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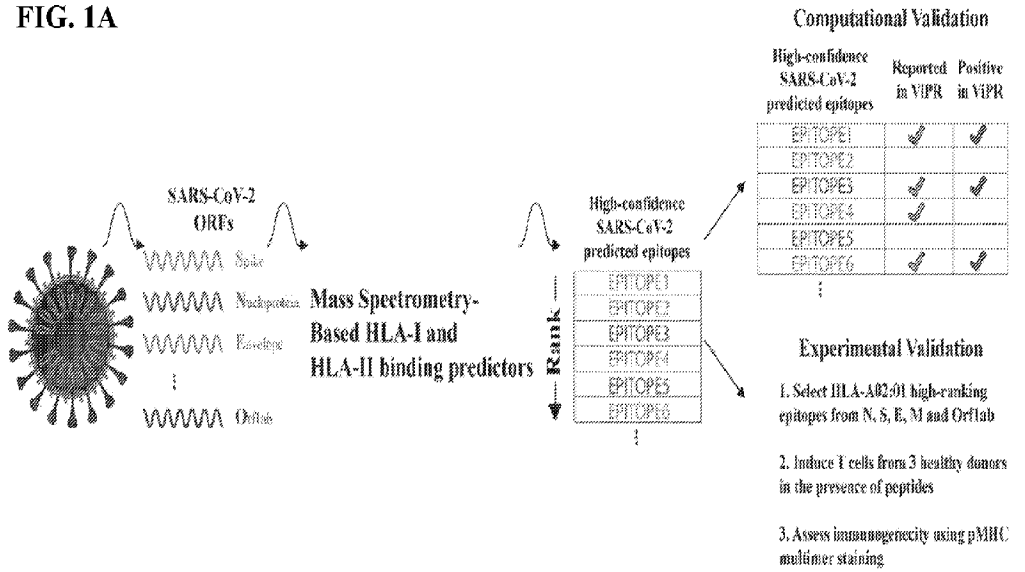
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(54) **Titre : VACCINS CONTRE LE CORONAVIRUS ET METHODES D'UTILISATION**
(54) **Title: CORONAVIRUS VACCINES AND METHODS OF USE**

FIG. 1A



(57) **Abrégé/Abstract:**
Compositions and methods for the prevention and/or treatment of a viral infection, in particular of the Coronaviridae family.

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Abstract:

Compositions and methods for the prevention and/or treatment of a viral infection, in particular of the Coronaviridae family.

DEMANDE OU BREVET VOLUMINEUX

LA PRÉSENTE PARTIE DE CETTE DEMANDE OU CE BREVET COMPREND PLUS D'UN TOME.

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CORONAVIRUS VACCINES AND METHODS OF USE

CROSS-REFERENCE TO RELATED APPLICATIONS

[001] This application claims the benefit of U.S. Provisional Application No. US 63/246,902 filed September 22, 2021, and U.S. Provisional Application No. 63/320,187 filed March 15, 2022, the content of each of which is hereby incorporated herein in its entirety.

BACKGROUND

[002] Newly emerging acute respiratory virus infections caused by novel coronavirus is a significant public health concern. Importantly, there are no vaccines or specific antivirals at the time of an outbreak, specifically, for example the MERS-CoV of 2015, or 2019 SARS CoV-2 infections. The 2019 SARS CoV-2 infection outbreak in December of 2019 claimed more than 2000 lives in less than 2 months from the first reported case. Accordingly, novel and easily scalable therapeutics are necessary to combat a disease caused by such a viral infection.

SUMMARY

[003] Patients who are immunocompromised because of autoimmunity, organ transplant or immunosuppressive treatment have reduced ability to produce antibody responses to vaccinations (Rousseau et al., A H1N1v 2009 vaccine in cancer patients treated with cytotoxic chemotherapy and/or targeted therapy: the VACANCE study. Ann Oncol. 2012 Feb;23(2):450-7). Seropositivity after vaccination is decreased in immunocompromised patients (Haidar et al., Immunogenicity of COVID-19 Vaccination in Immunocompromised Patients: An Observational, Prospective Cohort Study Interim Analysis. medRxiv 2021.06.28.21259576). While immunocompromised patients were excluded from the original clinical trials testing current SARS-CoV-2 vaccines targeting spike protein, follow-up analysis of immunocompromised patients have shown reduced capacity for patients to mount broad and durable anti-spike antibody responses, particularly in older patient cohorts (Boyarsky, et al., Immunogenicity of a Single Dose of SARS-CoV-2 Messenger RNA Vaccine in Solid Organ Transplant Recipients. JAMA. 2021;325(17):1784–1786; Rincon-Arevalo, et al., Impaired antigen-specific memory B cell and plasma cell responses including lack of specific IgG upon SARS-CoV-2 BNT162b2 vaccination among Kidney Transplant and Dialysis patients. medRxiv 2021.04.15.21255550). Thus, induction of T cell responses to other SARS-CoV-2 viral proteins may be beneficial to enhance both cellular and humoral immunity. Thus, there is a need for a SARS-CoV-2 vaccine that specifically targets T cell responses. Patients undergoing anti-CD20 treatment were shown to be able to develop functional T cells with vaccination (Apostolidis et al., Altered cellular and humoral immune responses following SARS-CoV-2 mRNA vaccination in patients with multiple sclerosis on anti-CD20 therapy. *Nature Medicine*, vol. 27, pp. 1990–2001 (2021)), indicating

that patients with impaired B cells may still develop SARS-COV 2-specific T cells in response to vaccination.

[004] Provided herein is an immunogenic composition (e.g., a vaccine) that specifically targets one or more T cell responses to a pathogen (e.g., in some embodiments a virus), including CD4+ T cell responses and/or CD8+ T cell responses, and/or leverages long term persistence of T cell immunity. In some embodiments, an immunogenic composition (e.g., vaccine) provided herein can specifically target one or more T cell responses to one or more polypeptide antigens of a pathogen (e.g., in some embodiments one or more viral antigens), including, e.g., non-structural proteins, nucleocapsid, membrane protein and/or envelope protein of one or more viruses.

[005] In one aspect, provided herein is a SARS-CoV-2 immunogenic composition (e.g., a vaccine) that specifically targets one or more T cell responses, including CD4+ T cell responses and/or CD8+ T cell responses, and/or leverages long term persistence of T cell immunity. In some embodiments, a SARS-CoV-2 vaccine provided herein can specifically target one or more T cell responses to a polypeptide antigen of SARS-CoV-2, including, e.g., nucleocapsid, membrane protein and/or envelope protein of SARS-CoV-2. SARS-CoV-2 immunogenic compositions (e.g., a vaccines) provided herein can be useful for eliciting one or more T cell responses to SARS-CoV-2 in all patients. Protection from COVID19 has been observed in patients deficient in humoral immunity when T cell responses were present (Bange, et al., CD8+ T cells contribute to survival in patients with COVID-19 and hematologic cancer. Nat Med 27, 1280–1289 (2021)) and the longevity of T cell responses from related infections from the original SARS-CoV epidemic (Le Bert et al., SARS-CoV-2-specific T cell immunity in cases of COVID-19 and SARS, and uninfected controls. Nature 584, 457–462 (2020)). In some embodiments, the present disclosure, among other things, provides a particular insight that SARS-CoV-2 immunogenic compositions (e.g., a vaccines) provided herein can be particularly useful for eliciting one or more T cell responses to SARS-CoV-2 in patients that have been immunocompromised in their humoral immunity, such as, for example, in some embodiments through cancer (e.g., B cell lymphoma), treatment with rituximab, methotrexate or other immunosuppressive treatment targeting the humoral immune response, or patients undergoing organ transplant. In some embodiments, T cell responses induced by SARS-CoV-2 immunogenic compositions (e.g., a vaccines) described herein can protect patients from severe COVID-19 and provide long lasting protection through T cell immunity to the SARS-CoV-2 immunogenic composition (e.g., a vaccine) provided herein. Additionally or alternatively, in some embodiments, SARS-CoV-2 immunogenic compositions (e.g., a vaccines) provided herein can be used to overcome SARS-CoV-2 variants that could reduce efficacy of other vaccines, such as those that do not target T cell responses (Davis et al., Reduced neutralisation of the Delta (B.1.617.2) SARS-CoV-2 variant of concern following vaccination. *PLoS Pathog.*, 17(12): e1010022 (2021); Tada et al., Comparison of Neutralizing Antibody Titers Elicited by mRNA and Adenoviral Vector Vaccine against SARS-CoV-2 Variants. bioRxiv 2021.07.19.452771). In

some embodiments, the immunogenic compositions described herein are used to treat a subject with SARS-CoV-2 B1.1.529 (omicron) variant or to immunize a subject against SARS-CoV-2 B1.1.529 (omicron) variant. In some embodiments, SARS-CoV-2 immunogenic compositions (e.g., a vaccines) provided herein can be used to complement and/or enhance other immunogenic compositions (e.g., a vaccines), such as those that do not target T cell responses. For example, in some embodiments, SARS-CoV-2 immunogenic compositions (e.g., a vaccines) provided herein can be used to enhance B cell responses through increased CD4+ T cell activation.

[006] Coronaviruses are single positive stranded RNA viruses that have emerged occasionally from zoonotic sources to infect human populations. Most of the infections in humans cause mild respiratory symptoms, though some recent coronavirus infections in the last decade have resulted in severe morbidity and mortality. These include the severe acute respiratory syndrome coronavirus (SARS-CoV), middle east respiratory syndrome coronavirus (MERS-CoV) and the currently ongoing pandemic of SARS-CoV-2. Infection with these viruses can lead to acute respiratory distress resulting in a high mortality rate. SARS-CoV originated in 2002 in South China and its global spread led to 8096 cases and 774 deaths. The first case of MERS-CoV emerged in 2012 in Saudi Arabia and since then a total of 2494 cases and 858 associated deaths have been reported. 2019 SARS CoV-2 emerged in Wuhan, China at the end of December 2019 and by March 8th 2020 had resulted in 118,096 cases including 4262 deaths globally. The rapid spread of 2019 SARS-CoV-2 resulted in the World Health Organization declaring a global pandemic of international concern.

[007] All three coronaviruses SARS-CoV, MERS-CoV and the recently emergent SARS CoV-2 belong to the genus beta coronaviridae. SARS CoV-2 has a genome size of 30 kilobases that encodes for at least four (4) structural (spike [S], envelope [E], membrane [M], and nucleocapsid [N]) and at least sixteen (16) non-structural (NSP 1-16) proteins. S protein facilitates viral entry into target cells and entry depends on binding of the spike protein to a cellular receptor ACE2 for both SARS-CoV and SARS-CoV-2. Both viruses share a 76% amino acid identity across the genome.

[008] The field of the present disclosure relates to immunotherapeutic peptides, nucleic acids encoding the peptides, peptide binding agents, and their use, for example, in the immunotherapy of a viral disease. In one aspect, the present disclosure provides viral epitopes expressed in virus infected cells, useful alone or in combination with other anti-viral, or immunomodulatory agents to treat viral infection. The present disclosure is useful in immunotherapy for a coronavirus infection.

[009] Provided herein is a method of treating or preventing an infection by a virus (e.g., SARS-CoV-2) or treating a respiratory disease or condition associated with an infection by a virus (e.g., SARS-CoV-2) comprising administering to a subject with a B cell immunodeficiency a pharmaceutical composition comprising: (i) a polypeptide comprising at least two of the following (a) a sequence comprising an epitope sequence from ORF1ab, (b) a sequence comprising an epitope sequence from membrane glycoprotein (M)

and (c) a sequence comprising an epitope sequence from nucleocapsid phosphoprotein (N); (ii) a polynucleotide encoding a polypeptide, wherein the polypeptide comprises at least two of the following (a) a sequence comprising an epitope sequence from ORF1ab, (b) a sequence comprising an epitope sequence from membrane glycoprotein (M) and (c) a sequence comprising an epitope sequence from nucleocapsid phosphoprotein (N); (iii) a T cell receptor (TCR) or a T cell comprising the TCR, wherein the TCR binds to an epitope sequence of the polypeptide in complex with a corresponding HLA class I or class II molecule; (iv) an antigen presenting cell comprising (i) or (ii); or (v) an antibody or B cell comprising the antibody, wherein the antibody binds to an epitope sequence of the polypeptide.

[0010] In some embodiments, the subject has a reduced ability to produce an antibody response to an antigen compared to a subject without a B cell immunodeficiency.

[0011] In some embodiments, the subject has a reduced ability to produce an antibody response to a vaccination compared to a subject without a B cell immunodeficiency.

[0012] In some embodiments, the subject has a reduced ability to produce an anti-spike protein antibody response and/or an anti-RBD antibody response compared to a subject without a B cell immunodeficiency.

[0013] In some embodiments, the subject can produce a T cell response or does not have a reduced ability to produce a T cell response compared to a subject without a B cell immunodeficiency.

[0014] In some embodiments, the pharmaceutical composition is protective against a variant of 2019 SARS CoV-2.

[0015] In some embodiments, the variant of 2019 SARS CoV-2 is alpha, beta, gamma, delta, epsilon, zeta, eta, theta, iota, kappa or lambda.

[0016] In some embodiments, the subject produces a T cell response to an epitope of the polypeptide.

[0017] In some embodiments, the subject produces a T cell response to the epitope sequence from ORF1ab, the epitope sequence from membrane glycoprotein (M) and/or the epitope sequence from nucleocapsid phosphoprotein (N).

[0018] In some embodiments, the subject is an organ transplant recipient.

[0019] In some embodiments, the organ transplant recipient is a sold organ transplant recipient, a stem cell transplant recipient or a bone marrow transplant recipient.

[0020] In some embodiments, the subject received an organ transplant less than 1 year, less than 6 months or less than 3 months after the pharmaceutical composition is administered.

[0021] In some embodiments, the subject is expected to receive an organ transplant less than 1 year, less than 6 months or less than 3 months prior to the pharmaceutical composition being administered.

[0022] In some embodiments, the subject has a cancer.

[0023] In some embodiments, the cancer is a B cell cancer.

[0024] In some embodiments, the B cell cancer is a B cell lymphoma or a B cell leukemia.

[0025] In some embodiments, the subject has an autoimmune disease or condition.

[0026] In some embodiments, the autoimmune disease or condition is Addison disease, Anti-NMDA receptor encephalitis, antisynthetase syndrome, Aplastic anemia, autoimmune anemias, Autoimmune hemolytic anemia, Autoimmune pancreatitis, Behcet's Disease, bullous skin disorders, Celiac disease - sprue, chronic fatigue syndrome, Chronic inflammatory demyelinating polyneuropathy, chronic lymphocytic leukemia, Crohn's disease, Dermatomyositis, Devic's disease, Erythroblastopenia, Evans syndrome, Focal segmental glomerulosclerosis, Granulomatosis with polyangiitis, Graves disease, Graves' ophthalmopathy, Guillain-Barre syndrome, Hashimoto thyroiditis, idiopathic thrombocytopenic purpura (ITP), IgA nephropathy, IgA-mediated autoimmune diseases, IgG4-related disease, Inflammatory bowel disease, Juvenile idiopathic arthritis, Multiple sclerosis, Myasthenia gravis, myeloma, non-Hodgkin's lymphoma, Opsoclonus myoclonus syndrome (OMS), Pemphigoid, Pemphigus, pemphigus vulgaris, Pernicious anemia, polymyositis, Psoriasis, pure red cell aplasia, Reactive arthritis, Rheumatoid arthritis, Sarcoidosis, scleroderma, Sjögren syndrome, Systemic lupus erythematosus, Thrombocytopenic purpura, Thrombotic thrombocytopenic purpura, Type I diabetes, Ulcerative colitis, Vasculitis and Vitiligo.

[0027] In some embodiments, the subject does not have congenital agammaglobulinemia or congenital IgA deficiency.

[0028] In some embodiments, the subject does not have HIV or AIDS.

[0029] In some embodiments, the subject is receiving an immunosuppressive agent or has received an immunosuppressive agent less than 1 year, less than 6 months or less than 3 months prior to the administering of the pharmaceutical composition.

[0030] In some embodiments, the immunosuppressive agent is abatacept, abrilumab, acalabrutinib, adalimumab, adrenocorticotropic hormone, agatolimod sodium, aldesleukin, alefacept, alemtuzumab, alisertib, alvespimycin hydrochloride, alvocidib, ambrisentan, aminocamptothecin, amiselimod, anakinra, andecaliximab, andrographolides, anifrolumab, antithymocyte Ig, apatinib, apelisib, asparaginase, atacicept, atezolizumab, avelumab, azacitidine, azathioprine, bafetinib, baminercept, baricitinib, basiliximab, becatecarin, begelomab, belatacept, belimumab, bemcentinib, bendamustine, bendamustine, betalutin with lilotomab, bevacizumab, BIIB033, BIIB059, BIIB061, bimekizumab, binimetinib, bleomycin, blinatumomab, bortezomib, brentuximab vedotin, bryostatin 1, bucillamine, buparlisib, busulfan, canakinumab, capecitabine, carboplatin, carfilzomib, carmustine, cediranib maleate, cemiplimab, ceralifimod, cerdulatinib, certolizumab, cetuximab, chidamide, chlorambucil, cilengitide, cirmtuzumab, cisplatin, cladribine, clazakizumab, clemastine, clioquinol, corticosteroids, cyclophosphamide, cyclosporine, cytarabine, cytotoxic chemotherapy, daclizumab, dalfampridine, daprolizumab pegol, daratumumab, dasatinib, defactinib, defibrotide, denosumab, dexamethasone, diacerein, dimethyl fumarate, dinaciclib, diroximel fumarate, doxorubicin, doxorubicin, durvalumab, duvelisib, duvortuxizumab, eculizumab, efalizumab, eftilagimod alpha, a neuropeptide combination of metenkefalin and tridecactide, elezanumab, elotuzumab, encorafenib, enfuvirtida, entinostat, entospletinib, enzastaurin,

epacadostat, epirubicin, epratuzumab, eritoran tetrasodium, etanercept, etoposide, etrolizumab, everolimus, evobrutinib, filgotinib, fingolimod, firategrast, fludarabine, fluorouracil, fontolizumab, forodesine hydrochloride, fostamatinib, galunisertib, ganetespib, ganitumab, gemcitabine, gemtuzumab ozogamicin, gerilimzumab, glasdegib, glassia, glatiramer acetate, glembatumumab vedotin, glesatinib, golimumab, guadecitabine, hydrocortisone, hydroxychloroquine sulfate, hydroxyurea, ibritumomab tiuxetan, ibrutinib, ibudilast, idarubicin, idebenone, idelalisib, ifosfamide, iguratimod, imatinib, imexon, infliximab, inotuzumab ozogamicin, interferon alfa-2, interferon beta-1a, interferon beta-1b, interferon gamma-1, ipilimumab, irofulven, isatuximab, ispinesib, itacitinib, ixazomib, lapatinib, laquinimod, laromustine, ld-aminopterin, leflunomide, lenalidomide, lenvatinib, letrozole, levamisole, levocabastine, lipoic acid, lirilumab, lonafarnib, lumiliximab, maraviroc, masitinib, mavrilimumab, melphalan, mercaptopurine, methotrexate, methoxsalen, methylprednisone, milatuzumab, mitoxantrone, mizoribine, mocetinostat, monalizumab, mosunetuzumab, motesanib diphosphate, moxetumomab pasudotox, muromonab-CD3, mycophenolate mofetil, mycophenolic acid, namilumab, natalizumab, navitoclax, neihulizumab, nerispirdine, neurovax, niraparib, nivolumab, obatoclax mesylate, obinutuzumab, oblimersen sodium, ocrelizumab, ofatumumab, olokizumab, opicinumab, oprelvekin, osimertinib, otelixizumab, oxaliplatin, oxcarbazepine, ozanimod, paclitaxel, pacritinib, palifermin, panobinostat, pazopanib, peficitinib, pegfilgrastim, peginterferon beta-1a, pegsunercept (peg stnf-ri), pembrolizumab, pemetrexed, penclomedine, pentostatin, perifosine, pevonedistat, pexidartinib, picoplatin, pidilizumab, pivanex, pixantrone, pleneva, plovamer acetate, polatuzumab vedotin, pomalidomide, ponatinib, ponesimod, prednisone/prednisolone, pyroxamide, ravulizimab-cwvz, recombinant il-12, relatlimab, rhigf-1, rhigm22, rigosertib, rilonacept, ritonavir, rituximab, ruxolitinib, sarilumab, secukinumab, selumetinib, simvastatin, sintilimab, siplizumab, siponimod, sirolimus (rapamycin), sirukumab, sitravatinib, sonidegib, sorafenib, sotrastaurin acetate, sunitinib, sunphenon epigallocatechin-gallate, tabalumab, tacrolimus, talabostat mesylate, talacotuzumab, tanespimycin, tegafur/gimeracil/oteracil, temozolomide, temsirolimus, tenalisib, terameprocol, teriflunomide, thalidomide, thiarabine, thiotepa, tipifarnib, tirabrutinib, tislelizumab, tivozanib, tocilizumab, tofacitinib, tregalizumab, tremelimumab, treosulfan, ublituximab, umbralisib, upadacitinib, urelumab, ustekinumab, varlilumab, vatelizumab, vedolizumab, veliparib, veltuzumab, venetoclax, vinblastine, vincristine, vinorelbine ditartrate, visilizumab, vismodegib, vistusertib, voriconazole, vorinostat, vosaroxin, ziv-aflibercept or any combination thereof.

[0031] In some embodiments, the immunosuppressive agent is A2aR antagonist, Akt inhibitor, anti CD20, Anti-amyloidotic (AA) Agent, anti-CD37 protein therapeutic, anti-CTLA4 mAb, Anti-CXCR4, anti-huCD40 mAb, anti-LAG3 mAb, anti-PD-1 mAb, anti-PD-L1 agent, anti-PD-L1 agent, anti-PD-L1 mAb, anti-TGFb mAb, anti-TIGIT mAb, anti-TIM-3 mAb, Aurora kinase inhibitor, Bcl-2 Inhibitor, bifunctional fusion protein targeting TGFb and PD-L1, bispecific anti-PD-1 and anti-LAG3 mAb, CD1d ligand, CD40 agonist, Complement C5a inhibitor, CSF1R inhibitor, EZH2 inhibitor, FGFR3 inhibitor,

FGFR4 inhibitor, FGFrR3 inhibitor, glucocorticoid-induced tumor necrosis factor receptor–related gene agonist, glutaminase inhibitor, Human monoclonal antibody against IL-12, ICOS agonist, IDO1 inhibitor, IL2 mutein, IL2 receptor agonist, MEK inhibitor, multitargeted receptor tyrosine kinase inhibitor, neutrophil elastase inhibitor, Notch Inhibitor, p38 MAPK inhibitor, PD-1 inhibitor, recombinant human Flt3L, ROCK inhibitor, selective sphingosine-1-phosphate receptor modulator, Src kinase inhibitor, TLR4 agonist, TLR9 agonist, or any combination thereof.

[0032] In some embodiments, the subject is greater than 55, 56, 57, 58, 59, 60, 65, 70, 75 or 80 years of age.

[0033] In some embodiments, the polypeptide comprises (a) a sequence comprising an epitope sequence from ORF1ab, (b) a sequence comprising an epitope sequence from membrane glycoprotein (M) and (c) a sequence comprising an epitope sequence from nucleocapsid phosphoprotein (N).

[0034] In some embodiments, the sequence comprising an epitope sequence from ORF1ab is C-terminal to the sequence comprising an epitope sequence from nucleocapsid phosphoprotein (N).

[0035] In some embodiments, the sequence comprising an epitope sequence from ORF1ab is N-terminal to the sequence comprising an epitope sequence from membrane glycoprotein (M).

[0036] In some embodiments, the sequence comprising an epitope sequence from nucleocapsid phosphoprotein (N) is N-terminal to the sequence comprising an epitope sequence from membrane glycoprotein (M).

[0037] In some embodiments, the polypeptide comprises (a) 2, 3, 4, 5, 6, 7, 8, 9 or 10 or more epitope sequences from ORF1ab, (b) a sequence comprising an epitope sequence from membrane glycoprotein (M) and (c) a sequence comprising an epitope sequence from nucleocapsid phosphoprotein (N).

[0038] In some embodiments, the epitope sequence from ORF1ab is an epitope sequence from a non-structural protein (NSP).

[0039] In some embodiments, the non-structural protein (NSP) is selected from the group consisting of NSP1, NSP2, NSP3, NSP4 and combinations thereof.

[0040] In some embodiments, the polypeptide comprises a sequence comprising an epitope sequence from NSP1, a sequence comprising an epitope sequence from NSP2, a sequence comprising an epitope sequence from NSP3 and a sequence comprising an epitope sequence from NSP4.

[0041] In some embodiments, the epitope sequence from ORF1ab is selected from the group consisting of YLFDESGEFKL, YLFDESGEF, FGDDTVIEV, QLMCQPILL, TTDPSFLGRY, PTDNYITTY, PSFLGRY, AEAELAKNV, KTIQPRVEK and any combination thereof.

[0042] In some embodiments, the epitope sequence from nucleocapsid glycoprotein (N) is LLLDRLNQL.

[0043] In some embodiments, the epitope sequence from membrane phosphoprotein (M) is VATSRTLSY.

[0044] In some embodiments, the polypeptide comprises an epitope sequence from nucleocapsid glycoprotein (N) that is LLLDRLNQL and an epitope sequence from membrane phosphoprotein (M) that is VATSRTLSY.

[0045] In some embodiments, the polypeptide comprises (a) each of the following epitope sequences from ORF1ab: YLFDESGEFKL, YLFDESGEF, FGDDTVIEV, QLMCQPILL, TTDPSFLGRY, PTDNYITTY, PSFLGRY, AEAELAKNV, KTIQPRVEK; (b) an epitope sequence from nucleocapsid glycoprotein (N) that is LLLDRLNQL; and (c) an epitope sequence from membrane phosphoprotein (M) that is VATSRTLSY.

[0046] In some embodiments, the sequence comprising an epitope sequence from ORF1ab is selected from the group consisting of the following sequences or fragments thereof: MVTNNTFTLKVPHVGEIPVAYRKVLLKTIQPRVEKYLFDESGEFKLSEVGPEHSLAEYYIFFASFY Y; MVTNNTFTLKVPHVGEIPVAYRKVLLKTIQPRVEKYLFDESGEFKLSEVGPEHSLAEY; APKEIIFLEGETLFGDDTVIEVAIILASFSAST; APKEIIFLEGETLFGDDTVIEV; HTTDPSFLGRYMSALFADDLNQLTGYHTDFSSEIIGYQLMCQPILLAEAELAKNVSLILGTVSWN L;

TTDPSFLGRYMSALFADDLNQLTGYHTDFSSEIIGYQLMCQPILLAEAELAKNVSLILGTVSWNL; LLSAGIFGAITDVFYKENSYKVPTDNYITTY; and combinations thereof.

[0047] In some embodiments, the sequence comprising an epitope sequence from membrane glycoprotein (M) is selected from the group consisting of the following sequences or fragments thereof: ADSNGTITVEELKKLLEQWNLVIGFLFLTWICLLQFAYANRNRFLYIIKLIFLWLLWPVTLACFVL AAVYRINWITGGIAIAMACLVGLMWLSYFIASFRLFARTRSMWSFNPETNILLNVPLHGTILTRPL LESELVIGAVILRGHLRIAGHHLGRCDIKDLPKEITVATSRTLSYYKLGASQRVAGDSGFAAYSR YRIGNYKLNTDHSSSSDNIALLVQ;

[0048] FAYANRNRFLYIIKLIFLWLLWPVTLACFVLAAVYRINWITGGIAIAMACLVGLMWLS YFIASFRLF; LGRCDIKDLPKEITVATSRTLSYYKLGASQRVA; KLLEQWNLVIGF; NRNRFLYIIKLIFLWLLWPVTLACFVLAAVY; SELVIGAVILRGHLRIAGHHLGR; VATSRTLSYYKLGASQRV; GLMWLSYF; and combinations thereof.

[0049] In some embodiments, the sequence comprising an epitope sequence from nucleocapsid phosphoprotein (N) is selected from the group consisting of the following sequences or fragments thereof: KDLSPRWYFYYLGTGPEAGLPYGANKDGIIWVATEGALNTPKDHIGTRNPANNAAIVLQLPQGT TLPKGFYAEGSRGGSQASSRSSSRSRNSSRNSTPGSSRGTSPARMAGNGGDAALALLLLDRLNQL ESKMSGKGQQQQGQTVTKKSAAEASKKPRQKRTATKAYNVTQAFGRRGPEQTQGNFGDQELI RQGTDYKHWPQIAQFAPSASAFFGMSRIGMEVTPSGTWLTYTGAIKLDDKDPNFKDQVILLNKH IDAYKTFPPTEPKKDKKKKADETQALPQRQKKQQTVTLLPAADLDDFSKQLQQSMSSADSTQA; RMAGNGGDAALALLLLDRLNQLESKMSGKGQQQ;

YKHWPQIAQFAPSASAFFGMSRIGMEVTPSGTWLTYTGAIKLDDKDPNFKDQVILLNKHIDAYK TFP;
SPARMAGNGGDAALALLLLDRLNQLESKMSGKGQQQQGQTVTKKSAAEASKKPRQKRTATKA YNVTQAFGRRGPEQTQGNFGDQELIRQGTDYKHWPQIAQFAPSASAFFGMSRIGMEVTPSGTWL TYTGAIKLDDKDPNFKDQVILLNKHIDAYKTFPPTEPKKDK and combinations thereof.

[0050] In some embodiments, the polypeptide comprises one or more linker sequences.

[0051] In some embodiments, the one or more linker sequences are selected from the group consisting of GGSGGGGSGG, GGSLGGGGSG.

[0052] In some embodiments, the one or more linker sequences comprise cleavage sequences.

[0053] In some embodiments, the one or more cleavage sequences are selected from the group consisting of FRAC, KRCF, KKRY, ARMA, RRSG, MRAC, KMCG, ARCA, KKQG, YRSY, SFMN, FKAA, KRNG, YNSF, KKNG, RRRG, KRYS, and ARYA.

[0054] In some embodiments, the polypeptide comprises a transmembrane domain sequence.

[0055] In some embodiments, the transmembrane domain sequence is C-terminal to the sequence comprising an epitope sequence from ORF1ab, the sequence comprising an epitope sequence from membrane glycoprotein (M) and the sequence comprising an epitope sequence from nucleocapsid phosphoprotein (N).

[0056] In some embodiments, the transmembrane domain sequence is EQYIKWPWYIWLGFIAGLIAIVMVTIMLCCMTSCCSCLKGCCSCGSCCKFDEDDSEPVLKGVKL HYT.

[0057] In some embodiments, the polypeptide comprises an SEC sequence.

[0058] In some embodiments, the SEC sequence is N-terminal to the sequence comprising an epitope sequence from ORF1ab, the sequence comprising an epitope sequence from membrane glycoprotein (M) and the sequence comprising an epitope sequence from nucleocapsid phosphoprotein (N).

[0059] In some embodiments, the SEC sequence is MFVFLVLLPLVSSQCVNLT.

[0060] In some embodiments, the composition comprises the polynucleotide encoding the polypeptide.

[0061] In some embodiments, the polynucleotide is an mRNA.

[0062] In some embodiments, the polynucleotide comprises a codon optimized sequence for expression in a human.

[0063] In some embodiments, the polynucleotide comprises a dEarI-hAg sequence.

[0064] In some embodiments, the dEarI-hAg sequence is ATTCTTCTGGTCCCCACAGACTCAGAGAGAACCC, optionally wherein each T is a U.

[0065] In some embodiments, the polynucleotide comprises a Kozak sequence.

[0066] In some embodiments, the Kozak sequence is GCCACC.

[0067] In some embodiments, the polynucleotide comprises an F element sequence.

[0068] In some embodiments, the F element sequence is a 3 UTR of amino-terminal enhancer of split (AES).

[0069] In some embodiments, the F element sequence is CTGGTACTGCATGCACGCAATGCTAGCTGCCCCTTTCCCGTCCTGGGTACCCCGAGTCTCCC CCGACCTCGGGTCCCAGGTATGCTCCCACCTCCACCTGCCCCACTCACCACCTCTGCTAGTTC CAGACACCTCC, optionally wherein each T is a U.

[0070] In some embodiments, the polynucleotide comprises an I element sequence.

[0071] In some embodiments, the I element sequence is a 3' UTR of mitochondrially encoded 12S rRNA (mtRNR1).

[0072] In some embodiments, the I element sequence is CAAGCACGCAGCAATGCAGCTCAAAACGCTTAGCCTAGCCACACCCCCACGGGAAACAGCA GTGATTAACCTTTAGCAATAAACGAAAGTTTAACTAAGCTATACTAACCCCAGGGTTGGTCA ATTTCGTGCCAGCCACACC, optionally wherein each T is a U.

[0073] In some embodiments, the polynucleotide comprises a poly A sequence.

[0074] In some embodiments, the poly A sequence is AAAAAAAAAAAAAAAAAAAAAAAAAAAAAAGCATATGACTAAAAAAAAAAAAAAAAAAAA AAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA, optionally wherein each T is a U.

[0075] In some embodiments, each of the epitope sequences from the ORF1ab, the membrane glycoprotein, and the nucleocapsid phosphoprotein are from 2019 SARS-CoV-2.

[0076] In some embodiments, one or more or each epitope elicits a T cell response.

[0077] In some embodiments, one or more or each epitope has been observed by mass spectrometry as being presented by an HLA molecule.

[0078] In some embodiments, the composition comprises (i) a polypeptide with at least 70%, at least 75%, at least 80%, at least 85%, 90%, at least 95%, or 100% sequence identity to a sequence selected from the group consisting of RS C1p1full, RS C2p1full, RS C3p1full, RS C4p1full, RS C5p1, RS C5p2, RS C5p2full, RS C6p1, RS C6p2, RS C6p2full, RS C7p1, RS C7p2, RS C7p2full, RS C7p4, RS C7p4full, RS C8p1, RS C8p2 and RS C8p2full; (ii) a polynucleotide encoding a polypeptide with at least 70%, at least 75%, at least 80%, at least 85%, 90%, at least 95%, or 100% sequence identity to a sequence selected from the group consisting of RS C1p1full, RS C2p1full, RS C3p1full, RS C4p1full, RS C5p1, RS C5p2, RS C5p2full, RS C6p1, RS C6p2, RS C6p2full, RS C7p1, RS C7p2, RS C7p2full, RS C7p4, RS C7p4full, RS C8p1, RS C8p2 and RS C8p2full; or (iii) a polynucleotide with at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, or 100% sequence identity to a sequence selected from the group consisting of SEQ ID NOs: RS C1n1, RS C2n1, RS C3n1, RS C4n1, RS C5n1, RS C6n1, RS C7n1, RS

C8n1, RS C5n2, RS C6n2, RS C7n2, RS C7n4, RS C7n4full, RS C8n2, RS C5n2full, RS C6n2full, RS C7n2full and RS C8n2full.

[0079] In some embodiments, the composition comprises (i) a polypeptide with at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, or 100% sequence identity to a sequence selected from the group consisting of RS C7p1, RS C7p2, RS C7p2full, RS C7p4 and RS C7p4full, ; or (ii) a polynucleotide with at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, or 100% sequence identity to a sequence selected from the group consisting of SEQ ID NOs: RS C7n1, RS C7n2, RS C7n2full, RS C7n4 and RS C7n4full.

[0080] In some embodiments, the pharmaceutical composition comprises a pharmaceutically acceptable excipient, carrier, or diluent.

[0081] Provided herein is a method of treating or preventing an infection by a virus or treating a respiratory disease or condition associated with an infection by a virus comprising administering to a subject with a B cell immunodeficiency a pharmaceutical composition comprising: (i)a polypeptide comprising an epitope sequence of Table 1A, Table 1B, Table 1C, Table 2Ai, Table 2Aii, Table 2B and/or Table 16; (ii) a polynucleotide encoding the polypeptide comprising an epitope sequence of Table 1A, Table 1B, Table 1C, Table 2Ai, Table 2Aii, Table 2B and/or Table 16; (iii) a T cell receptor (TCR) or a T cell comprising the TCR, wherein the TCR binds to the epitope sequence in complex with a corresponding HLA class I or class II molecule; (iv) an antigen presenting cell comprising (i) or (ii); or (v) an antibody or B cell comprising the antibody, wherein the antibody binds to the epitope sequence.

[0082] In some embodiments, the epitope sequence comprises one or more or each of the following: YLFDESGEFKL, YLFDESGEF, FGDDTVIEV, LLLDRLNQL, QLMCQPILL, TTDPSFLGRY, PTDNYITTY, PSFLGRY, AEAELAKNV, VATSRTLSY and KTIQPRVEK.

[0083] In some embodiments, the epitope sequence comprises one or more or each of the following: SAPPAQYEL, AVASKILGL, EYADVFHLY, DEFTPFDVV, VRIQPGQTF, SFRLFARTR, KFLPFQQF, VVQEGVLTA, RLDKVEAEV, FGADPIHSL, NYNYLYRLF, KYIKWPWYI, KWPWYIWLGF, LPFNDGVYF, QPTESIVRF, IPFAMQMAY, YLQPRTFLL and RLQSLQTYV.

[0084] In some embodiments, the epitope sequence is from an orf1ab protein.

[0085] In some embodiments, the epitope sequence is from an orf1a protein

[0086] In some embodiments, the epitope sequence is from a surface glycoprotein (S) or a shifted reading frame thereof.

[0087] In some embodiments, the epitope sequence is from a nucleocapsid phosphoprotein (N).

[0088] In some embodiments, the epitope sequence is from an ORF3a protein.

[0089] In some embodiments, the epitope sequence is from a membrane glycoprotein (M).

[0090] In some embodiments, the epitope sequence is from an ORF7a protein.

[0091] In some embodiments, the epitope sequence is from an ORF8 protein.

[0092] In some embodiments, the epitope sequence is from an envelope protein (E).

[0093] In some embodiments, the epitope sequence is from an ORF6 protein.

[0094] In some embodiments, the epitope sequence is from an ORF7b protein.

[0095] In some embodiments, the epitope sequence is from an ORF10 protein.

[0096] In some embodiments, the epitope sequence is from an ORF9b protein.

[0097] Provided herein is a method of treating or preventing an infection by a virus or treating a respiratory disease or condition associated with an infection by a virus comprising administering to a subject with a B cell immunodeficiency a pharmaceutical composition comprising: a polypeptide having an amino acid sequence with at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, at least 95% or 100% sequence identity to a sequence of any one of the sequences depicted in column 2 of Table 11, column 2 of Table 12 or column 3 of Table 15; or a recombinant polynucleotide encoding a polypeptide having an amino acid sequence with at least at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, or 100% sequence identity to a sequence of any one of the sequences depicted in column 2 of Table 11, column 2 of Table 12 or column 3 of Table 15.

[0098] In some embodiments, the pharmaceutical composition comprises a polypeptide with at least 70%, at least 75%, at least 80%, at least 85%, 90%, at least 95% or 100% sequence identity to a sequence selected from the group consisting of RS C1p1full, RS C2p1full, RS C3p1full, RS C4p1full, RS C5p1, RS C5p2, RS C5p2full, RS C6p1, RS C6p2, RS C6p2full, RS C7p1, RS C7p2, RS C7p2full, RS C7p4, RS C7p4full, RS C8p1, RS C8p2 and RS C8p2full; or a polynucleotide encoding a polypeptide with at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, or 100% sequence identity to a sequence selected from the group consisting of RS C1p1full, RS C2p1full, RS C3p1full, RS C4p1full, RS C5p1, RS C5p2, RS C5p2full, RS C6p1, RS C6p2, RS C6p2full, RS C7p1, RS C7p2, RS C7p2full, RS C7p4, RS C7p4full, RS C8p1, RS C8p2 and RS C8p2full.

[0099] In some embodiments, the pharmaceutical composition comprises a polynucleotide with at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, at least 95% or 100% sequence identity to a sequence selected from the group consisting of SEQ ID NOs: RS C1n1, RS C2n1, RS C3n1, RS C4n1, RS C5n1, RS C6n1, RS C7n1, RS C8n1, RS C5n2, RS C6n2, RS C7n2, RS C8n2, RS C5n2full, RS C6n2full, RS C7n2full, RS C8n2full, RS C7n4, and RS C7n4full.

[00100] In some embodiments, the polynucleotide is an mRNA.

[00101] In some embodiments, the pharmaceutical composition further comprises one or more lipid components.

[00102] In some embodiments, the one or more lipid components comprise a lipid nanoparticle (LNP).

[00103] In some embodiments, the LNP encapsulates the recombinant polynucleotide construct.

[00104] In some embodiments, the polypeptide is synthetic.

[00105] In some embodiments, the polypeptide is recombinant.

[00106] In some embodiments, the polypeptide is from 8-1000 amino acids in length.

[00107] In some embodiments, the epitope sequence binds to or is predicted to bind to an HLA class I or class II molecule with a KD of 1000 nM or less.

[00108] In some embodiments, the epitope sequence binds to or is predicted to bind to an HLA class I or class II molecule with a KD of 500 nM or less.

[00109] In some embodiments, the epitope sequence comprises a sequence of a viral protein expressed by a virus-infected cell of the subject.

[00110] In some embodiments, the virus is a coronavirus.

[00111] In some embodiments, the virus is 2019 SARS-CoV 2.

[00112] In some embodiments, an HLA molecule expressed by the subject is unknown at the time of administration.

[00113] In some embodiments, the ability of the virus to avoid escape of recognition by an immune system of the subject is less compared to the ability of the virus to avoid escape of recognition by an immune system of a subject administered a pharmaceutical composition containing an epitope from a single protein or epitopes from fewer proteins than in the pharmaceutical composition administered according a method described herein.

[00114] In some embodiments, the subject expresses an HLA molecule encoded by an HLA allele of any one of Table 1A, Table 1B, Table 1C, Table 2Ai, Table 2Aii, Table 2B and Table 16 and the epitope sequence is an HLA allele-matched epitope sequence.

[00115] In some embodiments, the epitope sequence comprises one or more or each of the following: SAPPAQYEL, AVASKILGL, EYADVFHLY, DEFTPFDVV, VRIQPGQTF, SFRLFARTR, KFLPFQQF, VVQEGVLTA, RLDKVEAEV and FGADPIHSL.

[00116] In some embodiments, the method further comprises administering to the subject an additional therapy for a 2019 SARS-CoV 2 viral infection.

[00117] In some embodiments, the method further comprises administering to the subject (a) a polypeptide having an amino acid sequence of a 2019 SARS-CoV 2 spike protein or a variant or fragment thereof; (b) a recombinant polynucleotide encoding a 2019 SARS-CoV 2 spike protein or a variant or fragment thereof; or a 2019 SARS-CoV 2 spike protein pharmaceutical composition comprising (a) or (b).

[00118] In some embodiments, the vaccine or therapeutic of (a) or (b) is administered to the subject once.

[00119] In some embodiments, the vaccine or therapeutic of (a) or (b) is administered to the subject more than once.

[00120] In some embodiments, the vaccine or therapeutic is administered at least two times, wherein the first administered dose is a priming dose, and the second and subsequent doses are booster dose(s).

[00121] In some embodiments, the priming and the booster doses are administered at an interval of at least 21 days.

[00122] In some embodiments, an interval between two booster doses is at least 30 days, at least 60 days, or at least 90 days.

[00123] In some embodiments, the vaccine or therapeutic is administered once each year.

[00124] In some embodiments, the vaccine or therapeutic is administered twice each year.

[00125] In some embodiments, the vaccine or therapeutic is administered at a high priming or loading dose for the first dose, and at a reduced boosting or maintenance dose for the subsequent doses.

[00126] In some embodiments, the subject receives a lower dose of or a lower frequency of a SARS-CoV spike vaccine than a subject receiving the SARS-CoV spike vaccine alone.

[00127] Provided herein is a method of treating or preventing an infection by a virus or treating a respiratory disease or condition associated with an infection by a virus comprising administering to a subject in need thereof a pharmaceutical composition comprising: (i) a recombinant polynucleotide encoding a polypeptide comprising at least two of the following: a sequence comprising an epitope sequence from ORF1ab, a sequence comprising an epitope sequence from membrane glycoprotein (M), and a sequence comprising an epitope sequence from nucleocapsid phosphoprotein (N); and (ii) a recombinant polynucleotide encoding a 2019 SARS-CoV 2 spike protein or a variant or fragment thereof; wherein the ratio (e.g., mass ratio) of (i):(ii) is greater than 20:1 or less than 1:20.

[00128] In some embodiments, the ratio (e.g., mass ratio) of (i):(ii) is greater than 20:1, 30:1, 40:1, 50:1, 60:1, 70:1, 80:1, 90:1 or 100:1

[00129] In some embodiments, the ratio (e.g., mass ratio) of (i):(ii) is less than 1:20, 1:30, 1:40, 1:50, 1:60, 1:70, 1:80, 1:90 or 1:100.

[00130] Provided herein is a method of treating or preventing an infection by a virus or treating a respiratory disease or condition associated with an infection by a virus comprising administering to a subject in need thereof: (i) a first pharmaceutical composition comprising a first recombinant polynucleotide encoding a polypeptide comprising at least two of the following: a sequence comprising an epitope sequence from ORF1ab, a sequence comprising an epitope sequence from membrane glycoprotein (M), and a sequence comprising an epitope sequence from nucleocapsid phosphoprotein (N); and (ii) a second pharmaceutical composition comprising a second recombinant polynucleotide encoding a 2019 SARS-CoV 2 spike protein or a variant or fragment thereof; wherein the ratio (e.g., mass ratio) of the recombinant polynucleotide in (i) to the recombinant polynucleotide in (ii) is from 1:50 to 50:1.

[00131] In some embodiments, the ratio (e.g., mass ratio) of the recombinant polynucleotide in (i) to the recombinant polynucleotide in (ii) is from about 1:25 to 25:1.

[00132] In some embodiments, the ratio (e.g., mass ratio) of the recombinant polynucleotide in (i) to the recombinant polynucleotide in (ii) is from about 1:10 to 10:1.

[00133] In some embodiments, the ratio (e.g., mass ratio) of the recombinant polynucleotide in (i) to the recombinant polynucleotide in (ii) is about 1:10, 1:9, 1:8, 1:7, 1:6, 1:5, 1:4, 1:3, 1:2, 1:1, 2:1, 3:1, 4:1, 5:1,

6:1, 7:1, 8:1, 9:1, 10:1, 1:9.5, 1:8.5, 1:7.5, 1:6.5, 1:5.5, 1:4.5, 1:3.5, 1:2.5, 1:1.5, 2.5:1, 3.5:1, 4.5:1, 5.5:1, 6.5:1, 7.5:1, 8.5:1, 9.5:1, 2:9, 2:8, 2:7, 2:6, 2:5, 2:4, 2:3, 3:2, 4:2, 5:2, 6:2, 7:2, 8:2, 9:2, 3:8, 3:7, 3:5, 3:4, 4:3, 5:3, 7:3, 8:3, 4:9, 4:7, 4:5, 5:4, 7:4, 9:4, 5:9, 5:8, 5:7, 5:6, 6:5, 7:5, 8:5, 9:5, 6:7, 7:6, 7:8, 8:7, 8:9 or 9:8. In some embodiments, the ratio (e.g., mass ratio) of the recombinant polynucleotide in (i) to the recombinant polynucleotide in (ii) is about 1:6. In some embodiments, the ratio (e.g., mass ratio) of the recombinant polynucleotide in (i) to the recombinant polynucleotide in (ii) is about 1:3. In some embodiments, the ratio (e.g., mass ratio) of the recombinant polynucleotide in (i) to the recombinant polynucleotide in (ii) is about 1:2.

[00134] In some embodiments, the recombinant polynucleotide in (i) is present in a pharmaceutical composition at a dose of from 0.1 microgram to 100 micrograms, or 1 microgram to 50 micrograms, or 1 microgram to 30 micrograms, or 1 microgram to 20 micrograms, or 3 micrograms to 20 micrograms, or 5 micrograms to 15 micrograms. In some embodiments, the recombinant polynucleotide in (i) is present in a pharmaceutical composition at a dose of from 0.05 microgram to 10 micrograms, or 0.1 microgram to 5 micrograms, or 0.3 microgram to 5 micrograms. In some embodiments, the recombinant polynucleotide in (i) is present in a pharmaceutical composition at a dose of from 0.1 microgram to 20 micrograms or from 0.5 microgram to 15 micrograms.

[00135] In some embodiments, the recombinant polynucleotide in (ii) is present in a pharmaceutical composition at a dose of from 0.1 microgram to 100 micrograms, or 1 microgram to 100 micrograms, or 1 microgram to 30 micrograms, or 1 microgram to 20 micrograms, or 3 micrograms to 30 micrograms.

[00136] In some embodiments, the recombinant polynucleotide in (i) is present in a pharmaceutical composition at a dose of about 5 micrograms and the recombinant polynucleotide in (ii) is present in a pharmaceutical composition at a dose of about 30 micrograms. In some embodiments, the recombinant polynucleotide in (i) is present in a pharmaceutical composition at a dose of about 10 micrograms and the recombinant polynucleotide in (ii) is present in a pharmaceutical composition at a dose of about 30 micrograms. In some embodiments, the recombinant polynucleotide in (i) is present in a pharmaceutical composition at a dose of about 15 micrograms and the recombinant polynucleotide in (ii) is present in a pharmaceutical composition at a dose of about 30 micrograms.

[00137] In some embodiments, the recombinant polynucleotide in (ii) encompasses at least two separate recombinant polynucleotides, each encoding a SARS-CoV-2 S protein of a different strain or variant thereof, or an immunogenic variant or fragment thereof (e.g., in some embodiments RBD). For example, in some embodiments, the recombinant polynucleotide in (ii) encompasses a recombinant polynucleotide encoding a SARS-CoV-2 S protein of an ancestral strain (e.g., Wuhan strain) or an immunogenic variant or fragment thereof (e.g., in some embodiments RBD) and a recombinant polynucleotide encoding a SARS-CoV-2 S protein of a SARS-CoV-2 variant strain that is prevalent or rapidly spreading at the time of administration. For example, in some embodiments, the recombinant polynucleotide in (ii) encompasses

a recombinant polynucleotide encoding a SARS-CoV-2 S protein of an ancestral strain (e.g., Wuhan strain) or an immunogenic variant or fragment thereof (e.g., in some embodiments RBD) and a recombinant polynucleotide encoding a SARS-CoV-2 S protein of a variant strain having one or more mutations that are characteristics of a SARS-CoV-2 variant (e.g., in some embodiments an Omicron variant such as, e.g., a Omicron BA.1, BA.2, BA.4 or BA.5 variant), or an immunogenic variant or fragment thereof. In some embodiments, at least two recombinant polynucleotides, each encoding a SARS-CoV-2 S protein of a different strain or variant thereof, or an immunogenic variant or fragment thereof, can be present in a pharmaceutical composition at a ratio (e.g., mass ratio) of 3:1 to 1:3, or 2:1 to 1:2 or 1:1.

[00138] In some embodiments, a pharmaceutical composition described herein may further comprise (iii) a recombinant polynucleotide encoding a peptide or polypeptide antigen from a pathogen associated with a non-SARS-CoV-2 respiratory disease. In some embodiments, such a non-SARS-CoV-2 respiratory disease may be flu (influenza), and/or respiratory syncytial virus.

[00139] Provided herein is a method of treating or preventing an infection by a virus or treating a respiratory disease or condition associated with an infection by a virus comprising administering to a subject in need thereof a pharmaceutical composition comprising a nanoparticle, wherein the nanoparticle comprises: (i) a first recombinant polynucleotide encoding a polypeptide comprising at least two of the following: a sequence comprising an epitope sequence from ORF1ab, a sequence comprising an epitope sequence from membrane glycoprotein (M), and a sequence comprising an epitope sequence from nucleocapsid phosphoprotein (N); and (ii) a second recombinant polynucleotide encoding a 2019 SARS-CoV 2 spike protein or a variant or fragment thereof. In some embodiments, a first recombinant polynucleotide encodes a polypeptide comprising all of the following: a sequence comprising an epitope sequence from ORF1ab, a sequence comprising an epitope sequence from membrane glycoprotein (M), and a sequence comprising an epitope sequence from nucleocapsid phosphoprotein (N).

[00140] In some embodiments, the nanoparticle is present in the pharmaceutical composition at a dose of from 100 ng to 500 micrograms.

[00141] In some embodiments, the nanoparticle is present in the pharmaceutical composition at a dose of from 1 microgram to 100 micrograms.

[00142] In some embodiments, the nanoparticle is present in the pharmaceutical composition at a dose of from 1 microgram to 30 micrograms, 5 micrograms to 40 micrograms or 10 microgram to 50 micrograms.

[00143] In some embodiments, the nanoparticle is present in the pharmaceutical composition at a dose of 0.1, 0.2, 0.3, 0.4, 0.5, 0.6, 0.7, 0.8, 0.9, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25, 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, 100, 150, 200, 250, 300, 350, 400, 450, 500, 600, 700, 800, 900 or 1,000 micrograms.

[00144] In some embodiments, the ratio (e.g., mass ratio) of the first recombinant polynucleotide to the second recombinant polynucleotide is from about 1:50 to 50:1.

[00145] In some embodiments, the ratio (e.g., mass ratio) of the first recombinant polynucleotide to the second recombinant polynucleotide is from about 1:25 to 25:1.

[00146] In some embodiments, the ratio (e.g., mass ratio) of the first recombinant polynucleotide to the second recombinant polynucleotide is from about 1:10 to 10:1.

[00147] In some embodiments, the ratio of the first recombinant polynucleotide to the second recombinant polynucleotide is about 1:10, 1:9, 1:8, 1:7, 1:6, 1:5, 1:4, 1:3, 1:2, 1:1, 2:1, 3:1, 4:1, 5:1, 6:1, 7:1, 8:1, 9:1, 10:1, 1:9.5, 1:8.5, 1:7.5, 1:6.5, 1:5.5, 1:4.5, 1:3.5, 1:2.5, 1:1.5, 2.5:1, 3.5:1, 4.5:1, 5.5:1, 6.5:1, 7.5:1, 8.5:1, 9.5:1, 2:9, 2:8, 2:7, 2:6, 2:5, 2:4, 2:3, 3:2, 4:2, 5:2, 6:2, 7:2, 8:2, 9:2, 3:8, 3:7, 3:5, 3:4, 4:3, 5:3, 7:3, 8:3, 4:9, 4:7, 4:5, 5:4, 7:4, 9:4, 5:9, 5:8, 5:7, 5:6, 6:5, 7:5, 8:5, 9:5, 6:7, 7:6, 7:8, 8:7, 8:9 or 9:8. In some embodiments, the ratio (e.g., mass ratio) of the first recombinant polynucleotide to the second recombinant polynucleotide is about 1:6. In some embodiments, the ratio (e.g., mass ratio) of the first recombinant polynucleotide to the second recombinant polynucleotide is about 1:3. In some embodiments, the ratio (e.g., mass ratio) of the first recombinant polynucleotide to the second recombinant polynucleotide is about 1:2.

[00148] In some embodiments, the first recombinant polynucleotide is present in a pharmaceutical composition at a dose of from 0.1 microgram to 100 micrograms, or 1 microgram to 50 micrograms, or 1 microgram to 30 micrograms, or 1 microgram to 20 micrograms, or 3 micrograms to 20 micrograms, or 5 micrograms to 15 micrograms. In some embodiments, the first recombinant polynucleotide is present in a pharmaceutical composition at a dose of from 0.05 microgram to 10 micrograms, or 0.1 microgram to 5 micrograms, or 0.3 microgram to 5 micrograms. In some embodiments, the first recombinant polynucleotide is present in a pharmaceutical composition at a dose of from 0.1 microgram to 20 micrograms or from 0.5 microgram to 15 micrograms.

[00149] In some embodiments, the second recombinant polynucleotide is present in a pharmaceutical composition at a dose of from 0.1 microgram to 100 micrograms, or 1 microgram to 100 micrograms, or 1 microgram to 30 micrograms, or 1 microgram to 20 micrograms, or 3 micrograms to 30 micrograms.

[00150] In some embodiments, the second recombinant polynucleotide encompasses at least two separate recombinant polynucleotides, each encoding a SARS-CoV-2 S protein of a different strain or variant thereof, or an immunogenic variant or fragment thereof (e.g., in some embodiments RBD). For example, in some embodiments, the second recombinant polynucleotide encompasses a recombinant polynucleotide encoding a SARS-CoV-2 S protein of an ancestral strain (e.g., Wuhan strain) or an immunogenic variant or fragment thereof (e.g., in some embodiments RBD) and a recombinant polynucleotide encoding a SARS-CoV-2 S protein of a SARS-CoV-2 variant strain that is prevalent or rapidly spreading at the time of administration. For example, in some embodiments, the second recombinant polynucleotide encompasses a recombinant polynucleotide encoding a SARS-CoV-2 S protein of an ancestral strain (e.g., Wuhan strain) or an immunogenic variant or fragment thereof (e.g., in some embodiments RBD) and a recombinant

polynucleotide encoding a SARS-CoV-2 S protein of a variant strain having one or more mutations that are characteristics of a SARS-CoV-2 variant (e.g., in some embodiments an Omicron variant such as, e.g., an Omicron BA.1, BA.2, BA.4 or BA.5 variant), or an immunogenic variant or fragment thereof. In some embodiments, the two recombinant polynucleotides, each encoding a SARS-CoV-2 S protein of a different strain or variant thereof, or an immunogenic variant or fragment thereof, can be present in a pharmaceutical composition at a ratio (e.g., mass ratio) of 3:1 to 1:3, or 2:1 to 1:2 or 1:1.

[00151] In some embodiments, a pharmaceutical composition described herein may comprise a third recombinant polynucleotide encoding a peptide or polypeptide antigen from a pathogen associated with a non-SARS-CoV-2 respiratory disease. In some embodiments, such a non-SARS-CoV-2 respiratory disease may be, but not limited to flu (influenza), and/or respiratory syncytial virus.

[00152] Provided herein is a method of treating or preventing an infection by a virus or treating a respiratory disease or condition associated with an infection by a virus comprising administering to a subject in need thereof: (i) a first pharmaceutical composition comprising a first nanoparticle, wherein the first nanoparticle comprises a recombinant polynucleotide encoding a polypeptide comprising at least two of the following: a sequence comprising an epitope sequence from ORF1ab, a sequence comprising an epitope sequence from membrane glycoprotein (M), and a sequence comprising an epitope sequence from nucleocapsid phosphoprotein (N); and (ii) a second pharmaceutical composition comprising a second nanoparticle, wherein the second nanoparticle comprises a recombinant polynucleotide encoding a 2019 SARS-CoV 2 spike protein or a variant or fragment thereof. In some embodiments, a first pharmaceutical composition comprising a first nanoparticle, wherein the first nanoparticle comprises a recombinant polynucleotide encoding a polypeptide comprising all of the following: a sequence comprising an epitope sequence from ORF1ab, a sequence comprising an epitope sequence from membrane glycoprotein (M), and a sequence comprising an epitope sequence from nucleocapsid phosphoprotein (N).

[00153] In some embodiments, the ratio (e.g., mass ratio) of the recombinant polynucleotide in (i) to the recombinant polynucleotide in (ii) is from about 1:50 to 50:1.

[00154] In some embodiments, the ratio (e.g., mass ratio) of the recombinant polynucleotide in (i) to the recombinant polynucleotide in (ii) is from about 1:25 to 25:1.

[00155] In some embodiments, the ratio (e.g., mass ratio) of the recombinant polynucleotide in (i) to the recombinant polynucleotide in (ii) is from about 1:10 to 10:1.

[00156] In some embodiments, the ratio (e.g., mass ratio) of the recombinant polynucleotide in (i) to the recombinant polynucleotide in (ii) is about 1:10, 1:9, 1:8, 1:7, 1:6, 1:5, 1:4, 1:3, 1:2, 1:1, 2:1, 3:1, 4:1, 5:1, 6:1, 7:1, 8:1, 9:1, 10:1, 1:9.5, 1:8.5, 1:7.5, 1:6.5, 1:5.5, 1:4.5, 1:3.5, 1:2.5, 1:1.5, 2.5:1, 3.5:1, 4.5:1, 5.5:1, 6.5:1, 7.5:1, 8.5:1, 9.5:1, 2:9, 2:8, 2:7, 2:6, 2:5, 2:4, 2:3, 3:2, 4:2, 5:2, 6:2, 7:2, 8:2, 9:2, 3:8, 3:7, 3:5, 3:4, 4:3, 5:3, 7:3, 8:3, 4:9, 4:7, 4:5, 5:4, 7:4, 9:4, 5:9, 5:8, 5:7, 5:6, 6:5, 7:5, 8:5, 9:5, 6:7, 7:6, 7:8, 8:7, 8:9 or 9:8. In some embodiments, the ratio (e.g., mass ratio) of the recombinant polynucleotide in (i)

to the recombinant polynucleotide in (ii) is about 1:6. In some embodiments, the ratio (e.g., mass ratio) of the recombinant polynucleotide in (i) to the recombinant polynucleotide in (ii) is about 1:3. In some embodiments, the ratio (e.g., mass ratio) of the recombinant polynucleotide in (i) to the recombinant polynucleotide in (ii) is about 1:2.

[00157] In some embodiments, the recombinant polynucleotide in (i) is present in a pharmaceutical composition at a dose of from 0.1 microgram to 100 micrograms, or 1 microgram to 50 micrograms, or 1 microgram to 30 micrograms, or 1 microgram to 20 micrograms, or 3 micrograms to 20 micrograms, or 5 micrograms to 15 micrograms. In some embodiments, the recombinant polynucleotide in (i) is present in a pharmaceutical composition at a dose of from 0.05 microgram to 10 micrograms, or 0.1 microgram to 5 micrograms, or 0.3 microgram to 5 micrograms. In some embodiments, the recombinant polynucleotide in (i) is present in a pharmaceutical composition at a dose of from 0.1 microgram to 20 micrograms or from 0.5 microgram to 15 micrograms.

[00158] In some embodiments, the recombinant polynucleotide in (ii) is present in a pharmaceutical composition at a dose of from 0.1 microgram to 100 micrograms, or 1 microgram to 100 micrograms, or 1 microgram to 30 micrograms, or 1 microgram to 20 micrograms, or 3 micrograms to 30 micrograms.

[00159] In some embodiments, the recombinant polynucleotide in (ii) encompasses at least two separate recombinant polynucleotides, each encoding a SARS-CoV-2 S protein of a different strain or variant thereof, or an immunogenic variant or fragment thereof (e.g., in some embodiments RBD). For example, in some embodiments, the recombinant polynucleotide in (ii) encompasses a recombinant polynucleotide encoding a SARS-CoV-2 S protein of an ancestral strain (e.g., Wuhan strain) or an immunogenic variant or fragment thereof (e.g., in some embodiments RBD) and a recombinant polynucleotide encoding a SARS-CoV-2 S protein of a SARS-CoV-2 variant strain that is prevalent or rapidly spreading at the time of administration. For example, in some embodiments, the recombinant polynucleotide in (ii) encompasses a recombinant polynucleotide encoding a SARS-CoV-2 S protein of an ancestral strain (e.g., Wuhan strain) or an immunogenic variant or fragment thereof (e.g., in some embodiments RBD) and a recombinant polynucleotide encoding a SARS-CoV-2 S protein of a variant strain having one or more mutations that are characteristics of a SARS-CoV-2 variant (e.g., in some embodiments an Omicron variant such as, e.g., a Omicron BA.1, BA.2, BA.4 or BA.5 variant), or an immunogenic variant or fragment thereof. In some embodiments, at least two recombinant polynucleotides, each encoding a SARS-CoV-2 S protein of a different strain or variant thereof, or an immunogenic variant or fragment thereof, can be present in a pharmaceutical composition at a ratio (e.g., mass ratio) of 3:1 to 1:3, or 2:1 to 1:2 or 1:1.

[00160] In some embodiments, a third pharmaceutical composition (iii) may be administered to a subject in need thereof, which comprises a third nanoparticle, wherein the third nanoparticle comprises a recombinant polynucleotide encoding a peptide or polypeptide antigen from a pathogen associated with a

non-SARS-CoV-2 respiratory disease. In some embodiments, such a non-SARS-CoV-2 respiratory disease may be flu (influenza), and/or respiratory syncytial virus.

[00161] In some embodiments, the first nanoparticle is present in the first pharmaceutical composition at a dose of from about 100 ng to 500 micrograms.

[00162] In some embodiments, the first nanoparticle is present in the first pharmaceutical composition at a dose of from about 1 microgram to 100 micrograms.

[00163] In some embodiments, the first nanoparticle is present in the first pharmaceutical composition at a dose of from about 1 microgram to 30 micrograms, 5 micrograms to 40 micrograms or 10 microgram to 50 micrograms.

[00164] In some embodiments, the first nanoparticle is present in the first pharmaceutical composition at a dose of about 0.1, 0.2, 0.3, 0.4, 0.5, 0.6, 0.7, 0.8, 0.9, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25, 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, 100, 150, 200, 250, 300, 350, 400, 450, 500, 600, 700, 800, 900 or 1,000 micrograms.

[00165] In some embodiments, the second nanoparticle is present in the second pharmaceutical composition at a dose of from about 100 ng to 500 micrograms.

[00166] In some embodiments, the second nanoparticle is present in the second pharmaceutical composition at a dose of from about 1 microgram to 100 micrograms.

[00167] In some embodiments, the second nanoparticle is present in the second pharmaceutical composition at a dose of from about 1 microgram to 30 micrograms, 5 micrograms to 40 micrograms or 10 microgram to 50 micrograms.

[00168] In some embodiments, the second nanoparticle is present in the second pharmaceutical composition at a dose of about 0.1, 0.2, 0.3, 0.4, 0.5, 0.6, 0.7, 0.8, 0.9, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25, 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, 100, 150, 200, 250, 300, 350, 400, 450, 500, 600, 700, 800, 900 or 1,000 micrograms.

[00169] Provided herein is a method of treating or preventing an infection by a virus or treating a respiratory disease or condition associated with an infection by a virus comprising administering to a subject in need thereof: (i) a pharmaceutical composition comprising (a) a polypeptide comprising at least two of the following: a sequence comprising an epitope sequence from ORF1ab, a sequence comprising an epitope sequence from membrane glycoprotein (M), and a sequence comprising an epitope sequence from nucleocapsid phosphoprotein (N); or (b) a polynucleotide encoding a polypeptide comprising at least two of the following: a sequence comprising an epitope sequence from ORF1ab, a sequence comprising an epitope sequence from membrane glycoprotein (M), and a sequence comprising an epitope sequence from nucleocapsid phosphoprotein (N); and (ii) a pharmaceutical composition comprising (a) a polypeptide having an amino acid sequence of a 2019 SARS-CoV 2 spike protein or a variant or fragment thereof; or (b) a recombinant polynucleotide encoding a 2019 SARS-CoV 2 spike protein or a variant or fragment

thereof; or a 2019 SARS-CoV 2 spike protein pharmaceutical composition comprising (ii)(a) or (ii)(b); wherein the subject receives a dose of (ii)(a) or (ii)(b) that is lower than a dose of (ii)(a) or (ii)(b) administered to a subject alone.

