shows a model for RNA based, frame-shift peptide production in tumor cells—normal cells. Errors in DNA replication are very rare and repaired. Transcription error rates are higher but also rare as are mis-splicing during intron excision. Additionally, the FS transcript with a premature termination may be degraded by Nonsense Mediated Decay (NMD). Aberrant proteins, including those with frameshifts are largely eliminated by the protein quality control system, Ubiquitin/Proteasome System (UPS). The net result is that very few frameshift peptides are presented on MHC I/II or escape the cell to be presented to the immune system. Cancer Cell: All levels of information transfer become more error prone. More errors are made in DNA replication, but only when cells divide. Most DNA mutations are point mutations and encode low or non-immunogenic epitopes. Global transcription is increased and is generally less accurate and even more so through MSs producing INDELS. Most transcribed genes with MSs in the coding region will have more FS transcripts. RNA splicing is also far less accurate, creating more FS transcripts from each out-of-frame splicing between exons from the same gene and different genes. The substantial increase of the FS transcripts from INDELS of MS and mis-splicing overwhelms the RNA quality control systems, such as NMD. Consequently, more truncated proteins with the FS peptide will be translated. These unfolded truncated proteins, combined with aberrant proteins from other mutations, overwhelms the protein quality control system, leading to more frameshift peptides being presented on MHC I/II and mis-secreted or released from the cancer cell which the immune system can respond to.

[0014] FIG. 2A: shows end-point RT-PCR analysis of the mSMC1A-1⁴ in mouse tumor cell lines and human hSMC1A-1⁴.

[0015] FIG. 2B: shows end-point RT-PCR analysis and RT-qPCR of the human hSMC1A-1⁴ expression in human primary breast tumor tissues and normal mammary tissues. All values are normalized relative to the expression levels in sample 1259 (set as 1). Data are mean 2- $\Delta\Delta C$ of triplicates with SD.

[0016] FIG. 2C: shows an analysis of the human EST database for FS variants by exon skipping and trans-splicing.

[0017] FIG. 2D: shows an analysis of the frequency of the expression of the 35 trans-splicing variants in 50 human breast cancer cell lines and 54 primary human breast tumors.

[0018] FIG. 2E: is an example of a sequence trace of the MS region in SEC62 dog and human genes in paired DNA/cDNA samples.

[0019] FIG. 2F: shows an ex vivo analysis of the MS INDEL in transcription and translation of the MS INDEL variants. eGFP was fused to the 3rd reading frame after 11A MS of SEC62 or after 11 non-MS nucleotides. The eGFP directly fused to 12A MS was the positive control. The three different plasmids were transfected individually into 293T cells and GFP fluorescence was measured 24 hrs after transfection.

[0020] FIG. 2G: shows a FACS analysis of the GFP positive cells.

[0021] FIG. 2H: is a summary of sequencing results of microsatellite candidates in human (4 breast cancer cell lines) and dog (primary dog tumor tissues)

[0022] FIGS. 3A-3I: show detection of antibody response against FS in cancer patients.

[0023] FIG. 3A: shows a design of human FS array with microsatellite FS peptides from all coding MS regions and predicted mis-splicing FS peptides from every exon of human genes.

[0024] FIG. 3B: shows common reactivity and cancer-type reactivity against FS peptides were represented by ~7000 selected FS peptides. LC: lung cancer; BC: breast cancer; GBM: glioblastoma; GC: gastric cancer; and PC: pancreatic cancer (n=17/each cancer type) and a set of non-cancer samples (n=64), as control.

[0025] FIG. 3C: shows p-value and fold change volcano plot analysis of 5 cancer's IgG reactivity on the 400K FS array compared to normal. The horizontal line represents the significant p-value cut-off= $\frac{1}{\sqrt{92328}}$ (the number of the array peptides).

[0026] FIG. 3D: shows a positive rate of all 400K FS peptides in each cancer type, overall cancer and normal group (calculated by counting samples with higher reactivity than $\text{AVG}(\text{Normal})+6*\text{SD}(\text{Normal})$), error bar represents $\text{Mean}\pm\text{SEM}$.

[0027] FIG. 3E: shows a distribution of personal anti-FS response and shared anti-FS response in all 5 cancer types.

[0028] FIG. 3F: shows the top 20 FS peptides for each GBM sample were selected for personal vaccines.

[0029] FIG. 3G: shows components of cancer-type specific FS vaccines, top 100 FS peptides for each cancer type were selected with highest positive rate in corresponding cancer type. Shading in normal represents negative sample; other shading is indicative of a positive sample.

[0030] FIG. 3H: shows components of a general FS vaccine, top 100 FS peptides were selected with highest positive rate in cancer group. Shading in normal represents negative sample; other shading is indicative of a positive sample.

[0031] FIG. 3I: shows a heat map of the positive rate distribution of the FS peptides in Stage I and late stages pancreatic cancer.

[0032] FIGS. 4A-4F: show protection of FS antigens as cancer vaccine candidates in different mouse tumor models.

[0033] FIG. 4A: shows tumor growth curve of mSMC1A-1⁴ immunization in the B16F10-C57BL6 tumor model compared to the control antigen, non-protective Cowpox viral antigen (CPV 172 (3I)) immunization. Mice (n=10 per group) were genetically immunized at 8 weeks of age and challenged with 1×10^5 B16-F10 cells 4 weeks later.

[0034] FIG. 4B: shows tumor growth curve after mSMC1A-1⁴ immunization in the 4T1-BALB/c tumor model. Mice (n=10 per group) were prophylactically immunized and challenged 2.5 weeks after the last immunization by 5×10^3 4T1 cells. The CD8 and CD4 T cell depletion started 2 weeks after the last immunization. The control groups were genetically immunized with empty vectors and boosted with the KLH protein.

[0035] FIG. 4C: shows tumor growth curve after FS neo-antigen immunization in the 4T1-BALB/c tumor model. Mice (n=4 per group) were genetic immunized with SLAIN2 FS, ZDHHC17 FS and mock control three times in two week intervals and challenged 2 weeks after the last immunization by subcutaneous injection of 2×10^3 4T1 cells.

[0036] FIG. 4D: shows three MS FS antigens were selected based on the best predicted H2D binding epitopes for BALB/C mice. The tumor growth curve is after three MS FS antigen immunizations in the 4T1-BALB/c tumor model. Mice (n=10 per group) were prophylactically immunized

with the different FS antigens or control antigen and challenged 2 weeks later with 5×10^3 4T1 cells.

[0037] FIG. 4E: shows ELISPOT analysis of the three MS FS neo-antigens immunizations. 3 mice were genetically immunized with a pool of the three MS FS neo-antigens and challenged with 5×10^3 4T1 cells. Splenocytes were collected 19 days after tumor challenge and a pool of three splenocytes were used in the assay. Error bars represent SD of triplicates.

[0038] FIG. 4F: shows three FS antigens were selected and immunized individually or pooled in the BALB-NeuT mouse breast tumor model. A tumor free curve is presented of BALB-NeuT mice immunized with individual FS neo-antigens (SMC1A-1⁴, n=32; RBM FS, n=22; and SLAIN2 FS, n=14) (total n=68), pool of these three FS neo-antigens (n=37) and control group (total n=44), including untreated (n=14) and immunized with control antigens (n=30). Control vs individual or 3 FS pool, $p \leq 0.0001$; individual vs 3FS pool, $p = 0.005$. Error bars in all mouse growth curves represent SEM, *, $p < 0.05$ and **, $p < 0.005$ by two tailed t-test. Statistical analysis of the tumor free curve was with Mantal-Cox test.

[0039] FIGS. 5A-5D: are a schematic of FS mis-splicing.

[0040] FIG. 5A: is a schematic of exon mis-splicing of mSMC1A. The asterisk indicates the stop codon that is generated by a shift in reading frame upon joining exon 1 with exon 4.

[0041] FIG. 5B: is a schematic of exon mis-splicing of ZDHHC17. The asterisk indicates the stop codon that is generated by a shift in reading frame upon joining exon 15 with exon 17.

[0042] FIG. 5C: is a schematic of exon mis-splicing of SLAIN2 by splicing exon 6 with exon 8.

[0043] FIG. 5D: is a schematic of exon mis-splicing of RBM by splicing RBM14 exon 1 with RBM4 exon 2.

[0044] FIG. 5E: shows an RT-PCR of human SMC1A (hSMC1A), human SMC1A FS (hSMC1A-1⁴) and β -actin in 33 human breast tumor cell lines.

[0045] FIG. 5F: shows an RT-PCR analysis of the ZDHHC17_FS and SLAIN2_FS in B16F10 and 4T1 tumor cell cDNA.

[0046] FIG. 5G: shows an RT-PCR analysis of SLAIN2_FS and ZDHHC17 FS in different human tumor cells.

[0047] FIG. 5H: shows an RT-PCR analysis of SMC1A_FS, SLAIN_FS and ZDHHC17_FS variants in B16 melanoma cells and normal tissues from C57BL6 mouse.

[0048] FIGS. 6A-6H: show components of frameshift peptide array and characteristics.

[0049] FIG. 6A: is an example of INDEL Frameshift peptides from dog gene SEC62

[0050] FIG. 6B: shows examples of mis-splicing Frame-shift peptides from 2nd frame and 3rd frame of human exons.

[0051] FIG. 6C: shows a distribution of MS FS peptides in human FS array with insertion or deletion events.

[0052] FIG. 6D: shows a distribution of MS FS peptide lengths in human FS array with corresponding FS antigen length.

[0053] FIG. 6E: shows a distribution of MS Type in human FS array.

[0054] FIG. 6F: shows a distribution of MS repeat length in human FS array.

[0055] FIG. 6G: shows a distribution of Mis-splicing FS antigen length in human FS array.

[0056] FIG. 6H: shows a distribution of Exon numbers of FS antigens in human FS array.

[0057] FIGS. 7A-7G: show a personal frameshift response in 4 cancer types.

[0058] FIG. 7A: shows a hierarchical clustering of all 400K FS peptides in 17 GBM samples.

[0059] FIG. 7B: shows a personal anti-FS response in 17 GBM cancer patients.

[0060] FIG. 7C: shows a personal anti-FS response in 17 gastric cancer patients.

[0061] FIG. 7D: shows a personal anti-FS response in 17 breast cancer patients.

[0062] FIG. 7E: shows a personal anti-FS response in 17 pancreatic cancer patients.

[0063] FIG. 7F: shows a personal anti-FS response in 17 lung cancer patients.

[0064] FIG. 7G: shows a correlation matrix of anti-FS response in all cancer samples from 5 cancer types.

[0065] FIG. 8: shows tumor free curve of each FS neo-antigen immunized group in BALB-NeuN mice. BALB-NeuT mice were immunized with individual FS antigens (mSMC1A-1⁴, n=32; RBM, n=22; and SLAIN2, n=14) (total n=68), pool of these three FS antigens (n=37) and control group (total n=44), including untreated (n=14) and immunized with control antigens (n=30). All of the mice were immunized with the same regime as in FIG. 4D. Detail immunization regime see the method. Control vs. each of individual FS group, $p < 0.05$; 3FS pool vs. mSMC1A-1⁴ or RBM FS, $p < 0.005$; 3FS pool vs. SLAIN2, $p = 0.43$. All statistical analysis were with Mantal-Cox test. Detail immunization regimes were described in the methods.

[0066] FIG. 9: shows pooled FS vaccines are more protective than personal vaccines. Mouse 4T1 model was used to test pooled FS peptides as vaccines relative to personal vaccines used in the field. Pooled vaccines were made to 4T1 based on screening 30 mice injected with 4T1 and assayed on the FS arrays (BC-FAST). Personal vaccines also made to each mouse injected with 4T1 (BC-PCV) or a pancreatic tumor line (PC-FAST). As shown the BC-FAST vaccine was more protective than the personal vaccines.

[0067] FIG. 10: shows pooled FSP vaccines can be constructed for any tumor in humans. The blood of 15 to 17 individuals with one of the 5 designated cancers, including breast, stomach, glioblastoma (GBM), lung, and pancreatic, were screened on FSP arrays to determine reactivity. High reactivity relative to non-cancer individuals is designated by a bars. The 100 most recurrently reactive peptides for each cancer are shown.

DETAILED DESCRIPTION

[0068] Provided herein are methods and compositions for preventing, treating, and diagnosing cancer comprising the use of neoantigens. Neoantigens herein comprise peptides encoded by nucleic acids having frameshift mutations, such as insertions or deletions, causing a frameshift in the mRNA and a long stretch of mutant amino acids that are, in some cases, recognized as a non-self peptide by the immune system.

[0069] The success of checkpoint inhibitors in cancer therapy is largely attributed to activating the patient's immune response to their tumor's neoantigens arising from DNA mutations. This realization has motivated the interest in personal cancer vaccines based on sequencing the patient's tumor DNA to discover neoantigens. Embodiments

provided herein relate to an additional, unrecognized source of tumor neoantigens. In some embodiments, errors in transcription of microsatellites (MS) and mis-splicing of exons create highly immunogenic frameshift (FS) neoantigens in tumors. The sequence of these FS neoantigens are predictable, allowing creation of a peptide array representing all possible neoantigen FS peptides. This array can be used to detect the antibody response in a patient to the FS peptides. A survey of 5 types of cancers reveals peptides that are personally reactive for each patient. This source of neoantigens and the method to discover them may be useful in developing cancer vaccines.

[0070] Personal cancer vaccines are promising as a new therapeutic treatment. These vaccines are currently based on mutations in tumor DNA. In some embodiments, variants in RNA production create frameshift neoantigens that may be another source of neoantigens for personal vaccines. Because there are only ~220K of these antigens a simple peptide array can be used for their detection.

[0071] Checkpoint inhibitor immunotherapeutics are revolutionizing cancer therapy. However, even in the most responsive cancers a substantial portion (50%-80%) of the patients have poor to no positive response (1-5). A surprising finding in the analysis of these patients was that one of the best correlates of response has been the total number of neoantigens in the tumor (6-8). This is also the case for patients with high microsatellite instability (MSI) where the production of FS neoantigens drives the effective anti-tumor immune responses (9-11). The realization of the immunological importance of these DNA mutations has spawned the effort to develop personal vaccines (12). As promising as early studies are of these vaccines, a major problem is that the majority of tumors will not have enough neoantigen-generating mutations to sustain development of a personal vaccine (13-15). For example, melanoma tumors have a high mutational level with an average of 200 neoepitope mutations. This provides a large number to algorithmically screen for optimal antigenic presentation. In recent reports of two Phase I clinical trials of personal melanoma vaccines, starting with 90-2,000 personal neoantigens, 10 or 20 were identified for the vaccine (16, 17). However, in glioblastoma multiforme (GBM) only 3.5% patients had a high tumor mutation load, and further analysis showed that only a very small subset of GBM patients would potentially benefit from checkpoint blockade treatment (18). This is also consistent with a lack of response in GBM patients to checkpoint inhibitors (19). Massive genomic sequencing results indicated that GBM, ovarian cancer, breast adenocarcinoma and many other cancer types had very low number non-synonymous mutations, which will make these cancers difficult targets for personalized cancer vaccines (14, 20).

[0072] To solve this problem, methods and compositions are provided herein related to an alternative source of neoantigens which expand the scope of the application and efficacy of the neoantigen based cancer vaccines. In the process of becoming a tumor, not only does the DNA mutation rate increase with faster cell divisions, but also there is a disruption of basic cellular functions, including RNA transcription, splicing and the quality control system on peptides (21). The disrupted RNA processes increase the FS transcripts generated by RNA splicing errors and the insertions and deletions (INDELs) of MSs (22). Both of these processes, combined with the disrupted quality control system in tumor cells, can lead to the production of FS

peptides and exposure of the FS epitopes to the immune system. Embodiments provided herein relate to FS variants produced by errors in RNA processing as a source of cancer neoantigens and a simple system to detect them.

[0073] Disclosed herein are models for how errors in transcription microsatellites and mis-splicing of exons could create frameshift neoantigens. Embodiments provided herein include examples in the RNA of tumors for both mis-splicing and of mis-transcription of an INDEL where the errors are present at the RNA but not DNA level. Also provided are methods for analysis of the NCBI EST library to reveal other examples of FS variants. Using an array comprising all predicted FS peptides with specific qualifications, human sera from patients with 5 different cancers have higher antibody reactivity than people without cancer. Three different patterns of high antibody reactivity can be determined—pan-cancer, cancer-type focused and personal. Several examples are presented demonstrating that the FS variants offer at least partial protection in mouse models and that the protection is additive for each FS antigen.

[0074] The methods and compositions provided herein indicates that variants produced at the RNA level in tumor cells may be a good source of neoantigens for vaccines for several reasons. First, these FS variants produce neoantigens which are more likely to be immunogenic than neo-epitopes encoded by single nucleotide mutations (7). Second, FS from MS INDELs would be particularly attractive sources. There are a limited number of possible variants (8600 of homopolymers ≥ 7 bp), which encode about 7,000 FS peptides longer than 10 aa, thus reducing the search space for neoantigens. Third, because of the predictable number of candidates it should be possible to use a peptide array to screen for immune reactive neoantigens. This approach would be much simpler than sequencing tumor DNA obtained from a biopsy. Fourth, because any expressed gene has the potential to produce neoantigens, it may not be necessary to limit the vaccine to oncological driver genes. Finally, it should be difficult for the tumor cells to evolve away from the vaccine since these FSs are variants, not heritable mutations. Particularly if the FS antigen was produced in RNA from an essential gene, the tumor cells would need to restrict MHC presentation (17, 52) or create an immune suppressive environment (53) to escape an immune response.

[0075] Elements of the model are supported by other published work. The immunological reactivity of FS neoantigens is the presumed basis of the effectiveness of PD-1 in most MSI-H cancers (54, 55). It also explains the responsiveness of renal cancer to CPI therapy—these cancers have low point mutation levels but high FS mutations (3, 7, 20). It has also been shown that cancer cells have much higher mis-splicing rates than normal cells (39, 41, 56). Recently, Andre et al. (56) showed informatically that cancer cells could make neofusion sites by mis-splicing. However, their analysis did not include fusions that created FS peptides. Also, Alicia et.al. (57) analyzed intron retention in tumor databases. This process can also create FS neoepitopes, though apparently much less frequently than mis-splicing of exons. The only aspects of the model not independently confirmed are 1) that the FS peptides potentially generated at the RNA level are made in tumors, 2) that the RNA-generated FSPs can generate immune responses, and 3) that

these peptides can be protective against tumors. However, the methods provided herein support these 3 remaining aspects of the model.

[0076] An important aspect of this source of neoantigens is that it may allow extending the personal vaccines to more patients and tumor types. Many tumors have relatively low numbers of DNA mutations and probably could not support constructing a vaccine (58). Estimates from published mutational surveys of various tumors (59) indicate that only 40% of patients could be treated with personal vaccines. However, the methods and compositions provided herein predicts that the RNA FS variants would be produced in any cancer type, even if the DNA mutation level is low. This is substantiated, for example, in GBM (FIGS. 3B and G), which is a low mutation rate cancer (14, 20), but elicits similar overall immune response to FS peptides as other high mutation cancers.

[0077] The model also predicts that there may be recurrent FSs produced in different tumors. This is substantiated, for example, at the RNA level for SMC1 FS in breast cancers (FIG. 2D), and also confirmed by antibody reactivity using the FS arrays. This data shows 4641 FS peptides that were positive in 10% or more of all the samples across all five tumor types.

[0078] Sets of FS peptides were found that had enriched activity in individual tumor types. A collection of a set of these peptides could potentially be used to constitute a general, therapeutic vaccine or one focused on a particular tumor or set of tumors. Such vaccines would have an advantage over a personal vaccine of being pre-made but would have fewer antigens in common with the tumor. Conceivably, pan-cancer peptides could be used to create a prophylactic cancer vaccine, as has been proposed for cancer associated antigens (60). However, as shown in comparing late and early stage pancreatic cancer profiles, a prophylactic vaccine from FS neoantigens would be best constituted from peptides reactive at early stages of cancer. Clinical trials in dogs were recently initiated of a prophylactic vaccine that is designed to be broadly protective (data not shown).

[0079] FIG. 3F and FIGS. 7A-7G show refinement of the collection of reactive peptides to the personal level. Using GBM as an example, a set of peptides that are personal for each patient are found. In the 17 patients analyzed there were 1316-8299 personal peptides which were reactive only in that individual. Approximately 70% of all cancer-specific reactivity on the arrays was personal. A set of 20 personal FS antigens for each GBM patient is presented in FIG. 3F. The high antibody reactive indicates the high expression and/or high immunogenic of the FS antigen in the patient, with potential reactive CD4+ T cell response.

[0080] In FIGS. 3G and 3H, people without cancer have sporadic antibody reactivity to some of the peptides. This has also been noted that healthy individuals have antibody and T-cell responses to tumor associated antigens (61, 62). This could be due to random background cross-reactive IgG antibodies unrelated to cancer. It was previously shown that monoclonal antibodies are capable of binding random sequence peptides with high affinity, even though the peptides do not contain a sequence resembling the cognate site (63). Alternatively, this reactivity could be a manifestation of immune surveillance (64) eliminating potential tumor cells. Any cell that produced and presented FS antigens, whether tumor or not, could be susceptible to this elimination, effectively a "bad cell" response.

[0081] The vaccines tested did not produce complete protection by themselves in the models tested. However, it should be noted that both these models are very stringent and probably do not completely replicate natural tumors. One reason for this may be due to low level production of each FS neoantigen, consistent with the additive effects of the FS peptides in vaccines (FIG. 4F). Only occasional identification by mass spectrometry of FS peptide from MHC I elution of tumor cells is achieved, consistent with other reports (57). The quantitative analysis of transcription errors reported by Gout et al recently is consistent with this proposition (22, 32). However, this could also be due to the tumor cells deleting the antigen and evolving resistance, or that the T cell epitopes have low affinity, as is predicted for the mSMC1A FS peptide in the BALB/c mouse strain. Neoantigens produced by mutations in the DNA will produce 50-100% variant RNA and therefore potentially more presented antigen than would be expected for RNA based neoantigens. Pre-existing T-cell responses were not detected in mouse tumor models, even though vaccination with the FS is at least partially protective. The level of RNA-error-based FS production in the tumor is generally not enough to elicit a T-cell response, but is enough to elicit T-cells elicited by a vaccine to kill the tumor cell. This is consistent with analysis of three clinical trials of personal vaccines (16, 17, 65), where most of the antigens which produced a T-cell response had no pre-existing T-cell response detectable. Recently, complete protection in the 4T1 model using pools of 10 selected FS antigens with both personal and cancer-type specific vaccines was shown (MTB, LS and SAJ, data not shown).

[0082] The arrays detect antibody responses to FS peptides. B-cell responses are not commonly considered important for an anti-tumor effect. It was recently shown that antibodies generated by dogs with cancer could be detected on an 800 FS peptide array. Peptides reactive on the dog array, whose homolog was also present in a mouse tumor line, were protective in the mouse models, while non-reactive peptides on the array did not confer protection. This study establishes that antibody response is an indicator of vaccine effectiveness. The level of antibody response correlated with protection in the mouse models. One explanation for this observation is that the IgG antibody response depends on CD4+ T-cell help. FS with good CD4+ T cell epitopes may also elicit tumor cell killing. It has been noted that CD4+ T cell responses to vaccines correlate with protection (66, 67).

[0083] In summary, the methods and compositions provided herein relate to another class of neoantigens that are useful in developing different types of cancer vaccines. Also provided herein are array formats for directly detecting immune responses to these tumor antigens. Dog and human clinical trials for use of the tumor antigens identified by the methods disclosed herein are underway.

[0084] As used herein, the term "detect," "detection," "detectable," or "detecting" is understood both on a quantitative and a qualitative level, as well as a combination thereof. It thus includes quantitative, semi-quantitative, and qualitative measurements of measuring a cancer in a subject, using the methods and compositions as disclosed herein.

[0085] As used herein, the expression "a subject in need thereof" means a human or non-human mammal that exhibits one or more symptoms or indications of cancer, and/or who has been diagnosed with cancer, including a solid tumor

and who needs treatment for the same. In many embodiments, the term “subject” may be interchangeably used with the term “patient”. For example, a human subject may be diagnosed with a primary or a metastatic tumor and/or with one or more symptoms or indications including, but not limited to, unexplained weight loss, general weakness, persistent fatigue, loss of appetite, fever, night sweats, bone pain, shortness of breath, swollen abdomen, chest pain/pressure, enlargement of spleen, and elevation in the level of a cancer-related biomarker.

[0086] The term “malignancy” refers to a non-benign tumor or a cancer. As used herein, the term “cancer” includes a malignancy characterized by deregulated or uncontrolled cell growth. Exemplary cancers include: carcinomas, sarcomas, leukemias, and lymphomas. Cancer includes primary malignant tumors (e.g., those whose cells have not migrated to sites in the subject’s body other than the site of the original tumor) and secondary malignant tumors (e.g., those arising from metastasis, the migration of tumor cells to secondary sites that are different from the site of the original tumor). A cancer may include, for example, gastric, myeloid, colon, nasopharyngeal, esophageal, and prostate tumors, glioma, neuroblastoma, breast cancer, lung cancer, ovarian cancer, colorectal cancer, thyroid cancer, leukemia (e.g., Adult T-cell leukemia, Acute monocytic leukemia, Acute myeloid leukemia, Acute promyelocytic leukemia, myelogenous leukemia, lymphocytic leukemia, acute myelogenous leukemia (AML), chronic myeloid leukemia (CML), acute lymphoblastic leukemia (ALL), T-lineage acute lymphoblastic leukemia or T-ALL chronic lymphocytic leukemia (CLL), myelodysplastic syndrome (MDS), hairy cell leukemia), lymphoma (Hodgkin’s lymphoma (HL), non-Hodgkin’s lymphoma (NHL)), multiple myeloma, bladder, renal, gastric (e.g., gastrointestinal stromal tumors (GIST)), liver, melanoma and pancreatic cancer, sarcoma, Adenocarcinoma, Astrocytoma, Bone Cancer, Brain Tumor, Burkitt’s lymphoma, Carcinoma, Cervical Cancer, Chronic Lymphocytic Leukemia, Chronic myelogenous leukemia, Endometrial cancer, Glioblastoma multiforme, Glioma, Hepatocellular carcinoma, Hodgkin’s lymphoma, Inflammatory breast cancer, Kidney Cancer, Leukemia, Lymphoma, Malignant Mesothelioma, Medulloblastoma, Melanoma, Multiple myeloma, Neuroblastoma, Non-Hodgkin Lymphoma, Non-Small Cell Lung Cancer, Pancreatic Cancer, Pituitary tumor, Retinoblastoma, Skin Cancer, Small Cell Lung Cancer, Squamous cell carcinoma, Stomach cancer, T-cell leukemia, T-cell lymphoma, and Wilms’ tumor.

[0087] As used herein the term “frameshift mutation” is a mutation causing a change in the frame of the protein. Thus, a frameshift variant peptide is a peptide in which a frame has changed due to a frameshift mutation. In some embodiments provided herein, a frameshift includes two or more pooled frameshifts. As used herein, the term “pooled” refers to a plurality of frameshift samples that have been combined to create a new composition.

[0088] As used herein, the term “microsatellite instability,” also known as “MSI” refers to the changes in microsatellite repeats in tumor cells or genetic hypermutability caused due to deficient DNA mismatch repair. Microsatellites, also known as simple sequence repeats, are repeated sequences of DNA comprising repeating units 1-6 base pairs in length. Although the length of microsatellites is highly variable from person to person and contributes to the DNA fingerprint, each individual has microsatellites of a set

length. MSI results from the inability of the mismatch repair (MMR) proteins to fix a DNA replication error. MSI comprises DNA polymorphisms, wherein the replication errors vary in length instead of sequence. MSI comprises frameshift mutations, either through insertions or deletions, or hypermethylation, leading to gene silencing. It is known in the art that microsatellite instability may result in colon cancer, gastric cancer, endometrium cancer, ovarian cancer, hepatobiliary tract cancer, urinary tract cancer, brain cancer, and skin cancers.

EXAMPLES

Example 1: Materials and Methods for Isolating Neoantigens

[0089] Cell Lines and Tissues

[0090] HEK293, B16-F10 and 4T1 cell lines were purchased from ATCC in 2006. Upon receipt, cells were cultured for three passages in RPMI medium (ATCC) with 10% FBS, 100 U/mL penicillin, and 100 mg/mL streptomycin and stored in aliquots under liquid nitrogen. Cells were maintained at 37° C. under humidified 5% CO₂, 95% air. Cells between 2 and 20 passages were used. Cell lines were not re-authenticated. Other cells lines are listed in Table 2 and were cultured in ATCC-recommended media.

[0091] Mice and Mouse Tumor Models

[0092] BALB/c and C57BL/6 mice were from Charles River Laboratories or Jackson Laboratories. For the tumor challenge, 5×10³ 4T1 cells were injected in the mammary pad at the right flank of the mice, or 1×10⁵ B16F10 cells were injected subcutaneously in the right flank of the mice. Tumor volumes were measured and calculated by (Length²× Width/2) daily after the size was larger than 1 mm³. Breeding pairs of BALB-neuT and FVB-neuN (FVB/N-Tg (MMTVneu) 202Mul) mice were obtained from Joseph Lustgarten, Mayo Clinic Arizona. Mice were monitored weekly for the tumor incidence after tumor size reached 1 mm³. All experiments were performed in accordance with protocols approved by the Institutional Animal Care and Use Committee of Arizona State University. Statistical significance of differences was analyzed by a Student t-test.

[0093] EST Analysis

[0094] To identify potential putative chimeric transcripts, that when translated would result in a frame-shifted neopeptide, two publicly available datasets and applied an algorithm that was used to identify chimeric transcripts were used. Specifically, the sequences found within the Expressed Sequence Tag (EST) library and the Human RefSeq database (23) from the National Center for Biotechnology Information (NCBI) were used. Using the stand-alone BLAST program, all EST sequences were aligned to RefSeq. ESTs that aligned with 50-85 base pairs and had 95% homology to RefSeqs that have been previously annotated by National Center Institute (NCI) were selected. The alignment data was filtered by eliminating the EST sequences that did not align to multiple RefSeqs or were aligned in the 3'-5' orientation. Lastly, the sequences that aligned with non-coding sequence regions were eliminated. The remaining EST sequences were then used to identify the chimeric transcripts. Only the ESTs that aligned to two or more distinct RefSeq in consecutive positions were considered to be potential candidates. To be defined as a coding chimeric transcript, the EST sequences had to be at least 100 bp long with sequence similarity greater than or equal to 95% to the

RefSeq. Also, the junction points between the two genes had to occur within the coding sequence of the upstream gene and orientation of the upstream gene alignment had to be in the positive (5'-3') orientation. To eliminate false calls, all potential chimeric EST sequences had to be either present in more than one cDNA library or supported by three or more independent EST sequences. In addition, chimeric transcripts were classified based on the relative position of two genes. Classification of types of chimeric transcript was based on relative position of two fusion genes on the chromosome. Specifically, genes found on different chromosomes resulted in inter-chromosomal fusion while genes found in same chromosome were intra-chromosomal or read-through chimeric transcripts. Read-through chimeric transcripts resulted from two neighboring genes on same strand, otherwise intra-chromosomal.

[0095] PCR Screen for EST FS Candidates

[0096] The 50 Human Breast cancer cell lines were obtained from the American Type Culture Collection (ATCC) and were grown according to recommendations. Human breast cancer tissue specimens were acquired from Mayo Clinic, and were informed consent and approval by the Mayo Clinic Institutional Review Board. All specimens were coded and anonymized. All experiments were performed in accordance with the approval protocol. Total RNA was extracted from breast cancer cell lines and primary breast tissues using the TRIzol LS reagent (Life Technologies, Carlsbad, Calif.) following the manufacturers protocol. RNA integrity was determined by gel electrophoresis and concentration was determined by measuring absorbance at 260/280 on the Nano-drop (NanoDrop Products, Wilmington, Del.). cDNA was prepared by using the SuperScript™ III First-Strand Synthesis SuperMix (Life Technologies, Carlsbad, Calif.) that includes random hexamers and oligo dT's following the manufacturer's recommended protocol. cDNA integrity and quality were assessed by performing a β -actin control PCR. End Point PCR primers for each chimeric transcript were designed using Primer3 (24) so that the forward and reverse primers both bind 80 bp to 280 bp upstream/downstream from the junction point. End-point PCR reactions using approximately 25 ng of cDNA, reagents from (Life Technologies, Carlsbad, Calif.) and 35 cycles were performed using Mastercycler ep gradient S (Eppendorf, Hamburg, Germany). PCR products were analyzed on 1.5% agarose gels. PCR products were purified, and sequence confirmed by Applied Biosystems 3730 (Life Technologies, Carlsbad, Calif.) sequencing.

[0097] End-Point RT-PCR

[0098] cDNAs from human primary breast tumors and normal mammary glands were from BioChain (Newark, Calif.). Total RNA from other sources was extracted with TRIzol (Life Technologies, Carlsbad, Calif.). cDNA was synthesized from total RNA using the SuperScript III First-Strand Synthesis SuperMix (Life Technologies). The primer sequences used for end-point RT-PCR were synthesized by Life Technologies or Sigma. End-point RT-PCR reactions (25 μ L) used the GoTaq PCR kit (Promega, Madison, Wis.) and the following conditions: 95° C. for 2 min; 35 cycles of 95° C. for 30 secs, 60° C. for 30 sec (annealing), and 72° C. for 10 to 30 sec (extension); and 72° C. for 5 min. Exceptions were that mouse SMC1A primers used an annealing temperature of 55° C., and β -actin primers were done with 25 cycles and 30 sec of extension time. Sequence verification was performed on RT-PCR products in initial reactions

and later during intermittent reactions. The following primers (from 5' to 3') for the PCR were used: SEC62 DNA human forward: TGCCATACCTGTTTTTCCC (SEQ ID NO: 1); SEC62 human DNA reverse: AGT-TATCTCAGGTAGGTGTTGC (SEQ ID NO: 2); SEC62 DNA dog forward: AAGGGAGTCTGTGGTTGA (SEQ ID NO: 3); SEC62 DNA dog reverse: CAAAGAGG-GAAGAGAGTGG (SEQ ID NO: 4); SEC62 cDNA human forward: AAAGGAAAAGCTGAAAGTGGAA (SEQ ID NO: 5); SEC62 human cDNA reverse: GCAACAGCAAGGAGAAGAATAC (SEQ ID NO: 6); SEC62 cDNA dog forward: AAGGGAGTCTGTGGTTGA (SEQ ID NO: 7); SEC62 cDNA dog reverse: CAAAGAGG-GAAGAGAGTGG (SEQ ID NO: 8); SMC1A mouse forward: CTGTCATGGGTTTCTG (SEQ ID NO: 9); SMC1A mouse reverse: GAGCTGCTCTCTCTTG (SEQ ID NO: 10); SMC1A human forward: CCTGAACTGAT-TGAGATTGAG (SEQ ID NO: 11); SMC1A human reverse: TCTTCAGCCTTCACCATTC (SEQ ID NO: 12); β -actin mouse forward: CCAACCGTGAAGATGACC (SEQ ID NO: 13); β -actin mouse reverse: TGCCAATAGT-GATGACCTGG (SEQ ID NO: 14); β -actin human forward: CCAACCGGAGAAGATGACC (SEQ ID NO: 15); β -actin human reverse: TGCCAATGGTATGACCTGG (SEQ ID NO: 16); Rat Her-2 forward: ATCGGTGATGTCGGC-GATAT (SEQ ID NO: 17); Rat Her-2 reverse: GTAACACAGGCAGATGTAGGA (SEQ ID NO: 18).

[0099] Sec62 Transfection and Flow Analysis

[0100] HEK293 cell line were purchased from ATCC and cultured with standard protocols. Lipofectamine 2000 Transfection Reagent (Thermo Fisher Scientific, MA) was used to transfect plasmids into cell lines for overnight. Cells were then prepared in FACS buffer and quantified with flow cytometry. The three open reading frames (ORFs) were assembled by PCR and inserted into pCMV1 vector at EcoR I MCS site. Detailed sequences of three ORFs were included in Table 6.

[0101] Gene Expression

[0102] Gene expression was measured with the TaqMan Gene Expression Assay (Life Technologies) according to the manufacturer's directions. The hSMC1A-specific labeled probe was 5'-CAATGGCTCTGGGTGCTGTGGAATC-3' (SEQ ID NO: 19). The unlabeled forward and reverse primers were 5'-GGGTCGACAGATTATCGGACC-3' (SEQ ID NO: 20) and 5'-GTCACTACTCCTGCGCCAGCT-3' (SEQ ID NO: 21), respectively. Results were normalized by human GAPDH.

Example 2: Human Frameshift Peptide Array Synthesis and Analysis

[0103] Microsatellite Frameshift antigens: human mRNA sequences were acquired from NCBI CCDS databases (25). Microsatellite regions (homopolymers of 7 runs or more) were mapped to human coding genes, 2nd and 3rd reading frame peptide sequences after MS regions were predicted and stored in Microsatellite FS database, MS FS peptides 10 aa or longer were included in the human FS peptide array.

[0104] Mis-splicing Frameshift antigens: human mRNA sequences and exon coordinates were acquired from NCBI Refseq database (23). 2nd and 3rd reading frame FS peptide sequences were predicted from the start of every exon. Then all the FS peptides were aligned against the human proteome, FS peptides with higher than 98% homology to wild type proteome were removed. FS peptides 10 aa or longer

were then included in the human FS peptide array. Table 7 depicts exemplary variant FS peptides.

[0105] A total number of 64 non-cancer control samples and 13 pancreatic stage 1 cancer samples, 85 late stage cancer samples from 5 cancer types were tested on the FS array, detailed information was summarized in Table 5. All samples were acquired from collaborators and were informed consent upon collection through the institute's own IRB. All samples were anonymized before receipt at Arizona State University (ASU) via Institutional Review Board (IRB) protocol No. STUDY00003722, 'Receipt of Deidentified Human Serum for Immunosignature Analysis' and protocol No. 0912004625, 'Profiling Biological Sera for Unique Antibody Signatures'. All experiments were performed in accordance with the approval protocol.