[00170] Provided herein is a method of treating or preventing an infection by a virus or treating a respiratory disease or condition associated with an infection by a virus comprising administering to a subject in need thereof: (i) a pharmaceutical composition comprising (a) a polypeptide comprising at least two of the following: a sequence comprising an epitope sequence from ORF1ab, a sequence comprising an epitope sequence from membrane glycoprotein (M), and a sequence comprising an epitope sequence from nucleocapsid phosphoprotein (N); or (b) a polynucleotide encoding a polypeptide comprising at least two of the following: a sequence comprising an epitope sequence from ORF1ab, a sequence comprising an epitope sequence from membrane glycoprotein (M), and a sequence comprising an epitope sequence from nucleocapsid phosphoprotein (N); and (ii) a pharmaceutical composition comprising (a) a polypeptide having an amino acid sequence of a 2019 SARS-CoV 2 spike protein or a variant or fragment thereof; or (b) a recombinant polynucleotide encoding a 2019 SARS-CoV 2 spike protein or a variant or fragment thereof; or a 2019 SARS-CoV 2 spike protein pharmaceutical composition comprising (ii)(a) or (ii)(b).

[00171] Provided herein is a method of treating or preventing an infection by a virus or treating a respiratory disease or condition associated with an infection by a virus comprising administering to a subject in need thereof: (i) a pharmaceutical composition comprising (a) a polypeptide comprising at least two of the following: a sequence comprising an epitope sequence from ORF1ab, a sequence comprising an epitope sequence from membrane glycoprotein (M), and a sequence comprising an epitope sequence from nucleocapsid phosphoprotein (N); or (b) a polynucleotide encoding a polypeptide comprising at least two of the following: a sequence comprising an epitope sequence from ORF1ab, a sequence comprising an epitope sequence from membrane glycoprotein (M), and a sequence comprising an epitope sequence from nucleocapsid phosphoprotein (N); and (ii) a pharmaceutical composition comprising (a) a polypeptide having an amino acid sequence of a 2019 SARS-CoV 2 spike protein or a variant or fragment thereof; (b) a recombinant polynucleotide encoding a 2019 SARS-CoV 2 spike protein or a variant or fragment thereof; or a 2019 SARS-CoV 2 spike protein pharmaceutical composition comprising (ii)(a) or (ii)(b); wherein the subject receives a number of doses of (ii)(a) or (ii)(b) that is lower than a number of doses of (ii)(a) or (ii)(b) administered to a subject alone.

[00172] In some embodiments, the subject receives a dose of (ii)(a) or (ii)(b) that is at least 1.1, 1, 1.5, 2, 3, 4, 5, 6, 7, 8, 9, 10, 20, 30, 40, 50, 60, 70, 80, 90 or 100 times lower than a dose of (ii)(a) or (ii)(b) administered to a subject alone.

[00173] In some embodiments, the subject receives 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 fewer doses of (ii)(a) or (ii)(b) than the number of doses of (ii)(a) or (ii)(b) administered to a subject alone.

[00174] In some embodiments, the pharmaceutical composition of (i) is co-formulated with the pharmaceutical composition of (ii).

[00175] In some embodiments, the pharmaceutical composition of (i) is formulated separately from the pharmaceutical composition of (ii).

[00176] In some embodiments, the pharmaceutical composition of (i) is administered separately from the pharmaceutical composition of (ii).

[00177] Provided herein is a method of treating or preventing an infection by a virus or treating a respiratory disease or condition associated with an infection by a virus comprising administering to a subject in need thereof: (i) a pharmaceutical composition comprising (a) a polypeptide comprising at least two of the following: a sequence comprising an epitope sequence from ORF1ab, a sequence comprising an epitope sequence from membrane glycoprotein (M), and a sequence comprising an epitope sequence from nucleocapsid phosphoprotein (N); or (b) a polynucleotide encoding a polypeptide comprising at least two of the following: a sequence comprising an epitope sequence from ORF1ab, a sequence comprising an epitope sequence from membrane glycoprotein (M), and a sequence comprising an epitope sequence from nucleocapsid phosphoprotein (N); and (ii) a pharmaceutical composition comprising (a) a polypeptide having an amino acid sequence of a 2019 SARS-CoV 2 spike protein or a variant or fragment thereof; (b) a recombinant polynucleotide encoding a 2019 SARS-CoV 2 spike protein or a variant or fragment thereof; or a 2019 SARS-CoV 2 spike protein pharmaceutical composition comprising (ii)(a) or (ii)(b); wherein the subject receives a dose of (i)(a) or (i)(b) that is lower than a dose of (i)(a) or (i)(b) administered to a subject alone.

[00178] Provided herein is a method of treating or preventing an infection by a virus or treating a respiratory disease or condition associated with an infection by a virus comprising administering to a subject in need thereof: (i) a pharmaceutical composition comprising (a) a polypeptide comprising at least two of the following: a sequence comprising an epitope sequence from ORF1ab, a sequence comprising an epitope sequence from membrane glycoprotein (M), and a sequence comprising an epitope sequence from nucleocapsid phosphoprotein (N); or (b) a polynucleotide encoding a polypeptide comprising at least two of the following: a sequence comprising an epitope sequence from ORF1ab, a sequence comprising an epitope sequence from membrane glycoprotein (M), and a sequence comprising an epitope sequence from nucleocapsid phosphoprotein (N); and (ii) a pharmaceutical composition comprising (a) a polypeptide having an amino acid sequence of a 2019 SARS-CoV 2 spike protein or a variant or fragment thereof; (b) a recombinant polynucleotide encoding a 2019 SARS-CoV 2 spike protein or a variant or fragment thereof; or a 2019 SARS-CoV 2 spike protein pharmaceutical composition comprising (ii)(a) or (ii)(b); wherein the subject receives a number of doses of (i)(a) or (i)(b) that is lower than a number of doses of (i)(a) or (i)(b) administered to a subject alone.

[00179] In some embodiments, the subject receives a dose of (i)(a) or (i)(b) that is at least 1.1, 1, 1.5, 2, 3, 4, 5, 6, 7, 8, 9, 10, 20, 30, 40, 50, 60, 70, 80, 90 or 100 times lower than a dose of (i)(a) or (i)(b) administered to a subject alone.

[00180] In some embodiments, the subject receives 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 fewer doses of (i)(a) or (i)(b) than the number of doses of (i)(a) or (i)(b) administered to a subject alone.

[00181] In some embodiments, the pharmaceutical composition of (i) is co-formulated with the pharmaceutical composition of (ii).

[00182] In some embodiments, the pharmaceutical composition of (i) is formulated separately from the pharmaceutical composition of (ii).

[00183] In some embodiments, the pharmaceutical composition of (i) is administered separately from the pharmaceutical composition of (ii).

[00184] In some embodiments, the pharmaceutical composition is a coformulation.

[00185] In some embodiments, the first pharmaceutical composition is administered with or on the same day as the second pharmaceutical composition

[00186] In some embodiments, the first pharmaceutical composition is administered simultaneously with the second pharmaceutical composition.

[00187] In some embodiments, the first pharmaceutical composition is administered at a first location of the subject and the second pharmaceutical composition is administered at a second location of the subject that is different than the first location.

[00188] In some embodiments, the first location is at an appendage of the subject and second location is at an opposing appendage of the subject,

[00189] In some embodiments, the first appendage is an arm and the second appendage is an arm.

[00190] In some embodiments, the first pharmaceutical composition and the second pharmaceutical composition are administered to the same location of the subject.

[00191] In some embodiments, the pharmaceutical composition is administered at a first time point and a second time point, wherein the second time point is at least about, at most about or about 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35 or 36 days after the first time point; at least about, at most about or about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35 or 36 weeks after the first time point; or at least about, at most about or about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35 or 36 months after the first time point.

[00192] In some embodiments, the pharmaceutical composition is administered at a third time point, wherein the third time point is at least about, at most about or about 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35 or 36 days after the second time point; at least about, at most about or about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18,

19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35 or 36 weeks after the second time point; or at least about, at most about or about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35 or 36 months after the second time point.

[00193] In some embodiments, the third time point is at least about, at most about or about 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49 or 50 days after the first time point; at least about, at most about or about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35 or 36 weeks after the first time point; or at least about, at most about or about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35 or 36 months after the first time point.

[00194] In some embodiments, the first pharmaceutical composition is administered at a first time point and a second time point, wherein the second time point is at least about, at most about or about 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35 or 36 days after the first time point; at least about, at most about or about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35 or 36 weeks after the first time point; or at least about, at most about or about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35 or 36 months after the first time point.

[00195] In some embodiments, the first pharmaceutical composition is administered at a third time point, wherein the third time point is at least about, at most about or about 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35 or 36 days after the second time point; at least about, at most about or about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35 or 36 weeks after the second time point; or at least about, at most about or about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35 or 36 months after the second time point.

[00196] In some embodiments, the third time point is at least about, at most about or about 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49 or 50 days after the first time point; at least about, at most about or about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35 or 36 weeks after the first time point; or at least about, at most about or about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35 or 36 months after the first time point.

[00197] In some embodiments, the second pharmaceutical composition is administered at the first time point.

[00198] In some embodiments, the second pharmaceutical composition is administered at the second time point.

[00199] In some embodiments, the second pharmaceutical composition is administered at the third time point.

[00200] In some embodiments, the second pharmaceutical composition is administered at least about, at most about or about 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35 or 36 days after the first time point; at least about, at most about or about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35 or 36 weeks after the first time point; or at least about, at most about or about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35 or 36 months after the first time point.

[00201] In some embodiments, the second pharmaceutical composition is administered at least about, at most about or about 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35 or 36 days after the second time point; at least about, at most about or about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35 or 36 weeks after the second time point; or at least about, at most about or about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35 or 36 months after the second time point.

[00202] Provided herein is a method of treating or preventing an infection by a virus or treating a respiratory disease or condition associated with an infection by a virus comprising administering to a subject in need thereof: (i) a pharmaceutical composition comprising (a) a polypeptide comprising at least two of the following: a sequence comprising an epitope sequence from ORF1ab, a sequence comprising an epitope sequence from membrane glycoprotein (M), and a sequence comprising an epitope sequence from nucleocapsid phosphoprotein (N); or (b) a polynucleotide encoding a polypeptide comprising at least two of the following: a sequence comprising an epitope sequence from ORF1ab, a sequence comprising an epitope sequence from membrane glycoprotein (M), and a sequence comprising an epitope sequence from nucleocapsid phosphoprotein (N); wherein the pharmaceutical composition is administered at a first time point, a second time point and a third time point, wherein the second time point is at least about 2 days after the first time point and the third time point is at least about 2 days after the second time point.

[00203] In some embodiments, the second time point is at least about 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, or 35 days after the first time point, at least about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, or 35 weeks after the first time point, or at least about 1, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, or 35 months after the first time point.

[00204] In some embodiments, the second time point is at most about 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, or 35 days after the first time point, at most about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, or 35 weeks after the first time point, or at most about 1, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, or 35 months after the first time point.

[00205] In some embodiments, the second time point is about 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, or 35 days after the first time point, about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, or 35 weeks after the first time point, or about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, or 35 months after the first time point.

[00206] In some embodiments, the third time point is at least about 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, or 35 days after the second time point, at least about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, or 35 weeks after the second time point, or at least about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, or 35 months after the second time point.

[00207] In some embodiments, the third time point is at most about 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, or 35 days after the second time point, at most about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, or 35 weeks after the second time point, or at most about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, or 35 months after the second time point.

[00208] In some embodiments, the third time point is about 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34 or 35 days after the second time point, about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, or 35 weeks after the second time point, or about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, or 35 months after the second time point.

[00209] In some embodiments, the third time point is at least about 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35 or 36 days after the first time point, at least about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, or 35 weeks after the first time point, or at least about 1, 2, 3, 4, 5, 6, 7, 8, 9,

10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, or 35 months after the first time point.

[00210] In some embodiments, the third time point is at most about 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35 or 36 days after the first time point, at most about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, or 35 weeks after the first time point, or at most about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, or 35 months after the first time point.

[00211] In some embodiments, the third time point about 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35 or 36 days after the first time point, about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, or 35 weeks after the first time point, or about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, or 35 months after the first time point.

[00212] In some embodiments, the method further comprises administering to the subject: (ii) (a) a polypeptide having an amino acid sequence of a 2019 SARS-CoV 2 spike protein or a variant or fragment thereof; (b) a recombinant polynucleotide encoding a 2019 SARS-CoV 2 spike protein or a variant or fragment thereof; or a 2019 SARS-CoV 2 spike protein pharmaceutical composition comprising (ii)(a) or (ii)(b).

[00213] In some embodiments, the subject has an immunodeficiency.

[00214] In some embodiments, the subject has a B cell immunodeficiency.

[00215] In some embodiments, the pharmaceutical composition is administered prophylactically.

[00216] Provided herein is a pharmaceutical composition comprising: (i) a recombinant polynucleotide encoding a polypeptide comprising at least two of the following: a sequence comprising an epitope sequence from ORF1ab, a sequence comprising an epitope sequence from membrane glycoprotein (M), and a sequence comprising an epitope sequence from nucleocapsid phosphoprotein (N); and (ii) a recombinant polynucleotide encoding a 2019 SARS-CoV 2 spike protein or a variant or fragment thereof; wherein the ratio (e.g., mass ratio) of (i):(ii) is greater than 20:1 or less than 1:20.

[00217] In some embodiments, the ratio (e.g., mass ratio) of (i):(ii) is greater than 20:1, 30:1, 40:1, 50:1, 60:1, 70:1, 80:1, 90:1 or 100:1

[00218] In some embodiments, the ratio (e.g., mass ratio) of (i):(ii) is less than 1:20, 1:30, 1:40, 1:50, 1:60, 1:70, 1:80, 1:90 or 1:100.

[00219] Provided herein is a composition comprising: (i) a first pharmaceutical composition comprising a first recombinant polynucleotide encoding a polypeptide comprising at least two of the following: a sequence comprising an epitope sequence from ORF1ab, a sequence comprising an epitope sequence from

membrane glycoprotein (M), and a sequence comprising an epitope sequence from nucleocapsid phosphoprotein (N); and (ii) a second pharmaceutical composition comprising a second recombinant polynucleotide encoding a 2019 SARS-CoV 2 spike protein or a variant or fragment thereof; wherein the ratio (e.g., mass ratio) of the recombinant polynucleotide in (i) to the recombinant polynucleotide in (ii) is from 1:50 to 50:1.

[00220] In some embodiments, the ratio (e.g., mass ratio) of the recombinant polynucleotide in (i) to the recombinant polynucleotide in (ii) is from about 1:25 to 25:1.

In some embodiments, the ratio (e.g., mass ratio) of the recombinant polynucleotide in (i) to the recombinant polynucleotide in (ii) is from about 1:10 to 10:1.

[00221] In some embodiments, the ratio (e.g., mass ratio) of the recombinant polynucleotide in (i) to the recombinant polynucleotide in (ii) is about 1:10, 1:9, 1:8, 1:7, 1:6, 1:5, 1:4, 1:3, 1:2, 1:1, 2:1, 3:1, 4:1, 5:1, 6:1, 7:1, 8:1, 9:1, 10:1, 1:9.5, 1:8.5, 1:7.5, 1:6.5, 1:5.5, 1:4.5, 1:3.5, 1:2.5, 1:1.5, 2.5:1, 3.5:1, 4.5:1, 5.5:1, 6.5:1, 7.5:1, 8.5:1, 9.5:1, 2:9, 2:8, 2:7, 2:6, 2:5, 2:4, 2:3, 3:2, 4:2, 5:2, 6:2, 7:2, 8:2, 9:2, 3:8, 3:7, 3:5, 3:4, 4:3, 5:3, 7:3, 8:3, 4:9, 4:7, 4:5, 5:4, 7:4, 9:4, 5:9, 5:8, 5:7, 5:6, 6:5, 7:5, 8:5, 9:5, 6:7, 7:6, 7:8, 8:7, 8:9 or 9:8. In some embodiments, the ratio (e.g., mass ratio) of the recombinant polynucleotide in (i) to the recombinant polynucleotide in (ii) is about 1:6. In some embodiments, the ratio (e.g., mass ratio) of the recombinant polynucleotide in (i) to the recombinant polynucleotide in (ii) is about 1:3. In some embodiments, the ratio (e.g., mass ratio) of the recombinant polynucleotide in (i) to the recombinant polynucleotide in (ii) is about 1:2.

[00222] In some embodiments, the recombinant polynucleotide in (i) is present at a dose of from 0.1 microgram to 100 micrograms, or 1 microgram to 50 micrograms, or 1 microgram to 30 micrograms, or 1 microgram to 20 micrograms, or 3 micrograms to 20 micrograms, or 5 micrograms to 15 micrograms. In some embodiments, the recombinant polynucleotide in (i) is present at a dose of from 0.05 microgram to 10 micrograms, or 0.1 microgram to 5 micrograms, or 0.3 microgram to 5 micrograms. In some embodiments, the recombinant polynucleotide in (i) is present at a dose of from 0.1 microgram to 20 micrograms or from 0.5 microgram to 15 micrograms.

[00223] In some embodiments, the recombinant polynucleotide in (ii) is present at a dose of from 0.1 microgram to 100 micrograms, or 1 microgram to 100 micrograms, or 1 microgram to 30 micrograms, or 1 microgram to 20 micrograms, or 3 micrograms to 30 micrograms.

[00224] In some embodiments, the recombinant polynucleotide in (ii) encompasses at least two recombinant polynucleotide, each encoding a SARS-CoV-2 S protein of a different strain or variant thereof. For example, in some embodiments, the recombinant polynucleotide in (ii) encompasses a recombinant polynucleotide encoding a SARS-CoV-2 protein of a Wuhan strain and a recombinant polynucleotide encoding a SARS-CoV-2 protein having one or more mutations that are characteristics of a SARS-CoV-2 variant (e.g., in some embodiments an Omicron variant such as, e.g., a Omicron BA.4 or BA.5).

[00225] In some embodiments, the recombinant polynucleotide in (i) is present at a dose of about 5 micrograms and the recombinant polynucleotide in (ii) is present at a dose of about 30 micrograms. In some embodiments, the recombinant polynucleotide in (i) is present at a dose of about 10 micrograms and the recombinant polynucleotide in (ii) is present at a dose of about 30 micrograms. In some embodiments, the recombinant polynucleotide in (i) is present at a dose of about 15 micrograms and the recombinant polynucleotide in (ii) is present at a dose of about 30 micrograms.

[00226] Provided herein is a pharmaceutical composition comprising a nanoparticle, wherein the nanoparticle comprises: (i) a first recombinant polynucleotide encoding a polypeptide comprising at least two of the following: a sequence comprising an epitope sequence from ORF1ab, a sequence comprising an epitope sequence from membrane glycoprotein (M), and a sequence comprising an epitope sequence from nucleocapsid phosphoprotein (N); and (ii) a second recombinant polynucleotide encoding a 2019 SARS-CoV 2 spike protein or a variant or fragment thereof.

[00227] In some embodiments, the nanoparticle is present in the pharmaceutical composition at a dose of from 100 ng to 500 micrograms.

[00228] In some embodiments, the nanoparticle is present in the pharmaceutical composition at a dose of from 1 microgram to 100 micrograms.

[00229] In some embodiments, the nanoparticle is present in the pharmaceutical composition at a dose of from 1 microgram to 30 micrograms, 5 micrograms to 40 micrograms or 10 microgram to 50 micrograms.

[00230] In some embodiments, the nanoparticle is present in the pharmaceutical composition at a dose of 0.1, 0.2, 0.3, 0.4, 0.5, 0.6, 0.7, 0.8, 0.9, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25, 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, 100, 150, 200, 250, 300, 350, 400, 450, 500, 600, 700, 800, 900 or 1,000 micrograms.

[00231] In some embodiments, the ratio (e.g., mass ratio) of the first recombinant polynucleotide to the second recombinant polynucleotide is from about 1:50 to 50:1.

[00232] In some embodiments, the ratio (e.g., mass ratio) of the first recombinant polynucleotide to the second recombinant polynucleotide is from about 1:25 to 25:1.

[00233] In some embodiments, the ratio (e.g., mass ratio) of the first recombinant polynucleotide to the second recombinant polynucleotide is from about 1:10 to 10:1.

[00234] In some embodiments, the ratio (e.g., mass ratio) of the first recombinant polynucleotide to the second recombinant polynucleotide is about 1:10, 1:9, 1:8, 1:7, 1:6, 1:5, 1:4, 1:3, 1:2, 1:1, 2:1, 3:1, 4:1, 5:1, 6:1, 7:1, 8:1, 9:1, 10:1, 1:9.5, 1:8.5, 1:7.5, 1:6.5, 1:5.5, 1:4.5, 1:3.5, 1:2.5, 1:1.5, 2.5:1, 3.5:1, 4.5:1, 5.5:1, 6.5:1, 7.5:1, 8.5:1, 9.5:1, 2:9, 2:8, 2:7, 2:6, 2:5, 2:4, 2:3, 3:2, 4:2, 5:2, 6:2, 7:2, 8:2, 9:2, 3:8, 3:7, 3:5, 3:4, 4:3, 5:3, 7:3, 8:3, 4:9, 4:7, 4:5, 5:4, 7:4, 9:4, 5:9, 5:8, 5:7, 5:6, 6:5, 7:5, 8:5, 9:5, 6:7, 7:6, 7:8, 8:7, 8:9 or 9:8. In some embodiments, the ratio (e.g., mass ratio) of the first recombinant polynucleotide to the second recombinant polynucleotide is about 1:6. In some embodiments, the ratio (e.g., mass ratio) of the first recombinant polynucleotide to the second recombinant polynucleotide is about 1:3. In some

embodiments, the ratio (e.g., mass ratio) of the first recombinant polynucleotide to the second recombinant polynucleotide is about 1:2.

[00235] In some embodiments, the first recombinant polynucleotide is present in a pharmaceutical composition at a dose of from 0.1 microgram to 100 micrograms, or 1 microgram to 50 micrograms, or 1 microgram to 30 micrograms, or 1 microgram to 20 micrograms, or 3 micrograms to 20 micrograms, or 5 micrograms to 15 micrograms. In some embodiments, the first recombinant polynucleotide is present in a pharmaceutical composition at a dose of from 0.05 microgram to 10 micrograms, or 0.1 microgram to 5 micrograms, or 0.3 microgram to 5 micrograms. In some embodiments, the first recombinant polynucleotide is present in a pharmaceutical composition at a dose of from 0.1 microgram to 20 micrograms or from 0.5 microgram to 15 micrograms.

[00236] In some embodiments, the second recombinant polynucleotide is present in a pharmaceutical composition at a dose of from 0.1 microgram to 100 micrograms, or 1 microgram to 100 micrograms, or 1 microgram to 30 micrograms, or 1 microgram to 20 micrograms, or 3 micrograms to 30 micrograms.

[00237] In some embodiments, the second recombinant polynucleotide encompasses at least two recombinant polynucleotide, each encoding a SARS-CoV-2 S protein of a different strain or variant thereof. For example, in some embodiments, the second recombinant polynucleotide encompasses a recombinant polynucleotide encoding a SARS-CoV-2 S protein of a Wuhan strain and a recombinant polynucleotide encoding a SARS-CoV-2 S protein having one or more mutations that are characteristics of a SARS-CoV-2 variant (e.g., in some embodiments an Omicron variant such as, e.g., an Omicron BA.1, BA.2, BA.4 or BA.5 variant).

[00238] Provided herein is a composition comprising: (i) a first pharmaceutical composition comprising a first nanoparticle, wherein the first nanoparticle comprises a recombinant polynucleotide encoding a polypeptide comprising at least two of the following: a sequence comprising an epitope sequence from ORF1ab, a sequence comprising an epitope sequence from membrane glycoprotein (M), and a sequence comprising an epitope sequence from nucleocapsid phosphoprotein (N); and (ii) a second pharmaceutical composition comprising a second nanoparticle, wherein the second nanoparticle comprises a recombinant polynucleotide encoding a 2019 SARS-CoV 2 spike protein or a variant or fragment thereof.

[00239] In some embodiments, the ratio (e.g., mass ratio) of the recombinant polynucleotide in (i) to the recombinant polynucleotide in (ii) is from about 1:50 to 50:1.

[00240] In some embodiments, the ratio (e.g., mass ratio) of the recombinant polynucleotide in (i) to the recombinant polynucleotide in (ii) is from about 1:25 to 25:1.

[00241] In some embodiments, the ratio (e.g., mass ratio) of the recombinant polynucleotide in (i) to the recombinant polynucleotide in (ii) is from about 1:10 to 10:1.

[00242] In some embodiments, the ratio (e.g., mass ratio) of the recombinant polynucleotide in (i) to the recombinant polynucleotide in (ii) is about 1:10, 1:9, 1:8, 1:7, 1:6, 1:5, 1:4, 1:3, 1:2, 1:1, 2:1, 3:1, 4:1, 5:1, 6:1, 7:1, 8:1, 9:1, 10:1, 1:9.5, 1:8.5, 1:7.5, 1:6.5, 1:5.5, 1:4.5, 1:3.5, 1:2.5, 1:1.5, 2.5:1, 3.5:1, 4.5:1, 5.5:1, 6.5:1, 7.5:1, 8.5:1, 9.5:1, 2:9, 2:8, 2:7, 2:6, 2:5, 2:4, 2:3, 3:2, 4:2, 5:2, 6:2, 7:2, 8:2, 9:2, 3:8, 3:7, 3:5, 3:4, 4:3, 5:3, 7:3, 8:3, 4:9, 4:7, 4:5, 5:4, 7:4, 9:4, 5:9, 5:8, 5:7, 5:6, 6:5, 7:5, 8:5, 9:5, 6:7, 7:6, 7:8, 8:7, 8:9 or 9:8. In some embodiments, the ratio (e.g., mass ratio) of the recombinant polynucleotide in (i) to the recombinant polynucleotide in (ii) is about 1:6. In some embodiments, the ratio (e.g., mass ratio) of the recombinant polynucleotide in (i) to the recombinant polynucleotide in (ii) is about 1:3. In some embodiments, the ratio (e.g., mass ratio) of the recombinant polynucleotide in (i) to the recombinant polynucleotide in (ii) is about 1:2.

[00243] In some embodiments, the recombinant polynucleotide in (i) is present at a dose of from 0.1 microgram to 100 micrograms, or 1 microgram to 50 micrograms, or 1 microgram to 30 micrograms, or 1 microgram to 20 micrograms, or 3 micrograms to 20 micrograms, or 5 micrograms to 15 micrograms. In some embodiments, the recombinant polynucleotide in (i) is present at a dose of from 0.05 microgram to 10 micrograms, or 0.1 microgram to 5 micrograms, or 0.3 microgram to 5 micrograms. In some embodiments, the recombinant polynucleotide in (i) is present at a dose of from 0.1 microgram to 20 micrograms or from 0.5 microgram to 15 micrograms.

[00244] In some embodiments, the recombinant polynucleotide in (ii) is present at a dose of from 0.1 microgram to 100 micrograms, or 1 microgram to 100 micrograms, or 1 microgram to 30 micrograms, or 1 microgram to 20 micrograms, or 3 micrograms to 30 micrograms.

[00245] In some embodiments, the recombinant polynucleotide in (ii) encompasses at least two recombinant polynucleotide, each encoding a SARS-CoV-2 S protein of a different strain or variant thereof. For example, in some embodiments, the recombinant polynucleotide in (ii) encompasses a recombinant polynucleotide encoding a SARS-CoV-2 protein of a Wuhan strain and a recombinant polynucleotide encoding a SARS-CoV-2 protein having one or more mutations that are characteristics of a SARS-CoV-2 variant (e.g., in some embodiments an Omicron variant such as, e.g., a Omicron BA.4 or BA.5).

[00246] In some embodiments, the first nanoparticle is present in the first pharmaceutical composition at a dose of from about 100 ng to 500 micrograms.

[00247] In some embodiments, the first nanoparticle is present in the first pharmaceutical composition at a dose of from about 1 microgram to 100 micrograms.

[00248] In some embodiments, the first nanoparticle is present in the first pharmaceutical composition at a dose of from about 1 microgram to 30 micrograms, 5 micrograms to 40 micrograms or 10 microgram to 50 micrograms.

[00249] In some embodiments, the first nanoparticle is present in the first pharmaceutical composition at a dose of about 0.1, 0.2, 0.3, 0.4, 0.5, 0.6, 0.7, 0.8, 0.9, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25, 30, 35, 40, 45,

50, 55, 60, 65, 70, 75, 80, 85, 90, 95, 100, 150, 200, 250, 300, 350, 400, 450, 500, 600, 700, 800, 900 or 1,000 micrograms.

[00250] In some embodiments, the second nanoparticle is present in the second pharmaceutical composition at a dose of from about 100 ng to 500 micrograms.

[00251] In some embodiments, the second nanoparticle is present in the second pharmaceutical composition at a dose of from about 1 microgram to 100 micrograms.

[00252] In some embodiments, the second nanoparticle is present in the second pharmaceutical composition at a dose of from about 1 microgram to 30 micrograms, 5 micrograms to 40 micrograms or 10 microgram to 50 micrograms.

[00253] In some embodiments, the second nanoparticle is present in the second pharmaceutical composition at a dose of about 0.1, 0.2, 0.3, 0.4, 0.5, 0.6, 0.7, 0.8, 0.9, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25, 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, 100, 150, 200, 250, 300, 350, 400, 450, 500, 600, 700, 800, 900 or 1,000 micrograms.

[00254] In some embodiments, the recombinant polynucleotide in (i) is present in the first pharmaceutical composition at a dose of from about 50 ng to 250 micrograms.

[00255] In some embodiments, the recombinant polynucleotide in (i) is present in the first pharmaceutical composition at a dose of from about 0.5 to 50 micrograms.

[00256] In some embodiments, the recombinant polynucleotide in (i) is present in the first pharmaceutical composition at a dose of from about 0.5 microgram to 15 micrograms, 2.5 micrograms to 20 micrograms or 5 microgram to 25 micrograms.

[00257] In some embodiments, the recombinant polynucleotide in (i) is present in the first pharmaceutical composition at a dose of about 0.05, 0.1, 0.2, 0.3, 0.4, 0.5, 0.6, 0.7, 0.8, 0.9, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25, 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, 100, 150, 200, 250, 300, 350, 400, 450 or 500 micrograms.

[00258] In some embodiments, the recombinant polynucleotide in (ii) is present in the second pharmaceutical composition at a dose of from about 50 ng to 250 micrograms.

[00259] In some embodiments, the recombinant polynucleotide in (ii) is present in the second pharmaceutical composition at a dose of from about 0.5 to 50 micrograms.

[00260] In some embodiments, the recombinant polynucleotide in (ii) is present in the second pharmaceutical composition at a dose of from about 0.5 microgram to 15 micrograms, 2.5 micrograms to 20 micrograms or 5 microgram to 25 micrograms.

[00261] In some embodiments, the recombinant polynucleotide in (ii) is present in the second pharmaceutical composition at a dose of about 0.05, 0.1, 0.2, 0.3, 0.4, 0.5, 0.6, 0.7, 0.8, 0.9, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25, 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, 100, 150, 200, 250, 300, 350, 400, 450 or 500 micrograms.

[00262] In some embodiments, the nanoparticle is a lipid nanoparticle.

[00263] Provided herein is a method of treating or preventing an infection by a virus or treating a respiratory disease or condition associated with an infection by a virus comprising administering to a subject in need thereof a pharmaceutical composition comprising: (i) a polypeptide comprising at least two of the following (a) a sequence comprising an epitope sequence from ORF1ab, (b) a sequence comprising an epitope sequence from membrane glycoprotein (M) and (c) a sequence comprising an epitope sequence from nucleocapsid phosphoprotein (N); (ii) a polynucleotide encoding a polypeptide, wherein the polypeptide comprises at least two of the following (a) a sequence comprising an epitope sequence from ORF1ab, (b) a sequence comprising an epitope sequence from membrane glycoprotein (M) and (c) a sequence comprising an epitope sequence from nucleocapsid phosphoprotein (N); (iii) a T cell receptor (TCR) or a T cell comprising the TCR, wherein the TCR binds to an epitope sequence of the polypeptide in complex with a corresponding HLA class I or class II molecule; (iv) an antigen presenting cell comprising (i) or (ii); or (v) an antibody or B cell comprising the antibody, wherein the antibody binds to an epitope sequence of the polypeptide.

[00264] In some embodiments, the subject has an immunodeficiency.

[00265] In some embodiments, the subject has a B cell immunodeficiency.

[00266] In some embodiments, the subject has a reduced ability to produce an antibody response to an antigen compared to a subject without an immunodeficiency.

[00267] In some embodiments, the subject has a reduced ability to produce an antibody response to a vaccination compared to a subject without an immunodeficiency.

[00268] In some embodiments, the subject has a reduced ability to produce an anti-spike protein antibody response and/or an anti-RBD antibody response compared to a subject without an immunodeficiency.

[00269] In some embodiments, the subject can produce a T cell response or does not have a reduced ability to produce a T cell response compared to a subject without an immunodeficiency.

[00270] In some embodiments, the pharmaceutical composition is protective against a variant of 2019 SARS CoV-2.

[00271] In some embodiments, the variant of 2019 SARS CoV-2 is alpha, beta, gamma, delta, epsilon, zeta, eta, theta, iota, kappa or lambda.

[00272] In some embodiments, the subject produces a T cell response to an epitope of the polypeptide.

[00273] In some embodiments, the subject produces a T cell response to the epitope sequence from ORF1ab, the epitope sequence from membrane glycoprotein (M) and/or the epitope sequence from nucleocapsid phosphoprotein (N).

[00274] In some embodiments, the subject is an organ transplant recipient.

[00275] In some embodiments, the organ transplant recipient is a sold organ transplant recipient, a stem cell transplant recipient or a bone marrow transplant recipient.

[00276] In some embodiments, the subject received an organ transplant less than 1 year, less than 6 months or less than 3 months after the pharmaceutical composition is administered.

[00277] In some embodiments, the subject is expected to receive an organ transplant less than 1 year, less than 6 months or less than 3 months prior to the pharmaceutical composition being administered.

[00278] In some embodiments, the subject has a cancer.

[00279] In some embodiments, the cancer is a B cell cancer.

[00280] In some embodiments, the B cell cancer is a B cell lymphoma or a B cell leukemia.

[00281] In some embodiments, the subject has an autoimmune disease or condition.

[00282] In some embodiments, the autoimmune disease or condition is Addison disease, Anti-NMDA receptor encephalitis, antisynthetase syndrome, Aplastic anemia, autoimmune anemias, Autoimmune hemolytic anemia, Autoimmune pancreatitis, Behcet's Disease, bullous skin disorders, Celiac disease - sprue, chronic fatigue syndrome, Chronic inflammatory demyelinating polyneuropathy, chronic lymphocytic leukemia, Crohn's disease, Dermatomyositis, Devic's disease, Erythroblastopenia, Evans syndrome, Focal segmental glomerulosclerosis, Granulomatosis with polyangiitis, Graves disease, Graves' ophthalmopathy, Guillain-Barre syndrome, Hashimoto thyroiditis, idiopathic thrombocytopenic purpura (ITP), IgA nephropathy, IgA-mediated autoimmune diseases, IgG4-related disease, Inflammatory bowel disease, Juvenile idiopathic arthritis, Multiple sclerosis, Myasthenia gravis, myeloma, non-Hodgkin's lymphoma, Opsoclonus myoclonus syndrome (OMS), Pemphigoid, Pemphigus, pemphigus vulgaris, Pernicious anemia, polymyositis, Psoriasis, pure red cell aplasia, Reactive arthritis, Rheumatoid arthritis, Sarcoidosis, scleroderma, Sjögren syndrome, Systemic lupus erythematosus, Thrombocytopenic purpura, Thrombotic thrombocytopenic purpura, Type I diabetes, Ulcerative colitis, Vasculitis and Vitiligo.

[00283] In some embodiments, the subject has congenital agammaglobulinemia or congenital IgA deficiency.

[00284] In some embodiments, the subject has HIV or AIDS. In some embodiments, the subject has an age-related decline in immunity, immunosenescence, multifactoral immunodeficiency, or is an elderly or older aldut with an age-related immuodeficiency.

[00285] In some embodiments, the subject is receiving an immunosuppressive agent or has received an immunosuppressive agent less than 1 year, less than 6 months or less than 3 months prior to the administering of the pharmaceutical composition.

[00286] In some embodiments, the immunosuppressive agent is abatacept, abrilumab, acalabrutinib, adalimumab, adrenocorticotropic hormone, agatolimod sodium, aldesleukin, alefacept, alemtuzumab, alisertib, alvespimycin hydrochloride, alvocidib, ambrisentan, aminocamptothecin, amiselimod, anakinra, andecaliximab, andrographolides, anifrolumab, antithymocyte Ig, apatinib, apelisib, asparaginase, atacicept, atezolizumab, avelumab, azacitidine, azathioprine, bafetinib, baminercept, baricitinib, basiliximab, becatecarin, begelomab, belatacept, belimumab, bemcentinib, bendamustine, bendamustine,

betalutin with lilotomab, bevacizumab, BIIB033, BIIB059, BIIB061, bimekizumab, binimetinib, bleomycin, blinatumomab, bortezomib, brentuximab vedotin, bryostatin 1, bucillamine, buparlisib, busulfan, canakinumab, capecitabine, carboplatin, carfilzomib, carmustine, cediranib maleate, cemiplimab, ceralifimod, cerdulatinib, certolizumab, cetuximab, chidamide, chlorambucil, cilengitide, cirmtuzumab, cisplatin, cladribine, clazakizumab, clemastine, clioquinol, corticosteroids, cyclophosphamide, cyclosporine, cytarabine, cytotoxic chemotherapy, daclizumab, dalfampridine, daprolizumab pegol, daratumumab, dasatinib, defactinib, defibrotide, denosumab, dexamethasone, diacerein, dimethyl fumarate, dinaciclib, diroximel fumarate, doxorubicin, doxorubicin, durvalumab, duvelisib, duvortuxizumab, eculizumab, efalizumab, eftilagimod alpha, a neuropeptide combination of metenkefalin and tridecactide, elezanumab, elotuzumab, encorafenib, enfuvirtida, entinostat, entospletinib, enzastaurin, epacadostat, epirubicin, epratuzumab, eritoran tetrasodium, etanercept, etoposide, etrolizumab, everolimus, evobrutinib, filgotinib, fingolimod, firategrast, fludarabine, fluorouracil, fontolizumab, forodesine hydrochloride, fostamatinib, galunisertib, ganetespib, ganitumab, gemcitabine, gemtuzumab ozogamicin, gerilimzumab, glasdegib, glassia, glatiramer acetate, glembatumumab vedotin, glesatinib, golimumab, guadecitabine, hydrocortisone, hydroxychloroquine sulfate, hydroxyurea, ibritumomab tiuxetan, ibrutinib, ibudilast, idarubicin, idebenone, idelalisib, ifosfamide, iguratimod, imatinib, imexon, infliximab, inotuzumab ozogamicin, interferon alfa-2, interferon beta-1a, interferon beta-1b, interferon gamma-1, ipilimumab, irofulven, isatuximab, ispinesib, itacitinib, ixazomib, lapatinib, laquinimod, laromustine, ld-aminopterin, leflunomide, lenalidomide, lenvatinib, letrozole, levamisole, levocabastine, lipoic acid, lirilumab, lonafarnib, lumiliximab, maraviroc, masitinib, mavrilimumab, melphalan, mercaptopurine, methotrexate, methoxsalen, methylprednisone, milatuzumab, mitoxantrone, mizoribine, mocetinostat, monalizumab, mosunetuzumab, motesanib diphosphate, moxetumomab pasudotox, muromonab-CD3, mycophenolate mofetil, mycophenolic acid, namilumab, natalizumab, navitoclax, neihulizumab, nerispirdine, neurovax, niraparib, nivolumab, obatoclax mesylate, obinutuzumab, oblimersen sodium, ocrelizumab, ofatumumab, olokizumab, opicinumab, oprelvekin, osimertinib, otelixizumab, oxaliplatin, oxcarbazepine, ozanimod, paclitaxel, pacritinib, palifermin, panobinostat, pazopanib, peficitinib, pegfilgrastim, peginterferon beta-1a, pegsunercept (peg stnf-ri), pembrolizumab, pemetrexed, penclomedine, pentostatin, perifosine, pevonedistat, pexidartinib, picoplatin, pidilizumab, pivanex, pixantrone, pleneva, plovamer acetate, polatuzumab vedotin, pomalidomide, ponatinib, ponesimod, prednisone/prednisolone, pyroxamide, ravulizimab-cwvz, recombinant il-12, relatlimab, rhigf-1, rhigm22, rigosertib, rilonacept, ritonavir, rituximab, ruxolitinib, sarilumab, secukinumab, selumetinib, simvastatin, sintilimab, siplizumab, siponimod, sirolimus (rapamycin), sirukumab, sitravatinib, sonidegib, sorafenib, sotrastaurin acetate, sunitinib, sunphenon epigallocatechin-gallate, tabalumab, tacrolimus, talabostat mesylate, talacotuzumab, tanespimycin, tegafur/gimeracil/oteracil, temozolomide, temsirolimus, tenalisib, terameprocol, teriflunomide, thalidomide, thiarabine, thiotepa, tipifarnib, tirabrutinib, tislelizumab,

tivozanib, tocilizumab, tofacitinib, tregalizumab, tremelimumab, treosulfan, ublituximab, umbralisib, upadacitinib, urelumab, ustekinumab, varlilumab, vatelizumab, vedolizumab, veliparib, veltuzumab, venetoclax, vinblastine, vincristine, vinorelbine ditartrate, visilizumab, vismodegib, vistusertib, voriconazole, vorinostat, vosaroxin, ziv-aflibercept or any combination thereof.

[00287] In some embodiments, the immunosuppressive agent is A2aR antagonist, Akt inhibitor, anti CD20, Anti-amyloidotic (AA) Agent, anti-CD37 protein therapeutic, anti-CTLA4 mAb, Anti-CXCR4, anti-huCD40 mAb, anti-LAG3 mAb, anti-PD-1 mAb, anti-PD-L1 agent, anti-PD-L1 agent, anti-PD-L1 mAb, anti-TGFb mAb, anti-TIGIT mAb, anti-TIM-3 mAb, Aurora kinase inhibitor, Bcl-2 Inhibitor, bifunctional fusion protein targeting TGFb and PD-L1, bispecific anti-PD-1 and anti-LAG3 mAb, CD1d ligand, CD40 agonist, Complement C5a inhibitor, CSF1R inhibitor, EZH2 inhibitor, FGFR3 inhibitor, FGFR4 inhibitor, FGFrR3 inhibitor, glucocorticoid-induced tumor necrosis factor receptor–related gene agonist, glutaminase inhibitor, Human monoclonal antibody against IL-12, ICOS agonist, IDO1 inhibitor, IL2 mutein, IL2 receptor agonist, MEK inhibitor, multitargeted receptor tyrosine kinase inhibitor, neutrophil elastase inhibitor, Notch Inhibitor, p38 MAPK inhibitor, PD-1 inhibitor, recombinant human Flt3L, ROCK inhibitor, selective sphingosine-1-phosphate receptor modulator, Src kinase inhibitor, TLR4 agonist, TLR9 agonist, or any combination thereof.

[00288] In some embodiments, the subject is greater than 55, 56, 57, 58, 59, 60, 65, 70, 75 or 80 years of age.

[00289] In some embodiments, the polypeptide comprises (a) a sequence comprising an epitope sequence from ORF1ab, (b) a sequence comprising an epitope sequence from membrane glycoprotein (M) and (c) a sequence comprising an epitope sequence from nucleocapsid phosphoprotein (N).

[00290] In some embodiments, the sequence comprising an epitope sequence from ORF1ab is C-terminal to the sequence comprising an epitope sequence from nucleocapsid phosphoprotein (N).

[00291] In some embodiments, the sequence comprising an epitope sequence from ORF1ab is N-terminal to the sequence comprising an epitope sequence from membrane glycoprotein (M).

[00292] In some embodiments, the sequence comprising an epitope sequence from nucleocapsid phosphoprotein (N) is N-terminal to the sequence comprising an epitope sequence from membrane glycoprotein (M).

[00293] In some embodiments, the polypeptide comprises (a) 2, 3, 4, 5, 6, 7, 8, 9 or 10 or more epitope sequences from ORF1ab, (b) a sequence comprising an epitope sequence from membrane glycoprotein (M) and (c) a sequence comprising an epitope sequence from nucleocapsid phosphoprotein (N).

[00294] In some embodiments, the epitope sequence from ORF1ab is an epitope sequence from a non-structural protein (NSP).

[00295] In some embodiments, the non-structural protein (NSP) is selected from the group consisting of NSP1, NSP2, NSP3, NSP4 and combinations thereof.

[00296] In some embodiments, the polypeptide comprises a sequence comprising an epitope sequence from NSP1, a sequence comprising an epitope sequence from NSP2, a sequence comprising an epitope sequence from NSP3 and a sequence comprising an epitope sequence from NSP4.

[00297] In some embodiments, the epitope sequence from ORF1ab is selected from the group consisting of YLFDESGEFKL, YLFDESGEF, FGDDTVIEV, QLMCQPILL, TTDPSFLGRY, PTDNYITTY, PSFLGRY, AEAELAKNV, KTIQPRVEK and any combination thereof.

[00298] In some embodiments, the epitope sequence from nucleocapsid glycoprotein (N) is LLLDRLNQL.

[00299] In some embodiments, the epitope sequence from membrane phosphoprotein (M) is VATSRTLSY.

[00300] In some embodiments, the polypeptide comprises an epitope sequence from nucleocapsid glycoprotein (N) that is LLLDRLNQL and an epitope sequence from membrane phosphoprotein (M) that is VATSRTLSY.

[00301] In some embodiments, the polypeptide comprises (a) each of the following epitope sequences from ORF1ab: YLFDESGEFKL, YLFDESGEF, FGDDTVIEV, QLMCQPILL, TTDPSFLGRY, PTDNYITTY, PSFLGRY, AEAELAKNV, KTIQPRVEK; (b) an epitope sequence from nucleocapsid glycoprotein (N) that is LLLDRLNQL; and (c) an epitope sequence from membrane phosphoprotein (M) that is VATSRTLSY.

[00302] In some embodiments, the sequence comprising an epitope sequence from ORF1ab is selected from the group consisting of the following sequences or fragments thereof: MVTNNTFTLKVPHVGEIPVAYRKVLLKTIQPRVEKYLFDESGEFKLSEVGPEHSLAEYYIFFASFY Y; MVTNNTFTLKVPHVGEIPVAYRKVLLKTIQPRVEKYLFDESGEFKLSEVGPEHSLAEY; APKEIIFLEGETLFGDDTVIEVAIILASFSAST; APKEIIFLEGETLFGDDTVIEV; HTTDPSFLGRYMSALFADDLNQLTGYHTDFSSEIIGYQLMCQPILLAEAELAKNVSLILGTVSWN L;

TTDPSFLGRYMSALFADDLNQLTGYHTDFSSEIIGYQLMCQPILLAEAELAKNVSLILGTVSWNL; LLSAGIFGAITDVFYKENSYKVPTDNYITTY; and combinations thereof.

[00303] In some embodiments, the sequence comprising an epitope sequence from membrane glycoprotein (M) is selected from the group consisting of the following sequences or fragments thereof: ADSNGTITVEELKKLLEQWNLVIGFLFLTWICLLQFAYANRNRFLYIIKLIFLWLLWPVTLACFVL AAVYRINWITGGIAIAMACLVGLMWLSYFIASFRLFARTRSMWSFNPETNILLNVPLHGTILTRPL LESELVIGAVILRGHLRIAGHHLGRCDIKDLPKEITVATSRTLSYYKLGASQRVAGDSGFAAYSR YRIGNYKLNTDHSSSSDNIALLVQ;

FAYANRNRFLYIIKLIFLWLLWPVTLACFVLAAVYRINWITGGIAIAMACLVGLMWLSYFIASFR LF; LGRCDIKDLPKEITVATSRTLSYYKLGASQRVA; KLLEQWNLVIGF;

NRNRFLYIIKLIFLWLLWPVTLACFVLAAVY; SELVIGAVILRGHLRIAGHHLGR; VATSRTLSYYKLGASQRV; GLMWLSYF; and combinations thereof.

[00304] In some embodiments, the sequence comprising an epitope sequence from nucleocapsid phosphoprotein (N) is selected from the group consisting of the following sequences or fragments thereof: KDLSPRWYFYYLGTGPEAGLPYGANKDGIIWVATEGALNTPKDHIGTRNPANNAAIVLQLPQGT TLPKGFYAEGSRGGSQASSRSSSRSRNSSRNSTPGSSRGTSPARMAGNGGDAALALLLLDRLNQL ESKMSGKGQQQQGQTVTKKSAAEASKKPRQKRTATKAYNVTQAFGRRGPEQTQGNFGDQELI RQGTDYKHWPQIAQFAPSASAFFGMSRIGMEVTPSGTWLTYTGAIKLDDKDPNFKDQVILLNKH IDAYKTFPPTEPKKDKKKKADETQALPQRQKKQQTVTLLPAADLDDFSKQLQQSMSSADSTQA; RMAGNGGDAALALLLLDRLNQLESKMSGKGQQQ; YKHWPQIAQFAPSASAFFGMSRIGMEVTPSGTWLTYTGAIKLDDKDPNFKDQVILLNKHIDAYK TFP; SPARMAGNGGDAALALLLLDRLNQLESKMSGKGQQQQGQTVTKKSAAEASKKPRQKRTATKA YNVTQAFGRRGPEQTQGNFGDQELIRQGTDYKHWPQIAQFAPSASAFFGMSRIGMEVTPSGTWL TYTGAIKLDDKDPNFKDQVILLNKHIDAYKTFPPTEPKKDK and combinations thereof.

[00305] In some embodiments, the polypeptide comprises one or more linker sequences.

[00306] In some embodiments, the one or more linker sequences are selected from the group consisting of GGSGGGGSGG, GGSLGGGGSG.

[00307] In some embodiments, the one or more linker sequences comprise cleavage sequences.

[00308] In some embodiments, the one or more cleavage sequences are selected from the group consisting of FRAC, KRCF, KKRY, ARMA, RRSG, MRAC, KMCG, ARCA, KKQG, YRSY, SFMN, FKAA, KRNG, YNSF, KKNG, RRRG, KRYS, and ARYA.

[00309] In some embodiments, the polypeptide comprises a transmembrane domain sequence.

[00310] In some embodiments, the transmembrane domain sequence is C-terminal to the sequence comprising an epitope sequence from ORF1ab, the sequence comprising an epitope sequence from membrane glycoprotein (M) and the sequence comprising an epitope sequence from nucleocapsid phosphoprotein (N).

[00311] In some embodiments, the transmembrane domain sequence is EQYIKWPWYIWLGFIAGLIAIVMVTIMLCCMTSCCSCLKGCCSCGSCCKFDEDDSEPVLKGVKL HYT.

[00312] In some embodiments, the polypeptide comprises a secretory signal sequence (SEC sequence).

[00313] In some embodiments, the SEC sequence is N-terminal to the sequence comprising an epitope sequence from ORF1ab, the sequence comprising an epitope sequence from membrane glycoprotein (M) and the sequence comprising an epitope sequence from nucleocapsid phosphoprotein (N).

[00314] In some embodiments, the SEC sequence is MFVFLVLLPLVSSQCVNLT.

[00315] In some embodiments, the composition comprises the polynucleotide encoding the polypeptide.

[00316] In some embodiments, the polynucleotide is an mRNA.

[00317] In some embodiments, the polynucleotide comprises a codon optimized sequence for expression in a human.

[00318] In some embodiments, the polynucleotide comprises a dEarI-hAg sequence.

[00319] In some embodiments, the dEarI-hAg sequence is ATTCTTCTGGTCCCCACAGACTCAGAGAGAACCC, optionally wherein each T is a U.

[00320] In some embodiments, the polynucleotide comprises a Kozak sequence.

[00321] In some embodiments, the Kozak sequence is GCCACC.

[00322] In some embodiments, the polynucleotide comprises an F element sequence.

[00323] In some embodiments, the F element sequence is a 3 UTR of amino-terminal enhancer of split (AES).

[00324] In some embodiments, the F element sequence is CTGGTACTGCATGCACGCAATGCTAGCTGCCCCTTTCCCGTCCTGGGTACCCCGAGTCTCCC CCGACCTCGGGTCCCAGGTATGCTCCCACCTCCACCTGCCCCACTCACCACCTCTGCTAGTTC CAGACACCTCC, optionally wherein each T is a U.

[00325] In some embodiments, the polynucleotide comprises an I element sequence.

[00326] In some embodiments, the I element sequence is a 3' UTR of mitochondrially encoded 12S rRNA (mtRNR1).

[00327] In some embodiments, the I element sequence is CAAGCACGCAGCAATGCAGCTCAAAACGCTTAGCCTAGCCACACCCCCACGGGAAACAGCA GTGATTAACCTTTAGCAATAAACGAAAGTTTAACTAAGCTATACTAACCCCAGGGTTGGTCA ATTTCGTGCCAGCCACACC, optionally wherein each T is a U.

[00328] In some embodiments, the polynucleotide comprises a poly A sequence.

[00329] In some embodiments, the poly A sequence is AAAAAAAAAAAAAAAAAAAAAAAAAAAAAAGCATATGACTAAAAAAAAAAAAAAAAAAAA AAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA, optionally wherein each T is a U.

[00330] In some embodiments, each of the epitope sequences from the ORF1ab, the membrane glycoprotein, and the nucleocapsid phosphoprotein are from 2019 SARS-CoV-2.

[00331] In some embodiments, one or more or each epitope elicits a T cell response.

[00332] In some embodiments, one or more or each epitope has been observed by mass spectrometry as being presented by an HLA molecule.

[00333] In some embodiments, the composition comprises (i) a polypeptide with at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, at least 95% or 100% sequence identity to a sequence selected

from the group consisting of RS C1p1full, RS C2p1full, RS C3p1full, RS C4p1full, RS C5p1, RS C5p2, RS C5p2full, RS C6p1, RS C6p2, RS C6p2full, RS C7p1, RS C7p2, RS C7p2full, RS C7p4, RS C7p4full, RS C8p1, RS C8p2 and RS C8p2full; (ii) a polynucleotide encoding a polypeptide with at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, or 100% sequence identity to a sequence selected from the group consisting of RS C1p1full, RS C2p1full, RS C3p1full, RS C4p1full, RS C5p1, RS C5p2, RS C5p2full, RS C6p1, RS C6p2, RS C6p2full, RS C7p1, RS C7p2, RS C7p2full, RS C7p4, RS C7p4full, RS C8p1, RS C8p2 and RS C8p2full; or (iii) a polynucleotide with at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, or 100% sequence identity to a sequence selected from the group consisting of SEQ ID NOs: RS C1n1, RS C2n1, RS C3n1, RS C4n1, RS C5n1, RS C6n1, RS C7n1, RS C8n1, RS C5n2, RS C6n2, RS C7n2, RS C8n2, RS C5n2full, RS C6n2full, RS C7n2full, RS C8n2full, RS C7n4, RS C7n4full.

[00334] In some embodiments, the composition comprises (i) a polypeptide with at least 70%, 80%, 90% or 100% sequence identity to a sequence selected from the group consisting of RS C7p1, RS C7p2, RS C7p2full, RS C7p4, and RS C7p4full; or (iii) a polynucleotide with at least at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, or 100% sequence identity to a sequence selected from the group consisting of SEQ ID NOs: RS C7n1, RS C7n2, RS C7n2full, RS C7n4, RS and C7n4full.

[00335] In some embodiments, the pharmaceutical composition comprises a pharmaceutically acceptable excipient, carrier, or diluent.

[00336] Provided herein is a method of treating or preventing an infection by a virus or treating a respiratory disease or condition associated with an infection by a virus comprising administering to a subject in need thereof a pharmaceutical composition comprising: (i) a polypeptide comprising an epitope sequence of Table 1A, Table 1B, Table 1C, Table 2Ai, Table 2Aii, Table 2B and/or Table 16; (ii) a polynucleotide encoding the polypeptide comprising an epitope sequence of Table 1A, Table 1B, Table 1C, Table 2Ai, Table 2Aii, Table 2B and/or Table 16; (iii) a T cell receptor (TCR) or a T cell comprising the TCR, wherein the TCR binds to the epitope sequence in complex with a corresponding HLA class I or class II molecule; (iv) an antigen presenting cell comprising (i) or (ii); or (v) an antibody or B cell comprising the antibody, wherein the antibody binds to the epitope sequence.

[00337] In some embodiments, the subject has an immunodeficiency.

[00338] In some embodiments, the subject has a B cell immunodeficiency.

[00339] In some embodiments, the epitope sequence comprises one or more or each of the following: YLFDESGEFKL, YLFDESGEF, FGDDTVIEV, LLLDRLNQL, QLMCQPILL, TTDPSFLGRY, PTDNYITTY, PSFLGRY, AEAELAKNV, VATSRTLSY and KTIQPRVEK.

[00340] In some embodiments, the epitope sequence comprises one or more or each of the following: SAPPAQYEL, AVASKILGL, EYADVFHLY, DEFTPFDVV, VRIQPGQTF, SFRLFARTR,

KFLPFQQF, VVQEGVLTA, RLDKVEAEV, FGADPIHSL, NYNYLYRLF, KYIKWPWYI, KWPWYIWLGF, LPFNDGVYF, QPTESIVRF, IPFAMQMAY, YLQPRTFLL and RLQSLQTYV.

[00341] In some embodiments, the epitope sequence is from an orf1ab protein.

[00342] In some embodiments, the epitope sequence is from an orf1a protein

[00343] In some embodiments, the epitope sequence is from a surface glycoprotein (S) or a shifted reading frame thereof.

[00344] In some embodiments, the epitope sequence is from a nucleocapsid phosphoprotein (N).

[00345] In some embodiments, the epitope sequence is from an ORF3a protein.

[00346] In some embodiments, the epitope sequence is from a membrane glycoprotein (M).

[00347] In some embodiments, the epitope sequence is from an ORF7a protein.

[00348] In some embodiments, the epitope sequence is from an ORF8 protein.

[00349] In some embodiments, the epitope sequence is from an envelope protein (E).

[00350] In some embodiments, the epitope sequence is from an ORF6 protein.

[00351] In some embodiments, the epitope sequence is from an ORF7b protein.

[00352] In some embodiments, the epitope sequence is from an ORF10 protein.

[00353] In some embodiments, the epitope sequence is from an ORF9b protein.

[00354] Provided herein is a method of treating or preventing an infection by a virus or treating a respiratory disease or condition associated with an infection by a virus comprising administering to a subject in need thereof a pharmaceutical composition comprising: a polypeptide having an amino acid sequence with at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, or 100% sequence identity to a sequence of any one of the sequences depicted in column 2 of Table 11, column 2 of Table 12 or column 3 of Table 15; or a recombinant polynucleotide encoding a polypeptide having an amino acid sequence with at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, or 100% sequence identity to a sequence of any one of the sequences depicted in column 2 of Table 11, column 2 of Table 12 or column 3 of Table 15.

[00355] In some embodiments, the subject has an immunodeficiency.

[00356] In some embodiments, the subject has a B cell immunodeficiency.

[00357] In some embodiments, the pharmaceutical composition comprises a polypeptide with at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, or 100% sequence identity to a sequence selected from the group consisting of RS C1p1full, RS C2p1full, RS C3p1full, RS C4p1full, RS C5p1, RS C5p2, RS C5p2full, RS C6p1, RS C6p2, RS C6p2full, RS C7p1, RS C7p2, RS C7p2full, RS C7p4, RS C7p4full, RS C8p1, RS C8p2 and RS C8p2full; or a polynucleotide encoding a polypeptide with at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, or 100% sequence identity to a sequence selected from the group consisting of RS C1p1full, RS C2p1full, RS C3p1full, RS C4p1full,

RS C5p1, RS C5p2, RS C5p2full, RS C6p1, RS C6p2, RS C6p2full, RS C7p1, RS C7p2, RS C7p2full, RS C7p4, RS C7p4full, RS C8p1, RS C8p2 and RS C8p2full.

[00358] In some embodiments, the pharmaceutical composition comprises a polynucleotide with at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, or 100% sequence identity to a sequence selected from the group consisting of SEQ ID NOs: RS C1n1, RS C2n1, RS C3n1, RS C4n1, RS C5n1, RS C6n1, RS C7n1, RS C8n1, RS C5n2, RS C6n2, RS C7n2, RS C8n2, RS C5n2full, RS C6n2full, RS C7n2full, RS C8n2full, RS C7n4, and RS C7n4full.

[00359] In some embodiments, the polynucleotide is an mRNA.

[00360] In some embodiments, the pharmaceutical composition further comprises one or more lipids.

[00361] In some embodiments, the one or more lipids comprise a lipid nanoparticle (LNP).

[00362] In some embodiments, the LNP encapsulates the recombinant polynucleotide construct.

[00363] In some embodiments, the polypeptide is synthetic.

[00364] In some embodiments, the polypeptide is recombinant.

[00365] In some embodiments, the polypeptide is from 8-1000 amino acids in length.

[00366] In some embodiments, the epitope sequence binds to or is predicted to bind to an HLA class I or class II molecule with a KD of 1000 nM or less.

[00367] In some embodiments, the epitope sequence binds to or is predicted to bind to an HLA class I or class II molecule with a KD of 500 nM or less.

[00368] In some embodiments, the epitope sequence comprises a sequence of a viral protein expressed by a virus-infected cell of the subject.

[00369] In some embodiments, the virus is a coronavirus.

[00370] In some embodiments, the virus is 2019 SARS-CoV 2.

[00371] In some embodiments, an HLA molecule expressed by the subject is unknown at the time of administration.

[00372] In some embodiments, the ability of the virus to avoid escape of recognition by an immune system of the subject is less compared to the ability of the virus to avoid escape of recognition by an immune system of a subject administered a pharmaceutical composition containing an epitope from a single protein or epitopes from fewer proteins than in the pharmaceutical composition administered according to a method described herein.

[00373] In some embodiments, the subject expresses an HLA molecule encoded by an HLA allele of any one of Table 1A, Table 1B, Table 1C, Table 2Ai, Table 2Aii, Table 2B and Table 16 and the epitope sequence is an HLA allele-matched epitope sequence.

[00374] In some embodiments, the epitope sequence comprises one or more or each of the following: SAPPAQYEL, AVASKILGL, EYADVFHLY, DEFTPFDVV, VRIQPGQTF, SFRLFARTR, KFLPFQQF, VVQEGVLTA, RLDKVEAEV and FGADPIHSL.

[00375] In some embodiments, the method further comprises administering to the subject an additional therapy for a 2019 SARS-CoV 2 viral infection.

[00376] In some embodiments, the method further comprises administering to the subject (a) a polypeptide having an amino acid sequence of a 2019 SARS-CoV 2 spike protein or a variant or fragment thereof; (b) a recombinant polynucleotide encoding a 2019 SARS-CoV 2 spike protein or a variant or fragment thereof; or a 2019 SARS-CoV 2 spike protein pharmaceutical composition comprising (a) or (b).

[00377] In some embodiments, the vaccine or therapeutic of (a) or (b) is administered to the subject once.

[00378] In some embodiments, the vaccine or therapeutic of (a) or (b) is administered to the subject more than once.

[00379] In some embodiments, the vaccine or therapeutic of (a) or (b) is administered at least two times, wherein the first administered dose is a priming dose, and the second and subsequent doses are booster dose(s). In some embodiments, the vaccine or therapeutic of (a) or (b) is administered at least three times, wherein the first administered dose is a priming dose, and the second, third, and subsequent doses are booster dose(s).

[00380] In some embodiments, the priming and the booster doses are administered at an interval of at least 21 days.

[00381] In some embodiments, an interval between two booster doses is at least 30 days, at least 60 days or at least 90 days.

[00382] In some embodiments, the vaccine or therapeutic is administered once each year.

[00383] In some embodiments, the vaccine or therapeutic is administered twice each year.

[00384] In some embodiments, the vaccine or therapeutic is administered at a high priming or loading dose for the first dose, and at a reduced boosting or maintenance dose for the subsequent doses.

[00385] In some embodiments, the subject receives a lower dose of or a lower frequency of a SARS-CoV spike vaccine than a subject receiving the SARS-CoV spike vaccine alone.

[00386] Provided herein is a method of treating or preventing an infection by a virus or treating a respiratory disease or condition associated with an infection by a virus comprising administering to a subject in need thereof a pharmaceutical composition comprising: (i) a recombinant polynucleotide encoding a polypeptide comprising at least two of the following (a) a sequence comprising an epitope sequence from ORF1ab, a sequence comprising an epitope sequence from membrane glycoprotein (M), and a sequence comprising an epitope sequence from nucleocapsid phosphoprotein (N); and (ii) a recombinant polynucleotide encoding a 2019 SARS-CoV 2 spike protein or a variant or fragment thereof.

[00387] In some embodiments, provided herein is a method of treating or preventing an infection by a virus or treating a respiratory disease or condition associated with an infection by a virus comprising administering to a subject in need thereof: (i) a first pharmaceutical composition comprising a first recombinant polynucleotide encoding a polypeptide comprising at least two of the following (a) a sequence

comprising an epitope sequence from ORF1ab, a sequence comprising an epitope sequence from membrane glycoprotein (M), and a sequence comprising an epitope sequence from nucleocapsid phosphoprotein (N); and (ii) a second pharmaceutical composition comprising a second recombinant polynucleotide encoding a 2019 SARS-CoV 2 spike protein or a variant or fragment thereof.

[00388] In some embodiments, the ratio (e.g., mass ratio) of the recombinant polynucleotide in (i) to the recombinant polynucleotide in (ii) is from 20:1 to 1:20.

[00389] In some embodiments, the ratio (e.g., mass ratio) of the recombinant polynucleotide in (i) to the recombinant polynucleotide in (ii) is from 1:10 to 10:1.

[00390] In some embodiments, the ratio (e.g., mass ratio) of the recombinant polynucleotide in (i) to the recombinant polynucleotide in (ii) is from about 1:5 to 5:1.

[00391] In some embodiments, the ratio (e.g., mass ratio) of the recombinant polynucleotide in (i) to the recombinant polynucleotide in (ii) is from about 1:3 to 3:1.

[00392] In some embodiments, the ratio (e.g., mass ratio) of the recombinant polynucleotide in (i) to the recombinant polynucleotide in (ii) is about 1:10, 1:9, 1:8, 1:7, 1:6, 1:5, 1:4, 1:3, 1:2, 1:1, 2:1, 3:1, 4:1, 5:1, 6:1, 7:1, 8:1, 9:1, 10:1, 1:9.5, 1:8.5, 1:7.5, 1:6.5, 1:5.5, 1:4.5, 1:3.5, 1:2.5, 1:1.5, 2.5:1, 3.5:1, 4.5:1, 5.5:1, 6.5:1, 7.5:1, 8.5:1, 9.5:1, 2:9, 2:8, 2:7, 2:6, 2:5, 2:4, 2:3, 3:2, 4:2, 5:2, 6:2, 7:2, 8:2, 9:2, 3:8, 3:7, 3:5, 3:4, 4:3, 5:3, 7:3, 8:3, 4:9, 4:7, 4:5, 5:4, 7:4, 9:4, 5:9, 5:8, 5:7, 5:6, 6:5, 7:5, 8:5, 9:5, 6:7, 7:6, 7:8, 8:7, 8:9 or 9:8.

[00393] In some embodiments, a method of treating or preventing an infection comprises administering the first pharmaceutical composition (i) and the second pharmaceutical composition (ii), to a subject who has previously been administered one or more doses of a SARS-CoV-2 vaccine (e.g., a SARS-CoV-2 vaccine that comprises (a) a polypeptide that includes a SARS-CoV-2 spike protein, or a fragment or variant thereof, or (b) a recombinant polynucleotide comprising a sequence that encodes a SARS-CoV-2 spike protein or a fragment or variant thereof). In some embodiments, a method of treating or preventing an infection comprises administering the first pharmaceutical composition (i) and the second pharmaceutical composition (ii) to a subject who has previously been administered two or more (e.g., three) doses of a SARS-CoV-2 vaccine.

[00394] In some embodiments, provided herein is a method of treating or preventing an infection by a virus or treating a respiratory disease or condition associated with an infection by a virus comprising administering to a subject in need thereof a pharmaceutical composition comprising: (i) a first recombinant polynucleotide encoding a polypeptide comprising at least two of the following (a) a sequence comprising an epitope sequence from ORF1ab, a sequence comprising an epitope sequence from membrane glycoprotein (M), and a sequence comprising an epitope sequence from nucleocapsid phosphoprotein (N); and (ii) a second recombinant polynucleotide encoding a 2019 SARS-CoV 2 spike protein or a variant or fragment thereof.

[00395] In some embodiments, the pharmaceutical composition comprises a nanoparticle, wherein the nanoparticle comprises the first recombinant polynucleotide and the second recombinant polynucleotide.

[00396] In some embodiments, the nanoparticle is present in the pharmaceutical composition at a dose of from 100 ng to 500 micrograms.

[00397] In some embodiments, the nanoparticle is present in the pharmaceutical composition at a dose of from 1 microgram to 100 micrograms.

[00398] In some embodiments, the nanoparticle is present in the pharmaceutical composition at a dose of from 1 microgram to 30 micrograms, 5 micrograms to 40 micrograms or 10 microgram to 50 micrograms.

[00399] In some embodiments, the nanoparticle is present in the pharmaceutical composition at a dose of 0.1, 0.2, 0.3, 0.4, 0.5, 0.6, 0.7, 0.8, 0.9, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25, 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, 100, 150, 200, 250, 300, 350, 400, 450, 500, 600, 700, 800, 900 or 1,000 micrograms.

[00400] In some embodiments, the ratio (e.g., mass ratio) of the first recombinant polynucleotide to the second recombinant polynucleotide is from about 1:50 to 50:1.

[00401] In some embodiments, the ratio (e.g., mass ratio) of the first recombinant polynucleotide to the second recombinant polynucleotide is from about 1:25 to 25:1.

[00402] In some embodiments, the ratio (e.g., mass ratio) of the first recombinant polynucleotide to the second recombinant polynucleotide is from about 1:10 to 10:1.

[00403] In some embodiments, the ratio (e.g., mass ratio) of the first recombinant polynucleotide to the second recombinant polynucleotide is about 1:10, 1:9, 1:8, 1:7, 1:6, 1:5, 1:4, 1:3, 1:2, 1:1, 2:1, 3:1, 4:1, 5:1, 6:1, 7:1, 8:1, 9:1, 10:1, 1:9.5, 1:8.5, 1:7.5, 1:6.5, 1:5.5, 1:4.5, 1:3.5, 1:2.5, 1:1.5, 2.5:1, 3.5:1, 4.5:1, 5.5:1, 6.5:1, 7.5:1, 8.5:1, 9.5:1, 2:9, 2:8, 2:7, 2:6, 2:5, 2:4, 2:3, 3:2, 4:2, 5:2, 6:2, 7:2, 8:2, 9:2, 3:8, 3:7, 3:5, 3:4, 4:3, 5:3, 7:3, 8:3, 4:9, 4:7, 4:5, 5:4, 7:4, 9:4, 5:9, 5:8, 5:7, 5:6, 6:5, 7:5, 8:5, 9:5, 6:7, 7:6, 7:8, 8:7, 8:9 or 9:8.

[00404] Provided herein is a method of treating or preventing an infection by a virus or treating a respiratory disease or condition associated with an infection by a virus comprising administering to a subject in need thereof: (i) a first pharmaceutical composition comprising a recombinant polynucleotide encoding a polypeptide comprising at least two of the following (a) a sequence comprising an epitope sequence from ORF1ab, a sequence comprising an epitope sequence from membrane glycoprotein (M), and a sequence comprising an epitope sequence from nucleocapsid phosphoprotein (N); and (ii) a second pharmaceutical composition comprising a recombinant polynucleotide encoding a 2019 SARS-CoV 2 spike protein or a variant or fragment thereof.

[00405] In some embodiments, the ratio (e.g., mass ratio) of the recombinant polynucleotide in (i) to the recombinant polynucleotide in (ii) is from about 1:50 to 50:1.

[00406] In some embodiments, the ratio (e.g., mass ratio) of the recombinant polynucleotide in (i) to the recombinant polynucleotide in (ii) is from about 1:25 to 25:1.

[00407] In some embodiments, the ratio (e.g., mass ratio) of the recombinant polynucleotide in (i) to the recombinant polynucleotide in (ii) is from about 1:10 to 10:1.

[00408] In some embodiments, the ratio (e.g., mass ratio) of the recombinant polynucleotide in (i) to the recombinant polynucleotide in (ii) is about 1:10, 1:9, 1:8, 1:7, 1:6, 1:5, 1:4, 1:3, 1:2, 1:1, 2:1, 3:1, 4:1, 5:1, 6:1, 7:1, 8:1, 9:1, 10:1, 1:9.5, 1:8.5, 1:7.5, 1:6.5, 1:5.5, 1:4.5, 1:3.5, 1:2.5, 1:1.5, 2.5:1, 3.5:1, 4.5:1, 5.5:1, 6.5:1, 7.5:1, 8.5:1, 9.5:1, 2:9, 2:8, 2:7, 2:6, 2:5, 2:4, 2:3, 3:2, 4:2, 5:2, 6:2, 7:2, 8:2, 9:2, 3:8, 3:7, 3:5, 3:4, 4:3, 5:3, 7:3, 8:3, 4:9, 4:7, 4:5, 5:4, 7:4, 9:4, 5:9, 5:8, 5:7, 5:6, 6:5, 7:5, 8:5, 9:5, 6:7, 7:6, 7:8, 8:7, 8:9 or 9:8.

[00409] In some embodiments, the first pharmaceutical composition comprises a first nanoparticle, wherein the first nanoparticle comprises the recombinant polynucleotide encoding a polypeptide comprising at least two of the following (a) a sequence comprising an epitope sequence from ORF1ab, a sequence comprising an epitope sequence from membrane glycoprotein (M), and a sequence comprising an epitope sequence from nucleocapsid phosphoprotein (N); and wherein the second pharmaceutical composition comprises a second nanoparticle, wherein the second nanoparticle comprises the recombinant polynucleotide encoding a 2019 SARS-CoV 2 spike protein or a variant or fragment thereof.

[00410] In some embodiments, the first nanoparticle is present in the first pharmaceutical composition at a dose of from about 100 ng to 500 micrograms.

[00411] In some embodiments, the first nanoparticle is present in the first pharmaceutical composition at a dose of from about 1 microgram to 100 micrograms.

[00412] In some embodiments, the first nanoparticle is present in the first pharmaceutical composition at a dose of from about 1 microgram to 30 micrograms, 5 micrograms to 40 micrograms or 10 microgram to 50 micrograms.

[00413] In some embodiments, the first nanoparticle is present in the first pharmaceutical composition at a dose of about 0.1, 0.2, 0.3, 0.4, 0.5, 0.6, 0.7, 0.8, 0.9, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25, 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, 100, 150, 200, 250, 300, 350, 400, 450, 500, 600, 700, 800, 900 or 1,000 micrograms.

[00414] In some embodiments, the second nanoparticle is present in the second pharmaceutical composition at a dose of from about 100 ng to 500 micrograms.

[00415] In some embodiments, the second nanoparticle is present in the second pharmaceutical composition at a dose of from about 1 microgram to 100 micrograms.

[00416] In some embodiments, the second nanoparticle is present in the second pharmaceutical composition at a dose of from about 1 microgram to 30 micrograms, 5 micrograms to 40 micrograms or 10 microgram to 50 micrograms.

[00417] In some embodiments, the second nanoparticle is present in the second pharmaceutical composition at a dose of about 0.1, 0.2, 0.3, 0.4, 0.5, 0.6, 0.7, 0.8, 0.9, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20,

25, 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, 100, 150, 200, 250, 300, 350, 400, 450, 500, 600, 700, 800, 900 or 1,000 micrograms.

[00418] Provided herein is a method of treating or preventing an infection by a virus or treating a respiratory disease or condition associated with an infection by a virus comprising administering to a subject in need thereof: (i) a pharmaceutical composition comprising (a) a polypeptide comprising at least two of the following (a) a sequence comprising an epitope sequence from ORF1ab, a sequence comprising an epitope sequence from membrane glycoprotein (M), and a sequence comprising an epitope sequence from nucleocapsid phosphoprotein (N); or (b) a polynucleotide encoding a polypeptide comprising at least two of the following (a) a sequence comprising an epitope sequence from ORF1ab, a sequence comprising an epitope sequence from membrane glycoprotein (M), and a sequence comprising an epitope sequence from nucleocapsid phosphoprotein (N); and (ii) (a) a pharmaceutical composition comprising a polypeptide having an amino acid sequence of a 2019 SARS-CoV 2 spike protein or a variant or fragment thereof; (b) a recombinant polynucleotide encoding a 2019 SARS-CoV 2 spike protein or a variant or fragment thereof; or a 2019 SARS-CoV 2 spike protein pharmaceutical composition comprising (ii)(a) or (ii)(b);

[00419] wherein the subject receives a dose of (ii)(a) or (ii)(b) that is lower than a dose of (ii)(a) or (ii)(b) administered to a subject alone.

[00420] Provided herein is a method of treating or preventing an infection by a virus or treating a respiratory disease or condition associated with an infection by a virus comprising administering to a subject in need thereof: (i) a pharmaceutical composition comprising (a) a polypeptide comprising at least two of the following (a) a sequence comprising an epitope sequence from ORF1ab, a sequence comprising an epitope sequence from membrane glycoprotein (M), and a sequence comprising an epitope sequence from nucleocapsid phosphoprotein (N); or (b) a polynucleotide encoding a polypeptide comprising at least two of the following (a) a sequence comprising an epitope sequence from ORF1ab, a sequence comprising an epitope sequence from membrane glycoprotein (M), and a sequence comprising an epitope sequence from nucleocapsid phosphoprotein (N); and (ii) (a) a pharmaceutical composition comprising a polypeptide having an amino acid sequence of a 2019 SARS-CoV 2 spike protein or a variant or fragment thereof; (b) a recombinant polynucleotide encoding a 2019 SARS-CoV 2 spike protein or a variant or fragment thereof; or a 2019 SARS-CoV 2 spike protein pharmaceutical composition comprising (ii)(a) or (ii)(b);

[00421] wherein the subject receives a number of doses of (ii)(a) or (ii)(b) that is lower than a number of doses of (ii)(a) or (ii)(b) administered to a subject alone.

[00422] In some embodiments, the subject receives a dose of (ii)(a) or (ii)(b) that is at least 1.1, 1, 1.5, 2, 3, 4, 5, 6, 7, 8, 9, 10, 20, 30, 40, 50, 60, 70, 80, 90 or 100 times lower than a dose of (ii)(a) or (ii)(b) administered to a subject alone.

[00423] In some embodiments, the subject receives 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 fewer doses of (ii)(a) or (ii)(b) than the number of doses of (ii)(a) or (ii)(b) administered to a subject alone.

[00424] In some embodiments, the pharmaceutical composition of (i) is co-formulated with the pharmaceutical composition of (ii).

[00425] In some embodiments, the pharmaceutical composition of (i) is formulated separately from the pharmaceutical composition of (ii).

[00426] In some embodiments, the pharmaceutical composition of (i) is administered separately from the pharmaceutical composition of (ii).

[00427] Provided herein is a method of treating or preventing an infection by a virus or treating a respiratory disease or condition associated with an infection by a virus comprising administering to a subject in need thereof: (i) a pharmaceutical composition comprising (a) a polypeptide comprising at least two of the following (a) a sequence comprising an epitope sequence from ORF1ab, a sequence comprising an epitope sequence from membrane glycoprotein (M), and a sequence comprising an epitope sequence from nucleocapsid phosphoprotein (N); or (b) a polynucleotide encoding a polypeptide comprising at least two of the following (a) a sequence comprising an epitope sequence from ORF1ab, a sequence comprising an epitope sequence from membrane glycoprotein (M), and a sequence comprising an epitope sequence from nucleocapsid phosphoprotein (N); and (ii) a pharmaceutical composition comprising (a) a polypeptide having an amino acid sequence of a 2019 SARS-CoV 2 spike protein or a variant or fragment thereof; (b) a recombinant polynucleotide encoding a 2019 SARS-CoV 2 spike protein or a variant or fragment thereof; or a 2019 SARS-CoV 2 spike protein pharmaceutical composition comprising (ii)(a) or (ii)(b); wherein the subject receives a dose of (i)(a) or (i)(b) that is lower than a dose of (i)(a) or (i)(b) administered to a subject alone.

[00428] Provided herein is a method of treating or preventing an infection by a virus or treating a respiratory disease or condition associated with an infection by a virus comprising administering to a subject in need thereof: (i) a pharmaceutical composition comprising (a) a polypeptide comprising at least two of the following (a) a sequence comprising an epitope sequence from ORF1ab, a sequence comprising an epitope sequence from membrane glycoprotein (M), and a sequence comprising an epitope sequence from nucleocapsid phosphoprotein (N); or (b) a polynucleotide encoding a polypeptide comprising at least two of the following (a) a sequence comprising an epitope sequence from ORF1ab, a sequence comprising an epitope sequence from membrane glycoprotein (M), and a sequence comprising an epitope sequence from nucleocapsid phosphoprotein (N); and (ii) a pharmaceutical composition comprising (a) a polypeptide having an amino acid sequence of a 2019 SARS-CoV 2 spike protein or a variant or fragment thereof; (b) a recombinant polynucleotide encoding a 2019 SARS-CoV 2 spike protein or a variant or fragment thereof; or a 2019 SARS-CoV 2 spike protein pharmaceutical composition comprising (ii)(a) or (ii)(b); wherein the subject receives a number of doses of (i)(a) or (i)(b) that is lower than a number of doses of (i)(a) or (i)(b) administered to a subject alone.

[00429] In some embodiments, the subject receives a dose of (i)(a) or (i)(b) that is at least 1.1, 1, 1.5, 2, 3, 4, 5, 6, 7, 8, 9, 10, 20, 30, 40, 50, 60, 70, 80, 90 or 100 times lower than a dose of (i)(a) or (i)(b) administered to a subject alone.

[00430] In some embodiments, the subject receives 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 fewer doses of (i)(a) or (i)(b) than the number of doses of (i)(a) or (i)(b) administered to a subject alone.

[00431] In some embodiments, the pharmaceutical composition of (i) is co-formulated with the pharmaceutical composition of (ii).

[00432] In some embodiments, the pharmaceutical composition of (i) is formulated separately from the pharmaceutical composition of (ii).

[00433] In some embodiments, the pharmaceutical composition of (i) is administered separately from the pharmaceutical composition of (ii).

[00434] In some embodiments, the pharmaceutical composition is a coformulation.

[00435] In some embodiments, the first pharmaceutical composition is administered with or on the same day as the second pharmaceutical composition.

[00436] In some embodiments, the first pharmaceutical composition is administered simultaneously with the second pharmaceutical composition.

[00437] In some embodiments, the first pharmaceutical composition is administered at a first location of the subject and the second pharmaceutical composition is administered at a second location of the subject that is different than the first location.

[00438] In some embodiments, the first location is at an appendage of the subject and second location is at an opposing appendage of the subject,

[00439] In some embodiments, the first appendage is an arm and the second appendage is an arm.

[00440] In some embodiments, the first pharmaceutical composition and the second pharmaceutical composition are administered to the same location of the subject.

[00441] In some embodiments, the pharmaceutical composition is administered at a first time point and a second time point, wherein the second time point is at least about, at most about or about 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35 or 36 days after the first time point; at least about, at most about or about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35 or 36 weeks after the first time point; or at least about, at most about or about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35 or 36 months after the first time point.

[00442] In some embodiments, the pharmaceutical composition is administered at a third time point, wherein the third time point is at least about, at most about or about 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35 or 36 days after the second time point; at least about, at most about or about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18,

19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35 or 36 weeks after the second time point; or at least about, at most about or about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35 or 36 months after the second time point.

[00443] In some embodiments, the third time point is at least about, at most about or about 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49 or 50 days after the first time point; at least about, at most about or about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35 or 36 weeks after the first time point; or at least about, at most about or about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35 or 36 months after the first time point.

[00444] In some embodiments, the first pharmaceutical composition is administered at a first time point and a second time point, wherein the second time point is at least about, at most about or about 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35 or 36 days after the first time point; at least about, at most about or about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35 or 36 weeks after the first time point; or at least about, at most about or about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35 or 36 months after the first time point.

[00445] In some embodiments, the first pharmaceutical composition is administered at a third time point, wherein the third time point is at least about, at most about or about 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35 or 36 days after the second time point; at least about, at most about or about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35 or 36 weeks after the second time point; or at least about, at most about or about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35 or 36 months after the second time point.

[00446] In some embodiments, the third time point is at least about, at most about or about 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49 or 50 days after the first time point; at least about, at most about or about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35 or 36 weeks after the first time point; or at least about, at most about or about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35 or 36 months after the first time point.

[00447] In some embodiments, the second pharmaceutical composition is administered at the first time point.

[00448] In some embodiments, the second pharmaceutical composition is administered at the second time point.

[00449] In some embodiments, the second pharmaceutical composition is administered at the third time point.

[00450] In some embodiments, the second pharmaceutical composition is administered at least about, at most about or about 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35 or 36 days after the first time point; at least about, at most about or about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35 or 36 weeks after the first time point; or at least about, at most about or about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35 or 36 months after the first time point.

[00451] In some embodiments, the second pharmaceutical composition is administered at least about, at most about or about 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35 or 36 days after the second time point; at least about, at most about or about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35 or 36 weeks after the second time point; or at least about, at most about or about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35 or 36 months after the second time point.

[00452] Provided herein is a method of treating or preventing an infection by a virus or treating a respiratory disease or condition associated with an infection by a virus comprising administering to a subject in need thereof: (i) a pharmaceutical composition comprising (a) a polypeptide comprising at least two of the following (a) a sequence comprising an epitope sequence from ORF1ab, a sequence comprising an epitope sequence from membrane glycoprotein (M), and a sequence comprising an epitope sequence from nucleocapsid phosphoprotein (N); or (b) a polynucleotide encoding a polypeptide comprising at least two of the following (a) a sequence comprising an epitope sequence from ORF1ab, a sequence comprising an epitope sequence from membrane glycoprotein (M), and a sequence comprising an epitope sequence from nucleocapsid phosphoprotein (N); wherein the pharmaceutical composition is administered at a first time point and a second time point, wherein the second time point is at least about 2 days after the first time point.

[00453] In some embodiments, the pharmaceutical composition is administered at a third time point, wherein the third time point is at least about 2 days after the second time point.

[00454] In some embodiments, the second time point is at least about 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, or 35 days after the first time point, at least about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, or 35 weeks after the first time point, or at least about 1, 3, 4, 5, 6, 7, 8, 9,

10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, or 35 months after the first time point.

[00455] In some embodiments, the second time point is at most about 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, or 35 days after the first time point, at most about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, or 35 weeks after the first time point, or at most about 1, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, or 35 months after the first time point.

[00456] In some embodiments, the second time point is about 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, or 35 days after the first time point, about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, or 35 weeks after the first time point, or about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, or 35 months after the first time point.

[00457] In some embodiments, the third time point is at least about 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, or 35 days after the second time point, at least about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, or 35 weeks after the second time point, or at least about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, or 35 months after the second time point.

[00458] In some embodiments, the third time point is at most about 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, or 35 days after the second time point, at most about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, or 35 weeks after the second time point, or at most about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, or 35 months after the second time point.

[00459] In some embodiments, the third time point is about 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34 or 35 days after the second time point, about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, or 35 weeks after the second time point, or about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, or 35 months after the second time point.

[00460] In some embodiments, the third time point is at least about 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35 or 36 days after the first time point, at least about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26,

27, 28, 29, 30, 31, 32, 33, 34, or 35 weeks after the first time point, or at least about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, or 35 months after the first time point.

[00461] In some embodiments, the third time point is at most about 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35 or 36 days after the first time point, at most about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, or 35 weeks after the first time point, or at most about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, or 35 months after the first time point.

[00462] In some embodiments, the third time point about 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35 or 36 days after the first time point, about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, or 35 weeks after the first time point, or about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, or 35 months after the first time point.

[00463] In some embodiments, the method further comprises administering to the subject: (ii) (a) a polypeptide having an amino acid sequence of a 2019 SARS-CoV 2 spike protein or a variant or fragment thereof; (b) a recombinant polynucleotide encoding a 2019 SARS-CoV 2 spike protein or a variant or fragment thereof; or a 2019 SARS-CoV 2 spike protein pharmaceutical composition comprising (ii)(a) or (ii)(b).

[00464] In some embodiments, the subject has an immunodeficiency.

[00465] In some embodiments, the subject has a B cell immunodeficiency.

[00466] In some embodiments, the pharmaceutical composition is administered prophylactically.

[00467] Provided herein is a pharmaceutical composition comprising: (i) a recombinant polynucleotide encoding a polypeptide comprising at least two of the following (a) a sequence comprising an epitope sequence from ORF1ab, a sequence comprising an epitope sequence from membrane glycoprotein (M), and a sequence comprising an epitope sequence from nucleocapsid phosphoprotein (N); and (ii) a recombinant polynucleotide encoding a 2019 SARS-CoV 2 spike protein or a variant or fragment thereof.

[00468] In some embodiments, the ratio (e.g., mass ratio) of (i):(ii) is from 20:1 to 1:20.

[00469] In some embodiments, the ratio (e.g., mass ratio) of (i):(ii) is less than 20:1, 30:1, 40:1, 50:1, 60:1, 70:1, 80:1, 90:1 or 100:1.

[00470] In some embodiments, the ratio (e.g., mass ratio) of (i):(ii) is greater than 1:20, 1:30, 1:40, 1:50, 1:60, 1:70, 1:80, 1:90 or 1:100.

[00471] Provided herein is a composition comprising: (i) a first pharmaceutical composition comprising a first recombinant polynucleotide encoding a polypeptide comprising at least two of the following (a) a

sequence comprising an epitope sequence from ORF1ab, a sequence comprising an epitope sequence from membrane glycoprotein (M), and a sequence comprising an epitope sequence from nucleocapsid phosphoprotein (N); and (ii) a second pharmaceutical composition comprising a second recombinant polynucleotide encoding a 2019 SARS-CoV 2 spike protein or a variant or fragment thereof.

[00472] In some embodiments, the ratio (e.g., mass ratio) of the recombinant polynucleotide in (i) to the recombinant polynucleotide in (ii) is from 1:50 to 50:1.

[00473] In some embodiments, the ratio (e.g., mass ratio) of the recombinant polynucleotide in (i) to the recombinant polynucleotide in (ii) is from about 1:25 to 25:1.

[00474] In some embodiments, the ratio (e.g., mass ratio) of the recombinant polynucleotide in (i) to the recombinant polynucleotide in (ii) is from about 1:10 to 10:1.

[00475] In some embodiments, the ratio (e.g., mass ratio) of the recombinant polynucleotide in (i) to the recombinant polynucleotide in (ii) is about 1:10, 1:9, 1:8, 1:7, 1:6, 1:5, 1:4, 1:3, 1:2, 1:1, 2:1, 3:1, 4:1, 5:1, 6:1, 7:1, 8:1, 9:1, 10:1, 1:9.5, 1:8.5, 1:7.5, 1:6.5, 1:5.5, 1:4.5, 1:3.5, 1:2.5, 1:1.5, 2.5:1, 3.5:1, 4.5:1, 5.5:1, 6.5:1, 7.5:1, 8.5:1, 9.5:1, 2:9, 2:8, 2:7, 2:6, 2:5, 2:4, 2:3, 3:2, 4:2, 5:2, 6:2, 7:2, 8:2, 9:2, 3:8, 3:7, 3:5, 3:4, 4:3, 5:3, 7:3, 8:3, 4:9, 4:7, 4:5, 5:4, 7:4, 9:4, 5:9, 5:8, 5:7, 5:6, 6:5, 7:5, 8:5, 9:5, 6:7, 7:6, 7:8, 8:7, 8:9 or 9:8.

[00476] Provided herein is a pharmaceutical composition comprising: (i) a first recombinant polynucleotide encoding a polypeptide comprising at least two of the following (a) a sequence comprising an epitope sequence from ORF1ab, a sequence comprising an epitope sequence from membrane glycoprotein (M), and a sequence comprising an epitope sequence from nucleocapsid phosphoprotein (N); and (ii) a second recombinant polynucleotide encoding a 2019 SARS-CoV 2 spike protein or a variant or fragment thereof.

[00477] In some embodiments, the pharmaceutical composition comprises a nanoparticle, wherein the nanoparticle comprises the first recombinant polynucleotide and the second recombinant polynucleotide.

[00478] In some embodiments, the nanoparticle is present in the pharmaceutical composition at a dose of from 100 ng to 500 micrograms.

[00479] In some embodiments, the nanoparticle is present in the pharmaceutical composition at a dose of from 1 microgram to 100 micrograms.

[00480] In some embodiments, the nanoparticle is present in the pharmaceutical composition at a dose of from 1 microgram to 30 micrograms, 5 micrograms to 40 micrograms or 10 microgram to 50 micrograms.

[00481] In some embodiments, the nanoparticle is present in the pharmaceutical composition at a dose of 0.1, 0.2, 0.3, 0.4, 0.5, 0.6, 0.7, 0.8, 0.9, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25, 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, 100, 150, 200, 250, 300, 350, 400, 450, 500, 600, 700, 800, 900 or 1,000 micrograms.

[00482] In some embodiments, the ratio (e.g., mass ratio) of the first recombinant polynucleotide to the second recombinant polynucleotide is from about 1:50 to 50:1.

[00483] In some embodiments, the ratio (e.g., mass ratio) of the first recombinant polynucleotide to the second recombinant polynucleotide is from about 1:25 to 25:1.

[00484] In some embodiments, the ratio (e.g., mass ratio) of the first recombinant polynucleotide to the second recombinant polynucleotide is from about 1:10 to 10:1.

[00485] In some embodiments, the ratio (e.g., mass ratio) of the first recombinant polynucleotide to the second recombinant polynucleotide is about 1:10, 1:9, 1:8, 1:7, 1:6, 1:5, 1:4, 1:3, 1:2, 1:1, 2:1, 3:1, 4:1, 5:1, 6:1, 7:1, 8:1, 9:1, 10:1, 1:9.5, 1:8.5, 1:7.5, 1:6.5, 1:5.5, 1:4.5, 1:3.5, 1:2.5, 1:1.5, 2.5:1, 3.5:1, 4.5:1, 5.5:1, 6.5:1, 7.5:1, 8.5:1, 9.5:1, 2:9, 2:8, 2:7, 2:6, 2:5, 2:4, 2:3, 3:2, 4:2, 5:2, 6:2, 7:2, 8:2, 9:2, 3:8, 3:7, 3:5, 3:4, 4:3, 5:3, 7:3, 8:3, 4:9, 4:7, 4:5, 5:4, 7:4, 9:4, 5:9, 5:8, 5:7, 5:6, 6:5, 7:5, 8:5, 9:5, 6:7, 7:6, 7:8, 8:7, 8:9 or 9:8.

[00486] Provided herein is a composition comprising: (i) a first pharmaceutical composition comprising a recombinant polynucleotide encoding a polypeptide comprising at least two of the following (a) a sequence comprising an epitope sequence from ORF1ab, a sequence comprising an epitope sequence from membrane glycoprotein (M), and a sequence comprising an epitope sequence from nucleocapsid phosphoprotein (N); and (ii) a second pharmaceutical composition comprising a recombinant polynucleotide encoding a 2019 SARS-CoV 2 spike protein or a variant or fragment thereof.

[00487] In some embodiments, the first pharmaceutical composition comprises a first nanoparticle, wherein the first nanoparticle comprises the recombinant polynucleotide encoding a polypeptide comprising at least two of the following (a) a sequence comprising an epitope sequence from ORF1ab, a sequence comprising an epitope sequence from membrane glycoprotein (M), and a sequence comprising an epitope sequence from nucleocapsid phosphoprotein (N); and wherein the second pharmaceutical composition comprises a second nanoparticle, wherein the second nanoparticle comprises the recombinant polynucleotide encoding a 2019 SARS-CoV 2 spike protein or a variant or fragment thereof.

[00488] In some embodiments, the ratio (e.g., mass ratio) of the recombinant polynucleotide in (i) to the recombinant polynucleotide in (ii) is from about 1:50 to 50:1.

[00489] In some embodiments, the ratio (e.g., mass ratio) of the recombinant polynucleotide in (i) to the recombinant polynucleotide in (ii) is from about 1:25 to 25:1.

[00490] In some embodiments, the ratio (e.g., mass ratio) of the recombinant polynucleotide in (i) to the recombinant polynucleotide in (ii) is from about 1:10 to 10:1.

[00491] In some embodiments, the ratio (e.g., mass ratio) of the recombinant polynucleotide in (i) to the recombinant polynucleotide in (ii) is about 1:10, 1:9, 1:8, 1:7, 1:6, 1:5, 1:4, 1:3, 1:2, 1:1, 2:1, 3:1, 4:1, 5:1, 6:1, 7:1, 8:1, 9:1, 10:1, 1:9.5, 1:8.5, 1:7.5, 1:6.5, 1:5.5, 1:4.5, 1:3.5, 1:2.5, 1:1.5, 2.5:1, 3.5:1, 4.5:1, 5.5:1, 6.5:1, 7.5:1, 8.5:1, 9.5:1, 2:9, 2:8, 2:7, 2:6, 2:5, 2:4, 2:3, 3:2, 4:2, 5:2, 6:2, 7:2, 8:2, 9:2, 3:8, 3:7, 3:5, 3:4, 4:3, 5:3, 7:3, 8:3, 4:9, 4:7, 4:5, 5:4, 7:4, 9:4, 5:9, 5:8, 5:7, 5:6, 6:5, 7:5, 8:5, 9:5, 6:7, 7:6, 7:8, 8:7, 8:9 or 9:8.

[00492] In some embodiments, the first nanoparticle is present in the first pharmaceutical composition at a dose of from about 100 ng to 500 micrograms.

[00493] In some embodiments, the first nanoparticle is present in the first pharmaceutical composition at a dose of from about 1 microgram to 100 micrograms.

[00494] In some embodiments, the first nanoparticle is present in the first pharmaceutical composition at a dose of from about 1 microgram to 30 micrograms, 5 micrograms to 40 micrograms or 10 microgram to 50 micrograms.

[00495] In some embodiments, the first nanoparticle is present in the first pharmaceutical composition at a dose of about 0.1, 0.2, 0.3, 0.4, 0.5, 0.6, 0.7, 0.8, 0.9, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25, 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, 100, 150, 200, 250, 300, 350, 400, 450, 500, 600, 700, 800, 900 or 1,000 micrograms.

[00496] In some embodiments, the second nanoparticle is present in the second pharmaceutical composition at a dose of from about 100 ng to 500 micrograms.

[00497] In some embodiments, the second nanoparticle is present in the second pharmaceutical composition at a dose of from about 1 microgram to 100 micrograms.

[00498] In some embodiments, the second nanoparticle is present in the second pharmaceutical composition at a dose of from about 1 microgram to 30 micrograms, 5 micrograms to 40 micrograms or 10 microgram to 50 micrograms.

[00499] In some embodiments, the second nanoparticle is present in the second pharmaceutical composition at a dose of about 0.1, 0.2, 0.3, 0.4, 0.5, 0.6, 0.7, 0.8, 0.9, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25, 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, 100, 150, 200, 250, 300, 350, 400, 450, 500, 600, 700, 800, 900 or 1,000 micrograms.

[00500] In some embodiments, the recombinant polynucleotide in (i) is present in the first pharmaceutical composition at a dose of from about 50 ng to 250 micrograms.

[00501] In some embodiments, the recombinant polynucleotide in (i) is present in the first pharmaceutical composition at a dose of from about 0.5 to 50 micrograms.

[00502] In some embodiments, the recombinant polynucleotide in (i) is present in the first pharmaceutical composition at a dose of from about 0.5 microgram to 15 micrograms, 2.5 micrograms to 20 micrograms or 5 microgram to 25 micrograms.

[00503] In some embodiments, the recombinant polynucleotide in (i) is present in the first pharmaceutical composition at a dose of about 0.05, 0.1, 0.2, 0.3, 0.4, 0.5, 0.6, 0.7, 0.8, 0.9, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25, 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, 100, 150, 200, 250, 300, 350, 400, 450 or 500 micrograms.

[00504] In some embodiments, the recombinant polynucleotide in (ii) is present in the second pharmaceutical composition at a dose of from about 50 ng to 250 micrograms.

[00505] In some embodiments, the recombinant polynucleotide in (ii) is present in the second pharmaceutical composition at a dose of from about 0.5 to 50 micrograms.

[00506] In some embodiments, the recombinant polynucleotide in (ii) is present in the second pharmaceutical composition at a dose of from about 0.5 microgram to 15 micrograms, 2.5 micrograms to 20 micrograms or 5 microgram to 25 micrograms.

[00507] In some embodiments, the recombinant polynucleotide in (ii) is present in the second pharmaceutical composition at a dose of about 0.05, 0.1, 0.2, 0.3, 0.4, 0.5, 0.6, 0.7, 0.8, 0.9, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25, 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, 100, 150, 200, 250, 300, 350, 400, 450 or 500 micrograms.

[00508] In some embodiments, the nanoparticle is a lipid nanoparticle.

[00509] Provided herein is a composition comprising: (i) a polypeptide comprising at least two of the following (a) a sequence comprising an epitope sequence from ORF1ab, (b) a sequence comprising an epitope sequence from membrane glycoprotein (M) and (c) a sequence comprising an epitope sequence from nucleocapsid phosphoprotein (N); (ii) a polynucleotide encoding a polypeptide, wherein the polypeptide comprises at least two of the following (a) a sequence comprising an epitope sequence from ORF1ab, (b) a sequence comprising an epitope sequence from membrane glycoprotein (M) and (c) a sequence comprising an epitope sequence from nucleocapsid phosphoprotein (N); (iii) a T cell receptor (TCR) or a T cell comprising the TCR, wherein the TCR binds to an epitope sequence of the polypeptide in complex with a corresponding HLA class I or class II molecule; (iv) an antigen presenting cell comprising (i) or (ii); or (v) an antibody or B cell comprising the antibody, wherein the antibody binds to an epitope sequence of the polypeptide; and a pharmaceutically acceptable excipient.

[00510] In some embodiments, the polypeptide comprises (a) a sequence comprising an epitope sequence from ORF1ab, (b) a sequence comprising an epitope sequence from membrane glycoprotein (M) and (c) a sequence comprising an epitope sequence from nucleocapsid phosphoprotein (N). In some embodiments, the sequence comprising an epitope sequence from ORF1ab is C-terminal to the sequence comprising an epitope sequence from nucleocapsid phosphoprotein (N). In some embodiments, the sequence comprising an epitope sequence from ORF1ab is N-terminal to the sequence comprising an epitope sequence from membrane glycoprotein (M). In some embodiments, the sequence comprising an epitope sequence from nucleocapsid phosphoprotein (N) is N-terminal to the sequence comprising an epitope sequence from membrane glycoprotein (M).

[00511] In some embodiments, the polypeptide comprises at least two of the following (a) a sequence comprising an epitope sequence from ORF1ab, (b) a sequence comprising an epitope sequence from membrane glycoprotein (M) and (c) a sequence comprising an epitope sequence from nucleocapsid phosphoprotein (N)

[00512] In some embodiments, the polypeptide comprises (a) 2, 3, 4, 5, 6, 7, 8, 9 or 10 or more epitope sequence from ORF1ab, (b) a sequence comprising an epitope sequence from membrane glycoprotein (M) and (c) a sequence comprising an epitope sequence from nucleocapsid phosphoprotein (N).

[00513] In some embodiments, the epitope sequence from ORF1ab is an epitope sequence from a non-structural protein. In some embodiments, the non-structural protein is selected from the group consisting of NSP1, NSP2, NSP3, NSP4 and combinations thereof. In some embodiments, the polypeptide comprises a sequence comprising an epitope sequence from NSP1, a sequence comprising an epitope sequence from NSP2, a sequence comprising an epitope sequence from NSP3 and a sequence comprising an epitope sequence from NSP4.

[00514] In some embodiments, the epitope sequence from ORF1ab is selected from the group consisting of YLFDESGEFKL, YLFDESGEF, FGDDTVIEV, QLMCQPILL, TTDPSFLGRY, PTDNYITTY, PSFLGRY, AEAELAKNV, KTIQPRVEK and any combination thereof.

[00515] In some embodiments, the epitope sequence from nucleocapsid glycoprotein (N) is LLLDRLNQL. In some embodiments, the epitope sequence from membrane phosphoprotein (M) is VATSRTLSY. In some embodiments, the polypeptide comprises an epitope sequence from nucleocapsid glycoprotein (N) that is LLLDRLNQL and an epitope sequence from membrane phosphoprotein (M) that is VATSRTLSY.

[00516] In some embodiments, the polypeptide comprises (a) each of the following epitope sequences from ORF1ab: YLFDESGEFKL, YLFDESGEF, FGDDTVIEV, QLMCQPILL, TTDPSFLGRY, PTDNYITTY, PSFLGRY, AEAELAKNV, KTIQPRVEK; (b) an epitope sequence from nucleocapsid glycoprotein (N) that is LLLDRLNQL; and (c) an epitope sequence from membrane phosphoprotein (M) that is VATSRTLSY.

[00517] In some embodiments, the sequence comprising an epitope sequence from ORF1ab is selected from the group consisting of the following sequences or fragments thereof: MVTNNTFTLKVPHVGEIPVAYRKVLLKTIQPRVEKYLFDESGEFKLSEVGPEHSLAEYYIFFASFY Y; MVTNNTFTLKVPHVGEIPVAYRKVLLKTIQPRVEKYLFDESGEFKLSEVGPEHSLAEY; APKEIIFLEGETLFGDDTVIEVAIILASFSAST; APKEIIFLEGETLFGDDTVIEV; HTTDPSFLGRYMSALFADDLNQLTGYHTDFSSEIIGYQLMCQPILLAEAELAKNVSLILGTVSWN L;

TTDPSFLGRYMSALFADDLNQLTGYHTDFSSEIIGYQLMCQPILLAEAELAKNVSLILGTVSWNL; LLSAGIFGAITDVFYKENSYKVPTDNYITTY; and combinations thereof.

[00518] In some embodiments, the sequence comprising an epitope sequence from membrane glycoprotein (M) is selected from the group consisting of the following sequences or fragments thereof: ADSNGTITVEELKKLLEQWNLVIGFLFLTWICLLQFAYANRNRFLYIIKLIFLWLLWPVTLACFVL AAVYRINWITGGIAIAMACLVGLMWLSYFIASFRLFARTRSMWSFNPETNILLNVPLHGTILTRPL

LESELVIGAVILRGHLRIAGHHLGRCDIKDLPKEITVATSRTLSYYKLGASQRVAGDSGFAAYSR YRIGNYKLNTDHSSSSDNIALLVQ;
FAYANRNRFLYIIKLIFLWLLWPVTLACFVLAAVYRINWITGGIAIAMACLVGLMWLSYFIASFR LF; LGRCDIKDLPKEITVATSRTLSYYKLGASQRVA; KLLEQWNLVIGF; NRNRFLYIIKLIFLWLLWPVTLACFVLAAVY; SELVIGAVILRGHLRIAGHHLGR; VATSRTLSYYKLGASQRV; GLMWLSYF; and combinations thereof.

[00519] In some embodiments, the sequence comprising an epitope sequence from nucleocapsid phosphoprotein (N) is selected from the group consisting of the following sequences or fragments thereof: KDLSPRWYFYYLGTGPEAGLPYGANKDGIIWVATEGALNTPKDHIGTRNPANNAAIVLQLPQGT TLPKGFYAEGSRGGSQASSRSSSRSRNSSRNSTPGSSRGTSPARMAGNGGDAALALLLLDRLNQL ESKMSGKGQQQQGQTVTKKSAAEASKKPRQKRTATKAYNVTQAFGRRGPEQTQGNFGDQELI RQGTDYKHWPQIAQFAPSASAFFGMSRIGMEVTPSGTWLTYTGAIKLDDKDPNFKDQVILLNKH IDAYKTFPPTEPKKDKKKKADETQALPQRQKKQQTVTLLPAADLDDFSKQLQQSMSSADSTQA; RMAGNGGDAALALLLLDRLNQLESKMSGKGQQQ;
YKHWPQIAQFAPSASAFFGMSRIGMEVTPSGTWLTYTGAIKLDDKDPNFKDQVILLNKHIDAYK TFP;
SPARMAGNGGDAALALLLLDRLNQLESKMSGKGQQQQGQTVTKKSAAEASKKPRQKRTATKA YNVTQAFGRRGPEQTQGNFGDQELIRQGTDYKHWPQIAQFAPSASAFFGMSRIGMEVTPSGTWL TYTGAIKLDDKDPNFKDQVILLNKHIDAYKTFPPTEPKKDK and combinations thereof.

[00520] In some embodiments, the polypeptide comprises one or more linker sequences. In some embodiments, the one or more linker sequences are selected from the group consisting of GGSGGGGSGG, GGSLGGGGSG. In some embodiments, the one or more linker sequences comprise cleavage sequences. In some embodiments, the one or more cleavage sequences are selected from the group consisting of FRAC, KRCF, KKRY, ARMA, RRSG, MRAC, KMCG, ARCA, KKQG, YRSY, SFMN, FKAA, KRNG, YNSF, KKNG, RRRG, KRYS, and ARYA.

[00521] In some embodiments, the polypeptide comprises a transmembrane domain sequence. In some embodiments, the transmembrane sequence is C-terminal to the sequence comprising an epitope sequence from ORF1ab, the sequence comprising an epitope sequence from membrane glycoprotein (M) and the sequence comprising an epitope sequence from nucleocapsid phosphoprotein (N). In some embodiments, the transmembrane sequence is EQYIKWPWYIWLGFIAGLIAIVMVTIMLCCMTSCCSCLKGCCSCGSCCKFDEDDSEPVLKGVKL HYT.

[00522] In some embodiments, the polypeptide comprises an SEC sequence. In some embodiments, the SEC sequence is N-terminal to the sequence comprising an epitope sequence from ORF1ab, the sequence comprising an epitope sequence from membrane glycoprotein (M) and the sequence comprising an epitope

sequence from nucleocapsid phosphoprotein (N). In some embodiments, the SEC sequence is MFVFLVLLPLVSSQCVNLT.

[00523] In some embodiments, the composition comprises the polynucleotide encoding the polypeptide. In some embodiments, the polynucleotide is an mRNA. In some embodiments, the polynucleotide comprises a codon optimized sequence for expression in a human.

[00524] In some embodiments, the polynucleotide comprises a dEarI-hAg sequence. In some embodiments, the dEarI-hAg sequence is ATTCTTCTGGTCCCCACAGACTCAGAGAGAACCC, optionally wherein each T is a U.

[00525] In some embodiments, the polynucleotide comprises a Kozak sequence. In some embodiments, the a Kozak sequences is GCCACC.

[00526] In some embodiments, the polynucleotide comprises an F element sequence. In some embodiments, the F element sequence is a 3 UTR of amino-terminal enhancer of split (AES). In some embodiments, the F element sequence is CTGGTACTGCATGCACGCAATGCTAGCTGCCCCTTTCCCGTCCTGGGTACCCCGAGTCTCCC CCGACCTCGGGTCCCAGGTATGCTCCCACCTCCACCTGCCCCACTCACCACCTCTGCTAGTTC CAGACACCTCC, optionally wherein each T is a U.

[00527] In some embodiments, the polynucleotide comprises an I element sequence. In some embodiments, the I element sequence is a 3' UTR of mitochondrially encoded 12S rRNA (mtRNR1). In some embodiments, the I element sequence is CAAGCACGCAGCAATGCAGCTCAAAACGCTTAGCCTAGCCACACCCCCACGGGAAACAGCA GTGATTAACCTTTAGCAATAAACGAAAGTTTAACTAAGCTATACTAACCCCAGGGTTGGTCA ATTTCGTGCCAGCCACACC, optionally wherein each T is a U.

[00528] In some embodiments, the polynucleotide comprises a poly A sequence. In some embodiments, the poly A sequence is AAAAAAAAAAAAAAAAAAAAAAAAAAAAAAGCATATGACTAAAAAAAAAAAAAAAAAAAA AAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA, optionally wherein each T is a U.

[00529] In some embodiments, each of the epitope sequences from the ORF1ab, the membrane glycoprotein, and the nucleocapsid phosphoprotein are from 2019 SARS-CoV-2.

[00530] In some embodiments, one or more or each epitope elicits a T cell response.

[00531] In some embodiments, one or more or each epitope has been observed by mass spectrometry as being presented by an HLA molecule.

[00532] In some embodiments, the composition comprises (i) a polypeptide with at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, or 100% sequence identity to a sequence selected from the group consisting of RS C1p1full, RS C2p1full, RS C3p1full, RS C4p1full, RS C5p1, RS

C5p2, RS C5p2full, RS C6p1, RS C6p2, RS C6p2full, RS C7p1, RS C7p2, RS C7p2full, RS C7p4, RS C7p4full, RS C8p1, RS C8p2 and RS C8p2full; (ii) a polynucleotide encoding a polypeptide with at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, or 100% sequence identity to a sequence selected from the group consisting of RS C1p1full, RS C2p1full, RS C3p1full, RS C4p1full, RS C5p1, RS C5p2, RS C5p2full, RS C6p1, RS C6p2, RS C6p2full, RS C7p1, RS C7p2, RS C7p2full, RS C7p4, RS C7p4full, RS C8p1, RS C8p2 and RS C8p2full; or (iii) a polynucleotide with at least at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, or 100% sequence identity to a sequence selected from the group consisting of SEQ ID NOs: RS C1n1, RS C2n1, RS C3n1, RS C4n1, RS C5n1, RS C6n1, RS C7n1, RS C8n1, RS C5n2, RS C6n2, RS C7n2, RS C8n2, RS C5n2full, RS C6n2full, RS C7n2full, RS C8n2full, RS C7n4, RS C7n4full.

[00533] Also provided herein is a pharmaceutical composition comprising any of the compositions described herein.

[00534] Also provided herein is a pharmaceutical composition comprising: (i) a polypeptide comprising an epitope sequence of Table 1A, Table 1B, Table 1C, Table 2Ai, Table 2Aii, Table 2B and/or Table 16; (ii) a polynucleotide encoding the polypeptide; (iii) a T cell receptor (TCR) or a T cell comprising the TCR, wherein the TCR binds to the epitope sequence in complex with a corresponding HLA class I or class II molecule; (iv) an antigen presenting cell comprising (i) or (ii); or (v) an antibody or B cell comprising the antibody, wherein the antibody binds to the epitope sequence; and a pharmaceutically acceptable excipient.

[00535] In some embodiments, the epitope sequence comprises one or more or each of the following: YLFDESGEFKL, YLFDESGEF, FGDDTVIEV, LLLDRLNQL, QLMCQPILL, TTDPSFLGRY, PTDNYITTY, PSFLGRY, AEAELAKNV, VATSRTLSY and KTIQPRVEK. In some embodiments, the epitope sequence comprises one or more or each of the following: SAPPAQYEL, AVASKILGL, EYADVFHLY, DEFTPFDVV, VRIQPGQTF, SFRLFARTR, KFLPFQQF, VVQEGVLTA, RLDKVEAEV, FGADPIHSL, NYNYLYRLF, KYIKWPWYI, KWPWYIWLGF, LPFNDGVYF, QPTESIVRF, IPFAMQMAY, YLQPRTFLL and RLQSLQTYV.

[00536] In some embodiments, the epitope sequence is from an orf1ab protein. In some embodiments, the epitope sequence is from an orf1a protein In some embodiments, the epitope sequence is from a surface glycoprotein (S) or a shifted reading frame thereof. In some embodiments, the epitope sequence is from a nucleocapsid phosphoprotein (N). In some embodiments, the epitope sequence is from an ORF3a protein. In some embodiments, the epitope sequence is from a membrane glycoprotein (M). In some embodiments, the epitope sequence is from an ORF7a protein. In some embodiments, the epitope sequence is from an ORF8 protein. In some embodiments, the epitope sequence is from an envelope protein (E). In some embodiments, the epitope sequence is from an ORF6 protein. In some embodiments, the epitope sequence is from an ORF7b protein. In some embodiments, the epitope sequence is from an ORF10 protein. In some embodiments, the epitope sequence is from an ORF9b protein.

[00537] Also provided herein is a pharmaceutical composition comprising: a polypeptide having an amino acid sequence with at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, or 100% sequence identity to a sequence of any one of the sequences depicted in column 2 of Table 11, column 2 of Table 12 or column 3 of Table 15; or a recombinant polynucleotide encoding a polypeptide having an amino acid sequence with at least at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, or 100% sequence identity to a sequence of any one of the sequences depicted in column 2 of Table 11, column 2 of Table 12 or column 3 of Table 15.

[00538] In some embodiments, the pharmaceutical composition comprises a polypeptide with at least at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, or 100% sequence identity to a sequence selected from the group consisting of RS C1p1full, RS C2p1full, RS C3p1full, RS C4p1full, RS C5p1, RS C5p2, RS C5p2full, RS C6p1, RS C6p2, RS C6p2full, RS C7p1, RS C7p2, RS C7p2full, RS C7p4, RS C7p4full, RS C8p1, RS C8p2 and RS C8p2full; or a polynucleotide encoding a polypeptide with at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, or 100% sequence identity to a sequence selected from the group consisting of RS C1p1full, RS C2p1full, RS C3p1full, RS C4p1full, RS C5p1, RS C5p2, RS C5p2full, RS C6p1, RS C6p2, RS C6p2full, RS C7p1, RS C7p2, RS C7p2full, RS C7p4, RS C7p4full, RS C8p1, RS C8p2 and RS C8p2full. In some embodiments, the pharmaceutical composition comprises a polynucleotide with at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, or 100% sequence identity to a sequence selected from the group consisting of SEQ ID NOs: RS C1n1, RS C2n1, RS C3n1, RS C4n1, RS C5n1, RS C6n1, RS C7n1, RS C8n1, RS C5n2, RS C6n2, RS C7n2, RS C8n2, RS C5n2full, RS C6n2full, RS C7n2full, RS C8n2full, RS C7n4 and RS C7n4full, .

[00539] In some embodiments, the polynucleotide is an mRNA.

[00540] In some embodiments, the pharmaceutical composition further comprises one or more lipid components. In some embodiments, the one or more lipids comprise a lipid nanoparticle (LNP). In some embodiments, the LNP encapsulates the recombinant polynucleotide construct.

[00541] In some embodiments, the polypeptide is synthetic. In some embodiments, the polypeptide is recombinant.

[00542] In some embodiments, the polypeptide is from 8-1000 amino acids in length.

[00543] In some embodiments, the epitope sequence binds to or is predicted to bind to an HLA class I or class II molecule with a K_D of 1000 nM or less. In some embodiments, the epitope sequence binds to or is predicted to bind to an HLA class I or class II molecule with a K_D of 500 nM or less.

[00544] In some embodiments, the epitope sequence comprises a sequence of a viral protein expressed by a virus-infected cell of a subject.

[00545] Also provided herein is a method of treating or preventing an infection by a virus or treating a respiratory disease or condition associated with an infection by a virus comprising administering to a subject in need thereof a pharmaceutical composition described herein.

[00546] In some embodiments, the virus is a coronavirus. In some embodiments, the virus is 2019 SARS-CoV 2. In some embodiments, an HLA molecule expressed by the subject is unknown at the time of administration. In some embodiments, the ability of the virus to avoid escape of recognition by an immune system of the subject is less compared to the ability of the virus to avoid escape of recognition by an immune system of a subject administered a pharmaceutical composition containing an epitope from a single protein or epitopes from fewer proteins than in a pharmaceutical composition described herein. In some embodiments, the subject express an HLA molecule encoded by an HLA allele of any one of Table 1A, Table 1B, Table 1C, Table 2Ai or Table 2Aii, Table 2B or Table 16 and the epitope sequence is an HLA allele-matched epitope sequence.

[00547] In some embodiments, the epitope sequence comprises one or more or each of the following: SAPPAQYEL, AVASKILGL, EYADVFHLY, DEFTPFDVV, VRIQPGQTF, SFRLFARTR, KFLPFQQF, VVQEGVLTA, RLDKVEAEV and FGADPIHSL.

[00548] Also provided herein is a method of treating or preventing a 2019 SARS-CoV 2 infection in a subject in need thereof, comprising administering to the subject a pharmaceutical composition described herein.

[00549] In some embodiments, the pharmaceutical composition is administered in addition to one or more therapeutics for the 2019 SARS-CoV 2 viral infection in the subject. In some embodiments, the pharmaceutical composition is administered in combination with (a) a polypeptide having an amino acid sequence of a 2019 SARS-CoV 2 spike protein or a variant or fragment thereof; (b) a recombinant polynucleotide encoding a 2019 SARS-CoV 2 spike protein or a variant or fragment thereof; or a 2019 SARS-CoV 2 spike protein pharmaceutical composition comprising (a) or (b). In some embodiments, the 2019 SARS-CoV 2 spike protein or a variant or fragment thereof is a SARS-CoV-2 spike protein or a fragment thereof.

[00550] In some embodiments, the pharmaceutical composition is administered 1-10 weeks after a first administration of the 2019 SARS-CoV 2 spike protein pharmaceutical composition. In some embodiments, the pharmaceutical composition is administered 1-6 weeks, 1-6 months or 1-2 years or later after a first administration of the 2019 SARS-CoV 2 spike protein pharmaceutical composition. In some embodiments, the pharmaceutical composition is administered on the same day or simultaneously with an administration of the 2019 SARS-CoV 2 spike protein pharmaceutical composition. In some embodiments, the pharmaceutical composition is co-formulated with the polypeptide having an amino acid sequence of a 2019 SARS-CoV 2 spike protein or a variant or fragment thereof or the recombinant polynucleotide encoding a 2019 SARS-CoV 2 spike protein or a variant or fragment thereof. In some embodiments, the

pharmaceutical composition is administered before an administration of the 2019 SARS-CoV 2 spike protein pharmaceutical composition, such as 2-10 weeks before an administration of the 2019 SARS-CoV 2 spike protein pharmaceutical composition. In some embodiments, the pharmaceutical composition is administered prophylactically. In some embodiments, the pharmaceutical composition is administered once every 1, 2, 3, 4, 5, 6 or more weeks; or once every 1-7, 7-14, 14-21, 21-28, or 28-35 days; or once every 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, or 35 days.

[00551] Also provided herein is a use of a composition described herein for preparing a therapeutic for treating or preventing a respiratory viral infection caused by 2019 SARS CoV-2 virus.

[00552] Also provided herein is a composition described herein or a pharmaceutical composition described herein for use as a medicament.

[00553] Also provided herein is a composition described herein or a pharmaceutical composition described herein for use in the treatment or prevention of a respiratory viral infection caused by 2019 SARS CoV-2 virus.

[00554] Provided herein is an antigenic peptide comprising an epitope sequence from Table 1A, Table 1B, Table 1C, Table 2Ai, Table 2Aii or Table 2B. Also provided herein is a polynucleotide encoding and antigenic peptide comprising an epitope sequence from Table 1A, Table 1B, Table 1C, Table 2Ai, Table 2Aii or Table 2B. The antigenic peptide and/or polynucleotide may be recombinant. The antigenic peptide and/or polynucleotide may be isolated or purified. The antigenic peptide may be synthetic or expressed from a polynucleotide.

[00555] Also provided herein is an antibody or B cell comprising an antibody that binds to an antigenic peptide comprising an epitope sequence from Table 1A, Table 1B, Table 1C, Table 2Ai, Table 2Aii or Table 2B.

[00556] Also provided herein is a T cell receptor (TCR) or T cell comprising a TCR that binds an epitope sequence from Table 1A or Table 1B in complex with a corresponding MHC class I molecule according to Table 1A or Table 1B. For example, the TCR can bind to an epitope sequence from column 2 (set 1) of Table 1A in complex with a corresponding MHC class I molecule from column 3 (set 1) in the same row of Table 1A. For example, the TCR can bind to an epitope sequence from column 4 (set 2) of Table 1A in complex with a corresponding MHC class I molecule from column 5 (set 2) in the same row of Table 1A. For example, the TCR can bind to an epitope sequence from column 6 (set 3) of Table 1A in complex with a corresponding MHC class I molecule from column 7 (set 3) in the same row of Table 1A. For example, the TCR can bind to an epitope sequence from column 2 (set 1) of Table 1B in complex with a corresponding MHC class I molecule from column 3 (set 1) in the same row of Table 1B. For example, the TCR can bind to an epitope sequence from column 4 (set 2) of Table 1B in complex with a corresponding MHC class I molecule from column 5 (set 2) in the same row of Table 1B.

[00557] Also provided herein is a T cell receptor (TCR) or T cell comprising a TCR that binds to an epitope sequence from Table 2Ai or Table 2Aii in complex with a corresponding MHC class II molecule according to Table 2Ai or Table 2Aii. For example, the TCR can bind to an epitope sequence from column 2 (set 1) of Table 2Ai in complex with a corresponding MHC class II molecule from column 3 (set 1) in the same row of Table 2Ai. For example, the TCR can bind to an epitope sequence from column 4 (set 2) of Table 2Ai in complex with a corresponding MHC class II molecule from column 5 (set 2) in the same row of Table 2Ai. Likewise, a TCR can bind to an epitope sequence from the left column of Table 2Aii in complex with a corresponding MHC class II molecule from the right column of Table 2Aii.

[00558] Provided herein is a method of treating or preventing viral infection in a subject in need thereof comprising administering to the subject an antigenic peptide comprising an epitope sequence from Table 1A, Table 1B, Table 1C, Table 2Ai, Table 2Aii or Table 2B. Also provided herein is a method of treating or preventing viral infection in a subject in need thereof comprising administering to the subject a polynucleotide encoding and antigenic peptide comprising an epitope sequence from Table 1A, Table 1B, Table 1C, Table 2Ai, Table 2Aii or Table 2B.

[00559] Also provided herein is a method of treating or preventing a viral infection in a subject in need thereof comprising administering to the subject an antibody or B cell comprising an antibody that binds to an antigenic peptide comprising an epitope sequence from Table 1A, Table 1B, Table 1C, Table 2Ai, Table 2Aii or Table 2B.

[00560] Also provided herein is a method of treating or preventing viral infection in a subject in need thereof comprising administering to the subject a T cell receptor (TCR) or T cell comprising a TCR that that binds an epitope sequence from Table 1A or Table 1B in complex with a corresponding MHC class I molecule according to Table 1A or Table 1B.

[00561] For example, the method can comprise administering to the subject a TCR or T cell comprising a TCR that can bind to an epitope sequence from column 2 (set 1) of Table 1A in complex with a corresponding MHC class I molecule from column 3 (set 1) in the same row of Table 1A. For example, the method can comprise administering to a TCR or T cell comprising a TCR that can bind to an epitope sequence from column 2 (set 1) of Table 1A in complex with a corresponding MHC class I molecule from column 3 (set 1) in the same row of Table 1A to a subject that expresses the corresponding MHC class I molecule from column 3 (set 1). For example, the method can comprise administering to the subject a TCR or T cell comprising a TCR that can bind to an epitope sequence from column 4 (set 2) of Table 1A in complex with a corresponding MHC class I molecule from column 5 (set 2) in the same row of Table 1A. For example, the method can comprise administering to a TCR or T cell comprising a TCR that can bind to an epitope sequence from column 4 (set 2) of Table 1A in complex with a corresponding MHC class I molecule from column 5 (set 2) in the same row of Table 1A to a subject that expresses the corresponding MHC class I molecule from column 5 (set 2). For example, the method can comprise administering to the

subject a TCR or T cell comprising a TCR that can bind to an epitope sequence from column 6 (set 3) of Table 1A in complex with a corresponding MHC class I molecule from column 7 (set 3) in the same row of Table 1A. For example, the method can comprise administering to a TCR or T cell comprising a TCR that can bind to an epitope sequence from column 6 (set 3) of Table 1A in complex with a corresponding MHC class I molecule from column 7 (set 3) in the same row of Table 1A to a subject that expresses the corresponding MHC class I molecule from column 7 (set 3).

[00562] For example, the method can comprise administering to the subject a TCR or T cell comprising a TCR that can bind to an epitope sequence from column 2 (set 1) of Table 1B in complex with a corresponding MHC class I molecule from column 3 (set 1) in the same row of Table 1B. For example, the method can comprise administering to a TCR or T cell comprising a TCR that can bind to an epitope sequence from column 2 (set 1) of Table 1B in complex with a corresponding MHC class I molecule from column 3 (set 1) in the same row of Table 1B to a subject that expresses the corresponding MHC class I molecule from column 3 (set 1). For example, the method can comprise administering to the subject a TCR or T cell comprising a TCR that can bind to an epitope sequence from column 4 (set 2) of Table 1B in complex with a corresponding MHC class I molecule from column 5 (set 2) in the same row of Table 1B. For example, the method can comprise administering to a TCR or T cell comprising a TCR that can bind to an epitope sequence from column 4 (set 2) of Table 1B in complex with a corresponding MHC class I molecule from column 5 (set 2) in the same row of Table 1B to a subject that expresses the corresponding MHC class I molecule from column 5 (set 2).

[00563] For example, the method can comprise administering to the subject a TCR or T cell comprising a TCR that can bind to an epitope sequence from column 2 (set 1) of Table 2Ai in complex with a corresponding MHC class II molecule from column 3 (set 1) in the same row of Table 2Ai. For example, the method can comprise administering to a TCR or T cell comprising a TCR that can bind to an epitope sequence from column 2 (set 1) of Table 2Ai in complex with a corresponding MHC class II molecule from column 3 (set 1) in the same row of Table 2Ai to a subject that expresses the corresponding MHC class II molecule from column 3 (set 1). For example, the method can comprise administering to the subject a TCR or T cell comprising a TCR that can bind to an epitope sequence from column 4 (set 2) of Table 2Ai in complex with a corresponding MHC class II molecule from column 5 (set 2) in the same row of Table 2Ai. For example, the method can comprise administering to a TCR or T cell comprising a TCR that can bind to an epitope sequence from column 4 (set 2) of Table 2Ai in complex with a corresponding MHC class II molecule from column 5 (set 2) in the same row of Table 2Ai to a subject that expresses the corresponding MHC class II molecule from column 5 (set 2). For example, the method can comprise administering to the subject a TCR or T cell comprising a TCR that can bind to an epitope sequence from the left column of Table 2Aii in complex with a corresponding MHC class II molecule from the right column in the same row of Table 2Aii.

[00564] In one embodiment, the antigenic peptide is a viral antigen. In another embodiment, the antigenic peptide is a non-mutated overexpressed antigen. In some embodiments, the viral antigen is derived from publicly disclosed information on the viral genetic information. In some embodiments, the viral antigen is derived from analysis of the viral genome to predict suitable epitopes for T cell activation. In some embodiments, the viral antigen is derived from analysis of the sequence of the viral genome in a MHC-peptide presentation prediction algorithm implemented in a computer processor. In some embodiments, the viral antigen is derived from analysis of the viral sequences in an MHC-peptide presentation prediction algorithm implemented in a computer processor that has been trained by a machine learning software, which predicts the likelihood of binding and presentation of an epitope by an MHC class I or an MHC class II antigen. In some embodiments, the MHC-peptide presentation predictor is *neonmhc2*.

[00565] In some embodiments, the MHC-peptide presentation prediction algorithm or MHC-peptide presentation predictor is NetMHCpan or NetMHCIIpan and in addition, further analyzed in MHC-peptide presentation predictor NetMHCpan or NetMHCIIpan for comparison. In some embodiments, a skilled artisan may use hidden markov model approach for MHC-peptide presentation prediction. In some embodiments, the peptide prediction model MARIA may be utilized. In some embodiments, the MHC-peptide presentation prediction algorithm or MHC-peptide presentation predictor used is not NetMHCpan or NetMHCIIpan. In some embodiments, the viral sequences are analyzed in MHC-peptide presentation prediction algorithm implemented in a computer processor where the MHC-peptide presentation predictor is *neonmhc 1* or *neonmhc2*, that refer respectively to class I and class II binding prediction. In some embodiments, the MHC-peptide presentation predictor model is RECON, which offers high quality MHC-peptide presentation prediction based on expression, processing and binding capabilities.