[0106] 400K Frameshift Peptide Array Assay

[0107] Serum was diluted 1:100 in binding buffer (0.01M Tris-HCl, pH 7.4, 1% alkali-soluble casein, 0.05% Tween-20) and 150 μ l diluted samples were loaded into each compartment of the 12-plex array and incubated overnight at room temperature or 4° C. After sample binding, the arrays were washed 3 \times in wash buffer (1 \times TBS, 0.05% Tween-20), 10 min per wash. Primary sample binding was detected via Alexa Fluor® 647-conjugated goat anti-human IgG secondary antibody (Jackson ImmunoResearch #109-605-098). The secondary antibody was diluted 1:10,000 (final concentration 0.15 ng/ μ l) in secondary binding buffer (1 \times TBS, 1% alkali-soluble casein, 0.05% Tween-20). Arrays were incubated with secondary antibody for 3 h at room temperature, washed 3 \times in wash buffer (10 min per wash), 30 secs in reagent-grade water, and then dried by centrifuging at 690 RPM for 5 mins. All washes and centrifugations were done on a Little Dipper 650C Microarray Processor (SciGene) with preset programs. Fluorescent signal of the secondary antibody was detected by scanning at 635 nm at 2 μ m resolution and 15% gain, using an MS200 microarray scanner (Roche NimbleGen).

Example 3: Genetic Immunization

[0108] Plasmids for Genetic Immunization

[0109] The DNA fragments encoding FS peptides were cloned as a C-terminal fusion into the genetic immunization vectors pCMVi-UB (26) and pCMVi-LSrCOMPTT (27, 28) with the Bgl II and Hind III and mixed with 1:1 ratio as the vaccine antigen. Three adjuvants were encoded by genetic immunization vectors. The pCMVi-mGM-CSF vector expresses the adjuvant mouse granulocyte/macrophage colony-stimulating factor (mGM-CSF) under control of the human cytomegalovirus (CMV) promoter (27). LTAB indicates immunization with 1:5 ratio by weight of two plasmids, pCMVi-LTA and pCMVi-LTB, expressing the heat-labile enterotoxins LTA and LTB from *Escherichia coli*. These plasmids express LTA and LTB as C terminal fusions to the secretion leader sequence from the human al antitrypsin gene (29). Vectors pCMVi-UB, pCMVi-LSrCOMPTT, pCMVi-LTA (also called pCMVi-LS-LTA-R192G) and pCMVi-LTB are available from the PSI: Biology-Materials Repository DNASU (dnasu.org) at Arizona State University. Additional adjuvants were the class A CpG 2216 single-stranded oligodeoxynucleotide obtained from Sigma and alum from Pierce.

[0110] Bullet Preparation for Genetic Immunization with Gene Gun

[0111] Bullets for biolistic genetic immunization used the gold micronanoplex approach and were prepared as described (30) with the following changes. Two grams of 1-micron gold was used. Prior to addition of N-hydroxysuccinimide and N-(3-dimethylaminopropyl)-N'-ethylcarbodiimide hydrochloride, the gold was resuspended in 20 mL of a 0.1 M solution of 2-(N-morpholino) ethanesulfonic acid (MES), pH 6.0. DNA-gold micronanoplexes were prepared by combining, per bullet, 57 μ L of cysteamine-gold solution with precipitated DNA (\leq 10 μ g) that had been resuspended in \leq 15 μ L of water, and then vortexing for 10 min. To the DNA-cysteamine-gold was added 6 μ L/bullet of a freshly made solution of PEI-micron gold (167 mg/mL in 0.1 M MES, pH 6, without NaCl). The pelleted micronanoplexes were washed with ethanol prior to resuspension in n-butanol (55 μ L/bullet), followed by bullet formation under nitrogen gas.

[0112] Immunization Dosage and Regime and Tumor Challenge

[0113] C57BL/B16-F10 Mouse Melanoma Model

[0114] Six week old mice (n=10 per group) received one genetic immunization with the Gene Gun in the pinna of the ear (4 shots/mouse) with 20 ng of antigen (SMC1A-1⁴ and non-protective Cowpox viral antigen CPV 172 (31)) in pCMVi vectors plus the adjuvants pCMVi-mGM-CSF (0.5 μ g) and CpG 2216 (5 μ g) for each shot. All of the mice were challenged with 1 \times 10⁵ B16-F10 cells 4 weeks after the immunization.

[0115] BALB/C-4T1 Mouse Breast Tumor Model

[0116] For the three MS FS experiments, all mice (n=10 per group) were genetically immunized in the ear by Gene Gun at 8 weeks of age (2 shots/mouse, 60 ng pooled antigens plus 0.25 μ g LTAB and 2.5 μ g CpG2216 as the adjuvant for each shot) and boosted twice (two days apart) in three weeks with 1 μ g pooled antigens plus the same adjuvants dosage. All mice were boosted again in two weeks with 50 μ g KLH conjugated MS FS peptides with 50 μ g CpG 2216 and 50 ul alum in total 100 ul PBS. The negative groups were immunized with the empty vectors and KLH protein with the same dosage. All mice were challenged with 5 \times 10³ 4T1 cells two weeks after the last immunization.

[0117] For the mSMC1A-1⁴ experiment, all mice were (n=10 per group) genetically immunized in the ear by Gene Gun at 8 weeks of age (2 shots/mouse, 1 μ g antigen plus 0.25 μ g LTAB and 2.5 μ g CpG2216 as the adjuvant for each shot), and boosted in two weeks with KLH conjugated SMC1A-1⁴ peptide plus 50 μ g Poly:IC (Sigma) in 100 ul PBS. The same regime was repeated in two weeks. The negative groups were immunized with the empty vectors and KLH protein with the same dosage. All mice were challenged with 5 \times 10³ 4T1 cells 4 weeks after the last immunization. The CD8 and CD4 T cell depletion started 2 weeks after the last immunization by i.p injection of 100 μ g antibody (anti CD8, clone 2.43; anti CD4, clone GK 1.5; BioXCell, West Lebanon, N.H.) every 3 days until the end of the experiment.

[0118] BALB-neuT Mice

[0119] Mice were genetically immunized by Gene Gun at 4-6 weeks with 100 ng of antigen(s) in pCMVi vectors, boosted twice (3-4 days apart) at 9-10 weeks with 1 μ g of the same antigen(s), and boosted once at 13-14 weeks with protein. Genetic immunizations included adjuvants LTAB (0.5 μ g) and CpG 2216 (5 μ g). Protein boosts were 50 μ g of

KLH conjugated FS peptides (SMC1A-1⁴, n=32; RBM FS, n=22; SLAIN2 FS, n=14 and pool of three FS neoantigens, n=37). The protein boost included 50 µg CpG 2216 and 50 µl alum in 100 µl PBS as the adjuvant. The negative groups (n=30) were immunized with the empty vectors and GST or KLH protein with the same adjuvants and dosage.

[0120] ELISPOT

[0121] Peptides used in the ELISPOT assays were synthesized in-house. The Mouse IFN-γ ELISPOT Set (BD Biosciences) was used according to the manufacturer's directions except that blocking was at 37° C. 10⁶ fresh mouse splenocytes were added to each well, followed by co-culturing for 48 hr with 20 µg of peptide in a volume of 200 µl RPMI medium. The plate was scanned and spots were analyzed by the AID EliSpot Reader System (Autoimmun Diagnostika GmbH, Germany).

[0122] Statistical Analysis

[0123] The statistical calculation software used was GraphPad Prism 7 (GraphPad Software, San Diego, Calif.) and JMP Pro (SAS Institute, NC). The data presentation and the statistical tests for each experiment are indicated in the legend of the corresponding figures, as well as the samples size and p-values.

Example 4: Model for the Production of
RNA-Based Frameshift Variants

[0124] Mistakes in RNA mis-splicing and transcription, particularly of INDELS of MSs in coding regions, in cancer cells may also be a source of neoantigens. FIG. 1 depicts an exemplary model of some embodiments provided herein. As information flows from DNA to RNA to protein there is a general increase in error rates (22, 32-35). These errors include mis-splicing and INDELS of MSs. Both errors will produce a background level of FS transcripts, which encode truncated proteins with a FS peptide at the C-terminus. The level of the FS peptides in normal cells is managed by the quality control mechanisms, such as nonsense mediated decay (36) and ER-associated degradation (37), such that these FS peptides are not presented to the immune system. However, the initiation event of a potentially cancerous cell will destabilize basic cellular processes including transcription, RNA splicing and the quality control system (21, 38-41). These global errors can be augmented due to chromosomal instability (42) or key, broadly effective mutations (43, 44). Consequently, the number of FS peptides produced, combining with other aberrant proteins, exceeds the disrupted quality control system, allowing FS peptides to be presented in MHC I/MHC II complexes or externally to dendritic cells. The level of FS production may be sufficient to be presented in MHC complexes but not induce a T-cell response. In most cases the aberrant cells are killed due to inherent dysfunction or by the immune system. Those escaping to become cancer cells could do so by decreasing MHC expression and/or establishing an immune suppressive environment. An important aspect of the model is that because of the global increase in the errors of transcription and splicing, the FS neoantigens will be constantly produced. Thus, in contrast to the commonly held view (45), bystander FS neoantigens would be good immunological targets. The production of these variants is not dependent on DNA replication as is the case for DNA mutations nor are they heritable and subject to selection.

[0125] As seen in FIG. 1, errors in DNA replication are very rare and repaired. Transcription error rates are higher

but also rare as are mis-splicing during intron excision. Additionally, the FS transcript with a premature termination may be degraded by Nonsense Mediated Decay (NMD). Aberrant proteins, including those with frameshifts are largely eliminated by the protein quality control system, Ubiquitin/Proteasome System (UPS). The net result is that very few frameshift peptides are presented on MHC I/II or escape the cell to be presented to the immune system. Cancer Cell: All levels of information transfer become more error prone. More errors are made in DNA replication, but only when cells divide. Most DNA mutations are point mutations and encode low or non-immunogenic epitopes. Global transcription is increased and is generally less accurate and even more so through MSs producing INDELS. Most transcribed genes with MSs in the coding region will have more FS transcripts. RNA splicing is also far less accurate, creating more FS transcripts from each out-of-frame splicing between exons from the same gene and different genes. The substantial increase of the FS transcripts from INDELS of MS and mis-splicing overwhelms the RNA quality control systems, such as NMD. Consequently, more truncated proteins with the FS peptide will be translated. These unfolded truncated proteins, combined with aberrant proteins from other mutations, overwhelms the protein quality control system, leading to more frameshift peptides being presented on MHC I/II and mis-secreted or released from the cancer cell which the immune system can respond to.

Example 5: Detection of Frameshift Transcripts

[0126] This model makes several specific predictions. First, frequent FS variants in different cancers will be produced by errors in RNA splicing and transcription, not as DNA mutations. As an example of errors in mis-splicing, substantial levels of a FS transcript, SMC1A1⁴ (exon 1 to exon 4), from the gene SMC1A in different mouse and human tumors were found (FIGS. 2A, 5A, 5E and 5F). The SMC1A1⁴ encodes a 17 amino acids (aa) FS peptide (FIG. 5A). Corresponding exon deletion in the DNA of mouse tumor cell lines was not detected, nor in the 12 TCGA cohorts (N=4730) via Cancer Genomics Browser analysis (data not shown) (46). Quantitative PCR demonstrates more expression of the SMC1A1⁴ transcript in breast cancers than normal breast samples (FIG. 2B). To establish an estimate of the frequency of mis-splicing FS variants, 500 clones from a poly A-primed cDNA library of the mouse melanoma cell line, B16F10 were sequenced. Two FS variants SLAIN2 FS and ZDHHHC17_FS were identified, which skip exon 7 and 16 respectively (FIGS. 5B and 5C). Table 3 depicts mouse mis-splicing FS antigens in the vaccine. Interestingly, only SLAIN2 was detected in 4T1, a mouse breast tumor cell line (FIG. 5G). The same conserved FS variants were also detected in different human cancers (FIG. 5H). While there were usually more (3-100-fold) frameshift transcripts in mis-splicing of these exons from tumor tissues or cancer cell lines, a low level of frameshift transcripts could be detected in some normal tissues (FIGS. 2B and 5H), which is consistent with the prediction of the model.

[0127] The analysis of RNA-generated FS variants was expanded by comparing NCBI tumor EST libraries to normal EST libraries. To simplify the analysis, FS variants caused by exon skipping or trans-splicing were focused on, i.e. splicing exons from different genes. A total of 12,456 exon skipping variants and 5,234 trans-splicing variants were found (FIG. 2C). 96 tumor associated FS variants from

exon skipping passed the filters described in FIG. 2C, which also encode a FS peptide longer than 7 aa (Table 1). 230 FS trans-splicing variants that encode FS peptides longer than 6 aa were also identified. Primers were designed to screen 220 of these in different pools of cDNAs from 50 human breast cancer cell lines (Table 2) and 48 were successfully validated. Two of these 48 FS variants, BCAS4-BCAS3 and MDS1-EVI1, have been described elsewhere (47, 48). 35 of these 48 FS variants were also found in 54 human primary breast tumors. The frequency of FS variants detected in tumor cell lines or tumor tissue is summarized in FIG. 2D. The expression frequency of these 48 variants range from 2% to 98% in tumor cell lines and primary tumors. Overall, a total of 27 out of 35 variants were expressed in over 50% of 50 tumor cell lines or 54 primary tumors. 12 of 35 variants tested were not detected in three normal tissues.

[0128] Another source of FS transcripts in tumors predicted by embodiments of the model provided herein is INDELs in MSs generated in transcription. As an example, the microsatellite region in the Sec62 gene contains 9 and 11 repeats of Adenine in human and dog, respectively. The sequence of Sec62 and the corresponding INDEL frameshift peptides are shown in FIG. 2A. Human breast cancer cell lines and dog primary tumor tissues from 7 different cancer types were used for sequencing. No INDELs were detected at the genomic level. However, there was a significant level of one A insertion in the cDNA samples from the same tumor for both MSs (FIG. 2E). Two clones with one A insertion and one clone with one A deletion were found in sequencing 15 PCR clones from dog Sec62 cDNA. The INDEL rate was similar as estimated from the PCR sequence trace. 9 human MS candidates and 18 dog MS candidates were further sequenced in cDNA samples from cancer cell lines or primary tumor tissues. INDELs were frequently detected in MS candidates with repeat length of 9 or longer (FIG. 2F). This is consistent with large scale sequencing results in yeast (22). The INDEL rate in transcription for MSs with repeat length of 7, 8 and 9 was very high compared to the genomic mutation rate but was not detected in the PCR sequencing trace due to low sensitivity of the assay. There is no evidence of INDELs in the MS in DNA in published reports except for Microsatellite Instability-High cancer patients with a defective mis-match repair system (15, 49, 50).

[0129] To further validate the INDELs in the transcription and the translation of the FS peptide, three plasmids based on the dog Sec62 gene were constructed. One has the eGFP fused in the 3rd reading frame to the MS region of 11 A in the dog Sec62 CDS. The eGFP protein will be correctly translated if there is one A insertion during the transcription. The 11A with 11 nucleotides of non-MS sequence in another plasmid as the negative control was replaced, so there is no MS related INDEL in the transcription and no expression of eGFP. The 11A with 12A as the positive control was also replaced, so the eGFP is in the 1st reading frame and would be translated with the upstream dog Sec62 gene. (FIG. 2G). Plasmids were transfected into 293T cells. 12.77% of the cells were GFP positive in the first construct which indicates this portion of the cells had 1A insertions at the mRNA level and then successfully translated the FS protein. In contrast, none of cells were GFP positive in the negative control which indicates the MS region was crucial for INDELs (FIG. 2H). This experiment not only shows that the transcription could induce translatable FS variants with the INDELs in the MS region, but also indicates that FS

peptides could be globally expressed in cancer cells with the defects in the quality control system.

Example 6: Detection of Antibodies to Frameshift Peptides

[0130] The model also predicts that the increased expression of FS variants, combined with other aberrant proteins, would overwhelm the quality control system and could potentially elicit immune responses to these FS peptides. To test this, an array of all possible predicted RNA-defined frameshift peptides was designed, meeting specific qualifications that the tumor cell could produce from INDELs in coding MS and mis-splicing of exons.

[0131] There are over 8000 MS in the coding region of the human genome that are runs of 7 or more repeats of homopolymers. The majority of MS regions meeting selection criteria are A runs and the number of MS candidates decreases exponentially as the repeat length or frameshift peptide length criteria increases. Each MS could generate 2 predictable FS peptides depending on whether there was an insertion or deletion. In addition, there are ~200,000 possible FS peptides that could be generated by mis-splicing of exons in the human genome, such as the examples of mis-splicing FSs. Similar to MS FSs, the number of mis-splicing FSs decreases exponentially as the FS peptide length requirement increases. Most of mis-splicing FSs are generated from the first 10 exons of human genes. The restriction of the peptide being longer than 10 amino acids for both sources of FS was applied. By these criteria there are over 220,000 possible FS antigens. Each FS antigen that was longer than 15 aa was divided into 15 aa, non-overlapping peptides. This produced a total of ~400,000 peptides. Peptides that share more than 10 aa identical sequences with any human reference proteins were excluded. Finally, each FS array was designed to contain a total of 392,318 FS peptides (FIG. 3A).

[0132] NimbleGen (Roche, Madison, Wis.) synthesized the FS peptide array, processed the array assay and summarized the IgG signals of each array with their standard protocol (51). The specific IgG reactivities was analyzed to these FSPs in 64 non-cancer control samples and a total of 85 cancers from 5 different late stage cancer types with 17 samples each (LC: lung cancer, BC: breast cancer, GBM: glioblastoma, GC: gastric cancer, PC: pancreatic cancer) and 12 stage I pancreatic cancer samples.

[0133] Each array was normalized to its median fluorescence for analysis. Three patterns of FS feature reactivity that were higher in cancer than non-cancer were found: common reactivity against FS peptides across all 5 cancer types; cancer type specific reactivity and personal reactivity. Reactivity against ~7000 selected peptides are shown in FIG. 3B. Common reactivity and cancer type reactivity in 5 cancer types were marked with black squares. Non-cancer control samples had very low, sporadic reactivity in these FS peptides.

[0134] Total reactivity on the 400K arrays was evaluated in the 5 cancer types and non-cancer samples with two methods. The first method compares the number of significant peptides in the cancer and control samples using fold change and p-values. By this method, BC, GC, PC and LC cancer samples had significantly more FS peptides compared to control samples which met the fold change and p-value criteria described in FIG. 3C. The exception is GBM where the reactivity in the controls was higher than the GBM

samples. The second method used a scoring method for each FS peptide. A peptide is scored as positive (red) if it is higher than six times the standard deviation (6SD) from the mean value of non-cancers for the peptide. All 5 cancer types had more positive FS peptides than the non-cancer controls (p-value<0.0001, FIG. 3D).

[0135] The analysis of individual cancer samples within the same cancer type using the scoring method showed that there were three patterns of reactivity. Most of the positive FS peptides (69%-80%) were personal for that individual. However, 16%-19% of the positive peptides were shared between two samples in that cancer type, with 1.5%-6.9% shared between 3 or more. The distribution of these classes is shown in FIG. 3E. Gastric cancer samples had the highest shared FS response (6.9% were shared in 3 or more). This is consistent with the very high correlation coefficients in several gastric cancer samples (FIG. 7F). Hierarchical clustering results of all positive FS peptides in the 5 cancer types are shown in FIGS. 7A-7G.

[0136] Embodiments of the model provided herein predicts that a FS peptide with high antibody reactivity is highly immunogenic and/or highly expressed in the tumor cells. These FS peptides could be cancer vaccine candidates. Analysis of the distribution of positive peptides allows the formulation 3 types of potential vaccines. One type is a personal vaccine. As an example, the personal vaccines for the 17 GBM patients are shown. Each patient had ~5800 positive FS peptides using the 6SD cut-off criterion and ~4500 positive FS peptides being unique for that patient (FIG. 7B). A filter for highest binding signals was applied to choose the 20 top peptides for each patient. These are depicted in FIG. 3F. This same system was applied to each of the other 4 cancer types with similar results (data not shown). It is noteworthy that even though GBM has been found to have a low DNA mutation rate (14), there appear to be an abundance of reactive RNA variant FS peptide for which to create a vaccine.

[0137] As noted in FIG. 3B, there were also peptides that were commonly reactive in a cancer type. Based on this analysis a set of peptides could be chosen to optimize the number in common for a particular cancer. This is depicted in FIG. 3G for the 5 tumor types. The top 100 peptides based on the maximum coverage for the particular cancer type were chosen. These vaccine compositions are referred to herein as "focused" vaccines, as it is clear from the FIG. 3G that many of the peptides optimal for a particular cancer are shared across other cancer types.

[0138] Finally, it was determined if there were FS peptides that were common across all 5 cancer types that met the p-value and frequency requirements. In FIG. 3H, exemplary 100 candidate FS peptides for a pan-cancer (at least for the 5 considered) vaccine are presented. It has been found that there are extremely few recurrent mutations in the DNA of certain tumors types (49) and with low chance of being immunogenic. In contrast common reactive FS variants can readily be identified.

[0139] All of the samples used for this analysis were from patients with late stage cancer. Cancer vaccines could also potentially be used for treatment of early stage cancers, and it is unclear whether early and late stage cancer vaccines would require different components. 20,000 most reactive and recurrent peptides were compared to non-cancer for both the late stage and stage 1 pancreatic cancer. As evident in FIG. 3I, most of the peptides did not overlap between the

late and early stages of pancreatic cancer. This implies that an early and late stage vaccine would require distinct peptide compositions.

Example 7: Frameshift Peptides Offer Partial Protection as Vaccines

[0140] The data presented herein shows that FS variants are present at the RNA level in tumors and that antibody responses to these FS peptides are present in cancer patients. However, the clinically relevant question is whether these FS variants can afford therapeutic value as vaccines, which is explored using mouse tumor models.

[0141] It was determined if the SMC1A 1⁴ FS peptide confers protection in the B16F10 mouse melanoma cancer model and/or the 4T1 mouse breast cancer model. This FS variant was shown to be common in both human and these mouse tumors (FIGS. 2A, and 5E). The FS peptide was encoded on a plasmid in a standard genetic immunization vector and introduced with a gene gun. 1×10⁵B16F10 tumor cells were injected and the animals vaccinated 4 weeks later. The tumor volume was monitored and compared to control mice receiving a mock vaccination. As shown in FIG. 4A, the vaccine conferred significant retardation of tumor growth. The SMC1A 1⁴ FS immunization also significantly retarded the 4T1 tumor growth in BALB/c mice (FIG. 4B). Depletion of CD8 or CD4 T-cells in the immunized mice indicates that this protection is CD8 T cell dependent (FIG. 4B).

[0142] It was tested whether the detection of FS variants in the RNA correlated with protection. The SLAIN2 and ZDHHC17 FSs had been identified in sequencing B16F10 cDNA. The SLAIN2 FS was present in the 4T1 mammary cancer cell line, but ZDHHC17 FS was not (FIG. 5F). When tested as gene vaccines in the mouse tumor injection model of 4T1, SLAIN2-FS conferred tumor retardation but ZDHHC17 did not (FIG. 4C).

[0143] The model (FIG. 1) implies that most transcribed genes with MS s in exons will produce FS peptides and these also may confer protection as vaccines. To test this prediction, three MS FSPs were selected based on the peptide size and best predicted H2-D binding epitopes in the mouse MS FS database (FIG. 4D and Table 4). As predicted, each FS neoantigen vaccination significantly retarded the tumor growth compared to the control group (FIG. 4D). Each FS antigen also elicited specific IFN γ releasing splenocytes (FIG. 4E).

[0144] Embodiments of the model provided herein also predicts that each tumor cell will present multiple FS neoantigens. These peptides could be presented at low levels as only a fraction of each RNA would be defective. Therefore, multiplexing neoantigens in a vaccine would be predicted to be more protective. To test this prediction, three FS neoantigens were tested individually and pooled together as vaccines in the BALB-NeuT transgenic mouse mammary cancer model. Each FS neoantigen-based vaccine individually showed similar protection by significantly delaying the tumor growth. As predicted, the pooled neoantigen vaccine produced a significant additive increase in delaying tumor initiation and growth (FIG. 4F). This suggests that pooling multiple FS neoantigens will increase efficacy.

[0145] Furthermore, as shown in FIGS. 8 and 9, pooled FS vaccines have increased efficacy compared to personal vaccines. Specifically, a mouse 4T1 model was used to test pooled FS peptides as vaccines relative to personal vaccines

used in the field. Pooled vaccines were made to 4T1 based on screening 30 mice injected with 4T1 and assayed on the FS arrays (BC-FAST). Personal vaccines also made to each mouse injected with 4T1 (BC-PCV) or a pancreatic tumor line (PC-FAST). As shown the BC-FAST vaccine was more protective than the personal vaccines (FIG. 9). In addition, pooled FS vaccines can be constructed for any tumor in humans (FIG. 10). The blood of 15 to 17 individuals with one of the 5 designated cancers, including breast, stomach, glioblastoma (GBM), lung, and pancreatic, were screened on FSP arrays to determine reactivity. High reactivity relative to non-cancer individuals is designated by a bars. The 100 most recurrently reactive peptides for each cancer are shown.

REFERENCES

- [0146] 1. J. W. Riess, P. N. Lara, Jr., D. R. Gandara, Theory Meets Practice for Immune Checkpoint Blockade in Small-Cell Lung Cancer. *J Clin Oncol*, (2016).
- [0147] 2. D. Schadendorf et al., Pooled Analysis of Long-Term Survival Data From Phase II and Phase III Trials of Ipilimumab in Unresectable or Metastatic Melanoma. *J Clin Oncol* 33, 1889-1894 (2015).
- [0148] 3. R. J. Motzer et al., Nivolumab versus Everolimus in Advanced Renal-Cell Carcinoma. *N Engl J Med* 373, 1803-1813 (2015).
- [0149] 4. E. B. Garon et al., Pembrolizumab for the treatment of non-small-cell lung cancer. *N Engl J Med* 372, 2018-2028 (2015).
- [0150] 5. J. Larkin et al., Combined Nivolumab and Ipilimumab or Monotherapy in Untreated Melanoma. *N Engl J Med* 373, 23-34 (2015).
- [0151] 6. A. M. Goodman et al., Tumor Mutational Burden as an Independent Predictor of Response to Immunotherapy in Diverse Cancers. *Mol Cancer Ther* 16, 2598-2608 (2017).
- [0152] 7. S. Turajlic et al., Insertion-and-deletion-derived tumour-specific neoantigens and the immunogenic phenotype: a pan-cancer analysis. *Lancet Oncol* 18, 1009-1021 (2017).
- [0153] 8. N. A. Rizvi et al., Cancer immunology. Mutational landscape determines sensitivity to PD-1 blockade in non-small cell lung cancer. *Science* 348, 124-128 (2015).
- [0154] 9. S. Bae, J. Tie, J. Desai, P. Gibbs, Microsatellite instability status is critical to analysis of survival in stage II colon cancer. *J Clin Oncol* 30, 675-676; author reply 676-677 (2012).
- [0155] 10. K. Bauer et al., T cell responses against microsatellite instability-induced frameshift peptides and influence of regulatory T cells in colorectal cancer. *Cancer Immunol Immunother* 62, 27-37 (2013).
- [0156] 11. J. C. Dudley, M. T. Lin, D. T. Le, J. R. Eshleman, Microsatellite Instability as a Biomarker for PD-1 Blockade. *Clin Cancer Res* 22, 813-820 (2016).
- [0157] 12. R. H. Vonderheide, K. L. Nathanson, Immunotherapy at large: the road to personalized cancer vaccines. *Nat Med* 19, 1098-1100 (2013).
- [0158] 13. A. Vitiello, M. Zanetti, Neoantigen prediction and the need for validation. *Nat Biotechnol* 35, 815-817 (2017).
- [0159] 14. Z. R. Chalmers et al., Analysis of 100,000 human cancer genomes reveals the landscape of tumor mutational burden. *Genome Med* 9, 34 (2017).
- [0160] 15. B. Vogelstein et al., Cancer genome landscapes. *Science* 339, 1546-1558 (2013).
- [0161] 16. P. A. Ott et al., An immunogenic personal neoantigen vaccine for patients with melanoma. *Nature* 547, 217-221 (2017).
- [0162] 17. U. Sahin et al., Personalized RNA mutanome vaccines mobilize poly-specific therapeutic immunity against cancer. *Nature* 547, 222-226 (2017).
- [0163] 18. T. R. Hodges et al., Mutational burden, immune checkpoint expression, and mismatch repair in glioma: implications for immune checkpoint immunotherapy. *Neuro Oncol* 19, 1047-1057 (2017).
- [0164] 19. A. C. Filley, M. Henriquez, M. Dey, Recurrent glioma clinical trial, CheckMate-143: the game is not over yet. *Oncotarget* 8, 91779-91794 (2017).
- [0165] 20. C. Kandoth et al., Mutational landscape and significance across 12 major cancer types. *Nature* 502, 333-339 (2013).
- [0166] 21. D. Hanahan, R. A. Weinberg, Hallmarks of cancer: the next generation. *Cell* 144, 646-674 (2011).
- [0167] 22. J. F. Gout et al., The landscape of transcription errors in eukaryotic cells. *Sci Adv* 3, e1701484(2017).
- [0168] 23. N. A. O'Leary et al., Reference sequence (RefSeq) database at NCBI: current status, taxonomic expansion, and functional annotation. *Nucleic Acids Res* 44, D733-745 (2016).
- [0169] 24. A. Untergasser et al., Primer3Plus, an enhanced web interface to Primer3. *Nucleic Acids Res* 35, W71-74 (2007).
- [0170] 25. K. D. Pruitt et al., The consensus coding sequence (CCDS) project: Identifying a common protein-coding gene set for the human and mouse genomes. *Genome Res* 19, 1316-1323 (2009).
- [0171] 26. K. F. Sykes, S. A. Johnston, Genetic live vaccines mimic the antigenicity but not pathogenicity of live viruses. *DNA Cell Biol* 18, 521-531 (1999).
- [0172] 27. R. S. Chambers, S. A. Johnston, High-level generation of polyclonal antibodies by genetic immunization. *Nat Biotechnol* 21, 1088-1092 (2003).
- [0173] 28. D. T. Hansen et al., Polyclonal Antibody Production for Membrane Proteins via Genetic Immunization. *Sci Rep* 6, 21925 (2016).
- [0174] 29. G. C. Whitlock et al., Protective antigens against glanders identified by expression library immunization. *Front Microbiol* 2, 227 (2011).
- [0175] 30. S. A. Svarovsky, M. J. Gonzalez-Moa, M. D. Robida, A. Y. Borovkov, K. Sykes, Self-assembled micro-nanoplexes for improved biolistic delivery of nucleic acids. *Mol Pharm* 6, 1927-1933 (2009).
- [0176] 31. A. Borovkov et al., New classes of orthopox-virus vaccine candidates by functionally screening a synthetic library for protective antigens. *Virology* 395, 97-113 (2009).
- [0177] 32. J. F. Gout, W. K. Thomas, Z. Smith, K. Okamoto, M. Lynch, Large-scale detection of in vivo transcription errors. *Proc Natl Acad Sci USA* 110, 18584-18589 (2013).
- [0178] 33. B. Schwanhaussner et al., Global quantification of mammalian gene expression control. *Nature* 473, 337-342 (2011).
- [0179] 34. M. Imashimizu, T. Oshima, L. Lubkowska, M. Kashlev, Direct assessment of transcription fidelity by high-resolution RNA sequencing. *Nucleic Acids Res* 41, 9090-9104 (2013).

- [0180] 35. H. S. Zaher, R. Green, Fidelity at the molecular level: lessons from protein synthesis. *Cell* 136, 746-762 (2009).
- [0181] 36. S. Lykke-Andersen, T. H. Jensen, Nonsense-mediated mRNA decay: an intricate machinery that shapes transcriptomes. *Nat Rev Mol Cell Biol* 16, 665-677 (2015).
- [0182] 37. A. Ruggiano, O. Foresti, P. Carvalho, Quality control: ER-associated degradation: protein quality control and beyond. *J Cell Biol* 204, 869-879 (2014).
- [0183] 38. J. E. Bradner, D. Hnisz, R. A. Young, Transcriptional Addiction in Cancer. *Cell* 168, 629-643 (2017).
- [0184] 39. S. C. Lee, O. Abdel-Wahab, Therapeutic targeting of splicing in cancer. *Nat Med* 22, 976-986 (2016).
- [0185] 40. T. I. Lee, R. A. Young, Transcriptional regulation and its misregulation in disease. *Cell* 152, 1237-1251 (2013).
- [0186] 41. S. Oltean, D. O. Bates, Hallmarks of alternative splicing in cancer. *Oncogene* 33, 5311-5318 (2014).
- [0187] 42. S. Negrini, V. G. Gorgoulis, T. D. Halazonetis, Genomic instability—an evolving hallmark of cancer. *Nat Rev Mol Cell Biol* 11, 220-228 (2010).
- [0188] 43. C. Y. Lin et al., Transcriptional amplification in tumor cells with elevated c-Myc. *Cell* 151, 56-67 (2012).
- [0189] 44. D. Silvera, S. C. Formenti, R. J. Schneider, Translational control in cancer. *Nat Rev Cancer* 10, 254-266 (2010).
- [0190] 45. P. L. Lollini et al., Vaccines and other immunological approaches for cancer immunoprevention. *Curr Drug Targets* 12, 1957-1973 (2011).
- [0191] 46. M. Goldman et al., The UCSC Cancer Genomics Browser: update 2015. *Nucleic Acids Res* 43, D812-817 (2015).
- [0192] 47. C. A. Maher et al., Transcriptome sequencing to detect gene fusions in cancer. *Nature* 458, 97-101 (2009).
- [0193] 48. C. A. Maher et al., Chimeric transcript discovery by paired-end transcriptome sequencing. *Proc Natl Acad Sci USA* 106, 12353-12358 (2009).
- [0194] 49. M. T. Chang et al., Identifying recurrent mutations in cancer reveals widespread lineage diversity and mutational specificity. *Nat Biotechnol* 34, 155-163 (2016).
- [0195] 50. R. J. Hause, C. C. Pritchard, J. Shendure, S. J. Salipante, Classification and characterization of microsatellite instability across 18 cancer types. *Nat Med* 22, 1342-1350 (2016).
- [0196] 51. B. Forsstrom et al., Proteome-wide epitope mapping of antibodies using ultra-dense peptide arrays. *Mol Cell Proteomics* 13, 1585-1597 (2014).
- [0197] 52. M. Sade-Feldman et al., Resistance to checkpoint blockade therapy through inactivation of antigen presentation. *Nat Commun* 8, 1136 (2017).
- [0198] 53. M. D. Vesely, R. D. Schreiber, Cancer immunoeediting: antigens, mechanisms, and implications to cancer immunotherapy. *Ann N Y Acad Sci* 1284, 1-5 (2013).
- [0199] 54. D. T. Le et al., Mismatch repair deficiency predicts response of solid tumors to PD-1 blockade. *Science* 357, 409-413 (2017).
- [0200] 55. D. T. Le et al., PD-1 Blockade in Tumors with Mismatch-Repair Deficiency. *N Engl J Med* 372, 2509-2520 (2015).
- [0201] 56. A. Kahles et al., Comprehensive Analysis of Alternative Splicing Across Tumors from 8,705 Patients. *Cancer Cell* 34, 211-224 e216 (2018).
- [0202] 57. A. C. Smart et al., Intron retention is a source of neoepitopes in cancer. *Nat Biotechnol* 36, 1056-1058 (2018).
- [0203] 58. S. D. Martin et al., Low Mutation Burden in Ovarian Cancer May Limit the Utility of Neoantigen-Targeted Vaccines. *PLoS One* 11, e0155189 (2016).
- [0204] 59. T. N. Schumacher, R. D. Schreiber, Neoantigens in cancer immunotherapy. *Science* 348, 69-74 (2015).
- [0205] 60. T. Kimura et al., MUC1 vaccine for individuals with advanced adenoma of the colon: a cancer immunoprevention feasibility study. *Cancer Prev Res (Phila)* 6, 18-26 (2013).
- [0206] 61. L. A. Vella et al., Healthy individuals have T-cell and antibody responses to the tumor antigen cyclin B1 that when elicited in mice protect from cancer. *Proc Natl Acad Sci USA* 106, 14010-14015 (2009).
- [0207] 62. D. W. Cramer et al., Conditions associated with antibodies against the tumor-associated antigen MUC1 and their relationship to risk for ovarian cancer. *Cancer Epidemiol Biomarkers Prev* 14, 1125-1131 (2005).
- [0208] 63. P. Stafford et al., Physical characterization of the “immunosignaturing effect”. *Mol Cell Proteomics* 11, M111 011593 (2012).
- [0209] 64. G. P. Dunn, A. T. Bruce, H. Ikeda, L. J. Old, R. D. Schreiber, Cancer immunoeediting: from immunosurveillance to tumor escape. *Nat Immunol* 3, 991-998 (2002).
- [0210] 65. D. B. Keskin et al., Neoantigen vaccine generates intratumoral T cell responses in phase Ib glioblastoma trial. *Nature* 565, 234-239 (2019).
- [0211] 66. S. Kreiter et al., Mutant MHC class II epitopes drive therapeutic immune responses to cancer. *Nature* 520, 692-696 (2015).
- [0212] 67. C. Linnemann et al., High-throughput epitope discovery reveals frequent recognition of neo-antigens by CD4+ T cells in human melanoma. *Nat Med* 21, 81-85 (2015).