[00566] In one aspect, provided herein is a method of treating a viral disease in a subject caused by a coronavirus, comprising: administering to the subject a composition comprising one or more viral peptide antigens, wherein the viral peptide antigens are predicted to bind to an MHC class I or an MHC class II peptide of the subject, and are predicted to be presented by an antigen presenting cell to a T cell of the subject such that an antiviral response is initiated in the subject. In some embodiments, the viral antigen is derived from analysis of the sequence of the viral genome in a MHC-peptide presentation prediction algorithm implemented in a computer processor. In some embodiments, the viral antigen is derived from analysis of the viral sequences in an MHC-peptide presentation prediction algorithm implemented in a computer processor that has been trained by a machine learning software, which predicts the likelihood of binding and presentation of an epitope by an MHC class I or an MHC class II antigen. In some embodiments, the MHC-peptide presentation predictor is *neonmhc2*. In some embodiments, the method further comprises analyzing nucleic acid sequence derived from viral genome in an MHC-peptide presentation prediction model, comprising an algorithm implemented in a computer processor that has been trained by a machine learning software, wherein the MHC-peptide presentation prediction model predicts

the likelihood of binding and presentation of an epitope encoded by the viral genome by an MHC class I or an MHC class II antigen. In some embodiments, the method further comprises analyzing a biological sample from a subject for identification of the MHC class I and MHC class II repertoire, wherein the analyzing comprises analyzing by genome or whole exome sequencing or by analysis of proteins encoded by an HLA gene. In some embodiments, the method further comprises matching the epitopes predicted by the MHC-peptide presentation prediction model that have a high affinity for an MHC class I or an MHC class II peptide encoded by an HLA gene of the subject, and selecting one or more peptides that are predicted to bind an MHC peptide encoded by an HLA gene of the subject with a high affinity ranked by the MHC-peptide presentation prediction model. In some embodiments, the one or more peptides that are selected have been predicted to bind an MHC peptide encoded by an HLA gene of the subject with an affinity of at least 1000 nM. In some embodiments, the one or more peptides that are selected have been predicted to bind an MHC class I peptide encoded by an HLA gene of the subject with an affinity of at least 500 nM. In some embodiments, the one or more peptides that are selected have been predicted to bind an MHC class II peptide encoded by an HLA gene of the subject with an affinity of at least 1000 nM.

[00567] In some embodiments, the MHC-peptide presentation prediction model is programmed to provide a ranking order in decreasing order of a likelihood for a particular epitope or antigenic peptide to bind to an HLA allele that would present the peptide to a T cell receptor. In some embodiments, epitope sequences that have the highest likelihood of binding and being presented by an HLA are selected for preparing a therapeutic. In some embodiments, the selection of the HLA may be restricted by HLA expressed in a subject. In some embodiments, the selection of the HLA may be based on the prevalence (e.g., higher prevalence) of the allele in a population. In some embodiments the epitopes may be selected for preparing a therapeutic based on the higher likelihood for the peptide (epitope) of binding to and being presented by an HLA allele, e.g., an HLA allele of interest. In some embodiments, this % rank value may be determined by evaluating the percentile in which a query peptide scores for a specific allele compared to a fixed set of reference peptides (with a different set of reference peptides for class I and class II). In some embodiments the top 10% of the epitopes that have the highest likelihood of binding to an HLA allele may be selected. In some embodiments the top 2% of the epitopes that have the highest likelihood of binding to an HLA allele may be selected. In some embodiments the top 5% of the epitopes that have the highest likelihood of binding to an HLA allele may be selected. In some embodiments the top 8% of the epitopes that have the highest likelihood of binding to an HLA allele may be selected. In some embodiments the top 1% of the epitopes that have the highest likelihood of binding to an HLA allele may be selected. In some embodiments the top 0.5 % of the epitopes that have the highest likelihood of binding to an HLA allele may be selected. In some embodiments the top 0.1 % of the epitopes that have the highest likelihood of binding to an HLA allele may be selected. In some embodiments the top 0.01 % of the epitopes that have the highest likelihood of binding to an HLA allele may be selected. In some embodiments the selection of the cut off may be

dependent on the availability and number of epitopes predicted to have a high likelihood of binding to an HLA allele as determined by the prediction model.

[00568] In some embodiments, the subject may be infected by the virus. In some embodiments, the subject may be at risk of infection by the virus. In some embodiments, the virus is a coronavirus. In some embodiments, the coronavirus is selected from a SARS virus, a MERS coronavirus or a 2019 SARS CoV-2 virus. In some embodiments, the one or more viral peptide antigen comprises a peptide comprising at least 8 contiguous amino acids of a sequence in Table 1A, Table 1B, Table 1C, Table 2Ai, Table 2Aii, Table 2B, Table 9, Table 10, Table 11, Table 12, Table 14A, Table 14B, Table 15 or Table 16. In some embodiments, the one or more viral peptide antigen comprises a peptide comprising at least 7 contiguous amino acids of a sequence in Table 1A, Table 1B, Table 1C, Table 2Ai, Table 2Aii, Table 2B, Table 9, Table 10, Table 11, Table 12, Table 14A, Table 14B, Table 15 or Table 16. In some embodiments, the one or more viral peptide antigen comprises a peptide comprising at least 6 contiguous amino acids of a sequence in Table 1A, Table 1B, Table 1C, Table 2Ai, Table 2Aii, Table 2B, Table 9, Table 10, Table 11, Table 12, Table 14A, Table 14B, Table 15 or Table 16.

[00569] In one embodiment, the antigenic peptide is between about 5 to about 50 amino acids in length. In another embodiment, the antigenic peptide is between about 15 to about 35 amino acids in length. In another embodiment, the antigenic peptide is about 15 amino acids or less in length. In another embodiment, the antigenic peptide is between about 8 and about 11 amino acids in length. In another embodiment, the antigenic peptide is 9 or 10 amino acids in length. In one embodiment, the antigenic peptide binds major histocompatibility complex (MHC) class I. In another embodiment, the antigenic peptide binds MHC class I with a binding affinity of less than about 500 nM.

In one embodiment, the antigenic peptide is about 30 amino acids or less in length. In another embodiment, the antigenic peptide is between about 6 and about 25 amino acids in length. In another embodiment, the antigenic peptide is between about 15 and about 24 amino acids in length. In another embodiment, the antigenic peptide is between about 9 and about 15 amino acids in length. In one embodiment, the antigenic peptide binds MHC class II. In another embodiment, the antigenic peptide binds MHC class II with a binding affinity of less than about 1000 nM.

[00570] In one embodiment, the antigenic peptide further comprises flanking amino acids. In another embodiment, the flanking amino acids are not native flanking amino acids. In one embodiment, the antigenic peptide is linked to at least a second antigenic peptide. In another embodiment, the peptides are linked using a poly-glycine or poly-serine linker. In another embodiment, the second antigenic peptide binds MHC class I or class II with a binding affinity of less than about 1000 nM. In another embodiment, the second antigenic peptide binds MHC class I or class II with a binding affinity of less than about 500 nM. In another embodiment, both of the epitopes bind to human leukocyte antigen (HLA) -A, -B, -C, -DP, -DQ, or -DR. In another embodiment, the antigenic peptide binds a class I HLA and the second antigenic

peptide binds a class II HLA. In another embodiment, the antigenic peptide binds a class II HLA and the second antigenic peptide binds a class I HLA.

[00571] In one embodiment, the antigenic peptide further comprises modifications which increase in vivo half-life, cellular targeting, antigen uptake, antigen processing, MHC affinity, MHC stability, or antigen presentation. In another embodiment, the modification is conjugation to a carrier protein, conjugation to a ligand, conjugation to an antibody, PEGylation, polysialylation HESylation, recombinant PEG mimetics, Fc fusion, albumin fusion, nanoparticle attachment, nanoparticulate encapsulation, cholesterol fusion, iron fusion, acylation, amidation, glycosylation, side chain oxidation, phosphorylation, biotinylation, the addition of a surface active material, the addition of amino acid mimetics, or the addition of unnatural amino acids, for example, synthetic amino acids, or f-moc amino acids, D-amino acids N-methyl amino acids. In one embodiment, the cells that are targeted are antigen presenting cells. In another embodiment, the antigen presenting cells are dendritic cells. In another embodiment, the dendritic cells are targeted using DEC205, XCR1, CD197, CD80, CD86, CD123, CD209, CD273, CD283, CD289, CD184, CD85h, CD85j, CD85k, CD85d, CD85g, CD85a, CD141, CD11 c, CD83, TSLP receptor, or CD1a marker. In another embodiment, the dendritic cells are targeted using the CD141, DEC205, or XCR1 marker.

[00572] In one embodiment, provided herein is an *in vivo* delivery system comprising an antigenic peptide described herein. In another embodiment, the delivery system includes cell-penetrating peptides, nanoparticulate encapsulation, virus like particles, or liposomes. In another embodiment, the cell-penetrating peptide is TAT peptide, herpes simplex virus VP22, transportan, or Antp.

[00573] In one embodiment, provided herein is a cell comprising an antigenic peptide described herein. In another embodiment, the cell is an antigen presenting cell. In another embodiment, the cell is a dendritic cell.

[00574] In one embodiment, provided herein is a composition comprising an antigenic peptide described herein. In another embodiment, the composition comprises at least 2, at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, at least 10, at least 11, at least 12, at least 13, at least 14, at least 15, at least 16, at least 17, at least 18, at least 19, at least 20, at least 21, at least 22, at least 23, at least 24, at least 25, at least 26, at least 27, at least 28, at least 29, or at least 30 of the antigenic peptides comprising an epitope of Table 1A. In another embodiment, the composition comprises at least 2, at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, at least 10, at least 11, at least 12, at least 13, at least 14, at least 15, at least 16, at least 17, at least 18, at least 19, at least 20, at least 21, at least 22, at least 23, at least 24, at least 25, at least 26, at least 27, at least 28, at least 29, or at least 30 of the antigenic peptides comprising an epitope of Table 1B. In another embodiment, the composition comprises at least 2, at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, at least 10, at least 11, at least 12, at least 13, at least 14, at least 15, at least 16, at least 17, at least 18, at least 19, at least 20, at least 21, at least 22, at least 23, at least 24, at least 25, at least 26,at least 27, at least 28, at least 29, or at least 30 of the antigenic

peptides comprising an epitope of Table 2B. In another embodiment, the composition comprises between 2 and 20 antigenic peptides. In another embodiment, the composition further comprises at least 1, at least 2, at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, at least 10, at least 11, at least 12, at least 13, at least 14, at least 15, at least 16, at least 17, at least 18, at least 19, at least 20, at least 21, at least 22, at least 23, at least 24, or at least 25, at least 26, at least 27, at least 28, at least 29, or at least 30 additional antigenic peptides. In another embodiment, the composition comprises between about 4 and about 20 additional antigenic peptides. In another embodiment, the additional antigenic peptide is specific for coronavirus.

[00575] In one embodiment, provided herein is a polynucleotide encoding the antigenic peptide described herein. In another embodiment, the polynucleotide is RNA, optionally a self-amplifying RNA. In some embodiments the polynucleotide is DNA. In another embodiment, the RNA is modified to increase stability, increase cellular targeting, increase translation efficiency, adjuvanticity, cytosol accessibility, and/or decrease cytotoxicity. In another embodiment, the modification is conjugation to a carrier protein, conjugation to a ligand, conjugation to an antibody, codon optimization, increased GC-content, incorporation of modified nucleosides, incorporation of 5'-cap or cap analog, and/or incorporation of a poly-A sequence e.g., an unmasked poly-A sequence, or a disrupted poly-A sequence in which two segments of contiguous A sequences linked by a linker.

[00576] In one embodiment, provided herein is a cell comprising a polynucleotide described herein.

[00577] In one embodiment, provided herein is a vector comprising a polynucleotide described herein. In another embodiment, the polynucleotide is operably linked to a promoter. In another embodiment, the vector is a self-amplifying RNA replicon, plasmid, phage, transposon, cosmid, virus, or virion. In another embodiment, the vector is an adeno-associated virus, herpesvirus, lentivirus, or pseudotypes thereof

[00578] In one embodiment, provided herein is an in vivo delivery system comprising an polynucleotide described herein. In another embodiment, the delivery system includes spherical nucleic acids, viruses, virus-like particles, plasmids, bacterial plasmids, or nanoparticles.

[00579] In one embodiment, provided herein is a cell comprising a vector or delivery system described herein. In another embodiment, the cell is an antigen presenting cell. In another embodiment, the cell is a dendritic cell. In another embodiment, the cell is an immature dendritic cell.

[00580] In some embodiments, provided herein is a composition comprising at least one polynucleotide described herein. In some embodiments, provided herein is a composition comprising one or more antigenic peptides described herein in combination with one or more 2019 SARS CoV-2 vaccines (e.g., mRNA-based vaccines, DNA-based vaccines, AAV-based vaccines, protein-based vaccines). In some embodiments, provided herein is a composition comprising one or more polynucleotides encoding at least one antigenic peptide described herein in combination with one or more 2019 SARS CoV-2 vaccines (e.g., mRNA-based vaccines, DNA-based vaccines, AAV-based vaccines, protein-based vaccines). In some

embodiments, provided herein is a single polynucleotide encoding more than one antigenic peptide as described herein. In some embodiments, provided herein is a single polynucleotide encoding (i) at least one antigenic peptide as described herein and (ii) a 2019 SARS CoV-2 protein (e.g., S protein) and/or immunogenic fragments thereof (e.g., receptor binding domain (RBD) of S protein). In another embodiment, the composition comprises at least 2, at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, at least 10, at least 11, at least 12, at least 13, at least 14, at least 15, at least 16, at least 17, at least 18, at least 19, at least 20, at least 21, at least 22, at least 23, at least 24, at least 25, at least 26, at least 27, at least 28, at least 29, or at least 30 of the polynucleotides. In another embodiment, the composition comprises between about 2 and about 20 polynucleotides. In another embodiment, the composition further comprises at least 1, at least 2, at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, at least 10, at least 11, at least 12, at least 13, at least 14, at least 15, at least 16, at least 17, at least 18, at least 19, at least 20, at least 21, at least 22, at least 23, at least 24, at least 25, at least 26, at least 27, at least 28, at least 29, or at least 30 additional antigenic polynucleotides encoding for additional antigenic peptides. In another embodiment, the composition comprises between about 4 and about 20 additional antigenic polynucleotides. In another embodiment, the polynucleotides and the additional antigenic polynucleotides are linked. In another embodiment, the polynucleotides are linked using nucleic acids that encode a poly-glycine or poly-serine linker.

[00581] In one embodiment, provided herein is a T cell receptor (TCR) capable of binding at least one antigenic peptide described herein. In another embodiment, the TCR is capable of binding the antigenic peptide in the context of MHC class I or class II.

[00582] In one embodiment, provided herein is a chimeric antigen receptor comprising: (i) a T cell activation molecule; (ii) a transmembrane region; and (iii) an antigen recognition moiety capable of binding an antigenic peptide described herein. In another embodiment, CD3-zeta is the T cell activation molecule. In another embodiment, the chimeric antigen receptor further comprises at least one costimulatory signaling domain. In another embodiment, the signaling domain is CD28, 4-1BB, ICOS, OX40, ITAM, or Fc epsilon RI-gamma. In another embodiment, the antigen recognition moiety is capable of binding the antigenic peptide in the context of MHC class I or class II. In another embodiment, the chimeric antigen receptor comprises the CD3-zeta, CD28, CTLA-4, ICOS, BTLA, KIR, LAG3, CD137, OX40, CD27, CD4OL, Tim-3, A2aR, or PD-1 transmembrane region.

[00583] In one embodiment, provided herein is a T cell comprising the T cell receptor or chimeric antigen receptor described herein. In one embodiment, the T cell is a helper or cytotoxic T cell.

[00584] In one embodiment, provided herein is a nucleic acid comprising a promoter operably linked to a polynucleotide encoding a T cell receptor described herein. In another embodiment, the TCR is capable of binding the at least one antigenic peptide in the context of major histocompatibility complex (MHC) class I or class II. In one embodiment, the nucleic acid comprises a promoter operably linked to a polynucleotide

encoding a chimeric antigen receptor described herein. In another embodiment, the antigen recognition moiety is capable of binding the at least one antigenic peptide in the context of major histocompatibility complex (MHC) class I or class II.

[00585] In one embodiment, provided herein is an antibody capable of binding a peptide comprising an epitope of Table 1A, Table 1B, Table 1C, Table 2Ai, Table 2Aii, Table 2B, Table 9, Table 10, Table 11, Table 12, Table 14A, Table 14B, Table 15 or Table 16. In one embodiment, provided herein is an antibody capable of binding a peptide comprising an epitope of Table 1B. In one embodiment, provided herein is an antibody capable of binding a peptide comprising an epitope of Table 2Ai or Table 2Aii.

[00586] In one embodiment, provided herein is a modified cell transfected or transduced with a nucleic acid described herein. In one embodiment, the modified cell is a T cell, tumor infiltrating lymphocyte, NK-T cell, TCR-expressing cell, CD4+ T cell, CD8+ T cell, or NK cell.

[00587] In one embodiment, provided herein is a composition comprising a T cell receptor or chimeric antigen receptor described herein. In another embodiment, a composition comprises autologous patient T cells containing a T cell receptor or chimeric antigen receptor described herein. In another embodiment, the composition further comprises an immune checkpoint inhibitor. In another embodiment, the composition further comprises at least two immune checkpoint inhibitors. In another embodiment, each of the immune checkpoint inhibitors inhibits a checkpoint protein selected from the group consisting of CTLA-4, PDL1, PDL2, PD1, B7-H3, B7-H4, BTLA, HVEM, TIM3, GAL9, LAG3, VISTA, KIR, 2B4, CD160, CGEN-15049, CLIK 1, CHK2, A2aR, and B-7 family ligands or a combination thereof. In another embodiment, each of the immune checkpoint inhibitors interacts with a ligand of a checkpoint protein selected from the group consisting of CTLA-4, PDL1, PDL2, PD1, B7-H3, B7-H4, BTLA, HVEM, TIM3, GAL9, LAG3, VISTA, KIR, 2B4, CD160, CGEN-15049, CHK 1, CHK2, A2aR, and B-7 family ligands or a combination thereof.

[00588] In one embodiment, the composition further comprises an immune modulator or adjuvant. In another embodiment, the immune modulator is a co-stimulatory ligand, a TNF ligand, an Ig superfamily ligand, CD28, CD80, CD86, ICOS, CD4OL, OX40, CD27, GITR, CD30, DR3, CD69, or 4-1BB. In another embodiment, the immune modulator is at least one an infected cell extract. In another embodiment, the infected cell is autologous to the subject in need of the composition. In another embodiment, the infected cell has undergone lysis or been exposed to UV radiation. In another embodiment, the composition further comprises an adjuvant. In another embodiment, the adjuvant is selected from the group consisting of: Poly(I:C), Poly-ICLC, STING agonist, 1018 ISS, aluminum salts, Amplivax, AS15, BCG, CP-870,893, CpG7909, CyaA, dSLIM, GM-CSF, IC30, IC31, Imiquimod, ImuFact IMP321, IS Patch, ISS, ISCOMATRIX, JuvImmune, LipoVac, MF59, monophosphoryl lipid A, Montanide IMS 1312 VG, Montanide ISA 206 VG, Montanide ISA 50 V2, Montanide ISA 51 VG, OK-432, OM-174, OM-197-MP-EC, ISA-TLR2 agonist, ONTAK, PepTel®. vector system, PLG microparticles, resiquimod, SRL172,

virosomes and other virus-like particles, YF-17D, VEGF trap, R848, beta-glucan, Pam3Cys, Pam3CSK4, acrylic or methacrylic polymers, copolymers of maleic anhydride, and QS21 stimulon. In another embodiment, the adjuvant induces a humoral when administered to a subject. In another embodiment, the adjuvant induces a T helper cell type 1 when administered to a subject.

[00589] In one embodiment, provided herein is a method of inhibiting infection by a virus by administering to a subject who has a likelihood of getting infected by the virus, a vaccine composition comprising one or more peptides comprising at least 8 contiguous amino acids from the epitopes defined in Table 1A, Table 1B, Table 1C, Table 2Ai, Table 2Aii or Table 2B, comprising contacting a cell with a peptide, polynucleotide, delivery system, vector, composition, antibody, or cells of the present disclosure.

[00590] In one embodiment, provided herein is a method of treating a viral infection specifically, a coronaviral infection, for example a 2019 SARS CoV-2 infection by enhancing, or prolonging an antiviral response in a subject in need thereof comprising administering to the subject the peptide, polynucleotide, vector, composition, antibody, or cells described herein.

[00591] In one embodiment, the subject is a human. In another embodiment, the subject has a viral infection. In one embodiment, the subject is infected by a respiratory virus, such as an acute respiratory virus, for example, a SARS-like virus or a MERS or MERS-like virus, or more specifically, a coronavirus of the 2019 SARS CoV-2 strain. In some embodiments, the subject is infected with a 2019 SARS CoV-2 coronavirus. In some embodiments, the subject has been detectably infected with the 2019 SARS CoV-2 coronavirus. In some embodiments, the subject is asymptomatic. In some embodiments, the subject is symptomatic. In some embodiments, the subject is not detected to have been infected by a 2019 SARS CoV-2 virus or a related virus, but the subject is in close proximity of an infected person, in an infected area or otherwise at risk of infection.

[00592] In one embodiment of the method, a peptide is administered. In another embodiment, the administration is systemic. In another embodiment of the method, a polynucleotide, optionally RNA, is administered. In one embodiment, the polynucleotide is administered parenterally. In one embodiment, the polynucleotide is administered intravenously. In another embodiment, the polynucleotide is administered intradermally or intramuscularly, or subcutaneously. In one embodiment, the polynucleotide is administered intramuscularly. In one embodiment of the method, a cell is administered. In another embodiment, the cell is a T cell or dendritic cell. In another embodiment, the peptide or polynucleotide comprises an antigen presenting cell targeting moiety.

[00593] In one embodiment, the peptide, polynucleotide, vector, composition, or cells is administered prior to administering concurrent with another therapy, such as another antiviral therapy. In another embodiment, the peptide, polynucleotide, vector, composition, or cells is administered before or after the another antiviral therapy. In another embodiment, administration of the another antiviral therapy is continued throughout antigen peptide, polynucleotide, vector, composition, or cell therapy.

[00594] In one embodiment of the method, an additional agent is administered. In another embodiment, the agent is a chemotherapeutic agent, an immunomodulatory drug, an immune metabolism modifying drug, a targeted therapy, radiation an anti-angiogenesis agent, or an agent that reduces immune-suppression. In another embodiment, the administration of a pharmaceutical composition described herein elicits or promotes a CD4+ T cell immune response. In another embodiment, the administration of a pharmaceutical composition described herein elicits or promotes a CD4+ T cell immune response and a CD8+ T cell immune response.

[00595] In another embodiment, the patient received a chemotherapeutic agent, an immunomodulatory drug, an immune metabolism modifying drug, targeted therapy or radiation prior to and/or during receipt of the antigen peptide or nucleic acid vaccine. In another embodiment, the autologous T cells are obtained from a patient that has already received at least one round of T cell therapy containing an antigen. In another embodiment, the method further comprises adoptive T cell therapy. In another embodiment, the adoptive T cell therapy comprises autologous T cells. In another embodiment, the autologous T cells are targeted against viral antigens. In another embodiment, the adoptive T cell therapy further comprises allogenic T cells. In another embodiment, the allogenic T cells are targeted against viral antigens.

[00596] In one embodiment, provided herein is a method for evaluating the efficacy of treatment comprising: (i) measuring the number or concentration of target cells in a first sample obtained from the subject before administering the modified cell, (ii) measuring the number or concentration of target cells in a second sample obtained from the subject after administration of the modified cell, and (iii) determining an increase or decrease of the number or concentration of target cells in the second sample compared to the number or concentration of target cells in the first sample. In another embodiment, the treatment efficacy is determined by monitoring a clinical outcome; an increase, enhancement or prolongation of antiviral activity by T cells; an increase in the number of antiviral T cells or activated T cells as compared with the number prior to treatment; B cell activity; CD4 T cell activity; or a combination thereof. In another embodiment, the treatment efficacy is determined by monitoring a biomarker. In another embodiment, the treatment effect is predicted by presence of T cells or by presence of a gene signature indicating T cell inflammation or a combination thereof.

[00597] Provided herein a pharmaceutical composition comprising: one or more polypeptides having an amino acid sequence of any one of the sequences depicted in column 2 of Table 11 and 12; or one or more recombinant polynucleotide constructs each encoding a polypeptide having an amino acid sequence of any one of the sequences depicted in column 2 of Table 11 and 12.

[00598] In some embodiments, the one or more polypeptides comprises at least 2, 3, 4, 5, 6, 7 or 8 different polypeptides having an amino acid sequence of any one of the sequences depicted in column 2 of Table 11 and 12; or wherein the one or more recombinant polynucleotide constructs comprises at least 2, 3, 4, 5, 6, 7 or 8 recombinant polynucleotide constructs each encoding a different polypeptide having an amino acid

sequence of any one of the sequences depicted in column 2 of Table 11 and 12. In some embodiments, the pharmaceutical composition comprises at least 8 recombinant polynucleotide strings. In some embodiments, the one or more recombinant polynucleotide strings encoding a plurality of coronavirus peptide antigens, comprises a sequence selected from a group of sequences depicted in SEQ ID RS C1n, RS C2n, RS C3n, RSC4n, RS C5n, RS C6n, RS C7n, and RS C8n, or a sequence that is at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, or 100% sequence identity to any one of the above. In some embodiments, the recombinant polynucleotide construct comprises an mRNA. In some embodiments, the recombinant polynucleotide construct is an mRNA. In some embodiments, the pharmaceutical composition further comprises one or more lipid components. In some embodiments, the one or more lipids comprise a lipid nanoparticle (LNP). In some embodiments, the LNP encapsulates the recombinant polynucleotide construct. In some embodiments, the pharmaceutical composition is administered to a subject in need thereof.

[00599] Provided herein is a method of treating COVID in a subject in need thereof, comprising administering to the subject a pharmaceutical composition described above. In some embodiments, the pharmaceutical composition is administered in addition to one or more therapeutic for COVID. In some embodiments, the pharmaceutical composition is administered in combination with one or more polypeptides having an amino acid sequence of a 2019 SARS CoV-2 spike protein or fragment thereof; or one or more recombinant polynucleotide constructs encoding a 2019 SARS CoV-2 spike protein or fragment thereof. In some embodiments, the 2019 SARS CoV-2 spike protein or fragment thereof is a SARS-CoV-2 spike protein or a fragment thereof. In some embodiments, the pharmaceutical composition is administered 2-10 weeks after a first administration of the 2019 SARS CoV-2 spike protein or fragment thereof. In some embodiments, the pharmaceutical composition is administered 1-6 months after a first administration of the 2019 SARS CoV-2 spike protein or fragment thereof. In some embodiments, the pharmaceutical composition is administered simultaneously with an administration of the 2019 SARS CoV-2 spike protein or fragment thereof. In some embodiments, the pharmaceutical composition is administered 2-10 weeks before an administration of the 2019 SARS CoV-2 spike protein or fragment thereof. In some embodiments, the pharmaceutical composition is administered 2-10 weeks after the first administration of vaccine comprising a SARS-CoV-2 spike protein or polynucleotide encoding the same. In some embodiments, the pharmaceutical composition is administered 1-6 months after the first administration of a SARS-CoV-2 spike protein or polynucleotide encoding the same. In some embodiments, the pharmaceutical composition is administered simultaneously with the administration of a SARS-CoV-2 spike protein or polynucleotide encoding the same. In some embodiments, the pharmaceutical composition is administered prophylactically. In some embodiments, the pharmaceutical composition is administered once every 1, 2, 3, 4, 5, 6 or more weeks.

[00600] Provided herein is an use of any one of the compositions described herein for preparing a therapeutic for treating or preventing a respiratory viral infection caused by 2019 SARS CoV-2 virus.

[00601] Where aspects or embodiments of the present disclosure are described in terms of a Markush group or other grouping of alternatives, the present disclosure encompasses not only the entire group listed as a whole, but also each member of the group individually and all possible subgroups of the main group, and also the main group absent one or more of the group members. The present disclosure also envisages the explicit exclusion of one or more of any of the group members in the embodiments of the present disclosure.

BRIEF DESCRIPTION OF THE DRAWINGS

[00602] FIG. 1A depicts an exemplary flow diagram of a method to identify peptides most relevant to the generation of CD8+ T cell responses against the viral epitopes described herein.

[00603] FIG. 1B shows a graphic representation of the SARS-CoV 2 genome.

[00604] FIG. 2 depicts exemplary graphs of results obtained using a T cell epitope prediction algorithm applied to class I peptide-MHC allele pairs in a validation dataset and comparison of the computed percent-ranks of these pairs with reported MHC-binding assay results. The percent-ranks of peptide-MHC allele pairs which had a binary "Positive" result in the MHC-binding assay were significantly lower than pairs with a "Negative" result. In the more granular positive results, stronger assay results (low <intermediate < high) were associated with significantly lower percent-ranks.

[00605] FIG. 3 depicts experimental validation of HLA-A02:01 predicted epitopes from 2019 SARS CoV-2 in human T cell induction assays. 23 peptides that were predicted to be high binders to HLA-A02:01 (see Table 4 of Example 8) were synthesized and assayed in T cell inductions using PBMCs from three human donors. Epitopes were considered to be immunogenic if at least one donor raised a T cell response to the peptide as determined by pMHC multimer technology. Representative flow cytometry plots of pMHC staining using peptides from Table 4 of Example 8 are shown. Multimer positive populations are circled, with the frequency of multimer positive CD8+ T cells shown in the upper right-hand corner of each plot.

[00606] FIG. 4A depicts exemplary graphs of cumulative USA population coverage of HLA alleles for the indicated peptides predicted to be MHC class I epitopes (left) and the cumulative USA population coverage of HLA alleles for 25mer peptides predicted to be MHC class II epitopes (right).

[00607] FIG. 4B depicts a small number of predicted multi-allele binding epitopes from individual 2019 SARS- CoV-2 proteins (alternatively termed 2019-CoV-2 proteins) can achieve broad population coverage. The upper panel shows cumulative HLA-I coverage for USA, EUR, and API populations versus the number of included prioritized HLA-I epitopes for M, N, and S proteins, respectively. Peptide sequences corresponding to the upper panel are shown in Table 6. The lower panel shows cumulative HLA-II coverage for each population versus the number of included prioritized HLA-II 25mers for M, N, and S proteins, respectively. Peptide sequences corresponding to the lower panel are shown in Table 7.

[00608] FIG. 5 depicts results from analysis of publicly available proteomic datasets showing relative 2019 SARS CoV-2 protein expression levels that can be leveraged to prioritize potential vaccine targets. Three datasets examining the proteomic response to 2019 SARS CoV-2 infection (alternatively termed 2019 SARS CoV-2 infection) were re-analyzed and protein abundance was estimated by spectral counts normalized to protein length. Any annotated ORF not shown in the figure was not detected in these proteomic studies. Across all three studies, the nucleocapsid protein is the most abundant protein during 2019 SARS CoV-2 infection.

[00609] FIG. 6A depicts a graphical representation of a string construct described as group 1, also described in Tables 9 and 11.

[00610] FIG. 6B provides a detailed and expanded view of the constructs in **FIG. 6A**.

[00611] FIG. 7A depicts a graphical representation of a string construct described as group 2, also described in Tables 10 and 12.

[00612] FIG. 7B provides a detailed and expanded view of the constructs in **FIG. 7A**.

[00613] FIG. 8Ai-8Aii show characterization of BNT mRNA vaccine-induced T cells on a single epitope level. Included data shows epitope responsive T cells for the indicated epitopes in three different participants. The vaccine comprises mRNA encoding a SARS-CoV-2 spike protein of 2019 SARS COV-2 encapsulated in a lipid nanoparticle.

[00614] FIG. 8B shows multimer positive CD8+ cells analysed by flow cytometry for cell surface markers, CCR7, CD45RA, CD3, PD-1, CD38, HLA-DR, CD28 and CD27.

[00615] FIG. 8C shows a mRNA vaccine including the spike proteins S1 and S2, with indicated epitope regions that can bind to specific MHC molecules indicated by the solid shapes along the length, corresponding HLA allele to which it binds is indicated below.

[00616] FIG. 8D shows time course of T cell responses after vaccination of patients with Spike protein mRNA vaccines at different doses (10, 20 and 30 micrograms as indicated). Upper panel shows CD4+ T cell responses, indicated by IFN-g expression using ELISPOT assay. Lower panel shows CD8+ T cell responses, indicated by IFN-g expression using ELISPOT assay. CEF and CEFT are controls CMV, EBV and influenza pools.

[00617] FIG. 8E shows time course of CD4+ T cells and CD8+ T cell responses in older adult population who are administered Spike protein mRNA vaccine (30 microgram each).

[00618] FIG. 9 shows design of vaccine strings comprising ORF-1ab epitopes, with specific use of MS-based HLA-I cleavage predictor information in ordering the epitopes. The design utilizes minimum number of linker sequences.

[00619] FIG. 10A shows experimental design for validating immunogenicity of the string vaccine compositions in an animal model.

[00620] FIG. 10B shows a representative experimental set up of an animal model study to determine the immunogenicity of the four CorVac 2.0 strings when administered in vivo. 5 Groups (16 animals/8-10 take down at d14/8-10 at d28).

[00621] FIG. 11A is a schematic of different dosing schedules for spike vaccine (BNT162b2) and CorVac 2.0.

[00622] FIG. 11B depicts a schematic of an animal study for determining the immune responses elicited by different formulation ratios and doses of CorVac 2.0 strings with BNT162b2 in HLA-A02 transgenic mice.

[00623] FIG. 11C depicts a schematic of an animal study for determining the immune responses elicited by different formulation ratios and doses of CorVac 2.0 strings with BNT162b2 in transgenic mice expressing human ACE2.

[00624] FIG. 12A demonstrates sequence variants and mutants across the spike protein in various SARS CoV-2 isolates, and the respective mapping of the vaccine epitope sequences.

[00625] FIG. 12B is a chart showing spike variant frequencies over time.

[00626] FIG. 13A demonstrates sequence variants and mutants across the nucleocapsid protein in various SARS CoV-2 isolates, and the respective mapping of the vaccine epitope sequences.

[00627] FIG. 13B is a chart showing nucleocapsid variant frequencies over time.

[00628] FIG. 14 demonstrates sequence variants and mutants across the membrane protein in various SARS CoV-2 isolates, and the respective mapping of the vaccine epitope sequences.

[00629] FIG. 15 demonstrates sequence variants and mutants across the NSP1 protein in various SARS CoV-2 isolates, and the respective mapping of the vaccine epitope sequences.

[00630] FIG. 16 demonstrates sequence variants and mutants across the NSP2 protein in various SARS CoV-2 isolates, and the respective mapping of the vaccine epitope sequences.

[00631] FIG. 17 demonstrates sequence variants and mutants across the NSP3 protein in various SARS CoV-2 isolates, and the respective mapping of the vaccine epitope sequences.

[00632] FIG. 18 demonstrates sequence variants and mutants across the NSP4 protein in various SARS CoV-2 isolates, and the respective mapping of the vaccine epitope sequences.

[00633] FIG. 19A shows CorVac 2.0 – String Design for maximal CD8 and CD4 T cell responses.

[00634] FIG. 19B shows RS-C7 is enriched for known ORF1ab T cell epitopes and avoids most variants of concern/variants of interest (VOC/VOI) mutations.

[00635] FIG. 19C shows RS-C7 is enriched for known nucleocapsid and membrane T cell epitopes and avoids most variants of concern/variants of interest (VOC/VOI) mutations.

[00636] FIG. 20 shows an exemplary experimental set up outlined to test the polynucleotide strings for peptide presentation in complex with the MHC protein.

[00637] FIG. 21 depicts representative data showing an exemplary target epitope presentation verified by mass spectrometry; endogenous, in an experimental set up when the epitope is expressed on A375 cells expressing endogenous HLAs; synthetic, in an experimental set up when the epitope is expressed in cells expressing exogenous HLA.

[00638] FIG. 22 shows a diagrammatic representation of a list of epitopes identified by the above methods using mass spectrometry. The identified epitopes span the viral genome, covering epitopes of the nucleocapsid protein, ORF1ab domains and the membrane protein.

[00639] FIG. 23 shows a representation of a map of all identified CorVac 2.0 epitopes across the viral nucleocapsid, ORF1ab and membrane regions.

[00640] FIG. 24 shows representative data demonstrating Corvac 2.0 strings elicit T cell responses from the nucleocapsid region after one injection at day 0 in BALB/C mice. Immunoreactive T cells are determined by elispot assay (# spots/1 x 10^6 cells). Statistical significance determined by two-way ANOVA with Sidak's multiple comparisons tests.

[00641] FIG. 25 shows representative data demonstrating Corvac 2.0 strings elicit T cell responses from the membrane region. after one injection at day 0 in BALB/C mice. Immunoreactive T cells are determined by elispot assay (# spots/1 x 10^6 cells). Statistical significance determined by two-way ANOVA with Sidak's multiple comparisons tests.

[00642] FIG. 26 shows a graphical representation of the summary of performances of the different strings tested thus far. Number of stars are proportional to the statistical significance of immunogenicity of each string compared to the vehicle control.

[00643] FIG. 27 shows representative data demonstrating Corvac 2.0 strings elicit T cell responses to epitopes from the nucleocapsid region after one injection at day 0 in HLA-A2tg mice (mice that express humanized HLA-A02:01). T cell immunoreactivity was determined by ELISpot assay (# spots/1 x 10^6 cells). Statistical significance was determined by two-way ANOVA with Sidak's multiple comparisons tests. Data is from mice at day 28 after injection of the string composition.

[00644] FIG. 28 shows representative data demonstrating Corvac 2.0 strings elicit T cell responses to epitopes from the membrane region after one injection at day 0 in HLA-A2tg mice (mice that express humanized HLA-A02:01). T cell immunoreactivity was determined by ELISpot assay (# spots/1 x 10^6 cells). Statistical significance was determined by two-way ANOVA with Sidak's multiple comparisons tests. Data from mice at day 28 after injection of the string composition.

[00645] FIG. 29 shows representative data demonstrating Corvac 2.0 strings elicit T cell responses to epitopes from the ORF1ab region after one injection at day 0 in HLA-A2tg mice (mice that express humanized HLA-A02:01). T cell immunoreactivity was determined by ELISpot assay (# spots/1 x 10^6 cells). Statistical significance was determined by two-way ANOVA with Sidak's multiple comparisons tests. Data is from mice at day 28 after injection of the string composition.

[00646] FIG. 30 is a graphical representation summarizing the statistical significance of immunogenicity of the different strings tested in the HLA-A02 transgenic mouse model compared to vehicle controls and results depicted in **FIG. 27, FIG. 28** and **FIG. 29**. The representation indicates RS-C7 has the most T cell responses across pools in the HLA-A02 transgenic mouse model.

[00647] FIG. 31 shows a graphical representation of the RS-C7 string design showing regions of the string that elicited immune responses as determined by ELISpot assay and epitopes that were confirmed process and presented by HLA using mass spectrometry.

[00648] FIG. 32A shows a graphical representation of the string designs where the encoded nucleocapsid sequence contain, inter alia, tiled overlapping 15-mer epitope sequences with 11 amino acid overlaps.

[00649] FIG. 32B shows a graphical representation of the string designs where the encoded membrane sequence contain, inter alia, tiled 15-mer sequences with 11 amino acid overlaps.

[00650] FIG. 32C shows a graphical representation of the string designs where the encoded ORF 1ab sequence contain, inter alia, tiled 15-mer sequences with 11 amino acid overlaps.

[00651] FIG. 32D shows results from the experimental design shown in **FIG. 10B** indicating CorVac 2.0 strings do not raise T cell responses from the ORF1ab region in the BALB/C mouse model. In contrast, results shown in **FIG. 29**, (left, pool 11), (right, pool 12) indicates CorVac 2.0 strings do raise T cell responses from the ORF1ab region in an HLA-A02 transgenic mouse model. Statistical significance determined by one-way ANOVA with Sidak's multiple comparisons tests.

[00652] FIG. 32E is a graphical representation of the summary of performances of the different strings tested in the BALB/C mouse model and demonstrates that RS-C7 has the most T cell responses across pools in the BALB/C mouse model. The RS-C7 string raised the most T cell responses across pools in the BALB/C mouse model.

[00653] FIG. 33 is a graphical representation showing that the CorVac 2.0 String C7 epitopes overlap with few or no regions with mutations of variants of concern.

[00654] FIG. 34A depicts data related to assessment of B cell responses by ELISA for S1 binding antibodies in mouse serum at the indicated timepoints and serum dilutions using the indicated dosing schedules according to **FIG. 11A**.

[00655] FIG. 34B depicts data related to assessment of B cell responses by ELISA for NP binding antibodies in mouse serum at the indicated timepoints and serum dilutions using the indicated dosing schedules according to **FIG. 11A**.

[00656] FIG. 35 shows results from ELISA for serum IgG concentrations at day 14, 21 and 35 after treatment (injection) with saline control (NaCl), BNT162b2, the C7 string, or the combinations as indicated using the dosing schedules according to **FIG. 11A**. Results indicate that inclusion of CorVac 2.0 in a co-formulation setting does not impact Spike-specific Ab development.

[00657] FIG. 36 shows results from a pseudovirus neutralization test (pVNT) using viral particles pseudotyped with VSV envelope containing SARS-CoV-2 spike protein at day 14, 21 and 35 after treatment (injection) with saline control (NaCl), BNT162b2, the C7 string, or the combinations as indicated using the dosing schedules according to **FIG. 11A**. Results indicate that CorVac 2.0 does not negatively impact formation of neutralizing antibodies against the SARS-CoV-2 viral protein (Wuhan strain).

[00658] FIG. 37A shows lymph node phenotyping results at day 35 using the dosing schedules according to **FIG. 11A**. B cell populations are indicated by the % of CD19+ cells of the CD45+ cell population. Percentage of activated B cells was determined by the % of IgD-CD3-CD4-CD8- cells; switched B cell percentage is determined by the % of Activated/B220+IgM-CD19+CD138- cells; and % GC B cells was determined by the % of Activated/B220+IgM-CD19+CD138- cells of the total CD45+ cells in the population. Results indicate that inclusion of CorVac 2.0 in a 1:1 coformulation does not affect BNT162b2-driven B cell response, and slightly enhances it.

[00659] FIG. 37B shows lymph node phenotyping results at day 35 using the dosing schedules according to **FIG. 11A**. Results indicate that inclusion of CorVac 2.0 maintains the frequency of Tfh cells in the lymph node.

[00660] FIG. 38 depicts activation of splenocyte cells that have been stimulated with peptides present in BNT162b2 on day 35 and assessed by flow cytometry for the presence of the activation marker CD69 on bulk T cell population (left panel) or CD4 T cells (middle panel) or CD8 T cells (right panel) using the dosing schedules according to **FIG. 11A**. Results indicate that activation of T cells when restimulated with spike peptides (spike 1 pool) are increased in vaccine groups that have BNT162b2 (Group 2) and not inhibited in groups that have both CorVac 2.0 and BNT162b2 (Groups 4-7).

[00661] FIG. 39 depicts activation of splenocyte cells that have been stimulated with peptides present in BNT162b2 on day 35 and assessed by flow cytometry for the presence of the activation marker IFN-gamma on bulk T cell population (left panel) or CD8 T cells (middle panel) or CD4 T cells (right panel) using the dosing schedules according to **FIG. 11A**. Results indicate that activation of T cells when restimulated with spike peptides (spike 1 pool) are increased in vaccine groups that have BNT162b2 (Group 2) and not inhibited in groups that have both CorVac 2.0 and BNT162b2 (Groups 4-7) in the CD3 T cell population and CD8 T cell population, but not significantly increased in any groups in the CD4 T cell population.

[00662] FIG. 40 depicts activation of splenocyte cells that have been stimulated with peptides present in BNT162b2 on day 35 and assessed by flow cytometry for the presence of the activation marker CD69 on bulk T cell population (left panel) or CD4 T cells (middle panel) or CD8 T cells (right panel) using the dosing schedules according to **FIG. 11A**. Results indicate that activation of T cells when restimulated with spike peptides (spike 2 pool) are increased most dramatically in groups that have been given the BNT162b2 co-formulated in the same LNP (Groups 5-7).

[00663] FIG. 41A depicts activation of splenocyte cells that have been stimulated with peptides present in the nucleocapsid sequence present in the CorVac 2.0 string on day 35 and assessed by flow cytometry for the presence of the activation marker CD69 on bulk T cell population (left panel) or CD4 T cells (middle panel) or CD8 T cells (right panel) using the dosing schedules according to **FIG. 11A**. Results indicate that activation of T cells when restimulated with nucleocapsid peptides are increased in vaccine groups that have CorVac 2.0 (Group 3) and separately formulated and co-formulated strings of both BNT162b2 and CorVac 2.0 (Group 4 and 5) in the CD3 T cell population and CD8 T cell population, and modestly in the CD4 T cell population.

[00664] FIG. 41B depicts activation of splenocyte cells that have been stimulated with peptides present in the nucleocapsid sequence present in the CorVac 2.0 string on day 35 and assessed by flow cytometry for the presence of the functional marker IFN-gamma on bulk T cell population (left panel) or CD8 T cells (middle panel) or CD4 T cells (right panel) using the dosing schedules according to **FIG. 11A**. Results indicate that production of INF-gamma in T cells when restimulated with nucleocapsid peptides are increased in vaccine groups that have CorVac 2.0 (Group 3) and co-formulated strings of both BNT162b2 and CorVac 2.0 at the same ratio (Group 5) in the CD3 T cell population and CD4 T cell population, and modestly in the CD8 T cell population.

[00665] FIG. 42 depicts results showing Spike (N and C-terminal) antigen-specific T cell responses by ELISpot assay on samples from day 35 using the dosing schedules according to **FIG. 11A**. Results indicate that Ag-specific Spike T-cell responses are not inhibited by addition of CorVac 2.0 and are slightly enhanced by the 1:1 co-formulation.

[00666] FIG. 43 depicts results showing nucleocapsid, membraneand Orf1ab antigen-specific T cell responses by ELISpot assay on samples from day 35 using the dosing schedules according to **FIG. 11A**. Results indicate that CorVac 2.0 string responses are stronger in the CorVac 2.0 only group but are still present when CorVac 2.0 string is combined with BNT162b2.

[00667] FIG. 44 depicts the effect of BNT162b2 and CorVac 2.0 alone or in combination on the anti-Spike antigen T cell responses by ELISPOT at day 14 and day 35 using the dosing schedules according to **FIG. 11A**. The kinetic study depicted herein indicates that Spike T cell responses increase after boost in all groups.

[00668] FIG. 45 depicts the effect of booster doses on the CorVac 2.0 immune responses at day 14 and day 35 using the dosing schedules according to **FIG. 11A**. The kinetic study depicted herein indicates that CorVac 2.0 responses did not increase after boost.

[00669] FIG. 46 depicts polyfunctionality of CD4 and CD8 responses elicited by BNT162b2 and CorVac 2.0 using the dosing schedules according to **FIG. 11A** after restimulation with cognate peptide groups (Spike N-term, Spike C-term, Nucleocapsid and Membrane, as noted) assayed by flow cytometry. CD4 and CD8 T cell responses were determined to be polyfunctional by the expression of IFNγ+IL-2+TNFα+.

[00670] FIG. 47 shows a graphical representation that summarizes the effects of the different formulations indicated on the left-hand column on spike N-terminal antigen specific responses by CD4/CD8 cells using the dosing schedules according to **FIG. 11A**. The number of stars is proportional to the statistical significance and intensity of the response compared to the vehicle control.

[00671] FIG. 48 shows a graphical representation summarizes the effects of the different formulations indicated on the left-hand column on spike C-terminal antigen specific responses by CD4/CD8 cells using the dosing schedules according to **FIG. 11A**. The number of stars is proportional to the statistical significance and intensity of the response compared to the vehicle control.

[00672] FIG. 49 shows a graphical representation that summarizes the effects of the different formulations indicated on the left-hand column on nucleocapsid antigen specific responses by CD4/CD8 cells using the dosing schedules according to **FIG. 11A**. The number of start is proportional to the statistical significance and intensity of the response compared to the vehicle control.

[00673] FIG. 50 shows a graphical representation that summarizes the effects of the different formulations indicated on the left-hand column on membrane antigen specific responses by CD4/CD8 cells using the dosing schedules according to **FIG. 11A**. The number of stars is proportional to the statistical significance and intensity of the response compared to the vehicle control.

[00674] FIG. 51 depicts a schematic of an animal study for determining the immune responses elicited by different formulation ratios and doses of CorVac 2.0 strings with BNT162b2 in transgenic mice expressing human ACE2.

[00675] FIG. 52 shows data from the animal study depicted in **FIG. 51**, demonstrating that boosting with separately formulated CorVac2.0 at 0.3 μg dose enhances anti-spike IgG production (quantified at day 56). CorVac2.0 alone slightly boosts anti-spike IgG production, separately formulated 3:1 boosts anti-spike IgG production and inclusion of multiple doses of separately formulated CorVac2.0 does not negatively impact anti-spike IgG responses.

[00676] FIG. 53 shows data from the animal study depicted in **FIG. 51**, demonstrating that boosting with separately formulated CorVac2.0 at 0.3 μg dose enhances anti-spike IgG production (as measured by optical density (OD) at day 56). CorVac2.0 alone slightly boosts anti-spike IgG production, separately formulated 3:1 boosts anti-spike IgG production and inclusion of multiple doses of separately formulated CorVac2.0 does not negatively impact anti-spike IgG responses.

[00677] FIG. 54 shows data from the animal study depicted in **FIG. 51**, demonstrating anti-spike IgG kinetics over time. A third boost increased anti-spike IgG under all CorVac2.0 variations.

[00678] FIG. 55 shows ELISA data from the animal study depicted in **FIG. 51**, demonstrating anti-spike IgG levels in serum on the indicated days using the indicated serum dilutions.

[00679] FIG. 56 shows pseudovirus neutralization test (pVNT) data from the animal study depicted in **FIG. 51**, demonstrating that inclusion of CorVac2.0 does not negatively impact neutralizing titers on the

indicated days following treatment with indicated dosing regimens. The pVNT was performed using viral particles pseudotyped with VSV envelope containing SARS-CoV-2 spike protein at the indicated dilutions.

[00680] FIG. 57 shows tetramer staining data using PBLs from the animal study depicted in **FIG. 51**, showing the percentage of CD8+T cells specific to the indicated membrane and spike epitopes or epitope combinations indicated, demonstrating that anti-spike responses are not impacted by addition of CorVac2.0.

[00681] FIG. 58 shows tetramer staining data using PBLs from the animal study depicted in **FIG. 51**, showing the percentage of CD8+T cells specific to the indicated spike epitopes, demonstrating that anti-spike responses are not impacted by addition of CorVac2.0.

[00682] FIG. 59 shows a spot forming assay from the animal study depicted in **FIG. 51**, showing the number of spots formed per 1x10^6 cells after treatment with the indicated regimens at day 56, demonstrating that addition of CorVac2.0 in the third booster shot as a separate formulation slightly improves anti-spike T cell responses. CorVac2.0 alone slightly boosts anti-spike T cell responses, separately formulated 3:1 and 9:1 slightly boost anti-spike T cells, and inclusion of multiple doses of separately formulated CorVac2.0 does not negatively impact anti-spike T cell responses.

[00683] FIG. 60 shows a spot forming assay from the animal study depicted in **FIG. 51**, showing the number of spots formed per 1x10^6 cells after treatment with the indicated regimens at day 56, demonstrating that weak anti-nucleocapsid responses were seen with 1 booster dose, and multiple doses of separately formulated BNT162b2+CorVac2.0 leads to increases in responses. Weak responses to nucleocapsid in K18-hACE2 mice with one CorVac2.0 boost was observed. Increased anti-nucleocapsid responses with increasing number of CorVac2.0 doses was also observed.

[00684] FIG. 61 shows a spot forming assay from the animal study depicted in **FIG. 51**, showing the number of spots formed per 1x10^6 cells after treatment with the indicated regimens at day 56, demonstrating that the strongest anti-membrane responses were seen in separately formulated groups as a booster; multiple doses of separately formulated BNT162b2+CorVac2.0 lead to increases in responses. Strongest anti-membrane responses were seen in separately formulated conditions. Increased anti-mmbrane responses with increasing number of CorVac2.0 doses was observed.

[00685] FIG. 62 shows data from the animal study depicted in **FIG. 51**, in which harvested inguinal lymph nodes (a draining lympgh node (dLN)) were dissected and live cell counts were determined after treatment with the indicated regimens. Three samples with 0% viability were removed (G5, G7, G9). The data demonstrate that groups containing a CorVac2.0 boost in combination with BNT162b2 show increased live LN cell counts.

[00686] FIG. 63 shows data from the animal study depicted in **FIG. 51**, in which harvested lymph nodes were dissected and cell counts of the indicated cell populations as a percentage of CD45.2 cells were determined after treatment with the indicated regimens. The data demonstrate a trend for increased

germinal center (GC) cells and CD27+ memory B cells in groups treated with with separately formulated CorVac2.0+BNT162.

[00687] FIG. 64A shows data from the animal study depicted in **FIG. 51**, in which harvested lymph nodes were dissected and cell counts of the indicated cell populations as a percentage of CD45.2 cells were determined after treatment with the indicated regimens. The data demonstrate slightly higher class-switched B cells in groups treated with with separately formulated CorVac2.0+BNT162.

[00688] FIG. 64B shows data from the animal study depicted in **FIG. 51**, in which harvested lymph nodes were dissected and toal cell counts of the indicated cell populations were determined after treatment with the indicated regimens. The data demonstrate slightly higher class-switched B cells in groups treated with with separately formulated CorVac2.0+BNT162

[00689] FIG. 65 shows tetramer-specific staing data from the animal study depicted in **FIG. 51**, from harvested lymph node samples showing the percentage of CD8+T cells specific to spike or membrane epitopes. Also depicted is a graph showing the percentage of central memory T cells, effector memory T cells, naive T cells and effector T cells cells as a percentage of spike positive CD8 T cells. Slightly less differentiated cells in CorVac2.0 treated groups were observed.

[00690] FIG. 66 depicts a schematic of an animal study for determining the immune responses elicited by different formulation ratios and doses of CorVac 2.0 strings with BNT162b2 in HLA-A02 transgenic mice.

[00691] FIG. 67A shows a spot forming assay from the animal study depicted in **FIG. 66**, showing the number of spots formed per 1x10^6 cells after treatment with the indicated regimens at day 14, demonstrating that CorVac2.0 induces the strongest immune responses at the highest dose.

[00692] FIG. 67B shows a spot forming assay from the animal study depicted in **FIG. 66**, showing the number of spots formed per 1x10^6 cells after treatment with the indicated regimens at day 35, demonstrating that Spike T cell responses are enhanced with CorVac2.0 inclusion. The dose of 1 ug yielded the strongest responses.

[00693] FIG. 67C shows a spot forming assay from the animal study depicted in **FIG. 66**, showing the number of spots formed per 1x10^6 cells over time. Improved T cell responses to all regions were observed after the boost.

[00694] FIG. 67D shows a co-culture spot forming assay from the animal study depicted in **FIG. 66**, showing the number of spots formed per 1x10^6 cells after treatment with the indicated regimens at day 35. Spike responses were seen in CD4 and CD8 T cells. Spike CD8 T cells show more cytokine secretion and degranulation than CD4 T cells.

[00695] FIG. 67E shows a co-culture spot forming assay from the animal study depicted in **FIG. 66**, showing the number of spots formed per 1x10^6 cells after treatment with the indicated regimens at day 35. Membrane responses were seen in CD4 and CD8 T cells and were strongest at the highest dose. IL2 secretion was seen in CD4 and CD8 T cells.

[00696] FIG. 67F shows a spot forming assay from the animal study depicted in **FIG. 66**, showing the number of spots formed per 1x10^6 cells after treatment with the indicated regimens at day 56. Spike responses were not negatively impacted by CorVac2.0. CorVac2.0 alone boosted spike responses. Boost with CorVac2.0 alone increased spike responses. No statistically significant changes in spike responses were seen with inclusion of CorVac2.0. The strongest membrane responses were observed in the highest dose groups. The strongest N responseswere observed in CorVac2.0 alone at the highest dose. The strongest Orf1ab responses were observed in CorVac2.0 alone and the separately formulated 3:1 dose.

[00697] FIG. 67G shows a co-culture spot forming assay from the animal study depicted in **FIG. 66**, showing the number of spots formed per 1x10^6 cells after treatment with the indicated regimens at day 56. Spike responses were seen in CD4 and CD8 T cells and some were boosted by inclusion of CorVac2.0.

[00698] FIG. 67H shows a co-culture spot forming assay from the animal study depicted in **FIG. 66**, showing the number of spots formed per 1x10^6 cells after treatment with the indicated regimens at day 56. Polyfunctional spike CD4 and CD8 T cells were slightly enhanced in higher dose CorVac2.0 conditions.

[00699] FIG. 67I shows a co-culture spot forming assay from the animal study depicted in **FIG. 66**, showing the number of spots formed per 1x10^6 cells after treatment with the indicated regimens at day 56. Membrane responses seen more strongly in CD8 T cells.

[00700] FIG. 67J shows a co-culture spot forming assay from the animal study depicted in **FIG. 66**, showing the number of spots formed per 1x10^6 cells after treatment with the indicated regimens at day 56. Polyfunctional membrane CD4 and CD8 T cells were observed.

[00701] FIG. 68A shows phenotyping data from the animal study depicted in **FIG. 66**, in which harvested lymph nodes were dissected and cell counts of the indicated cell populations as a percentage of CD45.2 cells were determined after treatment with the indicated regimens at day 14. Memory B cells: CD3-IgD-IgM-CD27+; Activated B cells: IgD-CD3-CD4-CD8-; Switched B cells: IgD-CD3-CD4-CD8-B220+IgM-CD19+CD138-. GC B cells: IgD-CD3-CD4-CD8-B220+IgM-CD19+CD138-CD95+CD38-.

[00702] FIG. 68B shows phenotyping data from the animal study depicted in **FIG. 66**, in which harvested lymph nodes were dissected and cell counts of the indicated cell populations as a percentage of CD45.2 cells were determined after treatment with the indicated regimens at day 35. Memory B cells: CD3-IgD-IgM-CD27+; Activated B cells: IgD-CD3-CD4-CD8-; Switched B cells: IgD-CD3-CD4-CD8-B220+IgM-CD19+CD138-. GC B cells: IgD-CD3-CD4-CD8-B220+IgM-CD19+CD138-CD95+CD38-. The addition of CorVac2.0 to BNT162b2 slightly enhances class-switching and GC B cells. CorVac2.0 leads to a slight increase in Tfh cells.

[00703] FIG. 68C shows phenotyping data from the animal study depicted in **FIG. 66**, in which harvested lymph nodes were dissected and cell counts of the indicated cell populations as a percentage of CD45.2 cells were determined after treatment with the indicated regimens at day 56. Memory B cells: CD3-IgD-IgM-CD27+; Activated B cells: IgD-CD3-CD4-CD8-; Switched B cells: IgD-CD3-CD4-CD8-B220+IgM-CD19+CD138-. GC B cells: IgD-CD3-CD4-CD8-B220+IgM-CD19+CD138-CD95+CD38-. Boosting with CorVac2.0 alone enhances B cell responses compared to no boost. CorVac2.0 does not significantly affect B cells responses in combination with BNT162b2.

[00704] FIG. 69 shows an exemplary clinical study design to evaluate safety of CorVac 2.0 vaccines in healthy human subjects.

[00705] FIG. 70 shows an exemplary clinical study design to evaluate safety of CorVac 2.0 vaccines in immunocompromised human subjects.

[00706] FIG. 71 shows an exemplary clinical study design to evaluate safety of CorVac 2.0 vaccines in immunocompromised human subjects.

[00707] FIG. 72 demonstrates sequence variants and mutants across the Spike protein in various SARS CoV-2 isolates as indicated on the right hand side. The data shows that the Spike protein is highly mutated putitively due to selective pressure.

[00708] FIG. 73 demonstrates sequence variants and mutants across the nucleocapsid (N) and membrane (M) protein in various SARS CoV-2 isolates as indicated on the right hand side, and the respective mapping of the vaccine epitope sequences in encoded by CorVac 2.0. The data shows that the CorVac2.0 vaccine sequence is rarely impacted by variant mutations in N, M.

[00709] FIG. 74 demonstrates sequence variants and mutants across the ORF 1ab in various SARS CoV-2 isolates as indicated on the right hand side, and the respective mapping of the vaccine epitope sequences in encoded by CorVac 2.0. The data shows that the CorVac2.0 vaccine sequence is rarely impacted by variant mutations in ORF1ab.

[00710] FIG. 75A shows a representation of a map of an exemplary CorVac2.0 RS-C7 string depicting linkers, the SEC domain, the transmembrane (TM) domain and the viral epitopes contained within the string, including nucleocapsid epitopes, ORF1ab epitopes, and membrane epitopes.

[00711] FIG. 75B shows a representation of a map of an exemplary CorVac2.0 RS-C7 string depicting the viral epitopes contained within the string that were observed as being presented by mass spectrometry (MS), including nucleocapsid epitopes, ORF1ab epitopes, and membrane epitopes.

[00712] FIG. 76 shows a representation of an MS-based HLA-I cleavage predictor used to optimize ordering of candidate ORF1ab sequences, adding as few linkers as possible while retaining efficient epitope cleavage (top) and 18 ORF1ab epitopes optimized for GSS linker contexts.

[00713] FIG. 77A-C shows a representation of a map of an exemplary CorVac2.0 RS-C7 string Antigens chosen for CorVac 2.0 are rarely mutated: across all WHO-designated variants, RS-C7 is only impacted

by 3 mutations, leaving the vast majority of epitopes unchanged. As shown in **FIG. 77B-C**, even in the highly mutated Omicron variants, only one mutation impacts CorVac 2.0 strings (in contrast to ~39 amino acid changes in Spike protein).

[00714] FIG. 78A-78B shows kinetics of the antibody concentration against the Spike protein.

[00715] FIG. 79 depicts an exemplary structure of RS C7, and illustrates certain factors that were considered when designing a CorVac 2.0 string. "Count", as used in **FIG. 79**, refers to the number of pMHC-allele pairs that overlap with an indicated residue of a protein sequence. Counts can be determined by reference to a database of epitopes (e.g., a database of epitopes that have been observed, for example, in experimental studies, and/or predicted). "Entropy" as used in **FIG.79** refers to Shannon entropy, and is a measure of conservation level (where lower entropy indicates higher conservation).

[00716] FIG. 80A depicts epitopes present in an exemplary CorVac 2.0 string (e.g., RS C7 string) that were observed via mass spectrometery as processed and presented by MHC complexes.

[00717] FIG. 80B depicts data for one exemplary epitope observed by mass spectrometry (epitope 23 of Table 19).

[00718] FIG. 81 depicts a study design to test the immunogenicity of various BNT162b2 + CorVac2.0 string dosing regimens in K18-hACE2 mice.

[00719] FIG. 82A-82B show anti-Spike protein, IgG concentrations measured over time, from serum samples collected from the experiment depicted in **FIG. 81**. IgG concentrations measured by ELISA. Error bars indicate standard error of the mean.

[00720] FIG. 83A-83B show neutralization titers measured from the serum samples collected from the experiment depicted in **FIG. 81**. Neutralization titers were measured using a pseudovirus neutralization assay, using pseudoviruses comprising an SARS-CoV-2 S protein from a Wuhan stain.

[00721] FIG. 84 depicts an experimental protocol for measuring the efficacy of a CorVac2.0 string, administered alone or in combination with RNA encoding a SARS-CoV-2 S protein in Syrian Hamsters.

[00722] FIG. 85 shows results from the study depicted in **FIG. 84**. Specifically, **FIG. 85** shows changes in body weight of hamsters, following challenge with SARS-CoV-2 (Wuhan strain).

[00723] FIG. 86 shows an exemplary protocol for clonotype analysis of Spike-specific B cells and T cells.

[00724] FIG. 87 summarizes T cell clonotypes observed in animals administered (i) two doses of RNA encoding a SARS-CoV-2 S protein (BNT162b2) or (ii) two doses of RNA encoding a SARS-CoV-2 S protein and one dose of CorVac2.0 (String C7). Circles correspond to samples having the same clonotype, with clonotypes in the same "clonotype cluster" (i.e., clonotypes having similar sequences) indicated with lines connecting dots. As shown in the figure, administration of a CorVac2.0 construct increases the trend towards higher clonal expansion, but does not negatively impact clonality.

[00725] FIG. 88 shows an exemplary clinical study design to evaluate safety of CorVac 2.0 vaccines in healthy human subjects. "Spike Vac" refers to RNA encoding a SARS-CoV-2 S protein and comprising

one or more mutations that stabilize the prefusion conformation (e.g., one or more mutations disclosed herein or known in the art); in the exemplary clinical study design, a bivalent vaccine is administered, comprising RNA encoding a SARS-CoV-2 S polypeptide of a Wuhan strain and a SARS-CoV-2 S polypeptide comprising one or more mutations characteristic of a BA.4/5 Omicron variant (e.g., one or more mutations disclosed herein). [a]Further dosing of subjects or opening of new cohorts may proceed if acceptable tolerability is shown and no stopping/pausing rules are met. [b]An exemplary SpikeVac Bivalent is BNT162b2 Bivalent (Wuhan + OMI BA.4/BA.5). Abbreviations: d = days; h = hour(s); FIH = first-in-human; IRC = Internal Review Committee; N = number of subjects; OMI = Omicron; WT = Wild Type. Trial population: Healthy volunteers aged 18-55 years, who have been previously vaccinated with at least three doses of any authorized COVID19 RNA vaccine (the last COVID19 RNA vaccine dose must have been administered at least 4 months before Visit 1). Subjects who have had SARS-CoV-2 infection 60 d or more prior to randomization are not excluded from the trial.

DETAILED DESCRIPTION

[00726] Described herein are novel therapeutics and vaccines based on viral epitopes. Accordingly, the present disclosure described herein provides peptides, polynucleotides encoding the peptides, and peptide binding agents that can be used, for example, to stimulate an immune response to a viral antigen, to create an immunogenic composition or vaccine for use in treating or preventing a viral infection.

Definitions

[00727] To facilitate an understanding of the present disclosure, a number of terms and phrases are defined below.

[00728] "Viral antigens" refer to antigens encoded by a virus. They include, but are not limited to, antigens of coronaviruses, such as COVID19.

[00729] Throughout this disclosure, "binding data" results can be expressed in terms of "IC50." IC50 is the concentration of the tested peptide in a binding assay at which 50% inhibition of binding of a labeled reference peptide is observed. Given the conditions in which the assays are run (i.e., limiting HLA protein and labeled reference peptide concentrations), these values approximate K_D values. Assays for determining binding are well known in the art and are described in detail, for example, in PCT publications WO 94/20127 and WO 94/03205, and other publications such Sidney et al., Current Protocols in Immunology 18.3.1 (1998); Sidney, et al., J. Immunol. 154:247 (1995); and Sette, et al., Mol. Immunol. 31:813 (1994). Alternatively, binding can be expressed relative to binding by a reference standard peptide. For example, can be based on its IC_{50}, relative to the IC_{50} of a reference standard peptide. Binding can also be determined using other assay systems including those using: live cells (e.g., Ceppellini et al., Nature 339:392 (1989); Christnick et al., Nature 352:67 (1991); Busch et al., Int. Immunol. 2:443 (1990); Hill et al., J. Immunol. 147:189 (1991); del Guercio et al., J. Immunol. 154:685 (1995)), cell free systems using detergent lysates

(e.g., Cerundolo et al., J. Immunol 21:2069 (1991)), immobilized purified MHC (e.g., Hill et al., J. Immunol. 152, 2890 (1994); Marshall et al., J. Immunol. 152:4946 (1994)), ELISA systems (e.g., Reay et al., EMBO J. 11:2829 (1992)), surface plasmon resonance (e.g., Khilko et al., J. Biol. Chem. 268:15425 (1993)); high flux soluble phase assays (Hammer et al., J. Exp. Med. 180:2353 (1994)), and measurement of class I MHC stabilization or assembly (e.g., Ljunggren et al., Nature 346:476 (1990); Schumacher et al., Cell 62:563 (1990); Townsend et al., Cell 62:285 (1990); Parker et al., J. Immunol. 149:1896 (1992)).

[00730] The term "derived" when used to discuss an epitope is a synonym for "prepared." A derived epitope can be from a natural source, or it can be synthesized according to standard protocols in the art. Synthetic epitopes can comprise artificial amino acid residues "amino acid mimetics," such as D isomers of natural occurring L amino acid residues or non-natural amino acid residues such as cyclohexylalanine. A derived or prepared epitope can be an analog of a native epitope.

[00731] A "diluent" includes sterile liquids, such as water and oils, including those of petroleum, animal, vegetable or synthetic origin, such as peanut oil, soybean oil, mineral oil, sesame oil and the like. Water is also a diluent for pharmaceutical compositions. Saline solutions and aqueous dextrose and glycerol solutions can also be employed as diluents, for example, in injectable solutions.

[00732] An "epitope" is the collective features of a molecule, such as primary, secondary and tertiary peptide structure, and charge, that together form a site recognized by, for example, an immunoglobulin, T cell receptor, HLA molecule, or chimeric antigen receptor. Alternatively, an epitope can be a set of amino acid residues which is involved in recognition by a particular immunoglobulin, or in the context of T cells, those residues necessary for recognition by T cell receptor proteins, chimeric antigen receptors, and/or Major Histocompatibility Complex (MHC) receptors. Epitopes can be prepared by isolation from a natural source, or they can be synthesized according to standard protocols in the art. Synthetic epitopes can comprise artificial amino acid residues, "amino acid mimetics," such as D isomers of naturally-occurring L amino acid residues or non-naturally-occurring amino acid residues such as cyclohexylalanine. Throughout this disclosure, epitopes may be referred to in some cases as peptides or peptide epitopes.

[00733] It is to be appreciated that proteins or peptides that comprise an epitope or an analog described herein as well as additional amino acid(s) are still within the bounds of the present disclosure. In certain embodiments, the peptide comprises a fragment of an antigen.

[00734] In certain embodiments, there is a limitation on the length of a peptide of the present disclosure. The embodiment that is length-limited occurs when the protein or peptide comprising an epitope described herein comprises a region (i.e., a contiguous series of amino acid residues) having 100% identity with a native sequence. In order to avoid the definition of epitope from reading, e.g., on whole natural molecules, there is a limitation on the length of any region that has 100% identity with a native peptide sequence. Thus, for a peptide comprising an epitope described herein and a region with 100% identity with a native peptide sequence, the region with 100% identity to a native sequence generally has a length of: less than

or equal to 600 amino acid residues, less than or equal to 500 amino acid residues, less than or equal to 400 amino acid residues, less than or equal to 250 amino acid residues, less than or equal to 100 amino acid residues, less than or equal to 85 amino acid residues, less than or equal to 75 amino acid residues, less than or equal to 65 amino acid residues, and less than or equal to 50 amino acid residues. In certain embodiments, an "epitope" described herein is comprised by a peptide having a region with less than 51 amino acid residues that has 100% identity to a native peptide sequence, in any increment down to 5 amino acid residues; for example 50, 49, 48, 47, 46, 45, 44, 43, 42, 41, 40, 39, 38, 37, 36, 35, 34, 33, 32, 31, 30, 29, 28, 27, 26, 25, 24, 23, 22, 21, 20, 19, 18, 17, 16, 15, 14, 13, 12, 11, 10, 9, 8, 7, 6, or 5 amino acid residues.

[00735] "Human Leukocyte Antigen" or "HLA" is a human class I or class II Major Histocompatibility Complex (MITC) protein (see, e.g., Stites, et al., IMMUNOLOGY, 8TH ED., Lange Publishing, Los Altos, Calif. (1994).

An "HLA supertype or HLA family", as used herein, describes sets of HLA molecules grouped on the basis of shared peptide-binding specificities. HLA class I molecules that share somewhat similar binding affinity for peptides bearing certain amino acid motifs are grouped into such HLA supertypes. The terms HLA superfamily, HLA supertype family, HLA family, and HLA xx-like molecules (where "xx" denotes a particular HLA type), are synonyms.

[00736] The terms "identical" or percent "identity," in the context of two or more peptide sequences or antigen fragments, refer to two or more sequences or subsequences that are the same or have a specified percentage of amino acid residues that are the same, when compared and aligned for maximum correspondence over a comparison window, as measured using a sequence comparison algorithm or by manual alignment and visual inspection.

[00737] An "immunogenic" peptide or an "immunogenic" epitope or "peptide epitope" is a peptide that comprises an allele-specific motif such that the peptide will bind an HLA molecule and induce a cell-mediated or humoral response, for example, cytotoxic T lymphocyte (CTL), helper T lymphocyte (HTL) and/or B lymphocyte response. Thus, immunogenic peptides described herein are capable of binding to an appropriate HLA molecule and thereafter inducing a CTL (cytotoxic) response, or a HTL (and humoral) response, to the peptide.

[00738] As used herein, a "chimeric antigen receptor" or "CAR" refers to an antigen binding protein in that includes an immunoglobulin antigen binding domain (e.g., an immunoglobulin variable domain) and a T cell receptor (TCR) constant domain. As used herein, a "constant domain" of a TCR polypeptide includes a membrane-proximal TCR constant domain, and may also include a TCR transmembrane domain and/or a TCR cytoplasmic tail. For example, in some embodiments, the CAR is a dimer that includes a first polypeptide comprising a immunoglobulin heavy chain variable domain linked to a TCR-beta constant domain and a second polypeptide comprising an immunoglobulin light chain variable domain (e.g., a lc or

2\., variable domain) linked to a TCRα constant domain. In some embodiments, the CAR is a dimer that includes a first polypeptide comprising a immunoglobulin heavy chain variable domain linked to a TCRα constant domain and a second polypeptide comprising an immunoglobulin light chain variable domain linked to a TCRβ constant domain.

[00739] The phrases "isolated" or "biologically pure" refer to material which is substantially or essentially free from components which normally accompany the material as it is found in its native state. Thus, peptides described herein do not contain some or all of the materials normally associated with the peptides in their in situ environment. An "isolated" epitope refers to an epitope that does not include the whole sequence of the antigen from which the epitope was derived. Typically, the "isolated" epitope does not have attached thereto additional amino acid residues that result in a sequence that has 100% identity over the entire length of a native sequence. The native sequence can be a sequence such as a viral antigen from which the epitope is derived. Thus, the term "isolated" means that the material is removed from its original environment (e.g., the natural environment if it is naturally occurring). For example, a naturally-occurring polynucleotide or peptide present in a living animal is not isolated, but the same polynucleotide or peptide, separated from some or all of the coexisting materials in the natural system, is isolated. Such a polynucleotide could be part of a vector, and/or such a polynucleotide or peptide could be part of a composition, and still be "isolated" in that such vector or composition is not part of its natural environment. RNA molecules include in vivo or in vitro RNA transcripts of the DNA molecules described herein, and further include such molecules produced synthetically.

[00740] "Major Histocompatibility Complex" or "MHC" is a cluster of genes that plays a role in control of the cellular interactions responsible for physiologic immune responses. In humans, the MHC complex is also known as the human leukocyte antigen (HLA) complex. For a detailed description of the MHC and HLA complexes, see, Paul, FUNDAMENTAL IMMUNOLOGY, 3.sup.RD ED., Raven Press, New York (1993).

[00741] A "native" or a "wild type" sequence refers to a sequence found in nature. Such a sequence can comprise a longer sequence in nature.

[00742] A "T cell epitope" is to be understood as meaning a peptide sequence which can be bound by the MHC molecules of class I or II in the form of a peptide-presenting MHC molecule or MHC complex and then, in this form, be recognized and bound by cytotoxic T-lymphocytes or T-helper cells, respectively.

[00743] A "receptor" is to be understood as meaning a biological molecule or a molecule grouping capable of binding a ligand. A receptor may serve, to transmit information in a cell, a cell formation or an organism. The receptor comprises at least one receptor unit, for example, where each receptor unit may consist of a protein molecule. The receptor has a structure which complements that of a ligand and may complex the ligand as a binding partner. The information is transmitted in particular by conformational changes of the receptor following complexation of the ligand on the surface of a cell. In some embodiments, a receptor is

to be understood as meaning in particular proteins of MHC classes I and II capable of forming a receptor/ligand complex with a ligand, in particular a peptide or peptide fragment of suitable length.

[00744] A "ligand" is to be understood as meaning a molecule which has a structure complementary to that of a receptor and is capable of forming a complex with this receptor. In some embodiments, a ligand is to be understood as meaning a peptide or peptide fragment which has a suitable length and suitable binding motifs in its amino acid sequence, so that the peptide or peptide fragment is capable of forming a complex with proteins of MHC class I or MHC class II.

[00745] In some embodiments, a "receptor/ligand complex" is also to be understood as meaning a "receptor/peptide complex" or "receptor/peptide fragment complex", including a peptide- or peptide fragment-presenting MHC molecule of class I or of class II.

[00746] "Proteins or molecules of the major histocompatibility complex (MHC)", "MHC molecules", "MHC proteins" or "HLA proteins" are to be understood as meaning proteins capable of binding peptides resulting from the proteolytic cleavage of protein antigens and representing potential lymphocyte epitopes, (e.g., T cell epitope and B cell epitope) transporting them to the cell surface and presenting them there to specific cells, in particular cytotoxic T-lymphocytes, T-helper cells, or B cells. The major histocompatibility complex in the genome comprises the genetic region whose gene products expressed on the cell surface are important for binding and presenting endogenous and/or foreign antigens and thus for regulating immunological processes. The major histocompatibility complex is classified into two gene groups coding for different proteins, namely molecules of MHC class I and molecules of MHC class II. The cellular biology and the expression patterns of the two MHC classes are adapted to these different roles.

[00747] The terms "peptide" and "peptide epitope" are used interchangeably with "oligopeptide" in the present specification to designate a series of residues connected one to the other, typically by peptide bonds between the a-amino and carboxyl groups of adjacent amino acid residues.

[00748] "Synthetic peptide" refers to a peptide that is obtained from a non-natural source, e.g., is man-made. Such peptides can be produced using such methods as chemical synthesis or recombinant DNA technology. "Synthetic peptides" include "fusion proteins."

[00749] A "PanDR binding" peptide, a "PanDR binding epitope" is a member of a family of molecules that binds more than one HLA class II DR molecule.

[00750] "Pharmaceutically acceptable" refers to a generally non-toxic, inert, and/or physiologically compatible composition or component of a composition.

[00751] A "pharmaceutical excipient" or "excipient" comprises a material such as an adjuvant, a carrier, pH-adjusting and buffering agents, tonicity adjusting agents, wetting agents, preservatives, and the like. A "pharmaceutical excipient" is an excipient which is pharmaceutically acceptable. The term "motif' refers to a pattern of residues in an amino acid sequence of defined length, for example, a peptide of less than

about 15 amino acid residues in length, or less than about 13 amino acid residues in length, for example, from about 8 to about 13 amino acid residues (e.g., 8, 9, 10, 11, 12, or 13) for a class I HLA motif and from about 6 to about 25 amino acid residues (e.g., 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, or 25) fora class II HLA motif, which is recognized by a particular HLA molecule. Motifs are typically different for each HLA protein encoded by a given human HLA allele. These motifs differ in their pattern of the primary and secondary anchor residues. In some embodiments, an MHC class I motif identifies a peptide of 9, 10, or 11 amino acid residues in length.

[00752] A "supermotif' is a peptide binding specificity shared by HLA molecules encoded by two or more HLA alleles. In some embodiments, a supermotif-bearing peptide described herein is recognized with high or intermediate affinity (as defined herein) by two or more HLA antigens.

[00753] The term "naturally occurring" as used herein refers to the fact that an object can be found in nature. For example, a peptide or nucleic acid that is present in an organism (including viruses) and can be from a source in nature and which has not been intentionally modified by man in the laboratory is naturally occurring.

[00754] According to the present disclosure, the term "vaccine" relates to a pharmaceutical preparation (pharmaceutical composition) or product that upon administration induces an immune response, for example, a cellular or humoral immune response, which recognizes and attacks a pathogen or a diseased cell such as a cell infected with a virus. A vaccine may be used for the prevention or treatment of a disease.

[00755] A "protective immune response" or "therapeutic immune response" refers to a CTL and/or an HTL response to an antigen derived from an pathogenic antigen (e.g., a viral antigen), which in some way prevents or at least partially arrests disease symptoms, side effects or progression. The immune response can also include an antibody response which has been facilitated by the stimulation of helper T cells.

[00756] "Antigen processing" or "processing" refers to the degradation of a polypeptide or antigen into procession products, which are fragments of said polypeptide or antigen (e.g., the degradation of a polypeptide into peptides) and the association of one or more of these fragments (e.g., via binding) with MHC molecules for presentation by cells, for example, antigen presenting cells, to specific T cells.

[00757] "Antigen presenting cells" (APC) are cells which present peptide fragments of protein antigens in association with MHC molecules on their cell surface. Some APCs may activate antigen specific T cells. Professional antigen-presenting cells are very efficient at internalizing antigen, either by phagocytosis or by receptor-mediated endocytosis, and then displaying a fragment of the antigen, bound to a class II MHC molecule, on their membrane. The T cell recognizes and interacts with the antigen-class II MHC molecule complex on the membrane of the antigen presenting cell. An additional co-stimulatory signal is then produced by the antigen presenting cell, leading to activation of the T cell. The expression of co-stimulatory molecules is a defining feature of professional antigen-presenting cells.

[00758] The main types of professional antigen-presenting cells are dendritic cells, which have the broadest range of antigen presentation, and are probably the most important antigen presenting cells, macrophages, B-cells, and certain activated epithelial cells.

[00759] Dendritic cells (DCs) are leukocyte populations that present antigens captured in peripheral tissues to T cells via both MHC class II and I antigen presentation pathways. It is well known that dendritic cells are potent inducers of immune responses and the activation of these cells is a critical step for the induction of antiviral immunity.

[00760] Dendritic cells are conveniently categorized as "immature" and "mature" cells, which can be used as a simple way to discriminate between two well characterized phenotypes. However, this nomenclature should not be construed to exclude all possible intermediate stages of differentiation.

[00761] Immature dendritic cells are characterized as antigen presenting cells with a high capacity for antigen uptake and processing, which correlates with the high expression of Fey receptor and mannose receptor. The mature phenotype is typically characterized by a lower expression of these markers, but a high expression of cell surface molecules responsible for T cell activation such as class I and class II MHC, adhesion molecules (e. g. CD54 and CD11) and costimulatory molecules (e. g., CD40, CD80, CD86 and 4-1 BB).

[00762] The term "residue" refers to an amino acid residue or amino acid mimetic residue incorporated into a peptide or protein by an amide bond or amide bond mimetic, or nucleic acid (DNA or RNA) that encodes the amino acid or amino acid mimetic.

[00763] The nomenclature used to describe peptides or proteins follows the conventional practice wherein the amino group is presented to the left (the amino- or N-terminus) and the carboxyl group to the right (the carboxy- or C-terminus) of each amino acid residue. When amino acid residue positions are referred to in a peptide epitope they are numbered in an amino to carboxyl direction with position one being the residue located at the amino terminal end of the epitope, or the peptide or protein of which it can be a part.

[00764] In the formulae representing selected specific embodiments of the present disclosure, the amino- and carboxyl-terminal groups, although not specifically shown, are in the form they would assume at physiologic pH values, unless otherwise specified. In the amino acid structure formulae, each residue is generally represented by standard three letter or single letter designations. The L-form of an amino acid residue is represented by a capital single letter or a capital first letter of a three-letter symbol, and the D-form for those amino acid residues having D-forms is represented by a lower case single letter or a lower case three letter symbol. However, when three letter symbols or full names are used without capitals, they can refer to L amino acid residues. Glycine has no asymmetric carbon atom and is simply referred to as "Gly" or "G". The amino acid sequences of peptides set forth herein are generally designated using the standard single letter symbol. (A, Alanine; C, Cysteine; D, Aspartic Acid; E, Glutamic Acid; F, Phenylalanine; G, Glycine; H, Histidine; I, Isoleucine; K, Lysine; L, Leucine; M, Methionine; N,

Asparagine; P, Proline; Q, Glutamine; R, Arginine; S, Serine; T, Threonine; V, Valine; W, Tryptophan; and Y, Tyrosine.)

[00765] The terms "polynucleotide" and "nucleic acid" are used interchangeably herein and refer to polymers of nucleotides of any length, and include DNA and RNA, for example, mRNA. The nucleotides can be deoxyribonucleotides, ribonucleotides, modified nucleotides or bases, and/or their analogs, or any substrate that can be incorporated into a polymer by DNA or RNA polymerase. In some embodiments, the polynucleotide and nucleic acid can be in vitro transcribed mRNA. In some embodiments, the polynucleotide that is administered is mRNA.

[00766] The terms "identical" or percent "identity" in the context of two or more nucleic acids or polypeptides, refer to two or more sequences or subsequences that are the same or have a specified percentage of nucleotides or amino acid residues that are the same, when compared and aligned (introducing gaps, if necessary) for maximum correspondence, not considering any conservative amino acid substitutions as part of the sequence identity. The percent identity can be measured using sequence comparison software or algorithms or by visual inspection. Various algorithms and software that can be used to obtain alignments of amino acid or nucleotide sequences are well-known in the art. These include, but are not limited to, BLAST, ALIGN, Megalign, BestFit, GCG Wisconsin Package, and variations thereof. In some embodiments, two nucleic acids or polypeptides described herein are substantially identical, meaning they have at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, and in some embodiments at least 95%, at least 96%, at least 97%, at least 98%, at least 99% nucleotide or amino acid residue identity, when compared and aligned for maximum correspondence, as measured using a sequence comparison algorithm or by visual inspection. In some embodiments, identity exists over a region of the sequences that is at least about 10, at least about 20, at least about 40-60 residues, at least about 60-80 residues in length or any integral value between. In some embodiments, identity exists over a longer region than 60-80 residues, such as at least about 80-100 residues, and in some embodiments the sequences are substantially identical over the full length of the sequences being compared, such as the coding region of a nucleotide sequence.

[00767] A "conservative amino acid substitution" is one in which one amino acid residue is replaced with another amino acid residue having a similar side chain. Families of amino acid residues having similar side chains have been defined in the art, including basic side chains (e.g., lysine, arginine, histidine), acidic side chains (e.g., aspartic acid, glutamic acid), uncharged polar side chains (e.g., glycine, asparagine, glutamine, serine, threonine, tyrosine, cysteine), nonpolar side chains (e.g., alanine, valine, leucine, isoleucine, proline, phenylalanine, methionine, tryptophan), beta-branched side chains (e.g., threonine, valine, isoleucine) and aromatic side chains (e.g., tyrosine, phenylalanine, tryptophan, histidine). For example, substitution of a phenylalanine for a tyrosine is a conservative substitution. Methods of identifying nucleotide and amino acid conservative substitutions which do not eliminate peptide function are well-known in the art.

[00768] The term "vector" as used herein means a construct, which is capable of delivering, and usually expressing, one or more gene(s) or sequence(s) of interest in a host cell. Examples of vectors include, but are not limited to, viral vectors, naked DNA or RNA expression vectors, plasmid, cosmid, or phage vectors, DNA or RNA expression vectors associated with cationic condensing agents, and DNA or RNA expression vectors encapsulated in liposomes.

[00769] A polypeptide, antibody, polynucleotide, vector, cell, or composition which is "isolated" is a polypeptide, antibody, polynucleotide, vector, cell, or composition which is in a form not found in nature. Isolated polypeptides, antibodies, polynucleotides, vectors, cells, or compositions include those which have been purified to a degree that they are no longer in a form in which they are found in nature. In some embodiments, a polypeptide, antibody, polynucleotide, vector, cell, or composition which is substantially pure. In one embodiment, a "polynucleotide" encompasses a PCR or quantitative PCR reaction comprising the polynucleotide amplified in the PCR or quantitative PCR reaction.

[00770] The term "substantially pure" as used herein refers to material which is at least 50% pure (i.e., free from contaminants), at least 90% pure, at least 95% pure, at least 98% pure, or at least 99% pure.

[00771] The term "subject" refers to any animal (e.g., a mammal), including, but not limited to, humans, non-human primates, canines, felines, rodents, and the like, which is to be the recipient of a particular treatment. Typically, the terms "subject" and "patient" are used interchangeably herein in reference to a human subject.

[00772] The terms "effective amount" or "therapeutically effective amount" or "therapeutic effect" refer to an amount of a therapeutic effective to "treat" a disease or disorder in a subject or mammal. The therapeutically effective amount of a drug has a therapeutic effect and as such can prevent the development of a disease or disorder; slow down the development of a disease or disorder; slow down the progression of a disease or disorder; relieve to some extent one or more of the symptoms associated with a disease or disorder; reduce morbidity and mortality; improve quality of life; or a combination of such effects.

[00773] The terms "treating" or "treatment" or "to treat" or "alleviating" or "to alleviate" refer to both 1) therapeutic measures that cure, slow down, lessen symptoms of, and/or halt progression of a diagnosed pathologic condition or disorder and 2) prophylactic or preventative measures that prevent or slow the development of a targeted pathologic condition or disorder. Thus, those in need of treatment include those already with the disorder; those prone to have the disorder; and those in whom the disorder is to be prevented.

[00774] As used in the present disclosure and embodiments, the singular forms "a", "an" and "the" include plural forms unless the context clearly dictates otherwise.

[00775] The term "therapeutic" refers a composition that is used to treat or prevent a disease or a condition, such as viral infection, e.g., in some embodiments coronaviral infection. For example, in some embodiments, a therapeutic is or comprises a vaccine. In some embodiments, a therapeutic may be a drug,

e.g., a small molecule drug. A therapeutic may be administered to a subject in need thereof, to prevent a disease or an infection, or to reduce or ameliorate one or more symptoms associated with a disease. A therapeutic may also be considered to treat at least a symptom of the disease.

[00776] It is understood that terms such as "comprises", "comprised", "comprising" and the like can have the meaning attributed to it in U.S. Patent law; e.g., they can mean "includes", "included", "including", and the like; and that terms such as "consisting essentially of and "consists essentially of have the meaning ascribed to them in U.S. Patent law, e.g., they allow for elements not explicitly recited, but exclude elements that are found in the prior art or that affect a basic or novel characteristic of the present disclosure. Nothing herein is intended as a promise.

[00777] The term "and/or" as used in a phrase such as "A and/or B" herein is intended to include both A and B; A or B; A (alone); and B (alone). Likewise, the term "and/or" as used in a phrase such as "A, B, and/or C" is intended to encompass each of the following embodiments: A, B, and C; A, B, or C; A or C; A or B; B or C; A and C; A and B; B and C; A (alone); B (alone); and C (alone).

[00778] The term "2019 SARS-CoV 2" when, for example, referring to a virus, includes, but is not limited to, the 2019 SARS-CoV 2 virus and any mutant or variant thereof. A variant of a 2019 SARS-CoV 2 virus, or simply a variant as referred to here may mean a virus strain that is mutated with respect to the originally sequenced 2019 SARS-CoV 2 virus strain, e.g., the Wuhan strain. A mutation can be present in a coding region, e.g., spike protein encoding region, a nucleocapsid protein encoding region or any viral protein encoding region. A mutation may be in the genome of the virus that changes or has the potential to change its infectivity and/or virulence.

[00779] 2019 SARS-CoV 2 variants include, but are not limited to, the variants in the table below:

Table A - Exemplary 2019 SARS-CoV 2 variants

Name	SNPs	Notes
Alpha (B.1.1.7; 20I; S.501Y.V1)	orf1ab:T1001I orf1ab:A1708D orf1ab:I2230T del:11288:9 del:21765:6 del:21991:3 S:N501Y S:A570D S:P681H S:T716I S:S982A S:D1118H Orf8:Q27* Orf8:R52I Orf8:Y73C N:D3L N:S235F	Initially a UK lineage, associated with a variant of concern with N501Y, P681H and numerous other mutations. Pangolin assigns B.1.1.7 to sequences with at least 5 of the 17 defining B.1.1.7 SNPs
	S:H69- S:V70-	Announced on the 14 Dec 2020, this variant appears to have arisen and/or initially expanded in the South East of England.

Name	SNPs	Notes
	S:Y144- S:N501Y S:A570D S:D614G S:P681H S:T716I S:S982A S:D1118H ORF1a:T1001I ORF1a:A1708D ORF1a:I2230T ORF1a:S3675- ORF1a:G3676- ORF1a:F3677- N:D3L N:R203K N:G204R N:S235F ORF1b:P314L ORF8:Q27* ORF8:R52I ORF8:Y73C	
Beta (B.1.351; 20H; S.501Y.V2)	E:P71L N:T205I orf1a:K1655N S:D80A S:D215G S:K417N S:A701V S:N501Y S:E484K	A lineage first identified in South Africa and defined by new variant of concern 501Y.V2 Pangolin assigns B.1.351 to sequences with at least 5 of the 9 defining B.1.351 SNPs
	S:D80A S:D215G S:L241- S:L242- S:A243- S:K417N S:E484K S:N501Y S:D614G S:A701V ORF3a:Q57H ORF1a:T265I ORF1a:K1655N ORF1a:K3353R ORF1a:S3675- ORF1a:G3676- ORF1a:F3677- N:T205I ORF1b:P314L E:P71L	Announced in December 2020, 20H (Beta, V2) originated and/or initially expanded in South Africa

Name	SNPs	Notes
Delta (B.1.617.2; 21A; 21A/S:478K)	S:T19R S:L452R S:T478K S:P681R S:D950N ORF3a:S26L M:I82T ORF7a:V82A ORF7a:T120I N:D63G N:R203M N:D377Y	A lineage circulating with variants of biological significance S:P681R and S:L452R, first detected in India and international cases with travel history from India. Pangolin assigns B.1.617.2 to sequences with at least 5 of the 15 defining B.1.617.2 SNPs
	S:T19R S:E156- S:F157- S:R158G S:L452R S:T478K S:D614G S:P681R S:D950N ORF1b:P314L ORF1b:P1000L M:I82T N:D63G N:R203M N:D377Y ORF3a:S26L ORF7a:V82A ORF7a:T120I	B.1.617 was first detected in late 2020 in India, and has appeared to expand rapidly
Gamma (B.1.1.28.1; P.1; 20J; S.501Y.V3)	orf1ab:S1188L orf1ab:K1795Q del:11288:9 S:L18F S:T20N S:P26S S:D138Y S:R190S S:K417T S:E484K S:N501Y S:H655Y S:T1027I orf3a:G174C orf8:E92K N:P80R	A lineage first identified in Brazil with variants of biological significance E484K, N501Y and K417T Pangolin assigns P.1 to sequences with at least 10 of the 17 defining P.1 SNPs
	S:L18F S:T20N S:P26S S:D138Y S:R190S S:K417T S:E484K	Announced in January 2021, originated and/or initially expanded in Brazil, and was particularly associated with Manaus, Amazonas

Name	SNPs	Notes
	S:N501Y S:D614G S:H655Y S:T1027I S:V1176F ORF3a:S253P ORF1a:S1188L ORF1a:K1795Q ORF1a:S3675- ORF1a:G3676- ORF1a:F3677- N:P80R N:R203K N:G204R ORF1b:P314L ORF1b:E1264D ORF8:E92K	
Epsilon (21C; 20C/S:452R)	S:S13I S:W152C S:L452R S:D614G ORF1a:I4205V ORF1b:D1183Y	Was first identified in California and appears to have increased in frequency
	orf1ab:L4715F S:Q52R S:E484K S:Q677H S:F888L E:L21F E:I82T del:11288:9 del:21765:6 del:28278:3	International lineage with variants of biological significance E484K, Q677H, F888L and a similar suite of deletions to B.1.1.7.
Eta (B.1.525; 21D; 20A/S:484K)	S:Q52R S:A67V S:H69- S:V70- S:Y144- S:E484K S:D614G S:Q677H S:F888L ORF1b:P314F N:S2- N:D3Y N:A12G N:T205I M:I82T ORF1a:T2007I ORF1a:S3675- ORF1a:G3676- ORF1a:F3677- E:L21F	Appears to have arisen in late 2020, and as of March 2021 has been detected in North America, Europe, Asia, Africa, and Australia

Name	SNPs	Notes
	ORF6:F2-	
Iota (B.1.526; 21F; 20C/S:484K)	S:L5F S:T95I S:D253G S:E484K S:D614G S:A701V ORF1b:P314L ORF1b:Q1011H ORF3a:P42L ORF3a:Q57H ORF1a:T265I ORF1a:L3201P ORF1a:S3675- ORF1a:G3676- ORF1a:F3677- N:P199L N:M234I ORF8:T11I	Largely found within the USA, particularly in New York state, and seems to have arisen in late 2020. A lineage predominantly circulating in New York but with a few exports to other countries. Characterised by spike mutations T95I and D253G, plus others. The most frequent spike mutation pattern is L5F T95I D253G E484K D614G A701V, with a smaller fraction having S477N instead of E484K. Spike mutation E484K is present in about half of this lineage (as of 2021-02-10)
Kappa (B.1.617.1; 21B; 21A/S:154K)	S:E154K S:L452R S:E484Q S:D614G S:P681R S:Q1071H ORF1b:P314L ORF1b:G1129C ORF1b:M1352I ORF1b:K2310R ORF1b:S2312A N:R203M N:D377Y M:I82S ORF3a:S26L ORF1a:T1567I ORF1a:T3646A ORF7a:V82A	Predominantly India lineage with 484Q B.1.617 was first detected in late 2020 in India, and has appeared to expand rapidly
Lambda (C.37; 21G; B.1.1.1.37)	S:G75V S:T76I S:R246- S:S247- S:Y248- S:L249- S:T250- S:P251- S:G252- S:D253N S:L452Q S:F490S S:D614G S:T859N ORF1a:T1246I ORF1a:P2287S	Lineage in Peru, Chile, USA and Germany. Appears to have arisen in late 2020 in South America. Early sequences are predominantly from Peru and Chile.

Name	SNPs	Notes
	ORF1a:F2387V ORF1a:L3201P ORF1a:T3255I ORF1a:G3278S ORF1a:S3675- ORF1a:G3676- ORF1a:F3677- ORF1b:P314L N:P13L N:R203K N:G204R N:G214C	
Mu (B.1.621; 21H)	S:T95I S:Y144S S:Y145N S:R346K S:E484K S:N501Y S:D614G S:P681H S:D950N ORF1a:T1055A ORF1a:T1538I ORF1a:T3255I ORF1a:Q3729R ORF1b:P314L ORF1b:P1342S N:T205I ORF3a:Q57H ORF3a:V256I ORF3a:N257Q ORF3a:P258* ORF8:T11K ORF8:P38S ORF8:S67F	Lineage predominantly in Colombia with several spike mutations. Appears to have arisen in early 2021 in South America.
Omicron (B.1.1.529)	del:6513:3 del:11283:9 nuc:C241T ORF1A:K856R nuc:C3037T nuc:T5386G ORF1A:A2710T ORF1A:T3255I ORF1A:P3395H ORF1A:I3758V nuc:T13195C ORF1B:P314L nuc:C15240T ORF1B:I1566V S:A67V S:T95I S:G339D S:S371L	A lineage detected in a number of countries with a high number of spike protein mutations. Since initial detection, a number of Omicron variants have arisen, including BA.1, BA.2, BA.2.12.1, BA.4, BA.5, and BA.2.75 (mutations shown in the present table correspond to the BA.1 Omicron variant). First reported to WHO from South Africa on 24 November 2021.

Name	SNPs	Notes
	S:S373P S:K417N S:N440K S:G446S S:S477N S:T478K S:E484A S:Q493R S:G496S S:Q498R S:N501Y S:T547K S:D614G S:H655Y S:N679K S:P681H S:N764K S:D796Y S:N856K S:Q954H S:N969K nuc:C25000T E:T9I M:D3G M:Q19E M:A63T nuc:A27259C nuc:C27807T N:RG203KR	

[00780] In some embodiments, sequencing methods may be used to identify virus specific epitopes. Any suitable sequencing method can be used according to the present disclosure, for example, Next Generation Sequencing (NGS) technologies. Third Generation Sequencing methods might substitute for the NGS technology in the future to speed up the sequencing step of the method. For clarification purposes: the terms "Next Generation Sequencing" or "NGS" in the context of the present disclosure mean all novel high throughput sequencing technologies which, in contrast to the "conventional" sequencing methodology known as Sanger chemistry, read nucleic acid templates randomly in parallel along the entire genome by breaking the entire genome into small pieces. Such NGS technologies (also known as massively parallel sequencing technologies) are able to deliver nucleic acid sequence information of a whole genome, exome, transcriptome (all transcribed sequences of a genome) or methylome (all methylated sequences of a genome) in very short time periods, e.g. within 1-2 weeks, for example, within 1-7 days or within less than 24 hours and allow, in principle, single cell sequencing approaches. Multiple NGS platforms which are commercially available or which are mentioned in the literature can be used in the context of the present disclosure e.g. those described in detail in WO 2012/159643.

[00781] In certain embodiments a viral epitope peptide described herein molecule can comprise, but is not limited to, about 5, about 6, about 7, about 8, about 9, about 10, about 11, about 12, about 13, about 14, about 15, about 16, about 17, about 18, about 19, about 20, about 21, about 22, about 23, about 24, about 25, about 26, about 27, about 28, about 29, about 30, about 31, about 32, about 33, about 34, about 35, about 36, about 37, about 38, about 39, about 40, about 41, about 42, about 43, about 44, about 45, about 46, about 47, about 48, about 49, about 50, about 60, about 70, about 80, about 90, about 100, about 110, about 120 or greater amino acid residues, and any range derivable therein. In specific embodiments, a viral epitope peptide molecule is equal to or less than 100 amino acids.

[00782] In some embodiments, viral epitope peptides described herein for MHC Class I are 13 residues or less in length and usually consist of between about 8 and about 11 residues, particularly 9 or 10 residues. In some embodiments, viral epitope peptides described herein for MHC Class II are 9-24 residues in length.

[00783] A longer viral protein epitope peptide can be designed in several ways. In some embodiments, when HLA-binding peptides are predicted or known, a longer viral protein epitope peptide could consist of (1) individual binding peptides with extensions of 2-5 amino acids toward the N- and C-terminus of each corresponding peptide; or (2) a concatenation of some or all of the binding peptides with extended sequences for each. In some embodiments, use of a longer peptide is presumed to allow for endogenous processing by patient cells and can lead to more effective antigen presentation and induction of T cell responses. In some embodiments, two or more peptides can be used, where the peptides overlap and are tiled over the long viral epitope peptide.

[00784] In some embodiments, the viral epitope peptides and polypeptides bind an HLA protein (e.g., HLA class I or HLA class II). In specific embodiments the viral epitope peptide or polypeptide has an IC_{50} of at least less than 5000 nM, at least less than 500 nM, at least less than 100 nM, at least less than 50 nM or less.

[00785] In some embodiments, a viral protein epitope peptide described herein can be in solution, lyophilized, or can be in crystal form.

[00786] In some embodiments, a viral protein epitope peptide described herein can be prepared synthetically, by recombinant DNA technology or chemical synthesis, or can be from natural sources such as native viruses. Epitopes can be synthesized individually or joined directly or indirectly in a peptide. Although a viral epitope peptide described herein will be substantially free of other naturally occurring host cell proteins and fragments thereof, in some embodiments the peptide can be synthetically conjugated to be joined to native fragments or particles.

[00787] In some embodiments, a viral protein epitope peptide described herein can be prepared in a wide variety of ways. In some embodiments, the peptides can be synthesized in solution or on a solid support according to conventional techniques. Various automatic synthesizers are commercially available and can be used according to known protocols. (See, for example, Stewart & Young, Solid Phase Peptide Synthesis,

2D. ED., Pierce Chemical Co., 1984). Further, individual peptides can be joined using chemical ligation to produce larger peptides that are still within the bounds of the present disclosure.

[00788] Alternatively, recombinant DNA technology can be employed wherein a nucleotide sequence which encodes a peptide inserted into an expression vector, transformed or transfected into an appropriate host cell and cultivated under conditions suitable for expression. These procedures are generally known in the art, as described generally in Sambrook et al., MOLECULAR CLONING, A LABORATORY MANUAL, Cold Spring Harbor Press, Cold Spring Harbor, N.Y. (1989). Thus, recombinant peptides, which comprise or consist of one or more epitopes described herein, can be used to present the appropriate T cell epitope.

[00789] In one aspect, the present disclosure described herein also provides compositions comprising one, at least two, or more than two viral epitope peptides. In some embodiments a composition described herein contains at least two distinct peptides. In some embodiments, the at least two distinct peptides are derived from the same polypeptide. By distinct polypeptides is meant that the peptide vary by length, amino acid sequence or both. The peptides are derived from any polypeptide known to or have been found to contain a viral-specific epitope.

Viral epitope polynucleotides

[00790] Polynucleotides encoding each of the peptides described herein are also within the scope of the present disclosure. As appreciated by one of ordinary skill in the art, various nucleic acids can encode the same peptide due to the redundancy of the genetic code. Each of these nucleic acids falls within the scope of the present disclosure. This embodiment of the present disclosurecomprises DNA and RNA, for example, mRNA, and in certain embodiments a combination of DNA and RNA. In one embodiment, the mRNA is a self-amplifying mRNA. (Brito et al., Adv. Genet. 2015; 89:179-233). It is to be appreciated that any polynucleotide that encodes a peptide described herein falls within the scope of this present disclosure.

[00791] The term "RNA" includes and in some embodiments relates to "mRNA". The term "mRNA" means "messenger-RNA" and relates to a "transcript" which is generated by using a DNA template and encodes a peptide or polypeptide. Typically, an mRNA comprises a 5'-UTR, a protein coding region, and a 3'-UTR. mRNA only possesses limited half-life in cells and in vitro. In one embodiment, the mRNA is self-amplifying mRNA. In the context of the present disclosure, mRNA may be generated by in vitro transcription from a DNA template. The in vitro transcription methodology is known to the skilled person. For example, there is a variety of in vitro transcription kits commercially available.

[00792] The stability and/or translation efficiency of RNA may be modified as required. For example, RNA may be stabilized and its translation increased by one or more modifications having a stabilizing effects and/or increasing translation efficiency of RNA. Such modifications are described,

for example, in PCT/EP2006/009448, PCT/EP15/073180, and PCT/EP2015/065357, each of which are incorporated herein by reference. In order to increase expression of the RNA used according to the present disclosure, it may be modified within the coding region, i.e. the sequence encoding the expressed peptide or protein, without altering the sequence of the expressed peptide or protein, so as to increase the GC-content to increase mRNA stability and to perform a codon optimization and, thus, enhance translation in cells.

[00793] The term "modification" in the context of the RNA used in the present disclosure includes any modification of an RNA which is not naturally present in said RNA. In one embodiment of the present disclosure, the RNA used according to the present disclosure does not have uncapped 5'-triphosphates. Removal of such uncapped 5'-triphosphates can be achieved by treating RNA with a phosphatase. The RNA according to the present disclosure may have modified ribonucleotides in order to increase its stability and/or decrease cytotoxicity. For example, in one embodiment, in the RNA used according to the present disclosure cytidine may be substituted by 5-methylcytidine; 5-methylcytidine is substituted partially or completely, for example, completely, for cytidine. Alternatively, or additionally, in one embodiment, in the RNA used according to the present disclosure uridine may be substituted by a modified uridine. In some embodiments pseudouridine or 1-methyl pseudouridine; pseudouridine or 1-methyl pseudouridine is substituted partially or completely, for example, completely, for uridine.

[00794] In one embodiment the term "modification" relates to providing an RNA with a 5'-cap or 5'- cap analog. The term "5'-cap" refers to a cap structure found on the 5'-end of an mRNA molecule and generally consists of a guanosine nucleotide connected to the mRNA via an unusual 5' to 5' triphosphate linkage. In one embodiment, this guanosine is methylated at the 7-position. The term "conventional 5'-cap" refers to a naturally occurring RNA 5'-cap, to the 7-methylguanosine cap (m G). In the context of the present disclosure, the term "5'-cap" includes a 5'-cap analog that resembles the RNA cap structure and is modified to possess the ability to stabilize RNA and/or enhance translation of RNA if attached thereto, in vivo and/or in a cell.

[00795] In certain embodiments, an mRNA encoding a viral epitope is administered to a subject in need thereof. In one embodiment, the present disclosure provides RNA, oligoribonucleotide, and polyribonucleotide molecules comprising a modified nucleoside, gene therapy vectors comprising same, gene therapy methods and gene transcription silencing methods comprising same. In one embodiment, the mRNA to be administered comprises at least one modified nucleoside.

[00796] The polynucleotides encoding peptides described herein can be synthesized by chemical techniques, for example, the phosphotriester method of Matteucci, et al., J. Am. Chem. Soc. 103:3185 (1981). Polynucleotides encoding peptides comprising or consisting of an analog can be made simply by substituting the appropriate and desired nucleic acid base(s) for those that encode the native epitope.

[00797] A large number of vectors and host systems suitable for producing and administering a viral epitope peptide described herein are known to those of skill in the art, and are commercially available. The following vectors are provided by way of example. Bacterial: pQE70, pQE60, pQE-9 (Qiagen), pBS, pD10, phagescript, psiX174, pBluescript SK, pbsks, pNH8A, pNH16a, pNH18A, pNH46A (Stratagene); ptrc99a, pKK223-3, pKK233-3, pDR540, pRIT5 (Pharmacia); pCR (Invitrogen). Eukaryotic: pWLNEO, pSV2CAT, pOG44, pXT1, pSG (Stratagene) pSVK3, pBPV, pMSG, pSVL (Pharmacia); p75.6 (Valentis); pCEP (Invitrogen); pCEI (Epimmune). However, any other plasmid or vector can be used as long as it is replicable and viable in the host.

[00798] As representative examples of appropriate hosts, there can be mentioned: bacterial cells, such as *E. coli, Bacillus subtilis, Salmonella typhimurium* and various species within the genera *Pseudomonas, Streptomyces,* and *Staphylococcus;* fungal cells, such as yeast; insect cells such as Drosophila and Sf9; animal cells such as COS-7 lines of monkey kidney fibroblasts, described by Gluzman, Cell 23:175 (1981), and other cell lines capable of expressing a compatible vector, for example, the C127, 3T3, CHO, HeLa and BHK cell lines or Bowes melanoma; plant cells, etc. The selection of an appropriate host is deemed to be within the scope of those skilled in the art from the teachings herein.

[00799] Thus, the present disclosure is also directed to vectors, and expression vectors useful for the production and administration of the viral epitope peptides described herein, and to host cells comprising such vectors.

[00800] Host cells are genetically engineered (transduced or transformed or transfected) with the vectors which can be, for example, a cloning vector or an expression vector. The vector can be, for example, in the form of a plasmid, a viral particle, a phage, etc. The engineered host cells can be cultured in conventional nutrient media modified as appropriate for activating promoters, selecting transformants or amplifying the polynucleotides. The culture conditions, such as temperature, pH and the like, are those previously used with the host cell selected for expression, and will be apparent to the ordinarily skilled artisan.

[00801] For expression of the viral epitope peptides described herein, the coding sequence will be provided operably linked start and stop codons, promoter and terminator regions, and in some embodiments, and a replication system to provide an expression vector for expression in the desired cellular host. For example, promoter sequences compatible with bacterial hosts are provided in plasmids containing convenient restriction sites for insertion of the desired coding sequence. The resulting expression vectors are transformed into suitable bacterial hosts.

[00802] Generally, recombinant expression vectors will include origins of replication and selectable markers permitting transformation of the host cell, e.g., the ampicillin resistance gene of E. coli and S. cerevisiae TRP1 gene, and a promoter derived from a highly-expressed gene to direct transcription of a downstream structural sequence. Such promoters can be derived from operons encoding glycolytic enzymes such as 3-phosphoglycerate kinase (PGK), acid phosphatase, or heat shock proteins, among

others. The heterologous structural sequence is assembled in appropriate phase with translation initiation and termination sequences, and in some embodiments, a leader sequence capable of directing secretion of translated protein into the periplasmic space or extracellular medium. Optionally, the heterologous sequence can encode a fusion protein including an N-terminal identification peptide imparting desired characteristics, e.g., stabilization or simplified purification of expressed recombinant product.

[00803] Yeast, insect or mammalian cell hosts can also be used, employing suitable vectors and control sequences. Examples of mammalian expression systems include the COS-7 lines of monkey kidney fibroblasts, described by Gluzman, Cell 23:175 (1981), and other cell lines capable of expressing a compatible vector, for example, the C127, 3T3, CHO, HeLa and BHK cell lines. Mammalian expression vectors will comprise an origin of replication, a suitable promoter and enhancer, and also any necessary ribosome binding sites, polyadenylation site, splice donor and acceptor sites, transcriptional termination sequences, and 5' flanking non-transcribed sequences. Such promoters can also be derived from viral sources, such as, e.g., human cytomegalovirus (CMV-IE promoter) or herpes simplex virus type-1 (HSV TK promoter). Nucleic acid sequences derived from the SV40 splice, and polyadenylation sites can be used to provide the non-transcribed genetic elements.

[00804] Polynucleotides encoding viral epitope peptides described herein can also comprise a ubiquitination signal sequence, and/or a targeting sequence such as an endoplasmic reticulum (ER) signal sequence to facilitate movement of the resulting peptide into the endoplasmic reticulum.

[00805] Polynucleotides described herein can be administered and expressed in human cells (e.g., immune cells, including dendritic cells). A human codon usage table can be used to guide the codon choice for each amino acid. Such polynucleotides comprise spacer amino acid residues between epitopes and/or analogs, such as those described above, or can comprise naturally-occurring flanking sequences adjacent to the epitopes and/or analogs (and/or CTL, HTL, and B cell epitopes).

[00806] In some embodiments, a viral epitope peptide described herein can also be administered/expressed by viral or bacterial vectors. Examples of expression vectors include attenuated viral hosts, such as vaccinia or fowlpox. As an example of this approach, vaccinia virus is used as a vector to express nucleotide sequences that encode the viral epitope peptides described herein. Vaccinia vectors and methods useful in immunization protocols are described in, e.g., U.S. Pat. No. 4,722,848. Another vector is BCG (Bacille Calmette Guerin). BCG vectors are described by Stover et al., Nature 351:456-460 (1991). A wide variety of other vectors useful for therapeutic administration or immunization of the viral epitope polypeptides described herein, e.g. adeno and adeno-associated virus vectors, retroviral vectors, Salmonella typhi vectors, detoxified anthrax toxin vectors, Sendai virus vectors, poxvirus vectors, canarypox vectors, and fowlpox vectors, and the like, will be apparent to those skilled in the art from the description herein. In some embodiments, the vector is Modified Vaccinia Ankara (VA) (e.g. Bavarian Nordic (MVA-BN)).

[00807] Standard regulatory sequences well known to those of skill in the art can be included in the vector to ensure expression in the human target cells. Several vector elements are desirable: a promoter with a downstream cloning site for polynucleotide, e.g., minigene insertion; a polyadenylation signal for efficient transcription termination; an E. coli origin of replication; and an E. coli selectable marker (e.g. ampicillin or kanamycin resistance). Numerous promoters can be used for this purpose, e.g., the human cytomegalovirus (hCMV) promoter. See, e.g., U.S. Pat. Nos. 5,580,859 and 5,589,466 for other suitable promoter sequences. In some embodiments, the promoter is the CMV-IE promoter.

[00808] Polynucleotides described herein can comprise one or more synthetic or naturally-occurring introns in the transcribed region. The inclusion of mRNA stabilization sequences and sequences for replication in mammalian cells can also be considered for increasing polynucleotide expression.

[00809] In addition, a polynucleotide described herein can comprise immunostimulatory sequences (ISSs or CpGs). These sequences can be included in the vector, outside the polynucleotide coding sequence to enhance immunogenicity.

Viral epitopes

[00810] Coronaviruses are enveloped positive-stranded RNA viruses that belong to the family Coronaviridae and the order Nidovirales. Coronaviruses frequently infect people around the globe. There are a large number of coronaviruses, most of which circulate among peridomestic animals including pigs, camels, bats and cats. Of the seven coronaviruses identified in human so far, Coronaviruses 229E, NL63 were classified as Group 1 antigenic viruses, OC43 and HKU1 were classified as Group 2 antigenic viruses. They typically infect upper respiratory tract in human and can bring about acute respiratory syndrome and can be fatal. Coronaviruses may be zoonotic in origin. The SARS-CoV, MERS-CoV and 2019 SARS CoV-2 have human transmission and infective capability and have caused major public health concern worldwide over a short period within the century. The expansion of genetic diversity among coronaviruses and their consequent ability to cause disease in human beings is mainly achieved through infecting peridomestic animals, which serve as intermediate hosts, nurturing recombination and mutation events. The spike glycoprotein (S glycoprotein), which attaches the virion to the host cell membrane, is postulated to play a dominant role in host range restriction. While SARS-CoV and 2019 SARS CoV-2 infect type 2 pneumocytes and ciliated bronchial epithelial cells utilizing angiotensin converting enzyme 2 (ACE2) as a receptor, MERS-CoV exploits dipeptidyl peptidase 4 (DPP4), a transmembrane glycoprotein, to infect type 2 pneumocytes and unciliated bronchial epithelial cells.

[00811] Coronaviruses first replicate in epithelial cells of the respiratory and enteric cells. Human airway epithelial cells facilitate high growth rate for the 2019 SARS CoV-2 virus. Coronavirus infected human beings can present with influenza-like symptoms and can develop pneumonia. Associated symptoms with the disease include cough, fever, dyspnea, myalgia or fatigue. Some human patients present with mild

clinical manifestation of the disease. However, the manifestation of the disease in human population can span a wide range from asymptomatic to fatal. In some cases, human coronavirus has an incubation period of 2–4 days; 2019 SARS CoV-2 is estimated to be 3-6 days, and SARS-CoV can be 4-6 days. SARS coronavirus was identified in 2003 and may have originated from an animal reservoir, and first infected humans in Guangdong province in southern China in 2002. Patients presented respiratory distress and diarrhea. MERS-CoV was identified in Saudi Arabia in 2012. Dromedary camels may have been the major reservoirs of MERS-CoV. Typical MERS symptoms include fever, cough, shortness of breath, pneumonia, gastrointestinal symptoms including diarrhea. 2019 SARS CoV-2 is also called SARS CoV-2 or simply CoV-2.

[00812] Human-to-human transmission of SARS-CoV occurred after early importation of cases were Toronto in Canada, Hong Kong Special Administrative Region of China, Chinese Taipei, Singapore, and Hanoi in Viet Nam during the global epidemic of 2003; at least four resurgences have since been reported. MERS is reported to have spread to countries, including at least Algeria, Austria, Bahrain, China, Egypt, France, Germany, Greece, Islamic Republic of Iran, Italy, Jordan, Kuwait, Lebanon, Malaysia, the Netherlands, Oman, Philippines, Qatar, Republic of Korea, Kingdom of Saudi Arabia, Thailand, Tunisia, Turkey, United Arab Emirates, United Kingdom, United States, and Yemen during the 2012 outbreak. The 2019 SARS CoV-2 was first identified in Wuhan, China and spread worldwide between December 2019 and early 2020.

[00813] As of March 20, 2019, no vaccines had been approved for these viruses. Novel therapeutics against the virus are needed. The present disclosure comprises methods and compositions for developing immunotherapy using subject's own immune cells to activate immune response against the virus.

[00814] In one aspect the method comprises one or more of the following:

- Analyzing the virus genome sequence to obtain information on potential viral epitopes.
- Analyzing a subject's MHC class I and MHC class II expression profiles.
- Analyzing the viral sequences in MHC-peptide presentation prediction algorithm implemented in a computer processor wherein the MHC-peptide presentation prediction algorithm implemented in a computer processor has been trained by a machine learning training module that incorporates a large number of characteristics related to the peptide and peptide MHC interactions in order to provide an output of a selection of peptides that are predicted to bind to a certain MHC molecule. In some embodiments, the MHC-peptide presentation predictor is *neonmhc2*. In some embodiments, a further analysis using MHC-peptide presentation predictor NetMHCpan or NetMHCpan II is performed for comparison. In some embodiments, the MHC-peptide presentation predictor is NetMHCpan. In some embodiments, the MHC-peptide presentation predictor is NetMHCpan II.
- Identifying which viral epitopes can bind to an MHC present in the subject.

- Ranking aided by a machine learning the viral peptides that bind to the subjects' MHC molecules according to the binding affinities, where higher rank infers higher binding affinity and presentation efficiency.
- Select at least one, at least two, at least three or at least four or more viral peptides from the ranked peptides that have high binding affinity to the subject's one or more MHC molecules and prepare a composition. The viral peptides that are selected, taken together may bind to one or more class I MHCs, or a class II MHCs or a mixture of class I and class II MHCs, wherein each of the MHCs is expressed by the subject.

[00815] Provided herein an antigenic peptide comprising an epitope sequence from Table 1A, Table 1B, Table 1C, Table 2Ai, Table 2Aii, Table 2B, Table 9, Table 10, Table 11, Table 12, Table 14A, Table 14B, Table 15 or Table 16. Also provided herein is a polynucleotide encoding and antigenic peptide comprising an epitope sequence from Table 1A, Table 1B, Table 1C, Table 2Ai, Table 2Aii, Table 2B, Table 9, Table 10, Table 11, Table 12, Table 14A, Table 14B, Table 14C, Table 15 or Table 16. The antigenic peptide and/or polynucleotide may be recombinant. The antigenic peptide and/or polynucleotide may be isolated or purified. The antigenic peptide may be synthetic or expressed from a polynucleotide.

[00816] Also provided herein is an antibody or B cell comprising an antibody that binds to an antigenic peptide comprising an epitope sequence from Table 1A, Table 1B, Table 1C, Table 2Ai, Table 2Aii, Table 2B, Table 9, Table 10, Table 11, Table 12, Table 14A, Table 14B, Table 14C, Table 15 or Table 16.

[00817] Also provided herein is a T cell receptor (TCR) or T cell comprising a TCR that that binds an epitope sequence from Table 1A or Table 1B in complex with a corresponding MHC class I molecule according to Table 1A or Table 1B. For example, the TCR can bind to an epitope sequence from column 2 (set 1) of Table 1A in complex with a corresponding MHC class I molecule from column 3 (set 1) in the same row of Table 1A. For example, the TCR can bind to an epitope sequence from column 4 (set 2) of Table 1A in complex with a corresponding MHC class I molecule from column 5 (set 2) in the same row of Table 1A. For example, the TCR can bind to an epitope sequence from column 6 (set 3) of Table 1A in complex with a corresponding MHC class I molecule from column 7 (set 3) in the same row of Table 1A. For example, the TCR can bind to an epitope sequence from column 2 (set 1) of Table 1B in complex with a corresponding MHC class I molecule from column 3 (set 1) in the same row of Table 1B. For example, the TCR can bind to an epitope sequence from column 4 (set 2) of Table 1B in complex with a corresponding MHC class I molecule from column 5 (set 2) in the same row of Table 1B.

[00818] Also provided herein is a T cell receptor (TCR) or T cell comprising a TCR that that binds to an epitope sequence from Table 2Ai in complex with a corresponding MHC class II molecule according to Table 2Ai. For example, the TCR can bind to an epitope sequence from column 2 (set 1) of Table 2Ai in complex with a corresponding MHC class II molecule from column 3 (set 1) in the same row of Table 2Ai. For example, the TCR can bind to an epitope sequence from column 4 (set 2) of Table 2Ai in complex with

a corresponding MHC class II molecule from column 5 (set 2) in the same row of Table 2Ai. Also provided herein is a T cell receptor (TCR) or T cell comprising a TCR that that binds to an epitope sequence from Table 2Aii in complex with a corresponding MHC class II molecule according to Table 2Aii. For example, the TCR can bind to an epitope sequence from column 2 (set 1) of Table 2Aii in complex with a corresponding MHC class II molecule from column 3 (set 1) in the same row of Table 2Aii.

[00819] Provided herein is a method of treating or preventing viral infection in a subject in need thereof comprising administering to the subject an antigenic peptide comprising an epitope sequence from Table 1A, Table 1B, Table 1C, Table 2Ai, Table 2Aii, Table 2B, Table 9, Table 10, Table 11, Table 12, Table 14A, Table 14B, Table 14C, Table 15 or Table 16. Also provided herein is a method of treating or preventing viral infection in a subject in need thereof comprising administering to the subject a polynucleotide encoding and antigenic peptide comprising an epitope sequence from Table 1A, Table 1B, Table 1C, Table 2Ai, Table 2Aii, Table 2B, Table 9, Table 10, Table 11, Table 12, Table 14A, Table 14B, Table 14C, Table 15 or Table 16.

[00820] Also provided herein is a method of treating or preventing a viral infection in a subject in need thereof comprising administering to the subject an antibody or B cell comprising an antibody that binds to an antigenic peptide comprising an epitope sequence from Table 1A, Table 1B, Table 1C, Table 2Ai, Table 2Aii, Table 2B, Table 9, Table 10, Table 11, Table 12, Table 14A, Table 14B, Table 14C, Table 15 or Table 16.

[00821] Also provided herein is a method of treating or preventing viral infection in a subject in need thereof comprising administering to the subject a T cell receptor (TCR) or T cell comprising a TCR that that binds an epitope sequence from Table 1A, Table 1B, Table 1C, Table 2Ai, Table 2Aii, Table 2B, Table 9, Table 10, Table 11, Table 12, Table 14A, Table 14B, Table 15 or Table 16 in complex with a corresponding MHC class I molecule according to Table 1A, Table 1B, Table 1C, Table 2Ai, Table 2Aii, Table 2B, Table 9, Table 10, Table 11, Table 12, Table 14A, Table 14B, Table 14C, Table 15 or Table 16.

[00822] For example, the method can comprise administering to the subject a TCR or T cell comprising a TCR that can bind to an epitope sequence from column 2 (set 1) of Table 1A in complex with a corresponding MHC class I molecule from column 3 (set 1) in the same row of Table 1A. For example, the method can comprise administering to a TCR or T cell comprising a TCR that can bind to an epitope sequence from column 2 (set 1) of Table 1A in complex with a corresponding MHC class I molecule from column 3 (set 1) in the same row of Table 1A to a subject that expresses the corresponding MHC class I molecule from column 3 (set 1). For example, the method can comprise administering to the subject a TCR or T cell comprising a TCR that can bind to an epitope sequence from column 4 (set 2) of Table 1A in complex with a corresponding MHC class I molecule from column 5 (set 2) in the same row of Table 1A. For example, the method can comprise administering to a TCR or T cell comprising a TCR that can bind to an epitope sequence from column 4 (set 2) of Table 1A in complex with a corresponding MHC class I

molecule from column 5 (set 2) in the same row of Table 1A to a subject that expresses the corresponding MHC class I molecule from column 5 (set 2). For example, the method can comprise administering to the subject a TCR or T cell comprising a TCR that can bind to an epitope sequence from column 6 (set 3) of Table 1A in complex with a corresponding MHC class I molecule from column 7 (set 3) in the same row of Table 1A. For example, the method can comprise administering to a TCR or T cell comprising a TCR that can bind to an epitope sequence from column 6 (set 3) of Table 1A in complex with a corresponding MHC class I molecule from column 7 (set 3) in the same row of Table 1A to a subject that expresses the corresponding MHC class I molecule from column 7 (set 3).

[00823] For example, the method can comprise administering to the subject a TCR or T cell comprising a TCR that can bind to an epitope sequence from column 2 (set 1) of Table 1B in complex with a corresponding MHC class I molecule from column 3 (set 1) in the same row of Table 1B. For example, the method can comprise administering to a TCR or T cell comprising a TCR that can bind to an epitope sequence from column 2 (set 1) of Table 1B in complex with a corresponding MHC class I molecule from column 3 (set 1) in the same row of Table 1B to a subject that expresses the corresponding MHC class I molecule from column 3 (set 1). For example, the method can comprise administering to the subject a TCR or T cell comprising a TCR that can bind to an epitope sequence from column 4 (set 2) of Table 1B in complex with a corresponding MHC class I molecule from column 5 (set 2) in the same row of Table 1B. For example, the method can comprise administering to a TCR or T cell comprising a TCR that can bind to an epitope sequence from column 4 (set 2) of Table 1B in complex with a corresponding MHC class I molecule from column 5 (set 2) in the same row of Table 1B to a subject that expresses the corresponding MHC class I molecule from column 5 (set 2).

[00824] For example, the method can comprise administering to the subject a TCR or T cell comprising a TCR that can bind to an epitope sequence from column 2 (set 1) of Table 2Ai in complex with a corresponding MHC class II molecule from column 3 (set 1) in the same row of Table 2Ai. For example, the method can comprise administering to a TCR or T cell comprising a TCR that can bind to an epitope sequence from column 2 (set 1) of Table 2Ai in complex with a corresponding MHC class II molecule from column 3 (set 1) in the same row of Table 2Ai to a subject that expresses the corresponding MHC class II molecule from column 3 (set 1). For example, the method can comprise administering to the subject a TCR or T cell comprising a TCR that can bind to an epitope sequence from column 4 (set 2) of Table 2Ai in complex with a corresponding MHC class II molecule from column 5 (set 2) in the same row of Table 2Ai. For example, the method can comprise administering to a TCR or T cell comprising a TCR that can bind to an epitope sequence from column 4 (set 2) of Table 2Ai in complex with a corresponding MHC class II molecule from column 5 (set 2) in the same row of Table 2Ai to a subject that expresses the corresponding MHC class II molecule from column 5 (set 2). Likewise, the method can comprise administering to the subject a TCR or T cell comprising a TCR that can bind to an epitope sequence from

column on the left of Table 2Aii in complex with a corresponding MHC class II molecule from the respective column on the right in the same row of Table 2Aii. A protein encoded by the corresponding allele to the right adjacent column of a peptide in any single row of Table 2Ai or Table 2Aii is an MHC protein that binds to the peptide and is presented to T cells by APCs. A peptide listed on the immediate left column of an HLA allele(s) in each row is matched with the HLA in the row.