TABLE 1

RefSeq_ ID	Encode FS peptides	Joint_ pos	#Total_ EST	EST_Ids	#Total_ Lib	# Tumor lib	# Normal_ lib
NM_001640.3	SPSQAMWATR M (SEQ ID NO: 22)	1940- 2047	7	14679393, 16524005, 18802412, 18807797, 19365353, 19366001, 33261912,	3	3	0

TABLE 1-continued

RefSeq_ ID	Encode FS peptides	Joint_ pos	#Total_ EST	EST_Ids	#Total_ Lib	# Tumor_ lib	# Normal_ lib
NM_199002.1	GVGGGILPPETP PVSAWGEIICPP AWLHL (SEQ ID NO: 23)	2623- 2788	3	10264060, 19733507, 23301501,	3	3	0
NM_014154.2	RHEKCCNWKQ QAESQSHCFRS CSKIVVLASARN LKHRAEN (SEQ ID NO: 24)	370- 448	5	20492217, 22518928, 45367569, 146009855, 146104793,	3	3	0
NM_001686.3	TTNPSRISLPSW VWMNFLRKTS (SEQ ID NO: 25)	1183- 1398	4	11106585, 12431398, 19143008, 20486863,	4	3	1
NM_004217.2	DHGGVGRCSNV LPWEEGDSQRH KARKSALRAQG RAEDC (SEQ ID NO: 26)	317- 599	3	10342556, 14654109, 22671315,	3	3	0
NM_016561.2	WSSSITGAAG NLNTTSWSTRL WPNGRRKKLSS GWSSWALGHLF TGKGFYLNE (SEQ ID NO: 27)	545- 751	6	19376801, 28113628, 45652559, 47036548, 52114251, 52114353,	4	3	1
NM_024808.2	FSLKMSSYPLLG LIMKGN SFHNVI PVNALT (SEQ ID NO: 28)	379- 426	4	9808442, 17166915, 146059308, 146063843,	4	3	0
NM_013265.2	PCTGLSLHPMA PRIWSRWSFPA GRCQDRPNKHV WPPQKKKKK KKKK (SEQ ID NO: 29)	2168- 2397	4	4311385, 46230323, 46834109, 47020765,	4	4	0
NM_020314.5	GSADRDDGKV (SEQ ID NO: 30)	1339- 1540	4	8407623, 9889142, 10213802, 80934926,	4	3	1
NM_018553.3	CYQHFPKKSQ FPGAYWTSFEG EEEGSQQLTLP P (SEQ ID NO: 31)	1845- 2308	3	8618242, 14448310, 14469670,	3	3	0
NM_134447.1	GFAASWLFKKP RPSECHTVIFKE ESYMN (SEQ ID NO: 32)	1419- 2068	20	2111082, 3151384, 3405187, 3801503, 5395116, 5446288, 5636075, 6451167, 7152982, 7319964, 8634237, 8634238, 19587294, 19753219, 21251126, 23295375, 24791739, 24792974, 154727570, 154730372,	18	12	4

TABLE 1-continued

RefSeq_ ID	Encode FS peptides	Joint_ pos	#Total_ EST	EST_Ids	#Total_ Lib	# Tumor_ lib	# Normal_ lib
NM_152266.3	DAAFFMSPKLI WWQEMATERG LFGLEIPIILKEL (SEQ ID NO: 33)	224- 283	4	10744663, 11064241, 22668651, 32210516,	4	3	1
NM_080571.1	CFTSSPLRW (SEQ ID NO: 34)	241- 360	7	12272400, 20501581, 22824741, 45697997, 46272730, 146043981, 146121376,	7	4	0
NM_178448.3	RVQGTLVHCPT RHLSQRRGPR QRGNSLPEPSS MLTCPQQPHRA TFPAAPGLQGCP RTGPSQPSMQL PSYPEDGSGLSR GHKDVRPGPPG QERVQVLRACA PQPQHVDCSA VGGPVAAREKP PVSRLGSAHQG LPTSAPFEGACH ALGDPGIFTGLE AGDRTVSVPG (SEQ ID NO: 35)	2485- 2522	4	10217199, 13329041, 14652514, 71054789,	4	3	1
NM_000070.2	CLQKHLPVALS TSLC (SEQ ID NO: 36)	2741- 3083	3	2222976, 4124403, 7038190,	3	3	0
NM_032830.2	MTSLSSHPLK RRNLEP (SEQ ID NO: 37)	1977- 2102	13	1720716, 2269339, 4332045, 5397085, 5638770, 5769282, 7317235, 11450365, 13719026, 13734654, 24787788, 24808260, 45860690,	9	6	2
NM_032830.2	LLSSHPLKRRN LEP (SEQ ID NO: 38)	1986- 2111	4	13908790, 18392074, 46257227, 92180377,	4	3	0
NM_001040648.1	TSASQIQAILVP (SEQ ID NO: 39)	1865- 2258	3	4630123, 4899627, 5676137,	3	3	0
NM_001161452.1	LLLQLRPGSRPF PVTYVSVTGRQ PYKSW (SEQ ID NO: 40)	889- 1669	4	1940552, 3933437, 13402321, 14509526,	4	4	0
NM_001039712.1	AAAAHHHSPR PAALRHPQEET GCVP (SEQ ID NO: 41)	225- 429	3	13914233, 21175318, 45699401,	3	3	0
NM_015954.2	LLQPPFVFIPPG CVML (SEQ ID NO: 42)	263- 412	5	10202290, 11101998, 13284397, 15434305, 52108714,	5	3	1

TABLE 1-continued

RefSeq_ ID	Encode FS peptides	Joint_ pos	#Total_ EST	EST_Ids	#Total_ Lib	# Tumor_ lib	# Normal_ lib
NM_213566.1	SPKLPLVRRWM Q (SEQ ID NO: 43)	540- 731	3	9183529, 10729953, 13583484,	3	3	0
NM_001384.4	LPCSSLTSYWE MLWLWLHDWR RRQGQRCSFWV TQPTAAAWM CWVLSKLELRL SYILALPA (SEQ ID NO: 44)	292- 345	9	9141503, 9341726, 9720673, 11614383, 12102395, 13326770, 22703054, 22813642, 56794883,	7	6	1
NM_130443.2	HFPACQLLPLCD LISSALPYVE (SEQ ID NO: 45)	2342- 2439	4	6594041, 6974193, 24809933, 31153484,	4	3	0
NM_001402.5	CLQNWYWC SCWPSGDWCSQ TRYGGHLCSSQ RYNGSKICRNA P (SEQ ID NO: 46)	119- 818	4	10201484, 16001157, 19093438, 19204512,	3	3	0
NM_014285.5	GFWSRFPFPW (SEQ ID NO: 47)	448- 528	5	9137001, 46278258, 145993595, 146042851, 146123968,	5	3	1
NM_001113378.1	VSPGVSELRNS KKYKGAGEAV WFSSDPPVLPFH FLRTE (SEQ ID NO: 48)	3439- 3628	4	6444477, 6870295, 6870449, 83195477,	3	3	0
NM_001018078.1	VLGSQRHPGQG SCGSCPWHLCS SPHPTCGSGPGT RSGRAGRRCRG AGPSFGTWTVR TPPAARRPACA GSARRCRAARG RAVAPRFESCSS MLPGTGTRRPC (SEQ ID NO: 49)	860- 1009	3	10218110, 19144710, 46186123,	3	3	0
NM_006098.4	GWPGHVMGSQ RRQTPLHARW WGHHPVLPQP (SEQ ID NO: 50)	637- 748	8	2574599, 9807168, 13524413, 33203609, 52715305, 58413416, 58566171, 90906220,	7	5	1
NM_015666.3	GPRGHAGEGGR QSCGRPVLGR (SEQ ID NO: 51)	390- 507	4	13133604, 145997763, 146023828, 146095508,	4	3	1
NM_016426.6	VQMKMMKSSS DPLDIKKDVLPP AWN (SEQ ID NO: 52)	291- 350	24	14072238, 14079103, 14080406, 14176079, 52197802, 52282171, 52282469, 52282506, 52282657, 84914016,	15	9	3

TABLE 1-continued

RefSeq_ ID	Encode FS peptides	Joint_ pos	#Total_ EST	EST_Ids	#Total_ Lib	# Tumor_ lib	# Normal_ lib
				145998391, 146023882, 146039486, 146039586, 146040214, 146050613, 146052038, 146057369, 146057491, 146062991, 146072037, 146080660, 146102605, 146107434,			
NM_031243.2	EGVLLQVTNEE VVNHRVFKK (SEQ ID NO: 53)	1300- 3179	4	12422802, 13033025, 13047121, 24132471,	4	3	1
NM_031243.2	KEGVLLQVTNE EVVNHRVFKK (SEQ ID NO: 54)	2581- 3176	3	2466855, 4569115, 5659331,	3	3	0
NM_006644.2	DSCGIVNSY (SEQ ID NO: 55)	2925- 3176	6	2077398, 10153160, 10993881, 12672555, 13911640, 51668448,	5	4	1
NM_006644.2	DSCGIVNSY (SEQ ID NO: 56)	2924- 3175	6	4074102, 10032700, 10153621, 19588875, 19608035, 45695863,	4	3	1
NM_024660.2	NCPVWRHNPCL ASWMSWRCWK S (SEQ ID NO: 57)	441- 821	6	2033361, 9124825, 9141800, 9332671, 10216854, 23253517,	6	4	1
NM_014761.2	IVGPGPKPEASA KLPSRPADNYD NFVLPPELPSVPD TLPTASAGASTS ASEDIDFDDLSR RFEEL (SEQ ID NO: 58)	916- 955	5	19137983, 19193502, 28140121, 46922603, 283449919,	5	3	1
NM_001130089.1	VGSMPKELLGE SSSSMIFEERG (SEQ ID NO: 59)	450- 617	7	9329185, 9335633, 9336682, 14810814, 22365213, 45711902, 45715554,	5	4	1
NM_199187.1	HRDSRGSGRNG RHPEREGDHAK PERPPGLLPQGS EPPGDREPEAGE QNPALGEGT PGQRLEPLLQD HRGPEGSDLRK YCGQCPHR SAD (SEQ ID NO: 60)	197- 260	18	10141571, 10142544, 10402934, 10586887, 12758550, 14177331, 19893549, 21768308, 21774629, 21774763, 21777572, 21811780,	10	8	2

TABLE 1-continued

RefSeq_ ID	Encode FS peptides	Joint_ pos	#Total_ EST	EST_Ids	#Total_ Lib	# Tumor_ lib	# Normal_ lib
				21815923, 22682079, 22908399, 24042754, 24045349, 56795793,			
NM_002273.3	LLRSRHSTRILP TAAGLRLRACT RSSMRSCRAWL GSTGMTCGAQR LRSLR (SEQ ID NO: 61)	831- 881	9	9340416, 9759824, 9759932, 9897110, 9897831, 10156714, 21813841, 21814354, 21816557,	4	4	0
NM_177433.1	RCQPDHSHIW ALRWPPWSWC QHQQWLWCLW FLLQV (SEQ ID NO: 62)	1731- 1809	6	2054843, 5511019, 5673765, 5853954, 20203884, 23531396,	4	3	1
NM_153450.1	ETPSDSHKKK KKKKEEDPERK RKKKEKKKKK VE (SEQ ID NO: 63)	590- 830	8	3151481, 3750732, 4223069, 6139460, 11444683, 11451179, 11452422, 18988750,	5	3	1
NM_015950.3	AGNVRNSRPSI QR (SEQ ID NO: 64)	749- 824	4	2252141, 3277351, 19588584, 23291327,	4	3	1
NM_032112.2	PASGGSDLVNH SFLCKWHP (SEQ ID NO: 65)	541- 717	3	12308492, 12339978, 22813610,	3	3	0
NM_032112.2	CLLLGAVTL (SEQ ID NO: 66)	599- 713	5	10154760, 13408766, 20201885, 20493143, 21494992,	3	3	0
NM_014018.2	EIPERNQGPVAA IRS (SEQ ID NO: 67)	237- 420	5	1295506, 6898484, 10246880, 33209502, 34555226,	5	4	1
NM_001145839.1	LHWGSTKVHLL LI (SEQ ID NO: 68)	415- 801	4	10738994, 80835964, 146091479, 146109603,	4	3	1
NM_001114185.1	GGPRRIWS (SEQ ID NO: 69)	410- 712	8	10147163, 10989026, 16773154, 16776609, 16779119, 22853771, 22902798, 145986212,	4	4	0
NM_000431.2	GGPRRIWS (SEQ ID NO: 70)	419- 721	5	16773347, 16777501, 28132078, 47402601, 146062357,	4	3	1

TABLE 1-continued

RefSeq_ ID	Encode FS peptides	Joint_ pos	#Total_ EST	EST_Ids	#Total_ Lib	# Tumor_ lib	# Normal_ lib
NM_003491.2	RSVKWSPNTMQ MGRTMP (SEQ ID NO: 71)	452- 499	5	9151226, 9345658, 19210146, 27947049, 126672362,	5	4	0
NM_024313.2	VPTACCRCCFC WDV (SEQ ID NO: 72)	788- 2696	16	9141107, 9803380, 12427492, 13328739, 13908466, 14678515, 21780385, 21785028, 22345418, 22361309, 22361754, 46290768, 68292178, 82116561, 90837311, 92186397,	12	9	1
NM_016391.4	SGKTSSILCRRG RWRWS (SEQ ID NO: 73)	391- 483	13	2054860, 2932939, 2942143, 3601044, 4535246, 5425877, 5438639, 5596079, 5659519, 7151152, 19723340, 19738445, 24795292,	10	8	2
NM_007243.1	AGDAVLGAHTQ RPCVVGSG (SEQ ID NO: 74)	151- 349	3	12766042, 46616730, 145998555,	3	3	0
NM_001042549.1	GAKPGGLALGA V (SEQ ID NO: 75)	533- 12194	3	3887573, 4991027, 6451223,	3	3	0
NM_181843.1	DEVFALPLAHL LQTQNGYTHF CRGGHFRYTLF VFLHGPHRVWG LTAVITEFALQL LAPGTYQPLA GLTCSGAEGLA RPKQPLASPCQ ASSTPGLNKGL (SEQ ID NO: 76)	426- 498	5	10326854, 11970552, 18510936, 19030548, 46555631,	5	4	1
NM_198887.1	QENCSPGGRG CSDPRSCHFTPA WAKEQNAISK IHI (SEQ ID NO: 77)	2448- 3467	4	1192583, 3280105, 5636736, 24792671,	4	3	0
NM_007342.2	AKFCPTFNKSM EEQGK (SEQ ID NO: 78)	704- 782	5	11617690, 52065044, 52097801, 52298172, 80768446,	5	3	1

TABLE 1-continued

RefSeq_ ID	Encode FS peptides	Joint_ pos	#Total_ EST	EST_Ids	#Total_ Lib	# Tumor_ lib	# Normal_ lib
NM_001199462.1	GLWLFPRQNVL QMPOSILLQQG ASDPRLEIGT (SEQ ID NO: 79)	257- 383	9	3988478, 4076572, 4268320, 4268335, 6700534, 10373888, 10984780, 11512824, 11512860,	5	4	0
NM_002618.3	DYRRLPPGPAN FFCIFSIRDGVSP CYPGWSPPDL VMSPLRSPKVL GLQA (SEQ ID NO: 80)	2760- 3281	4	9808150, 11159219, 13459444, 22920343,	4	3	1
NM_031948.3	PLRRPCTRSW GQGS (SEQ ID NO: 81)	465- 629	3	14807581, 19210482, 146069312,	3	3	0
NM_004577.3	CDLNSLCIFVAI FHTKCFKCGESI KHLYS (SEQ ID NO: 82)	1630- 1940	5	2159346, 13709277, 13742243, 14506129, 27939669,	4	3	1
NM_020387.2	GTIVVQWGPSW CLT (SEQ ID NO: 83)	269- 466	18	2277936, 9146588, 10156678, 10742718, 14380528, 14511202, 19128358, 19180556, 19196633, 19199578, 19199919, 23272326, 24184393, 38619719, 52187412, 52187724, 52259400, 52288970,	14	10	3
NM_006743.4	GLWMVRSVW IMQASLLGEPEE VALGPMGVVA ATLEVVGTRAM GVAGIMTVGLE GMDMDMDVPE TIMAETRVVMT ATQEEITETIMT T (SEQ ID NO: 84)	338- 445	6	10885369, 12600212, 12600293, 13460579, 19132700, 21168881,	4	3	1
NM_016026.3	SLPPNPSAARET KGISPIKDKCV FPRTSPGKDLPL (SEQ ID NO: 85)	165- 546	3	1679208, 22269010, 80545142,	3	3	0
NM_152553.2	GLFVFPIYCLC (SEQ ID NO: 86)	1017- 1133	5	10400124, 13908341, 14428408, 52261877, 83255255,	5	3	1

TABLE 1-continued

RefSeq_ ID	Encode FS peptides	Joint_ pos	#Total_ EST	EST_Ids	#Total_ Lib	# Tumor_ lib	# Normal_ lib
NM_198486.2	EVWRHLLGRPH S (SEQ ID NO: 87)	427- 538	5	21985536, 21986341, 145986153, 145999838, 146106725,	4	3	1
NM_000973.3	IRELCHRYLPQP (SEQ ID NO: 88)	225- 453	8	1154529, 6937038, 9128356, 19091430, 19200294, 20486488, 22907262, 24044064,	6	5	1
NM_001002.3	GVRQWQHLQP (SEQ ID NO: 89)	646- 754	13	9124850, 10205674, 13031883, 13403621, 13466151, 13666955, 14173427, 14175419, 19817898, 19895213, 21816494, 22689525, 47384119,	8	7	1
NM_001005.3	GLLWCAAVHH GEWGQRLRGC GVWETPRTEG (SEQ ID NO: 90)	285- 381	3	9125003, 9139471, 22695855,	3	3	0
NM_001006.3	FGKAHGASW (SEQ ID NO: 91)	614- 725	6	10160942, 12602739, 19378611, 21773234, 22849872, 22908519,	4	4	0
NM_138421.2	GDGGSGSKGRP VEQTEVFLCISK PSSFL (SEQ ID NO: 92)	1088- 1286	3	1801795, 7155873, 16771906,	3	3	0
NM_017827.3	LHARAPGPRGP PLLCPCCLRVSH (SEQ ID NO: 93)	1708- 1833	4	4890586, 5746185, 13915028, 23284022,	4	4	0
NM_001005914.1	LPQQDLWHLQF HQGLPRRCHPV CAEPPPHVQLCP AHWGAPSFPTS WSQLHLHSNCR GFGCSR (SEQ ID NO: 94)	1164- 1377	3	9896956, 52185731, 80585087,	3	3	0
NM_021627.2	GIFELFIL (SEQ ID NO: 95)	328- 463	4	19184218, 52117054, 80576973, 82328796,	4	3	1
NM_001193342.1	GIGAVCMDWW AAAPPGECAPR PGCAAHHCGRH LLH (SEQ ID NO: 96)	1086- 1200	4	19211503, 146039032, 146045087, 146056161,	4	3	0

TABLE 1-continued

RefSeq_ ID	Encode FS peptides	Joint_ pos	#Total_ EST	EST_Ids	#Total_ Lib	# Tumor_ lib	# Normal_ lib
NM_001532.2	SPCPSSPPSQPW (SEQ ID NO: 97)	1096- 1137	4	21176693, 24044445, 28133989, 80539035,	4	3	1
NM_178148.2	VLSDLGCAAGK SDDPQLWGHSH ITG (SEQ ID NO: 98)	343- 499	4	13997158, 46283786, 78233770, 80883909,	4	3	1
NM_006306.2	CCGIYCHEEPQR EDSSI (SEQ ID NO: 99)	179- 482	6	10204155, 10350966, 20396212, 20413818, 52288176, 84940096,	4	3	1
NM_030918.5	HFPDGEVTAER CGHLAFPYPLPF PSPSSYSFHVP FQTE (SEQ ID NO: 100)	1593- 2370	10	1162267, 2324233, 2356934, 2552335, 2557157, 3765160, 4328216, 12300356, 24781036, 24803854,	10	7	2
NM_006461.3	ISVSIMWTQRRK L (SEQ ID NO: 101)	269- 862	5	24952240, 45703140, 46182693, 46185076, 52109618,	5	3	0
NM_006925.3	VKGVLHSLTAA GQTH (SEQ ID NO: 102)	1055- 1428	6	2952696, 4286279, 18979142, 21477426, 21982089, 24787231,	6	5	1
NM_006374.3	KHQAMDHHGV PGRRLSTGLA (SEQ ID NO: 103)	426- 477	7	9183882, 11256565, 17161793, 17163262, 17174422, 22286625, 24120773,	5	4	1
NM_014760.3	GDQQPDRTQAG LKSVSQVEDVF RELIGTQKTRTG CFPPSGS (SEQ ID NO: 104)	2877- 2907	8	6883317, 10991109, 12385448, 21770848, 46184886, 58050995, 82074179, 91879091,	8	6	2
NM_006521.4	CSAQARNRSED ETQPLPLGTLA F (SEQ ID NO: 105)	2451- 2492	8	9149080, 9330710, 9331155, 9336773, 9344551, 9344576, 10734097, 10734771,	3	3	0

TABLE 1-continued

RefSeq_ ID	Encode FS peptides	Joint_ pos	#Total_ EST	EST_Ids	#Total_ Lib	# Tumor_ lib	# Normal_ lib
NM_199293.2	HQALGAVPSCE GV (SEQ ID NO: 106)	112- 370	6	16526130, 45700010, 45704764, 45705693, 45717940, 46847261,	4	3	1
NM_207379.1	QFRTPGWPLKA LAGRGWPEDas PGQEPSKGAGR GWA (SEQ ID NO: 107)	543- 1313	10	3933593, 3933605, 4111770, 4312229, 4684269, 6504772, 6838403, 10031991, 10940483, 11083896,	4	3	0
NM_006291.2	PRAAVSGIQW WNGRQNWKRK KEKMSRLAGA FRVLWRAVSTA SIRRHIVAPRP LQAGPAMGP (SEQ ID NO: 108)	2087- 2545	11	9176343, 10210944, 11290536, 19369027, 22342759, 22374168, 22662093, 22852902, 22853464, 22853646, 22902765,	5	4	1
NM_015140.3	LIVGGGAPDRK GFQ (SEQ ID NO: 109)	2096- 2811	10	21980643, 46551962, 46552370, 46845450, 46876330, 46920760, 46925643, 46929343, 46951310, 47021176,	5	4	1
NM_012473.3	CQRCPLCWP (SEQ ID NO: 110)	343- 468	3	12687717, 21780390, 28088991,	3	3	0
NM_001184977.1	GVRCLIHSHIGF L (SEQ ID NO: 111)	308- 382	6	11265100, 18775927, 19897757, 51485275, 81213059, 82161427,	6	4	1
NM_003370.3	WPQLLEPNSG KSASRRRPQGG PQPPKLRVVEA EVGDSWKR (SEQ ID NO: 112)	567- 1019	4	8608901, 14173570, 46181698, 46269629,	3	3	0
NM_052844.3	VAARAWQPPL PGAECGHRREG ATLAGHRGPA AAHRGLRPGHA AAATEHQAE SPRGDRGGRHG SGLLQL (SEQ ID NO: 113)	828- 939	7	10145344, 10147104, 16526305, 21773170, 21777139, 31447502, 46265826,	5	4	1
NM_001033519.1	RYGRCVHCREI VLQQFSGHRQP (SEQ ID NO: 114)	290- 374	5	10391746, 10393365, 12339226, 14653998, 78233952,	4	3	1

TABLE 1-continued

RefSeq_ ID	Encode FS peptides	Joint_ pos	#Total_ EST	EST_Ids	#Total_ Lib	# Tumor_ lib	# Normal_ lib
NM_152858.1	GLMASDYSEEV ATSEKFPF (SEQ ID NO: 115)	674-895	3	11158199, 12338537, 21118493,	3	3	0
NM_182969.1	DRKRGCCPTSSS LPISLRVRLS (SEQ ID NO: 116)	1312-1480	4	22340486, 27841540, 27878857, 83526847,	4	3	1
NM_005741.4	SHSQSGGPRHP GGTRRKAMGSQ CPQLQGGPEPQR PSSRRREI (SEQ ID NO: 117)	722-1106	4	9155377, 16534738, 16535238, 22701945,	3	3	0

TABLE 2

The 50 human breast cancer cell lines.			
No.	Cell Line	ATCC_Name	Tissue
1	MCF-10A	CRL-10317	Breast
2	BT-474	HTB-20	Breast
3	Hs 319.T	CRL-7236	Breast
4	HCC1428	CRL-2327	Breast
5	HCC1599	CRL-2331	Breast
6	Hs 605.T	CRL-7365	Breast
7	Hs 362.T	CRL-7253	Breast
8	ZR-75-1	CRL-1500	Breast
9	MCF-7	HTB-22	Breast
10	Hs 281.T	CRL-7227	Breast
11	HCC1500	CRL-2329	breast
12	BT-20	HTB-19	breast
13	HCC1143	CRL-2321	breast
14	UACC-812	CRL-1897	breast
15	SW527	CRL-7940	breast
16	MDA-MB-453	HTB-131	breast
17	ZR-75-30	CRL-1504	breast
18	MDA-MB-468	HTB-132	breast
19	HCC1187	CRL-2322	breast
20	SK-BR-3	HTB-30	breast
21	MDA-MB-175-VII	HTB-25	breast
22	Hs 574.T	CRL-7345	breast
23	HCC 1008	CRL-2320	breast
24	Hs 742.T	CRL-7482	breast
25	Hs 748.T	CRL-7486	breast
26	BT-483	HTB-121	breast
27	HCC202	CRL-2316	breast
28	HCC 2157	CRL-2340	breast
29	BT-549	HTB-122	breast
30	MDA-MB-415	HTB-128	breast
31	HCC1395	CRL-2324	breast
32		HTB-127	breast
33	MDA-MB-231	HTB-26	breast
34	CAMA-1	HTB-21	breast
35	MDA-MB-134-VI	HTB-23	breast
36	Hs 606.T	CRL-7368	breast
37	HCC1806	CRL-2335	breast
38	HCC1419	CRL-2326	breast
39	AU565	CRL-2351	breast
40	HCC1937	CRL-2336	breast
41	Hs 578T	HTB-126	breast

TABLE 2-continued

The 50 human breast cancer cell lines.			
No.	Cell Line	ATCC_Name	Tissue
42	Hs 739.T	CRL-7477	breast
43	DU4475	HTB-123	breast
44	HCC70	CRL-2315	breast
45	HCC38	CRL-2314	breast
46	HCC1954	CRL-2338	breast
47	MB 157	CRL-7721	breast
48	HCC2218	CRL-2343	breast
49	Hs 343.T	CRL-7245	breast
50	UACC-893	CRL-1902	breast

TABLE 3

Mouse mis-splicing FS antigens in the vaccine			
Antigen Name	Peptide size	Peptide sequence	
ZDHC17 FS	21	AVLLMCQLYQPWMCKEYYRLL (SEQ ID NO: 118)	
SLAIN2 FS	21	IIPRMQPQASANHCQLLKVMA (SEQ ID NO: 119)	
mSMC1A-1 ⁴	27	TAIIGPNGSGCGSVYCHEEPQGEDSSV (SEQ ID NO: 120)	
RBM FS	45	GRVIECDVVKGSCQDGEAVHWKSAPGGHRAGD PLTLRAVREGAGM (SEQ ID NO: 121)	

TABLE 4

Three mouse MS FS antigens with predicted H2-D epitope					
Antigen ID	Access #	MS type	INDEL	Peptide size	peptide sequence (Kd/Ld epitope score > 20)
MS927	NM_053009.3	9_A	Del	33	ICMSPPLLWATLQAPETTSACKASYRPEGLYL (SEQ ID NO: 122)
MS255	NM_010086.4	9_A	In	24	YFSCDKRCKIKHYAGNKSLLTFSGY (SEQ ID NO: 123)
MS518	NM_153511.3	10_A	Del	59	TLCMEVMLRWNTRELGYLYLQLCFLNTHLHLSQEEKLLTLGR FLTWTSRCSFVIRPL (SEQ ID NO: 124)

TABLE 5

Samples tested on Human 400K FS array		
Sample Type	Number of Samples	Source
Breast Cancer	17	UT Southwestern
Lung Cancer	17	UT Southwestern
GBM	17	Barrows Neurological Institute

TABLE 5-continued

Samples tested on Human 400K FS array		
Sample Type	Number of Samples	Source
Pancreatic Cancer	17	TGEN
Pancreatic Cancer Stage 1	13	TGEN
Gastric Cancer	17	Japan
Control	64	Varied Sources

TABLE 6

Three ORFs of Sec62 gene
<p>Sec62-12A: atggcggagcgcaggagacacaagaagcggatccaggaagtgggtgaaccatctaaagaagagaaggctgtagccaagatctctcgattta actgtccaacaaagtctaccaatgatggggcaccgagttgattatctcattgcttcaaaagcagtggtatgacctttggattcaaaagtgggcaa aggccaaagaaggagaggaagctttattacaacaagggagctctgtggttgactactgcaacaggcttttaagaagcagttttttcaccgggc actaaaagtaataaaaatgaagtatgataaagacataaaaaagaaaaagagaaaggaaggccgaaagtggaaaagaagaagataaaaa gagcaggaaaagaaatctaaaggatgaaaagacgaaaaaggagaaagaaaaaaagatggggaaggaagaggattacaagga cgacgcagcaagtgaatctcatggtgagcaaggcggagagctgttaccggggtgggtgccatcctgggtcgagctggacggcgacgta aacggccacaagttcagcgtgtccggcgaggggcagggggatgccacctacggcaagctgacctgaagttcatctgaccaccggcaag ctgcccgtgcccggcccacctcgtgaccacctgacctacggcgtgcagtgcttcagccactaccggaccacatgaagcagcagcactt ctccaagtccgcatgccgaaggctacgtccagagcgcacctctcttcaaggacgacggcaactacaagaccggcggaggtgaa gtccgagggcgacacctgggtgaaccgcatcgagctgaagggcatcgactcaaggaggacggcaacatcctggggcacaagctggagta caactacaacagccacaagctctatcatggcgcgacaagcagaagacggcatcaaggtgaactcaagatccgcccacaacatcgaggac ggcagcgtgcagctcgccgacctaccagcagaacccccatcgggcagggccccgctgctgctgcccgaacacctactctgagcac ccagtcgcacctgagcaaaagaccacaagcagaagcgcgcatcacatggtctgctggagttcgtgaccggcggcgggatcactctcgcatg gacgagctgtacaagagatctggtaccacgctatcgataaagcttgcctgcaggtcgactctagaggatcgtga (SEQ ID NO: 125);</p> <p>Sec62-11A: atggcggagcgcaggagacacaagaagcggatccaggaagtgggtgaaccatctaaagaagagaaggctgtagccaagatctctcgattta actgtccaacaaagtctaccaatgatggggcaccgagttgattatctcattgcttcaaaagcagtggtatgacctttggattcaaaagtgggcaa aggccaaagaaggagaggaagctttattacaacaagggagctctgtggttgactactgcaacaggcttttaagaagcagttttttcaccgggc actaaaagtaataaaaatgaagtatgataaagacataaaaaagaaaaagagaaaggaaggccgaaagtggaaaagaagaagataaaaa gagcaggaaaagaaatctaaaggatgaaaagacgaaaaaggagaaagaaaaaaagatggggaaggaagaggattacaagga cgacgcagcaagtgaatctcatggtgagcaaggcggagagctgttaccggggtgggtgccatcctgggtcgagctggacggcgacgta aacggccacaagttcagcgtgtccggcgaggggcaggggcgatgccacctacggcaagctgacctgaagttcatctgaccaccggcgaag ctgcccgtgcccggcccacctcgtgaccacctgacctacggcgtgcagtgcttcagccactaccggaccacatgaagcagcagcactt ctccaagtccgcatgccgaaggctacgtccagagcgcacctctcttcaaggacgacggcaactacaagaccggcggaggtgaa gtccgagggcgacacctgggtgaaccgcatcgagctgaagggcatcgactcaaggaggacggcaacatcctggggcacaagctggagta caactacaacagccacaagctctatcatggcgcgacaagcagaagacggcatcaaggtgaactcaagatccgcccacaacatcgaggac ggcagcgtgcagctcgccgacctaccagcagaacccccatcgggcagggccccgctgctgctgcccgaacacctactctgagcac ccagtcgcacctgagcaaaagaccacaagcagaagcgcgcatcacatggtctgctggagttcgtgaccggcggcgggatcactctcgcatg gacgagctgtacaagagatctggtaccacgctatcgataaagcttgcctgcaggtcgactctagaggatcgtga (SEQ ID NO: 126);</p> <p>Sec62-Non MS: atggcggagcgcaggagacacaagaagcggatccaggaagtgggtgaaccatctaaagaagagaaggctgtagccaagatctctcgattta actgtccaacaaagtctaccaatgatggggcaccgagttgattatctcattgcttcaaaagcagtggtatgacctttggattcaaaagtgggcaa aggccaaagaaggagaggaagctttattacaacaagggagctctgtggttgactactgcaacaggcttttaagaagcagttttttcaccgggc actaaaagtaataaaaatgaagtatgataaagacataaaaaagaaaaagagaaaggaaggccgaaagtggaaaagaagaagataaaaa gagcaggaaaagaaatctaaaggatgaaaagacgaaaaaggagaaagagagaaagagagatggggaaggaagaggattacaagga cgacgcagcaagtgaatctcatggtgagcaaggcggagagctgttaccggggtgggtgccatcctgggtcgagctggacggcgacgta aacggccacaagttcagcgtgtccggcgaggggcaggggcgatgccacctacggcaagctgacctgaagttcatctgaccaccggcgaag ctgcccgtgcccggcccacctcgtgaccacctgacctacggcgtgcagtgcttcagccactaccggaccacatgaagcagcagcactt</p>

TABLE 6-continued

Three ORFs of Sec62 gene

cttcaagtccgccatgccgaaggctacgtccaggagcgcaccatctcttcaaggacgacggcaactacaagaccgcgccgaggtgaa
 gttcaggggcgacacccctggtgaaccgcacatcgagctgaaggccatcgacttcaaggaggacggcaacatcctggggcacaagctggagta
 caactacaacagccacaacgtctatcatggccgacagcagaagaacggcatcaaggtgaacttcaagatccgccacaacatcgaggac
 ggcagcgtgcagctcgcgcaccactaccagcagaacccccatcgggcagcggcccgctgctgctgcccgacaaccactacctgagcac
 ccagtcgcctgagcaagacccccaaagagaagcgcgatcacatggtcctgctggagttcgtgaccgcgcgggatcactctcgcatg
 gacgagctgtacaagagatctggtaccacgcgtatcgataagcttgcatgcctcgaggtcgactctagaggatcgtga (SEQ ID NO:
 127) .

TABLE 7

Trans-splicing ID	up-stream gene ACC#	down-stream gene ACC#	up WT sequence	down stream FS sequence
BOLA2_ Exon2_ SMG1_ Exon12	NM_001031827.1	NM_015092.3	MASAKSLDRWKARLLEGGST ALTYALVRAEVSFPAEVAPV RQQGSVAGARAGVSVLLGCR SSWTAAMELSAEYLRKLR DLEAEHVEVEDTTLNRCSCSF RVLVVSAKFEGKPLLQRHR (SEQ ID NO: 128)	LLNR (SEQ ID NO: 129)
GFOD1_ Exon1_ C6orf114_ Exon2	NM_018988.2	NM_033069.2	MLPGVGVPGTSLTARV I PLL KDEGFAVKALWGRTOEEAEE LAKEMSVPFYTSRIDEVLLHQ DVDLVCINLPPPLTRQIAVKT L (SEQ ID NO: 130)	EPGHQRKKISRQKNTGEEKMP RGSVQLSFCSLQHPHMGHLFTF HDAALGESQGTGFKPLGMQPV (SEQ ID NO: 131)
MDS1_ Exon2_EVI1_ Exon4	NM_004991.2	NM_001105078.2	MRSKGRARKLATNNECVYG NYPEIPLLEMPDADGVASTPS LNIQEPSPATSSSEAFPKEGS PYKAPIYIPDDIPIPAEFELRES NMPGAGLGIWTKRKIEVGEK FGPYVGEQRSNLKDPSTYGE (SEQ ID NO: 132)	ILDEFYNVKFCIDASQPDVGSW LKYIRFAGCYDQHNLVACQIND QIFYRVVADIAPGEBLLLFMKS EDYPHETMAPDIHEERQYRCED CDQLFESKAELADHQKPCSTP HSAFSMVEEDFQQKLESENDLQ EIHTIQECKECDQVFPDLQSLEK HMLSHTEEREYKCDQCPKAFN WKSNLIRHQMSHSDSKHYECE NCAKVFTDPSNLQRHIRSQHVG ARAHACPECGKTFATSSGLKQ HKHIHSSVKPFICEV (SEQ ID NO: 133)
C11orf79_ Exon3_ C11orf66_ Exon5	NM_017841.1	NM_145017.1	MAVSTVFTSSMLALSRHSL LSPLL SVTSFRFRYRGDSPTDS QKDMIEIPLPPWQERTDESIET KRARLLYBSRKRKMLENCILL SLFAKEHLQHMTEKQLNLYD RLINEPSNDWDIYWAT (SEQ ID NO: 134)	GPEGPFRHPGARASGHHGAGA QGSASAPPAAGPGPAGAGELPT WPTLHDVGVQFQVVSQGPSRPA RFLAEEIDRRKGGEWLHQTVPP EPHCLPTALTGPPWGPCPPRPE CHQVRLPPQDSPTWR (SEQ ID NO: 135)
ABHD14A_ Exon3_ ACY1_ Exon2	NM_015407.3	NM_000666.13	MVGALCGCWFRLLGGARPLIP LGPTVVQTSMSQSQVALLGL SLLMLLLLYVGLPGPPEQTS LWGDPNVTVLAGLTPGNSPIF YREVLPLNQAHREVVVLLHG KAFNSHTWEQLGTLQLLSQR GYRAVALDLP (SEQ ID NO: 136)	AHHAQRHDQQGSRGGAPIGDA LPPVPAYPHCPAQA (SEQ ID NO: 137)
RBM14_ NA_RBM4_ Exon2	NM_006328.3	NM_002896.2	MKIFVGNVDGADTTPPELAA LPAPYGTVMSCAVMKQPAFV HMRENAGALRAIEALHGHEL RPGRALVVMMSRPRPLNTWK IFVGNVSAACTSQELRSLFER RGRVIECDVVK (SEQ ID NO: 138)	GSCQDGEAVHRKPAPGGYRAG DSLTLRAVWEGAGM (SEQ ID NO: 139)
C20orf29_ Exon2_ VISA_ Exon2	NM_018347.1	NM_020746.3	MVHAFLIHTLRAPNTEDTGLC RVLYSCVPGAESKSPDDPRPH GAERDRLLRKEQILAVA (SEQ ID NO: 140)	SLVSSQSIHPSWGQSPLSRI (SEQ ID NO: 141)

TABLE 7-continued

Trans-splicing ID	up-stream gene ACC#	down-stream gene ACC#	up WT sequence	down stream FS sequence
RRM2_ Exon9_ C2orf48_ Exon2	NM_001034.1	NM_182626.1	<p>MLSLRVPLAPI TDPQQLQLSP LKGLSLVDKENTPPALSGTRV LASKTARRIFQEPTPEPKTKAA APGVEDEPLLRNPRRPFVIFPI EYHDIWQMYKKAASFWTA EEVDLSKDIQHWESLKPPEERY FISHVLAFFAASDGIVNENLV ERFVSQEVQITEARCFYGFQIA MENIHSEMYSLIDTYIKDPK EREFLFNAIETMPCVKKKAD WALRWIGDKEATYGERVVA FAAVEGIFPFGSFAPIFWLKKR GLMPGLTFSNELISRDEGLHC DFACLMFKHLVHKPSEERV EIIINAVRIEQEFLTEALPVKLI GMNCTLMKQYIEFVADRLML ELGFSKV</p>	<p>LG DREVQSRWSPGPRGDSTPVR EMETNHPPSVRG (SEQ ID NO: 143)</p> <p>(SEQ ID NO: 142)</p>
ELAC1_E Exon2_ SMAD4_ Exon2	NM_018696.2	NM_005359.5	<p>MSMDVTFVLGTGAAYPSPTRG ASAVVLRCEGECWLFDCGEG TQTQLMKSQLKAG (SEQ ID NO: 144)</p>	<p>YPEYMSNNPCNVSCCFSLFPK DQNCFRNWRHI (SEQ ID NO: 145)</p>
BCAS4_ Exon1_ BCAS3_ Exon24	NM_001010974.1	NM_001099432.1	<p>MQRTGGGAPRPRGNHGLFPGS LRQDPVALLMLLVADADQPE PMRSGARELALFLTPEPGAE (SEQ ID NO: 146)</p>	VPLTGA (SEQ ID NO: 147)
C22orf39_ Exon2_ HIRA_ Exon2	NM_173793.3	NM_003325.3	<p>MADGSGWQPPRCEAYRAE WKLCSARHFLHHYVHGE RPACQWQRDLASCRDWE RRNAEAQ (SEQ ID NO: 148)</p>	<p>ASRFFQLIFTLTGPSSQLEDKGR ILGRL (SEQ ID NO: 149)</p>
PMF1_ Exon4_ BGLAP_ Exon4	NM_007221.2	NM_199173.3	<p>MAEASSANLGSCEEKREHEG SSSESVPPGTTISRVLKLDTM VDTFLQKLVAAAGSYQRFTDC YKCFYQLQPAMTQQIYDKFI AQLQTSIREIISDIKEEGNLEA VLNALDKIVEEGKVRKEPAW RPSGIPEKDLHSMAPYFLQQ RDTLRRHVQKQEAENQQLAD AVLAGRQVEELQLQVQQAQ QQAWQ (SEQ ID NO: 150)</p>	<p>VRSPAVQSPAKVQPLCPSRRAA R (SEQ ID NO: 151)</p>
SDHD_ Exon3_ TEX12_ Exon3	NM_003002.1	NM_031275.4	<p>MAVLWRLSAVCGALGGRAL LLRTPVVRPAHISAFQDRPIP EWCQVQIHLSPSHHSKSA ASLHWTSEVVSVLLGLLP AAYLNPCSAMDYSLAAALTL HGH (SEQ ID NO: 152)</p>	<p>CLQCQIVHSCPLENQIHLSLKP PDYFIKMKPWRKI (SEQ ID NO: 153)</p>
PRR13_ Exon3b_ PCBP2_ Exon2	NM_001005354.2	NM_001128914.1	<p>MWNPNAGGPPHPVPQPGYPG CQPLGPPPPYPAPGIPPVN PLAPGMVGPVIVDKMKQK KMKKAHKMKHKQKHKY HKHGK (SEQ ID NO: 154)</p>	FLAFTPNQ (SEQ ID NO: 155)
RMND5A_ Exon2_ ANAPC1_ Exon25	NM_022780.2	NM_022662.2	<p>MDQCVTVERELEKVLHKFSG YGQLCERGLEELIDYTGGLK HEILQSHGQDAELSGTSLVL TQCKRKIKDTVQKLDHDKDI HSSVSRVGAIDK (SEQ ID NO: 156)</p>	DSL (SEQ ID NO: 157)
TYMP_ Exon9_ SCCO2_ Exon2	NM_001113756.1	NM_005138.2	<p>MAALMTPGTGAPPAGDFSG EGSQGLPDPSPPEKQLPELIR MKRDGGRLEADIRGFVA AVVNGSAQGAQIGAMLMAIRLR GMDLEETSVLTQALAQSGQQ LEWPEAWRQQLVDKHSSTGG VGDKVSLLVAPALAACGCKV</p>	ASDPCCC (SEQ ID NO: 159)

TABLE 7-continued

Trans-splicing ID	up-stream gene ACC#	down-stream gene ACC#	up WT sequence	down stream FS sequence
			PMISGRGLGHTGGTLDKLESI PGFNV IQSPEQMQLLDQAG CCIVGQSEQLVPADGILYAAR DVTATVDSLPLITASILSKKLV EGLSALVVDVKFGGAAVFPN QEQARELAKTLVGVGASLGL RVAAALTAMDKPLGRGVGH ALEVEEALLCMDGAGPPDLR DLVTTLGGALLWLSGHAGTQ AQGAARVAAALDDGSALGR FERMLAAQGVDPGLARALCS GSPAERRQLLPRAREQEELLA PADGTVELVRALPLALVLHE LGAGR SRAGEPLRLGVGAEL LVDVGQRLRRG (SEQ ID NO: 158)	
NAIP_ Exon13_ OCLN_ Exon5	NM_ 004536.2	NM_ 002538.2	MATQQKASDERISQFDHLL PELSALLGLDAVQLAKELEEE EQKERAKMQKGYNSQMRSE AKRLKTFVITYEPYSSWIPQEM AAAGPYFTGVKSGIQPCCSL ILFGAGLTRLP IEDHKRFHPDC GFLLNKDVGNIAKYDIRVKN LKSRLRGKMR YQEEEARLA SPFNWPFVYVQGISPCVLS EAG FVFTGKQDTVQCFCGGCLG NWEEGDDPWKEHAKWFPKC EFLRSKKSSEEITQYIQSYKGF VDITGEHFPVNSWVQRELPMA SAYCNDSIFAYEELRLDSFKD WPRESAVGVALAKAGLFYT GIKDIVQCFSCGGCLEKWQE GDDPLDDHTRCFPNCP LQN MKS SAEVTPDLQSRGELCELL ETTSESNLEDS IAVGPIVPEMA QGGAQWFQEAKNLNEQLRA AYTSASFRHMSLLDISDLAT DHLLGCDLSIASKHISKPVQE PLVLP EVFGNLNSVMCVEGE AGSGKTVLLKKIAPLWASGC CPLLNRQLVFYLSSLSTRPD EGLAS IICDQLEKEGSVTEM CVRNIIQQLKNQVLFLLDDYK EICSIPQVIGKLIQKNHLSRTC LLI AVRTNRARDIRRYLETILE IKAFPYNTVCILRKLFSHNM_ TRLRKFVYFVKQNSLQKIQ KTPLFVAAI CAHWFPYFPDPS FDDVAVFKSYMERLSLRNKA TAEILKATVSSCGELALKGFF SCCFEFDDDLAAGVDEDE DLTMCLMSKFTAQRLRPFYR FLSPAFQEF LAGMRLIELLDS DRQEHQDLGLYHLKQINSPM MTVSA YNNFLNYVSSL PSTK AGPKIVSHLLHLVDNKESLEN ISENDY LKHQPEISLQMQLL RGLWQICPQAYFSMVSEHLL VLALKTAYQSNVAACSPFV LQFLQGR TLTGALNLQYFFD HPESLSLLRSIHFP IRGNKTS RAHFSVLETCFDPKSQVPTIDQ DYASAFEPMNEWERNLAEKE DNVKS YMDMQRAS PDLST GYWKLSPKQYKIPCLEVDVN DIDVVGQDMLEILMTVFSAS QRIELHLNHSRGFIESIRPALE	G (SEQ ID NO: 161)

TABLE 7-continued

Trans-splicing ID	up-stream gene ACC#	down-stream gene ACC#	up WT sequence	down stream FS sequence
			LSKASVTKCSISKLELSAAEQ ELLTLPLSLESLEVSGTIQSQD QIFPNLDKFLCLKELSVDLEG NINVFSVIPEEFPNFHHMEKLL IQISAEYDPSKL (SEQ ID NO: 160)	
Clorf151 _Exon1_ NBL1_Exon3	NM_ 001032363.1	NM_ 182744.2	MSESELGRKWDRCLADAVV KIG (SEQ ID NO: 162)	LWRPRA (SEQ ID NO: 163)
DDIT3_ ^Exon3_ MARS_ ^Exon21	NM_ 004083.4	NM_ 004990.2	MAAESLPFSFGTLSSWELEA WYEDLQEVLLSSDENGGYVVS PP (SEQ ID NO: 164)	LPLGASGGPPSATANCFFRSKSF ATSAATSFLSAFCAFSSRTMFPC FVTSSISACICCGLAVVTVSTTA GFGDVFAWPPPKRCKLSIWSF SNFWNKGLTVPIWCPAGKVHR KFVSRILQAGGSCSWAWIVAL TVGM (SEQ ID NO: 165)
RIPK3_ Exon9_ADCY4_ Exon2	NM_ 006871.3	NM_ 139247.2	MSCVKLWPSGAPAPLVSIEEL ENQELVGGGFGTVFRAQHR KWGYDVAVKIVNSKAI SREV KAMASLDNEFVLRLEGVIEK VNWDQDPKPALVTKFMENG SLSGLLQSQCPRPWFLLCRL KEVVLGMFYLDHQNFLVLR DLKPSNVLLDPELVHVKLADF GLSTPQGGSQSGTSGEPGGT LGYLAPELFVNVRKASTAS DVYSFGILMWAVALAGREVEL PTEPSLVYEAVCNRQNRPSLA ELPQAGPETPGLLEGLKELMQL CWSSEPKDRPSFQECLPKTDE VFQMVENNNAAVSTVKDF LSQLRSSNRFPISIPESGQGGTE MDGFRRTIENQHNRNDVMVS EWLNKLNLEPPSSVPKCCPS LTKRSRAQEEQVPQAWTAGT SSDSMAQPPQTPETSTFRNQM PSPTSTGTSPGPRGNQGAER QGMNWSCRTPEFNPVTG (SEQ ID NO: 166)	ADLRPELDPDHCAVRAGRLAA AGPRFPGAATAALDASPVRG MGRAASARPRLPVHRGRGERL GPGVLFSLRHLHGVCCHAALGH AGRRRRGPRLTLASAGPRAVS WATAGLTACTAAAVGSKRSV PVRERGRSVPQADGARPAGH VPGGTQLPALTPAAGHREAPG TPSLVHPSCLPGPRDEGRDHGT AAGRTGVTAREH (SEQ ID NO: 167)
COMMD3_ Exon1_ BMI1_Exon2	NM_ 012071.2	NM_ 005180.5	MELSEVQKGFQMLADPRSF DSNAFTLLRAAFQSLDDAQ ADEAVL (SEQ ID NO: 168)	GFFIKQKCIQRESRSL (SEQ ID NO: 169)
MED8 #x0n7c_ ELOVL1_ Exon2	NM_ 052877.3	NM_ 022821.2	MQREEKQLEASLDALLSQVA DLKNSLGSFICKLENEYGRLT WPSVLDSFALLSGQLNTLNK VLKHEKTPFRNQV I I PLVLS DRDEDLMRQTEGRVPVFSHE VVPDHLRTPKDEVEEQEKQ LTTDAARIGADAAQKIQSLN KMCSNLEKISKEERESESGG LRPNKQTFNPTDTNALVAAV AFGKGLSNWRPSSGSGPGQA GQPGAGTILAGTSGLQQVQM AGAPSQQQPMLSGVQMAQA GQPGKMPSGIKTNIKSASMHP YQR (SEQ ID NO: 170)	VLSQDGGCCELVPRGDEARRSP DPGLPSDGVPLANDLHSPDLRV LRSLTWASHHG (SEQ ID NO: 171)
POLR2J3- ^Exon2_ UPK38_ ^Exon7	NM_ 001097615.1	XM_ 001717094.1	MNAPPAFESFLLEPEGEKITINK DTKVPNACLFMTNKEDHTLG NIIKS (SEQ ID NO: 172)	RACPPFAFCRDCQFPEASPATLS VQPAEL (SEQ ID NO: 173)
BGLAP_ ^Exon2_ pMF1_ ^Exon5	NM_ 199173.3	NM_ 007221.2	MAEASANLGSCEEKRHEG SSSESVPPTTISRKLLDTM VDTFLQKLVAAVGSYRPTDC YKCFYQLQPAMTQQIYDKFI AQLQTSIREEISDIKEGNLEA	VRSPAVQSPAKVQPLCPSRRAA R (SEQ ID NO: 175)

TABLE 7-continued

Trans-splicing ID	up-stream gene ACC#	down-stream gene ACC#	up WT sequence	down stream FS sequence
			VLNALDKIVEEGKVRKEPAW RPSGIPEKDLHSMAPYFLQQ RDTLRRHVQKQEAENQQLAD AVLAGRRQVEELQLQVQAO QQAWQ (SEQ ID NO: 174)	
TMEM199_ Exon5_ SARM1_ Exon2	NM_ 152464.1	NM_ 015077.2	MASSLLAGERLVRALGPGGE LEPERLPRKLRAELEAALGKK HKGDDSSSGPQRLVFSRLIRD LHQHLRERDSKLYLHELLEGS EIYLPFVVKPRNPPELVARLE KIKIQLANEYKRI TRNVTCQ DTRHGGLSDLGKQVRSKLA LVITIFNFIVTVVAAFVCTYLG SQYIFTEMASR (SEQ ID NO: 176)	PRGAHWAGRDPEPGEGRTRR AGAERGRHLGAHVQAFGGDM PEAGGRRRPGRGAVLVPPHGP RAAAPLRAGAGQLRAARGP AATHGREARSRVLPARLLQG GRAASAARLPRSSGVGD (SEQ ID NO: 177)
C1QTNF6_ Exon2_ IL2RB_ Exon2	NM_ 182486.1	NM_ 000878.2	MQWLRVRESPGEATGHRVT MGTAALGPVWAAALLFLLM CEIPMVELTFDRAVASGCQRC CDESDPLDPAHVSSASSGRF HALPEIRPYINITILKG (SEQ ID NO: 178)	LPSSAPPCGNGGPCSVLASAPP HPPPAGYLLGICSGEWHFPVH MLLQLESQHLLCLEPRWGSAG HFLPSPCLAGQTAVEPNL (SEQ ID NO: 179)
LOC100131434_ NA_ FLJ44451_ NA	XM_ 001713865.1	XM_ 001714058.1	MDPASRGCLGPTPAFRHRKE QSSASPRPSEATGARTMGSQA RRPPVIPPTKNETLFLSLPGPDA RQPTRPRPGDLETGSLDEEPE GGKGTGGRKISRIDFITKFWV PASGVPEDETKRLLVLHPRCYF QNSGLVVWSLHCMSLLSNL ESSVFLPSVRCAYFSLKLEE AGMLEM (SEQ ID NO: 180)	RPSTPCLHGAALHLHSGHSGS RLTNSSCFPGTRRLALQFTQQ TGTVGHPTWQPVIR (SEQ ID NO: 181)
COX19_ Exon2_ CENTA1_ Exon2	NM_ 001031617.2	NM_ 006869.2	MSTAMNFGTKSFQPRPPDKG SFPLDHLGECESFKEKFMKCL HNNNFENALCRKESKEYLEC RMER (SEQ ID NO: 182)	SRLGLLHSGRLHLPELLGNPPE YPPGQQGEVRRPGRLLGGPSPGV HGLPRERRRESQV (SEQ ID NO: 183)
ACSF2_ Exon10_ CHAD_ ^Exon4	NM_ 025149.4	NM_ 001267.2	MAVYVGMRLRGLRCAGSSG VLGARAALRSRWQEARLQGV RFLSSREVDRMVSTPIGGLSY VQGCTKHLNSKTGVQCLET TAQRVPEREALVVLHEDVRL TFAQLKEEVDKAASGLLSIGL CKGDRLGMWGPNSYAWVL MQLATAQAGIILVSVNPAYQ AMELEYVLKVKCKALVFPK QPKTQYYNVLKQICPEVEN AQPALKSQRLPDLTTVISVD APLPGTLLEDEVVAAGSTRQ HLDQLQYNQQFLSCHDPINIQ FTSGTTGSPKATLSHYNIVN NSNILGERLKLHEKTPQLRM ILFNPLYHCLGSGVAGTMMCL MYGATLILASPIFNGKKALEA ISRERGTFLYGTPTMFVDILN QPDFSSYDISTMCGGVIAGSP APPELLIRAIINKINMKDLV (SEQ ID NO: 184)	RNLRKKLQHGKMDSKAPMSC (SEQ ID NO: 185)
TIMM23_ B_ NA_ LOC100132418_ NA	XM_ 928114.3	XM_ 001719607.1	MEGGGGSGNKTGGLAGFFG AGGAGYSHADLAGVPLTGM NPLSPVLNVDPRLVQDTDEF ILPTGANKTRGRFELAFFTIGG CCMTGAAPGAMNGLRLGLK ETQNMMAWSKPRNVQILNMV TRQGALWANTLGSLLALYSA FGVIIKTRGAEDDLNTVAAG TMTGMLYKCT (SEQ ID NO: 186)	VSEMALDSPFCVLLSGS (SEQ ID NO: 187)

TABLE 7-continued

Trans-splicing ID	up-stream gene ACC#	down-stream gene ACC#	up WT sequence	down stream FS sequence
NDUFA13_ Exon4_ YJEPN3_ Exon2	NM_015965.5	NM_198537.2	MQEPRRVTPCLGKRGVKTPQ LQPGSAFLPRVRRQSFPARSD SYTTVRDLAVPRTISSASATL IMAVAVSHFRPGPEVWDTAS MAASKVKQDMPPPGGYGID YKRNLPRRGLSGYSMLAIGIG TLIYGHWSIMKWRERRRLQ IEDFEARIALPLLQAETDRRT LQMLRENLEEEAIIMKDVDP WK (SEQ ID NO: 188)	GLGAAAPTCRHGKSGA (SEQ ID NO: 189)
ADHFE1_ Exon13_ C8orf46_ NA	NM_144650.2	NM_152765.3	MAAARARVAYLLRQLQRA ACQCPHTSHTYSQAPGLSPSG KTDTYAFEMAVSNIRYGAAV TKEVGMDLKNMGAKNVCML TDKNLSKLPVQVAMDSLK NGIPTVYDNRVEPTDSSFM EAIEFAQKGFADYAVVAVGGG STMDTCKAANLYASSPHSDF LDYVSAPIGKGPVSVPLKPL IAVPTTSGTSETTGVAIFDYE HLKVKIGITSRRAIKPTLGLIDP LHTLHMPARVVANSQFDVLC HALESYTTLPYHLRSPCPSNFI TRPAYQGSNPISDIWAHALRI VAKYLKRAVRNPDDEARSH MHLASAFAGIGFGNAGVHLC HGMSYPI SGLVKMYKAKDY NVDHPLVPHGLSVLTS PAVF TFTAQMPPERHLEMAEILGA DTRTARIQDAGLVLADTLRK FLFDLDVDDGLAAVGYSKAD IPALVKGTLPQ (SEQ ID NO: 190)	YPVQPEEBPKALSTS (SEQ ID NO: 191)
HPS4_ Exon13_ ASPHD2_ ^Exon4	NM_022081.4	NM_020437.4	MATSTSTEAKSASWNYFFL YDGSVKKEGDPTRAGICYF YPSQTLDDQELLCCQIAGVV RCVSDISDSPPTLRLRKLKF AIKVDGDLWVLGC AVELPD VSCRFDLQLVGFNFYNGP VSLAYENCQEELSTEWDTFI EQILKNTSDLHKIPNSLWNL QTKVEPLLLK AARILQTCQR SPHILAGCILYKGLIVSTQLPP SLTAKVLLHRTAPQEQLPTG EDAPQEHGAALPPNVQIIPVF VTKEAISLHEFPVEQMTRSL ASPAGLQDGS AQHHPKGGST SALKENATGHVESMAWTPD PTSPDEACPDGRKENGCLSGH DLESIRPAGLHNSARGEVLGL SSSLGKELVFLQEELDLSEIHI PEAQEVEMASGHFAFLHVPV PDGRAPYCKASLSASSLEPT PPEDTAISSLRPPSAPEMLTQH GAQEQLLEDHPGHSSQAPI PRA DPLPRTRRPLLLPRLDFGQR GNKLPTEQGLDEDVDGVCE SHAAPGLECSSGSANCCGAG PSADGISSRLTPAESCMGLVR MNLTYHCVKGLVLSLLAEEP LLGDSAAIEEVYHSSLASLNG LEVHLKETLPRDEAASTSSTY NFTHYDRIQSLMANLPQVA TPQDRRFLQAVSLMHSEFAQ LPALYEMTV (SEQ ID NO: 192)	SNSCTS (SEQ ID NO: 193)

TABLE 7-continued

Trans-splicing ID	up-stream gene ACC#	down-stream gene ACC#	up WT sequence	down stream FS sequence
KIAA1267_ Exon2 ARL17P1 _Exon3	NM_ 015443.2	NM_ 001113738.1	MAAMAPALTDAAAEAHHIRF KLAPSSTLSPGSAENNGNAN ILIAANGTKRKAIAAEDPSLDF RNNPTKEDLGKLPVIVASYL CSDVTSVPSKESLKLQGVFSK QTVLKSHPLLSQSYELRAELL GRQPVLEFSLNLRMTMNTSG QTALPQAPVNGLAKKLTSS THSDHDNSTSLNGGKRALTSS ALHGGEMGGESGDLKGGM TNCTLPHRSLDVEHTTLYSNN STANKSSVNSMEQPALQSS RLSPGTDSSSNLGGVKLEGKK SPLSSILFSALDSDTRITALLRR QADIESRARRLQKRLQVVQA KQVERHIQHQLGGPLEKTLK LPNLESRLRPSQLMLTRKAEA ALRKAASETTTSEGLSNFLKS NSISELERFTASGIANLRCSE QAFDSVTDSSSGGESDIEE ELTRADPEQRHVPLRRSEW KWADRAAIVSRWNWLOAH VSDLEYRIRQQTDIYKQIRAN K (SEQ ID NO: 194)	VSVWRQ (SEQ ID NO: 195)
LOC100129406_ NA CTTNP2NL_ NA	XM_ 001722372.1	NM_ 018704.2	MAGRPGSQEQSKDRGTGSLP PPSQRPPLGSPGAGPSPPPP IPRGGSSSSSEGPSYPLSLVD SQLLRGPFPLTFLIQRHLPPRT SALAERTH (SEQ ID NO: 196)	SIGHISTMLMAF (SEQ ID NO: 197)
RNF216_ Exon7 RBAK_ Exon2	NM_ 207116.1	NM_ 021163.3	MEEGNNNEEVIHLNPFCHR GQEWLNLRDGPITISDSSDEER IPMLVTPAPQQHEEEDLDD VILTEDDSEDDYGEFLDLGPP GISEFTKPSGQTEREPKPGPSH NQAANDIVNPRSEQKVIILEE GSLLYTESDPLETQNSSEDS ETELLSNLGESAALADDQATE EDCWLDHPYFQSLNQQPREIT NQVVPQERQPEAELGRLLFQ HEFPGPAPFRPEPQQGGISGFS SPQPAHPLGEFEDQQLASDDE EPGPAFPMQESQEPNLENIWG QEAAEVDQELVELLVKTEA RFPDVANGFIEEIIHFKNYYDL NVLNCFLENPDYPKREDRII NPSSSLASQDETKLPKIDFFD YSKLTPLDQRCFIQAADLLM ADFKVLSQDIKWALHELK HYAITRK (SEQ ID NO: 198)	VYQPQSLHVKSSRK (SEQ ID NO: 199)
DEDD_ Exon4 NIT1_ Exon6	NM_ 032998.2	NM_ 005600.1	MAGLKRRASQVWPEEHGEQ EHGLYSLHRMFDIVGTHLTH RDVRLSPLFVDVIDDHERGL IRNGRDFLLALERQGRCDEN FRQVLQLLRITRHDLLPYVTL KRRA (SEQ ID NO: 200)	APSGLGL (SEQ ID NO: 201)
RAD54B_ Exon3 LOC100128414_ NA	NM_ 012415.2	XM_ 001722896.1	MRRSAAPSQLQNSFKKPKFI PPGRSNPGLNEEITKLNPDIKL FEGVAINNTFLPSQMDLRICSL NLPSEESTREINNRDNCSEK CFEAPTATLDPPHTV (SEQ ID NO: 202)	QTMRRHRLVPVHYR (SEQ ID NO: 203)
TOPORS_ Exon2 DDX58_ Exon2	NM_ 005802.2	NM_ 014314.3	MGSQPPLGSPLSREEGEAPP APASEGRRRRRVRRLRGS HRPSFLGCRELAASAPARPAP ASSE (SEQ ID NO: 204)	KRCSIFRLRKTTRAQWRP SSCSWSSRRKAGSVAFWMP (SEQ ID NO: 205)

TABLE 7-continued

Trans-splicing ID	up-stream gene ACC#	down-stream gene ACC#	up WT sequence	down stream FS sequence
NDUFC2 _Exon2_ KCTD14_ Exon2	NM_ 004549.4	NM_ 023930.3	MIARRNPEPLRFLPDEARSLPP PKLTDPRLLYIGFLGYCSGLID NLIRRRPIATAGLHRQLLYITA FFPAGYYLVKREDYLYAVRD REMFQYMKLHPEDPFEEED (SEQ ID NO: 206)	VYCCGAERRG (SEQ ID NO: 207)
LRRC57 ^Exon5_ SNAP23_Exon8	NM_ 153260.2	NM_ 003825.2	MGNSALRAHVETAQKTGVF QLKDRGLTEFPADLQKLTSNL RTIDLSENKIESLPFLIGKFTL LKSLSLNNKLTVPDEICNL KKLETLSLNNHRLPSTFG QLSALKTSLSGNQLGALPPQ LCSLRHLDMVLSKNQIRISIP DSVGEQVIELNINQNISQIS VKISCCPRLKILRL (SEQ ID NO: 208)	SALSVIRFICGF (SEQ ID NO: 209)
IPO11_NA_ SLRN_ NA	NM_ 001134779.1	NM_ 181506.4	MVQPIIHLGYVVYSLLYLGY KPVQHVLTALNTVSSCHMVS MDLNSASTVVLQVLTQATSQ DTAVLKPAEEQLKQWETQPG FYSVLLNIFTNHTLDINVRWL AVLYFKHGIDRYWRRVAPHA LSEEEKTLRAGLITNFNEPIN QIATQIAVLIAKVARLDCPRQ WPELIPTLIESVKVQDDLROH RALLTFFYHVTKTLASKRLAA DRKLFYDLASGIYNFACSLW NHHTDTFLQEVSSGNEAAILS SLERTLLSLKVLKLTVNGFV EPHKNMEVMGFLHGIFERLK QFLECSRSIGTDNVCRRLEK TIIILFTKVLDFLDQHPFSFTP LIQRSLEFSVSVYFTEVGEV TFERFIVQCMNLKMIVKNYA YKPSKNFEDSSPETLEAHKIK MAFFTYPPLTEICRRLVSHYF LLTEBELTMWEEDPEGFTVEE TGGDSWKYSLRPTCEVLFIDI FHEYNTLTPVLEMMQTLQ GPTNVEDMALLIKDAVYNA VGLAAYELFDSVDPDQWFKN QLLPELQVIHNRKPLRRRVI WLIQQWISVKFKSDLRPMPLY EAI CNLLQDQDLVVRIETAT LKLTVDDFEFRDQFLPYLET MFTLLFQLLQVTECDTKMH VLHVLSCVIERVNMQIRPYVG CLVQYLPLLWKQSEEHNNLR CAILTTLIHLVQGLGADSKNL YPFLLPVIQLSTDVSPPHVY LLEDGLELWLVTLNENPCITP ELLRIFQNMSPLELSENLR CPKIINGYIFLSSTEFLQTYAV GLCQSFCELLKEITTEGQVQV LKVVENALKVNPILGPQMFQ PILPYVFKGIEGERYPVVMST YLGVMGRVLLQNTSFFSLL NEMAHKFNQEMDQLGNMI EMWVDRMDNITQPERRKL LALLSLLPSDNS (SEQ ID NO: 210)	LASKGP (SEQ ID NO: 211)
SNRPF_ Exon2_ CCDC38_ ^Exon12	NM_ 003095.2	NM_ 182496.1	MSLPLNPKPFLNGLTGKPV VKLKWGMEYKGYLVSV MNMQ (SEQ ID NO: 212)	QDFHLHLGNIETK (SEQ ID NO: 213)

TABLE 7-continued

Trans-splicing ID	up-stream gene ACC#	down-stream gene ACC#	up WT sequence	down stream FS sequence
RNF139_	NM_007218.3	NM_005005.2	MAAVGPPQQQVRMAHQQV	ETNTDTLLV (SEQ ID NO: 215)
Exon1_ NDUFB9_ Exon2			WAALEVALRVPCLYIIDAI SYPDSSQSRFCIVLQIFLRL (SEQ ID NO: 214)	
NDUPB8_ Exon4_ SEC31B_ Exon2	NM_005004.2	NM_015490.3	MAVARAGVLGVQWLQRASR NVMLPGARTASHMTKDMFP GPYRTPBERAAAAKKYNMR VEDYEFYPDDGMGYDYPK LPDRSQHERDWPYSDQFGL RLNWGEPMHWHLDMYNRN RVDTSPTPVSWHVMCMQLFG FLAFMIFMCWGDVYPVYQP V (SEQ ID NO: 216)	DRP (SEQ ID NO: 217)
MIA_ Exon3_ RAB4B_ Exon2	NM_006533.2	NM_016154.3	MARSLVCLGVIIILLSAFSGPG VRGGPMPKLADRKLCAEQEC SHPISMAVALQDYMAPDCRF LTIHRGQVVYVFSKLGKGRGR LFWGGSVQGDYDGLAARL GYFPSSIVREDQTLKPKGV KTD (SEQ ID NO: 218)	TSSNSW (SEQ ID NO: 219)
THAP2_ Exon2_ TMEM19_ Exon2	NM_031435.2	NM_018279.3	MPTNCAAGCATTYNKHINI SFHRFPLDPKRKEWVRLVR RKNFVPGKHTFLCSKHFEASC FDLTGQTRRLKMDAVPTIFDF CTHIKSM (SEQ ID NO: 220)	VTYDLFLRGVGCFLLLFLF (SEQ ID NO: 221)
NIT1_ Exon6_DEDD_ Exon4	NM_005600.1	NM_032998.2	MLGFITRPPHRLSLLCPGLRI PQLSVLCAQPRPRAMAISSSS CELPLVAVCQVTSPTDKQQN FKTCAELVREARLGACLAF LPEAFDFIARDPAETLHLSEPL GKLLLEEYTLARECGLWLS LGGFHERGQDWEQTQKIYNC HVLNLSKGAVVATYRKTFLC DVEIPGQGMCESNSTMPGPS LESPVSTPAGKIGLAVCYDMR FPELSLALAQAGAEILTYPSAF GSITGPAHWE (SEQ ID NO: 222)	QPVSS (SEQ ID NO: 223)

[0213] While preferred embodiments of the present invention have been shown and described herein, it will be obvious to those skilled in the art that such embodiments are provided by way of example only. Numerous variations, changes, and substitutions will now occur to those skilled in the art without departing from the invention. It should be

understood that various alternatives to the embodiments of the invention described herein may be employed in practicing the invention. It is intended that the following claims define the scope of the invention and that methods and structures within the scope of these claims and their equivalents be covered thereby.

SEQUENCE LISTING

```

<160> NUMBER OF SEQ ID NOS: 223

<210> SEQ ID NO 1
<211> LENGTH: 19
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic Oligonucleotide

<400> SEQUENCE: 1

tgccataacct gtttttccc
    
```

-continued

<210> SEQ ID NO 2
<211> LENGTH: 22
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic Oligonucleotide

<400> SEQUENCE: 2

agttatctca ggtaggtggt gc 22

<210> SEQ ID NO 3
<211> LENGTH: 18
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic Oligonucleotide

<400> SEQUENCE: 3

aaggaggtct gtggttga 18

<210> SEQ ID NO 4
<211> LENGTH: 19
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic Oligonucleotide

<400> SEQUENCE: 4

caaagagga agagagtg 19

<210> SEQ ID NO 5
<211> LENGTH: 22
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic Oligonucleotide

<400> SEQUENCE: 5

aaagaaaag ctgaaagtgg aa 22

<210> SEQ ID NO 6
<211> LENGTH: 22
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic Oligonucleotide

<400> SEQUENCE: 6

gcaacagcaa ggagaagaat ac 22

<210> SEQ ID NO 7
<211> LENGTH: 18
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic Oligonucleotide

<400> SEQUENCE: 7

aaggaggtct gtggttga 18

<210> SEQ ID NO 8
<211> LENGTH: 19

-continued

<212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic Oligonucleotide
 <400> SEQUENCE: 8
 caaagagggga agagagtgg 19

<210> SEQ ID NO 9
 <211> LENGTH: 17
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic Oligonucleotide
 <400> SEQUENCE: 9
 ctgtcatggg tttcctg 17

<210> SEQ ID NO 10
 <211> LENGTH: 17
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic Oligonucleotide
 <400> SEQUENCE: 10
 gagctgtcct ctccctg 17

<210> SEQ ID NO 11
 <211> LENGTH: 22
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic Oligonucleotide
 <400> SEQUENCE: 11
 cctgaaactg attgagattg ag 22

<210> SEQ ID NO 12
 <211> LENGTH: 20
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic Oligonucleotide
 <400> SEQUENCE: 12
 ttttcagcct tcaccatttc 20

<210> SEQ ID NO 13
 <211> LENGTH: 20
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic Oligonucleotide
 <400> SEQUENCE: 13
 ccaaccgtga aaagatgacc 20

<210> SEQ ID NO 14
 <211> LENGTH: 20
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic Oligonucleotide

-continued

<400> SEQUENCE: 14
 tgccaatagt gatgacctgg 20

<210> SEQ ID NO 15
 <211> LENGTH: 20
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic Oligonucleotide

<400> SEQUENCE: 15
 ccaaccgcca gaagatgacc 20

<210> SEQ ID NO 16
 <211> LENGTH: 20
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic Oligonucleotide

<400> SEQUENCE: 16
 tgccaatggt gatgacctgg 20

<210> SEQ ID NO 17
 <211> LENGTH: 20
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic Oligonucleotide

<400> SEQUENCE: 17
 atcggatgat tcggcgatat 20

<210> SEQ ID NO 18
 <211> LENGTH: 21
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic Oligonucleotide

<400> SEQUENCE: 18
 gtaacacagg cagatgtagg a 21

<210> SEQ ID NO 19
 <211> LENGTH: 25
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic Oligonucleotide

<400> SEQUENCE: 19
 caatggctct ggggtctgtg gaatc 25

<210> SEQ ID NO 20
 <211> LENGTH: 21
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic Oligonucleotide

<400> SEQUENCE: 20
 gggtcgacag attatcggac c 21

-continued

<210> SEQ ID NO 21
 <211> LENGTH: 20
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic Oligonucleotide

<400> SEQUENCE: 21

gtcataactcc tgcgccagct

20

<210> SEQ ID NO 22
 <211> LENGTH: 11
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic Peptide

<400> SEQUENCE: 22

Ser Pro Ser Gln Ala Met Trp Ala Thr Arg Met
 1 5 10

<210> SEQ ID NO 23
 <211> LENGTH: 28
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic Peptide

<400> SEQUENCE: 23

Gly Val Gly Gly Gly Ile Leu Pro Pro Glu Thr Pro Pro Val Ser Ala
 1 5 10 15

Trp Gly Glu Leu Cys Pro Pro Ala Trp Leu His Leu
 20 25

<210> SEQ ID NO 24
 <211> LENGTH: 40
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic Peptide

<400> SEQUENCE: 24

Arg His Glu Lys Cys Cys Asn Trp Lys Gln Gln Ala Glu Ser Gln Ser
 1 5 10 15

His Cys Phe Arg Ser Cys Ser Lys Ile Val Val Leu Ala Ser Ala Arg
 20 25 30

Asn Leu Lys His Arg Ala Glu Asn
 35 40

<210> SEQ ID NO 25
 <211> LENGTH: 22
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic Peptide

<400> SEQUENCE: 25

Thr Thr Asn Pro Ser Arg Ile Ser Leu Pro Ser Trp Val Trp Met Asn
 1 5 10 15

Phe Leu Arg Lys Thr Ser
 20

-continued

<210> SEQ ID NO 26
 <211> LENGTH: 38
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic Peptide

<400> SEQUENCE: 26

Asp His Gly Gly Val Gly Arg Cys Ser Asn Val Leu Pro Trp Glu Glu
 1 5 10 15

Gly Asp Ser Gln Arg His Lys Ala Arg Lys Ser Ala Leu Arg Ala Gln
 20 25 30

Gly Arg Ala Glu Asp Cys
 35

<210> SEQ ID NO 27
 <211> LENGTH: 53
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic Peptide

<400> SEQUENCE: 27

Trp Ser Cys Ser Ser Ile Thr Gly Ala Ala Gly Asn Leu Asn Thr Thr
 1 5 10 15

Ser Trp Ser Thr Arg Leu Trp Pro Asn Gly Arg Arg Lys Lys Leu Ser
 20 25 30

Ser Gly Trp Ser Ser Trp Ala Leu Gly His Leu Phe Thr Gly Lys Gly
 35 40 45

Phe Tyr Leu Asn Glu
 50

<210> SEQ ID NO 28
 <211> LENGTH: 30
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic Peptide

<400> SEQUENCE: 28

Phe Ser Leu Lys Met Ser Ser Tyr Pro Leu Leu Gly Leu Ile Met Lys
 1 5 10 15

Gly Asn Ser Phe His Asn Val Ile Pro Val Asn Ala Leu Thr
 20 25 30

<210> SEQ ID NO 29
 <211> LENGTH: 48
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic Peptide

<400> SEQUENCE: 29

Pro Cys Thr Gly Leu Ser Leu His Pro Met Ala Pro Arg Ile Trp Ser
 1 5 10 15

Arg Trp Ser Phe Pro Ala Gly Arg Cys Gln Asp Arg Pro Asn Lys His
 20 25 30

Val Trp Pro Pro Gln Lys Lys Lys Lys Lys Lys Lys Lys Lys Lys Lys
 35 40 45

-continued

<210> SEQ ID NO 30
 <211> LENGTH: 10
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic Peptide