Table 1A. Peptides and Alleles

	Set 1	Set 1	Set 2	Set 2	Set 3	Set 3
	Peptide	**Allele**	**Peptide**	**Allele**	**Peptide**	**Allele**
1	AACCHLAKAL	L61	TPLVPFWI	L47	FLVLLPLV	L2;L47;L4
2	AADLDDFSKQL	L68	TPLVPFWITIA	L50	FLYENAFLP	L12;L2;L4
3	AADPAMHAAS	L68	TPLVPFWITIAY	L31	FMGRIRSVY	L14;L43;L69
4	AAGLEAPFLYL	L67	TPNNTDFSRV	L51	FNATRFASV	L3;L20;L73
5	AAISDYDY	L54	TPRDLGAC	L51	FNIDYDCVSF	L43;L71;L72
6	AAISDYDYYR	L15	TPSFKKGAKLL	L39	FPDLNGDVVAI	L68;L50;L49
7	AAITILDGI	L10	TPSKLIEYT	L49	FPFNKWGKA	L50;L51;L46
8	AAITILDGISQY	L14	TPVYSFLPGVY	L31	FPLCANGQVF	L31;L50;L32
9	AAKKNNLPFK	L13	TQEVFAQV	L48	FPLNSIIKT	L50;L31;L47
10	AALALLLLDR	L7	TQFNYYKK	L24	FPLNSIIKTI	L47;L50;L49
11	AALCTFLL	L74	TQGNFGDQEL	L34	FRIDGDMVP	L66;L35;L34
12	AALQIPFA	L50	TQGNFGDQELI	L34	FRKSNLKPF	L66;L30;L58
13	AALQPEEEQ	L67	TQHGKEDLKF	L26	FRLTLGVYDY	L66;L30;L12
14	AAMQRKLEK	L7	TQLPPAYTNSF	L8	FRSSVLHST	L66;L35;L64
15	AANTVIWDYKR	L15	TQLSTDTGV	L24	FSALEPLV	L48;L47;L70
16	AARDLICAQ	L43	TQLYLGGMSYY	L14	FSKLINIIIW	L52;L69;L70
17	AARDLICAQK	L13	TQQLIRAA	L48	FSSLPSYAAF	L59;L60;L43
18	AARVVRSIFSR	L15	TQRNFYEPQI	L48	FSTVFPPTSF	L43;L60;L59
19	AARYMRSLK	L13	TQSLLIVNN	L24	FTSLEIPRR	L19;L17;L21
20	AASGNLLLD	L69	TQYEYGTEDDY	L14	FTYICGFIQQK	L7;L6;L19
21	AASGNLLLDK	L7	TRAGCLIGA	L30	FVDGVPFVVS	L68;L5;L67
22	AAVDALCEKAL	L67	TRCLAVHEC	L35	FVDSDVET	L63;L68;L62
23	AAVINGDRWF	L52	TRCNLGGAV	L35	FVENPDILRV	L20;L5;L63
24	AAVNSVPW	L54	TRDIASTD	L65	FVENPDILRVY	L14;L1;L31
25	AAVYRINW	L54	TRDIASTDT	L35	FVETVKGL	L63;L68;L60
26	AAYSRYRIGNY	L14	TRDIASTDTCF	L34	FVETVKGLDY	L1;L12;L18
27	ACLVGLMWL	L4	TREVGFVV	L35	FVFKNIDGYF	L11;L58;L12
28	ACPLIAAVI	L57	TRFASVYAWNR	L30	FVKATCEF	L58;L59;L43
29	ACTDDNALA	L42	TRFQTLLALH	L30	FVLAAVYR	L17;L15;L21
30	ACTDDNALAYY	L14	TRFQTLLALHR	L30	FVRIIMRL	L74;L59;L23
31	ACVEEVTTTL	L36	TRGATVVIG	L65	FVRIIMRLW	L52;L49;L10
32	ACYNGSPSGV	L3	TRKLMPVCV	L64	FVTVYSHLLL	L74;L60;L61
33	ACYNGSPSGVY	L14	TRLQSLENVAF	L30	FYKGVITH	L71;L66;L72
34	ADAQSFLN	L33	TRNPANNAA	L35	FYLCFLAFLLF	L9;L12;L8
35	ADAQSFLNGF	L33	TRNPAWRKAVF	L65	FYPKLQSS	L71;L72;L66

36	ADDLNQLT	L33	TRQVVNVVT	L35	FYPKLQSSQ	L71;L72;L66
37	ADKFPVLHD	L65	TRSTNSRI	L35	FYTSKTTVA	L72;L71;L46
38	ADLKSFDL	L33	TRYVDNNFC	L34	FYVLGLAA	L50;L72;L71
39	ADLVYALR	L33	TSALLAGTI	L55	FYVLPNDDTL	L67;L9;L71
40	ADLVYALRH	L33	TSAMQTML	L74	FYYLGTGPEA	L50;L71;L72
41	ADLYKLMGH	L33	TSDLATNNLVV	L68	GADLKSFDL	L68;L63;L60
42	ADLYKLMGHF	L33	TSFGPLVRKIF	L52	GADPIHSLRV	L18;L63;L5
43	ADNKFALTC	L33	TSGDGTTS	L65	GAPTKVTF	L23;L63;L57
44	ADPAMHAA	L33	TSHTVMPL	L57	GAWNIGEQK	L13;L7;L19
45	ADPIHSLR	L33	TSITSAVLQ	L19	GCDGGSLY	L1;L18;L14
46	ADPIHSLRV	L33	TSLEIPRRNV	L13	GCDGGSLYV	L18;L2;L45
47	ADQAMTQM	L33	TSLLVLVQ	L48	GDDYVYLPY	L18;L1;L65
48	ADQAMTQMY	L14	TSNPTTFH	L43	GDFKLNEEI	L37;L24;L34
49	ADQLTPTW	L33	TSNPTTFHLD	L65	GDFSHSQL	L25;L33;L37
50	ADSFVIRG	L33	TSPDVDLGD	L65	GEAANFCALI	L45;L36;L41
51	ADSIIIGG	L33	TSQWLTNI	L48	GEAVKTQFN	L45;L36;L40
52	ADSIIIGGA	L33	TSQWLTNIF	L53	GEIKDATP	L38;L46;L37
53	ADSKIVQLS	L33	TSSIVITSG	L65	GEIPVAYRKVLL	L36;L40;L41
54	ADSTLIGD	L33	TSTDVVYRA	L20	GELGDVRETM	L36;L41;L37
55	ADVFHLYL	L33	TSWQTGDFVK	L7	GEVITFDNLKTL	L36;L37;L41
56	ADVFHLYLQ	L33	TTAAKLMV	L73	GEVPVSIINN	L36;L37;L41
57	ADVTKIKP	L33	TTADIVVFDEI	L20	GEYTFEKGD	L45;L46;L37
58	ADYNYKLPD	L65	TTAPAICHD	L20	GFELTSMKY	L12;L18;L1
59	ADYSVLYN	L33	TTAPAICHDGK	L19	GFFKEGSSV	L72;L24;L71
60	AEASKKPRQK	L46	TTAYANSV	L20	GFMGRIRSVY	L71;L14;L72
61	AECTIFKD	L33	TTDNTFVS	L1	GFNEKTHVQL	L8;L71;L62
62	AEETRKLM	L45	TTDPSFLGRYM	L1	GFNFSQIL	L62;L72;L71
63	AEGSRGGSQ	L40	TTEMLAKALR	L19	GFSTGVNL	L72;L71;L62
64	AEIRASAN	L45	TTETAHSC	L18	GHMLDMYSV	L35;L28;L34
65	AELAKNVS	L46	TTEVVGDIILK	L7	GHNLAKHCL	L35;L34;L28
66	AENVTGLFKDC	L40	TTFHLDGEV	L20	GHTDLMAAY	L27;L12;L14
67	AESHVDTD	L33	TTFHLDGEVI	L20	GHVETFYPKL	L28;L34;L35
68	AEVAVKMFD	L41	TTFHLDGEVITF	L52	GIATVREV	L48;L3;L64
69	AFACPDGVKHVY	L14	TTKGGRFV	L70	GIFGADPIHSL	L16;L2;L10
70	AFASEAARV	L24	TTLPVNVAFEL W	L52	GIIAMSAF	L43;L26;L59
71	AFDIYNDK	L62	TTNIVTRCLNR	L15	GINASVVNI	L24;L3;L4
72	AFDIYNDKV	L62	TTRQVVNV	L48	GLDSLDTY	L18;L1;L14
73	AFDKSAFVN	L62	TTSPISEHD	L20	GLEAPFLY	L1;L18;L12
74	AFEHIVYG	L62	TTTIQTIV	L48	GLIAIVMVTI	L3;L24;L2
75	AFFGMSRI	L48	TTTLNGLW	L52	GLNDNLLEIL	L4;L2;L3
76	AFGEYSHVVA	L42	TTTNIVTRCL	L20	GLNLEEAARY	L14;L12;L18
77	AFHTPAFDK	L7	TTTYKLNVGDY	L14	GLPGTILRT	L24;L5;L2
78	AFKQIVESC	L13	TTYKLNVGD	L19	GLVASIKNF	L10;L27;L26
79	AFLLFLVLIM	L71	TTYPGQGLN	L14	GMPSYCTGY	L26;L27;L12
80	AFLPFAMGIIAM	L71	TVAAFHQEC	L20	GNFGDQELI	L34;L24;L36

81	AFVNLKQLP	L46	TVAYFNMV	L20	GPFVDRQTA	L51;L50;L46
82	AFVNLKQLPFFY	L12	TVCTVCGMW	L10	GQVDLFRNA	L24;L13;L46
83	AGDSGFAAYSRY	L18	TVDNINLH	L1	GRCDIKDL	L66;L25;L64
84	AGFAKFLK	L7	TVDNINLHT	L68	GRVDGQVDLF	L30;L34;L65
85	AGGIVAIV	L48	TVDSSQGSEYDY	L18	GSSVELKHF	L53;L52;L26
86	AGLEAPFLYL	L67	TVFFDGRV	L20	GTAVLRQW	L52;L54;L55
87	AGLEAPFLYLY	L14	TVHTANKW	L54	GTDLEGNF	L1;L62;L63
88	AGSYKDWSY	L14	TVIEVQGYKSV	L10	GTDTTITV	L18;L63;L68
89	AHISTIGVCSM	L34	TVKGLDYKA	L51	GTGPEAGLPY	L18;L12;L7
90	AHVASCDAIM	L28	TVKNYFITD	L13	GTGTSTDVVYR	L7;L15;L19
91	AICHDGKAH	L43	TVKSVGKFCL	L39	GTITVEEL	L67;L55;L54
92	AIDAYPLTKH	L6	TVLKKCKSA	L23	GTITVEELK	L7;L13;L19
93	AIDGGVTRDI	L68	TVLKKCKSAF	L23	GTLMIERF	L54;L52;L53
94	AIFYLITPVHV	L20	TVLSFCAFAV	L4	GTLSYEQF	L54;L53;L52
95	AIKCVPQAD	L43	TVMFLARGI	L55	GTLSYEQFK	L7;L6;L13
96	AILTALRLC	L14	TVRTNVYLAVF	L52	GTNLPLQL	L73;L55;L60
97	AILTALRLCAY	L14	TVSALVYDNK	L7	GTSKFYGGW	L10;L54;L52
98	AIMQLFFSYF	L12	TVVIGTSK	L19	GVAGALNK	L7;L6;L19
99	AISSVLNDI	L24	TVVIGTSKFY	L14	GVEHVTFFIY	L12;L18;L1
100	AIVFITLCFTLK	L7	TVVVNAANV	L20	GVLTESNKK	L7;L13;L6
101	AKCWTETDL	L44	TVVVNAANVY	L14	GVYYHKNNK	L7;L6;L13
102	AKEIKESVQTF	L27	TVYEKLKPVL	L20	GWTAGAAAY	L12;L14;L27
103	AKFLKTNCC	L27	TVYSDVENP	L49	GYFCTCYF	L72;L71;L9
104	AKFLKTNCCRF	L27	TVYSHLLLVAA	L51	GYLPQNAV	L48;L71;L72
105	AKHCLHVVG	L44	TWICLLQFAY	L12	GYQPYRVV	L72;L71;L64
106	AKKNNLPFK	L13	TWLDMVDTSL	L8	HAEETRKLM	L32;L63;L49
107	AKKPTETIC	L27	TWLTYTGAI	L8	HDVSSAINR	L19;L17;L15
108	AKNRARTV	L48	TWLTYTGAIKL	L8	HEHEIAWYTE	L37;L46;L29
109	AKNVSLDNVL	L44	TYERHSLSH	L71	HEVLLAPLLSA	L46;L41;L38
110	AKPFLNKVV	L64	TYGQQFGPTYL	L9	HFAWWTAF	L72;L71;L62
111	AKRFKESPF	L27	TYKLNVGDYF	L9	HFDGQQGEV	L62;L68;L63
112	AKSASVYY	L27	TYNCCDDDY	L14	HFISNSWL	L72;L71;L62
113	AKVGILCIM	L44	TYTGAIKLD	L9	HFPREGVF	L62;L72;L71
114	ALAPNMMVTN	L3	TYYLFDESGEF	L9	HFPREGVFV	L62;L71;L72
115	ALGGSVAI	L24	VAAIFYLI	L47	HFVCNLLL	L62;L71;L72
116	ALGGSVAIKI	L24	VAAIVFITLCF	L52	HFVCNLLLLF	L8;L12;L9
117	ALGKLQDV	L24	VAALTNNVA	L50	HFVNLDNL	L71;L62;L72
118	ALHRSYLTP	L46	VADAVIKTLQ	L63	HFVNLDNLR	L17;L15;L19
119	ALITLATC	L3	VAEWFLAYIL	L67	HFYSKWYIR	L17;L15;L21
120	ALKGGKIVNNW	L16	VAFELWAKRN	L69	HGHVMVEL	L23;L25;L59
121	ALLADKFPVLH	L6	VAGDSGFAA	L50	HHANEYRLYL	L34;L28;L35
122	ALLAVFQSASK	L6	VAGFAKFLK	L7	HHSIGFDYV	L34;L28;L35
123	ALLLLDRLNQL	L4	VAGVSICST	L43	HIDAYKTF	L63;L62;L68
124	ALLTLQQIELK	L6	VAIDYKHYTP	L67	HLAKALNDF	L26;L11;L10

125	ALNKATNNA	L3	VAIHADQLTPTW	L52	HLYLQYIRK	L6;L13;L7
126	ALRANSAV	L3	VAKSHNIALI	L70	HPLADNKF	L32;L31;L47
127	ALTGIAVEQ	L24	VAKSHNIALIW	L52	HPNPKGFCD	L32;L49;L39
128	ALWEIQQVVD	L2	VALLAVFQSA	L50	HQKLLKSI	L48;L25;L23
129	ALWEIQQVVDA	L2	VAMKYNYEPL	L67	HQSDIEVT	L24;L35;L44
130	AMDEFIERYKL	L5	VANGDSEVVLK	L7	HSDKFTDGV	L18;L1;L63
131	AMPNMLRI	L48	VANYQKVGM	L58	HSMQNCVLK	L7;L13;L19
132	AMQMAYRF	L33	VAPGTAVLRQW	L52	HTDLMAAY	L18;L1;L68
133	AMRNAGIVGV	L3	VARDLSLQFK	L13	HTIDGSSGVV	L11;L20;L10
134	AMRPNFTI	L48	VASCDAIMTR	L19	HTPAFDKSAF	L57;L11;L10
135	AMSAFAMMF	L12	VASPNECNQM	L70	HTQVVDMSMTY	L18;L14;L1
136	ANFCALIL	L73	VAVLYQDVN	L67	HTSPDVDL	L53;L20;L54
137	ANFCALILA	L46	VAYSNNSIAI	L47	HVDILGPL	L68;L63;L62
138	ANFCALILAY	L12	VCRFDTRV	L48	HVDTDLTKPY	L18;L1;L14
139	ANGDSEVVLKK	L7	VCRFDTRVL	L39	HVSGTNGTK	L19;L7;L6
140	ANGGKGFCK	L7	VCRLMKTI	L48	HVYQLRAR	L17;L15;L21
141	ANLDSCKRV	L4	VCSVIDLL	L62	IADTTDAV	L68;L63;L67
142	ANLDSCKRVL	L65	VCTNYMPYF	L9	IAMSAFAM	L59;L61;L70
143	ANLGERVRQA	L65	VCTNYMPYFF	L9	IASFRLFAR	L17;L19;L15
144	ANNAAIVLQL	L73	VCVETKAI	L48	IAVLDMCASL	L67;L31;L60
145	ANNCTFEYV	L73	VDALCEKAL	L33	IAYIICISTK	L19;L47;L43
146	ANNTKGSL	L23	VDDIVKTD	L33	ICISTKHFY	L14;L12;L58
147	ANQFNSAIGK	L7	VDGQVDLF	L33	IDYVPLKSA	L46;L51;L43
148	ANQVIVNNL	L72	VDGVVQQL	L33	IEELFYSY	L29;L18;L1
149	ANRNRFLYI	L73	VDNSSLTI	L48	IEELFYSYA	L38;L42;L46
150	ANSIVCRF	L33	VDSDLNDF	L33	IELKFNPPA	L46;L38;L42
151	ANSIVCRFD	L65	VDSVTVKN	L33	IELKFNPPAL	L36;L37;L29
152	ANYQKVGM	L33	VDSYYSLL	L33	IELSLIDFYL	L40;L36;L41
153	ANYQKVGMQKY	L14	VDSYYSLLM	L33	IERFVSLAI	L45;L48;L46
154	APAHISTIG	L22	VDTDLTKPY	L43	IEYTDFATSA	L46;L38;L42
155	APFLYLYALVY	L31	VDTSLSGF	L33	IFFASFYY	L12;L71;L72
156	APHGVVFLH	L56	VDTVRTNVY	L29	IFYLITPVH	L72;L71;L48
157	APHGVVFLHVT	L56	VDTVSALV	L33	IGIVNNTVY	L26;L27;L29
158	APHGVVFLHVTY	L56	VDVELFENK	L7	IGVTQNVLY	L12;L52;L14
159	APISAMVRMY	L31	VDVVNFNL	L33	IHADQLTPTW	L28;L52;L54
160	APKEIIFLEG	L51	VEAEVQID	L29	IIAYTMSL	L59;L60;L61
161	APLIELCV	L47	VEAEVQIDR	L19	IKDATPSDF	L62;L27;L63
162	APLIELCVDEA	L50	VEAFEYYHT	L38	IKDLPKEI	L68;L62;L63
163	APLLSAGIFGA	L50	VEAFEYYHTT	L38	IKNFKSVLY	L27;L12;L18
164	APLTVFFD	L65	VECTTIVN	L29	IKWDLLKY	L27;L18;L66
165	APRITFGGP	L51	VECTTIVNGV	L45	ILAYCNKTV	L3;L2;L4
166	APRITFGGPSD	L22	VEEAKTVLK	L38	ILHCANFNV	L4;L2;L5
167	APRTLLTKGTL	L22	VEEVLSEA	L38	ILLLDQALV	L2;L4;L5
168	APTHLSVDT	L56	VEFLRDGW	L29	ILPDPSKPS	L57;L43;L5
169	APTKVTFGD	L56	VEGFNCYF	L33	ILQKEKVNI	L24;L2;L4

170	APTLVPQEHY	L31	VEIIKSQD	L45	ILSDDAVVC	L2;L26;L4
171	AQAAGTDTT	L44	VEIIKSQDLSV	L38	ILSPLYAFA	L3;L2;L5
172	AQFAPSASAFF	L27	VEKGIYQTS	L45	ILTLTRAL	L23;L59;L57
173	AQLPAPRT	L48	VELGTEVN	L29	IMSDRDLY	L18;L14;L1
174	AQLPAPRTLL	L44	VENPTIQK	L29	INIIIWFLL	L73;L9;L8
175	AQLPAPRTLLTK	L7	VENPTIQKDV	L45	INIIIWFLLL	L73;L8;L67
176	AQSFLNGFAV	L24	VENPTIQKDVL	L36	IPARARVEC	L56;L22;L39
177	AQTGSSKCV	L24	VESDDYIA	L38	IPCSVCLSGL	L56;L22;L39
178	AQVDVVNFNL	L44	VESSSKLW	L40	IPCTCGKQA	L51;L50;L39
179	AQVLSEMV	L48	VETKAIVS	L29	IPIGAGICA	L51;L50;L22
180	AQYELKHG	L48	VEVEKGVLPQL	L36	IPLMYKGL	L39;L47;L23
181	ARARVECF	L35	VEVQPQLEMEL	L36	IPMDSTVKN	L49;L31;L32
182	ARARVECFDK	L30	VEVVDKYF	L29	IPYNSVTSS	L51;L47;L50
183	ARDGCVPLNII	L34	VEWKFYDA	L46	IQASLPFGW	L52;L16;L54
184	ARDLICAQK	L30	VEYCPIFFITG	L46	IQLSSYSL	L44;L35;L25
185	ARDLSLQFK	L30	VFAFPFTI	L9	IRGWIFGTTL	L35;L30;L66
186	ARDLSLQFKR	L30	VFAFPFTIYSL	L8	IRKLHDEL	L25;L66;L67
187	ARFPKSDGT	L30	VFAQVKQI	L48	ISAARQGF	L54;L53;L52
188	ARFPKSDGTGT	L30	VFDEISMA	L62	ISAMVRMY	L55;L70;L52
189	ARFYFYTS	L65	VFDEISMATN	L62	ISQYSLRLI	L55;L48;L73
190	ARGIVFMC	L65	VFDGKSKCE	L62	ISSDVLVNN	L53;L54;L52
191	ARHINAQVAK	L30	VFDKNLYD	L62	ISTKHFYWFF	L53;L54;L52
192	ARIVYTACSH	L30	VFDKNLYDK	L62	ISTSHKLV	L48;L70;L73
193	ARLRAKHY	L66	VFDKNLYDKL	L62	ITEGSVKGL	L63;L60;L39
194	ARLRAKHYV	L30	VFITLCFTLK	L13	ITFELDER	L21;L15;L17
195	ARLTPCGTGT	L30	VFKNIDGYFK	L13	ITISSFKW	L54;L52;L53
196	ARLYYDSM	L66	VFKNIDGYFKI	L8	ITPVHVMSK	L57;L6;L7
197	ARQGFVDSD	L65	VFLGIITTVA	L8	ITSAVLQSGF	L52;L54;L53
198	ARSEDKRAK	L30	VFLHVTYVP	L8	IVAAIVFI	L20;L47;L74
199	ARSVSPKLFIR	L30	VFNATRFA	L71	IVDEPEEHVQI	L5;L68;L63
200	ARTAPHGHV	L30	VFNATRFASV	L71	IVFDGKSKC	L16;L11;L14
201	ARTVYDDGAR	L30	VFNATRFASVY	L71	IVMVTIML	L74;L68;L60
202	ARTVYDDGARR	L30	VFNGVSFS	L62	IVNGVRRSFY	L14;L12;L18
203	ARVECFDKFK	L30	VFNGVSFST	L8	IVNNATNVV	L58;L51;L73
204	ARVECFDKFKV	L30	VFPLNSIIK	L62	IVVFDEISM	L31;L32;L67
205	ARVVRSIF	L66	VFSAVGNICY	L12	IYDEPTTT	L62;L63;L68
206	ARVVRSIFSR	L30	VFTGYRVTK	L13	IYLYLTFY	L71;L72;L12
207	ASALGKLQD	L65	VFVLWAHGFEL	L71	IYSKHTPINL	L9;L8;L66
208	ASANIGCNH	L43	VGDFKLNEEI	L68	KAGQKTYER	L21;L15;L17
209	ASCTLSEQL	L53	VGEIPVAYR	L15	KAKKGAWNI	L55;L53;L70
210	ASDTYACWHH	L18	VGHTDLMAAY	L14	KASMPTTI	L55;L70;L54
211	ASEAARVV	L48	VGKPRPPLNR	L15	KCVPQADVEW	L54;L52;L16
212	ASEFSSLPS	L1	VGPEHSLAE	L57	KCYGVSPTK	L13;L6;L7
213	ASEYTGNYQC	L18	VGPKQASL	L57	KDFGGFNF	L33;L54;L65
214	ASFSASTS	L55	VGYLQPRT	L48	KDGHVETF	L33;L54;L65
215	ASFSTFKC	L54	VGYQPYRVVVL	L67	KDQVILLNK	L13;L7;L6

216	ASFYYVWKS	L69	VHFISNSW	L28	KEGFFTYIC	L42;L38;L37
217	ASHMYCSF	L43	VHFISNSWLM	L28	KEIIFLEG	L45;L37;L46
218	ASIKNFKSVLY	L18	VHFVCNLLLL	L34	KEIIFLEGE	L46;L37;L42
219	ASIKNFKSVLYY	L18	VHFVCNLLLLF	L34	KEIIFLEGETL	L36;L37;L41
220	ASIVAGGI	L55	VHNQDVNLH	L34	KEILVTYN	L33;L45;L29
221	ASIVAGGIVA	L42	VIDLLLDD	L68	KEITVATSRTL	L36;L37;L41
222	ASKIITLK	L13	VIGAVILR	L21	KEKVNINI	L45;L33;L37
223	ASKIITLKKR	L15	VIHFGAGSD	L43	KFCLEASF	L62;L71;L72
224	ASKIITLKKRW	L52	VIKVCEFQF	L26	KFKVNSTL	L71;L72;L62
225	ASKILGLPT	L43	VILLNKHI	L48	KFNPPALQD	L65;L13;L8
226	ASLVLARK	L7	VISTSHKL	L60	KFPVLHDI	L62;L71;L72
227	ASPNECNQM	L57	VIWDYKRD	L43	KGEDIQLL	L63;L55;L65
228	ASQGLVASIK	L7	VIYLYLTFYL	L67	KGLPWNVVR	L15;L21;L7
229	ASQSIIAYT	L14	VKDCVVLH	L62	KGLPWNVVRI	L8;L4;L16
230	ASQSIIAYTM	L55	VKGLDYKAF	L27	KGPKVKYL	L57;L64;L66
231	ASRELKVT	L43	VKIGPERTC	L27	KGTHHWLLL	L73;L69;L8
232	ASSRSSSRSR	L15	VKLQNNEL	L44	KGTLEPEYF	L54;L52;L9
233	ASTEKSNII	L55	VKNGSIHL	L66	KHFYWFFSNY	L27;L14;L16
234	ASTEKSNIIR	L7	VKNGSIHLYF	L27	KHLIPLMYK	L6;L13;L7
235	ASTSAFVET	L73	VKNKCVNF	L27	KHYTPSFKK	L6;L7;L13
236	ASVVNIQK	L7	VKPGGTSSG	L57	KIAEIPKEE	L16;L43;L3
237	ASVYAWNR	L15	VKPTVVVN	L66	KIFVDGVPFV	L13;L2;L4
238	ASVYAWNRK	L7	VKQGDDYVYL	L44	KIKACVEEV	L13;L3;L58
239	ASVYYSQLM	L54	VKRHTFSNY	L27	KIVDEPEEH	L16;L43;L54
240	ASWFTALTQ	L18	VKSREETGL	L44	KIYSKHTPI	L16;L24;L6
241	ASWVMRIM	L55	VKSREETGLL	L44	KKAGGTTEM	L27;L44;L66
242	ASYQTQTN	L48	VKSVGKFCL	L44	KKQQTVTL	L44;L27;L66
243	ATAEAELAKN	L10	VKYLYFIKGL	L27	KLALGGSVA	L51;L3;L46
244	ATALLTLQQI	L53	VLAAVYRI	L24	KLASHMYCSF	L16;L43;L26
245	ATAQEAYEQ	L53	VLCNSQTSLR	L21	KLDNDALNNI	L5;L2;L18
246	ATEGALNT	L18	VLDMCASLK	L1	KLFDRYFK	L13;L6;L21
247	ATEGALNTPK	L7	VLGSLAATVR	L21	KLIEYTDFA	L2;L5;L3
248	ATEVPANST	L18	VLHDIGNPKA	L2	KLINIIIW	L16;L54;L69
249	ATEVPANSTV	L18	VLHSTQDLFL	L57	KLKDCVMYA	L3;L13;L2
250	ATHGLAAVN	L14	VLKKCKSA	L23	KLLKSIAAT	L16;L2;L4
251	ATHSDKFTD	L53	VLKLKVDT	L23	KLMPVCVET	L2;L5;L4
252	ATKMSECVL	L70	VLKTGDLQPL	L3	KLMPVCVETK	L6;L16;L13
253	ATKYLVQQE	L13	VLLFLAFVVFL	L4	KLNDLCFTN	L16;L4;L21
254	ATNKATYK	L7	VLLILMTA	L23	KLNVGDYFV	L2;L4;L5
255	ATNYDLSV	L73	VLLPLVSS	L23	KLPDDFTGCV	L5;L2;L57
256	ATREAVGTN	L10	VLLRKNGNK	L6	KLRGTAVMSL	L16;L3;L2
257	ATREAVGTNL	L53	VLMDGSIIQ	L2	KLRSDVLLP	L6;L16;L13
258	ATRFASVYA	L13	VLMSNLGMPSY	L12	KMADQAMTQMY	L18;L14;L16
259	ATRFASVYAW	L52	VLPFNDGV	L57	KNLREFVFK	L13;L6;L7
260	ATRGATVV	L70	VLQKAAITIL	L74	KNNLPFKL	L73;L55;L33

261	ATRVECTTI	L53	VLQVRDVL	L23	KNSIDAFKL	L55;L53;L73
262	ATSACVLAA	L42	VLSDRELHLSW	L16	KPLEFGATS	L51;L56;L50
263	ATSRTLSYYK	L7	VLSEARQHLK	L6	KPRPPLNRN	L51;L22;L39
264	ATTAYANSVF	L52	VLSTFISAAR	L21	KPRQKRTA	L51;L39;L65
265	ATVCGPKK	L7	VLSVNPYV	L2	KPRQKRTAT	L22;L51;L39
266	ATYYLFDES	L67	VLTAVVIPTK	L6	KPTVVVNAA	L51;L50;L56
267	AVDAAKAYKDY	L18	VLTAVVIPTKK	L6	KQEILGTVSW	L16;L52;L18
268	AVDALCEK	L7	VLVPHVGEIPV	L2	KQQTVTLL	L48;L33;L44
269	AVDALCEKA	L5	VLYENQKLIA	L2	KQVEQKIAEI	L44;L3;L24
270	AVDALCEKALKY	L18	VLYNSASFSTF	L26	KQVVSDIDY	L26;L27;L14
271	AVDINKLCE	L18	VLYNSASFSTFK	L6	KRGDKSVY	L65;L66;L14
272	AVFISPYNS	L7	VLYQDVNCTEV	L2	KRSDARTA	L65;L66;L55
273	AVGTNLPLQL	L6	VLYYQNNV	L48	KRTIKGTHHW	L16;L54;L52
274	AVHECFVK	L7	VMAYITGGV	L3	KRVDFCGKGY	L30;L66;L14
275	AVHECFVKRV	L3	VMCGGSLYV	L2	KRWQLALSK	L30;L13;L6
276	AVILRGHL	L74	VMCGGSLYVK	L7	KSASVYYSQ	L54;L55;L53
277	AVILRGHLRI	L24	VMFTPLVPFW	L52	KSHFAIGL	L55;L73;L54
278	AVINGDRW	L54	VMHANYIFWR	L21	KSHFAIGLALY	L14;L18;L52
279	AVINGDRWFL	L16	VMLTNDNTSR	L15	KSVGKFCL	L65;L54;L55
280	AVITREVGFV	L3	VMLTNDNTSRY	L14	KSWMESEF	L53;L55;L54
281	AVKRTIKGTHHW	L52	VMPLSAPTLV	L5	KSYVHVVD	L55;L65;L54
282	AVKTQFNY	L14	VMRIMTWL	L48	KTDGTLMIER	L21;L18;L15
283	AVLQSGFRKM	L14	VMYASAVVLL	L74	KTFPPTEP	L54;L55;L73
284	AVSKGFFK	L7	VNAANVYL	L74	KTIQPRVEKK	L13;L7;L6
285	AVTAYNGY	L14	VNAANVYLK	L7	KTLLSLREVR	L21;L15;L52
286	AVTAYNGYL	L74	VNASSSEAF	L9	KTQSLLIV	L73;L70;L18
287	AVVLLILM	L74	VNEFYAYL	L62	KTQSLLIVN	L53;L13;L21
288	AVVLLILMT	L7	VNINIVGDF	L9	KTTEVVGDI	L55;L53;L54
289	AVVLLILMTA	L51	VNKGEDIQL	L39	KTTEVVGDII	L53;L54;L55
290	AWPLIVTA	L62	VNLHSSRLSF	L12	KTYERHSLSH	L16;L6;L18
291	AWPLIVTALR	L21	VNLKQLPFFY	L12	KVAGFAKFLK	L7;L6;L21
292	AWQPGVAMPNLY	L14	VNLKQLPFFYY	L12	KVEGCMVQV	L63;L5;L13
293	AWRKAVFISP	L42	VNLVAVPTGY	L12	KVFTTVDNI	L16;L54;L24
294	AWYTERSEKSY	L14	VNNATNKATY	L14	KVGGNYNY	L54;L14;L18
295	AYEQAVAN	L71	VNNATNVV	L48	KVKPTVVVNA	L13;L51;L3
296	AYFNMVYMPASW	L9	VNSFSGYLK	L7	KVLNEKCSAY	L14;L16;L6
297	AYSRYRIGNY	L14	VNSTLEQYVF	L9	KVNINIVGD	L16;L21;L65
298	AYTKRNVIP	L42	VNSVLLFL	L73	KVNSTLEQYVF	L16;L54;L52
299	AYTKRNVIPTI	L9	VNSVLLFLAF	L12	KVTLADAGF	L54;L52;L53
300	AYTNSFTR	L15	VNVVTTKI	L48	KVTSAMQTM	L54;L16;L53
301	AYTNSFTRG	L9	VPANSTVLS	L56	KVVSTTTNI	L54;L16;L24
302	AYTNSFTRGVY	L14	VPAQEKNF	L39	KWDLIISDMY	L18;L14;L1
303	AYTVELGTEV	L72	VPATVSVSSP	L51	KWGKARLY	L55;L14;L18
304	AYYFMRFR	L15	VPEVKILNN	L49	KWPWYIWL	L57;L62;L71

305	AYYNTTKGG	L72	VPFVVSTG	L47	KWYIRVGAR	L21;L15;L6
306	CAFAVDAA	L50	VPFWITIAYII	L47	KYAISAKNR	L15;L21;L17
307	CAFAVDAAK	L19	VPGLPGTI	L47	KYCALAPNM	L71;L72;L9
308	CAKEIKES	L43	VPGLPGTILR	L21	KYFKNHTSP	L8;L46;L71
309	CALAPNMMV	L47	VPHVGEIPVAY	L31	KYKGIKIQE	L13;L8;L15
310	CALDPLSET	L59	VPINTNSSP	L51	KYNYEPLTQ	L9;L8;L65
311	CAMRPNFTI	L47	VPLKSATCI	L47	KYTQLCQYL	L9;L8;L64
312	CANDPVGFTLK	L6	VPLNIIPLTT	L50	KYVQIPTTC	L8;L9;L66
313	CANFNVLF	L58	VPLNIIPLTTAA	L50	KYVRNLQHR	L15;L17;L8
314	CAQVLSEM	L59	VPQEHYVRIT	L39	KYWDQTYHP	L8;L9;L66
315	CATTRQVV	L70	VPVAIHAD	L51	LAAVYRINW	L49;L52;L69
316	CAYCCNIVN	L69	VPVSIINNTVY	L31	LAFVVFLLVT	L31;L47;L50
317	CAYCCNIVNV	L69	VPYNMRVIH	L47	LAGTITSGW	L49;L52;L54
318	CAYWVPRASA	L50	VQAGNVQLRV	L24	LAVFDKNL	L60;L61;L74
319	CCSLSHRF	L33	VQELYSPIF	L27	LAYILFTR	L47;L17;L59
320	CDAMRNAGI	L33	VQELYSPIFL	L68	LDDDSQQTV	L5;L68;L63
321	CDGTTFTY	L65	VQHMVVKAA	L51	LDDFSKQL	L33;L68;L62
322	CDIRQLLF	L33	VQIGEYTFEK	L7	LDGEVITF	L33;L65;L29
323	CDIRQLLFV	L73	VQIPCTCGK	L13	LDNVLSTF	L33;L59;L43
324	CDLKGKYV	L33	VQIPTTCA	L48	LEAPFLYLYA	L46;L42;L38
325	CDQLREPML	L33	VQLHNDILLAK	L6	LEAPFLYLYAL	L41;L40;L36
326	CDTLKEIL	L33	VQLRVIGHSM	L14	LECIKDLLA	L38;L46;L42
327	CDTLKEILV	L33	VQLSEISM	L44	LEMKSEKQV	L45;L38;L37
328	CEEMLDNRATL	L36	VQLSLPVLQ	L44	LENVAFNV	L33;L29;L45
329	CEFQFCNDPF	L29	VQLSLPVLQVR	L15	LEYHDVRV	L45;L48;L37
330	CEFQFCNDPFL	L36	VQMAPISAMVR	L21	LEYHDVRVVL	L36;L37;L41
331	CEIVGGQIVTC	L36	VQMLSDTLK	L7	LFFSYFAVH	L71;L72;L12
332	CEKALKYL	L37	VQPTESIV	L48	LFLPFFSNVTW	L52;L9;L8
333	CFDKFKVNS	L62	VQQESPFV	L48	LFLTWICL	L71;L72;L62
334	CFKMFYKGV	L13	VQSKMSDV	L48	LFLTWICLLQF	L8;L9;L12
335	CFLGYFCTC	L8	VQSTQWSLFF	L9	LFLVLIML	L71;L72;L62
336	CFLGYFCTCYF	L8	VQTFFKLV	L48	LFLVLIMLI	L47;L9;L8
337	CFVDDIVKT	L8	VQTFFKLVNK	L7	LFVAAIFY	L72;L71;L12
338	CGFIQQKLAL	L65	VQVTCGTTTL	L44	LGDIAARDL	L68;L63;L62
339	CGPKKSTNL	L57	VRDLPQGFSAL	L68	LGDVRETM	L63;L62;L68
340	CGYLPQNAV	L48	VRFPNITNLC	L30	LGLPTQTV	L47;L48;L25
341	CHATREAV	L28	VRKIFVDGV	L64	LHCANFNVL	L35;L28;L34
342	CHDGKAHFP	L34	VRLQAGNAT	L30	LHSTQDLFL	L28;L34;L35
343	CHIDHPNPK	L28	VRMYIFFASF	L30	LIAAVITR	L19;L21;L17
344	CHIDHPNPKGF	L8	VRTNVYLAVF	L66	LIDSYFVV	L68;L63;L5
345	CHNKCAYWV	L35	VRVLQKAA	L25	LIRKSNHNF	L58;L26;L52
346	CIKDLLARA	L3	VSAKPPPGD	L43	LITPVHVM	L59;L61;L60
347	CINANQVIV	L73	VSALVYDNK	L7	LIVAAIVFI	L20;L47;L5
348	CIRCLWSTK	L13	VSELLTPLG	L1	LIVGVALL	L74;L60;L61
349	CISTKHFY	L14	VSGNCDVVI	L53	LIVNSVLL	L60;L74;L61
350	CISTKHFYW	L54	VSGTNGTKRF	L52	LKEILVTY	L27;L18;L1

351	CKDGHVETFY	L27	VSIINNTVYTK	L7	LKRGDKSVY	L27;L26;L43
352	CLAVHECFV	L2	VSKVVKVT	L43	LKVGGSCVL	L44;L27;L61
353	CLAVHECFVKR	L19	VSKVVKVTIDY	L43	LKVPATVSV	L50;L51;L64
354	CLAYYFMR	L21	VSLAIDAYPL	L55	LLALHRSYL	L74;L3;L4
355	CLFLLPSLA	L3	VSLLSVLLS	L52	LLDQALVSD	L5;L68;L1
356	CLFWNCNVDR	L21	VSLLSVLLSM	L52	LLEIKDTEKY	L1;L18;L12
357	CLGDIAAR	L21	VSMTKTSV	L48	LLFVVEVV	L3;L23;L47
358	CLLNRYFR	L21	VSTIQRKYK	L13	LLKSIAATR	L21;L15;L17
359	CLNRVCTNY	L26	VSTQEFRY	L54	LLLDQALV	L2;L4;L5
360	CLSGLDSLDTY	L14	VTCLAYYF	L62	LLLSVCLGSL	L4;L2;L5
361	CLVGLMWL	L74	VTFFPDLNG	L7	LLPPKNSI	L57;L5;L23
362	CNVKTTEV	L48	VTFGDDTVIEV	L20	LLPSLATV	L5;L57;L3
363	CPACHNSEV	L22	VTFQSAVK	L7	LLPSLATVAY	L12;L57;L5
364	CPDGVKHV	L47	VTFQSAVKRTI	L52	LLSAGIFGA	L3;L2;L4
365	CPIFFITG	L50	VTHSKGLYRK	L7	LLSVCLGSL	L57;L4;L3
366	CPNFVFPL	L22	VTIDYTEISFM	L11	LLSVLQQL	L4;L59;L23
367	CPNFVFPLN	L50	VTKGKAKK	L13	LLTKSSEY	L26;L43;L1
368	CQAVTANV	L48	VTKNSKVQIGEY	L14	LLVTLAIL	L74;L23;L59
369	CQEPKLGSL	L44	VTLACFVL	L55	LMNVLTLV	L48;L62;L47
370	CQPILLLD	L48	VTLADAGF	L54	LMWLIINL	L47;L62;L74
371	CQVHGNAHV	L24	VTLADAGFI	L55	LNDILSRL	L63;L68;L62
372	CQYLNTLTLAV	L48	VTLADAGFIKQY	L14	LNLEEAARY	L12;L14;L31
373	CRFDTRVLSN	L65	VTLIGEAV	L48	LNRYFRLTL	L65;L73;L22
374	CRFDTRVLSNL	L30	VTLIGEAVK	L7	LNVGDYFVL	L65;L67;L32
375	CRFQEKDED	L65	VTLKQGEI	L55	LPDDFTGCV	L32;L49;L47
376	CRFVTDTPK	L30	VTLKQGEIK	L7	LPFKLTCAT	L50;L32;L51
377	CRHHANEY	L66	VTQNVLYENQK	L7	LPGVYSVIY	L31;L65;L49
378	CRKVQHMVV	L25	VTQQLIRAA	L51	LPGVYSVIYL	L56;L39;L22
379	CRMNSRNY	L65	VTRCLNRV	L48	LPIDKCSRI	L47;L49;L32
380	CRMNSRNYI	L34	VTRCLNRVC	L52	LPLTQYNRY	L31;L49;L12
381	CSFYPPDED	L65	VTRDIAST	L43	LPLVSSQCV	L47;L50;L51
382	CSLSHRFY	L55	VTSAMQTM	L70	LPNNTASW	L49;L50;L56
383	CSQHTMLV	L48	VTSNYSGVV	L70	LPQLEQPYV	L47;L50;L51
384	CSQHTMLVK	L7	VTTTLEETK	L7	LPQLEQPYVF	L31;L32;L39
385	CSRIIPAR	L48	VTYKLDGVV	L73	LPTGTLLV	L47;L50;L51
386	CTDDNALA	L1	VTYNCCDDDY	L14	LPVLQVRDVL	L31;L22;L32
387	CTFEYVSQPFL	L20	VVDGCNSSTCM	L63	LPWNVVRI	L47;L50;L49
388	CTLKSFTVEK	L7	VVDMSMTYG	L68	LPWNVVRIK	L31;L47;L32
389	CTQHQPYVV	L73	VVFVLWAH	L59	LPWNVVRIKI	L47;L50;L39
390	CTTIVNGVRR	L19	VVGPNVNK	L7	LPWNVVRIKIV	L50;L39;L47
391	CVCSVIDL	L74	VVIGIVNN	L74	LPYPDPSR	L47;L50;L51
392	CVDEAGSKS	L63	VVIGIVNNT	L20	LQAIASEF	L26;L59;L27
393	CVDTVRTNVYL	L68	VVIGIVNNTV	L20	LQSINFVRI	L24;L48;L34
394	CVEYCPIFF	L62	VVIPTKKAG	L43	LRIAGHHL	L66;L35;L25
395	CVIAWNSNNL	L10	VVKAALLA	L51	LSDRELHLS	L1;L53;L18
396	CVLGQSKR	L17	VVKAALLAD	L51	LSFKELLV	L73;L48;L47

397	CVLSGHNL	L60	VVLHSYFTSDY	L14	LSKGRLIIR	L15;L17;L21
398	CVRGTTVL	L59	VVLKKLKKSL	L23	LSPRWYFYY	L1;L12;L18
399	CVVADAVIKTL	L10	VVLKTGDL	L74	LSTDTGVEH	L43;L61;L59
400	CVVLHSYF	L74	VVNARLRAKHY	L14	LSYFIASFR	L19;L15;L17
401	CWHHSIGFDY	L14	VVQQLPETYF	L12	LTAFGLVAEW	L52;L10;L54
402	CYDHVIST	L62	VVREFLTRN	L43	LTALRLCAY	L1;L59;L18
403	CYDHVISTS	L62	VVRIKIVQ	L23	LTENKYSQL	L1;L63;L60
404	CYDTNVLE	L62	VVSDIDYV	L20	LTENLLLY	L1;L18;L12
405	CYDTNVLEG	L62	VVSTGYHF	L54	LTENLLLYI	L1;L18;L73
406	CYDYCIPY	L62	VVTCLAYY	L14	LTESNKKFL	L1;L63;L60
407	CYDYCIPYN	L62	VVTTVMFL	L74	LTGHMLDMY	L1;L18;L12
408	CYTPSKLI	L9	VVVNAANVYL	L20	LTILTSLLV	L73;L1;L18
409	DAALALLLLDR	L19	VVVNAANVYLK	L7	LTKEGATTC	L55;L53;L52
410	DADSTLIGD	L49	VWTLMNVLTL	L9	LTLQQIELK	L6;L7;L52
411	DAFKLNIK	L47	VYAADPAMH	L9	LTLQQIELKF	L52;L12;L53
412	DAGFIKQY	L70	VYANLGER	L17	LTNDNTSR	L21;L15;L17
413	DALCEKALK	L19	VYCCREHEH	L72	LTNMFTPL	L59;L61;L60
414	DAMRNAGI	L47	VYCFLGYFC	L9	LTPVVQTI	L47;L55;L57
415	DAMRNAGIV	L47	VYDDGARR	L62	LTRNPAWRK	L13;L6;L7
416	DAQGMDNL	L74	VYDNKLKA	L62	LVAEWFLAYI	L20;L3;L4
417	DATPSDFV	L47	VYDPLQPE	L62	LVASIKNF	L74;L52;L58
418	DATPSDFVRA	L50	VYDPLQPELDSF	L9	LVASIKNFK	L6;L7;L19
419	DAVIKTLQP	L49	VYDYLVST	L62	LVAVPTGY	L26;L43;L1
420	DAVNLLTN	L47	VYFASTEKS	L9	LVDFQVTI	L68;L63;L62
421	DAVNLLTNMF	L10	VYFASTEKSNI	L9	LVDLPIGI	L68;L62;L63
422	DAVVCFNSTY	L10	VYFLQSINFVR	L15	LVEVEKGVL	L68;L63;L1
423	DAYKTFPPT	L47	VYIGDPAQ	L71	LVFLFVAAIF	L31;L12;L52
424	DAYNMMIS	L47	VYKQFDTYNLW	L9	LVKQGDDYVY	L14;L26;L52
425	DAYNMMISAGF	L11	VYLAVFDKNLY	L12	LVKQLSSNF	L26;L58;L52
426	DAYVNTFSS	L47	VYNPFMID	L66	LVPFWITIAY	L12;L26;L6
427	DAYYRARAG	L25	VYNPFMIDVQ	L9	LWLDDVVYC	L31;L4;L8
428	DCATVHTANK	L19	VYNPFMIDVQQW	L9	LYDANYFL	L62;L68;L63
429	DCSARHINA	L25	VYQCAMRPN	L72	LYFDKAGQKTY	L71;L14;L12
430	DCVVLHSY	L29	VYRAFDIY	L66	LYLDAYNM	L71;L72;L66
431	DCVVLHSYF	L29	VYSVIYLYLT	L9	LYPTLNISD	L71;L72;L9
432	DDFTGCVI	L25	VYYSQLMCQ	L72	MADSNGTI	L68;L63;L47
433	DDFVEIIKS	L29	VYYTSNPTTFHL	L9	MADSNGTIT	L63;L68;L32
434	DDKKIKAC	L23	WCKDGHVET	L43	MAFPSGKV	L47;L70;L69
435	DDNALAYY	L29	WDLIISDM	L33	MCDIRQLL	L62;L63;L68
436	DDNLIDSY	L29	WDLLKYDF	L33	MDEFIERY	L18;L1;L29
437	DDNLIDSYF	L29	WDLTAFGL	L33	MEVTPSGTWL	L36;L37;L41
438	DDQIGYYR	L17	WEIVKFISTC	L45	MFVFLVLL	L62;L71;L72
439	DDQIGYYRR	L17	WEPEFYEA	L42	MFYKGVITH	L71;L72;L17
440	DDTLRVEA	L25	WESGVKDCVV	L38	MHAASGNLL	L34;L28;L35
441	DDTVIEVQGY	L29	WESGVKDCVVL	L36	MHAASGNLLL	L28;L34;L35

442	DDVVYCPRH	L29	WEVGKPRP	L46	MISAGFSL	L60;L61;L28
443	DDYQGKPL	L25	WEVGKPRPPL	L36	MLDMYSVM	L63;L68;L62
444	DDYVYLPY	L29	WFHAIHVSG	L71	MLTNDNTSRY	L14;L12;L18
445	DEAGSKSPIQY	L29	WFLAYILFT	L12	MLVKQGDDY	L26;L14;L12
446	DEDDNLID	L29	WFLNRFTTT	L8	MPVCVETKA	L50;L51;L32
447	DEDDNLIDS	L29	WHNMLKTV	L48	MPYFFTLLLQL	L31;L50;L47
448	DEDDNLIDSYF	L41	WHNMLKTVY	L27	MSAFAMMFV	L73;L20;L70
449	DEDDSEPV	L29	WHTNCYDYCI	L34	MSKFPLKLR	L15;L17;L21
450	DEDEEEGD	L29	WICLLQFAY	L12	MSYEDQDALF	L54;L53;L52
451	DEEQPMEID	L29	WKSYVHVVD	L44	MTQMYKQAR	L17;L15;L21
452	DEFIERYK	L29	WLCWKCRSK	L13	MVTNNTFTLK	L6;L7;L19
453	DEFIERYKLEGY	L29	WLDDVVYCPR	L21	MVYMPASWVMR	L21;L19;L15
454	DEGNCDTL	L29	WLDDVVYCPRH	L5	MYKGLPWNV	L13;L64;L3
455	DEISMATN	L29	WLDDVVYCPRHV	L5	NADIVEEA	L68;L67;L63
456	DELGTDPY	L29	WLDMVDTSLS	L1	NADLYKLM	L63;L68;L62
457	DELTGHMLDM	L29	WLGFIAGLI	L24	NAGDYILAN	L67;L69;L43
458	DELTGHMLDMY	L29	WLKQLIKVT	L3	NAGIVGVL	L67;L70;L74
459	DEMIAQYT	L29	WLKQLIKVTLV	L3	NALDQAISMW	L10;L49;L52
460	DEMIAQYTS	L29	WLLWPVTLA	L2	NAVASKILGL	L31;L49;L10
461	DEPEEHVQ	L29	WLSYFIASFR	L21	NCTEVPVAI	L35;L20;L34
462	DEPEEHVQIH	L29	WMVMFTPLV	L48	NDFNLVAM	L29;L33;L25
463	DEPTTTTS	L29	WNLVIGFLFL	L73	NDNLLEIL	L33;L25;L29
464	DERIDKVLN	L29	WNVKDFMSL	L32	NEFYAYLRK	L41;L40;L29
465	DETQALPQR	L29	WNVVRIKIV	L69	NEKTHVQLSL	L37;L41;L36
466	DEVRQIAPG	L29	WPLIVTALRA	L50	NENGTITDA	L42;L38;L46
467	DEWSMATY	L29	WPQIAQFAP	L50	NETLVTMPL	L37;L29;L41
468	DFAVSKGFF	L9	WPQIAQFAPSA	L50	NEYRLYLDAY	L29;L41;L40
469	DFCGKGYHL	L8	WPVTLACFV	L47	NFKSVLYY	L72;L71;L12
470	DFGDFIQTT	L17	WPVTLACFVLA	L50	NFNVLFSTV	L62;L71;L72
471	DFIDTKRGV	L11	WPWYIWLGFI	L47	NFSKLINII	L8;L34;L9
472	DFIPMDSTV	L71	WPWYIWLGFIA	L50	NFYGPFVDR	L17;L19;L15
473	DFLEYHDVR	L17	WQTGDFVKA	L24	NGDFLHFL	L68;L63;L62
474	DFLHFLPR	L17	WRVYSTGSNV	L30	NGLMLLEI	L25;L47;L48
475	DFLHFLPRVF	L9	WSFNPETNIL	L60	NGYPNMFITR	L19;L17;L15
476	DFQENWNTK	L17	WSLFFFLYE	L73	NHDLYCQVH	L35;L34;L28
477	DFVEIIKS	L29	WSYSGQSTQ	L55	NHTSPDVDL	L28;L35;L34
478	DGADVTKIK	L19	WTAFVTNV	L20	NIALIWNVK	L19;L7;L6
479	DGCVPLNI	L47	WTAFVTNVNA	L20	NIIPLTTA	L3;L25;L23
480	DGCVPLNII	L47	WTAGAAAYYV	L20	NINLHTQV	L25;L23;L48
481	DGDMVPHI	L47	WTIEYPIIG	L69	NIVNVSLVK	L19;L7;L6
482	DGGSLYVNK	L19	WTLMNVLTLVY	L52	NKGAGGHSY	L27;L66;L14
483	DGHVETFY	L29	WVATEGAL	L74	NLAKHCLHVV	L3;L2;L4
484	DGIIWVAT	L25	WVLNNDYY	L14	NLIDSYFVVKR	L19;L17;L21
485	DGKMKDLSP	L23	WYDFGDFI	L62	NLIIKNLSK	L6;L23;L7

486	DGKSKCEE	L23	WYDFVENP	L62	NLLEILQK	L6;L7;L4
487	DGTLMIERF	L29	WYIRVGAR	L17	NLLKDCPAV	L4;L2;L5
488	DGVDVELF	L29	WYIRVGARK	L8	NLLLQYGSF	L10;L27;L12
489	DGVKHVYQLR	L19	WYIWLGFIA	L50	NLSDRVVFVL	L4;L3;L2
490	DGVPFVVSTGY	L11	WYTERSEKSY	L14	NLWNTFTR	L21;L17;L19
491	DGVVCTEI	L25	YAADPAMHAAS	L67	NLYKMQRML	L64;L23;L74
492	DGWEIVKFI	L47	YAAFATAQ	L59	NNDYYRSL	L68;L62;L63
493	DGYVMHANYI	L47	YAAFATAQEAY	L31	NNLDKSAGF	L8;L12;L11
494	DHCGETSW	L28	YAAVINGDR	L19	NNLNRGMVL	L25;L23;L71
495	DHIGTRNPA	L28	YADSFVIRGD	L49	NPDILRVY	L31;L49;L1
496	DHSSSSDNIALL	L34	YAFASEAA	L50	NPFMIDVQQW	L49;L31;L41
497	DHVISTSH	L28	YAFEHIVYGD	L49	NQKLIANQF	L26;L27;L58
498	DIAANTVIWDY	L11	YAFEHIVYGDF	L31	NQMCLSTL	L25;L48;L35
499	DIAKKPTET	L23	YALVYFLQSI	L47	NRATLQAI	L25;L35;L64
500	DIDYVPLKS	L1	YANGGKGFC	L58	NRNYVFTGY	L30;L66;L65
501	DIGNPKAIK	L19	YANGGKGFCKL	L60	NRPQIGVV	L66;L64;L25
502	DILGPLSA	L25	YASAVVLLILM	L31	NRQFHQKL	L25;L35;L66
503	DINGNLHPD	L11	YASQGLVASI	L20	NRVCGVSAA	L25;L35;L30
504	DINKLCEEM	L29	YATHSDKFTD	L49	NSFSGYLK	L19;L55;L7
505	DIPGIPKD	L11	YAWNRKRIS	L69	NSFTRGVY	L14;L1;L70
506	DIPGIPKDMTY	L11	YAYLRKHFS	L23	NSPNLAWPL	L57;L67;L66
507	DIPIGAGIC	L11	YCALAPNMM	L28	NSRNYIAQV	L13;L70;L48
508	DIQLLKSA	L23	YCPACHNSE	L57	NSSPDDQIGYY	L1;L14;L18
509	DIRQLLFV	L23	YCPACHNSEV	L57	NSTNVTIATY	L14;L43;L10
510	DISGINASVV	L20	YCPIFFITG	L57	NSVPWDTIANY	L52;L14;L11
511	DISTEIYQA	L11	YCPIFFITGNTL	L57	NTFSSTFNV	L20;L70;L19
512	DITPCSFGGV	L11	YCRHGTCER	L43	NTVIWDYKR	L17;L19;L15
513	DIVEEAKK	L19	YDANYFLCW	L49	NVAKYTQL	L74;L25;L56
514	DIVEEAKKVK	L19	YDDGARRVW	L49	NVGDYFVL	L67;L66;L65
515	DIVKTDGTLM	L11	YDHVISTSH	L43	NVLSTFISA	L50;L51;L17
516	DIVVFDEI	L47	YDKLVSSFL	L33	NVLTLVYK	L7;L17;L6
517	DKAGQKTY	L27	YDNKLKAH	L33	NVPMEKLKTL	L57;L10;L5
518	DKAGQKTYER	L19	YDPKTKNV	L33	NVSLVKPSF	L31;L39;L12
519	DKKIKACV	L23	YDSMSYED	L33	NVYADSFVI	L49;L10;L20
520	DKNTQEVF	L29	YDYVIFTQ	L33	NVYLAVFDK	L7;L19;L6
521	DKVEAEVQI	L44	YDYYRYNL	L33	NWLKQLIKV	L4;L8;L25
522	DKYVRNLQH	L25	YDYYRYNLP	L33	NWYDFGDF	L9;L71;L62
523	DLATNNLVVM	L11	YEAMYTPHTVL	L36	NWYDFGDFI	L34;L8;L9
524	DLICAQKF	L11	YECDIPIGAGI	L45	NYIAQVDVVNF	L8;L9;L71
525	DLKGKYVQ	L23	YECLYRNRD	L45	NYIFWRNTN	L72;L8;L71
526	DLKPVSEE	L23	YEDFQENWN	L45	NYKLPDDF	L62;L9;L71
527	DLLIRKSN	L23	YEDLLIRK	L45	NYQKVGMQKY	L8;L14;L12
528	DLLIRKSNH	L23	YEDLLIRKSN	L41	PASWVMRIM	L70;L32;L69
529	DLNDFVSD	L23	YEGNSPFHP	L38	PAYTNSFTR	L19;L17;L15
530	DLNGNWYDF	L11	YEGNSPFHPL	L36	PEAGLPYGA	L46;L42;L38
531	DLPIGINITR	L19	YELKHGTFT	L45	PETTADIVV	L38;L37;L36

532	DLPIGINITRF	L11	YELKHGTFTC	L38	PETTADIVVF	L29;L41;L40
533	DLPKEITV	L23	YELKHGTFTCA	L46	PGIPKDMTY	L43;L26;L14
534	DLPKEITVA	L11	YENFNQHEVLL	L36	PGLPGTILR	L15;L21;L17
535	DLSVVNAR	L17	YEPLTQDH	L33	PHGHVMVEL	L35;L34;L28
536	DLSVVSKVVK	L19	YEPQIITT	L29	PLADNKFAL	L4;L2;L16
537	DLTAFGLVAEW	L10	YEQAVANGD	L38	PLHGTILTR	L21;L19;L17
538	DLYCQVHGN	L11	YEQFKKGVQ	L46	PLQPELDSF	L9;L26;L16
539	DMCASLKEL	L25	YEQFKKGVQIP	L38	PPIKDFGGF	L49;L11;L10
540	DMFLGTCR	L17	YEQYIKWP	L38	PPTSFGPLV	L50;L51;L47
541	DMYSVMLTN	L47	YERHSLSH	L29	PQNAVVKIY	L26;L14;L27
542	DNGPQNQR	L17	YERHSLSHFV	L45	PRPPLNRNY	L64;L65;L66
543	DNIALLVQ	L25	YFDCYDGG	L62	PTITQMNLKY	L11;L12;L18
544	DNLACEDL	L25	YFDCYDGGC	L62	PTLVPQEHY	L52;L12;L16
545	DNLKTLLSLR	L17	YFDCYDGGCI	L62	PTMCDIRQL	L55;L53;L10
546	DNQDLNGNW	L49	YFDKAGQK	L62	PTSFGPLVR	L19;L7;L21
547	DNSSLTIKK	L19	YFDKAGQKT	L62	PVAYRKVLL	L23;L20;L74
548	DNVTDFNAI	L10	YFFTLLLQ	L48	PVLDWLEEK	L7;L6;L13
549	DNYYKKDNSY	L11	YFFTLLLQLC	L12	PVSELLTPL	L20;L67;L56
550	DPAQLPAP	L50	YFGLFCLLNR	L17	PVYSFLPGVY	L14;L11;L12
551	DPAQLPAPRTL	L22	YFIASFRLFAR	L17	PWDTIANY	L1;L18;L62
552	DPIHSLRV	L47	YFIKGLNNLNR	L17	PYFFTLLL	L9;L71;L72
553	DPKTKNVT	L23	YFKNHTSP	L71	PYIKWDLLKY	L12;L8;L14
554	DPKTKNVTK	L23	YFLQSINFVR	L17	PYPDPSRI	L9;L8;L62
555	DPLSETKC	L47	YFLQSINFVRI	L8	QAAGTDTTI	L32;L49;L67
556	DPNFKDQVILL	L31	YFRLTLGV	L48	QADVEWKF	L63;L68;L62
557	DPQTLEILD	L32	YFRLTLGVYDY	L12	QADVEWKFY	L1;L18;L70
558	DPQTLEILDI	L47	YFTQSRNLQEF	L9	QAPTHLSV	L57;L47;L70
559	DPSRILGA	L50	YFYTSKTTVAS	L71	QECVRGTTVL	L36;L40;L37
560	DPVGFTLK	L47	YFYTSKTTVASL	L71	QEEVQELYSP	L42;L38;L46
561	DPYEDFQE	L47	YGADLKSFDL	L44	QEFRYMNSQ	L46;L29;L45
562	DPYEDFQENW	L49	YGDFSHSQ	L68	QEFRYMNSQGL	L40;L36;L41
563	DQALVSDV	L25	YGDSATLP	L63	QEILGTVSWNL	L40;L41;L36
564	DQDALFAY	L1	YGFQPTNGV	L47	QEKNFTTAP	L46;L42;L38
565	DQFKHLIP	L25	YGFQPTNGVGY	L27	QELIRQGTD	L40;L33;L46
566	DQLREPML	L25	YHDVRVVLDF	L34	QESPFVMMSA	L42;L46;L38
567	DQLTPTWR	L17	YHDVRVVLDFI	L34	QEVFAQVKQI	L41;L45;L40
568	DQVILLNK	L25	YHTTDPSF	L28	QFAYANRNR	L17;L15;L21
569	DQVILLNKH	L29	YHYQECVR	L28	QHEETIYNL	L34;L35;L28
570	DRCILHCA	L25	YICGDSTEC	L43	QHEETIYNLL	L34;L28;L35
571	DRCILHCAN	L25	YIDIGNYTVS	L68	QHMVVKAAL	L28;L35;L34
572	DRDAAMQRKL	L35	YIDIGNYTVSC	L68	QIAPGQTGK	L6;L7;L19
573	DRLITGRL	L25	YIFFASFYYV	L20	QKKQQTVTL	L44;L27;L39
574	DRLITGRLQ	L25	YILANTCTER	L17	QLDEEQPMEI	L5;L2;L68
575	DRLITGRLQSL	L25	YIRVGARK	L43	QLHNDILLA	L3;L2;L24
576	DRLNEVAK	L25	YITTYPGQGL	L60	QLPAPRTLL	L57;L5;L22
577	DRLNQLES	L25	YIWLGFIA	L50	QLPPAYTNSF	L9;L57;L5

578	DRLNQLESKM	L30	YKAFKQIVE	L44	QLPQGTTL	L57;L23;L5
579	DRQTAQAA	L25	YKAIDGGVTR	L19	QMAPISAMV	L20;L3;L28
580	DRVVFVLW	L25	YKENSYTTT	L27	QPGVAMPNL	L22;L56;L39
581	DRYFKYWD	L25	YKENSYTTTI	L34	QPITNCVKML	L32;L39;L22
582	DRYFKYWDQ	L25	YKHITSKETL	L44	QPPQTSITSA	L50;L51;L22
583	DRYFKYWDQTY	L30	YKHWPQIAQF	L27	QPQLEMEL	L39;L22;L56
584	DSAEVAVK	L19	YKKVDGVVQ	L27	QPRTFLLKY	L31;L11;L22
585	DSATLPKGI	L10	YKLEGYAFE	L44	QPSVGPKQA	L51;L22;L39
586	DSATLVSDI	L10	YKLMGHFAW	L27	QPTSEAVEA	L50;L51;L32
587	DSCKRVLNV	L73	YKLNVGDY	L27	QQLIRAAEI	L48;L25;L24
588	DSCNNYMLTY	L18	YKLNVGDYFVL	L44	QQQQGQTV	L48;L24;L28
589	DSDLNDFV	L1	YKLPDDFTGC	L27	QSASKIITLK	L7;L6;L19
590	DSDLNDFVS	L1	YKNTCDGTTF	L27	QSIIAYTM	L55;L48;L54
591	DSEPVLKGV	L20	YKNTCDGTTFTY	L27	QSINFVRI	L48;L73;L55
592	DSFKEELDK	L19	YKSVNITFEL	L44	QSINFVRIIMR	L19;L21;L7
593	DSFVIRGD	L65	YKYFSGAM	L27	QSSYIVDSV	L20;L73;L70
594	DSFVIRGDEV	L20	YKYFSGAMD	L27	QTFFKLVNKF	L11;L10;L52
595	DSKEGFFTYI	L10	YLALYNKYK	L6	QTLLALHRSY	L52;L14;L40
596	DSVEEVLSEAR	L19	YLASGGQPIT	L2	QTNSPRRAR	L15;L21;L17
597	DSVTVKNGSI	L10	YLDGADVT	L1	QVDLFRNAR	L21;L17;L15
598	DSYFVVKRH	L19	YLGKPREQI	L2	QVRDVLVR	L21;L15;L17
599	DTANPKTPKYK	L19	YLGTGPEAGL	L2	QVTCGTTTL	L32;L56;L10
600	DTDLTKPYI	L1	YLITPVHVMSK	L6	QVVSDIDYV	L20;L11;L5
601	DTFNGECPNFV	L20	YLKHGGGVAGA	L3	QWLPTGTL	L33;L71;L9
602	DTKRGVYCC	L10	YLKLRSDV	L23	QWNLVIGF	L33;L62;L29
603	DTLRVEAF	L29	YLKLRSDVL	L23	QYIDIGNYT	L9;L8;L72
604	DTPNNTDF	L11	YLKLRSDVLL	L23	QYIDIGNYTV	L8;L20;L9
605	DTSLSGFKLK	L19	YLNSTNVTIA	L3	QYNRYLAL	L71;L72;L66
606	DTTEAFEK	L19	YLNTLTLA	L3	RAAEIRASA	L51;L50;L46
607	DTTITVNVLAW	L10	YLPIDKCSR	L57	RAFDIYND	L65;L54;L55
608	DTVRTNVYLAVF	L10	YLPYPDPSRIL	L57	RAFGEYSHVV	L24;L70;L69
609	DTYPSLET	L25	YLRKHFSM	L23	RAKVTSAM	L43;L70;L59
610	DVDLGDISGI	L10	YLRKHFSMM	L3	RALTGIAVE	L52;L44;L53
611	DVENPHLMGWDY	L1	YLVQQESPF	L26	RDAAMQRKL	L33;L55;L37
612	DVETKDVV	L23	YLVQQESPFV	L2	REAACCHL	L33;L37;L36
613	DVGDSAEV	L20	YLYALVYFLQ	L12	REAACCHLA	L38;L42;L46
614	DVGDSAEVAV	L20	YLYRLFRKS	L24	REAACCHLAKA	L46;L38;L42
615	DVGDSAEVAVK	L19	YMGTLSYEQF	L9	REAVGTNLPL	L36;L41;L40
616	DVKCTSVV	L23	YMPASWVMRI	L5	REEAIRHVRAW	L40;L38;L41
617	DVKCTSVVLL	L11	YMRSLKVPA	L50	REGYLNSTNV	L45;L38;L36
618	DVLECNVKT	L11	YMRSLKVPATV	L3	RELGVVHN	L33;L37;L29
619	DVLECNVKTT	L10	YNLWNTFTR	L17	RELNGGAY	L29;L14;L27
620	DVLLPLTQ	L25	YNYEPLTQ	L48	RELNGGAYT	L36;L45;L40
621	DVLLPLTQYNR	L17	YNYKLPDDF	L12	RFASVYAWNR	L15;L21;L17