<400> SEQUENCE: 30

Gly Ser Ala Asp Arg Asp Asp Gly Lys Val
 1 5 10

<210> SEQ ID NO 31
 <211> LENGTH: 35
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic Peptide

<400> SEQUENCE: 31

Cys Tyr Gln His Pro Phe Pro Lys Lys Ser Gln Phe Pro Gly Ala Tyr
 1 5 10 15

Trp Thr Ser Phe Glu Gly Glu Glu Gly Ser Gly Gln Leu Thr Leu
 20 25 30

Pro Gly Pro
 35

<210> SEQ ID NO 32
 <211> LENGTH: 28
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic Peptide

<400> SEQUENCE: 32

Gly Phe Ala Ala Ser Trp Leu Phe Lys Lys Pro Arg Pro Ser Glu Cys
 1 5 10 15

His Thr Val Ile Phe Lys Glu Glu Ser Tyr Met Asn
 20 25

<210> SEQ ID NO 33
 <211> LENGTH: 34
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic Peptide

<400> SEQUENCE: 33

Asp Ala Ala Phe Phe Met Ser Pro Lys Leu Ile Trp Trp Gln Glu Met
 1 5 10 15

Ala Thr Glu Arg Gly Leu Phe Gly Leu Glu Ile Pro Ile Ile Leu Lys
 20 25 30

Glu Leu

<210> SEQ ID NO 34
 <211> LENGTH: 9
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic Peptide

<400> SEQUENCE: 34

-continued

Cys Phe Thr Ser Ser Pro Leu Arg Trp
1 5

<210> SEQ ID NO 35
<211> LENGTH: 167
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic Peptide

<400> SEQUENCE: 35

Arg Val Gln Gly Thr Leu Val His Cys Pro Thr Arg His Leu Ser Gln
1 5 10 15

Arg Arg Gly Pro Gly Arg Gln Arg Gly Asn Ser Leu Pro Glu Pro Ser
20 25 30

Ser Met Leu Thr Cys Pro Gln Gln Pro His Arg Ala Thr Phe Pro Ala
35 40 45

Ala Pro Gly Leu Gln Gly Cys Pro Arg Thr Gly Pro Ser Gln Pro Ser
50 55 60

Met Gln Leu Pro Ser Tyr Pro Glu Asp Gly Ser Gly Leu Ser Arg Gly
65 70 75 80

His Lys Asp Val Arg Pro Gly Pro Pro Gly Gln Glu Arg Val Gln Val
85 90 95

Leu Arg Ala Cys Ala Pro Gln Pro Gln His Gln Val Asp Cys Ser Ala
100 105 110

Val Gly Gly Pro Val Ala Ala Arg Glu Lys Pro Pro Val Ser Arg Leu
115 120 125

Gly Ser Ala His Gln Gly Leu Pro Thr Ser Ala Phe Glu Gly Ala Cys
130 135 140

His Ala Leu Gly Asp Pro Gly Ile Phe Thr Gly Leu Glu Ala Gly Asp
145 150 155 160

Arg Thr Val Ser Val Pro Gly
165

<210> SEQ ID NO 36
<211> LENGTH: 15
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic Peptide

<400> SEQUENCE: 36

Cys Leu Gln Lys His Leu Pro Val Ala Leu Ser Thr Ser Leu Cys
1 5 10 15

<210> SEQ ID NO 37
<211> LENGTH: 18
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic Peptide

<400> SEQUENCE: 37

Met Thr Ser Leu Leu Ser Ser His His Pro Leu Lys Arg Arg Asn Leu
1 5 10 15

Glu Pro

-continued

<210> SEQ ID NO 38
<211> LENGTH: 15
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic Peptide

<400> SEQUENCE: 38

Leu Leu Ser Ser His His Pro Leu Lys Arg Arg Asn Leu Glu Pro
1 5 10 15

<210> SEQ ID NO 39
<211> LENGTH: 12
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic Peptide

<400> SEQUENCE: 39

Thr Ser Ala Ser Gln Ile Gln Ala Ile Leu Val Pro
1 5 10

<210> SEQ ID NO 40
<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic Peptide

<400> SEQUENCE: 40

Leu Leu Leu Gln Leu Arg Pro Gly Ser Arg Pro Phe Pro Val Thr Tyr
1 5 10 15

Val Ser Val Thr Gly Arg Gln Pro Tyr Lys Ser Trp
20 25

<210> SEQ ID NO 41
<211> LENGTH: 26
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic Peptide

<400> SEQUENCE: 41

Ala Ala Ala Ala Ala His His His Ser Pro Arg Pro Ala Ala Leu Arg
1 5 10 15

His Pro Gln Glu Glu Thr Gly Cys Val Pro
20 25

<210> SEQ ID NO 42
<211> LENGTH: 16
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic Peptide

<400> SEQUENCE: 42

Leu Leu Gln Pro Pro Phe Val Phe Ile Pro Pro Gly Cys Val Met Leu
1 5 10 15

<210> SEQ ID NO 43
<211> LENGTH: 12
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:

-continued

 <223> OTHER INFORMATION: Synthetic Peptide

<400> SEQUENCE: 43

Ser Pro Lys Leu Pro Leu Val Arg Arg Trp Met Gln
 1 5 10

<210> SEQ ID NO 44

<211> LENGTH: 61

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic Peptide

<400> SEQUENCE: 44

Leu Pro Cys Ser Ser Leu Thr Ser Tyr Trp Glu Met Leu Trp Leu Trp
 1 5 10 15

Leu His Asp Trp Arg Arg Arg Gln Gly Gln Arg Cys Ser Phe Trp Val
 20 25 30

Thr Gln Pro Thr Ala Ala Ala Ala Trp Met Cys Trp Val Leu Ser Lys
 35 40 45

Leu Glu Leu Arg Leu Ser Tyr Ile Leu Ala Leu Pro Ala
 50 55 60

<210> SEQ ID NO 45

<211> LENGTH: 22

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic Peptide

<400> SEQUENCE: 45

His Phe Pro Ala Cys Gln Leu Leu Pro Leu Cys Asp Leu Ile Ser Ser
 1 5 10 15

Ala Leu Pro Tyr Val Glu
 20

<210> SEQ ID NO 46

<211> LENGTH: 44

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic Peptide

<400> SEQUENCE: 46

Cys Leu Gln Asn Trp Trp Tyr Trp Tyr Cys Ser Cys Trp Pro Ser Gly
 1 5 10 15

Asp Trp Cys Ser Gln Thr Arg Tyr Gly Gly His Leu Cys Ser Ser Gln
 20 25 30

Arg Tyr Asn Gly Ser Lys Ile Cys Arg Asn Ala Pro
 35 40

<210> SEQ ID NO 47

<211> LENGTH: 10

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic Peptide

<400> SEQUENCE: 47

Gly Phe Trp Ser Arg Phe Pro Pro Pro Trp
 1 5 10

-continued

<210> SEQ ID NO 48
 <211> LENGTH: 39
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic Peptide

 <400> SEQUENCE: 48

 Val Ser Pro Gly Val Ser Glu Leu Arg Arg Asn Ser Lys Lys Tyr Gly
 1 5 10 15

 Lys Ala Gly Glu Ala Val Trp Phe Ser Ser Asp Pro Pro Val Leu Phe
 20 25 30

 Phe His Phe Leu Arg Thr Glu
 35

<210> SEQ ID NO 49
 <211> LENGTH: 101
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic Peptide

 <400> SEQUENCE: 49

 Val Leu Gly Ser Gln Arg His Pro Gly Gln Gly Ser Cys Gly Ser Cys
 1 5 10 15

 Pro Trp His Leu Cys Ser Ser Pro His Pro Thr Cys Gly Ser Gly Phe
 20 25 30

 Gly Thr Arg Ser Gly Arg Ala Gly Arg Arg Cys Cys Gly Ala Gly Pro
 35 40 45

 Ser Pro Gly Thr Trp Thr Val Arg Thr Pro Pro Ala Arg Arg Pro
 50 55 60

 Ala Cys Ala Gly Ser Ala Arg Arg Cys Arg Ala Ala Arg Gly Arg Ala
 65 70 75 80

 Val Ala Pro Arg Phe Glu Ser Cys Ser Ser Met Leu Pro Gly Thr Gly
 85 90 95

 Thr Arg Arg Pro Cys
 100

<210> SEQ ID NO 50
 <211> LENGTH: 31
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic Peptide

 <400> SEQUENCE: 50

 Gly Trp Pro Gly His Val Met Gly Ser Gln Arg Arg Gln Thr Pro Leu
 1 5 10 15

 His Ala Arg Trp Trp Gly His His Gln Arg Pro Val Leu Gln Pro
 20 25 30

<210> SEQ ID NO 51
 <211> LENGTH: 22
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic Peptide

 <400> SEQUENCE: 51

-continued

Gly Pro Arg Gly His Ala Gly Glu Gly Gly Arg Gln Ser Cys Gly Arg
1 5 10 15

Pro Val Leu Arg Gly Arg
20

<210> SEQ ID NO 52
<211> LENGTH: 25
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic Peptide

<400> SEQUENCE: 52

Val Gln Met Lys Met Met Lys Ser Ser Ser Asp Pro Leu Asp Ile Lys
1 5 10 15

Lys Asp Val Leu Leu Pro Ala Trp Asn
20 25

<210> SEQ ID NO 53
<211> LENGTH: 20
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic Peptide

<400> SEQUENCE: 53

Glu Gly Val Leu Leu Gln Val Thr Asn Glu Glu Val Val Asn His Arg
1 5 10 15

Val Phe Lys Lys
20

<210> SEQ ID NO 54
<211> LENGTH: 21
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic Peptide

<400> SEQUENCE: 54

Lys Glu Gly Val Leu Leu Gln Val Thr Asn Glu Glu Val Val Asn His
1 5 10 15

Arg Val Phe Lys Lys
20

<210> SEQ ID NO 55
<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic Peptide

<400> SEQUENCE: 55

Asp Ser Cys Gly Ile Val Asn Ser Tyr
1 5

<210> SEQ ID NO 56
<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic Peptide

-continued

<400> SEQUENCE: 56

Asp Ser Cys Gly Ile Val Asn Ser Tyr
 1 5

<210> SEQ ID NO 57

<211> LENGTH: 22

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic Peptide

<400> SEQUENCE: 57

Asn Cys Pro Val Trp Arg His Asn Pro Cys Leu Ala Ser Trp Met Ser
 1 5 10 15

Trp Arg Cys Trp Lys Ser
 20

<210> SEQ ID NO 58

<211> LENGTH: 64

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic Peptide

<400> SEQUENCE: 58

Ile Val Gly Pro Gly Pro Lys Pro Glu Ala Ser Ala Lys Leu Pro Ser
 1 5 10 15

Arg Pro Ala Asp Asn Tyr Asp Asn Phe Val Leu Pro Glu Leu Pro Ser
 20 25 30

Val Pro Asp Thr Leu Pro Thr Ala Ser Ala Gly Ala Ser Thr Ser Ala
 35 40 45

Ser Glu Asp Ile Asp Phe Asp Asp Leu Ser Arg Arg Phe Glu Glu Leu
 50 55 60

<210> SEQ ID NO 59

<211> LENGTH: 22

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic Peptide

<400> SEQUENCE: 59

Val Gly Ser Met Pro Lys Glu Leu Leu Gly Glu Ser Ser Ser Ser Met
 1 5 10 15

Ile Phe Glu Glu Arg Gly
 20

<210> SEQ ID NO 60

<211> LENGTH: 90

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic Peptide

<400> SEQUENCE: 60

His Arg Asp Ser Arg Gly Ser Gly Arg Asn Gly Arg His Pro Glu Arg
 1 5 10 15

Glu Gly Asp His Ala Lys Pro Glu Arg Pro Pro Gly Leu Leu Pro Gly
 20 25 30

Gln Ser Glu Glu Pro Gly Asp Arg Glu Pro Glu Ala Gly Glu Gln Asn

-continued

```

          35          40          45
Pro Gly Ala Leu Gly Glu Glu Gly Thr Pro Gly Gln Arg Leu Glu Pro
  50          55          60
Leu Leu Gln Asp His Arg Gly Pro Glu Gly Ser Asp Leu Arg Lys Tyr
  65          70          75          80
Cys Gly Gln Cys Pro His Arg Ser Ala Asp
          85          90

```

```

<210> SEQ ID NO 61
<211> LENGTH: 50
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic Peptide

```

```

<400> SEQUENCE: 61

```

```

Leu Leu Arg Ser Arg His Ser Thr Arg Ile Leu Pro Thr Ala Ala Gly
  1          5          10          15
Leu Arg Leu Arg Ala Cys Thr Arg Ser Ser Met Arg Ser Cys Arg Ala
          20          25          30
Trp Leu Gly Ser Thr Gly Met Thr Cys Gly Ala Gln Arg Leu Arg Ser
          35          40          45
Leu Arg
          50

```

```

<210> SEQ ID NO 62
<211> LENGTH: 36
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic Peptide

```

```

<400> SEQUENCE: 62

```

```

Arg Cys Gln Pro Asp Arg His Ser His Ile Trp Ala Leu Arg Trp Pro
  1          5          10          15
Trp Trp Ser Trp Cys Gln His Gln Trp Gln Leu Trp Cys Leu Trp Phe
          20          25          30
Leu Leu Gln Val
          35

```

```

<210> SEQ ID NO 63
<211> LENGTH: 34
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic Peptide

```

```

<400> SEQUENCE: 63

```

```

Glu Thr Pro Ser Asp Ser Asp His Lys Lys Lys Lys Lys Lys Glu
  1          5          10          15
Glu Asp Pro Glu Arg Lys Arg Lys Lys Lys Glu Lys Lys Lys Lys
          20          25          30
Val Glu

```

```

<210> SEQ ID NO 64
<211> LENGTH: 14
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:

```

-continued

<223> OTHER INFORMATION: Synthetic Peptide

<400> SEQUENCE: 64

Ala Gly Asn Val Arg Ser Asn Ser Arg Pro Ser Ile Gln Arg
1 5 10

<210> SEQ ID NO 65

<211> LENGTH: 19

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic Peptide

<400> SEQUENCE: 65

Pro Ala Ser Gly Gly Ser Asp Leu Val Asn His Ser Phe Leu Cys Lys
1 5 10 15

Trp His Pro

<210> SEQ ID NO 66

<211> LENGTH: 9

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic Peptide

<400> SEQUENCE: 66

Cys Leu Leu Leu Gly Ala Val Thr Leu
1 5

<210> SEQ ID NO 67

<211> LENGTH: 15

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic Peptide

<400> SEQUENCE: 67

Glu Ile Pro Glu Arg Asn Gln Gly Pro Val Ala Ala Ile Arg Ser
1 5 10 15

<210> SEQ ID NO 68

<211> LENGTH: 13

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic Peptide

<400> SEQUENCE: 68

Leu His Trp Gly Ser Thr Lys Val His Leu Leu Leu Ile
1 5 10

<210> SEQ ID NO 69

<211> LENGTH: 8

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic Peptide

<400> SEQUENCE: 69

Gly Gly Pro Arg Arg Ile Trp Ser
1 5

<210> SEQ ID NO 70

-continued

<211> LENGTH: 8
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic Peptide

<400> SEQUENCE: 70

Gly Gly Pro Arg Arg Ile Trp Ser
 1 5

<210> SEQ ID NO 71
 <211> LENGTH: 18
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic Peptide

<400> SEQUENCE: 71

Arg Ser Val Lys Trp Ser Pro Asn Thr Met Gln Met Gly Arg Thr Pro
 1 5 10 15

Met Pro

<210> SEQ ID NO 72
 <211> LENGTH: 14
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic Peptide

<400> SEQUENCE: 72

Val Pro Thr Ala Cys Cys Arg Cys Cys Phe Cys Trp Asp Val
 1 5 10

<210> SEQ ID NO 73
 <211> LENGTH: 17
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic Peptide

<400> SEQUENCE: 73

Ser Gly Lys Thr Ser Ser Ile Leu Cys Arg Arg Gly Arg Trp Arg Trp
 1 5 10 15

Ser

<210> SEQ ID NO 74
 <211> LENGTH: 20
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic Peptide

<400> SEQUENCE: 74

Ala Gly Asp Ala Val Leu Gly Ala His Thr Gln Arg Pro Cys Val Val
 1 5 10 15

Gly Gly Ser Gly
 20

<210> SEQ ID NO 75
 <211> LENGTH: 12
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:

-continued

 <223> OTHER INFORMATION: Synthetic Peptide

<400> SEQUENCE: 75

Gly Ala Lys Pro Gly Gly Leu Ala Leu Gly Ala Val
 1 5 10

<210> SEQ ID NO 76

<211> LENGTH: 100

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic Peptide

<400> SEQUENCE: 76

Asp Glu Val Phe Ala Leu Pro Leu Ala His Leu Leu Gln Thr Gln Asn
 1 5 10 15

Gln Gly Tyr Thr His Phe Cys Arg Gly Gly His Phe Arg Tyr Thr Leu
 20 25 30

Pro Val Phe Leu His Gly Pro His Arg Val Trp Gly Leu Thr Ala Val
 35 40 45

Ile Thr Glu Phe Ala Leu Gln Leu Leu Ala Pro Gly Thr Tyr Gln Pro
 50 55 60

Arg Leu Ala Gly Leu Thr Cys Ser Gly Ala Glu Gly Leu Ala Arg Pro
 65 70 75 80

Lys Gln Pro Leu Ala Ser Pro Cys Gln Ala Ser Ser Thr Pro Gly Leu
 85 90 95

Asn Lys Gly Leu
 100

<210> SEQ ID NO 77

<211> LENGTH: 37

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic Peptide

<400> SEQUENCE: 77

Gln Glu Asn Cys Ser Asn Pro Gly Gly Arg Gly Cys Ser Asp Pro Arg
 1 5 10 15

Ser Cys His Phe Thr Pro Ala Trp Ala Lys Glu Gln Asn Ala Ile Ser
 20 25 30

Lys Asn Ile His Ile
 35

<210> SEQ ID NO 78

<211> LENGTH: 16

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic Peptide

<400> SEQUENCE: 78

Ala Lys Phe Cys Pro Thr Phe Asn Lys Ser Met Glu Glu Gln Gly Lys
 1 5 10 15

<210> SEQ ID NO 79

<211> LENGTH: 32

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

-continued

<223> OTHER INFORMATION: Synthetic Peptide

<400> SEQUENCE: 79

Gly Leu Trp Leu Phe Arg Pro Gln Asn Val Leu Gln Met Pro Gln Ser
 1 5 10 15
 Ile Leu Leu Gln Gln Gly Ala Ser Asp Pro Arg Leu Glu Ile Gly Thr
 20 25 30

<210> SEQ ID NO 80

<211> LENGTH: 49

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic Peptide

<400> SEQUENCE: 80

Asp Tyr Arg Arg Leu Pro Pro Gly Pro Ala Asn Phe Phe Cys Ile Phe
 1 5 10 15
 Ser Arg Asp Gly Val Ser Pro Cys Tyr Pro Gly Trp Ser Pro Ser Pro
 20 25 30
 Asp Leu Val Met Ser Pro Leu Arg Ser Pro Lys Val Leu Gly Leu Gln
 35 40 45

Ala

<210> SEQ ID NO 81

<211> LENGTH: 15

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic Peptide

<400> SEQUENCE: 81

Pro Leu Arg Arg Pro Cys Thr Arg Ser Cys Trp Gly Gln Gly Ser
 1 5 10 15

<210> SEQ ID NO 82

<211> LENGTH: 29

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic Peptide

<400> SEQUENCE: 82

Cys Asp Leu Asn Ser Leu Cys Ile Phe Val Ala Ile Phe His Thr Lys
 1 5 10 15
 Cys Phe Lys Cys Gly Glu Ser Ile Lys His Leu Tyr Ser
 20 25

<210> SEQ ID NO 83

<211> LENGTH: 14

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic Peptide

<400> SEQUENCE: 83

Gly Thr Ile Val Val Gln Trp Gly Pro Ser Trp Cys Leu Thr
 1 5 10

<210> SEQ ID NO 84

<211> LENGTH: 88

-continued

<212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic Peptide
 <400> SEQUENCE: 84
 Gly Leu Trp Met Val Val Arg Ser Val Trp Ile Met Gln Ala Ser Leu
 1 5 10 15
 Leu Gly Glu Pro Glu Glu Val Ala Leu Gly Pro Met Gly Val Val Ala
 20 25 30
 Ala Thr Leu Glu Val Val Gly Thr Arg Ala Met Gly Val Ala Gly Ile
 35 40 45
 Met Thr Val Asp Leu Glu Gly Met Asp Met Asp Met Asp Val Pro Glu
 50 55 60
 Thr Ile Met Ala Glu Thr Arg Val Val Met Thr Ala Thr Gln Glu Glu
 65 70 75 80
 Ile Thr Glu Thr Ile Met Thr Thr
 85

<210> SEQ ID NO 85
 <211> LENGTH: 36
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic Peptide
 <400> SEQUENCE: 85
 Ser Leu Pro Pro Asn Pro Ser Ala Ala Arg Glu Thr Lys Gly Ile Ser
 1 5 10 15
 Pro Ile Lys Asp Ser Lys Cys Val Phe Pro Arg Thr Ser Pro Gly Lys
 20 25 30
 Asp Pro Leu Pro
 35

<210> SEQ ID NO 86
 <211> LENGTH: 11
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic Peptide
 <400> SEQUENCE: 86
 Gly Leu Phe Val Phe Pro Ile Tyr Cys Leu Cys
 1 5 10

<210> SEQ ID NO 87
 <211> LENGTH: 12
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic Peptide
 <400> SEQUENCE: 87
 Glu Val Trp Arg His Leu Leu Gly Arg Pro His Ser
 1 5 10

<210> SEQ ID NO 88
 <211> LENGTH: 12
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:

-continued

<223> OTHER INFORMATION: Synthetic Peptide

<400> SEQUENCE: 88

Ile Arg Glu Leu Cys His Arg Tyr Leu Pro Gln Pro
1 5 10

<210> SEQ ID NO 89

<211> LENGTH: 10

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic Peptide

<400> SEQUENCE: 89

Gly Val Arg Gln Trp Gln His Leu Gln Pro
1 5 10

<210> SEQ ID NO 90

<211> LENGTH: 30

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic Peptide

<400> SEQUENCE: 90

Gly Leu Leu Trp Cys Ala Ala Val His His Gly Glu Trp Gly Gln Arg
1 5 10 15

Leu Arg Gly Cys Gly Val Trp Glu Thr Pro Arg Thr Glu Gly
 20 25 30

<210> SEQ ID NO 91

<211> LENGTH: 9

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic Peptide

<400> SEQUENCE: 91

Phe Gly Lys Ala His Gly Ala Ser Trp
1 5

<210> SEQ ID NO 92

<211> LENGTH: 28

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic Peptide

<400> SEQUENCE: 92

Gly Asp Gly Gly Ser Gly Ser Lys Gly Arg Pro Val Glu Gln Thr Glu
1 5 10 15

Val Phe Leu Cys Ile Ser Lys Pro Ser Ser Phe Leu
 20 25

<210> SEQ ID NO 93

<211> LENGTH: 23

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic Peptide

<400> SEQUENCE: 93

Leu His Ala Arg Ala Pro Gly Pro Arg Gly Pro Pro Leu Leu Cys Pro

-continued

1 5 10 15

Cys Cys Leu Arg Val Ser His
 20

<210> SEQ ID NO 94
<211> LENGTH: 62
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic Peptide

<400> SEQUENCE: 94

Leu Pro Gln Gln Asp Leu Trp His Leu Gln Phe His Gln Gly Leu Pro
1 5 10 15

Arg Arg Cys His Pro Val Cys Ala Glu Pro Pro Pro His Val Gln Leu
 20 25 30

Cys Pro Ala His Trp Gly Ala Pro Ser Phe Pro Thr Ser Trp Ser Gln
 35 40 45

Leu His Leu His Ser Asn Cys Arg Gly Pro Gly Cys Ser Arg
 50 55 60

<210> SEQ ID NO 95
<211> LENGTH: 8
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic Peptide

<400> SEQUENCE: 95

Gly Ile Phe Glu Leu Phe Ile Leu
1 5

<210> SEQ ID NO 96
<211> LENGTH: 35
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic Peptide

<400> SEQUENCE: 96

Gly Ile Gly Ala Val Cys Met Asp Trp Trp Ala Ala Ala Pro Pro Gly
1 5 10 15

Glu Cys Ala Pro Arg Pro Gly Cys Ala Ala His His Cys Gly His Arg
 20 25 30

Leu Leu His
 35

<210> SEQ ID NO 97
<211> LENGTH: 12
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic Peptide

<400> SEQUENCE: 97

Ser Pro Cys Pro Ser Ser Pro Pro Ser Gln Pro Trp
1 5 10

<210> SEQ ID NO 98
<211> LENGTH: 25
<212> TYPE: PRT

-continued

<213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic Peptide

<400> SEQUENCE: 98

Val Leu Ser Asp Leu Gly Cys Ala Ala Gly Lys Ser Asp Asp Pro Gln
 1 5 10 15

Leu Trp Gly His Ser His Ile Thr Gly
 20 25

<210> SEQ ID NO 99
 <211> LENGTH: 17
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic Peptide

<400> SEQUENCE: 99

Cys Cys Gly Ile Tyr Cys His Glu Glu Pro Gln Arg Glu Asp Ser Ser
 1 5 10 15

Ile

<210> SEQ ID NO 100
 <211> LENGTH: 39
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic Peptide

<400> SEQUENCE: 100

His Phe Pro Asp Gly Glu Val Thr Ala Glu Arg Cys Gly His Leu Ala
 1 5 10 15

Phe Pro Tyr Pro Leu Pro Phe Pro Ser Pro Pro Ser Ser Tyr Ser Phe
 20 25 30

His Val Pro Phe Gln Thr Glu
 35

<210> SEQ ID NO 101
 <211> LENGTH: 13
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic Peptide

<400> SEQUENCE: 101

Ile Ser Val Ser Ile Met Trp Thr Gln Arg Arg Lys Leu
 1 5 10

<210> SEQ ID NO 102
 <211> LENGTH: 15
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic Peptide

<400> SEQUENCE: 102

Val Lys Gly Val Leu His Ser Leu Thr Ala Ala Gly Gln Thr His
 1 5 10 15

<210> SEQ ID NO 103
 <211> LENGTH: 20
 <212> TYPE: PRT

-continued

<213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic Peptide

<400> SEQUENCE: 103

Lys His Gln Ala Met Asp His His Gly Val Pro Gly Arg Arg Leu Ser
 1 5 10 15

Thr Gly Leu Ala
 20

<210> SEQ ID NO 104
 <211> LENGTH: 41
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic Peptide

<400> SEQUENCE: 104

Gly Asp Gln Gln Pro Asp Arg Thr Gln Ala Gly Leu Lys Ser Val Ser
 1 5 10 15

Gln Val Glu Asp Val Phe Arg Glu Leu Ile Gly Thr Gln Lys Thr Arg
 20 25 30

Thr Gly Cys Phe Pro Pro Ser Gly Ser
 35 40

<210> SEQ ID NO 105
 <211> LENGTH: 24
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic Peptide

<400> SEQUENCE: 105

Cys Ser Ala Gln Ala Arg Asn Arg Ser Glu Asp Glu Thr Gln Pro Leu
 1 5 10 15

Pro Leu Gly Thr Leu Leu Ala Phe
 20

<210> SEQ ID NO 106
 <211> LENGTH: 13
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic Peptide

<400> SEQUENCE: 106

His Gln Ala Leu Gly Ala Val Pro Ser Cys Glu Gly Val
 1 5 10

<210> SEQ ID NO 107
 <211> LENGTH: 36
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic Peptide

<400> SEQUENCE: 107

Gln Phe Arg Thr Pro Gly Trp Pro Leu Lys Ala Leu Ala Gly Arg Gly
 1 5 10 15

Trp Pro Glu Asp Ala Ser Pro Gly Gln Glu Pro Ser Lys Gly Ala Gly
 20 25 30

-continued

Arg Gly Trp Ala
35

<210> SEQ ID NO 108
 <211> LENGTH: 64
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic Peptide

<400> SEQUENCE: 108

Pro Arg Ala Ala Val Ser Gly Ile Gln Gln Trp Trp Asn Gly Arg Gln
 1 5 10 15

Asn Trp Lys Arg Lys Lys Glu Lys Met Ser Ser Arg Leu Ala Gly Ala
 20 25 30

Phe Arg Val Leu Trp Arg Ala Val Ser Thr Ala Ser Ile Arg Arg His
 35 40 45

Ile Gln Val Ala Pro Arg Pro Leu Gln Ala Gly Pro Ala Met Gly Pro
 50 55 60

<210> SEQ ID NO 109
 <211> LENGTH: 14
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic Peptide

<400> SEQUENCE: 109

Leu Ile Val Gly Gly Gly Ala Pro Asp Arg Lys Gly Phe Gln
 1 5 10

<210> SEQ ID NO 110
 <211> LENGTH: 9
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic Peptide

<400> SEQUENCE: 110

Cys Gln Arg Cys Pro Leu Cys Trp Pro
 1 5

<210> SEQ ID NO 111
 <211> LENGTH: 13
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic Peptide

<400> SEQUENCE: 111

Gly Val Arg Cys Leu Ile His Ser Ile His Gly Phe Leu
 1 5 10

<210> SEQ ID NO 112
 <211> LENGTH: 41
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic Peptide

<400> SEQUENCE: 112

Trp Pro Gln Leu Leu Leu Glu Pro Asn Ser Gly Lys Ser Ala Ser Arg
 1 5 10 15

-continued

Arg Arg Pro Gln Gly Gly Pro Gln Pro Pro Lys Leu Arg Val Val Glu
 20 25 30
 Ala Glu Val Gly Asp Ser Trp Lys Arg
 35 40

<210> SEQ ID NO 113
 <211> LENGTH: 72
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic Peptide

<400> SEQUENCE: 113

Val Ala Ala Arg Ala Trp Ala Gln Pro Pro Leu Pro Gly Ala Glu Cys
 1 5 10 15
 Gly His Arg Arg Glu Gly Ala Thr Leu Ala Gly His Arg Gly Arg Pro
 20 25 30
 Ala Ala Ala His Arg Gly Leu Arg Pro Gly His Ala Ala Ala Thr
 35 40 45
 Glu His Gln Ala Gln Glu Ala Ser Pro Arg Gly Asp Arg Gly Gly Arg
 50 55 60
 His Gly Ser Gly Leu Leu Gln Leu
 65 70

<210> SEQ ID NO 114
 <211> LENGTH: 22
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic Peptide

<400> SEQUENCE: 114

Arg Tyr Gly Arg Cys Val His Cys Arg Glu Ile Val Leu Gln Gln Pro
 1 5 10 15
 Ser Gly His Arg Gln Pro
 20

<210> SEQ ID NO 115
 <211> LENGTH: 19
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic Peptide

<400> SEQUENCE: 115

Gly Leu Met Ala Ser Asp Tyr Ser Glu Glu Val Ala Thr Ser Glu Lys
 1 5 10 15
 Phe Pro Phe

<210> SEQ ID NO 116
 <211> LENGTH: 22
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic Peptide

<400> SEQUENCE: 116

Asp Arg Lys Arg Gly Cys Cys Pro Thr Ser Ser Ser Leu Pro Ile Ser
 1 5 10 15

-continued

Leu Arg Val Arg Leu Ser
20

<210> SEQ ID NO 117
 <211> LENGTH: 42
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic Peptide

<400> SEQUENCE: 117

Ser His Ser Gln Ser Gly Gly Pro Arg His Pro Gly Gly Thr Arg Arg
 1 5 10 15

Lys Ala Met Gly Ser Gln Cys Pro Glu Leu Gln Gly Gly Pro Glu Pro
 20 25 30

Gln Arg Pro Ser Ser Arg Arg Arg Glu Ile
 35 40

<210> SEQ ID NO 118
 <211> LENGTH: 21
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic Peptide

<400> SEQUENCE: 118

Ala Val Leu Leu Met Cys Gln Leu Tyr Gln Pro Trp Met Cys Lys Glu
 1 5 10 15

Tyr Tyr Arg Leu Leu
 20

<210> SEQ ID NO 119
 <211> LENGTH: 21
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic Peptide

<400> SEQUENCE: 119

Ile Pro Arg Met Gln Pro Gln Ala Ser Ala Asn His Cys Gln Leu Leu
 1 5 10 15

Lys Val Met Val Ala
 20

<210> SEQ ID NO 120
 <211> LENGTH: 27
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic Peptide

<400> SEQUENCE: 120

Thr Ala Ile Ile Gly Pro Asn Gly Ser Gly Cys Ser Gly Val Tyr Cys
 1 5 10 15

His Glu Glu Pro Gln Gly Glu Asp Ser Ser Val
 20 25

<210> SEQ ID NO 121
 <211> LENGTH: 45
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:

-continued

 <223> OTHER INFORMATION: Synthetic Peptide

<400> SEQUENCE: 121

Gly Arg Val Ile Glu Cys Asp Val Val Lys Gly Ser Cys Gln Asp Gly
 1 5 10 15
 Glu Ala Val His Trp Lys Ser Ala Pro Gly Gly His Arg Ala Gly Asp
 20 25 30
 Pro Leu Thr Leu Arg Ala Val Arg Glu Gly Ala Gly Met
 35 40 45

<210> SEQ ID NO 122

<211> LENGTH: 33

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic Peptide

<400> SEQUENCE: 122

Ile Cys Met Ser Pro Pro Leu Leu Trp Ala Thr Leu Gln Ala Pro Glu
 1 5 10 15
 Thr Thr Ser Ala Ala Cys Lys Ala Ser Tyr Arg Pro Glu Gly Leu Tyr
 20 25 30
 Leu

<210> SEQ ID NO 123

<211> LENGTH: 24

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic Peptide

<400> SEQUENCE: 123

Tyr Phe Ser Cys Asp Lys Arg Cys Ile Lys His Tyr Ala Gly Asn Lys
 1 5 10 15
 Ser Leu Leu Thr Phe Ser Gly Tyr
 20

<210> SEQ ID NO 124

<211> LENGTH: 59

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic Peptide

<400> SEQUENCE: 124

Thr Leu Cys Met Glu Val Met Leu Arg Trp Asn Thr Arg Glu Leu Gly
 1 5 10 15
 Tyr Leu Tyr Leu Gln Leu Cys Phe Leu Asn Thr His Phe Leu His Thr
 20 25 30
 Ser Gln Glu Glu Lys Leu Leu Thr Leu Gly Arg Phe Leu Thr Trp Thr
 35 40 45
 Ser Arg Cys Gly Ser Phe Val Ile Arg Pro Leu
 50 55

<210> SEQ ID NO 125

<211> LENGTH: 1260

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic oligonucleotide

-continued

<400> SEQUENCE: 125

```

atggcggagc gcaggagaca caagaagcgg atccaggaag ttggtgaacc atctaaagaa    60
gagaaggctg tagccaagta tcttcgattt aactgtccaa caaagtctac caatatgatg    120
gggcaccgag ttgattatct cattgcttca aaagcagtgg attgcctttt ggattcaaag    180
tgggcaaagg ccaagaaagg agaggaagct ttatttaca caaggggagtc tgtggttgac    240
tactgcaaca ggcttttaaa gaagcagttt tttcaccggg cactaaaagt aatgaaaatg    300
aagtatgata aagacataaa aaaagaaaa gagaaaggaa aggccgaaag tggaaaagaa    360
gaagataaaa agagcaggaa agaaaatcta aaggatgaaa agacgaaaaa ggagaaagaa    420
aaaaaaaaa gatggggaaa aggaagagga ttacaaggac gacgacgaca agtgaatttc    480
atggtgagca agggcgagga gctgttcacc ggggtggtgc ccatectggt cgagctggac    540
ggcgacgtaa acggccacaa gttcagcgtg tccggcgagg gcgagggcga tgccacctac    600
ggcaagctga cctgaagtt catctgcacc accggcaagc tgcccgtgcc ctggcccacc    660
ctcgtgacca cctgaccta cggcgtgcag tgcttcagcc actacccca ccacatgaag    720
cagcacgact tcttaagtc cgcctgccc gaaggctacg tccaggagcg caccatcttc    780
ttcaaggacg acggcaacta caagaccgc gccgaggtga agttcgaggg cgacaccctg    840
gtgaaccgca tcgagctgaa gggcatcgac ttcaaggagg acggcaacat cctggggcac    900
aagctggagt acaactacaa gaccacaac gtctatatca tggccgacaa gcagaagaac    960
ggcatcaagg tgaacttcaa gatccgccac aacatcgagg acggcagcgt gcagctcgcc   1020
gaccactacc agcagaacac ccccatcggc gacggccccg tgctgctgcc cgacaaccac   1080
tacctgagca ccagctccc cctgagcaaa gacccaacg agaagcgcga tcacatggtc   1140
ctgctggagt tcgtgaccgc cgcgggatc actctcggca tggacgagct gtacaagaga   1200
tctggtacca cgcgtatcga taagcttgca tgctgcagg tcgactctag aggatcgtga   1260

```

<210> SEQ ID NO 126

<211> LENGTH: 1260

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 126

```

atggcggagc gcaggagaca caagaagcgg atccaggaag ttggtgaacc atctaaagaa    60
gagaaggctg tagccaagta tcttcgattt aactgtccaa caaagtctac caatatgatg    120
gggcaccgag ttgattatct cattgcttca aaagcagtgg attgcctttt ggattcaaag    180
tgggcaaagg ccaagaaagg agaggaagct ttatttaca caaggggagtc tgtggttgac    240
tactgcaaca ggcttttaaa gaagcagttt tttcaccggg cactaaaagt aatgaaaatg    300
aagtatgata aagacataaa aaaagaaaa gagaaaggaa aggccgaaag tggaaaagaa    360
gaagataaaa agagcaggaa agaaaatcta aaggatgaaa agacgaaaaa ggagaaagaa    420
aaaaaaaaa gatggggaaa aggaagagga ttacaaggac gacgacgaca agtgaatttc    480
atggtgagca agggcgagga gctgttcacc ggggtggtgc ccatectggt cgagctggac    540
ggcgacgtaa acggccacaa gttcagcgtg tccggcgagg gcgagggcga tgccacctac    600
ggcaagctga cctgaagtt catctgcacc accggcaagc tgcccgtgcc ctggcccacc    660

```

-continued

```

ctcgtgacca ccttgaccta cggcgtgcag tgcttcagcc actacccca ccacatgaag 720
cagcagcact tcttcaagtc cgccatgccc gaaggctacg tccaggagcg caccatcttc 780
ttcaaggacg acggcaacta caagaccgcg gccgaggtga agttcgaggg cgacaccctg 840
gtgaaccgca tcgagctgaa gggcatcgac ttcaaggagg acggcaacat cctggggcac 900
aagctggagt acaactacaa cagccacaac gtctatatca tggccgacaa gcagaagaac 960
ggcatcaagg tgaacttcaa gatccgccc aacatcgagg acggcagcgt gcagctcgcc 1020
gaccactacc agcagaacac ccccatcggc gacggccccg tgctgctgcc cgacaaccac 1080
tacctgagca cccagtcgcc cctgagcaaa gaccccaacg agaagcgcga tcacatggtc 1140
ctgctggagt tcgtgaccgc cgcggggtgc actctcgcca tggacgagct gtacaagaga 1200
tctggtacca cgcgtatcga taagcttgca tgctgcagg tcgactctag aggatcgtga 1260

```

```

<210> SEQ ID NO 127
<211> LENGTH: 1259
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

```

```

<400> SEQUENCE: 127
atggcggagc gcaggagaca caagaagcgg atccaggaag ttggtgaacc atctaagaa 60
gagaaggctg tagccaagta tcttcgattt aactgtccaa caaagtctac caatatgatg 120
gggcaccgag ttgattatct cattgcttca aaagcagtggt attgcctttt ggattcaaag 180
tgggcaaagg ccaagaaagg agaggaagct ttatttacia caagggagtc tgtggttgac 240
tactgcaaca ggctttttaa gaagcagttt tttcacccgg cactaaaagt aatgaaaatg 300
aagtatgata aagacataaa aaaagaaaaa gagaagggaa aggccgaaag tggaaaagaa 360
gaagataaaa agagcagtaa agaaaatcta aaggatgaaa agacgaaaaa ggagaaagag 420
aggaagagag atggggaaaa ggaagaggat tacaaggacg acgacgacaa gtgaaattca 480
tggtgagcaa gggcgaggag ctgttcaccg gggtggtgcc catcctgtgc gagctggacg 540
gcgacgtaaa cggccacaag ttcagcgtgt cggcgagggg cgaggcgcgt gccacctacg 600
gcaagctgac cctgaagttc atctgcacca cggcaagct gccctgtccc tggccccacc 660
tcgtgaccac cctgacctac ggcgtgcagt gcttcagcca ctaccccgac cacatgaagc 720
agcacgactt cttcaagtcg gccatgcccc aaggctacgt ccaggagcgc accatcttct 780
tcaaggacga cggcaactac aagaccgcg ccgaggtgaa gttcgagggc gacaccctgg 840
tgaaccgcat cgagctgaag ggcacgact tcaaggagga cggcaacatc ctggggcaca 900
agctggagta caactacaac agccacaacg tctatatcat gggcgacaag cagaagaacg 960
gcatcaaggt gaacttcaag atccgccaca acatcgagga cggcagcgtg cagctcgccg 1020
accactacca gcagaacacc cccatcgcg cggccccgt gctgctgcc gacaaccact 1080
acctgagcac ccagtcgcc ctgagcaaa agcccaacga gaagcgcgat cacatggtcc 1140
tgctggagtt cgtgaccgcc gccgggatca ctctcgcat ggaagcagctg tacaagagat 1200
ctggtaccac cgcgtatcga aagcttgcat gcctgcaggt cgactctaga ggatcgtga 1259

```

```

<210> SEQ ID NO 128
<211> LENGTH: 120

```

-continued

```

<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic Peptide

<400> SEQUENCE: 128

Met Ala Ser Ala Lys Ser Leu Asp Arg Trp Lys Ala Arg Leu Leu Glu
1           5           10          15

Gly Gly Ser Thr Ala Leu Thr Tyr Ala Leu Val Arg Ala Glu Val Ser
20          25          30

Phe Pro Ala Glu Val Ala Pro Val Arg Gln Gln Gly Ser Val Ala Gly
35          40          45

Ala Arg Ala Gly Val Val Ser Leu Leu Gly Cys Arg Ser Ser Trp Thr
50          55          60

Ala Ala Met Glu Leu Ser Ala Glu Tyr Leu Arg Glu Lys Leu Gln Arg
65          70          75          80

Asp Leu Glu Ala Glu His Val Glu Val Glu Asp Thr Thr Leu Asn Arg
85          90          95

Cys Ser Cys Ser Phe Arg Val Leu Val Val Ser Ala Lys Phe Glu Gly
100         105         110

Lys Pro Leu Leu Gln Arg His Arg
115          120

```

```

<210> SEQ ID NO 129
<211> LENGTH: 4
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic Peptide

```

```

<400> SEQUENCE: 129

```

```

Leu Leu Asn Arg
1

```

```

<210> SEQ ID NO 130
<211> LENGTH: 84
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic Peptide

```

```

<400> SEQUENCE: 130

```

```

Met Leu Pro Gly Val Gly Val Phe Gly Thr Ser Leu Thr Ala Arg Val
1           5           10          15

Ile Ile Pro Leu Leu Lys Asp Glu Gly Phe Ala Val Lys Ala Leu Trp
20          25          30

Gly Arg Thr Gln Glu Glu Ala Glu Glu Leu Ala Lys Glu Met Ser Val
35          40          45

Pro Phe Tyr Thr Ser Arg Ile Asp Glu Val Leu Leu His Gln Asp Val
50          55          60

Asp Leu Val Cys Ile Asn Leu Pro Pro Pro Leu Thr Arg Gln Ile Ala
65          70          75          80

Val Lys Thr Leu

```

```

<210> SEQ ID NO 131
<211> LENGTH: 64
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence

```

-continued

<220> FEATURE:
 <223> OTHER INFORMATION: Synthetic Peptide

<400> SEQUENCE: 131

Glu Pro Gly His Gln Arg Lys Lys Ile Ser Arg Gln Lys Asn Thr Gly
 1 5 10 15

Glu Lys Lys Met Pro Arg Gly Ser Val Gln Leu Ser Phe Cys Ser Leu
 20 25 30

Gln His Pro His Met Gly His Leu Phe Thr Pro His Asp Ala Ala Leu
 35 40 45

Gly Glu Ser Gln Gly Thr Gly Phe Lys Pro Leu Gly Met Gln Pro Val
 50 55 60

<210> SEQ ID NO 132
 <211> LENGTH: 125
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic Peptide

<400> SEQUENCE: 132

Met Arg Ser Lys Gly Arg Ala Arg Lys Leu Ala Thr Asn Asn Glu Cys
 1 5 10 15

Val Tyr Gly Asn Tyr Pro Glu Ile Pro Leu Glu Glu Met Pro Asp Ala
 20 25 30

Asp Gly Val Ala Ser Thr Pro Ser Leu Asn Ile Gln Glu Pro Cys Ser
 35 40 45

Pro Ala Thr Ser Ser Glu Ala Phe Thr Pro Lys Glu Gly Ser Pro Tyr
 50 55 60

Lys Ala Pro Ile Tyr Ile Pro Asp Asp Ile Pro Ile Pro Ala Glu Phe
 65 70 75 80

Glu Leu Arg Glu Ser Asn Met Pro Gly Ala Gly Leu Gly Ile Trp Thr
 85 90 95

Lys Arg Lys Ile Glu Val Gly Glu Lys Phe Gly Pro Tyr Val Gly Glu
 100 105 110

Gln Arg Ser Asn Leu Lys Asp Pro Ser Tyr Gly Trp Glu
 115 120 125

<210> SEQ ID NO 133
 <211> LENGTH: 255
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic Peptide

<400> SEQUENCE: 133

Ile Leu Asp Glu Phe Tyr Asn Val Lys Phe Cys Ile Asp Ala Ser Gln
 1 5 10 15

Pro Asp Val Gly Ser Trp Leu Lys Tyr Ile Arg Phe Ala Gly Cys Tyr
 20 25 30

Asp Gln His Asn Leu Val Ala Cys Gln Ile Asn Asp Gln Ile Phe Tyr
 35 40 45

Arg Val Val Ala Asp Ile Ala Pro Gly Glu Glu Leu Leu Leu Phe Met
 50 55 60

Lys Ser Glu Asp Tyr Pro His Glu Thr Met Ala Pro Asp Ile His Glu
 65 70 75 80

-continued

Glu Arg Gln Tyr Arg Cys Glu Asp Cys Asp Gln Leu Phe Glu Ser Lys
 85 90 95
 Ala Glu Leu Ala Asp His Gln Lys Phe Pro Cys Ser Thr Pro His Ser
 100 105 110
 Ala Phe Ser Met Val Glu Glu Asp Phe Gln Gln Lys Leu Glu Ser Glu
 115 120 125
 Asn Asp Leu Gln Glu Ile His Thr Ile Gln Glu Cys Lys Glu Cys Asp
 130 135 140
 Gln Val Phe Pro Asp Leu Gln Ser Leu Glu Lys His Met Leu Ser His
 145 150 155 160
 Thr Glu Glu Arg Glu Tyr Lys Cys Asp Gln Cys Pro Lys Ala Phe Asn
 165 170 175
 Trp Lys Ser Asn Leu Ile Arg His Gln Met Ser His Asp Ser Gly Lys
 180 185 190
 His Tyr Glu Cys Glu Asn Cys Ala Lys Val Phe Thr Asp Pro Ser Asn
 195 200 205
 Leu Gln Arg His Ile Arg Ser Gln His Val Gly Ala Arg Ala His Ala
 210 215 220
 Cys Pro Glu Cys Gly Lys Thr Phe Ala Thr Ser Ser Gly Leu Lys Gln
 225 230 235 240
 His Lys His Ile His Ser Ser Val Lys Pro Phe Ile Cys Glu Val
 245 250 255

<210> SEQ ID NO 134
 <211> LENGTH: 123
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic Peptide

<400> SEQUENCE: 134

Met Ala Val Ser Thr Val Phe Ser Thr Ser Ser Leu Met Leu Ala Leu
 1 5 10 15
 Ser Arg His Ser Leu Leu Ser Pro Leu Leu Ser Val Thr Ser Phe Arg
 20 25 30
 Arg Phe Tyr Arg Gly Asp Ser Pro Thr Asp Ser Gln Lys Asp Met Ile
 35 40 45
 Glu Ile Pro Leu Pro Pro Trp Gln Glu Arg Thr Asp Glu Ser Ile Glu
 50 55 60
 Thr Lys Arg Ala Arg Leu Leu Tyr Glu Ser Arg Lys Arg Gly Met Leu
 65 70 75 80
 Glu Asn Cys Ile Leu Leu Ser Leu Phe Ala Lys Glu His Leu Gln His
 85 90 95
 Met Thr Glu Lys Gln Leu Asn Leu Tyr Asp Arg Leu Ile Asn Glu Pro
 100 105 110
 Ser Asn Asp Trp Asp Ile Tyr Tyr Trp Ala Thr
 115 120

<210> SEQ ID NO 135
 <211> LENGTH: 124
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic Peptide

<400> SEQUENCE: 135

-continued

Gly Pro Glu Gly Pro Phe Arg His Pro Gly Ala Arg Ala Ser Gly His
 1 5 10 15
 His Gly Ala Gly Ala Gln Gly Ser Ala Ser Ala Pro Pro Ala Ala Gly
 20 25 30
 Pro Gly Pro Ala Gly Ala Gly Glu Leu Pro Thr Trp Pro Thr Leu His
 35 40 45
 Asp Val Gly Val Gln Phe Gln Val Ser Gln Gly Pro Ser Arg Pro Ala
 50 55 60
 Arg Phe Leu Ala Glu Glu Ile Asp Arg Arg Lys Gly Gly Glu Trp Leu
 65 70 75 80
 His Gln Thr Val Pro Pro Glu Pro His Cys Leu Pro Thr Ala Leu Thr
 85 90 95
 Gly Pro Pro Trp Gly Pro Cys Pro Pro Pro Arg Pro Glu Cys His Gln
 100 105 110
 Val Arg Leu Pro Pro Gln Asp Ser Pro Thr Trp Arg
 115 120

<210> SEQ ID NO 136
 <211> LENGTH: 132
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic Peptide

<400> SEQUENCE: 136

Met Val Gly Ala Leu Cys Gly Cys Trp Phe Arg Leu Gly Gly Ala Arg
 1 5 10 15
 Pro Leu Ile Pro Leu Gly Pro Thr Val Val Gln Thr Ser Met Ser Gln
 20 25 30
 Ser Gln Val Ala Leu Leu Gly Leu Ser Leu Leu Leu Met Leu Leu Leu
 35 40 45
 Tyr Val Gly Leu Pro Gly Pro Pro Glu Gln Thr Ser Cys Leu Trp Gly
 50 55 60
 Asp Pro Asn Val Thr Val Leu Ala Gly Leu Thr Pro Gly Asn Ser Pro
 65 70 75 80
 Ile Phe Tyr Arg Glu Val Leu Pro Leu Asn Gln Ala His Arg Val Glu
 85 90 95
 Val Val Leu Leu His Gly Lys Ala Phe Asn Ser His Thr Trp Glu Gln
 100 105 110
 Leu Gly Thr Leu Gln Leu Leu Ser Gln Arg Gly Tyr Arg Ala Val Ala
 115 120 125
 Leu Asp Leu Pro
 130

<210> SEQ ID NO 137
 <211> LENGTH: 35
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic Peptide

<400> SEQUENCE: 137

Ala His His Ala Gln Arg His Asp Gln Gln Gly Ser Arg Gly Gly Ala
 1 5 10 15
 Pro Ile Gly Asp Ala Leu Pro Pro Val Pro Ala Tyr Pro His Cys Pro

-continued

20 25 30

Ala Gln Ala
35

<210> SEQ ID NO 138
<211> LENGTH: 112
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic Peptide

<400> SEQUENCE: 138

Met Lys Ile Phe Val Gly Asn Val Asp Gly Ala Asp Thr Thr Pro Glu
1 5 10 15
Glu Leu Ala Ala Leu Phe Ala Pro Tyr Gly Thr Val Met Ser Cys Ala
20 25 30
Val Met Lys Gln Phe Ala Phe Val His Met Arg Glu Asn Ala Gly Ala
35 40 45
Leu Arg Ala Ile Glu Ala Leu His Gly His Glu Leu Arg Pro Gly Arg
50 55 60
Ala Leu Val Val Glu Met Ser Arg Pro Arg Pro Leu Asn Thr Trp Lys
65 70 75 80
Ile Phe Val Gly Asn Val Ser Ala Ala Cys Thr Ser Gln Glu Leu Arg
85 90 95
Ser Leu Phe Glu Arg Arg Gly Arg Val Ile Glu Cys Asp Val Val Lys
100 105 110

<210> SEQ ID NO 139
<211> LENGTH: 35
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic Peptide

<400> SEQUENCE: 139

Gly Ser Cys Gln Asp Gly Glu Ala Val His Arg Lys Pro Ala Pro Gly
1 5 10 15
Gly Tyr Arg Ala Gly Asp Ser Leu Thr Leu Arg Ala Val Trp Glu Gly
20 25 30

Ala Gly Met
35

<210> SEQ ID NO 140
<211> LENGTH: 58
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic Peptide

<400> SEQUENCE: 140

Met Val His Ala Phe Leu Ile His Thr Leu Arg Ala Pro Asn Thr Glu
1 5 10 15
Asp Thr Gly Leu Cys Arg Val Leu Tyr Ser Cys Val Phe Gly Ala Glu
20 25 30
Lys Ser Pro Asp Asp Pro Arg Pro His Gly Ala Glu Arg Asp Arg Leu
35 40 45
Leu Arg Lys Glu Gln Ile Leu Ala Val Ala
50 55

-continued

```

<210> SEQ ID NO 141
<211> LENGTH: 20
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic Peptide

<400> SEQUENCE: 141

Ser Leu Val Ser Ser Gln Ser Ile His Pro Ser Trp Gly Gln Ser Pro
1           5           10           15

Leu Ser Arg Ile
                20

<210> SEQ ID NO 142
<211> LENGTH: 340
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic Peptide

<400> SEQUENCE: 142

Met Leu Ser Leu Arg Val Pro Leu Ala Pro Ile Thr Asp Pro Gln Gln
1           5           10           15

Leu Gln Leu Ser Pro Leu Lys Gly Leu Ser Leu Val Asp Lys Glu Asn
                20           25           30

Thr Pro Pro Ala Leu Ser Gly Thr Arg Val Leu Ala Ser Lys Thr Ala
35           40           45

Arg Arg Ile Phe Gln Glu Pro Thr Glu Pro Lys Thr Lys Ala Ala Ala
50           55           60

Pro Gly Val Glu Asp Glu Pro Leu Leu Arg Glu Asn Pro Arg Arg Phe
65           70           75           80

Val Ile Phe Pro Ile Glu Tyr His Asp Ile Trp Gln Met Tyr Lys Lys
85           90           95

Ala Glu Ala Ser Phe Trp Thr Ala Glu Glu Val Asp Leu Ser Lys Asp
100          105          110

Ile Gln His Trp Glu Ser Leu Lys Pro Glu Glu Arg Tyr Phe Ile Ser
115          120          125

His Val Leu Ala Phe Phe Ala Ala Ser Asp Gly Ile Val Asn Glu Asn
130          135          140

Leu Val Glu Arg Phe Ser Gln Glu Val Gln Ile Thr Glu Ala Arg Cys
145          150          155          160

Phe Tyr Gly Phe Gln Ile Ala Met Glu Asn Ile His Ser Glu Met Tyr
165          170          175

Ser Leu Leu Ile Asp Thr Tyr Ile Lys Asp Pro Lys Glu Arg Glu Phe
180          185          190

Leu Phe Asn Ala Ile Glu Thr Met Pro Cys Val Lys Lys Lys Ala Asp
195          200          205

Trp Ala Leu Arg Trp Ile Gly Asp Lys Glu Ala Thr Tyr Gly Glu Arg
210          215          220

Val Val Ala Phe Ala Ala Val Glu Gly Ile Phe Phe Ser Gly Ser Phe
225          230          235          240

Ala Ser Ile Phe Trp Leu Lys Lys Arg Gly Leu Met Pro Gly Leu Thr
245          250          255

Phe Ser Asn Glu Leu Ile Ser Arg Asp Glu Gly Leu His Cys Asp Phe

```

-continued

260 265 270

Ala Cys Leu Met Phe Lys His Leu Val His Lys Pro Ser Glu Glu Arg
 275 280 285

Val Arg Glu Ile Ile Ile Asn Ala Val Arg Ile Glu Gln Glu Phe Leu
 290 295 300

Thr Glu Ala Leu Pro Val Lys Leu Ile Gly Met Asn Cys Thr Leu Met
 305 310 315 320

Lys Gln Tyr Ile Glu Phe Val Ala Asp Arg Leu Met Leu Glu Leu Gly
 325 330 335

Phe Ser Lys Val
 340

<210> SEQ ID NO 143
 <211> LENGTH: 34
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic Peptide

<400> SEQUENCE: 143

Leu Gly Asp Arg Glu Val Gln Ser Arg Trp Ser Pro Gly Pro Arg Gly
 1 5 10 15

Asp Ser Thr Pro Val Arg Glu Met Glu Thr Asn His Pro Pro Ser Val
 20 25 30

Arg Gly

<210> SEQ ID NO 144
 <211> LENGTH: 53
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic Peptide

<400> SEQUENCE: 144

Met Ser Met Asp Val Thr Phe Leu Gly Thr Gly Ala Ala Tyr Pro Ser
 1 5 10 15

Pro Thr Arg Gly Ala Ser Ala Val Val Leu Arg Cys Glu Gly Glu Cys
 20 25 30

Trp Leu Phe Asp Cys Gly Glu Gly Thr Gln Thr Gln Leu Met Lys Ser
 35 40 45

Gln Leu Lys Ala Gly
 50

<210> SEQ ID NO 145
 <211> LENGTH: 33
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic Peptide

<400> SEQUENCE: 145

Tyr Pro Glu Tyr Met Ser Asn Asn Phe Pro Cys Asn Val Ser Cys Cys
 1 5 10 15

Phe Ser Leu Phe Pro Lys Asp Gln Asn Cys Phe Arg Asn Trp Arg His
 20 25 30

Ile

-continued

```

<210> SEQ ID NO 146
<211> LENGTH: 60
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic Peptide

<400> SEQUENCE: 146

Met Gln Arg Thr Gly Gly Gly Ala Pro Arg Pro Gly Arg Asn His Gly
1           5           10           15

Leu Pro Gly Ser Leu Arg Gln Pro Asp Pro Val Ala Leu Leu Met Leu
20           25           30

Leu Val Asp Ala Asp Gln Pro Glu Pro Met Arg Ser Gly Ala Arg Glu
35           40           45

Leu Ala Leu Phe Leu Thr Pro Glu Pro Gly Ala Glu
50           55           60

```

```

<210> SEQ ID NO 147
<211> LENGTH: 6
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic Peptide

<400> SEQUENCE: 147

```

```

Val Pro Leu Thr Gly Ala
1           5

```

```

<210> SEQ ID NO 148
<211> LENGTH: 64
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic Peptide

<400> SEQUENCE: 148

```

```

Met Ala Asp Gly Ser Gly Trp Gln Pro Pro Arg Pro Cys Glu Ala Tyr
1           5           10           15

Arg Ala Glu Trp Lys Leu Cys Arg Ser Ala Arg His Phe Leu His His
20           25           30

Tyr Tyr Val His Gly Glu Arg Pro Ala Cys Glu Gln Trp Gln Arg Asp
35           40           45

Leu Ala Ser Cys Arg Asp Trp Glu Glu Arg Arg Asn Ala Glu Ala Gln
50           55           60

```

```

<210> SEQ ID NO 149
<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic Peptide

<400> SEQUENCE: 149

```

```

Ala Ser Arg Phe Phe Gln Leu Ile Phe Thr Leu Thr Gly Pro Ser Ser
1           5           10           15

Gln Leu Glu Asp Lys Gly Arg Ile Leu Gly Arg Leu
20           25

```

```

<210> SEQ ID NO 150
<211> LENGTH: 188
<212> TYPE: PRT

```

-continued

```

<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic Peptide

<400> SEQUENCE: 150
Met Ala Glu Ala Ser Ser Ala Asn Leu Gly Ser Gly Cys Glu Glu Lys
1           5           10           15
Arg His Glu Gly Ser Ser Ser Glu Ser Val Pro Pro Gly Thr Thr Ile
20           25           30
Ser Arg Val Lys Leu Leu Asp Thr Met Val Asp Thr Phe Leu Gln Lys
35           40           45
Leu Val Ala Ala Gly Ser Tyr Gln Arg Phe Thr Asp Cys Tyr Lys Cys
50           55           60
Phe Tyr Gln Leu Gln Pro Ala Met Thr Gln Gln Ile Tyr Asp Lys Phe
65           70           75           80
Ile Ala Gln Leu Gln Thr Ser Ile Arg Glu Glu Ile Ser Asp Ile Lys
85           90           95
Glu Glu Gly Asn Leu Glu Ala Val Leu Asn Ala Leu Asp Lys Ile Val
100          105          110
Glu Glu Gly Lys Val Arg Lys Glu Pro Ala Trp Arg Pro Ser Gly Ile
115          120          125
Pro Glu Lys Asp Leu His Ser Val Met Ala Pro Tyr Phe Leu Gln Gln
130          135          140
Arg Asp Thr Leu Arg Arg His Val Gln Lys Gln Glu Ala Glu Asn Gln
145          150          155          160
Gln Leu Ala Asp Ala Val Leu Ala Gly Arg Arg Gln Val Glu Glu Leu
165          170          175
Gln Leu Gln Val Gln Ala Gln Gln Ala Trp Gln
180          185

```

```

<210> SEQ ID NO 151
<211> LENGTH: 23
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic Peptide

<400> SEQUENCE: 151
Val Arg Ser Pro Ala Val Gln Ser Pro Ala Lys Val Gln Pro Leu Cys
1           5           10           15
Pro Ser Arg Arg Ala Ala Arg
20

```

```

<210> SEQ ID NO 152
<211> LENGTH: 104
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic Peptide

<400> SEQUENCE: 152
Met Ala Val Leu Trp Arg Leu Ser Ala Val Cys Gly Ala Leu Gly Gly
1           5           10           15
Arg Ala Leu Leu Leu Arg Thr Pro Val Val Arg Pro Ala His Ile Ser
20           25           30
Ala Phe Leu Gln Asp Arg Pro Ile Pro Glu Trp Cys Gly Val Gln His
35           40           45

```

-continued

```

Ile His Leu Ser Pro Ser His His Ser Gly Ser Lys Ala Ala Ser Leu
 50          55          60
His Trp Thr Ser Glu Arg Val Val Ser Val Leu Leu Gly Leu Leu
65          70          75          80
Pro Ala Ala Tyr Leu Asn Pro Cys Ser Ala Met Asp Tyr Ser Leu Ala
          85          90          95
Ala Ala Leu Thr Leu His Gly His
          100

```

```

<210> SEQ ID NO 153
<211> LENGTH: 36
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic Peptide

```

```

<400> SEQUENCE: 153

```

```

Cys Leu Gln Cys Gln Ile Val His Ser Cys Pro Leu Leu Glu Asn Gln
1          5          10          15
Ile His Leu Ser Leu Lys Phe Pro Asp Tyr Phe Ile Lys Met Lys Pro
          20          25          30
Trp Arg Lys Ile
          35

```

```

<210> SEQ ID NO 154
<211> LENGTH: 84
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic Peptide

```

```

<400> SEQUENCE: 154

```

```

Met Trp Asn Pro Asn Ala Gly Gly Pro Pro His Pro Val Pro Gln Pro
1          5          10          15
Gly Tyr Pro Gly Cys Gln Pro Leu Gly Pro Tyr Pro Pro Pro Tyr Pro
          20          25          30
Pro Pro Ala Pro Gly Ile Pro Pro Val Asn Pro Leu Ala Pro Gly Met
          35          40          45
Val Gly Pro Ala Val Ile Val Asp Lys Lys Met Gln Lys Lys Met Lys
50          55          60
Lys Ala His Lys Lys Met His Lys His Gln Lys His His Lys Tyr His
65          70          75          80
Lys His Gly Lys

```

```

<210> SEQ ID NO 155
<211> LENGTH: 8
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic Peptide

```

```

<400> SEQUENCE: 155

```

```

Phe Leu Ala Phe Thr Pro Asn Gln
1          5

```

```

<210> SEQ ID NO 156
<211> LENGTH: 95
<212> TYPE: PRT

```

-continued

```

<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic Peptide

<400> SEQUENCE: 156
Met Asp Gln Cys Val Thr Val Glu Arg Glu Leu Glu Lys Val Leu His
1           5           10           15
Lys Phe Ser Gly Tyr Gly Gln Leu Cys Glu Arg Gly Leu Glu Glu Leu
20           25           30
Ile Asp Tyr Thr Gly Gly Leu Lys His Glu Ile Leu Gln Ser His Gly
35           40           45
Gln Asp Ala Glu Leu Ser Gly Thr Leu Ser Leu Val Leu Thr Gln Cys
50           55           60
Cys Lys Arg Ile Lys Asp Thr Val Gln Lys Leu Ala Ser Asp His Lys
65           70           75           80
Asp Ile His Ser Ser Val Ser Arg Val Gly Lys Ala Ile Asp Lys
85           90           95

```

```

<210> SEQ ID NO 157
<211> LENGTH: 3
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic Peptide

<400> SEQUENCE: 157

```

```

Asp Ser Leu
1

```

```

<210> SEQ ID NO 158
<211> LENGTH: 434
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic Peptide

<400> SEQUENCE: 158

```

```

Met Ala Ala Leu Met Thr Pro Gly Thr Gly Ala Pro Pro Ala Pro Gly
1           5           10           15
Asp Phe Ser Gly Glu Gly Ser Gln Gly Leu Pro Asp Pro Ser Pro Glu
20           25           30
Pro Lys Gln Leu Pro Glu Leu Ile Arg Met Lys Arg Asp Gly Gly Arg
35           40           45
Leu Ser Glu Ala Asp Ile Arg Gly Phe Val Ala Ala Val Val Asn Gly
50           55           60
Ser Ala Gln Gly Ala Gln Ile Gly Ala Met Leu Met Ala Ile Arg Leu
65           70           75           80
Arg Gly Met Asp Leu Glu Glu Thr Ser Val Leu Thr Gln Ala Leu Ala
85           90           95
Gln Ser Gly Gln Gln Leu Glu Trp Pro Glu Ala Trp Arg Gln Gln Leu
100          105          110
Val Asp Lys His Ser Thr Gly Gly Val Gly Asp Lys Val Ser Leu Val
115          120          125
Leu Ala Pro Ala Leu Ala Ala Cys Gly Cys Lys Val Pro Met Ile Ser
130          135          140
Gly Arg Gly Leu Gly His Thr Gly Gly Thr Leu Asp Lys Leu Glu Ser
145          150          155          160

```

-continued

```

Ile Pro Gly Phe Asn Val Ile Gln Ser Pro Glu Gln Met Gln Val Leu
    165                               170                               175
Leu Asp Gln Ala Gly Cys Cys Ile Val Gly Gln Ser Glu Gln Leu Val
    180                               185                               190
Pro Ala Asp Gly Ile Leu Tyr Ala Ala Arg Asp Val Thr Ala Thr Val
    195                               200                               205
Asp Ser Leu Pro Leu Ile Thr Ala Ser Ile Leu Ser Lys Lys Leu Val
    210                               215                               220
Glu Gly Leu Ser Ala Leu Val Val Asp Val Lys Phe Gly Gly Ala Ala
    225                               230                               235                               240
Val Phe Pro Asn Gln Glu Gln Ala Arg Glu Leu Ala Lys Thr Leu Val
    245                               250                               255
Gly Val Gly Ala Ser Leu Gly Leu Arg Val Ala Ala Ala Leu Thr Ala
    260                               265                               270
Met Asp Lys Pro Leu Gly Arg Cys Val Gly His Ala Leu Glu Val Glu
    275                               280                               285
Glu Ala Leu Leu Cys Met Asp Gly Ala Gly Pro Pro Asp Leu Arg Asp
    290                               295                               300
Leu Val Thr Thr Leu Gly Gly Ala Leu Leu Trp Leu Ser Gly His Ala
    305                               310                               315                               320
Gly Thr Gln Ala Gln Gly Ala Ala Arg Val Ala Ala Ala Leu Asp Asp
    325                               330                               335
Gly Ser Ala Leu Gly Arg Phe Glu Arg Met Leu Ala Ala Gln Gly Val
    340                               345                               350
Asp Pro Gly Leu Ala Arg Ala Leu Cys Ser Gly Ser Pro Ala Glu Arg
    355                               360                               365
Arg Gln Leu Leu Pro Arg Ala Arg Glu Gln Glu Glu Leu Leu Ala Pro
    370                               375                               380
Ala Asp Gly Thr Val Glu Leu Val Arg Ala Leu Pro Leu Ala Leu Val
    385                               390                               395                               400
Leu His Glu Leu Gly Ala Gly Arg Ser Arg Ala Gly Glu Pro Leu Arg
    405                               410                               415
Leu Gly Val Gly Ala Glu Leu Leu Val Asp Val Gly Gln Arg Leu Arg
    420                               425                               430
Arg Gly

```

```

<210> SEQ ID NO 159
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic Peptide

```

```

<400> SEQUENCE: 159

```

```

Ala Ser Asp Pro Cys Cys Cys
1           5

```

```

<210> SEQ ID NO 160
<211> LENGTH: 1147
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic Peptide

```

```

<400> SEQUENCE: 160

```

-continued

Met Ala Thr Gln Gln Lys Ala Ser Asp Glu Arg Ile Ser Gln Phe Asp
 1 5 10 15
 His Asn Leu Leu Pro Glu Leu Ser Ala Leu Leu Gly Leu Asp Ala Val
 20 25 30
 Gln Leu Ala Lys Glu Leu Glu Glu Glu Gln Lys Glu Arg Ala Lys
 35 40 45
 Met Gln Lys Gly Tyr Asn Ser Gln Met Arg Ser Glu Ala Lys Arg Leu
 50 55 60
 Lys Thr Phe Val Thr Tyr Glu Pro Tyr Ser Ser Trp Ile Pro Gln Glu
 65 70 75 80
 Met Ala Ala Ala Gly Phe Tyr Phe Thr Gly Val Lys Ser Gly Ile Gln
 85 90 95
 Cys Phe Cys Cys Ser Leu Ile Leu Phe Gly Ala Gly Leu Thr Arg Leu
 100 105 110
 Pro Ile Glu Asp His Lys Arg Phe His Pro Asp Cys Gly Phe Leu Leu
 115 120 125
 Asn Lys Asp Val Gly Asn Ile Ala Lys Tyr Asp Ile Arg Val Lys Asn
 130 135 140
 Leu Lys Ser Arg Leu Arg Gly Gly Lys Met Arg Tyr Gln Glu Glu Glu
 145 150 155 160
 Ala Arg Leu Ala Ser Phe Arg Asn Trp Pro Phe Tyr Val Gln Gly Ile
 165 170 175
 Ser Pro Cys Val Leu Ser Glu Ala Gly Phe Val Phe Thr Gly Lys Gln
 180 185 190
 Asp Thr Val Gln Cys Phe Ser Cys Gly Gly Cys Leu Gly Asn Trp Glu
 195 200 205
 Glu Gly Asp Asp Pro Trp Lys Glu His Ala Lys Trp Phe Pro Lys Cys
 210 215 220
 Glu Phe Leu Arg Ser Lys Lys Ser Ser Glu Glu Ile Thr Gln Tyr Ile
 225 230 235 240
 Gln Ser Tyr Lys Gly Phe Val Asp Ile Thr Gly Glu His Phe Val Asn
 245 250 255
 Ser Trp Val Gln Arg Glu Leu Pro Met Ala Ser Ala Tyr Cys Asn Asp
 260 265 270
 Ser Ile Phe Ala Tyr Glu Glu Leu Arg Leu Asp Ser Phe Lys Asp Trp
 275 280 285
 Pro Arg Glu Ser Ala Val Gly Val Ala Ala Leu Ala Lys Ala Gly Leu
 290 295 300
 Phe Tyr Thr Gly Ile Lys Asp Ile Val Gln Cys Phe Ser Cys Gly Gly
 305 310 315 320
 Cys Leu Glu Lys Trp Gln Glu Gly Asp Asp Pro Leu Asp Asp His Thr
 325 330 335
 Arg Cys Phe Pro Asn Cys Pro Phe Leu Gln Asn Met Lys Ser Ser Ala
 340 345 350
 Glu Val Thr Pro Asp Leu Gln Ser Arg Gly Glu Leu Cys Glu Leu Leu
 355 360 365
 Glu Thr Thr Ser Glu Ser Asn Leu Glu Asp Ser Ile Ala Val Gly Pro
 370 375 380
 Ile Val Pro Glu Met Ala Gln Gly Glu Ala Gln Trp Phe Gln Glu Ala
 385 390 395 400

-continued

Lys	Asn	Leu	Asn	Glu	Gln	Leu	Arg	Ala	Ala	Tyr	Thr	Ser	Ala	Ser	Phe
				405					410						415
Arg	His	Met	Ser	Leu	Leu	Asp	Ile	Ser	Ser	Asp	Leu	Ala	Thr	Asp	His
			420					425					430		
Leu	Leu	Gly	Cys	Asp	Leu	Ser	Ile	Ala	Ser	Lys	His	Ile	Ser	Lys	Pro
		435					440					445			
Val	Gln	Glu	Pro	Leu	Val	Leu	Pro	Glu	Val	Phe	Gly	Asn	Leu	Asn	Ser
	450					455					460				
Val	Met	Cys	Val	Glu	Gly	Glu	Ala	Gly	Ser	Gly	Lys	Thr	Val	Leu	Leu
	465				470					475					480
Lys	Lys	Ile	Ala	Phe	Leu	Trp	Ala	Ser	Gly	Cys	Cys	Pro	Leu	Leu	Asn
			485						490						495
Arg	Phe	Gln	Leu	Val	Phe	Tyr	Leu	Ser	Leu	Ser	Ser	Thr	Arg	Pro	Asp
			500					505						510	
Glu	Gly	Leu	Ala	Ser	Ile	Ile	Cys	Asp	Gln	Leu	Leu	Glu	Lys	Glu	Gly
		515					520					525			
Ser	Val	Thr	Glu	Met	Cys	Val	Arg	Asn	Ile	Ile	Gln	Gln	Leu	Lys	Asn
	530					535					540				
Gln	Val	Leu	Phe	Leu	Leu	Asp	Asp	Tyr	Lys	Glu	Ile	Cys	Ser	Ile	Pro
	545				550					555					560
Gln	Val	Ile	Gly	Lys	Leu	Ile	Gln	Lys	Asn	His	Leu	Ser	Arg	Thr	Cys
			565					570						575	
Leu	Leu	Ile	Ala	Val	Arg	Thr	Asn	Arg	Ala	Arg	Asp	Ile	Arg	Arg	Tyr
			580					585						590	
Leu	Glu	Thr	Ile	Leu	Glu	Ile	Lys	Ala	Phe	Pro	Phe	Tyr	Asn	Thr	Val
		595					600						605		
Cys	Ile	Leu	Arg	Lys	Leu	Phe	Ser	His	Asn	Met	Thr	Arg	Leu	Arg	Lys
	610					615						620			
Phe	Met	Val	Tyr	Phe	Gly	Lys	Asn	Gln	Ser	Leu	Gln	Lys	Ile	Gln	Lys
	625				630					635					640
Thr	Pro	Leu	Phe	Val	Ala	Ala	Ile	Cys	Ala	His	Trp	Phe	Gln	Tyr	Pro
			645						650					655	
Phe	Asp	Pro	Ser	Phe	Asp	Asp	Val	Ala	Val	Phe	Lys	Ser	Tyr	Met	Glu
			660					665						670	
Arg	Leu	Ser	Leu	Arg	Asn	Lys	Ala	Thr	Ala	Glu	Ile	Leu	Lys	Ala	Thr
		675					680							685	
Val	Ser	Ser	Cys	Gly	Glu	Leu	Ala	Leu	Lys	Gly	Phe	Phe	Ser	Cys	Cys
		690				695					700				
Phe	Glu	Phe	Asn	Asp	Asp	Asp	Leu	Ala	Glu	Ala	Gly	Val	Asp	Glu	Asp
	705				710					715					720
Glu	Asp	Leu	Thr	Met	Cys	Leu	Met	Ser	Lys	Phe	Thr	Ala	Gln	Arg	Leu
			725						730					735	
Arg	Pro	Phe	Tyr	Arg	Phe	Leu	Ser	Pro	Ala	Phe	Gln	Glu	Phe	Leu	Ala
			740					745						750	
Gly	Met	Arg	Leu	Ile	Glu	Leu	Leu	Asp	Ser	Asp	Arg	Gln	Glu	His	Gln
		755					760						765		
Asp	Leu	Gly	Leu	Tyr	His	Leu	Lys	Gln	Ile	Asn	Ser	Pro	Met	Met	Thr
	770					775						780			
Val	Ser	Ala	Tyr	Asn	Asn	Phe	Leu	Asn	Tyr	Val	Ser	Ser	Leu	Pro	Ser
		785			790					795					800
Thr	Lys	Ala	Gly	Pro	Lys	Ile	Val	Ser	His	Leu	Leu	His	Leu	Val	Asp