622	DVLVRGFGD	L17	YNYLYRLFR	L17	RFLYIIKLIF	L8;L9;L12
623	DVQQWGFTGN	L10	YPANSIVC	L47	RFYRLANEC	L72;L71;L8
624	DVRVVLDF	L23	YPGQGLNGYTV	L50	RGFGDSVEE	L65;L44;L27
625	DVSFLAHI	L20	YPLECIKDLL	L31	RGIVFMCVEY	L26;L43;L27
626	DVTQLYLGG	L11	YPLECIKDLLA	L50	RHFDEGNCDTL	L34;L28;L16
627	DVVECLKLSH	L11	YPLTKHPNQEY	L31	RHHANEYRLY	L14;L27;L18
628	DVVIGIVNNTV	L20	YPNMFITREEA	L50	RHVRAWIGF	L27;L34;L53
629	DVVYCPRHV	L20	YPSLETIQIT	L31	RIMTWLDMV	L73;L4;L24
630	DWTIEYPII	L47	YPSLETIQITI	L47	RKGGRTIAF	L27;L44;L33
631	DWYDFVENP	L11	YPTLNISD	L50	RLANECAQVL	L16;L24;L44
632	DYDCVSFC	L62	YQCAMRPNF	L58	RLIDAMMF	L26;L16;L54
633	DYDCVSFCYM	L62	YQCGHYKHI	L24	RLISMMGF	L26;L27;L16
634	DYDYYRYNL	L62	YQLYSTQLS	L24	RLKLFDRY	L14;L18;L26
635	DYFNKKDWYDF	L8	YQPYRVVV	L48	RLNQLESKM	L14;L16;L24
636	DYGARFYF	L9	YRAFDIYNDK	L30	RLQSLENVAF	L16;L26;L56
637	DYGARFYFY	L12	YREAACCHL	L34	RLYECLYR	L21;L15;L6
638	DYIATNGPLKV	L8	YREGYLNST	L35	RLYECLYRNR	L21;L15;L6
639	DYIINLIIK	L17	YRINWITGG	L30	RMYIFFASFYY	L14;L18;L12
640	DYILANTC	L71	YRKVLLRKN	L64	RNLQHRLY	L55;L14;L65
641	DYILANTCTER	L17	YRLANECAQV	L30	RNSTPGSSR	L15;L21;L17
642	DYKAFKQIV	L23	YRLANECAQVL	L35	RNYVFTGY	L27;L26;L65
643	DYLVSTQEFR	L17	YRLFRKSNLK	L30	RPINPTDQSSY	L14;L27;L31
644	DYNYKLPDDF	L9	YRLYLDAY	L66	RPLLESEL	L56;L22;L39
645	DYVPLKSA	L25	YRNRDVDTD	L65	RPNFTIKGSF	L39;L22;L56
646	DYYQLYSTQ	L17	YRRLISMM	L66	RPNFTIKGSFL	L56;L39;L22
647	DYYRSLPGV	L47	YRVVVLSFELL	L30	RPPLNRNYV	L39;L22;L51
648	DYYRSLPGVF	L9	YSDSPCES	L1	RPPLNRNYVF	L22;L39;L56
649	EAACCHLAK	L19	YSDSPCESHG	L63	RPQIGVVR	L56;L15;L39
650	EAALCTFL	L74	YSDVENPHLMGW	L1	RQALLKTV	L48;L24;L33
651	EAANFCALI	L20	YSFLPGVYSVIY	L1	RQKKQQTV	L48;L24;L26
652	EAARVVRSIFSR	L19	YSFVSEET	L43	RQKKQQTVT	L26;L27;L44
653	EAELAKNVSL	L68	YSLLLCRM	L59	RQKRTATKAY	L26;L27;L14
654	EAEVQIDR	L17	YSLRLIDAM	L67	RQRLTKYTM	L27;L44;L26
655	EAFLIGCNYL	L20	YSPIFLIVAA	L50	RSDVLLPLTQY	L18;L1;L14
656	EAGLPYGANK	L19	YSVIYLYLTFY	L1	RSGETLGV	L73;L48;L24
657	EAIRHVRAWI	L20	YSVLYNSA	L50	RSVSPKLFIR	L15;L21;L7
658	EAKTVLKKC	L10	YTDFATSACV	L1	RTTNGDFL	L55;L54;L53
659	EASFNYLK	L19	YTDFATSACVL	L68	RTVAGVSI	L55;L54;L53
660	EAVGTNLPLQL	L20	YTEISFMLWC	L1	RVDFCGKGYHL	L18;L63;L68
661	EAVMYMGTLSY	L11	YTEKWESGV	L1	RVDGQVDLFR	L21;L7;L18
662	EAYEQAVA	L50	YTEKWESGVK	L1	RVEAFEYY	L18;L1;L14
663	ECAQVLSEMV	L20	YTELEPPCR	L1	RVESSSKL	L63;L18;L54
664	ECFDKFKVN	L10	YTELEPPCRF	L1	RVLNVVCK	L7;L13;L6
665	ECFVKRVD	L65	YTERSEKS	L1	RVLNVVCKT	L13;L24;L6
666	ECNQMCLSTL	L10	YTGNYQCGHY	L1	RVLSNLNLP	L6;L16;L15

667	ECNVKTTEV	L23	YTKRNVIPTI	L10	RVQPTESI	L54;L16;L24
668	ECTTIVNGV	L20	YTKVDGVDVELF	L52	RVQPTESIV	L24;L14;L28
669	ECTTIVNGVRR	L19	YTMADLVYA	L20	RVRQALLK	L13;L6;L7
670	ECVRGTTV	L48	YTPHTVLQA	L11	RVRQALLKT	L13;L6;L51
671	ECVRGTTVLL	L20	YTSALLAGT	L20	RVRQALLKTV	L13;L3;L51
672	EDDSEPVL	L28	YTSKTTVASL	L20	RVYSSANNCTF	L16;L54;L52
673	EDDSEPVLK	L19	YTSNPTTFH	L58	RWVLNNDYY	L14;L18;L12
674	EDIQLLKSA	L46	YTTTIKPV	L70	RYWEPEFYE	L65;L8;L9
675	EDIQLLKSAY	L40	YTVELGTEVNEF	L10	SAEVAVKM	L63;L62;L68
676	EDLLFNKVTL	L23	YTVSCLPFTI	L20	SAFFGMSR	L19;L17;L15
677	EDMLNPNY	L29	YVDNSSLTIK	L6	SAFYILPSII	L69;L20;L70
678	EDNQTTTI	L48	YVDNSSLTIKK	L7	SAGFPFNKW	L49;L52;L54
679	EEAALCTFLLN	L41	YVGCHNKCAY	L43	SAIGKIQDS	L43;L49;L58
680	EEAARYMRS	L42	YVMHANYIFW	L10	SARHINAQV	L20;L58;L70
681	EEAKKVKPT	L42	YVPLKSAT	L57	SAVGNICY	L70;L58;L69
682	EEEEFEPST	L42	YVPLKSATC	L57	SCKRVLNVV	L51;L3;L39
683	EEEGDCEEE	L42	YVSQPFLMDL	L20	SDDAVVCF	L33;L62;L63
684	EEHFIETIS	L42	YVTQQLIRAA	L50	SDRVVFVL	L33;L65;L29
685	EELFYSYATH	L40	YVYIGDPA	L50	SEAFLIGCNY	L40;L41;L29
686	EEMLDNRA	L42	YVYIGDPAQ	L67	SEAFLIGCNYL	L40;L36;L41
687	EEQEEDWL	L29	YVYNPFMI	L47	SEAKCWTET	L46;L42;L37
688	EEQPMEID	L29	YVYNPFMIDV	L20	SEETGTLI	L45;L36;L37
689	EERLKLFDR	L17	YWDQTYHP	L62	SEFRVYSS	L29;L33;L37
690	EERLKLFDRYF	L40	YWDQTYHPN	L62	SEGLNDNL	L33;L36;L37
691	EESSAKSASVYY	L41	YWEPEFYEAMY	L1	SEISMDNSPNL	L36;L41;L40
692	EETGLLMPLKA	L42	YWFFSNYLK	L7	SEKQVEQKIA	L42;L38;L46
693	EETGTLIVNSVL	L41	YWFFSNYLKR	L19	SEKSYELQTP	L42;L46;L38
694	EETIYNLLKD	L41	YYDSMSYE	L62	SELLTPLGIDL	L36;L41;L40
695	EETKFLTENLL	L41	YYDSMSYED	L62	SEQLDFIDT	L42;L40;L38
696	EETKFLTENLLL	L41	YYFMRFRR	L17	SFCYMHHM	L62;L72;L71
697	EEVGHTDLMA	L42	YYFMRFRRA	L46	SFCYMHHMEL	L71;L72;L62
698	EEVKPFIT	L29	YYGNALDQ	L71	SFGGASCCL	L72;L71;L62
699	EEVLSEAR	L29	YYGNALDQAI	L9	SFGGVSVI	L72;L71;L48
700	EEVQELYSPIFL	L41	YYHTTDPS	L71	SFIEDLLFN	L12;L8;L72
701	EEVTTTLEE	L41	YYLFDESG	L71	SFIEDLLFNK	L7;L13;L6
702	EEVVLKTG	L29	YYLGTGPE	L71	SFKKGAKL	L72;L62;L71
703	EFCSQHTML	L8	YYLGTGPEAGL	L9	SFLEMKSEK	L71;L72;L13
704	EFDRDAAM	L62	YYNTTKGGR	L17	SFNYLKSPNF	L9;L8;L12
705	EFDRDAAMQR	L17	YYRARAGEA	L72	SFTRGVYY	L72;L71;L12
706	EFEPSTQY	L1	YYRRATRR	L17	SFTVEKGIY	L14;L12;L72
707	EFIERYKL	L8	YYRSLPGV	L48	SFVSEETGTL	L8;L72;L71
708	EFKLASHMY	L14	YYSLLMPILTL	L9	SFYPPDED	L72;L71;L62
709	EFLRDGWEIVKF	L8	AAAYYVGY	L43;L58	SGVKDCVVL	L44;L32;L56
710	EFLTRNPAWR	L17	AADPAMHA	L63;L68	SHAAVDAL	L35;L28;L34
711	EFQFCNDPF	L72	AAFATAQEA	L69;L46	SHEGKTFYV	L34;L35;L28

712	EFYAYLRKH	L17	AAIMQLFFSY	L12;L14	SHEGKTFYVL	L34;L35;L28
713	EGDCEEEEF	L34	AAISDYDYYRY	L12;L14	SHFVNLDNL	L34;L28;L35
714	EGFFTYICGF	L11	AAKLMVVI	L70;L69	SHQSDIEVT	L28;L34;L35
715	EGKTFYVL	L23	AAKLMVVIP	L69;L42	SHSQLGGLHL	L34;L28;L35
716	EGKTFYVLP	L42	AALALLLLD	L12;L7	SHSQLGGLHLL	L34;L28;L35
717	EGNFYGPFVDR	L17	AALCTFLLNK	L7;L6	SHVVAFNTLL	L34;L28;L35
718	EGVLTAVV	L48	AALGVLMSNL	L74;L67	SIFSRTLET	L43;L6;L3
719	EGVVDYGAR	L17	AALLADKF	L33;L54	SIINNTVYTK	L7;L19;L6
720	EGYAFEHIVY	L27	AALLADKFPVL	L67;L31	SIIQFPNTYL	L11;L20;L6
721	EGYLNSTNV	L48	AANFCALILAY	L12;L31	SIKNFKSVLYY	L12;L14;L6
722	EHDYQIGGYTE	L34	AAYSRYRI	L70;L47	SKLINIIIW	L44;L27;L52
723	EHEIAWYTE	L34	AAYSRYRIG	L69;L70	SKPSKRSF	L27;L66;L57
724	EHFIETISLA	L28	ACFVLAAV	L48;L33	SKRSFIEDL	L44;L27;L66
725	EHIVYGDFS	L34	ADDLNQLTGY	L18;L1	SKVQIGEYTF	L27;L44;L34
726	EHIVYGDFSH	L34	ADLDDFSKQL	L40;L37	SLAEYHNESGL	L2;L3;L4
727	EHSWNADLY	L34	ADLVYALRHF	L40;L33	SLDNVLSTFI	L5;L68;L2
728	EHVNNSYECDI	L34	ADSFVIRGD	L65;L33	SLFDMSKFPLK	L6;L7;L13
729	EHVTFFIY	L29	ADVEWKFYD	L65;L33	SLFDMSKFPLKL	L2;L3;L4
730	EHYVRITGLY	L11	AEETRKLMPV	L42;L38	SLGAENSVAY	L12;L26;L14
731	EIDRLNEVA	L42	AEHVNNSYEC	L42;L38	SLIDLQELG	L2;L4;L12
732	EIIGYKAI	L10	AEILLIIMRTFK	L40;L41	SLKELLQNG	L3;L13;L4
733	EIIGYKAID	L11	AEIPKEEVKPF	L41;L40	SLKVPATV	L3;L23;L43
734	EIIGYKAIDGG	L11	AEIVDTVSALVY	L41;L40	SLPSYAAF	L57;L43;L72
735	EIIKSQDL	L23	AELAKNVSLD	L40;L41	SLPVLQVRDV	L57;L64;L5
736	EIIKSQDLSV	L11	AELEGIQYGRSG	L41;L40	SLREVRTIK	L13;L6;L21
737	EIKDATPSD	L11	AETLKATEE	L45;L46	SLRVCVDTV	L3;L4;L2
738	EIKDTEKYCAL	L10	AETLKATEETF	L41;L36	SLSEQLRKQ	L3;L4;L14
739	EIKLAKKF	L23	AEVAVKMFDAY	L40;L41	SLSHFVNL	L74;L56;L4
740	EILGTVSW	L10	AEVQIDRLIT	L41;L40	SLVVRCSFY	L14;L12;L26
741	EILQKEKV	L23	AEWFLAYILFT	L40;L41	SNHNFLVQA	L46;L51;L42
742	EIPKEEVKP	L11	AEYHNESGLKTI	L45;L41	SNYLKRRV	L48;L45;L33
743	EIPVAYRKVL	L57	AFATAQEA	L72;L71	SPCESHGKQV	L39;L51;L22
744	EISFMLWCK	L19	AFDKSAFV	L62;L63	SPFVMMSA	L50;L51;L25
745	EITVATSRTL	L10	AFDKSAFVNL	L62;L68	SPIFLIVA	L50;L51;L22
746	EIVGGQIV	L20	AFFGMSRIGM	L71;L72	SPISEHDYQI	L32;L49;L34
747	EKCSAYTVEL	L44	AFKLNIKL	L62;L71	SPNLAWPL	L22;L56;L39
748	EKDEDDNLI	L34	AFLIGCNY	L71;L72	SPSGVYQCAM	L22;L32;L39
749	EKGDYGDAVVY	L27	AFPFTIYS	L71;L72	SQCVNLTTR	L15;L21;L17
750	EKQEILGTV	L20	AFPSGKVE	L71;L72	SQDLSVVSKV	L63;L68;L24
751	ELAKNVSLD	L11	AFPSGKVEG	L72;L71	SQILPDPSK	L13;L7;L28
752	ELDSFKEELDKY	L1	AFQTVKPG	L72;L71	SQLGGLHLLI	L24;L34;L8
753	ELFYSYATH	L10	AFVETVKGLDY	L12;L71	SQNAVASKI	L24;L48;L34
754	ELGKYEQYI	L24	AFVNLKQL	L72;L71	SQWLTNIF	L27;L48;L26
755	ELGTDPYEDF	L11	AFVTNVNAS	L72;L71	SRELKVTFF	L34;L30;L62
756	ELHLSWEV	L23	AGFPFNKW	L54;L48	SRIGMEVTP	L35;L34;L30
757	ELIRQGTDYKHW	L10	AGFPFNKWGK	L7;L13	SRIIPARAR	L30;L17;L15

758	ELKHGTFTC	L10	AGGIVAIVV	L69;L73	SRNYIAQV	L64;L35;L48
759	ELKINAAC	L23	AGLIAIVMV	L4;L73	SRNYIAQVD	L65;L64;L35
760	ELKINAACR	L17	AGNVQLRV	L48;L73	SRVPDLLV	L64;L35;L25
761	ELKKLLEQ	L23	AGNVQLRVI	L55;L48	SRYRIGNYKL	L30;L35;L34
762	ELSLIDFY	L1	AGSDKGVAP	L46;L42	SRYWEPEF	L65;L66;L28
763	ELSLIDFYL	L20	AGTDLEGNFY	L14;L12	SSRGTSPAR	L21;L15;L13
764	ELSPVALRQM	L11	AHIQWMVM	L28;L35	SSRSRNSSR	L15;L21;L17
765	ELSRVLGL	L23	AHISTIGV	L28;L35	SSSDNIALLV	L73;L20;L18
766	ELTGHMLDM	L11	AHKDKSAQCF	L43;L34	SSVELKHFFF	L52;L53;L54
767	ELTPVVQTIEV	L20	AHVASCDAI	L34;L28	STASALGK	L7;L19;L6
768	ELTSMKYFV	L20	AIAMACLVGL	L3;L4	STASDTYACW	L10;L52;L54
769	ELVAELEGIQY	L11	AIGKIQDSL	L67;L44	STDGNKIADKY	L18;L1;L14
770	ELVIGAVI	L23	AINRPQIGVVR	L21;L15	STFNVPMEKLK	L7;L6;L13
771	EMELTPVV	L48	AIPTNFTISV	L57;L5	STKPVETSNSF	L52;L53;L10
772	EMIAQYTSA	L42	AITILDGISQY	L14;L18	STMTNRQF	L52;L55;L53
773	EMIAQYTSAL	L10	AKDTTEAF	L27;L68	STQLGIEFLKR	L15;L7;L19
774	EMKSEKQV	L48	AKHDFFKF	L27;L66	STYASQGLV	L20;L73;L14
775	EMLAKALR	L17	AKHDFFKFR	L15;L21	SVEEVLSEA	L3;L5;L51
776	EMLAKALRK	L6	AKKVKPTVV	L23;L3	SVITPGTNT	L13;L11;L7
777	EMVMCGGSL	L10	AKNLNESL	L44;L27	SVMLTNDNTSR	L7;L19;L15
778	EMYLKLRSD	L23	AKNRARTVA	L42;L46	SVQTFFKLVNK	L7;L6;L15
779	ENFNQHEVLL	L20	AKSHNIALI	L44;L34	SVVNARLRAK	L7;L10;L6
780	ENSYTTTI	L48	ALALLLLDRL	L4;L3	SVVNIQKEI	L20;L10;L24
781	ENVAFNVVNK	L19	ALAPNMMVT	L3;L2	SVVSKVVK	L7;L19;L13
782	EPEFYEAMY	L31	ALDPLSETKC	L5;L18	SYCTGYREGY	L14;L72;L71
783	EPIYDEPTT	L32	ALDQAISMWAL	L5;L68	SYELQTPF	L71;L72;L62
784	EPKKDKKKK	L23	ALEPLVDLP	L1;L18	SYFVVKRH	L71;L48;L72
785	EPKKDKKKKAD	L23	ALFAYTKR	L21;L15	SYGIATVREV	L72;L64;L71
786	EPLTQDHV	L47	ALFAYTKRN	L24;L3	SYKDWSYSG	L8;L66;L15
787	EPLTQDHVD	L32	ALFAYTKRNV	L3;L2	TAALGVLM	L70;L31;L74
788	EPLVDLPI	L47	ALGGSVAIK	L6;L7	TADIVVFD	L68;L63;L62
789	EPLVDLPIG	L31	ALGKLQDVV	L24;L2	TADIVVFDEI	L67;L68;L49
790	EPMLQSADA	L50	ALIISVTSN	L3;L26	TANVNALL	L62;L68;L63
791	EPQIITTD	L23	ALITLATCEL	L2;L4	TAYNGYLTS	L49;L43;L69
792	EPTTTTSVPL	L22	ALKGGKIV	L23;L39	TCCSLSHRF	L49;L8;L34
793	EQDKNTQEVF	L34	ALKGGKIVN	L43;L26	TDDNALAYY	L1;L18;L14
794	EQIDGYVM	L35	ALKGGKIVNN	L3;L21	TDNYITTY	L29;L65;L33
795	EQIDGYVMHA	L11	ALLADKFPV	L2;L4	TEAFEKMV	L45;L37;L38
796	EQKSILSPL	L10	ALLAGTITS	L2;L4	TEAFEKMVSLL	L36;L40;L41
797	EQKSILSPLY	L14	ALLLLDRL	L4;L74	TECSNLLL	L45;L36;L37
798	EQLDFIDTKR	L17	ALLSDLQDLK	L6;L7	TEGSVKGL	L37;L33;L45
799	EQPTSEAV	L48	ALLSTDGNK	L6;L7	TEGSVKGLQP	L38;L42;L46
800	EQYIKWPW	L48	ALLSTDGNKI	L24;L2	TEIYQAGSTP	L38;L46;L42
801	EQYIKWPWYI	L48	ALLTKSSEYK	L6;L7	TEKYCALAP	L46;L42;L38
802	EQYVFCTVN	L48	ALLTLQQI	L4;L24	TELEPPCRFV	L45;L38;L36
803	ERLKLFAA	L25	ALNDFSNSG	L43;L16	TENLLLYIDI	L41;L40;L36

804	ERLKLFDR	L17	ALPETTAD	L57;L43	TESNKKFLP	L38;L42;L46
805	ERLKLFDRYF	L30	ALPETTADIV	L5;L2	TETICAPLTV	L45;L38;L46
806	ERSEAGVC	L35	ALPETTADIVV	L5;L2	TETICAPLTVF	L40;L41;L29
807	ERVRQALL	L35	ALQDAYYR	L21;L15	TFEEAALCTF	L62;L8;L9
808	ERVRQALLK	L30	ALQDAYYRAR	L21;L15	TFGAGAAL	L72;L71;L62
809	ERYKLEGY	L25	ALRANSAVK	L13;L6	TFISDEVAR	L17;L19;L15
810	ESCGNFKVTK	L19	ALRKVPTDNY	L26;L14	TFLLNKEMY	L12;L72;L71
811	ESDDYIAT	L1	ALSKGVHF	L26;L74	TFTYASAL	L72;L71;L62
812	ESDDYIATN	L1	ALTCFSTQF	L26;L27	TFVTHSKGL	L71;L8;L72
813	ESFGGASCC	L19	ALTNNVAF	L26;L43	TGSNVFQTR	L19;L17;L15
814	ESGLKTIL	L23	ALYYPSAR	L21;L6	TGYKKPASR	L17;L19;L15
815	ESGLKTILRK	L19	AMACLVGL	L56;L3	THDVSSAIN	L28;L35;L34
816	ESLRPDTR	L17	AMMFTSDL	L71;L72	THHWLLLTIL	L28;L34;L35
817	ESLVPGFNE	L17	AMPNMLRIM	L64;L57	THSDKFTDGVCL	L34;L35;L28
818	ESPFELEDF	L11	ANGDSEVVLK	L7;L6	THTGTGQAI	L35;L34;L28
819	ESSAKSASV	L20	ANGQVFGL	L65;L33	THTGTGQAITV	L28;L34;L35
820	ESSAKSASVY	L14	ANGQVFGLYK	L7;L6	THVQLSLPVL	L28;L34;L35
821	ESVQTFFKLV	L20	ANKDGIIWVA	L51;L42	TIDGSSGVV	L68;L63;L28
822	ETAHSCNV	L20	ANSTVLSF	L33;L65	TIFKDASGK	L19;L6;L7
823	ETAQNSVRVLQK	L19	ANYAKPFLNK	L6;L7	TISLAGSY	L14;L18;L1
824	ETDLTKGPH	L1	ANYQKVGMQK	L6;L7	TISLAGSYK	L6;L19;L7
825	ETDLTKGPHEF	L1	APFLYLYA	L50;L51	TITQMNLKY	L12;L18;L14
826	ETFKLSYGIA	L11	APGQTGKIA	L51;L39	TITVNVLAW	L10;L16;L49
827	ETFKLSYGIATV	L20	APGTAVLRQWL	L56;L22	TKDVVECL	L62;L68;L63
828	ETFVTHSKGLY	L11	APHGHVMVE	L51;L39	TKHPNQEY	L27;L66;L43
829	ETFYPKLQS	L20	APKEIIFLE	L39;L56	TKPYIKWDL	L44;L66;L57
830	ETGLLMPLK	L19	APLLSAGIF	L22;L31	TKVDGVDVEL	L44;L32;L66
831	ETGTLIVNSV	L20	APNMMVTNNTF	L39;L22	TLADAGFIK	L6;L7;L19
832	ETICAPLTVFF	L11	APRTLLTK	L22;L51	TLADAGFIKQY	L11;L10;L14
833	ETIQITISSFK	L19	APRTLLTKG	L51;L22	TLEPEYFNSV	L5;L2;L4
834	ETISLAGS	L11	APSASAFF	L22;L56	TLIVNSVL	L23;L68;L28
835	ETIYNLLK	L19	APSASAFFGM	L22;L56	TLKATEETF	L26;L9;L16
836	ETKDVVEC	L17	APYIVGDV	L47;L51	TLKKRWQLAL	L23;L3;L39
837	ETKDVVECLK	L19	APYIVGDVVQ	L56;L51	TLLSLREVR	L15;L21;L17
838	ETKFLTENLL	L20	AQAAGTDTTI	L34;L24	TLNGLWLDDV	L2;L4;L3
839	ETKFLTENLLLY	L1	AQALNTLV	L24;L48	TLQAENVTGL	L4;L3;L2
840	ETLGVLVPHV	L20	AQCFKMFYK	L7;L6	TLSYEQFKK	L6;L7;L19
841	ETLPTEVLT	L17	AQDGNAAISDY	L14;L18	TLVFLFVAA	L50;L46;L51
842	ETLYCIDGALL	L20	AQEAYEQAV	L24;L28	TMCDIRQLLF	L12;L8;L9
843	ETNILLNVPL	L20	AQNSVRVLQ	L44;L15	TNNLVVMAY	L14;L31;L65
844	ETQALPQRQ	L20	AQSFLNRV	L48;L24	TPLVPFWIT	L31;L47;L50
845	ETQALPQRQK	L19	AQTGIAVLD	L44;L24	TPLVPFWITI	L47;L50;L22
846	ETRKLMPVCV	L20	AQVAKSHNI	L24;L48	TPTWRVYST	L23;L32;L39
847	ETSNSFDV	L20	AQVDVVNFN	L24;L44	TQLGIEFL	L25;L35;L34
848	ETSNSFDVLK	L19	AQVKQIYKT	L24;L44	TQLGIEFLK	L7;L30;L6

849	ETSWQTGDFV	L20	AQYTSALLA	L24;L28	TQVVDMSMTY	L26;L27;L14
850	ETTADIVV	L20	ARAGKASCTL	L30;L35	TQWSLFFFLY	L14;L12;L27
851	ETTADIVVFD	L20	ARDGCVPLNI	L30;L34	TRAKVGILC	L30;L34;L35
852	ETYFTQSRN	L11	ARHINAQV	L35;L25	TREEAIRHV	L64;L35;L34
853	EVARDLSL	L20	ARLRAKHYVY	L66;L30	TRLQSLENV	L30;L34;L35
854	EVAVKMFDAYV	L20	ARNGVLIT	L65;L35	TRQVVNVV	L35;L25;L64
855	EVFAQVKQ	L20	ARNGVLITEG	L65;L30	TRVECTTI	L25;L35;L34
856	EVFNATRFAS	L20	ASAVVLLILM	L52;L7	TRVECTTIV	L64;L35;L25
857	EVFNATRFASV	L20	ASDTYACWH	L18;L1	TSAFVETV	L48;L20;L70
858	EVGKPRPPL	L20	ASEAARVVR	L15;L21	TSAMQTMLF	L53;L52;L54
859	EVGKPRPPLNR	L17	ASEFSSLP	L1;L18	TSDLATNNLV	L1;L68;L18
860	EVGPEHSLA	L20	ASEYTGNY	L1;L18	TSFGPLVRKI	L55;L20;L10
861	EVITFDNLKT	L11	ASEYTGNYQ	L1;L18	TSLEIPRR	L48;L17;L15
862	EVKILNNL	L23	ASFYYVWK	L7;L13	TSNSFDVL	L73;L55;L67
863	EVKILNNLGV	L11	ASGKPVPY	L43;L65	TSPISEHDY	L14;L1;L26
864	EVKPFITE	L23	ASGNLLLDK	L7;L6	TSSGDATTAY	L18;L14;L1
865	EVLLAPLL	L74	ASKKPRQK	L13;L55	TSTDVVYR	L19;L17;L15
866	EVLLAPLLSA	L50	ASLPFGWLIV	L73;L69	TSVDCTMYI	L70;L69;L73
867	EVLSDRELH	L17	ASLVLARKH	L55;L52	TSVVLLSV	L48;L73;L59
868	EVLSDRELHL	L10	ASSSEAFL	L74;L73	TTCCSLSHR	L17;L15;L19
869	EVNEFACV	L20	ASTDTCFANK	L7;L13	TTCFSVAAL	L20;L68;L57
870	EVPANSTV	L20	ATALLTLQQ	L7;L18	TTFTYASALW	L52;L10;L54
871	EVPVSIINNTV	L20	ATCDWTNAGDY	L14;L18	TTIAKNTVK	L7;L19;L6
872	EVQELYSPIF	L11	ATCFSTASDTY	L18;L14	TTIKPVTYKL	L20;L53;L11
873	EVQELYSPIFL	L20	ATEETFKLS	L1;L18	TTLDSKTQSL	L10;L16;L8
874	EVQGYKSVNI	L20	ATEGALNTP	L42;L18	TTLEETKF	L53;L54;L52
875	EVQPQLEMEL	L20	ATLVSDIDITF	L52;L53	TTLNGLWL	L55;L61;L60
876	EVRQIAPGQ	L11	ATNNAMQV	L73;L70	TTTLEETKF	L53;L52;L54
877	EVRTIKVFT	L20	ATNNLVVMA	L42;L69	TTVDNINL	L20;L70;L60
878	EVRTIKVFTTV	L20	ATNVVIKVCEF	L52;L16	TTYKLNVGDY	L14;L11;L10
879	EVTGDSCNNYM	L11	ATTAYANSV	L73;L70	TVCTVCGMWK	L7;L6;L19
880	EVTTTLEET	L10	ATVAYFNMV	L73;L20	TVEEAKTVLK	L19;L7;L6
881	EVVDKYFD	L20	ATVAYFNMVY	L14;L18	TVELGTEV	L63;L68;L23
882	EVVENPTI	L20	ATVREVLSD	L65;L10	TVFFDGRVD	L65;L55;L32
883	EWKFYDAQP	L42	AVAKHDFF	L74;L54	TVMPLSAPTL	L20;L28;L32
884	EYCRHGTCER	L17	AVAKHDFFK	L7;L6	TVNVLAWL	L62;L59;L23
885	EYDYVIFT	L62	AVANGDSEVVL	L44;L56	TVQFCDAMR	L19;L21;L17
886	EYDYVIFTQ	L17	AVANGDSEVVLK	L7;L6	TVYDDGARRVW	L16;L52;L10
887	EYFNSVCR	L17	AVCRHHANEY	L18;L14	TVYDPLQPE	L6;L43;L20
888	EYRLYLDAY	L14	AVDAAKAYK	L7;L6	TVYSHLLLVA	L51;L3;L46
889	EYTDFATSA	L17	AVINGDRWFLNR	L7;L15	TVYTKVDGV	L3;L20;L11
890	EYTFEKGDY	L14	AVKMFDAY	L14;L26	TWFSQRGGSY	L14;L10;L12
891	EYVSQPFL	L9	AVKTQFNYYK	L13;L7	TWICLLQF	L8;L9;L59
892	FAAYSRYR	L17	AVKTQFNYYKK	L7;L13	TYASALWEI	L9;L8;L64

893	FAFACPDGVKH	L31	AVLQSGFRK	L7;L6	TYEGNSPF	L72;L71;L62
894	FAKFLKTN	L70	AVRDPQTLE	L13;L6	TYICGFIQQ	L8;L17;L9
895	FAKFLKTNC	L58	AVSKGFFKE	L7;L24	TYKLNVGDY	L14;L72;L71
896	FAMMFVKH	L59	AVVIPTKK	L7;L6	TYLDGADVTK	L8;L9;L17
897	FANKHADFD	L58	AVVIPTKKA	L51;L46	TYLEGSVRVV	L8;L72;L71
898	FANKHADFDTW	L49	AVVYRGTTTYK	L7;L6	TYNKVENM	L71;L72;L62
899	FASEAARVVR	L19	AVYRINWI	L48;L24	TYNLWNTFTR	L17;L15;L21
900	FASFYYVWKSY	L31	AWQPGVAMP	L42;L38	TYRRLISM	L72;L71;L66
901	FATSACVLAA	L50	AYANRNRFLY	L12;L14	VAALTNNVAF	L31;L52;L58
902	FAVDAAKA	L50	AYANRNRFLYI	L9;L8	VAFNVVNKG	L69;L70;L47
903	FAYANRNR	L17	AYCNKTVGEL	L72;L71	VAITRAKV	L70;L47;L48
904	FAYANRNRFLY	L12	AYIICIST	L71;L72	VAKYTQLCQY	L43;L14;L58
905	FAYANRNRFLYI	L47	AYIICISTKHFY	L14;L40	VANGDSEV	L70;L58;L63
906	FAYTKRNVIPTI	L47	AYITGGVV	L72;L71	VAYESLRPD	L43;L49;L59
907	FCAFAVDAA	L50	AYKIEELFYSY	L14;L12	VAYSNNSI	L47;L70;L68
908	FCGKGYHL	L74	AYNGYLTS	L65;L71	VCTEIDPKL	L8;L9;L5
909	FCLLNRYFR	L17	AYNMMISA	L71;L72	VDDPCPIHFY	L18;L1;L14
910	FCSQHTML	L74	AYNMMISAG	L72;L71	VDILGPLSA	L46;L50;L51
911	FDEDDSEPVL	L67	AYNVTQAFGR	L15;L21	VDYGARFY	L65;L14;L55
912	FDEGNCDTL	L67	AYPLTKHP	L72;L71	VEGCMVQV	L45;L37;L33
913	FDEISMATNY	L1	AYPLTKHPN	L72;L71	VEHVTFFI	L45;L33;L48
914	FDKSAFVNL	L58	AYRFNGIGV	L13;L72	VEHVTFFIY	L29;L40;L41
915	FDRDAAMQR	L17	AYRKVLLR	L15;L17	VEKKKLDGF	L33;L37;L29
916	FDTRVLSNL	L74	AYTRYVDNNF	L9;L8	VELKHFFFA	L46;L42;L38
917	FDVEGCHATR	L19	AYVDNSSLT	L8;L9	VEQDKNTQEV	L38;L45;L37
918	FEEAALCTFL	L36	AYWVPRAS	L71;L72	VEQKIAEIP	L38;L42;L29
919	FEHIVYGD	L33	AYYFMRFRRA	L46;L42	VESSSKLWA	L46;L38;L42
920	FEKGDYGDA	L46	AYYFMRFRRAF	L71;L72	VETSNSFDV	L45;L38;L46
921	FEKGDYGDAV	L45	AYYNTTKGGRF	L8;L9	VEWKFYDAQP	L46;L42;L38
922	FELEDFIP	L38	AYYRARAG	L71;L72	VFAQVKQIY	L12;L14;L72
923	FELLHAPA	L50	AYYVGYLQPR	L15;L21	VFCGVDAV	L71;L62;L72
924	FELLHAPAT	L38	CANGQVFGLY	L14;L12	VFCTVNAL	L72;L71;L62
925	FELTSMKY	L29	CASLKELL	L23;L74	VFDEISMATNY	L12;L18;L62
926	FELTSMKYFV	L45	CATVHTANKW	L54;L49	VFHLYLQY	L71;L72;L12
927	FELWAKRN	L29	CAYWVPRA	L50;L47	VFKNIDGY	L14;L71;L72
928	FENKTTLP	L38	CAYWVPRAS	L59;L69	VFLFVAAI	L71;L72;L48
929	FFASFYYV	L62	CCDDDYFNK	L13;L7	VFLLVTLAIL	L9;L62;L8
930	FFDGRVDG	L62	CCYDHVIST	L69;L43	VFPLNSII	L62;L71;L72
931	FFDGRVDGQ	L62	CDNIKFAD	L65;L33	VFPPTSFG	L62;L72;L71
932	FFDGRVDGQV	L62	CDVTDVTQL	L37;L33	VFQSASKIITL	L72;L71;L8
933	FFIYNKIV	L71	CEEEEFEP	L38;L42	VFQTRAGCL	L72;L71;L62
934	FFSNYLKRR	L17	CEEMLDNRA	L38;L42	VFTTVDNINL	L9;L8;L72
935	FFTLLLQLC	L12	CEFQFCNDP	L46;L42	VGSDNVTDF	L26;L9;L8
936	FFYVLGLA	L62	CEIVGGQI	L45;L48	VHFVCNLL	L28;L34;L35
937	FFYVLGLAAIM	L71	CFSTQFAF	L72;L71	VHFVCNLLL	L34;L28;L35
938	FGADPIHSLR	L19	CFTNVYADSF	L9;L72	VHNQDVNL	L28;L34;L35

939	FGDDTVIEVQ	L68	CFVLAAVY	L72;L71	VIAWNSNNL	L60;L74;L58
940	FGDFIQTT	L68	CFVLAAVYR	L17;L15	VILRGHLRI	L24;L8;L48
941	FGDFIQTTP	L68	CGFIQQKL	L48;L25	VINGDRWFLNR	L15;L21;L17
942	FGGCVFSY	L66	CGPDGYPL	L57;L66	VIVFDGKSK	L7;L13;L43
943	FGLFCLLNR	L17	CHDGKAHF	L62;L63	VKDCVVLHSY	L14;L18;L27
944	FGLFCLLNRY	L12	CIDCSARHI	L68;L63	VKQGDDYVY	L27;L66;L14
945	FGLVAEWF	L59	CIKDLLAR	L17;L15	VKRVDWTIEY	L43;L27;L26
946	FGPLVRKIF	L57	CLAYYFMRF	L12;L10	VLAAECTIF	L26;L9;L74
947	FGWLIVGVA	L50	CLDDRCILH	L5;L18	VLHSTQDLF	L9;L12;L26
948	FHAIHVSGT	L28	CLDDRCILHC	L18;L5	VLHSYFTSDY	L43;L26;L14
949	FHLVDFQVT	L35	CLEASFNY	L1;L18	VLITEGSVK	L6;L13;L7
950	FHLVDFQVTI	L34	CLEASFNYL	L5;L1	VLKKCKSAF	L23;L43;L26
951	FHQKLLKSI	L34	CLLQFAYANR	L21;L15	VLLFLAFVV	L4;L2;L24
952	FHTPAFDKSAF	L28	CLTPVYSF	L23;L26	VLLILMTAR	L21;L15;L6
953	FIASFRLFA	L69	CMMCYKRNR	L15;L17	VLLSVLQQLR	L21;L15;L6
954	FIDTKRGVYC	L63	CNIVNVSLV	L73;L48	VLNNDYYRSL	L43;L57;L4
955	FIEDLLFN	L1	CNLLLLFV	L73;L48	VLPNDDTL	L57;L5;L62
956	FIETISLAGSY	L1	CPAEIVDTVSA	L50;L51	VLPNDDTLR	L21;L15;L5
957	FISDEVARD	L3	CPDGVKHVYQL	L32;L39	VLPNDDTLRV	L5;L2;L57
958	FISDEVARDL	L60	CPFGEVFNA	L50;L51	VLPPLLTD	L57;L5;L43
959	FISNSWLM	L58	CPIFFITGNTL	L56;L22	VLPQLEQPY	L12;L26;L57
960	FISPYNSQN	L58	CPIHFYSKW	L49;L10	VLQAVGACV	L2;L5;L4
961	FIYNKIVDE	L69	CPLIAAVI	L47;L48	VLQKAAITI	L4;L24;L2
962	FKDQVILLN	L1	CRFDTRVLS	L65;L30	VLQVRDVLV	L2;L4;L5
963	FKEELDKY	L1	CRSKNPLL	L35;L66	VLSFELLHA	L3;L2;L4
964	FKEELDKYF	L27	CSDKAYKI	L55;L63	VLSTFISAA	L3;L2;L51
965	FKELLVYAA	L50	CSVIDLLL	L73;L74	VLYQPPQTS	L43;L3;L24
966	FKFVCDNIKF	L27	CTCGKQATK	L7;L19	VMCGGSLY	L18;L1;L14
967	FKHLIPLM	L66	CTEIDPKLDNY	L1;L18	VMFLARGI	L48;L55;L47
968	FKLASHMY	L27	CTEIDPKLDNYY	L1;L18	VPFWITIA	L50;L51;L47
969	FKLNEEIAI	L44	CTFEYVSQP	L11;L10	VPNQPYPNA	L51;L50;L22
970	FKLSYGIAT	L44	CTFLLNKEM	L70;L69	VPQADVEW	L56;L49;L39
971	FKVNSTLEQY	L27	CTVCGMWKGY	L10;L11	VPVSIINNTV	L51;L50;L47
972	FKVSIWNLDY	L12	CVFSYVGCHNK	L7;L6	VQIDRLITG	L26;L69;L27
973	FKWDLTAFGL	L44	CVLAAECTIFK	L7;L6	VQLHNDILL	L44;L8;L34
974	FKYWDQTYH	L27	CVLSGHNLAK	L6;L7	VQQESPFVM	L66;L35;L28
975	FLAHIQWM	L74	CVVADAVIK	L7;L19	VQQLPETY	L26;L27;L48
976	FLALITLA	L3	CYFGLFCLLNR	L15;L17	VQQLPETYF	L26;L27;L9
977	FLALITLATC	L3	CYKRNRATR	L17;L15	VRAWIGFDV	L64;L30;L35
978	FLAYILFTRFFY	L12	CYNGSPSGV	L62;L72	VRCSFYEDF	L66;L30;L34
979	FLEGETLPTEV	L2	CYNGSPSGVY	L14;L72	VRETMSYLF	L9;L66;L34
980	FLGIITTVAA	L2	DAAMQRKL	L47;L70	VRIKIVQM	L66;L35;L25
981	FLGYFCTCY	L12	DALFAYTKR	L17;L19	VRTNVYLAV	L35;L64;L30
982	FLIGCNYLG	L2	DALNNIINN	L47;L17	VSCLPFTI	L55;L48;L68
983	FLIGCNYLGK	L6	DALNNIINNAR	L17;L19	VSDIDITFLK	L1;L18;L7
984	FLKKDAPY	L43	DAMMFTSDL	L25;L61	VSDIDITFLKK	L18;L1;L7

985	FLKTNCCRF	L43	DANYFLCW	L49;L47	VSDVGDSAE	L68;L1;L63
986	FLLKYNENG	L2	DAPYIVGDV	L47;L20	VSGTNGTKR	L15;L19;L21
987	FLLNKEMY	L12	DAQSFLNR	L17;L19	VSNGTHWFV	L73;L58;L70
988	FLLNKEMYLK	L6	DATPSDFVR	L19;L17	VSTSGRWV	L48;L70;L55
989	FLLPSLATVA	L2	DAYPLTKHP	L47;L49	VSWNLREML	L53;L16;L67
990	FLLVTLAI	L59	DDFTGCVIAW	L10;L29	VTDFNAIAT	L68;L1;L18
991	FLLVTLAILTA	L2	DDPCPIHFY	L11;L29	VTDTPKGPKV	L63;L1;L18
992	FLMDLEGKQ	L2	DDYQGKPLEF	L10;L49	VTHSKGLY	L1;L14;L18
993	FLMDLEGKQG	L2	DEFTPFDV	L29;L25	VTLLPAADL	L60;L61;L53
994	FLNKVVST	L23	DEFTPFDVVR	L29;L19	VTMPLGYVT	L52;L55;L53
995	FLNRVCGV	L3	DEFTPFDVVRQ	L41;L29	VTMPLGYVTH	L52;L53;L7
996	FLPFAMGI	L57	DELTGHMLD	L29;L25	VTQLYLGGMSY	L1;L14;L18
997	FLPFFSNVT	L57	DEMIAQYTSA	L38;L42	VTRDIASTD	L43;L55;L13
998	FLPFFSNVTWF	L57	DESGEFKL	L29;L37	VTTEILPV	L73;L48;L70
999	FLPGVYSVIYLY	L12	DEVRQIAP	L29;L46	VTVYSHLL	L60;L55;L70
1000	FLRDGWEIVK	L13	DEWSMATYYLF	L41;L40	VVDADSKIV	L63;L5;L68
1001	FLRDGWEIVKF	L43	DFATSACVL	L72;L71	VVDADSKIVQL	L68;L5;L63
1002	FLVFLGIITT	L2	DFLELAMDEF	L9;L8	VVDDPCPI	L68;L63;L62
1003	FLVLIMLI	L74	DFLHFLPRV	L47;L4	VVDDPCPIH	L63;L68;L5
1004	FLWLLWPV	L2	DFMSLSEQLR	L17;L19	VVDYGARFYF	L1;L63;L12
1005	FLWLLWPVT	L2	DFTGCVIAW	L49;L10	VVFDEISM	L69;L59;L58
1006	FLYIIKLIFLW	L12	DFVENPDIL	L62;L67	VVFLLVTLA	L50;L51;L3
1007	FMRFRRAF	L59	DFVENPDILR	L17;L19	VVFNGVSFSTF	L16;L26;L52
1008	FMRIFTIGTV	L3	DFVRATATI	L10;L8	VVIPDYNTYK	L7;L6;L13
1009	FNDGVYFAS	L68	DGADVTKI	L47;L25	VVKRHTFSNY	L14;L10;L26
1010	FNICQAVTA	L50	DGISQYSL	L23;L25	VVLLILMTAR	L15;L21;L17
1011	FNKWGKARLY	L14	DGNAAISDY	L14;L29	VVLSFELLH	L12;L7;L6
1012	FNLVAMKYNY	L12	DGYFKIYSK	L23;L19	VVNAANVY	L26;L18;L14
1013	FNPETNILLNV	L5	DIAKKPTETI	L10;L11	VVNARLRAK	L6;L7;L13
1014	FNPPALQDAY	L12	DIASTDTCF	L11;L10	VVNPVMEPIY	L12;L14;L31
1015	FNVAITRAKV	L20	DILGPLSAQ	L10;L11	VVNVVTTKI	L24;L49;L48
1016	FNYLKSPNF	L59	DILRVYANL	L10;L11	VVPGLPGTI	L5;L57;L9
1017	FPDLNGDV	L68	DIPGIPKDM	L11;L57	VVREFLTR	L15;L21;L17
1018	FPFNKWGKAR	L50	DIQLLKSAY	L14;L29	VVRQCSGVTF	L26;L52;L53
1019	FPFNKWGKARLY	L31	DIVKTDGTL	L10;L11	VVRSIFSR	L15;L21;L17
1020	FPKSDGTGTI	L49	DIYNDKVAGF	L11;L10	VVRSIFSRTL	L13;L39;L55
1021	FPLQSYGF	L31	DKFPVLHDI	L47;L20	VVYCPRHV	L48;L47;L64
1022	FPLQSYGFQP	L50	DKLQFTSL	L25;L23	VVYCPRHVI	L16;L47;L39
1023	FPNITNLC	L47	DKVFRSSVL	L25;L44	VYAADPAM	L71;L72;L66
1024	FPNITNLCP	L50	DLEGKQGNF	L11;L10	VYANLGERV	L9;L8;L72
1025	FPNTYLEG	L50	DLGDELGTD	L10;L11	VYCPRHVIC	L8;L66;L9
1026	FPPTEPKKD	L49	DLNDFVSDA	L3;L11	VYDDGARRVW	L9;L62;L52
1027	FPQSAPHGVVFL	L31	DLNQLTGY	L11;L26	VYDNKLKAH	L62;L71;L72
1028	FPSGKVEG	L50	DLQDLKWARF	L11;L10	VYDYLVSTQEF	L8;L9;L62
1029	FQEKDEDDNL	L34	DLQELGKYEQY	L11;L10	VYLAVFDKN	L9;L8;L12
1030	FQQFGRDI	L48	DLSVVNARL	L20;L4	VYLKHGGGV	L72;L71;L8

1031	FQSASKII	L48	DLSVVNARLR	L19;L17	VYLPYPDPS	L9;L72;L71
1032	FQTRAGCLI	L24	DLTKPYIKW	L10;L49	VYMPASWV	L72;L71;L62
1033	FQTVKPGNF	L58	DLVYALRHF	L10;L11	VYMPASWVMR	L15;L9;L21
1034	FQVTIAEI	L48	DLYDKLQFTSL	L10;L11	VYPVASPNE	L9;L71;L72
1035	FQVTIAEILL	L44	DLYKLMGHF	L11;L10	VYPVASPNEC	L72;L9;L71
1036	FRIDGDMV	L35	DMSKFPLKLR	L17;L19	VYQLRARSV	L72;L71;L64
1037	FRIDGDMVPH	L30	DMVDTSLSGF	L10;L11	VYSDVENPH	L72;L9;L71
1038	FRIDGDMVPHI	L34	DMVPHISRQ	L11;L10	VYSVIYLYLTF	L9;L8;L12
1039	FRKMAFPSG	L66	DMVPHISRQR	L19;L17	VYYGNALDQ	L71;L72;L8
1040	FRLTLGVY	L66	DNINLHTQV	L25;L20	VYYHKNNKSW	L9;L8;L71
1041	FRLTLGVYD	L30	DNLLEILQK	L17;L7	WAHGFELTSM	L58;L43;L59
1042	FRRAFGEY	L66	DPAQLPAPR	L19;L17	WAKRNIKPV	L70;L58;L69
1043	FRVQPTES	L66	DPLQPELDSF	L31;L47	WEVGKPRPP	L38;L46;L42
1044	FRYMNSQGLL	L30	DPLSETKCTL	L32;L23	WFFSNYLKR	L17;L15;L19
1045	FSALEPLVD	L69	DPNFKDQV	L23;L47	WFLAYILFTRF	L8;L12;L9
1046	FSGYLKLTD	L65	DQIGYYRRA	L11;L24	WFLLLSVCL	L71;L72;L62
1047	FSHSQLGGLHL	L60	DQLTPTWRV	L24;L48	WFLNRFTTTL	L71;L8;L72
1048	FSLELQDH	L59	DQLTPTWRVY	L27;L14	WHHSIGFDY	L14;L12;L43
1049	FSNVTWFHA	L50	DRAMPNML	L25;L35	WLDDDSQQT	L5;L2;L1
1050	FSNVTWFHAI	L61	DRDLYDKL	L25;L35	WLDDDSQQTV	L5;L2;L24
1051	FSNYLKRRVV	L73	DRDLYDKLQF	L34;L35	WLKQLIKVTL	L23;L3;L56
1052	FSSLPSYAA	L50	DRELHLSW	L25;L35	WLPTGTLL	L57;L74;L62
1053	FSSNVANYQK	L19	DRLNQLESK	L30;L25	WSYSGQSTQL	L60;L55;L53
1054	FSYVGCHNK	L7	DRVVFVLWA	L25;L35	WVMRIMTW	L10;L54;L52
1055	FTDGVCLFWN	L1	DRYPANSIVC	L25;L35	WWTAFVTNV	L20;L3;L64
1056	FTEERLKLFD	L1	DSAEVAVKMF	L10;L11	YAADPAMHAA	L50;L67;L61
1057	FTGNLQSNHDLY	L1	DSGFAAYSR	L19;L17	YAAVINGDRW	L52;L49;L54
1058	FTIGTVTLKQ	L11	DSIIIGGAK	L19;L11	YACWHHSIG	L59;L69;L70
1059	FTPLIQPI	L57	DSIIIGGAKL	L20;L11	YAFASEAAR	L19;L17;L31
1060	FTPLIQPIGAL	L57	DSSQGSEY	L1;L18	YAFASEAARV	L20;L47;L58
1061	FTRGVYYPDK	L13	DSVEEVLSE	L10;L11	YAKPFLNK	L13;L59;L70
1062	FTRSTNSRIK	L13	DSYFVVKR	L19;L17	YAKPFLNKVV	L70;L69;L58
1063	FTSDLATN	L59	DTANPKTPKY	L11;L10	YALRHFDEG	L67;L59;L61
1064	FTVEKGIY	L1	DTDFVNEFYAY	L1;L18	YALVYFLQS	L59;L61;L47
1065	FTYASALW	L54	DTDLTKPY	L1;L18	YANLGERVR	L17;L19;L32
1066	FVCNLLLLFV	L20	DTFNGECPNF	L10;L11	YANRNRFLYI	L47;L49;L73
1067	FVDDIVKTDGTL	L68	DTGVEHVTFF	L10;L11	YANSVFNI	L47;L70;L49
1068	FVDGVPFVVST	L68	DTIANYAKP	L11;L10	YATHSDKF	L58;L49;L54
1069	FVDRQTAQ	L68	DTIANYAKPF	L10;L11	YCIPYNSV	L28;L47;L45
1070	FVEIIKSQDL	L68	DTLKEILVT	L10;L11	YCQVHGNAH	L71;L72;L59
1071	FVETVKGLD	L1	DTLRVEAFEY	L12;L10	YDDGARRV	L63;L33;L62
1072	FVFLVLLP	L50	DTPKGPKV	L11;L47	YDFTEERL	L33;L65;L29
1073	FVIRGDEV	L67	DTPKGPKVK	L19;L11	YDKLQFTSL	L23;L37;L33
1074	FVLTSHTV	L47	DTPKGPKVKY	L11;L10	YDKLVSSF	L33;L43;L23
1075	FVMMSAPPA	L50	DTPNNTDFSR	L19;L17	YDYLVSTQEF	L33;L43;L27
1076	FVNLDNLRA	L50	DTSLSGFKL	L20;L19	YEDQDALF	L62;L33;L63

1077	FVNLKQLPFFY	L12	DTTDAVRDP	L11;L10	YEKLKPVLD	L45;L46;L23
1078	FVNLKQLPFFYY	L12	DTWFSQRGGSY	L11;L14	YELKHGTF	L33;L29;L37
1079	FVRATATI	L48	DVDTDFVNEFY	L1;L18	YENAFLPF	L29;L33;L59
1080	FVSDADSTLI	L20	DVEGCHATR	L19;L17	YENAFLPFAM	L29;L36;L40
1081	FVSEETGTLI	L20	DVENPHLMGW	L10;L11	YENQKLIA	L46;L38;L42
1082	FVSGNCDVVI	L32	DVFHLYLQYI	L20;L10	YENQKLIANQF	L29;L40;L41
1083	FVSLAIDA	L50	DVNLHSSR	L17;L19	YEQYIKWPWY	L41;L29;L40
1084	FVSNGTHWFV	L20	DVNLHSSRL	L11;L10	YESLRPDTRY	L29;L40;L41
1085	FVTDTPKGPKV	L20	DVRETMSYL	L11;L10	YEYGTEDDY	L29;L14;L27
1086	FVTNVNASS	L20	DVRETMSYLF	L11;L10	YFAVHFISN	L71;L72;L46
1087	FVVEVVDK	L19	DVSFLAHIQW	L19;L10	YFKNHTSPD	L71;L43;L72
1088	FVVFLLVT	L59	DVTQLYLGGM	L11;L10	YFLCWHTNC	L71;L72;L8
1089	FVVFLLVTLA	L50	DVVECLKLS	L11;L10	YFLCWHTNCY	L72;L71;L12
1090	FVVKRHTFS	L74	DVVECLKLSHQ	L10;L11	YFNKKDWYDF	L8;L9;L12
1091	FVVKRHTFSNY	L10	DVVNQNAQA	L11;L20	YFNSVCRL	L62;L71;L72
1092	FVVPGLPG	L61	DVVQEGVLTA	L11;L10	YFNSVCRLM	L62;L71;L72
1093	FVVPGLPGTILR	L19	DVVQEGVLTAV	L11;L20	YFSGAMDTTSY	L71;L72;L12
1094	FVVSTGYHFREL	L60	DVVRQCSGVTF	L11;L10	YFTQSRNL	L71;L72;L62
1095	FYDAQPCSD	L62	DVVYRAFDIY	L10;L11	YFVKIGPER	L17;L19;L8
1096	FYDFAVSKGFF	L62	DWYDFVEN	L25;L29	YFYTSKTTVA	L71;L72;L46
1097	FYFYTSKT	L71	DYDCVSFCY	L12;L1	YFYYLGTGP	L72;L71;L46
1098	FYGPFVDRQ	L66	DYIATNGPL	L72;L71	YHFRELGV	L28;L35;L48
1099	FYILPSIISN	L72	DYIINLII	L47;L25	YHNESGLKT	L28;L35;L34
1100	FYKENSYTTTI	L9	DYPKCDRAM	L72;L71	YHNESGLKTI	L34;L28;L35
1101	FYKGVITHD	L66	DYTEISFM	L72;L62	YIATNGPLK	L6;L7;L19
1102	FYLTNDVS	L71	DYTEISFMLW	L9;L8	YIDINGNLHP	L1;L68;L18
1103	FYPPDEDEEE	L66	DYVYNPFMI	L8;L9	YILFTRFFY	L12;L14;L1
1104	FYSKWYIR	L17	EAALCTFLL	L20;L74	YKHYTPSF	L66;L27;L59
1105	FYSYATHSDKF	L9	EAANFCALIL	L69;L20	YKIEELFY	L27;L66;L12
1106	FYVYSRVK	L71	EAEVQIDRL	L32;L63	YKKDNSYF	L58;L27;L66
1107	GAAAYYVGYL	L74	EAGVCVSTSGR	L19;L17	YKLNVGDYF	L27;L9;L12
1108	GAALQIPFA	L50	EAMYTPHTVL	L67;L32	YKQFDTYNL	L44;L66;L34
1109	GADLKSFD	L63	EAPFLYLYAL	L57;L20	YLALYNKYKY	L12;L1;L14
1110	GADVTKIKP	L63	EAPLVGTPV	L57;L20	YLCFLAFLLF	L12;L9;L1
1111	GAISSVLND	L49	EASKKPRQK	L19;L17	YLFDESGEFK	L6;L2;L13
1112	GAISSVLNDIL	L67	EASKKPRQKR	L17;L19	YLFDESGEFKL	L2;L4;L5
1113	GALDISASI	L44	EAVKTQFNYY	L11;L10	YLKRRVVF	L23;L26;L27
1114	GATTCGYL	L74	EAVMYMGTL	L10;L61	YLKSPNFSK	L13;L6;L43
1115	GAVILRGHLR	L19	ECFDKFKV	L20;L24	YLKSPNFSKL	L3;L10;L5
1116	GAWNIGEQKS	L24	ECPNFVFPL	L57;L20	YLPQNAVVKI	L5;L3;L2
1117	GCDVTDVTQL	L34	ECVLGQSKR	L19;L17	YLTNDVSF	L43;L26;L74
1118	GCDVTDVTQLY	L18	EDLLFNKV	L33;L48	YLVSTQEFRY	L12;L14;L1
1119	GCINANQV	L48	EEAIRHVR	L29;L42	YMPASWVM	L57;L66;L71
1120	GCVPLNII	L48	EEAKTVLKKC	L41;L40	YNDKVAGF	L62;L33;L63
1121	GCVPLNIIPL	L44	EEEEFEPSTQY	L41;L40	YNGSPSGVY	L65;L14;L12
1122	GDAALALL	L33	EEEFEPSTQY	L41;L40	YPDKVFRSS	L32;L49;L39

1123	GDAALALLL	L40	EEFEPSTQYE	L41;L40	YPDKVFRSSV	L32;L22;L39
1124	GDCEEEEF	L33	EEGDCEEEEF	L40;L41	YPKLQSSQA	L51;L50;L22
1125	GDELGTDPY	L18	EEIAIILASFS	L40;L41	YPNMFITR	L50;L17;L47
1126	GDELKINAA	L46	EELDKYFKNH	L41;L40	YPNMFITRE	L49;L32;L50
1127	GDFIQTTP	L65	EELFYSYAT	L42;L40	YQIGGYTEKW	L49;L10;L24
1128	GDFLHFLP	L33	EELKKLLEQW	L40;L41	YQPPQTSI	L48;L24;L57
1129	GDFLHFLPR	L7	EESSAKSA	L42;L38	YQVNGYPNM	L58;L28;L61
1130	GDFLHFLPRV	L33	EESSAKSASV	L42;L38	YQVNGYPNMF	L34;L27;L58
1131	GDFVKATC	L33	EESSAKSASVY	L41;L40	YRFNGIGV	L25;L35;L64
1132	GDIAARDL	L37	EETFKLSYGI	L40;L41	YRFNGIGVTQ	L30;L35;L34
1133	GDMVPHISR	L15	EETGLLMP	L42;L46	YRVVVLSFEL	L66;L30;L35
1134	GDQFKHLI	L33	EETKFLTENL	L41;L40	YSGVVTTV	L48;L73;L70
1135	GDSAEVAV	L33	EETRKLMP	L42;L46	YSVIYLYLTF	L52;L54;L10
1136	GDSCNNYM	L33	EETRKLMPV	L42;L45	YTDFATSA	L1;L68;L63
1137	GDSEVVLK	L33	EEVLSEARQ	L41;L40	YTEISFML	L1;L68;L60
1138	GDSEVVLKKL	L37	EEVLSEARQHL	L40;L41	YTERSEKSY	L1;L18;L14
1139	GDSVEEVL	L33	EEVQELYSPI	L41;L40	YTRYVDNNF	L53;L52;L58
1140	GDVRETMSY	L27	EEVQELYSPIF	L40;L41	YTSNPTTFHL	L20;L60;L61
1141	GDVVQEGV	L33	EEVTTTLEETKF	L40;L41	YVMHANYIF	L58;L12;L31
1142	GDYFVLTSH	L43	EEVVLKTGDL	L41;L40	YVPAQEKNF	L5;L10;L12
1143	GEGSEGLNDNL	L36	EFEPSTQYEY	L12;L1	YVRITGLY	L1;L14;L26
1144	GEGSEGLNDNLL	L36	EFGATSAAL	L72;L71	YVRNLQHRLY	L12;L14;L13
1145	GEIPVAYR	L45	EFIERYKLEGY	L11;L10	YVVDDPCPI	L20;L67;L49
1146	GEQKSILSPL	L36	EFLRDGWEI	L8;L9	YVVDDPCPIHFY	L11;L14;L12
1147	GETFVTHSKGL	L36	EFTPFDVVR	L17;L19	YVWKSYVHVV	L2;L5;L3
1148	GETLPTEVLT	L36	EFVFKNIDGY	L11;L10	YVYNPFMID	L61;L60;L59
1149	GEVFNATR	L45	EFYEAMYTP	L42;L8	YWVPRASA	L50;L46;L51
1150	GEVPVSIINNTV	L36	EGYAFEHI	L48;L47	YYFMRFRRAF	L71;L72;L9
1151	GEYSHVVAFNTL	L36	EGYAFEHIV	L48;L47	YYKKDNSY	L66;L72;L71
1152	GEYTFEKGDY	L41	EHEHEIAW	L35;L28	YYRRATRRI	L8;L48;L9
1153	GFDVEGCH	L62	EHSWNADL	L35;L28	YYSDSPCES	L66;L72;L9
1154	GFDYVYNP	L62	EHSWNADLYKL	L34;L35	AACRKVQHM	L70;L69;L58;L63
1155	GFDYVYNPF	L62	EIAWYTER	L17;L19	AADLDDFSK	L68;L7;L63;L18
1156	GFDYVYNPFM	L62	EIKDATPSDF	L10;L11	AAFATAQEAY	L31;L27;L14;L12
1157	GFFKEGSSVEL	L44	EIKESVQTFF	L10;L11	AAIFYLITP	L69;L42;L38;L46
1158	GFLFLTWI	L48	EILGTVSWNLR	L19;L17	AAKAYKDY	L43;L70;L58;L14
1159	GFQPTNGV	L48	EILLIIMR	L17;L19	AAKKNNLPF	L58;L43;L70;L52
1160	GFSALEPL	L72	EIPKEEVKPF	L10;L11	AARVVRSI	L48;L55;L70;L47
1161	GFSTGVNLV	L64	EIPVAYRKV	L11;L10	AATRGATVV	L69;L70;L58;L24
1162	GFTLKNTV	L48	EITVATSR	L17;L19	AAVDALCEK	L7;L19;L67;L69

1163	GGAYTRYV	L48	EIVDTVSALV	L20;L11	ADAVIKTL	L33;L37;L25;L23
1164	GGDGKMKDL	L63	EIVDTVSALVY	L11;L10	ADFDTWFSQR	L15;L21;L7;L19
1165	GGFNFSQI	L48	EIYQAGSTP	L10;L11	ADSKIVQL	L33;L37;L56;L65
1166	GGIVAIVV	L48	EKFKEGVEFL	L44;L20	AEAELAKNVSL	L36;L41;L40;L37
1167	GGIVAIVVT	L44	ELAMDEFIERY	L11;L10	AECTIFKDA	L42;L46;L38;L40
1168	GGKIVNNWL	L44	ELGDVRETMSY	L10;L11	AEILLIIMRTF	L41;L40;L37;L29
1169	GGKPCIKV	L48	ELKFNPPAL	L23;L3	AEIRASANLA	L38;L42;L46;L40
1170	GGNYNYLYR	L15	ELKKLLEQW	L10;L11	AESHVDTDL	L36;L37;L41;L40
1171	GGQPITNCV	L48	ELLQNGMNGR	L17;L19	AEWFLAYI	L45;L33;L48;L37
1172	GGRFVLALL	L44	ELSPVALRQ	L24;L20	AFATAQEAY	L72;L71;L12;L14
1173	GGSVAIKI	L48	ELSRVLGLK	L19;L6	AFAVDAAKAY	L14;L72;L71;L12
1174	GGTTEMLAK	L7	ELTGHMLDMY	L11;L10	AFEKMVSL	L62;L72;L71;L63
1175	GGVAGALNK	L7	ELYHYQECV	L24;L20	AFLPFAMGI	L71;L72;L8;L9
1176	GHFAWWTA	L28	ENFNQHEV	L48;L20	AFNTLLFL	L62;L71;L72;L73
1177	GHFAWWTAFV	L28	EPEEHVQI	L49;L25	AFYILPSI	L48;L71;L72;L47
1178	GHHLGRCDI	L34	EPKLGSLV	L23;L51	AGNGGDAAL	L44;L57;L56;L61
1179	GHMLDMYSVM	L28	EPKLGSLVVR	L17;L19	AGSKSPIQY	L26;L27;L14;L18
1180	GHMLDMYSVML	L28	EPTTTTSV	L23;L50	AGTDTTITV	L24;L69;L48;L2
1181	GHSMQNCV	L28	EQLDFIDTK	L24;L7	AHISTIGVC	L35;L28;L34;L27
1182	GHSMQNCVLKL	L28	ERFVSLAI	L25;L35	AHSCNVNRF	L34;L35;L28;L27
1183	GHTDLMAA	L28	ERHSLSHFV	L35;L64	AIDAYPLTK	L6;L7;L18;L68
1184	GHTDLMAAYV	L28	ERIDKVLNE	L30;L35	AIMTRCLAV	L23;L73;L3;L4
1185	GHVETFYPK	L7	ERIDKVLNEK	L30;L11	AISDYDYY	L14;L18;L1;L58
1186	GHVMVELV	L28	ESELVIGAV	L20;L1	AISDYDYYRY	L12;L14;L18;L16
1187	GIDLDEWSMATY	L18	ESIVRFPNI	L48;L20	ALALLLLDR	L21;L6;L7;L15
1188	GIKIQEGVVDY	L26	ESLRPDTRY	L11;L14	ALCEKALKYL	L3;L2;L4;L5
1189	GIPKDMTY	L26	ETAHSCNVNRF	L11;L10	ALDQAISM	L63;L68;L62;L18
1190	GIVAIVVTC	L19	ETAQNSVR	L17;L19	ALLKTVQF	L26;L27;L33;L74
1191	GIVNNTVY	L26	ETFVTHSK	L19;L17	ALNHTKKWKY	L14;L12;L18;L16