-continued

805				810				815							
Asn	Lys	Glu	Ser	Leu	Glu	Asn	Ile	Ser	Glu	Asn	Asp	Asp	Tyr	Leu	Lys
			820					825					830		
His	Gln	Pro	Glu	Ile	Ser	Leu	Gln	Met	Gln	Leu	Leu	Arg	Gly	Leu	Trp
		835					840					845			
Gln	Ile	Cys	Pro	Gln	Ala	Tyr	Phe	Ser	Met	Val	Ser	Glu	His	Leu	Leu
	850					855					860				
Val	Leu	Ala	Leu	Lys	Thr	Ala	Tyr	Gln	Ser	Asn	Thr	Val	Ala	Ala	Cys
865					870					875					880
Ser	Pro	Phe	Val	Leu	Gln	Phe	Leu	Gln	Gly	Arg	Thr	Leu	Thr	Leu	Gly
			885						890					895	
Ala	Leu	Asn	Leu	Gln	Tyr	Phe	Phe	Asp	His	Pro	Glu	Ser	Leu	Ser	Leu
		900						905					910		
Leu	Arg	Ser	Ile	His	Phe	Pro	Ile	Arg	Gly	Asn	Lys	Thr	Ser	Pro	Arg
	915					920						925			
Ala	His	Phe	Ser	Val	Leu	Glu	Thr	Cys	Phe	Asp	Lys	Ser	Gln	Val	Pro
930					935						940				
Thr	Ile	Asp	Gln	Asp	Tyr	Ala	Ser	Ala	Phe	Glu	Pro	Met	Asn	Glu	Trp
945					950					955					960
Glu	Arg	Asn	Leu	Ala	Glu	Lys	Glu	Asp	Asn	Val	Lys	Ser	Tyr	Met	Asp
			965						970					975	
Met	Gln	Arg	Arg	Ala	Ser	Pro	Asp	Leu	Ser	Thr	Gly	Tyr	Trp	Lys	Leu
			980					985					990		
Ser	Pro	Lys	Gln	Tyr	Lys	Ile	Pro	Cys	Leu	Glu	Val	Asp	Val	Asn	Asp
		995				1000						1005			
Ile	Asp	Val	Val	Gly	Gln	Asp	Met	Leu	Glu	Ile	Leu	Met	Thr	Val	Phe
	1010					1015					1020				
Ser	Ala	Ser	Gln	Arg	Ile	Glu	Leu	His	Leu	Asn	His	Ser	Arg	Gly	Phe
1025				1030						1035					1040
Ile	Glu	Ser	Ile	Arg	Pro	Ala	Leu	Glu	Leu	Ser	Lys	Ala	Ser	Val	Thr
			1045						1050					1055	
Lys	Cys	Ser	Ile	Ser	Lys	Leu	Glu	Leu	Ser	Ala	Ala	Glu	Gln	Glu	Leu
			1060				1065						1070		
Leu	Leu	Thr	Leu	Pro	Ser	Leu	Glu	Ser	Leu	Glu	Val	Ser	Gly	Thr	Ile
	1075					1080						1085			
Gln	Ser	Gln	Asp	Gln	Ile	Phe	Pro	Asn	Leu	Asp	Lys	Phe	Leu	Cys	Leu
	1090					1095					1100				
Lys	Glu	Leu	Ser	Val	Asp	Leu	Glu	Gly	Asn	Ile	Asn	Val	Phe	Ser	Val
1105					1110					1115					1120
Ile	Pro	Glu	Glu	Phe	Pro	Asn	Phe	His	His	Met	Glu	Lys	Leu	Leu	Ile
			1125						1130					1135	
Gln	Ile	Ser	Ala	Glu	Tyr	Asp	Pro	Ser	Lys	Leu					
		1140							1145						

<210> SEQ ID NO 161

<211> LENGTH: 1

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic Peptide

<400> SEQUENCE: 161

Gly

-continued

1

<210> SEQ ID NO 162
 <211> LENGTH: 22
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic Peptide

<400> SEQUENCE: 162

Met Ser Glu Ser Glu Leu Gly Arg Lys Trp Asp Arg Cys Leu Ala Asp
 1 5 10 15

 Ala Val Val Lys Ile Gly
 20

<210> SEQ ID NO 163
 <211> LENGTH: 6
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic Peptide

<400> SEQUENCE: 163

Leu Trp Arg Pro Arg Ala
 1 5

<210> SEQ ID NO 164
 <211> LENGTH: 42
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic Peptide

<400> SEQUENCE: 164

Met Ala Ala Glu Ser Leu Pro Phe Ser Phe Gly Thr Leu Ser Ser Trp
 1 5 10 15

 Glu Leu Glu Ala Trp Tyr Glu Asp Leu Gln Glu Val Leu Ser Ser Asp
 20 25 30

 Glu Asn Gly Gly Thr Tyr Val Ser Pro Pro
 35 40

<210> SEQ ID NO 165
 <211> LENGTH: 138
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic Peptide

<400> SEQUENCE: 165

Leu Pro Leu Gly Ala Ser Gly Gly Phe Pro Ser Ala Thr Ala Asn Cys
 1 5 10 15

 Phe Phe Arg Ser Lys Ser Phe Ala Thr Ser Ala Ala Thr Ser Phe Leu
 20 25 30

 Ser Ala Phe Cys Ala Phe Ser Ser Arg Thr Met Phe Pro Cys Phe Val
 35 40 45

 Thr Ser Ser Ile Ser Ala Cys Ile Cys Cys Gly Leu Ala Val Val Thr
 50 55 60

 Val Ser Thr Thr Ala Gly Phe Gly Asp Val Phe Ala Trp Pro Pro Pro
 65 70 75 80

 Lys Arg Cys Leu Lys Leu Ser Ile Trp Ser Phe Ser Asn Phe Trp Asn

-continued

```

                85                90                95
Lys Gly Leu Thr Val Pro Ile Trp Cys Pro Ala Gly Lys Val His Arg
                100                105                110
Lys Phe Val Ser Arg Ile Leu Gln Ala Gly Gly Gly Ser Cys Ser Trp
                115                120                125
Ala Trp Ile Val Ala Leu Thr Val Gly Met
                130                135

```

```

<210> SEQ ID NO 166
<211> LENGTH: 446
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic Peptide

```

```

<400> SEQUENCE: 166

```

```

Met Ser Cys Val Lys Leu Trp Pro Ser Gly Ala Pro Ala Pro Leu Val
1          5          10          15
Ser Ile Glu Glu Leu Glu Asn Gln Glu Leu Val Gly Lys Gly Gly Phe
20        25        30
Gly Thr Val Phe Arg Ala Gln His Arg Lys Trp Gly Tyr Asp Val Ala
35        40        45
Val Lys Ile Val Asn Ser Lys Ala Ile Ser Arg Glu Val Lys Ala Met
50        55        60
Ala Ser Leu Asp Asn Glu Phe Val Leu Arg Leu Glu Gly Val Ile Glu
65        70        75        80
Lys Val Asn Trp Asp Gln Asp Pro Lys Pro Ala Leu Val Thr Lys Phe
85        90        95
Met Glu Asn Gly Ser Leu Ser Gly Leu Leu Gln Ser Gln Cys Pro Arg
100       105       110
Pro Trp Pro Leu Leu Cys Arg Leu Leu Lys Glu Val Val Leu Gly Met
115      120      125
Phe Tyr Leu His Asp Gln Asn Pro Val Leu Leu His Arg Asp Leu Lys
130     135     140
Pro Ser Asn Val Leu Leu Asp Pro Glu Leu His Val Lys Leu Ala Asp
145     150     155     160
Phe Gly Leu Ser Thr Phe Gln Gly Gly Ser Gln Ser Gly Thr Gly Ser
165     170     175
Gly Glu Pro Gly Gly Thr Leu Gly Tyr Leu Ala Pro Glu Leu Phe Val
180     185     190
Asn Val Asn Arg Lys Ala Ser Thr Ala Ser Asp Val Tyr Ser Phe Gly
195     200     205
Ile Leu Met Trp Ala Val Leu Ala Gly Arg Glu Val Glu Leu Pro Thr
210     215     220
Glu Pro Ser Leu Val Tyr Glu Ala Val Cys Asn Arg Gln Asn Arg Pro
225     230     235     240
Ser Leu Ala Glu Leu Pro Gln Ala Gly Pro Glu Thr Pro Gly Leu Glu
245     250     255
Gly Leu Lys Glu Leu Met Gln Leu Cys Trp Ser Ser Glu Pro Lys Asp
260     265     270
Arg Pro Ser Phe Gln Glu Cys Leu Pro Lys Thr Asp Glu Val Phe Gln
275     280     285
Met Val Glu Asn Asn Met Asn Ala Ala Val Ser Thr Val Lys Asp Phe

```

-continued

290			295			300									
Leu	Ser	Gln	Leu	Arg	Ser	Ser	Asn	Arg	Arg	Phe	Ser	Ile	Pro	Glu	Ser
305					310					315					320
Gly	Gln	Gly	Gly	Thr	Glu	Met	Asp	Gly	Phe	Arg	Arg	Thr	Ile	Glu	Asn
				325						330				335	
Gln	His	Ser	Arg	Asn	Asp	Val	Met	Val	Ser	Glu	Trp	Leu	Asn	Lys	Leu
				340						345				350	
Asn	Leu	Glu	Glu	Pro	Pro	Ser	Ser	Val	Pro	Lys	Lys	Cys	Pro	Ser	Leu
		355						360						365	
Thr	Lys	Arg	Ser	Arg	Ala	Gln	Glu	Glu	Gln	Val	Pro	Gln	Ala	Trp	Thr
		370						375						380	
Ala	Gly	Thr	Ser	Ser	Asp	Ser	Met	Ala	Gln	Pro	Pro	Gln	Thr	Pro	Glu
		385			390						395				400
Thr	Ser	Thr	Phe	Arg	Asn	Gln	Met	Pro	Ser	Pro	Thr	Ser	Thr	Gly	Thr
				405						410				415	
Pro	Ser	Pro	Gly	Pro	Arg	Gly	Asn	Gln	Gly	Ala	Glu	Arg	Gln	Gly	Met
				420				425						430	
Asn	Trp	Ser	Cys	Arg	Thr	Pro	Glu	Pro	Asn	Pro	Val	Thr	Gly		
		435						440						445	

<210> SEQ ID NO 167
 <211> LENGTH: 203
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic Peptide

<400> SEQUENCE: 167

Asp	Leu	Arg	Pro	Glu	Leu	Pro	Asp	His	Cys	Ala	Val	Arg	Ala	Gly	Arg
1				5					10					15	
Leu	Leu	Ala	Ala	Ala	Gly	Pro	Arg	Phe	Pro	Gly	Ala	Ala	Thr	Ala	Ala
				20				25					30		
Leu	Asp	Ala	Ser	Pro	Val	Arg	Leu	Gly	Met	Gly	Arg	Ala	Ala	Ser	Ala
		35					40					45			
Arg	Pro	Arg	Leu	Pro	Val	His	Arg	Gly	Arg	Gly	Glu	Arg	Leu	Gly	Pro
		50				55					60				
Gly	Val	Leu	Phe	Ser	Leu	Arg	His	Leu	His	Gly	Val	Cys	His	Ala	Ala
		65			70					75				80	
Leu	Gly	His	Ala	Gly	Arg	Arg	Arg	Arg	Gly	Pro	Arg	Leu	Leu	Thr	Leu
				85					90					95	
Ala	Ser	Ala	Gly	Pro	Arg	Ala	Val	Ser	Trp	Ala	Thr	Ala	Gly	Leu	Thr
				100					105					110	
Ala	Cys	Thr	Ala	Ala	Ala	Val	Gly	Ser	Lys	Arg	Ser	Ala	Val	Pro	Val
		115					120						125		
Arg	Glu	Arg	Gly	Arg	Ser	Val	Pro	Gln	Gly	Ala	Asp	Gly	Ala	Arg	Pro
		130				135						140			
Ala	Gly	His	Val	Pro	Gly	Gly	Thr	Gln	Leu	Pro	Ala	Leu	Thr	Pro	Ala
				145		150				155				160	
Ala	Gly	His	Arg	Glu	Glu	Ala	Pro	Gly	Thr	Pro	Ser	Leu	Val	His	Pro
				165					170					175	
Ser	Cys	Leu	Pro	Gly	Pro	Arg	Asp	Glu	Gly	Arg	Asp	His	Gly	Thr	Ala
			180					185						190	
Ala	Gly	Arg	Thr	Gly	Val	Thr	Ala	Arg	Glu	His					

-continued

```

Ser Glu Ser Gly Gly Leu Arg Pro Asn Lys Gln Thr Phe Asn Pro Thr
      165                      170                      175
Asp Thr Asn Ala Leu Val Ala Ala Val Ala Phe Gly Lys Gly Leu Ser
      180                      185                      190
Asn Trp Arg Pro Ser Gly Ser Ser Gly Pro Gly Gln Ala Gly Gln Pro
      195                      200                      205
Gly Ala Gly Thr Ile Leu Ala Gly Thr Ser Gly Leu Gln Gln Val Gln
      210                      215                      220
Met Ala Gly Ala Pro Ser Gln Gln Gln Pro Met Leu Ser Gly Val Gln
      225                      230                      235
Met Ala Gln Ala Gly Gln Pro Gly Lys Met Pro Ser Gly Ile Lys Thr
      245                      250                      255
Asn Ile Lys Ser Ala Ser Met His Pro Tyr Gln Arg Ser Glu Gln Ile
      260                      265                      270

```

Asp Asn

```

<210> SEQ ID NO 171
<211> LENGTH: 55
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic Peptide

```

<400> SEQUENCE: 171

```

Val Leu Ser Gln Asp Gly Gly Cys Cys Glu Leu Val Pro Arg Gly Asp
 1      5                      10                      15
Glu Ala Arg Arg Ser Pro Asp Pro Gly Leu Pro Ser Asp Gly Val Pro
 20     25                      30
Leu Ala Asn Asp Leu His Ser Pro Asp Leu Arg Val Leu Arg Ser Leu
 35     40                      45
Thr Trp Ala Ser His His Gly
 50     55

```

```

<210> SEQ ID NO 172
<211> LENGTH: 47
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic Peptide

```

<400> SEQUENCE: 172

```

Met Asn Ala Pro Pro Ala Phe Glu Ser Phe Leu Leu Phe Glu Gly Glu
 1      5                      10                      15
Lys Ile Thr Ile Asn Lys Asp Thr Lys Val Pro Asn Ala Cys Leu Phe
 20     25                      30
Thr Met Asn Lys Glu Asp His Thr Leu Gly Asn Ile Ile Lys Ser
 35     40                      45

```

```

<210> SEQ ID NO 173
<211> LENGTH: 29
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic Peptide

```

<400> SEQUENCE: 173

```

Arg Ala Cys Phe Pro Phe Ala Phe Cys Arg Asp Cys Gln Phe Pro Glu
 1      5                      10                      15

```

-continued

Ala Ser Pro Ala Thr Leu Ser Val Gln Pro Ala Glu Leu
 20 25

<210> SEQ ID NO 174
 <211> LENGTH: 188
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic Peptide

<400> SEQUENCE: 174

Met Ala Glu Ala Ser Ser Ala Asn Leu Gly Ser Gly Cys Glu Glu Lys
 1 5 10 15

Arg His Glu Gly Ser Ser Ser Glu Ser Val Pro Pro Gly Thr Thr Ile
 20 25 30

Ser Arg Val Lys Leu Leu Asp Thr Met Val Asp Thr Phe Leu Gln Lys
 35 40 45

Leu Val Ala Ala Gly Ser Tyr Gln Arg Phe Thr Asp Cys Tyr Lys Cys
 50 55 60

Phe Tyr Gln Leu Gln Pro Ala Met Thr Gln Gln Ile Tyr Asp Lys Phe
 65 70 75 80

Ile Ala Gln Leu Gln Thr Ser Ile Arg Glu Glu Ile Ser Asp Ile Lys
 85 90 95

Glu Glu Gly Asn Leu Glu Ala Val Leu Asn Ala Leu Asp Lys Ile Val
 100 105 110

Glu Glu Gly Lys Val Arg Lys Glu Pro Ala Trp Arg Pro Ser Gly Ile
 115 120 125

Pro Glu Lys Asp Leu His Ser Val Met Ala Pro Tyr Phe Leu Gln Gln
 130 135 140

Arg Asp Thr Leu Arg Arg His Val Gln Lys Gln Glu Ala Glu Asn Gln
 145 150 155 160

Gln Leu Ala Asp Ala Val Leu Ala Gly Arg Arg Gln Val Glu Glu Leu
 165 170 175

Gln Leu Gln Val Gln Ala Gln Gln Ala Trp Gln
 180 185

<210> SEQ ID NO 175
 <211> LENGTH: 23
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic Peptide

<400> SEQUENCE: 175

Val Arg Ser Pro Ala Val Gln Ser Pro Ala Lys Val Gln Pro Leu Cys
 1 5 10 15

Pro Ser Arg Arg Ala Ala Arg
 20

<210> SEQ ID NO 176
 <211> LENGTH: 178
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic Peptide

<400> SEQUENCE: 176

-continued

Met Ala Ser Ser Leu Leu Ala Gly Glu Arg Leu Val Arg Ala Leu Gly
 1 5 10 15
 Pro Gly Gly Glu Leu Glu Pro Glu Arg Leu Pro Arg Lys Leu Arg Ala
 20 25 30
 Glu Leu Glu Ala Ala Leu Gly Lys Lys His Lys Gly Gly Asp Ser Ser
 35 40 45
 Ser Gly Pro Gln Arg Leu Val Ser Phe Arg Leu Ile Arg Asp Leu His
 50 55 60
 Gln His Leu Arg Glu Arg Asp Ser Lys Leu Tyr Leu His Glu Leu Leu
 65 70 75 80
 Glu Gly Ser Glu Ile Tyr Leu Pro Glu Val Val Lys Pro Pro Arg Asn
 85 90 95
 Pro Glu Leu Val Ala Arg Leu Glu Lys Ile Lys Ile Gln Leu Ala Asn
 100 105 110
 Glu Glu Tyr Lys Arg Ile Thr Arg Asn Val Thr Cys Gln Asp Thr Arg
 115 120 125
 His Gly Gly Thr Leu Ser Asp Leu Gly Lys Gln Val Arg Ser Leu Lys
 130 135 140
 Ala Leu Val Ile Thr Ile Phe Asn Phe Ile Val Thr Val Val Ala Ala
 145 150 155 160
 Phe Val Cys Thr Tyr Leu Gly Ser Gln Tyr Ile Phe Thr Glu Met Ala
 165 170 175
 Ser Arg

<210> SEQ ID NO 177
 <211> LENGTH: 121
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic Peptide

<400> SEQUENCE: 177

Pro Arg Gly Ala His Trp Ala Gly Arg Asp Pro Glu Pro Gly Glu Gly
 1 5 10 15
 Thr Arg Thr Arg Arg Ala Gly Ala Glu Arg Gly Arg His Leu Gly Ala
 20 25 30
 His Val Gln Ala Phe Gly Gly Asp Met Pro Glu Ala Gly Gly Gly Arg
 35 40 45
 Arg Pro Gly Arg Gly Ala Val Leu Val Pro Pro His Gly Pro Arg Ala
 50 55 60
 Ala Ala Pro Leu Arg Ala Gly Ala Gly Gln Leu Arg Ala Ala Arg Gly
 65 70 75 80
 Pro Gly Gly Ala Ala Thr His Gly Arg Glu Ala Arg Ser Arg Val Ala
 85 90 95
 Leu Pro Ala Arg Leu Leu Gln Gly Gly Arg Ala Ala Ser Ala Ala Arg
 100 105 110
 Leu Pro Arg Ser Ser Gly Val Gly Asp
 115 120

<210> SEQ ID NO 178
 <211> LENGTH: 97
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic Peptide

-continued

<400> SEQUENCE: 178

```

Met Gln Trp Leu Arg Val Arg Glu Ser Pro Gly Glu Ala Thr Gly His
1           5           10           15
Arg Val Thr Met Gly Thr Ala Ala Leu Gly Pro Val Trp Ala Ala Leu
          20           25           30
Leu Leu Phe Leu Leu Met Cys Glu Ile Pro Met Val Glu Leu Thr Phe
          35           40           45
Asp Arg Ala Val Ala Ser Gly Cys Gln Arg Cys Cys Asp Ser Glu Asp
          50           55           60
Pro Leu Asp Pro Ala His Val Ser Ser Ala Ser Ser Ser Gly Arg Pro
          65           70           75           80
His Ala Leu Pro Glu Ile Arg Pro Tyr Ile Asn Ile Thr Ile Leu Lys
          85           90           95

```

Gly

<210> SEQ ID NO 179

<211> LENGTH: 84

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic Peptide

<400> SEQUENCE: 179

```

Leu Pro Ser Ser Ala Pro Pro Cys Gly Cys Asn Gly Gly Pro Cys Ser
1           5           10           15
Val Leu Ala Ser Ala Pro Pro His Pro Pro Pro Ala Pro Gly Tyr Leu
          20           25           30
Leu Gly Ile Cys Ser Gly Glu Trp His Phe Pro Val His Met Leu Leu
          35           40           45
Gln Leu Glu Ser Gln His Leu Leu Cys Leu Glu Pro Arg Trp Gly Ser
          50           55           60
Ala Gly His Phe Leu Pro Ser Pro Cys Leu Ala Gly Gln Thr Ala Val
          65           70           75           80
Glu Pro Asn Leu

```

<210> SEQ ID NO 180

<211> LENGTH: 173

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic Peptide

<400> SEQUENCE: 180

```

Met Asp Pro Ala Ser Arg Gly Cys Leu Gly Pro Thr Pro Ala Phe Arg
1           5           10           15
His Arg Lys Glu Gln Ser Ser Ala Ser Pro Arg Pro Ser Glu Ala Thr
          20           25           30
Gly Ala Arg Thr Met Gly Ser Gln Ala Arg Arg Pro Pro Val Ile Pro
          35           40           45
Phe Thr Lys Asn Glu Thr Leu Phe Ser Leu Pro Gly Pro Asp Ala Arg
          50           55           60
Gln Pro Thr Arg Pro Arg Pro Gly Asp Leu Glu Thr Gly Ser Leu Asp
          65           70           75           80
Glu Glu Pro Glu Gly Gly Lys Gly Thr Gly Gly Arg Lys Ile Ser Arg

```

-continued

	85	90	95
Ile Asp Phe Ile Thr Lys Phe Trp Val Pro Ala Ser Gly Val Pro Asp	100	105	110
Glu Thr Lys Arg Leu Leu Val Leu His Pro Arg Cys Tyr Phe Gln Asn	115	120	125
Ser Gly Leu Val Val Trp Ser Leu His Cys Ser Met Ser Leu Leu Ser	130	135	140
Asn Leu Glu Ser Ser Val Phe Leu Pro Ser Val Arg Cys Ala Tyr Phe	145	150	155
Ser Leu Glu Lys Leu Glu Glu Ala Gly Met Leu Glu Met	165	170	

<210> SEQ ID NO 181
 <211> LENGTH: 58
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic Peptide

<400> SEQUENCE: 181

Arg Pro Ser Thr	Pro Cys Leu His Gly Ala Ala Leu His Leu His Ser		
1	5	10	
15			
Gly His Gly Ser Gly Ser Arg Leu Thr Asn Ser Ser Cys Phe Pro Gly	20	25	30
Thr Arg Arg Leu Leu Ala Leu Gln Phe Thr Gln Gln Thr Gly Thr Val	35	40	45
Gly His Pro Thr Trp Gln Pro Val Ile Arg	50	55	

<210> SEQ ID NO 182
 <211> LENGTH: 65
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic Peptide

<400> SEQUENCE: 182

Met Ser Thr Ala Met Asn Phe Gly Thr Lys Ser Phe Gln Pro Arg Pro			
1	5	10	
15			
Pro Asp Lys Gly Ser Phe Pro Leu Asp His Leu Gly Glu Cys Lys Ser	20	25	30
Phe Lys Glu Lys Phe Met Lys Cys Leu His Asn Asn Asn Phe Glu Asn	35	40	45
Ala Leu Cys Arg Lys Glu Ser Lys Glu Tyr Leu Glu Cys Arg Met Glu	50	55	60

Arg
65

<210> SEQ ID NO 183
 <211> LENGTH: 57
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic Peptide

<400> SEQUENCE: 183

Ser Arg Leu Gly Leu Leu His Ser Gly Arg Leu His Leu Pro Glu Leu		
1	5	10
15		

-continued

Leu Gly Asn Pro Pro Glu Tyr Pro Pro Gly Gln Gln Gly Glu Val Arg
 20 25 30
 Pro Pro Gly Arg Leu Gly Gly Gly Pro Ser Gly Val His Gly Leu Pro
 35 40 45
 Arg Glu Arg Arg Arg Glu Ser Gln Val
 50 55

<210> SEQ ID NO 184
 <211> LENGTH: 405
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic Peptide

<400> SEQUENCE: 184

Met Ala Val Tyr Val Gly Met Leu Arg Leu Gly Arg Leu Cys Ala Gly
 1 5 10 15
 Ser Ser Gly Val Leu Gly Ala Arg Ala Leu Ser Arg Ser Trp Gln
 20 25 30
 Glu Ala Arg Leu Gln Gly Val Arg Phe Leu Ser Ser Arg Glu Val Asp
 35 40 45
 Arg Met Val Ser Thr Pro Ile Gly Gly Leu Ser Tyr Val Gln Gly Cys
 50 55 60
 Thr Lys Lys His Leu Asn Ser Lys Thr Val Gly Gln Cys Leu Glu Thr
 65 70 75 80
 Thr Ala Gln Arg Val Pro Glu Arg Glu Ala Leu Val Val Leu His Glu
 85 90 95
 Asp Val Arg Leu Thr Phe Ala Gln Leu Lys Glu Glu Val Asp Lys Ala
 100 105 110
 Ala Ser Gly Leu Leu Ser Ile Gly Leu Cys Lys Gly Asp Arg Leu Gly
 115 120 125
 Met Trp Gly Pro Asn Ser Tyr Ala Trp Val Leu Met Gln Leu Ala Thr
 130 135 140
 Ala Gln Ala Gly Ile Ile Leu Val Ser Val Asn Pro Ala Tyr Gln Ala
 145 150 155 160
 Met Glu Leu Glu Tyr Val Leu Lys Lys Val Gly Cys Lys Ala Leu Val
 165 170 175
 Phe Pro Lys Gln Phe Lys Thr Gln Gln Tyr Tyr Asn Val Leu Lys Gln
 180 185 190
 Ile Cys Pro Glu Val Glu Asn Ala Gln Pro Gly Ala Leu Lys Ser Gln
 195 200 205
 Arg Leu Pro Asp Leu Thr Thr Val Ile Ser Val Asp Ala Pro Leu Pro
 210 215 220
 Gly Thr Leu Leu Leu Asp Glu Val Val Ala Ala Gly Ser Thr Arg Gln
 225 230 235 240
 His Leu Asp Gln Leu Gln Tyr Asn Gln Gln Phe Leu Ser Cys His Asp
 245 250 255
 Pro Ile Asn Ile Gln Phe Thr Ser Gly Thr Thr Gly Ser Pro Lys Gly
 260 265 270
 Ala Thr Leu Ser His Tyr Asn Ile Val Asn Asn Ser Asn Ile Leu Gly
 275 280 285
 Glu Arg Leu Lys Leu His Glu Lys Thr Pro Glu Gln Leu Arg Met Ile
 290 295 300

-continued

Leu Pro Asn Pro Leu Tyr His Cys Leu Gly Ser Val Ala Gly Thr Met
 305 310 315 320

Met Cys Leu Met Tyr Gly Ala Thr Leu Ile Leu Ala Ser Pro Ile Phe
 325 330 335

Asn Gly Lys Lys Ala Leu Glu Ala Ile Ser Arg Glu Arg Gly Thr Phe
 340 345 350

Leu Tyr Gly Thr Pro Thr Met Phe Val Asp Ile Leu Asn Gln Pro Asp
 355 360 365

Phe Ser Ser Tyr Asp Ile Ser Thr Met Cys Gly Gly Val Ile Ala Gly
 370 375 380

Ser Pro Ala Pro Pro Glu Leu Ile Arg Ala Ile Ile Asn Lys Ile Asn
 385 390 395 400

Met Lys Asp Leu Val
 405

<210> SEQ ID NO 185
 <211> LENGTH: 20
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic Peptide

<400> SEQUENCE: 185

Arg Asn Leu Arg Lys Lys Leu Gln His Gly Lys Met Asp Ser Lys Ala
 1 5 10 15

Pro Met Ser Cys
 20

<210> SEQ ID NO 186
 <211> LENGTH: 171
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic Peptide

<400> SEQUENCE: 186

Met Glu Gly Gly Gly Gly Ser Gly Asn Lys Thr Thr Gly Gly Leu Ala
 1 5 10 15

Gly Phe Phe Gly Ala Gly Gly Ala Gly Tyr Ser His Ala Asp Leu Ala
 20 25 30

Gly Val Pro Leu Thr Gly Met Asn Pro Leu Ser Pro Tyr Leu Asn Val
 35 40 45

Asp Pro Arg Tyr Leu Val Gln Asp Thr Asp Glu Phe Ile Leu Pro Thr
 50 55 60

Gly Ala Asn Lys Thr Arg Gly Arg Phe Glu Leu Ala Phe Phe Thr Ile
 65 70 75 80

Gly Gly Cys Cys Met Thr Gly Ala Ala Phe Gly Ala Met Asn Gly Leu
 85 90 95

Arg Leu Gly Leu Lys Glu Thr Gln Asn Met Ala Trp Ser Lys Pro Arg
 100 105 110

Asn Val Gln Ile Leu Asn Met Val Thr Arg Gln Gly Ala Leu Trp Ala
 115 120 125

Asn Thr Leu Gly Ser Leu Ala Leu Leu Tyr Ser Ala Phe Gly Val Ile
 130 135 140

Ile Glu Lys Thr Arg Gly Ala Glu Asp Asp Leu Asn Thr Val Ala Ala

-continued

Gly Leu Gly Ala Ala Ala Pro Thr Cys Arg His Gly Lys Ser Gly Ala
1 5 10 15

<210> SEQ ID NO 190
 <211> LENGTH: 440
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic Peptide

<400> SEQUENCE: 190

Met Ala Ala Ala Ala Arg Ala Arg Val Ala Tyr Leu Leu Arg Gln Leu
1 5 10 15

Gln Arg Ala Ala Cys Gln Cys Pro Thr His Ser His Thr Tyr Ser Gln
20 25 30

Ala Pro Gly Leu Ser Pro Ser Gly Lys Thr Thr Asp Tyr Ala Phe Glu
35 40 45

Met Ala Val Ser Asn Ile Arg Tyr Gly Ala Ala Val Thr Lys Glu Val
50 55 60

Gly Met Asp Leu Lys Asn Met Gly Ala Lys Asn Val Cys Leu Met Thr
65 70 75 80

Asp Lys Asn Leu Ser Lys Leu Pro Pro Val Gln Val Ala Met Asp Ser
85 90 95

Leu Val Lys Asn Gly Ile Pro Phe Thr Val Tyr Asp Asn Val Arg Val
100 105 110

Glu Pro Thr Asp Ser Ser Phe Met Glu Ala Ile Glu Phe Ala Gln Lys
115 120 125

Gly Ala Phe Asp Ala Tyr Val Ala Val Gly Gly Gly Ser Thr Met Asp
130 135 140

Thr Cys Lys Ala Ala Asn Leu Tyr Ala Ser Ser Pro His Ser Asp Phe
145 150 155 160

Leu Asp Tyr Val Ser Ala Pro Ile Gly Lys Gly Lys Pro Val Ser Val
165 170 175

Pro Leu Lys Pro Leu Ile Ala Val Pro Thr Thr Ser Gly Thr Gly Ser
180 185 190

Glu Thr Thr Gly Val Ala Ile Phe Asp Tyr Glu His Leu Lys Val Lys
195 200 205

Ile Gly Ile Thr Ser Arg Ala Ile Lys Pro Thr Leu Gly Leu Ile Asp
210 215 220

Pro Leu His Thr Leu His Met Pro Ala Arg Val Val Ala Asn Ser Gly
225 230 235 240

Phe Asp Val Leu Cys His Ala Leu Glu Ser Tyr Thr Thr Leu Pro Tyr
245 250 255

His Leu Arg Ser Pro Cys Pro Ser Asn Pro Ile Thr Arg Pro Ala Tyr
260 265 270

Gln Gly Ser Asn Pro Ile Ser Asp Ile Trp Ala Ile His Ala Leu Arg
275 280 285

Ile Val Ala Lys Tyr Leu Lys Arg Ala Val Arg Asn Pro Asp Asp Leu
290 295 300

Glu Ala Arg Ser His Met His Leu Ala Ser Ala Phe Ala Gly Ile Gly
305 310 315 320

Phe Gly Asn Ala Gly Val His Leu Cys His Gly Met Ser Tyr Pro Ile
325 330 335

-continued

Ser Gly Leu Val Lys Met Tyr Lys Ala Lys Asp Tyr Asn Val Asp His
 340 345 350

Pro Leu Val Pro His Gly Leu Ser Val Val Leu Thr Ser Pro Ala Val
 355 360 365

Phe Thr Phe Thr Ala Gln Met Phe Pro Glu Arg His Leu Glu Met Ala
 370 375 380

Glu Ile Leu Gly Ala Asp Thr Arg Thr Ala Arg Ile Gln Asp Ala Gly
 385 390 395 400

Leu Val Leu Ala Asp Thr Leu Arg Lys Phe Leu Phe Asp Leu Asp Val
 405 410 415

Asp Asp Gly Leu Ala Ala Val Gly Tyr Ser Lys Ala Asp Ile Pro Ala
 420 425 430

Leu Val Lys Gly Thr Leu Pro Gln
 435 440

<210> SEQ ID NO 191
 <211> LENGTH: 15
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic Peptide

<400> SEQUENCE: 191

Tyr Pro Val Gln Pro Glu Glu Glu Pro Lys Ala Leu Ser Thr Ser
 1 5 10 15

<210> SEQ ID NO 192
 <211> LENGTH: 651
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic Peptide

<400> SEQUENCE: 192

Met Ala Thr Ser Thr Ser Thr Glu Ala Lys Ser Ala Ser Trp Trp Asn
 1 5 10 15

Tyr Phe Phe Leu Tyr Asp Gly Ser Lys Val Lys Glu Glu Gly Asp Pro
 20 25 30

Thr Arg Ala Gly Ile Cys Tyr Phe Tyr Pro Ser Gln Thr Leu Leu Asp
 35 40 45

Gln Gln Glu Leu Leu Cys Gly Gln Ile Ala Gly Val Val Arg Cys Val
 50 55 60

Ser Asp Ile Ser Asp Ser Pro Pro Thr Leu Val Arg Leu Arg Lys Leu
 65 70 75 80

Lys Phe Ala Ile Lys Val Asp Gly Asp Tyr Leu Trp Val Leu Gly Cys
 85 90 95

Ala Val Glu Leu Pro Asp Val Ser Cys Lys Arg Phe Leu Asp Gln Leu
 100 105 110

Val Gly Phe Phe Asn Phe Tyr Asn Gly Pro Val Ser Leu Ala Tyr Glu
 115 120 125

Asn Cys Ser Gln Glu Glu Leu Ser Thr Glu Trp Asp Thr Phe Ile Glu
 130 135 140

Gln Ile Leu Lys Asn Thr Ser Asp Leu His Lys Ile Phe Asn Ser Leu
 145 150 155 160

Trp Asn Leu Asp Gln Thr Lys Val Glu Pro Leu Leu Leu Leu Lys Ala
 165 170 175

-continued

Ala Arg Ile Leu Gln Thr Cys Gln Arg Ser Pro His Ile Leu Ala Gly
180 185 190

Cys Ile Leu Tyr Lys Gly Leu Ile Val Ser Thr Gln Leu Pro Pro Ser
195 200 205

Leu Thr Ala Lys Val Leu Leu His Arg Thr Ala Pro Gln Glu Gln Arg
210 215 220

Leu Pro Thr Gly Glu Asp Ala Pro Gln Glu His Gly Ala Ala Leu Pro
225 230 235 240

Pro Asn Val Gln Ile Ile Pro Val Phe Val Thr Lys Glu Glu Ala Ile
245 250 255

Ser Leu His Glu Phe Pro Val Glu Gln Met Thr Arg Ser Leu Ala Ser
260 265 270

Pro Ala Gly Leu Gln Asp Gly Ser Ala Gln His His Pro Lys Gly Gly
275 280 285

Ser Thr Ser Ala Leu Lys Glu Asn Ala Thr Gly His Val Glu Ser Met
290 295 300

Ala Trp Thr Thr Pro Asp Pro Thr Ser Pro Asp Glu Ala Cys Pro Asp
305 310 315 320

Gly Arg Lys Glu Asn Gly Cys Leu Ser Gly His Asp Leu Glu Ser Ile
325 330 335

Arg Pro Ala Gly Leu His Asn Ser Ala Arg Gly Glu Val Leu Gly Leu
340 345 350

Ser Ser Ser Leu Gly Lys Glu Leu Val Phe Leu Gln Glu Glu Leu Asp
355 360 365

Leu Ser Glu Ile His Ile Pro Glu Ala Gln Glu Val Glu Met Ala Ser
370 375 380

Gly His Phe Ala Phe Leu His Val Pro Val Pro Asp Gly Arg Ala Pro
385 390 395 400

Tyr Cys Lys Ala Ser Leu Ser Ala Ser Ser Ser Leu Glu Pro Thr Pro
405 410 415

Pro Glu Asp Thr Ala Ile Ser Ser Leu Arg Pro Pro Ser Ala Pro Glu
420 425 430

Met Leu Thr Gln His Gly Ala Gln Glu Gln Leu Glu Asp His Pro Gly
435 440 445

His Ser Ser Gln Ala Pro Ile Pro Arg Ala Asp Pro Leu Pro Arg Arg
450 455 460

Thr Arg Arg Pro Leu Leu Leu Pro Arg Leu Asp Pro Gly Gln Arg Gly
465 470 475 480

Asn Lys Leu Pro Thr Gly Glu Gln Gly Leu Asp Glu Asp Val Asp Gly
485 490 495

Val Cys Glu Ser His Ala Ala Pro Gly Leu Glu Cys Ser Ser Gly Ser
500 505 510

Ala Asn Cys Gln Gly Ala Gly Pro Ser Ala Asp Gly Ile Ser Ser Arg
515 520 525

Leu Thr Pro Ala Glu Ser Cys Met Gly Leu Val Arg Met Asn Leu Tyr
530 535 540

Thr His Cys Val Lys Gly Leu Val Leu Ser Leu Leu Ala Glu Glu Pro
545 550 555 560

Leu Leu Gly Asp Ser Ala Ala Ile Glu Glu Val Tyr His Ser Ser Leu
565 570 575

-continued

Ala Ser Leu Asn Gly Leu Glu Val His Leu Lys Glu Thr Leu Pro Arg
580 585 590

Asp Glu Ala Ala Ser Thr Ser Ser Thr Tyr Asn Phe Thr His Tyr Asp
595 600 605

Arg Ile Gln Ser Leu Leu Met Ala Asn Leu Pro Gln Val Ala Thr Pro
610 615 620

Gln Asp Arg Arg Phe Leu Gln Ala Val Ser Leu Met His Ser Glu Phe
625 630 635 640

Ala Gln Leu Pro Ala Leu Tyr Glu Met Thr Val
645 650

<210> SEQ ID NO 193
<211> LENGTH: 6
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic Peptide

<400> SEQUENCE: 193

Ser Asn Ser Cys Thr Ser
1 5

<210> SEQ ID NO 194
<211> LENGTH: 477
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic Peptide

<400> SEQUENCE: 194

Met Ala Ala Met Ala Pro Ala Leu Thr Asp Ala Ala Ala Glu Ala His
1 5 10 15

His Ile Arg Phe Lys Leu Ala Pro Pro Ser Ser Thr Leu Ser Pro Gly
20 25 30

Ser Ala Glu Asn Asn Gly Asn Ala Asn Ile Leu Ile Ala Ala Asn Gly
35 40 45

Thr Lys Arg Lys Ala Ile Ala Ala Glu Asp Pro Ser Leu Asp Phe Arg
50 55 60

Asn Asn Pro Thr Lys Glu Asp Leu Gly Lys Leu Gln Pro Leu Val Ala
65 70 75 80

Ser Tyr Leu Cys Ser Asp Val Thr Ser Val Pro Ser Lys Glu Ser Leu
85 90 95

Lys Leu Gln Gly Val Phe Ser Lys Gln Thr Val Leu Lys Ser His Pro
100 105 110

Leu Leu Ser Gln Ser Tyr Glu Leu Arg Ala Glu Leu Leu Gly Arg Gln
115 120 125

Pro Val Leu Glu Phe Ser Leu Glu Asn Leu Arg Thr Met Asn Thr Ser
130 135 140

Gly Gln Thr Ala Leu Pro Gln Ala Pro Val Asn Gly Leu Ala Lys Lys
145 150 155 160

Leu Thr Lys Ser Ser Thr His Ser Asp His Asp Asn Ser Thr Ser Leu
165 170 175

Asn Gly Gly Lys Arg Ala Leu Thr Ser Ser Ala Leu His Gly Gly Glu
180 185 190

Met Gly Gly Ser Glu Ser Gly Asp Leu Lys Gly Gly Met Thr Asn Cys
195 200 205

-continued

Thr Leu Pro His Arg Ser Leu Asp Val Glu His Thr Thr Leu Tyr Ser
 210 215 220
 Asn Asn Ser Thr Ala Asn Lys Ser Ser Val Asn Ser Met Glu Gln Pro
 225 230 235 240
 Ala Leu Gln Gly Ser Ser Arg Leu Ser Pro Gly Thr Asp Ser Ser Ser
 245 250 255
 Asn Leu Gly Gly Val Lys Leu Glu Gly Lys Lys Ser Pro Leu Ser Ser
 260 265 270
 Ile Leu Phe Ser Ala Leu Asp Ser Asp Thr Arg Ile Thr Ala Leu Leu
 275 280 285
 Arg Arg Gln Ala Asp Ile Glu Ser Arg Ala Arg Arg Leu Gln Lys Arg
 290 295 300
 Leu Gln Val Val Gln Ala Lys Gln Val Glu Arg His Ile Gln His Gln
 305 310 315 320
 Leu Gly Gly Phe Leu Glu Lys Thr Leu Ser Lys Leu Pro Asn Leu Glu
 325 330 335
 Ser Leu Arg Pro Arg Ser Gln Leu Met Leu Thr Arg Lys Ala Glu Ala
 340 345 350
 Ala Leu Arg Lys Ala Ala Ser Glu Thr Thr Thr Ser Glu Gly Leu Ser
 355 360 365
 Asn Phe Leu Lys Ser Asn Ser Ile Ser Glu Glu Leu Glu Arg Phe Thr
 370 375 380
 Ala Ser Gly Ile Ala Asn Leu Arg Cys Ser Glu Gln Ala Phe Asp Ser
 385 390 395 400
 Asp Val Thr Asp Ser Ser Ser Gly Gly Glu Ser Asp Ile Glu Glu Glu
 405 410 415
 Glu Leu Thr Arg Ala Asp Pro Glu Gln Arg His Val Pro Leu Arg Arg
 420 425 430
 Arg Ser Glu Trp Lys Trp Ala Ala Asp Arg Ala Ala Ile Val Ser Arg
 435 440 445
 Trp Asn Trp Leu Gln Ala His Val Ser Asp Leu Glu Tyr Arg Ile Arg
 450 455 460
 Gln Gln Thr Asp Ile Tyr Lys Gln Ile Arg Ala Asn Lys
 465 470 475

<210> SEQ ID NO 195
 <211> LENGTH: 6
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic Peptide

<400> SEQUENCE: 195

Val Ser Val Trp Arg Gln
1 5

<210> SEQ ID NO 196
 <211> LENGTH: 94
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic Peptide

<400> SEQUENCE: 196

Met Ala Gly Arg Pro Gly Ser Gln Glu Gln Ser Lys Asp Arg Gly Thr

-continued

```

1           5           10           15
Gly Ser Leu Pro Pro Pro Ser Gln Arg Pro Leu Gly Pro Ser Pro Glu
                20                25                30
Gly Ala Gly Pro Ser Pro Pro Pro Pro Gly Ile Pro Arg Gly Gly Gly
                35                40                45
Ser Ser Ser Ser Glu Gly Pro His Ser Tyr Phe Leu Ser Leu Val Asp
                50                55                60
Ser Gln Leu Leu Arg Arg Gly Phe Pro Leu Thr Pro Leu Ile Gln Arg
        65                70                75                80
His Leu Pro Pro Arg Thr Ser Ala Leu Ala Glu Arg Thr His
                85                90

```

```

<210> SEQ ID NO 197
<211> LENGTH: 12
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic Peptide

```

```

<400> SEQUENCE: 197

```

```

Ser Ile Gly His Ile Ser Thr Met Leu Met Ala Phe
1           5           10

```

```

<210> SEQ ID NO 198
<211> LENGTH: 406
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic Peptide

```

```

<400> SEQUENCE: 198

```

```

Met Glu Glu Gly Asn Asn Asn Glu Glu Val Ile His Leu Asn Asn Phe
1           5           10           15
His Cys His Arg Gly Gln Glu Trp Ile Asn Leu Arg Asp Gly Pro Ile
        20                25                30
Thr Ile Ser Asp Ser Ser Asp Glu Glu Arg Ile Pro Met Leu Val Thr
        35                40                45
Pro Ala Pro Gln Gln His Glu Glu Glu Asp Leu Asp Asp Asp Val Ile
        50                55                60
Leu Thr Glu Asp Asp Ser Glu Asp Asp Tyr Gly Glu Phe Leu Asp Leu
        65                70                75                80
Gly Pro Pro Gly Ile Ser Glu Phe Thr Lys Pro Ser Gly Gln Thr Glu
        85                90                95
Arg Glu Pro Lys Pro Gly Pro Ser His Asn Gln Ala Ala Asn Asp Ile
        100               105               110
Val Asn Pro Arg Ser Glu Gln Lys Val Ile Ile Leu Glu Glu Gly Ser
        115               120               125
Leu Leu Tyr Thr Glu Ser Asp Pro Leu Glu Thr Gln Asn Gln Ser Ser
        130               135               140
Glu Asp Ser Glu Thr Glu Leu Leu Ser Asn Leu Gly Glu Ser Ala Ala
        145               150               155               160
Leu Ala Asp Asp Gln Ala Ile Glu Glu Asp Cys Trp Leu Asp His Pro
        165               170               175
Tyr Phe Gln Ser Leu Asn Gln Gln Pro Arg Glu Ile Thr Asn Gln Val
        180               185               190

```

-continued

Val Pro Gln Glu Arg Gln Pro Glu Ala Glu Leu Gly Arg Leu Leu Phe
 195 200 205

Gln His Glu Phe Pro Gly Pro Ala Phe Pro Arg Pro Glu Pro Gln Gln
 210 215 220

Gly Gly Ile Ser Gly Pro Ser Ser Pro Gln Pro Ala His Pro Leu Gly
 225 230 235 240

Glu Phe Glu Asp Gln Gln Leu Ala Ser Asp Asp Glu Glu Pro Gly Pro
 245 250 255

Ala Phe Pro Met Gln Glu Ser Gln Glu Pro Asn Leu Glu Asn Ile Trp
 260 265 270

Gly Gln Glu Ala Ala Glu Val Asp Gln Glu Leu Val Glu Leu Leu Val
 275 280 285

Lys Glu Thr Glu Ala Arg Phe Pro Asp Val Ala Asn Gly Phe Ile Glu
 290 295 300

Glu Ile Ile His Phe Lys Asn Tyr Tyr Asp Leu Asn Val Leu Cys Asn
 305 310 315 320

Phe Leu Leu Glu Asn Pro Asp Tyr Pro Lys Arg Glu Asp Arg Ile Ile
 325 330 335

Ile Asn Pro Ser Ser Ser Leu Leu Ala Ser Gln Asp Glu Thr Lys Leu
 340 345 350

Pro Lys Ile Asp Phe Phe Asp Tyr Ser Lys Leu Thr Pro Leu Asp Gln
 355 360 365

Arg Cys Phe Ile Gln Ala Ala Asp Leu Leu Met Ala Asp Phe Lys Val
 370 375 380

Leu Ser Ser Gln Asp Ile Lys Trp Ala Leu His Glu Leu Lys Gly His
 385 390 395 400

Tyr Ala Ile Thr Arg Lys
 405

<210> SEQ ID NO 199
 <211> LENGTH: 15
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic Peptide

<400> SEQUENCE: 199

Val Tyr Gln Pro Gln Ser Leu His Val Ser Lys Ser Ser Arg Lys
 1 5 10 15

<210> SEQ ID NO 200
 <211> LENGTH: 108
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic Peptide

<400> SEQUENCE: 200

Met Ala Gly Leu Lys Arg Arg Ala Ser Gln Val Trp Pro Glu Glu His
 1 5 10 15

Gly Glu Gln Glu His Gly Leu Tyr Ser Leu His Arg Met Phe Asp Ile
 20 25 30

Val Gly Thr His Leu Thr His Arg Asp Val Arg Val Leu Ser Phe Leu
 35 40 45

Phe Val Asp Val Ile Asp Asp His Glu Arg Gly Leu Ile Arg Asn Gly
 50 55 60

-continued

```

Arg Asp Phe Leu Leu Ala Leu Glu Arg Gln Gly Arg Cys Asp Glu Ser
65          70          75          80
Asn Phe Arg Gln Val Leu Gln Leu Leu Arg Ile Ile Thr Arg His Asp
          85          90          95
Leu Leu Pro Tyr Val Thr Leu Lys Arg Arg Arg Ala
          100          105

```

```

<210> SEQ ID NO 201
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic Peptide

```

```

<400> SEQUENCE: 201

```

```

Ala Pro Ser Gly Leu Gly Leu
1          5

```

```

<210> SEQ ID NO 202
<211> LENGTH: 102
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic Peptide

```

```

<400> SEQUENCE: 202

```

```

Met Arg Arg Ser Ala Ala Pro Ser Gln Leu Gln Gly Asn Ser Phe Lys
1          5          10          15
Lys Pro Lys Phe Ile Pro Pro Gly Arg Ser Asn Pro Gly Leu Asn Glu
          20          25          30
Glu Ile Thr Lys Leu Asn Pro Asp Ile Lys Leu Phe Glu Gly Val Ala
          35          40          45
Ile Asn Asn Thr Phe Leu Pro Ser Gln Asn Asp Leu Arg Ile Cys Ser
          50          55          60
Leu Asn Leu Pro Ser Glu Glu Ser Thr Arg Glu Ile Asn Asn Arg Asp
65          70          75          80
Asn Cys Ser Gly Lys Tyr Cys Phe Glu Ala Pro Thr Leu Ala Thr Leu
          85          90          95
Asp Pro Pro His Thr Val
          100

```

```

<210> SEQ ID NO 203
<211> LENGTH: 15
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic Peptide

```

```

<400> SEQUENCE: 203

```

```

Gln Thr Trp Met Arg Arg His Arg Leu Val Pro Val His Tyr Arg
1          5          10          15

```

```

<210> SEQ ID NO 204
<211> LENGTH: 66
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic Peptide

```

```

<400> SEQUENCE: 204

```

-continued

Met Gly Ser Gln Pro Pro Leu Gly Ser Pro Leu Ser Arg Glu Glu Gly
 1 5 10 15
 Glu Ala Pro Pro Pro Ala Pro Ala Ser Glu Gly Arg Arg Arg Ser Arg
 20 25 30
 Arg Val Arg Leu Arg Gly Ser Cys Arg His Arg Pro Ser Phe Leu Gly
 35 40 45
 Cys Arg Glu Leu Ala Ala Ser Ala Pro Ala Arg Pro Ala Pro Ala Ser
 50 55 60
 Ser Glu
 65

<210> SEQ ID NO 205
 <211> LENGTH: 41
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic Peptide

<400> SEQUENCE: 205

Lys Arg Cys Ser Ile Phe Arg Leu Arg Lys Thr Thr Arg Ala Gln Trp
 1 5 10 15
 Arg Leu Pro His Phe Phe Ser Ser Ser Cys Trp Ser Ser Arg Arg Lys
 20 25 30
 Ala Gly Ser Val Ala Phe Trp Met Pro
 35 40

<210> SEQ ID NO 206
 <211> LENGTH: 104
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic Peptide

<400> SEQUENCE: 206

Met Ile Ala Arg Arg Asn Pro Glu Pro Leu Arg Phe Leu Pro Asp Glu
 1 5 10 15
 Ala Arg Ser Leu Pro Pro Pro Lys Leu Thr Asp Pro Arg Leu Leu Tyr
 20 25 30
 Ile Gly Phe Leu Gly Tyr Cys Ser Gly Leu Ile Asp Asn Leu Ile Arg
 35 40 45
 Arg Arg Pro Ile Ala Thr Ala Gly Leu His Arg Gln Leu Leu Tyr Ile
 50 55 60
 Thr Ala Phe Phe Phe Ala Gly Tyr Tyr Leu Val Lys Arg Glu Asp Tyr
 65 70 75 80
 Leu Tyr Ala Val Arg Asp Arg Glu Met Phe Gly Tyr Met Lys Leu His
 85 90 95
 Pro Glu Asp Phe Pro Glu Glu Asp
 100

<210> SEQ ID NO 207
 <211> LENGTH: 10
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic Peptide

<400> SEQUENCE: 207

-continued

Val Tyr Cys Cys Gly Ala Glu Arg Arg Gly
1 5 10

<210> SEQ ID NO 208
<211> LENGTH: 183
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic Peptide

<400> SEQUENCE: 208

Met Gly Asn Ser Ala Leu Arg Ala His Val Glu Thr Ala Gln Lys Thr
1 5 10 15
Gly Val Phe Gln Leu Lys Asp Arg Gly Leu Thr Glu Phe Pro Ala Asp
20 25 30
Leu Gln Lys Leu Thr Ser Asn Leu Arg Thr Ile Asp Leu Ser Asn Asn
35 40 45
Lys Ile Glu Ser Leu Pro Pro Leu Leu Ile Gly Lys Phe Thr Leu Leu
50 55 60
Lys Ser Leu Ser Leu Asn Asn Asn Lys Leu Thr Val Leu Pro Asp Glu
65 70 75 80
Ile Cys Asn Leu Lys Lys Leu Glu Thr Leu Ser Leu Asn Asn Asn His
85 90 95
Leu Arg Glu Leu Pro Ser Thr Phe Gly Gln Leu Ser Ala Leu Lys Thr
100 105 110
Leu Ser Leu Ser Gly Asn Gln Leu Gly Ala Leu Pro Pro Gln Leu Cys
115 120 125
Ser Leu Arg His Leu Asp Val Met Asp Leu Ser Lys Asn Gln Ile Arg
130 135 140
Ser Ile Pro Asp Ser Val Gly Glu Leu Gln Val Ile Glu Leu Asn Leu
145 150 155 160
Asn Gln Asn Gln Ile Ser Gln Ile Ser Val Lys Ile Ser Cys Cys Pro
165 170 175
Arg Leu Lys Ile Leu Arg Leu
180

<210> SEQ ID NO 209
<211> LENGTH: 12
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic Peptide

<400> SEQUENCE: 209

Ser Ala Leu Ser Val Ile Arg Phe Ile Cys Gly Phe
1 5 10

<210> SEQ ID NO 210
<211> LENGTH: 901
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic Peptide

<400> SEQUENCE: 210

Met Val Gln Pro Ile Ile His Leu Gly Tyr Val Val Tyr Ser Leu Leu
1 5 10 15
Tyr Leu Gly Tyr Lys Pro Val Gln His Val Thr Ala Leu Asn Thr Val

-continued

Val Glu Glu Thr Gly Gly Asp Ser Trp Lys Tyr Ser Leu Arg Pro Cys
 435 440 445
 Thr Glu Val Leu Phe Ile Asp Ile Phe His Glu Tyr Asn Gln Thr Leu
 450 455 460
 Thr Pro Val Leu Leu Glu Met Met Gln Thr Leu Gln Gly Pro Thr Asn
 465 470 475 480
 Val Glu Asp Met Asn Ala Leu Leu Ile Lys Asp Ala Val Tyr Asn Ala
 485 490 495
 Val Gly Leu Ala Ala Tyr Glu Leu Phe Asp Ser Val Asp Phe Asp Gln
 500 505 510
 Trp Phe Lys Asn Gln Leu Leu Pro Glu Leu Gln Val Ile His Asn Arg
 515 520 525
 Tyr Lys Pro Leu Arg Arg Arg Val Ile Trp Leu Ile Gly Gln Trp Ile
 530 535 540
 Ser Val Lys Phe Lys Ser Asp Leu Arg Pro Met Leu Tyr Glu Ala Ile
 545 550 555 560
 Cys Asn Leu Leu Gln Asp Gln Asp Leu Val Val Arg Ile Glu Thr Ala
 565 570 575
 Thr Thr Leu Lys Leu Thr Val Asp Asp Phe Glu Phe Arg Thr Asp Gln
 580 585 590
 Phe Leu Pro Tyr Leu Glu Thr Met Phe Thr Leu Leu Phe Gln Leu Leu
 595 600 605
 Gln Gln Val Thr Glu Cys Asp Thr Lys Met His Val Leu His Val Leu
 610 615 620
 Ser Cys Val Ile Glu Arg Val Asn Met Gln Ile Arg Pro Tyr Val Gly
 625 630 635 640
 Cys Leu Val Gln Tyr Leu Pro Leu Leu Trp Lys Gln Ser Glu Glu His
 645 650 655
 Asn Met Leu Arg Cys Ala Ile Leu Thr Thr Leu Ile His Leu Val Gln
 660 665 670
 Gly Leu Gly Ala Asp Ser Lys Asn Leu Tyr Pro Phe Leu Leu Pro Val
 675 680 685
 Ile Gln Leu Ser Thr Asp Val Ser Gln Pro Pro His Val Tyr Leu Leu
 690 695 700
 Glu Asp Gly Leu Glu Leu Trp Leu Val Thr Leu Glu Asn Ser Pro Cys
 705 710 715 720
 Ile Thr Pro Glu Leu Leu Arg Ile Phe Gln Asn Met Ser Pro Leu Leu
 725 730 735
 Glu Leu Ser Ser Glu Asn Leu Arg Thr Cys Phe Lys Ile Ile Asn Gly
 740 745 750
 Tyr Ile Phe Leu Ser Ser Thr Glu Phe Leu Gln Thr Tyr Ala Val Gly
 755 760 765
 Leu Cys Gln Ser Phe Cys Glu Leu Leu Lys Glu Ile Thr Thr Glu Gly
 770 775 780
 Gln Val Gln Val Leu Lys Val Val Glu Asn Ala Leu Lys Val Asn Pro
 785 790 795 800
 Ile Leu Gly Pro Gln Met Phe Gln Pro Ile Leu Pro Tyr Val Phe Lys
 805 810 815
 Gly Ile Ile Glu Gly Glu Arg Tyr Pro Val Val Met Ser Thr Tyr Leu
 820 825 830

-continued

Gly Val Met Gly Arg Val Leu Leu Gln Asn Thr Ser Phe Phe Ser Ser
835 840 845

Leu Leu Asn Glu Met Ala His Lys Phe Asn Gln Glu Met Asp Gln Leu
850 855 860

Leu Gly Asn Met Ile Glu Met Trp Val Asp Arg Met Asp Asn Ile Thr
865 870 875 880

Gln Pro Glu Arg Arg Lys Leu Ser Ala Leu Ala Leu Leu Ser Leu Leu
885 890 895

Pro Ser Asp Asn Ser
900

<210> SEQ ID NO 211
<211> LENGTH: 6
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic Peptide

<400> SEQUENCE: 211

Leu Ala Ser Lys Gly Pro
1 5

<210> SEQ ID NO 212
<211> LENGTH: 43
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic Peptide

<400> SEQUENCE: 212

Met Ser Leu Pro Leu Asn Pro Lys Pro Phe Leu Asn Gly Leu Thr Gly
1 5 10 15

Lys Pro Val Met Val Lys Leu Lys Trp Gly Met Glu Tyr Lys Gly Tyr
20 25 30

Leu Val Ser Val Asp Gly Tyr Met Asn Met Gln
35 40

<210> SEQ ID NO 213
<211> LENGTH: 13
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic Peptide

<400> SEQUENCE: 213

Gln Asp Phe His Leu His Leu Gly Asn Ile Glu Thr Lys
1 5 10

<210> SEQ ID NO 214
<211> LENGTH: 60
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic Peptide

<400> SEQUENCE: 214

Met Ala Ala Val Gly Pro Pro Gln Gln Gln Val Arg Met Ala His Gln
1 5 10 15

Gln Val Trp Ala Ala Leu Glu Val Ala Leu Arg Val Pro Cys Leu Tyr
20 25 30

-continued

```
Ile Ile Asp Ala Ile Phe Asn Ser Tyr Pro Asp Ser Ser Gln Ser Arg
      35                40                45
```

```
Phe Cys Ile Val Leu Gln Ile Phe Leu Arg Leu Phe
      50                55                60
```

```
<210> SEQ ID NO 215
<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic Peptide
```

```
<400> SEQUENCE: 215
```

```
Glu Thr Asn Thr Asp Thr Leu Leu Val
1                5
```

```
<210> SEQ ID NO 216
<211> LENGTH: 156
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic Peptide
```

```
<400> SEQUENCE: 216
```

```
Met Ala Val Ala Arg Ala Gly Val Leu Gly Val Gln Trp Leu Gln Arg
1                5                10                15
```

```
Ala Ser Arg Asn Val Met Pro Leu Gly Ala Arg Thr Ala Ser His Met
      20                25                30
```

```
Thr Lys Asp Met Phe Pro Gly Pro Tyr Pro Arg Thr Pro Glu Glu Arg
      35                40                45
```

```
Ala Ala Ala Ala Lys Lys Tyr Asn Met Arg Val Glu Asp Tyr Glu Pro
      50                55                60
```

```
Tyr Pro Asp Asp Gly Met Gly Tyr Gly Asp Tyr Pro Lys Leu Pro Asp
      65                70                75                80
```

```
Arg Ser Gln His Glu Arg Asp Pro Trp Tyr Ser Trp Asp Gln Pro Gly
      85                90                95
```

```
Leu Arg Leu Asn Trp Gly Glu Pro Met His Trp His Leu Asp Met Tyr
      100               105               110
```

```
Asn Arg Asn Arg Val Asp Thr Ser Pro Thr Pro Val Ser Trp His Val
      115               120               125
```

```
Met Cys Met Gln Leu Phe Gly Phe Leu Ala Phe Met Ile Phe Met Cys
      130               135               140
```

```
Trp Val Gly Asp Val Tyr Pro Val Tyr Gln Pro Val
      145               150               155
```

```
<210> SEQ ID NO 217
<211> LENGTH: 3
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic Peptide
```

```
<400> SEQUENCE: 217
```

```
Asp Arg Pro
1
```

```
<210> SEQ ID NO 218
<211> LENGTH: 124
<212> TYPE: PRT
```

-continued

```

<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic Peptide

<400> SEQUENCE: 218

Met Ala Arg Ser Leu Val Cys Leu Gly Val Ile Ile Leu Leu Ser Ala
1           5           10           15
Phe Ser Gly Pro Gly Val Arg Gly Gly Pro Met Pro Lys Leu Ala Asp
20          25          30
Arg Lys Leu Cys Ala Asp Gln Glu Cys Ser His Pro Ile Ser Met Ala
35          40          45
Val Ala Leu Gln Asp Tyr Met Ala Pro Asp Cys Arg Phe Leu Thr Ile
50          55          60
His Arg Gly Gln Val Val Tyr Val Phe Ser Lys Leu Lys Gly Arg Gly
65          70          75          80
Arg Leu Phe Trp Gly Gly Ser Val Gln Gly Asp Tyr Tyr Gly Asp Leu
85          90          95
Ala Ala Arg Leu Gly Tyr Phe Pro Ser Ser Ile Val Arg Glu Asp Gln
100         105         110
Thr Leu Lys Pro Gly Lys Val Asp Val Lys Thr Asp
115         120

```

```

<210> SEQ ID NO 219
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic Peptide

<400> SEQUENCE: 219

```

```

Thr Ser Ser Ser Asn Ser Trp
1           5

```

```

<210> SEQ ID NO 220
<211> LENGTH: 89
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic Peptide

<400> SEQUENCE: 220

```

```

Met Pro Thr Asn Cys Ala Ala Ala Gly Cys Ala Thr Thr Tyr Asn Lys
1           5           10           15
His Ile Asn Ile Ser Phe His Arg Phe Pro Leu Asp Pro Lys Arg Arg
20          25          30
Lys Glu Trp Val Arg Leu Val Arg Arg Lys Asn Phe Val Pro Gly Lys
35          40          45
His Thr Phe Leu Cys Ser Lys His Phe Glu Ala Ser Cys Phe Asp Leu
50          55          60
Thr Gly Gln Thr Arg Arg Leu Lys Met Asp Ala Val Pro Thr Ile Phe
65          70          75          80
Asp Phe Cys Thr His Ile Lys Ser Met
85

```

```

<210> SEQ ID NO 221
<211> LENGTH: 19
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence

```

-continued

```

<220> FEATURE:
<223> OTHER INFORMATION: Synthetic Peptide

<400> SEQUENCE: 221

Val Thr Tyr Asp Leu Phe Leu Arg Gly Val Gly Cys Phe Leu Leu Leu
1           5           10           15

Phe Leu Phe

<210> SEQ ID NO 222
<211> LENGTH: 239
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic Peptide

<400> SEQUENCE: 222

Met Leu Gly Phe Ile Thr Arg Pro Pro His Arg Phe Leu Ser Leu Leu
1           5           10           15

Cys Pro Gly Leu Arg Ile Pro Gln Leu Ser Val Leu Cys Ala Gln Pro
20          25          30

Arg Pro Arg Ala Met Ala Ile Ser Ser Ser Ser Cys Glu Leu Pro Leu
35          40          45

Val Ala Val Cys Gln Val Thr Ser Thr Pro Asp Lys Gln Gln Asn Phe
50          55          60

Lys Thr Cys Ala Glu Leu Val Arg Glu Ala Ala Arg Leu Gly Ala Cys
65          70          75          80

Leu Ala Phe Leu Pro Glu Ala Phe Asp Phe Ile Ala Arg Asp Pro Ala
85          90          95

Glu Thr Leu His Leu Ser Glu Pro Leu Gly Gly Lys Leu Leu Glu Glu
100         105         110

Tyr Thr Gln Leu Ala Arg Glu Cys Gly Leu Trp Leu Ser Leu Gly Gly
115         120         125

Phe His Glu Arg Gly Gln Asp Trp Glu Gln Thr Gln Lys Ile Tyr Asn
130         135         140

Cys His Val Leu Leu Asn Ser Lys Gly Ala Val Val Ala Thr Tyr Arg
145         150         155         160

Lys Thr His Leu Cys Asp Val Glu Ile Pro Gly Gln Gly Pro Met Cys
165         170         175

Glu Ser Asn Ser Thr Met Pro Gly Pro Ser Leu Glu Ser Pro Val Ser
180         185         190

Thr Pro Ala Gly Lys Ile Gly Leu Ala Val Cys Tyr Asp Met Arg Phe
195         200         205

Pro Glu Leu Ser Leu Ala Leu Ala Gln Ala Gly Ala Glu Ile Leu Thr
210         215         220

Tyr Pro Ser Ala Phe Gly Ser Ile Thr Gly Pro Ala His Trp Glu
225         230         235

```

-continued

```

<210> SEQ ID NO 223
<211> LENGTH: 5
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic Peptide

<400> SEQUENCE: 223

Gln Pro Val Ser Ser
1           5

```

What is claimed is:

1. A method of detecting a cancer in a subject, the method comprising: (a) contacting a biological sample obtained from a subject to a peptide array comprising a plurality of frameshift variant peptides, (i) wherein the plurality of frameshift variant peptides comprise peptides encoded by genes having a variant in a microsatellite (MS) in a coding region of the gene; or (ii) wherein the plurality of frameshift variant peptides comprise peptides encoded by a mRNA having an RNA processing error; and (b) detecting binding of the biological sample to at least one peptide in the peptide array.

2. The method of claim 1, wherein the plurality of frameshift variant peptides comprise one or more peptides provided in any one of Tables 1 or 7.

3. The method of claim 1, wherein the plurality of frameshift variant peptides are fixed on a substrate.

4. The method of claim 3, wherein the substrate comprises glass, composite, resin, or combination thereof.

5. The method of claim 1, wherein detecting binding comprises at least one of fluorescence, luminescence, calorimetry, chromatography, radioactivity, Bio-Layer Interferometry, and surface plasmon resonance.

6. The method of claim 1, wherein the peptide array comprises at least about 25,000, about 50,000, about 75,000, about 100,000, about 125,000, about 150,000, about 175,000, about 200,000, about 225,000, about 250,000, about 275,000, about 300,000, about 325,000, about 350,000, about 375,000, or about 400,000 frameshift variant peptides.

7. The method of claim 1, wherein the biological sample comprises blood, serum, plasma, cerebrospinal fluid, saliva, urine, or combinations thereof.

8. The method of claim 1, wherein the biological sample comprises an antibody.

9. The method of claim 1, wherein the subject is a mammal.

10. The method of claim 1, wherein the subject is a human, a dog, a cat, a mouse, a rat, a rabbit, a horse, a cow, or a pig.

11. The method of claim 1, wherein the subject is suspected of having a cancer.

12. The method of claim 1, wherein the cancer is selected from the group consisting of acute lymphoblastic leukemia, acute monocytic leukemia, acute myeloid leukemia, acute promyelocytic leukemia, adenocarcinoma, adult T-cell leukemia, astrocytoma, bladder cancer, bone cancer, brain tumor, breast cancer, Burkitt's lymphoma, carcinoma, cervical cancer, chronic lymphocytic leukemia, chronic myelogenous leukemia, colon cancer, colorectal cancer, endome-

trial cancer, glioblastoma multiforme, glioma, hepatocellular carcinoma, Hodgkin's lymphoma, inflammatory breast cancer, kidney cancer, leukemia, lung cancer, lymphoma, malignant mesothelioma, medulloblastoma, melanoma, multiple myeloma, neuroblastoma, non-Hodgkin lymphoma, non-small cell lung cancer, ovarian cancer, pancreatic cancer, pituitary tumor, prostate cancer, retinoblastoma, skin cancer, small cell lung cancer, squamous cell carcinoma, stomach cancer, T-cell leukemia, T-cell lymphoma, thyroid cancer, and Wilms' tumor.

13. A method of measuring an immune response to a neoantigen peptide in a subject, the method comprising: (a) contacting a biological sample obtained from a subject to a peptide array comprising a plurality of frameshift variant peptides, (i) wherein the plurality of frameshift variant peptides comprise peptides encoded by genes having a variant in a microsatellite (MS) in a coding region of the gene; or (ii) wherein the plurality of frameshift variant peptides comprise peptides encoded by a mRNA having an RNA processing error; and (b) detecting binding of the biological sample to at least one peptide in the peptide array.

14. The method of claim 13, wherein the plurality of frameshift variant peptides comprise one or more peptides provided in any one of Tables 1 or 7.

15. The method of claim 13, wherein the plurality of frameshift variant peptides are fixed on a substrate.

16. The method of claim 15, wherein the substrate comprises glass, composite, resin, or combination thereof.

17. The method of claim 13, wherein detecting binding comprises at least one of fluorescence, luminescence, calorimetry, chromatography, radioactivity, Bio-Layer Interferometry, and surface plasmon resonance.

18. The method of claim 13, wherein the peptide array comprises at least about 25,000, about 50,000, about 75,000, about 100,000, about 125,000, about 150,000, about 175,000, about 200,000, about 225,000, about 250,000, about 275,000, about 300,000, about 325,000, about 350,000, about 375,000, or about 400,000 frameshift variant peptides.

19. The method of claim 13, wherein the biological sample comprises blood, serum, plasma, cerebrospinal fluid, saliva, urine, or combinations thereof.

20. The method of claim 13, wherein the biological sample comprises an antibody.

21. The method of claim 13, wherein the subject is a mammal.

22. The method of claim 13, wherein the subject is a human, a dog, a cat, a mouse, a rat, a rabbit, a horse, a cow, or a pig.

23. The method of claim **13**, wherein the subject is suspected of having a cancer.

24. The method of claim **23**, wherein the cancer is selected from the group consisting of acute lymphoblastic leukemia, acute monocytic leukemia, acute myeloid leukemia, acute promyelocytic leukemia, adenocarcinoma, adult T-cell leukemia, astrocytoma, bladder cancer, bone cancer, brain tumor, breast cancer, Burkitt's lymphoma, carcinoma, cervical cancer, chronic lymphocytic leukemia, chronic myelogenous leukemia, colon cancer, colorectal cancer, endometrial cancer, glioblastoma multiforme, glioma, hepatocellular carcinoma, Hodgkin's lymphoma, inflammatory breast cancer, kidney cancer, leukemia, lung cancer, lymphoma, malignant mesothelioma, medulloblastoma, melanoma, multiple myeloma, neuroblastoma, non-Hodgkin lymphoma, non-small cell lung cancer, ovarian cancer, pancreatic cancer, pituitary tumor, prostate cancer, retinoblastoma, skin cancer, small cell lung cancer, squamous cell carcinoma, stomach cancer, T-cell leukemia, T-cell lymphoma, thyroid cancer, and Wilms' tumor.

25. The method of claim **13**, wherein the plurality of frameshift variant peptides comprise two or more pooled frameshift peptides.

26. A peptide array comprising a plurality of frameshift variant peptides, (i) wherein the plurality of frameshift variant peptides comprise peptides encoded by genes having a variant in a microsatellite (MS) in a coding region of the gene; or (ii) wherein the plurality of frameshift variant peptides comprise peptides encoded by a mRNA having an RNA processing error.

27. The peptide array of claim **26**, wherein the plurality of frameshift variant peptides comprise one or more peptides provided in any one of Tables 1 or 7.

28. The peptide array of claim **26**, wherein the plurality of frameshift variant peptides are fixed on a substrate.

29. The peptide array of claim **28**, wherein the substrate comprises glass, composite, resin, or combination thereof.

30. The peptide array of claim **26**, wherein the peptide array comprises at least about 25,000, about 50,000, about 75,000, about 100,000, about 125,000, about 150,000, about 175,000, about 200,000, about 225,000, about 250,000, about 275,000, about 300,000, about 325,000, about 350,000, about 375,000, or about 400,000 frameshift variant peptides.

* * * * *