1192	GIYQTSNF	L26	ETFVTHSKGL	L10;L20	ALNLGETFV	L2;L4;L24;L3
1193	GKASCTLSE	L44	ETFYPKLQSS	L20;L10	ALYYPSARI	L24;L45;L2;L3
1194	GKASCTLSEQL	L44	ETICAPLTVF	L10;L11	AMDEFIER	L15;L21;L62;L68
1195	GKFCLEASFNY	L27	ETKDVVECLKL	L11;L10	ANGQVFGLY	L14;L12;L18;L40
1196	GKGYHLMSF	L27	ETLVTMPLGY	L11;L12	APAHISTIGV	L56;L22;L51;L39
1197	GKIADYNY	L27	ETMSYLFQHA	L20;L10	APHGHVMVEL	L56;L39;L22;L32
1198	GKIADYNYKL	L44	ETNILLNV	L48;L73	APPAQYEL	L56;L39;L22;L66
1199	GKIQDSLSS	L27	ETQALPQR	L17;L19	AQNSVRVLQK	L7;L6;L13;L24
1200	GKIQDSLSST	L27	ETSWQTGDF	L11;L10	AQYTSALL	L28;L48;L44;L27
1201	GKIVNNWL	L44	ETVKGLDY	L11;L1	ARDGCVPL	L35;L66;L63;L68
1202	GKIVNNWLKQL	L44	ETVKGLDYKAF	L10;L11	ARDLSLQF	L35;L33;L65;L62
1203	GKMKDLSPRWY	L27	ETYFTQSR	L17;L19	ARHINAQVA	L35;L25;L46;L28
1204	GKPCIKVAT	L44	EVAVKMFDAY	L10;L11	ARNGVLITE	L30;L65;L66;L35
1205	GKPREQIDGY	L27	EVEKGVLPQL	L11;L20	ARTRSMWSF	L66;L30;L35;L34
1206	GKPVPYCY	L66	EVFNATRFA	L20;L11	ASAVVLLI	L73;L48;L55;L24
1207	GKSHFAIGL	L44	EVGFVVPGL	L20;L11	ASFRLFARTR	L15;L19;L21;L55
1208	GKVEGCMVQ	L27	EVGHTDLMAAY	L11;L10	ASFYYVWKSY	L43;L16;L14;L52
1209	GKVEGCMVQV	L27	EVITFDNL	L20;L74	ASKKPRQKR	L15;L13;L21;L17
1210	GKYEQYIKWP	L27	EVITFDNLKTL	L10;L11	ASMPTTIAK	L7;L6;L13;L43
1211	GKYEQYIKWPWY	L27	EVKPFITESK	L11;L10	ASSSEAFLI	L55;L24;L53;L54
1212	GKYVQIPTTC	L27	EVLSDREL	L23;L55	ATAEAELAK	L7;L6;L19;L13
1213	GLAAIMQLFF	L12	EVLSEARQHL	L10;L20	ATCELYHY	L18;L1;L14;L54
1214	GLCVDIPGIPK	L6	EVNEFACVV	L20;L11	ATEETFKL	L63;L1;L18;L68
1215	GLFCLLNRYF	L12	EVNSFSGYLKL	L11;L10	ATLQAIASEF	L52;L53;L16;L10
1216	GLHLLIGL	L23	EVPANSTVLSF	L11;L10	ATNGPLKV	L73;L70;L48;L24
1217	GLHLLIGLA	L24	EVPVAIHAD	L10;L11	ATNNLVVM	L70;L73;L59;L58
1218	GLHLLIGLAK	L6	EVPVSIINN	L17;L11	ATNYDLSVV	L73;L70;L58;L18
1219	GLHPTQAP	L43	EVQIDRLITGR	L17;L19	ATRFASVY	L18;L14;L26;L1
1220	GLKTILRKG	L3	EVTPSGTW	L10;L54	ATRGATVVI	L53;L70;L52;L10

1221	GLKTLATHGL	L3	EVTPSGTWLTY	L11;L10	ATSRTLSY	L18;L1;L54;L14
1222	GLLMPLKAPK	L6	EVVDKYFDCY	L10;L11	AVDALCEKAL	L68;L5;L67;L63
1223	GLMWLSYF	L26	EVVENPTIQ	L11;L20	AYANRNRF	L9;L71;L72;L8
1224	GLNGYTVEE	L2	EWFLAYILFTR	L17;L19	AYANSVFNI	L9;L8;L72;L34
1225	GLPGTILR	L21	EWSMATYYLF	L9;L8	AYFNMVYM	L71;L72;L62;L66
1226	GLTGTGVL	L74	EYCPIFFI	L9;L8	AYFNMVYMP	L42;L71;L66;L72
1227	GLTGTGVLT	L2	EYHDVRVVLDF	L8;L9	AYIICISTK	L13;L72;L7;L71
1228	GLVAEWFL	L74	EYHNESGL	L71;L72	AYIICISTKHF	L8;L9;L72;L40
1229	GLVAEWFLA	L2	EYKGPITDV	L17;L11	AYITGGVVQ	L71;L72;L8;L9
1230	GLWLDDVVYC	L2	EYSHVVAFNTL	L8;L9	AYNGYLTSS	L72;L71;L15;L8
1231	GLYRKCVKS	L24	EYYHTTDPSF	L9;L8	AYSNNSIAI	L72;L9;L71;L8
1232	GLYRKCVKSR	L21	FADDLNQLTG	L67;L68	AYVDNSSLTI	L8;L9;L71;L72
1233	GMSRIGMEV	L24	FALTCFSTQ	L59;L61	AYVNTFSSTF	L8;L9;L71;L72
1234	GMVLGSLAA	L46	FAMGIIAMSA	L50;L61	AYYFMRFRR	L15;L17;L21;L12
1235	GNAAISDYDY	L12	FASTEKSNI	L49;L70	CCNIVNVSL	L56;L44;L32;L35
1236	GNCDVVIGI	L24	FATSACVLA	L50;L69	CEFCGTENL	L37;L36;L29;L45
1237	GNFGDQEL	L65	FCDLKGKY	L1;L18	CFSTASDTY	L14;L72;L71;L12
1238	GNFKVTKGK	L13	FCLEASFNY	L12;L31	CLHVVGPNV	L2;L24;L4;L5
1239	GNFYGPFV	L48	FCNDPFLGVYY	L31;L12	CLVGLMWLSY	L12;L16;L10;L11
1240	GNFYGPFVD	L65	FDAYVNTF	L33;L29	CSNLLLQY	L18;L59;L1;L48
1241	GNVQLRVI	L48	FDESGEFKL	L32;L63	CTSVVLLSV	L73;L20;L69;L70
1242	GPDGYPLEC	L49	FEKMVSLL	L33;L23	CVDIPGIPK	L7;L6;L13;L68
1243	GPEAGLPY	L18	FEKMVSLLSV	L45;L46	CVPLNIIPL	L57;L5;L74;L64
1244	GPEQTQGNF	L49	FELDERIDKVL	L40;L41	CVRGTTVLL	L74;L58;L13;L56
1245	GPITDVFYK	L7	FERDISTEIY	L43;L29	CYLATALL	L71;L72;L9;L62
1246	GPKQASLNGV	L51	FEYYHTTD	L25;L45	CYLATALLTL	L8;L9;L71;L72
1247	GPKQASLNGVTL	L56	FFGMSRIGM	L72;L71	CYTPSKLIEY	L12;L72;L66;L71
1248	GPKVKYLY	L23	FFITGNTLQ	L71;L72	DAAKAYKDY	L10;L11;L58;L49
1249	GPLKVGGSCV	L51	FFITGNTLQC	L71;L72	DAYNMMISA	L47;L50;L25;L69
1250	GPLKVGGSCVL	L56	FFIYNKIVD	L72;L71	DDTLRVEAF	L33;L29;L23;L25
1251	GPLVRKIF	L23	FFKEGSSVE	L71;L72	DEDDNLIDSY	L29;L41;L40;L1
1252	GPNVNKGED	L49	FFLYENAFLPF	L12;L8	DEFSSNVAN	L29;L46;L25;L41
1253	GQAITVTP	L48	FFYYSDSP	L71;L72	DEISMATNY	L29;L41;L11;L40

1254	GQINDMILS	L24	FFYYSDSPC	L71;L72	DELTGHML	L25;L29;L23;L37
1255	GQIVTCAKE	L24	FGAGAALQI	L64;L47	DEPTTTTSV	L45;L29;L57;L37
1256	GQKTYERHSL	L44	FGATSAAL	L61;L59	DFMSLSEQL	L8;L71;L9;L72
1257	GQQDGSEDN	L24	FGLVAEWFL	L61;L44	DISGINASV	L20;L11;L28;L19
1258	GQQGEVPV	L24	FHPLADNKF	L34;L62	DIVEEAKKV	L11;L10;L20;L24
1259	GQQGEVPVS	L24	FIAGLIAIVMV	L20;L2	DKFKVNSTL	L44;L25;L27;L35
1260	GQQGEVPVSI	L24	FIDTKRGV	L63;L68	DKVAGFAKF	L10;L11;L27;L29
1261	GQQQQGQTVTK	L7	FIEDLLFNKV	L5;L20	DLKGKYVQI	L23;L10;L11;L3
1262	GQQQTTLKG	L24	FIERYKLEGY	L1;L18	DLPQGFSAL	L57;L10;L11;L5
1263	GQSTQLGIEFL	L44	FIKGLNNLNR	L17;L21	DLQDLKWAR	L17;L19;L21;L15
1264	GQTFSVLAC	L24	FIPMDSTV	L57;L5	DLQELGKY	L14;L11;L1;L10
1265	GQTFSVLACY	L14	FISDEVAR	L19;L17	DLSPRWYFYY	L11;L12;L1;L18
1266	GQTGKIADYNY	L14	FISNSWLMW	L49;L69	DLYDKLQF	L23;L11;L43;L25
1267	GQTVTKKS	L48	FITGNTLQC	L60;L58	DLYDKLQFT	L11;L2;L3;L10
1268	GQVDLFRN	L24	FITLCFTLK	L6;L7	DMILSLLSK	L6;L19;L17;L7
1269	GQVDLFRNAR	L15	FIYNKIVD	L43;L23	DNLKTLLSL	L25;L23;L8;L73
1270	GQVFGLYKN	L24	FKESPFEL	L66;L68	DPCPIHFY	L49;L29;L31;L47
1271	GRCDIKDLPK	L30	FKKGAKLL	L66;L64	DPFLGVYY	L31;L29;L47;L49
1272	GRDIADTTD	L34	FKLKDCVMY	L27;L31	DPIHSLRVC	L47;L32;L49;L31
1273	GRFVLALLS	L30	FKLVNKFLAL	L61;L44	DPNFKDQVIL	L39;L32;L56;L23
1274	GRFVLALLSD	L30	FKNLREFVF	L66;L27	DPSFLGRYM	L31;L32;L49;L22
1275	GRLIIREN	L65	FKYWDQTY	L27;L66	DPVGFTLKN	L49;L11;L47;L32
1276	GRLIIRENN	L30	FLALITLAT	L2;L3	DQAISMWAL	L25;L44;L35;L28
1277	GRLIIRENNR	L30	FLAYILFTRF	L12;L10	DSNGTITV	L48;L47;L70;L73
1278	GRLQSLQTYV	L30	FLEYHDVRVV	L3;L2	DTDFVNEF	L62;L1;L68;L63
1279	GRSGETLGVLV	L30	FLGIITTVA	L2;L3	DTTEAFEKM	L11;L10;L29;L20
1280	GRTIAFGGC	L30	FLKKDAPYI	L2;L3	DTTITVNVL	L10;L25;L35;L11
1281	GRTILGSALL	L30	FLKKDAPYIV	L3;L2	DTVSALVYD	L11;L20;L19;L17
1282	GRVDGQVD	L65	FLKRGDKSV	L3;L2	DTYNLWNTFTR	L19;L17;L21;L7
1283	GRVDGQVDLFR	L30	FLLNKEMYLKL	L4;L2	DVDTDFVNEF	L10;L11;L68;L49

1284	GRWVLNNDY	L30	FLLPSLATVAY	L12;L31	DVKCTSVVL	L23;L10;L11;L39
1285	GRWVLNNDYY	L30	FLNRVCGVSA	L2;L50	DYFNKKDWY	L72;L12;L14;L71
1286	GRWVLNNDYYR	L30	FLPFAMGII	L57;L5	DYFVLTSH	L71;L25;L72;L17
1287	GRYMSALNH	L30	FLPFFSNV	L57;L5	DYGDAVVYR	L17;L19;L15;L21
1288	GRYMSALNHT	L30	FLPFFSNVTW	L57;L5	EAANFCAL	L67;L59;L61;L20
1289	GRYMSALNHTK	L30	FLTWICLLQF	L12;L5	EDQDALFAY	L40;L10;L14;L29
1290	GSCGSVGF	L54	FLVFLGIITTV	L2;L3	EEAALCTFL	L41;L40;L36;L20
1291	GSEGLNDNL	L1	FLVLIMLII	L69;L67	EEAALCTFLL	L41;L40;L42;L20
1292	GSEYDYVIF	L53	FLVLIMLIIF	L74;L69	EEAKTVLKK	L42;L19;L41;L40
1293	GSGVPVVD	L65	FLYENAFLPFA	L2;L3	EEEQEEDWL	L36;L41;L40;L34
1294	GSIHLYFDK	L7	FMGRIRSV	L48;L64	EEHFIETI	L45;L29;L48;L37
1295	GSLIYSTAA	L46	FNGECPNFV	L73;L64	EEKFKEGVEF	L40;L41;L42;L37
1296	GSLVVRCSFY	L14	FNGVSFSTF	L59;L9	EELDKYFKN	L41;L40;L29;L42
1297	GSLYVNKHAF	L52	FNQHEVLL	L62;L74	EELKKLLEQ	L42;L41;L40;L46
1298	GSNVFQTR	L15	FNVLFSTV	L47;L48	EEMLDNRATL	L40;L41;L36;L42
1299	GSRGGSQAS	L43	FNVPMEKL	L67;L74	EETKFLTEN	L42;L46;L29;L45
1300	GSSVELKHFF	L52	FPDLNGDVVA	L50;L32	EEVVLKTGD	L41;L42;L46;L40
1301	GSTPCNGV	L48	FPFNKWGKARL	L56;L31	EHDYQIGGY	L1;L11;L10;L18
1302	GTCGLVEVEK	L7	FPKSDGTGTIY	L31;L49	EHEHEIAWY	L11;L34;L1;L10
1303	GTDLEGNFYG	L1	FPLCANGQV	L50;L47	EHVQIHTI	L34;L48;L35;L28
1304	GTDTTITVNV	L18	FPLKLRGTA	L50;L51	EIIFLEGETL	L20;L10;L34;L11
1305	GTGVLTESNK	L7	FPNITNLCPF	L31;L49	EIKDTEKY	L11;L10;L26;L43
1306	GTHHWLLL	L73	FPPTSFGPLV	L47;L50	EILLIIMRTF	L10;L11;L40;L41
1307	GTHWFVTQRNF	L52	FPQSAPHGVV	L50;L22	EIVGGQIVTC	L11;L10;L19;L20
1308	GTILTRPLL	L13	FPREGVFVS	L50;L31	EKSNIIRGW	L10;L40;L41;L49
1309	GTKRFDNPVL	L53	FPSGKVEGC	L49;L31	ELAKNVSL	L23;L20;L35;L56
1310	GTLIVNSV	L48	FPVLHDIGN	L50;L31	ELGTEVNEF	L10;L9;L11;L26

1311	GTLIVNSVLLF	L52	FSALEPLVDL	L74;L60	ELIRQGTDY	L11;L10;L26;L12
1312	GTNGTKRF	L54	FSGAMDTTSY	L43;L1	ELLHAPATV	L2;L4;L20;L3
1313	GTNGTKRFD	L65	FSNSGSDV	L58;L70	ELNGGAYTRY	L11;L10;L14;L26
1314	GTNTSNQVAVLY	L18	FSSEIIGYK	L19;L7	ELVAELEGI	L10;L20;L24;L11
1315	GTRNPANNA	L13	FSTASDTY	L1;L54	ENFNQHEVL	L25;L20;L35;L34
1316	GTSTDVVY	L18	FTALTQHGK	L19;L7	EQYIKWPWY	L26;L27;L11;L48
1317	GTSTDVVYRAF	L52	FTEERLKLFDRY	L1;L18	ERDISTEIY	L1;L34;L35;L18
1318	GTTEMLAK	L7	FTIYSLLLCR	L19;L17	ERSEAGVCV	L35;L34;L28;L20
1319	GTTLPKGF	L55	FTLLLQLCTF	L52;L53	ESKPSVEQR	L17;L19;L11;L15
1320	GTTSPISEHDY	L14	FTPLVPFWI	L64;L20	ETAHSCNVNR	L19;L17;L20;L21
1321	GTTTYKLNV	L73	FTRSTNSR	L17;L21	ETICAPLTV	L20;L73;L11;L10
1322	GTVSWNLREM	L10	FTSDLATNNL	L20;L60	ETISLAGSYK	L19;L11;L17;L7
1323	GVAMPNLY	L18	FTTTLNDF	L59;L58	ETLGVLVPH	L17;L20;L7;L11
1324	GVAPGTAVLRQW	L52	FTVLCLTPV	L20;L59	ETVKGLDYK	L19;L11;L20;L17
1325	GVCSMTDIAK	L7	FVCDNIKFA	L3;L69	EVFAQVKQIYK	L19;L7;L6;L20
1326	GVCSMTDIAKK	L7	FVDRQTAQA	L5;L63	EVFNATRF	L11;L10;L29;L20
1327	GVDIAANTVI	L68	FVFKNIDGYFK	L6;L7	EVNSFSGY	L11;L10;L26;L14
1328	GVDVELFENK	L7	FVIRGDEVR	L19;L17	EVPANSTVL	L10;L11;L57;L20
1329	GVEGFNCYF	L12	FVLWAHGF	L59;L60	EVVDKYFDC	L11;L10;L20;L19
1330	GVEHVTFF	L63	FVNLKQLPFF	L58;L59	EVVGDIILKP	L11;L10;L20;L19
1331	GVEHVTFFI	L24	FVTHSKGL	L60;L61	EYHDVRVV	L64;L72;L48;L71
1332	GVGYQPYRV	L24	FVTHSKGLYR	L19;L17	EYVSQPFLM	L9;L8;L17;L66
1333	GVITHDVSSA	L3	FVVPGLPGT	L11;L20	FAAETLKA	L50;L69;L59;L61
1334	GVKHVYQL	L23	FVVSTGYHFR	L19;L17	FACPDGVKHV	L70;L69;L58;L47
1335	GVKHVYQLRAR	L15	FWITIAYI	L62;L47	FASFYYVWK	L7;L67;L19;L69
1336	GVLTAVVI	L55	FWRNTNPIQL	L62;L74	FATAQEAY	L59;L31;L58;L70
1337	GVLTESNKKF	L52	FYDFAVSKG	L62;L68	FAVHFISNS	L69;L70;L58;L49
1338	GVPVVDSY	L26	FYDFAVSKGF	L62;L9	FAWWTAFVTN	L67;L50;L49;L31

1339	GVQIPCTCGK	L7	FYEAMYTPH	L71;L72	FCGPDGYPL	L67;L61;L66;L60
1340	GVSAARLT	L55	FYFYTSKTT	L71;L72	FCTQLNRAL	L61;L60;L64;L32
1341	GVSICSTMTNR	L19	FYFYTSKTTV	L71;L72	FDKAGQKTY	L58;L43;L14;L70
1342	GVSPTKLND	L65	FYGPFVDR	L17;L66	FDYVYNPF	L33;L59;L71;L43
1343	GVTFQSAVK	L7	FYKENSYTT	L66;L9	FEEAALCTF	L38;L41;L36;L40
1344	GVTRELMREL	L10	FYLCFLAFLL	L9;L8	FELDERIDKV	L45;L36;L38;L37
1345	GVVCTEIDPK	L7	FYLITPVH	L71;L72	FELLHAPATV	L45;L46;L38;L36
1346	GVVDYGARFYF	L12	FYPPDEDE	L66;L71	FELTSMKYF	L41;L40;L29;L33
1347	GVVFLHVTYV	L20	FYRLANEC	L72;L71	FENKTTLPV	L45;L38;L37;L42
1348	GVVGEGSEGL	L10	FYSKWYIRV	L64;L62	FEPSTQYEY	L66;L12;L40;L41
1349	GVVTTVMF	L74	FYSYATHSD	L72;L71	FERDISTEI	L45;L43;L36;L37
1350	GVVTTVMFL	L74	FYTSKTTV	L71;L72	FFPDLNGDV	L62;L72;L71;L5
1351	GVYDYLVSTQ	L10	FYTSKTTVASL	L71;L72	FFSNVTWF	L72;L62;L71;L9
1352	GVYYHKNNKSW	L16	FYVLGLAAIM	L71;L72	FGAISSVL	L61;L59;L28;L25
1353	GWEIVKFI	L48	FYVYANGGKGF	L8;L9	FGDSVEEV	L63;L68;L62;L67
1354	GWLIVGVALL	L8	FYVYSRVKNL	L71;L72	FHLDGEVIT	L35;L34;L28;L44
1355	GYKAIDGGVTR	L15	FYYLGTGP	L71;L72	FIASFRLF	L58;L59;L74;L60
1356	GYKKPASREL	L13	FYYLGTGPE	L72;L71	FISAARQGF	L58;L12;L60;L16
1357	GYLNSTNV	L71	FYYSDSPC	L71;L72	FKWDLTAF	L59;L27;L66;L71
1358	GYLQPRTFLLK	L6	FYYVWKSYVH	L71;L72	FLARGIVF	L74;L59;L26;L23
1359	GYLQPRTFLLKY	L12	GAALQIPF	L74;L59	FLCWHTNCY	L43;L59;L26;L1
1360	GYLTSSSK	L71	GAENSVAY	L18;L27	FLEYHDVRV	L2;L63;L5;L4
1361	GYREGYLNS	L13	GALLTKSSEY	L27;L14	FLIVAAIVFI	L2;L3;L4;L5
1362	GYRVTKNSK	L13	GCFVDDIVK	L7;L13	FLMSFTVLC	L2;L4;L12;L5
1363	GYVMHANYI	L9	GDDTVIEV	L33;L37	FLNKVVSTT	L3;L2;L4;L43
1364	HAASGNLLLD	L49	GDYGDAVVYR	L15;L19	FLPGVYSVIY	L12;L66;L26;L43
1365	HAAVDALCE	L49	GEAANFCA	L38;L46	FLPGVYSVIYL	L2;L5;L57;L74
1366	HADQLTPTWR	L63	GEAANFCALIL	L36;L41	FLQSINFVR	L21;L17;L15;L19
1367	HADQLTPTWRVY	L18	GEAVKTQFNY	L40;L41	FLTENLLLYI	L3;L2;L4;L5

1368	HAFHTPAFD	L49	GECPNFVFPL	L37;L36	FLVQAGNVQL	L2;L4;L5;L74
1369	HAFLCLFLLP	L50	GEDIQLLKSAY	L41;L40	FLYLYALV	L62;L2;L3;L47
1370	HANEYRLYLD	L49	GEQKSILSPLY	L40;L41	FMIDVQQW	L49;L69;L54;L3
1371	HANLDSCKR	L17	GERSGARSK	L13;L45	FPLKLRGTAV	L50;L51;L22;L32
1372	HDELTGHM	L33	GETFVTHSK	L37;L38	FPREGVFVSN	L50;L51;L31;L22
1373	HDELTGHMLDMY	L18	GETSWQTGD	L46;L37	FRNARNGVL	L25;L66;L64;L35
1374	HDFFKFRI	L33	GEVFNATRFA	L46;L38	FSASTSAFV	L58;L70;L20;L73
1375	HDFFKFRID	L65	GEYTFEKG	L45;L29	FSHSQLGGL	L58;L60;L57;L61
1376	HDIGNPKAI	L37	GFAAYSRY	L12;L14	FSKLINII	L70;L48;L55;L47
1377	HDLYCQVH	L33	GFAAYSRYR	L15;L17	FSKLINIII	L70;L69;L55;L68
1378	HEFCSQHT	L29	GFCDLKGKY	L12;L14	FSNYLKRRV	L73;L64;L70;L69
1379	HEIAWYTE	L29	GFNEKTHV	L62;L48	FSQRGGSY	L1;L14;L59;L18
1380	HEVLLAPLLS	L41	GGAKLKAL	L23;L44	FSSNVANY	L58;L1;L70;L59
1381	HFDEGNCD	L62	GGDAALAL	L68;L63	FSTGVNLVA	L50;L61;L69;L73
1382	HFDEGNCDT	L62	GGHSYGADL	L57;L44	FSTGVNLVAV	L20;L73;L58;L50
1383	HFISNSWLMW	L8	GGLHLLIGL	L44;L4	FTEQPIDLV	L1;L20;L18;L63
1384	HFYSKWYI	L48	GGRFVLAL	L48;L23	FTISVTTEIL	L60;L67;L61;L20
1385	HGFELTSMK	L13	GHFDGQQG	L28;L35	FTIYSLLLC	L73;L1;L12;L58
1386	HGGGVAGAL	L44	GHFDGQQGEV	L28;L35	FTQSRNLQEF	L58;L10;L59;L60
1387	HGHVMVELV	L48	GHLRIAGHHL	L34;L44	FVCDNIKF	L58;L74;L68;L63
1388	HGKQVVSD	L23	GHSYGADL	L28;L35	FVENPDILR	L19;L17;L21;L15
1389	HGLNLEEAA	L50	GHVMVELVA	L28;L35	FVFPLNSIIK	L6;L7;L13;L19
1390	HGLNLEEAARY	L14	GIGVTQNVLY	L12;L18	FVKHKHAF	L23;L59;L58;L43
1391	HGVVFLHV	L48	GINASVVNIQK	L7;L6	FVLAAVYRI	L4;L47;L5;L20
1392	HHMELPTG	L28	GISQYSLRL	L24;L73	FVLWAHGFEL	L60;L61;L67;L59
1393	HHSIGFDYVY	L34	GKFCLEASF	L27;L44	FVNEFYAYLR	L15;L21;L17;L19
1394	HIDAYKTFP	L63	GKQGNFKNL	L44;L27	FVNLKQLPF	L59;L12;L58;L60
1395	HIDHPNPKG	L63	GKYVQIPTT	L27;L44	FVRIQPGQTF	L26;L43;L10;L58
1396	HIDHPNPKGF	L63	GLALYYPSA	L2;L3	FVSGNCDVV	L58;L67;L20;L69
1397	HISRQRLTK	L6	GLDSLDTYPSL	L2;L5	FVVPGLPGTI	L20;L10;L67;L3

1398	HITSKETL	L23	GLFCLLNR	L15;L21	FWNCNVDRY	L58;L12;L49;L14
1399	HKHAFLCLFL	L44	GLIAIVMVT	L3;L2	FYDFAVSK	L62;L71;L68;L72
1400	HKLVLSVNP	L44	GLKTILRK	L13;L6	FYEDFLEYH	L62;L72;L71;L12
1401	HKPIVWHV	L48	GLMWLSYFI	L24;L2	FYGGWHNM	L72;L66;L71;L62
1402	HKPIVWHVN	L44	GLNGYTVEEA	L3;L2	FYILPSII	L62;L71;L72;L47
1403	HLIPLMYK	L6	GLNLEEAAR	L21;L15	FYWFFSNY	L72;L71;L66;L12
1404	HLIPLMYKG	L24	GLQPSVGPK	L6;L7	GANKDGIIW	L54;L49;L52;L53
1405	HLKDGTCGLV	L3	GLVEVEKGVL	L44;L2	GEAVKTQF	L33;L29;L37;L45
1406	HLKDGTCGLVEV	L3	GLYKNTCV	L24;L2	GECPNFVF	L29;L37;L33;L36
1407	HLLIGLAKRF	L12	GLYPTLNIS	L24;L3	GEDIQLLKS	L45;L46;L37;L41
1408	HLMGWDYPK	L6	GNKGAGGHSY	L14;L26	GEDIQLLKSA	L46;L38;L42;L37
1409	HLRIAGHHL	L26	GNLQSNHDLY	L12;L14	GEFKLASHMY	L40;L29;L41;L27
1410	HLSVDTKFK	L6	GNYNYLYRL	L4;L24	GEIPVAYRKVL	L36;L41;L40;L37
1411	HLSWEVGKP	L24	GNYQCGHYK	L7;L6	GGDAALALL	L63;L62;L68;L34
1412	HLVDFQVTIA	L3	GPKKSTNLV	L51;L39	GGFNFSQIL	L44;L64;L28;L69
1413	HLYFDKAGQK	L6	GPLVRKIFV	L23;L47	GHFDGQQGE	L28;L34;L35;L24
1414	HLYLQYIR	L21	GPPGTGKSH	L39;L22	GHSMQNCVL	L35;L28;L34;L44
1415	HMELPTGV	L48	GQGLNGYTV	L24;L48	GIATVREVL	L44;L16;L28;L67
1416	HMLDMYSV	L48	GQGVPINTN	L24;L26	GIDLDEWSM	L68;L63;L28;L18
1417	HMLDMYSVM	L72	GQINDMIL	L28;L44	GIVFMCVEY	L26;L43;L12;L27
1418	HMLDMYSVML	L44	GQIVTCAKEI	L24;L48	GIYQTSNFR	L21;L7;L6;L19
1419	HNLAKHCL	L23	GQPITNCV	L48;L24	GKYEQYIKW	L27;L44;L49;L10
1420	HNSHEGKTFY	L12	GQSKRVDF	L27;L26	GLAAIMQL	L3;L74;L2;L4
1421	HPTQAPTH	L50	GQSTQLGI	L48;L24	GLAAVNSV	L3;L2;L4;L24
1422	HQECSLQSC	L24	GQSTQLGIEF	L26;L27	GLCVDIPGI	L4;L2;L24;L3
1423	HQSDIEVTGD	L44	GRIRSVYPV	L30;L35	GLEAPFLYLY	L18;L12;L1;L14
1424	HRFYRLAN	L25	GRRGPEQTQ	L65;L30	GLFKDCSKV	L24;L3;L2;L4
1425	HRFYRLANE	L25	GRSGETLGVL	L30;L35	GLIAIVMV	L24;L2;L3;L4
1426	HRLYECLY	L65	GSALLEDEF	L53;L52	GLPNNTASW	L57;L10;L16;L5

1427	HRLYECLYR	L30	GSDNVTDFN	L1;L18	GLYPTLNI	L24;L48;L3;L2
1428	HRLYECLYRNR	L30	GSGVPVVDSY	L14;L18	GPEHSLAEY	L49;L31;L18;L12
1429	HSCNVNRFN	L55	GSSGVVNPV	L20;L24	GPKKSTNL	L56;L39;L23;L22
1430	HSMQNCVL	L55	GSTPCNGVEGF	L52;L54	GQQFGPTY	L26;L27;L48;L14
1431	HSSSSDNIAL	L44	GSVAYESL	L67;L55	GQQFGPTYL	L44;L28;L24;L34
1432	HSTQDLFLP	L53	GSVAYESLR	L19;L7	GQTGKIADY	L26;L14;L27;L12
1433	HSTQDLFLPF	L52	GTAVLRQWL	L53;L16	GRSGETLGV	L30;L24;L35;L34
1434	HSTQDLFLPFF	L52	GTDPYEDFQ	L1;L18	GSFCTQLNR	L7;L15;L19;L21
1435	HSWNADLYKL	L53	GTDPYEDFQENW	L52;L54	GSLPINVI	L48;L55;L47;L53
1436	HTGTGQAITV	L20	GTDTTITVN	L18;L1	GTDLEGNFY	L1;L18;L14;L12
1437	HTKKWKYPQV	L13	GTEDDYQGK	L13;L7	GTGTIYTEL	L53;L10;L67;L65
1438	HTPINLVRD	L11	GTGTSTDVVY	L18;L52	GTITVEELKK	L7;L13;L6;L19
1439	HTPINLVRDL	L11	GTILTRPL	L55;L60	GTLEPEYF	L52;L55;L54;L53
1440	HTTCCSLSHRF	L54	GTLIVNSVLL	L53;L13	GTLIVNSVL	L53;L44;L55;L52
1441	HTTDPSFLG	L20	GTLSYEQFKK	L7;L6	GTTLPKGFY	L14;L1;L12;L18
1442	HTVLQAVGA	L50	GTNLPLQLGF	L12;L52	GVAMPNLYK	L6;L7;L13;L19
1443	HTVMPLSA	L50	GTPVCINGL	L57;L10	GVCVSTSGR	L19;L15;L21;L7
1444	HTVMPLSAP	L10	GTSSGDATTAY	L18;L14	GVKHVYQLR	L15;L21;L19;L17
1445	HVDILGPLS	L1	GTTSPISEH	L7;L10	GVPFVVSTGY	L11;L12;L26;L14
1446	HVDTDLTK	L18	GTTTLNGLW	L52;L54	GVVDYGARFY	L12;L14;L10;L11
1447	HVICTSEDM	L11	GTVSWNLR	L19;L15	GVYFASTEK	L7;L6;L13;L19
1448	HVISTSHKLV	L20	GVAGALNKA	L51;L3	GWHNMLKTV	L24;L3;L48;L45
1449	HVMSKHTD	L23	GVALLAVF	L26;L59	GYLPQNAVV	L72;L8;L71;L9
1450	HVNNATNKA	L51	GVDAVNLLT	L18;L1	HADFDTWFS	L68;L49;L18;L63
1451	HVNNATNKATY	L14	GVEGFNCY	L18;L1	HCANFNVL	L35;L28;L25;L44
1452	HVRAWIGF	L26	GVFVSNGTHW	L10;L52	HDVRVVLDF	L33;L49;L65;L29
1453	HVSGTNGTKRF	L11	GVFVSNGTHWF	L16;L26	HDYQIGGY	L29;L33;L14;L11
1454	HVTFFIYNKI	L20	GVGGKPCIK	L6;L7	HEETIYNL	L37;L33;L29;L36
1455	HVTYVPAQE	L20	GVKDCVVLH	L13;L7	HEFCSQHTML	L37;L36;L45;L25
1456	HVTYVPAQEK	L19	GVLITEGSVK	L6;L7	HEGKTFYV	L33;L45;L37;L29

DEMANDE OU BREVET VOLUMINEUX

LA PRÉSENTE PARTIE DE CETTE DEMANDE OU CE BREVET COMPREND PLUS D'UN TOME.

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JUMBO APPLICATIONS/PATENTS

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CLAIMS

WHAT IS CLAIMED IS:

1. A method of treating or preventing an infection by a virus or treating a respiratory disease or condition associated with an infection by a virus comprising administering to a subject with a B cell immunodeficiency a pharmaceutical composition comprising:
   (i) a polypeptide comprising at least two of the following (a) a sequence comprising an epitope sequence from ORF1ab, (b) a sequence comprising an epitope sequence from membrane glycoprotein (M) and (c) a sequence comprising an epitope sequence from nucleocapsid phosphoprotein (N);
   (ii) a polynucleotide encoding a polypeptide, wherein the polypeptide comprises at least two of the following (a) a sequence comprising an epitope sequence from ORF1ab, (b) a sequence comprising an epitope sequence from membrane glycoprotein (M) and (c) a sequence comprising an epitope sequence from nucleocapsid phosphoprotein (N);
   (iii) a T cell receptor (TCR) or a T cell comprising the TCR, wherein the TCR binds to an epitope sequence of the polypeptide in complex with a corresponding HLA class I or class II molecule;
   (iv) an antigen presenting cell comprising (i) or (ii); or
   (v) an antibody or B cell comprising the antibody, wherein the antibody binds to an epitope sequence of the polypeptide.
2. The method of claim 1, wherein the subject has a reduced ability to produce an antibody response to an antigen compared to a subject without a B cell immunodeficiency or wherein the subject has a reduced ability to produce an anti-spike protein antibody response and/or an anti-RBD antibody response compared to a subject without a B cell immunodeficiency.
3. The method of claim 1, wherein the subject can produce a T cell response or does not have a reduced ability to produce a T cell response compared to a subject without a B cell immunodeficiency.
4. The method of claim 1, wherein the pharmaceutical composition is protective against a variant of 2019 SARS CoV-2.
5. The method of claim 1, wherein the subject produces a T cell response to an epitope of the polypeptide.
6. The method of claim 1, wherein the subject is an organ transplant recipient, or has cancer or an autoimmune disease or HIV or AIDS or has an age-related decline in immunity, or immunosenescence, or multifactoral immunodeficiency, or an age-related immuodeficiency.
7. The method of claim 1, wherein the composition comprises the polynucleotide encoding the polypeptide.
8. The method of claim 7, wherein the polynucleotide is an mRNA.

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9. The method of claim 1, wherein the composition comprises (i) a polypeptide with at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, or 100% sequence identity to a sequence selected from the group consisting of RS C1p1full, RS C2p1full, RS C3p1full, RS C4p1full, RS C5p1, RS C5p2, RS C5p2full, RS C6p1, RS C6p2, RS C6p2full, RS C7p1, RS C7p2, RS C7p2full, RS C7p4, RS C7p4full, RS C8p1, RS C8p2 and RS C8p2full; (ii) a polynucleotide encoding a polypeptide with at least at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, or 100% sequence identity to a sequence selected from the group consisting of RS C1p1full, RS C2p1full, RS C3p1full, RS C4p1full, RS C5p1, RS C5p2, RS C5p2full, RS C6p1, RS C6p2, RS C6p2full, RS C7p1, RS C7p2, RS C7p2full, RS C7p4, RS C7p4full, RS C8p1, RS C8p2 and RS C8p2full; or (iii) a polynucleotide with at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, or 100% sequence identity to a sequence selected from the group consisting of SEQ ID NOs: RS C1n1, RS C2n1, RS C3n1, RS C4n1, RS C5n1, RS C6n1, RS C7n1, RS C8n1, RS C5n2, RS C6n2, RS C7n2, RS C8n2, RS C5n2full, RS C6n2full, RS C7n2full, RS C8n2full, RS C7n4 and RS C7n4full.

10. The method of claim 1, wherein the composition comprises (i) a polypeptide with at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, or 100% sequence identity to a sequence selected from the group consisting of RS C7p1, RS C7p2, RS C7p2full, RS C7p4 and RS C7p4full; or (iii) a polynucleotide with at least at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, or 100% sequence identity to a sequence selected from the group consisting of SEQ ID NOs: RS C7n1, RS C7n2, RS C7n2full, RS C7n4 and RS C7n4full.

11. A method of treating or preventing an infection by a virus or treating a respiratory disease or condition associated with an infection by a virus comprising administering to a subject with a B cell immunodeficiency a pharmaceutical composition comprising:
    (i) a polypeptide comprising an epitope sequence of Table 1A, Table 1B, Table 1C, Table 2Ai, Table 2Aii, Table 2B and/or Table 16;
    (ii) a polynucleotide encoding the polypeptide comprising an epitope sequence of Table 1A, Table 1B, Table 1C, Table 2Ai, Table 2Aii, Table 2B and/or Table 16;
    (iii) a T cell receptor (TCR) or a T cell comprising the TCR, wherein the TCR binds to the epitope sequence in complex with a corresponding HLA class I or class II molecule;
    (iv) an antigen presenting cell comprising (i) or (ii); or
    (v) an antibody or B cell comprising the antibody, wherein the antibody binds to the epitope sequence.

12. A method of treating or preventing an infection by a virus or treating a respiratory disease or condition associated with an infection by a virus comprising administering to a subject with a B cell immunodeficiency a pharmaceutical composition comprising: a polypeptide having an amino acid sequence with at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, or

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100% sequence identity to a sequence of any one of the sequences depicted in column 2 of Table 11, column 2 of Table 12 or column 3 of Table 15; or a recombinant polynucleotide encoding a polypeptide having an amino acid sequence with at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, or 100% sequence identity to a sequence of any one of the sequences depicted in column 2 of Table 11, column 2 of Table 12 or column 3 of Table 15.

13. The method of claim 12, wherein the pharmaceutical composition comprises a polypeptide with at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, or 100% sequence identity to a sequence selected from the group consisting of RS C1p1full, RS C2p1full, RS C3p1full, RS C4p1full, RS C5p1, RS C5p2, RS C5p2full, RS C6p1, RS C6p2, RS C6p2full, RS C7p1, RS C7p2, RS C7p2full, RS C7p4, RS C7p4full, RS C8p1, RS C8p2 and RS C8p2full; or a polynucleotide encoding a polypeptide with at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, or 100% sequence identity to a sequence selected from the group consisting of RS C1p1full, RS C2p1full, RS C3p1full, RS C4p1full, RS C5p1, RS C5p2, RS C5p2full, RS C6p1, RS C6p2, RS C6p2full, RS C7p1, RS C7p2, RS C7p2full, RS C7p4, RS C7p4full, RS C8p1, RS C8p2 and RS C8p2full.

14. The method of claim 12, wherein the pharmaceutical composition comprises a polynucleotide with at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, or 100% sequence identity to a sequence selected from the group consisting of SEQ ID NOs: RS C1n1, RS C2n1, RS C3n1, RS C4n1, RS C5n1, RS C6n1, RS C7n1, RS C8n1, RS C5n2, RS C6n2, RS C7n2, RS C8n2, RS C5n2full, RS C6n2full, RS C7n2full, RS C8n2full, RS C7n4, RS C7pn4full.

15. The method of any one of claims 1, 11 or 12, wherein the polynucleotide is an mRNA.

16. The method of any one of claims 1, 11 or 12, wherein the pharmaceutical composition further comprises one or more lipid components.

17. The method of claim 16, wherein the one or more lipids comprise a lipid nanoparticle (LNP).

18. The method of claim 17, wherein the LNP encapsulates the recombinant polynucleotide construct.

19. A method of treating or preventing an infection by a virus or treating a respiratory disease or condition associated with an infection by a virus comprising administering to a subject in need thereof a pharmaceutical composition comprising:

(i) a recombinant polynucleotide encoding a polypeptide comprising at least two of the following (a) a sequence comprising an epitope sequence from ORF1ab, a sequence comprising an epitope sequence from membrane glycoprotein (M), and a sequence comprising an epitope sequence from nucleocapsid phosphoprotein (N); and

(ii) a recombinant polynucleotide encoding a 2019 SARS-CoV 2 spike protein or a variant or fragment thereof;

wherein the ratio (e.g., mass ratio) of (i):(ii) is greater than 20:1 or less than 1:20.

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20. A method of treating or preventing an infection by a virus or treating a respiratory disease or condition associated with an infection by a virus comprising administering to a subject in need thereof:
(i) a first pharmaceutical composition comprising a first recombinant polynucleotide encoding a polypeptide comprising at least two of the following (a) a sequence comprising an epitope sequence from ORF1ab, a sequence comprising an epitope sequence from membrane glycoprotein (M), and a sequence comprising an epitope sequence from nucleocapsid phosphoprotein (N); and
(ii) a second pharmaceutical composition comprising a second recombinant polynucleotide encoding a 2019 SARS-CoV 2 spike protein or a variant or fragment thereof;
wherein the ratio (e.g., mass ratio) of the recombinant polynucleotide in (i) to the recombinant polynucleotide in (ii) is from 1:50 to 50:1.

21. A method of treating or preventing an infection by a virus or treating a respiratory disease or condition associated with an infection by a virus comprising administering to a subject in need thereof a pharmaceutical composition comprising a nanoparticle, wherein the nanoparticle comprises:
(i) a first recombinant polynucleotide encoding a polypeptide comprising at least two of the following (a) a sequence comprising an epitope sequence from ORF1ab, a sequence comprising an epitope sequence from membrane glycoprotein (M), and a sequence comprising an epitope sequence from nucleocapsid phosphoprotein (N); and
(ii) a second recombinant polynucleotide encoding a 2019 SARS-CoV 2 spike protein or a variant or fragment thereof.

22. The method of claim 21, wherein the nanoparticle is present in the pharmaceutical composition at a dose of from 100 ng to 500 micrograms.

23. The method of claim 21 or 22, wherein the ratio (e.g., mass ratio) of the first recombinant polynucleotide to the second recombinant polynucleotide is from about 1:50 to 50:1.

24. A method of treating or preventing an infection by a virus or treating a respiratory disease or condition associated with an infection by a virus comprising administering to a subject in need thereof:
(i) a first pharmaceutical composition comprising a first nanoparticle, wherein the first nanoparticle comprises a recombinant polynucleotide encoding a polypeptide comprising at least two of the following (a) a sequence comprising an epitope sequence from ORF1ab, a sequence comprising an epitope sequence from membrane glycoprotein (M), and a sequence comprising an epitope sequence from nucleocapsid phosphoprotein (N); and
(ii) a second pharmaceutical composition comprising a second nanoparticle, wherein the second nanoparticle comprises a recombinant polynucleotide encoding a 2019 SARS-CoV 2 spike protein or a variant or fragment thereof.

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25. The method of claim 24, wherein the ratio (e.g., mass ratio) of the recombinant polynucleotide in (i) to the recombinant polynucleotide in (ii) is from about 1:50 to 50:1.
26. The method of claims 24 or 25, wherein the first nanoparticle is present in the first pharmaceutical composition at a dose of from about 100 ng to 500 micrograms.
27. The method of any one of claims 24-26, wherein the second nanoparticle is present in the second pharmaceutical composition at a dose of from about 100 ng to 500 micrograms.
28. A method of treating or preventing an infection by a virus or treating a respiratory disease or condition associated with an infection by a virus comprising administering to a subject in need thereof:
    (i) a pharmaceutical composition comprising (a) a polypeptide comprising at least two of the following (a) a sequence comprising an epitope sequence from ORF1ab, a sequence comprising an epitope sequence from membrane glycoprotein (M), and a sequence comprising an epitope sequence from nucleocapsid phosphoprotein (N); or (b) a polynucleotide encoding a polypeptide comprising at least two of the following (a) a sequence comprising an epitope sequence from ORF1ab, a sequence comprising an epitope sequence from membrane glycoprotein (M), and a sequence comprising an epitope sequence from nucleocapsid phosphoprotein (N); and
    (ii) (a) a pharmaceutical composition comprising a polypeptide having an amino acid sequence of a 2019 SARS-CoV 2 spike protein or a variant or fragment thereof; (b) a recombinant polynucleotide encoding a 2019 SARS-CoV 2 spike protein or a variant or fragment thereof; or a 2019 SARS-CoV 2 spike protein pharmaceutical composition comprising (ii)(a) or (ii)(b);
    wherein the subject receives a dose of (ii)(a) or (ii)(b) that is lower than a dose of (ii)(a) or (ii)(b) administered to a subject alone.
29. A method of treating or preventing an infection by a virus or treating a respiratory disease or condition associated with an infection by a virus comprising administering to a subject in need thereof:
    (i) a pharmaceutical composition comprising (a) a polypeptide comprising at least two of the following (a) a sequence comprising an epitope sequence from ORF1ab, a sequence comprising an epitope sequence from membrane glycoprotein (M), and a sequence comprising an epitope sequence from nucleocapsid phosphoprotein (N); or (b) a polynucleotide encoding a polypeptide comprising at least two of the following (a) a sequence comprising an epitope sequence from ORF1ab, a sequence comprising an epitope sequence from membrane glycoprotein (M), and a sequence comprising an epitope sequence from nucleocapsid phosphoprotein (N); and
    (ii) (a) a pharmaceutical composition comprising a polypeptide having an amino acid sequence of a 2019 SARS-CoV 2 spike protein or a variant or fragment thereof; (b) a recombinant polynucleotide encoding a 2019 SARS-CoV 2 spike protein or a variant or fragment thereof; or a 2019 SARS-CoV 2 spike protein pharmaceutical composition comprising (ii)(a) or (ii)(b);

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wherein the subject receives a number of doses of (ii)(a) or (ii)(b) that is lower than a number of doses of (ii)(a) or (ii)(b) administered to a subject alone.

30. The method of claim 28, wherein the subject receives a dose of (ii)(a) or (ii)(b) that is at least 1.1, 1, 1.5, 2, 3, 4, 5, 6, 7, 8, 9, 10, 20, 30, 40, 50, 60, 70, 80, 90 or 100 times lower than a dose of (ii)(a) or (ii)(b) administered to a subject alone.

31. The method of claim 29, wherein the subject receives 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 fewer doses of (ii)(a) or (ii)(b) than the number of doses of (ii)(a) or (ii)(b) administered to a subject alone.

32. The method of claim 28 or 29, wherein the pharmaceutical composition of (i) is co-formulated with the pharmaceutical composition of (ii), wherein the pharmaceutical composition of (i) is formulated separately from the pharmaceutical composition of (ii) or wherein the pharmaceutical composition of (i) is administered separately from the pharmaceutical composition of (ii).

33. A method of treating or preventing an infection by a virus or treating a respiratory disease or condition associated with an infection by a virus comprising administering to a subject in need thereof:

(i) a pharmaceutical composition comprising (a) a polypeptide comprising at least two of the following (a) a sequence comprising an epitope sequence from ORF1ab, a sequence comprising an epitope sequence from membrane glycoprotein (M), and a sequence comprising an epitope sequence from nucleocapsid phosphoprotein (N); or (b) a polynucleotide encoding a polypeptide comprising at least two of the following (a) a sequence comprising an epitope sequence from ORF1ab, a sequence comprising an epitope sequence from membrane glycoprotein (M), and a sequence comprising an epitope sequence from nucleocapsid phosphoprotein (N); and

(ii) a pharmaceutical composition comprising (a) a polypeptide having an amino acid sequence of a 2019 SARS-CoV 2 spike protein or a variant or fragment thereof; (b) a recombinant polynucleotide encoding a 2019 SARS-CoV 2 spike protein or a variant or fragment thereof; or a 2019 SARS-CoV 2 spike protein pharmaceutical composition comprising (ii)(a) or (ii)(b);

wherein the subject receives a dose of (i)(a) or (i)(b) that is lower than a dose of (i)(a) or (i)(b) administered to a subject alone.

34. A method of treating or preventing an infection by a virus or treating a respiratory disease or condition associated with an infection by a virus comprising administering to a subject in need thereof:

(i) a pharmaceutical composition comprising (a) a polypeptide comprising at least two of the following (a) a sequence comprising an epitope sequence from ORF1ab, a sequence comprising an epitope sequence from membrane glycoprotein (M), and a sequence comprising an epitope sequence from nucleocapsid phosphoprotein (N); or (b) a polynucleotide encoding a polypeptide comprising at least two of the following (a) a sequence comprising an epitope sequence from ORF1ab, a sequence comprising an epitope sequence from membrane glycoprotein (M), and a sequence comprising an epitope sequence from nucleocapsid phosphoprotein (N); and

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(ii) a pharmaceutical composition comprising (a) a polypeptide having an amino acid sequence of a 2019 SARS-CoV 2 spike protein or a variant or fragment thereof; (b) a recombinant polynucleotide encoding a 2019 SARS-CoV 2 spike protein or a variant or fragment thereof; or a 2019 SARS-CoV 2 spike protein pharmaceutical composition comprising (ii)(a) or (ii)(b);

wherein the subject receives a number of doses of (i)(a) or (i)(b) that is lower than a number of doses of (i)(a) or (i)(b) administered to a subject alone.

35. The method of claim 33, wherein the subject receives a dose of (i)(a) or (i)(b) that is at least 1.1, 1, 1.5, 2, 3, 4, 5, 6, 7, 8, 9, 10, 20, 30, 40, 50, 60, 70, 80, 90 or 100 times lower than a dose of (i)(a) or (i)(b) administered to a subject alone.

36. The method of claim 34, wherein the subject receives 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 fewer doses of (i)(a) or (i)(b) than the number of doses of (i)(a) or (i)(b) administered to a subject alone.

37. The method of claim 33 or 34, wherein the pharmaceutical composition of (i) is co-formulated with the pharmaceutical composition of (ii), wherein the pharmaceutical composition of (i) is formulated separately from the pharmaceutical composition of (ii) or wherein the pharmaceutical composition of (i) is administered separately from the pharmaceutical composition of (ii).

38. A method of treating or preventing an infection by a virus or treating a respiratory disease or condition associated with an infection by a virus comprising administering to a subject in need thereof:

(i) a pharmaceutical composition comprising (a) a polypeptide comprising at least two of the following (a) a sequence comprising an epitope sequence from ORF1ab, a sequence comprising an epitope sequence from membrane glycoprotein (M), and a sequence comprising an epitope sequence from nucleocapsid phosphoprotein (N); or (b) a polynucleotide encoding a polypeptide comprising at least two of the following (a) a sequence comprising an epitope sequence from ORF1ab, a sequence comprising an epitope sequence from membrane glycoprotein (M), and a sequence comprising an epitope sequence from nucleocapsid phosphoprotein (N);

wherein the pharmaceutical composition is administered at a first time point, a second time point and a third time point, wherein the second time point is at least about 2 days after the first time point and the third time point is at least about 2 days after the second time point.

39. The method of claim 38, wherein the second time point is at least about, at most about or about 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, or 35 days after the first time point, at least about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, or 35 weeks after the first time point, or at least about 1, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, or 35 months after the first time point.

40. The method of claim 38 or 39, wherein the third time point is at least about, at most about or about 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31,

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32, 33, 34, or 35 days after the second time point, at least about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, or 35 weeks after the second time point, or at least about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, or 35 months after the second time point.

41. The method of any one of claims 38-40, wherein the third time point is at least about, at most about or about 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35 or 36 days after the first time point, at least about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, or 35 weeks after the first time point, or at least about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, or 35 months after the first time point.

42. A pharmaceutical composition comprising:

(i) a recombinant polynucleotide encoding a polypeptide comprising at least two of the following (a) a sequence comprising an epitope sequence from ORF1ab, a sequence comprising an epitope sequence from membrane glycoprotein (M), and a sequence comprising an epitope sequence from nucleocapsid phosphoprotein (N); and

(ii) a recombinant polynucleotide encoding a 2019 SARS-CoV 2 spike protein or a variant or fragment thereof;

wherein the ratio (e.g., mass ratio) of (i):(ii) is greater than 20:1 or less than 1:20.

43. A composition comprising:

(i) a first pharmaceutical composition comprising a first recombinant polynucleotide encoding a polypeptide comprising at least two of the following (a) a sequence comprising an epitope sequence from ORF1ab, a sequence comprising an epitope sequence from membrane glycoprotein (M), and a sequence comprising an epitope sequence from nucleocapsid phosphoprotein (N); and

(ii) a second pharmaceutical composition comprising a second recombinant polynucleotide encoding a 2019 SARS-CoV 2 spike protein or a variant or fragment thereof;

wherein the ratio (e.g., mass ratio) of the recombinant polynucleotide in (i) to the recombinant polynucleotide in (ii) is from 1:50 to 50:1.

44. A pharmaceutical composition comprising a nanoparticle, wherein the nanoparticle comprises:

(i) a first recombinant polynucleotide encoding a polypeptide comprising at least two of the following (a) a sequence comprising an epitope sequence from ORF1ab, a sequence comprising an epitope sequence from membrane glycoprotein (M), and a sequence comprising an epitope sequence from nucleocapsid phosphoprotein (N); and

(ii) a second recombinant polynucleotide encoding a 2019 SARS-CoV 2 spike protein or a variant or fragment thereof.

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45. The pharmaceutical composition of claim 44, wherein the nanoparticle is present in the pharmaceutical composition at a dose of from 100 ng to 500 micrograms.
46. The pharmaceutical composition of claim 44 or 45, wherein the ratio (e.g., mass ratio) of the first recombinant polynucleotide to the second recombinant polynucleotide is from about 1:50 to 50:1.
47. A composition comprising:
    (i) a first pharmaceutical composition comprising a first nanoparticle, wherein the first nanoparticle comprises a recombinant polynucleotide encoding a polypeptide comprising at least two of the following (a) a sequence comprising an epitope sequence from ORF1ab, a sequence comprising an epitope sequence from membrane glycoprotein (M), and a sequence comprising an epitope sequence from nucleocapsid phosphoprotein (N); and
    (ii) a second pharmaceutical composition comprising a second nanoparticle, wherein the second nanoparticle comprises a recombinant polynucleotide encoding a 2019 SARS-CoV 2 spike protein or a variant or fragment thereof.
48. The composition of claim 47, wherein the ratio (e.g., mass ratio) of the recombinant polynucleotide in (i) to the recombinant polynucleotide in (ii) is from about 1:50 to 50:1.
49. The composition of claim 47 or 48, wherein the first nanoparticle is present in the first pharmaceutical composition at a dose of from about 100 ng to 500 micrograms.
50. The composition of any one of claims 47-49, wherein the second nanoparticle is present in the second pharmaceutical composition at a dose of from about 100 ng to 500 micrograms.
51. The composition of any one of claims 47-50, wherein the recombinant polynucleotide in (i) is present in the first pharmaceutical composition at a dose of from about 50 ng to 250 micrograms.
52. The composition of any one of claims 47-51, wherein the recombinant polynucleotide in (ii) is present in the second pharmaceutical composition at a dose of from about 50 ng to 250 micrograms.
53. The composition of any one of claims 21-27 and 44-52 wherein the nanoparticle is a lipid nanoparticle.
54. A method of treating or preventing an infection by a virus or treating a respiratory disease or condition associated with an infection by a virus comprising administering to a subject in need thereof a pharmaceutical composition comprising:
    (i) a polypeptide comprising at least two of the following (a) a sequence comprising an epitope sequence from ORF1ab, (b) a sequence comprising an epitope sequence from membrane glycoprotein (M) and (c) a sequence comprising an epitope sequence from nucleocapsid phosphoprotein (N);
    (ii) a polynucleotide encoding a polypeptide, wherein the polypeptide comprises at least two of the following (a) a sequence comprising an epitope sequence from ORF1ab, (b) a sequence

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comprising an epitope sequence from membrane glycoprotein (M) and (c) a sequence comprising an epitope sequence from nucleocapsid phosphoprotein (N);

(iii) a T cell receptor (TCR) or a T cell comprising the TCR, wherein the TCR binds to an epitope sequence of the polypeptide in complex with a corresponding HLA class I or class II molecule;

(iv) an antigen presenting cell comprising (i) or (ii); or

(v) an antibody or B cell comprising the antibody, wherein the antibody binds to an epitope sequence of the polypeptide.

55. The method of claim 54, wherein the subject has an immunodeficiency.

56. The method of claim 55, wherein the subject has a B cell immunodeficiency.

57. The method of claim 54, wherein the composition comprises (i) a polypeptide with at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, or 100% sequence identity to a sequence selected from the group consisting of RS C1p1full, RS C2p1full, RS C3p1full, RS C4p1full, RS C5p1, RS C5p2, RS C5p2full, RS C6p1, RS C6p2, RS C6p2full, RS C7p1, RS C7p2, RS C7p2full, RS C7p4, RS C7p4full, RS C8p1, RS C8p2 and RS C8p2full; (ii) a polynucleotide encoding a polypeptide with at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, or 100% sequence identity to a sequence selected from the group consisting of RS C1p1full, RS C2p1full, RS C3p1full, RS C4p1full, RS C5p1, RS C5p2, RS C5p2full, RS C6p1, RS C6p2, RS C6p2full, RS C7p1, RS C7p2, RS C7p2full, RS C7p4, RS C7p4full, RS C8p1, RS C8p2 and RS C8p2full; or (iii) a polynucleotide with at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, or 100% sequence identity to a sequence selected from the group consisting of SEQ ID NOs: RS C1n1, RS C2n1, RS C3n1, RS C4n1, RS C5n1, RS C6n1, RS C7n1, RS C8n1, RS C5n2, RS C6n2, RS C7n2, RS C8n2, RS C5n2full, RS C6n2full, RS C7n2full, RS C8n2full, , RS C7n4 and RS C7n4full.

58. The method of claim 54, wherein the composition comprises (i) a polypeptide with at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, or 100% sequence identity to a sequence selected from the group consisting of RS C7p1, RS C7p2, RS C7p2full, RS C7p4 and RS C7p4full; or (iii) a polynucleotide with at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, or 100% sequence identity to a sequence selected from the group consisting of SEQ ID NOs: RS C7n1, RS C7n2, RS C7n2full, , RS C7n4 and RS C7n4full.

59. A method of treating or preventing an infection by a virus or treating a respiratory disease or condition associated with an infection by a virus comprising administering to a subject in need thereof a pharmaceutical composition comprising:

(i) a polypeptide comprising an epitope sequence of Table 1A, Table 1B, Table 1C, Table 2Ai, Table 2Aii, Table 2B and/or Table 16;

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(ii) a polynucleotide encoding the polypeptide comprising an epitope sequence of Table 1A, Table 1B, Table 1C, Table 2Ai, Table 2Aii, Table 2B and/or Table 16;

(iii) a T cell receptor (TCR) or a T cell comprising the TCR, wherein the TCR binds to the epitope sequence in complex with a corresponding HLA class I or class II molecule;

(iv) an antigen presenting cell comprising (i) or (ii); or(v) an antibody or B cell comprising the antibody, wherein the antibody binds to the epitope sequence.

60. The method of claim 59, wherein the subject has an immunodeficiency.

61. The method of claim 60, wherein the subject has a B cell immunodeficiency.

62. A method of treating or preventing an infection by a virus or treating a respiratory disease or condition associated with an infection by a virus comprising administering to a subject in need thereof a pharmaceutical composition comprising: a polypeptide having an amino acid sequence with at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, or 100% sequence identity to a sequence of any one of the sequences depicted in column 2 of Table 11, column 2 of Table 12 or column 3 of Table 15; or a recombinant polynucleotide encoding a polypeptide having an amino acid sequence with at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, or 100% sequence identity to a sequence of any one of the sequences depicted in column 2 of Table 11, column 2 of Table 12 or column 3 of Table 15

63. The method of claim 62, wherein the subject has an immunodeficiency.

64. The method of claim 63, wherein the subject has a B cell immunodeficiency.

65. The method of claim 62, wherein the pharmaceutical composition comprises a polypeptide with at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, or 100% sequence identity to a sequence selected from the group consisting of RS C1p1full, RS C2p1full, RS C3p1full, RS C4p1full, RS C5p1, RS C5p2, RS C5p2full, RS C6p1, RS C6p2, RS C6p2full, RS C7p1, RS C7p2, RS C7p2full, RS C7p4, RS C7p4full, RS C8p1, RS C8p2 and RS C8p2full; or a polynucleotide encoding a polypeptide with at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, or 100% sequence identity to a sequence selected from the group consisting of RS C1p1full, RS C2p1full, RS C3p1full, RS C4p1full, RS C5p1, RS C5p2, RS C5p2full, RS C6p1, RS C6p2, RS C6p2full, RS C7p1, RS C7p2, RS C7p2full, RS C7p4, RS C7p4full, RS C8p1, RS C8p2, and RS C8p2full.

66. The method of claim 62, wherein the pharmaceutical composition comprises a polynucleotide with at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, or 100% sequence identity to a sequence selected from the group consisting of SEQ ID NOs: RS C1n1, RS C2n1, RS C3n1, RS C4n1, RS C5n1, RS C6n1, RS C7n1, RS C8n1, RS C5n2, RS C6n2, RS C7n2, RS C8n2, RS C5n2full, RS C6n2full, RS C7n2full, RS C8n2full, RS C7n4, RS C7n4full.

67. The method of any one of claims 54, 59 or 62, wherein the polynucleotide is an mRNA.

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68. The method of any one of claims 54, 59 or 62, wherein the pharmaceutical composition further comprises one or more lipids.
69. The method of claim 68, wherein the one or more lipids comprise a lipid nanoparticle (LNP).
70. The method of claim 69, wherein the LNP encapsulates the recombinant polynucleotide construct.
71. A method of treating or preventing an infection by a virus or treating a respiratory disease or condition associated with an infection by a virus comprising administering to a subject in need thereof a pharmaceutical composition comprising:
    (i) a recombinant polynucleotide encoding a polypeptide comprising at least two of the following (a) a sequence comprising an epitope sequence from ORF1ab, a sequence comprising an epitope sequence from membrane glycoprotein (M), and a sequence comprising an epitope sequence from nucleocapsid phosphoprotein (N); and
    (ii) a recombinant polynucleotide encoding a 2019 SARS-CoV 2 spike protein or a variant or fragment thereof.
72. A method of treating or preventing an infection by a virus or treating a respiratory disease or condition associated with an infection by a virus comprising administering to a subject in need thereof:
    (i) a first pharmaceutical composition comprising a first recombinant polynucleotide encoding a polypeptide comprising at least two of the following (a) a sequence comprising an epitope sequence from ORF1ab, a sequence comprising an epitope sequence from membrane glycoprotein (M), and a sequence comprising an epitope sequence from nucleocapsid phosphoprotein (N); and
    (ii) a second pharmaceutical composition comprising a second recombinant polynucleotide encoding a 2019 SARS-CoV 2 spike protein or a variant or fragment thereof.
73. The method of claim 71 or 72, wherein the ratio (e.g., mass ratio) of the recombinant polynucleotide in (i) to the recombinant polynucleotide in (ii) is from 20:1 to 1:20.
74. A method of treating or preventing an infection by a virus or treating a respiratory disease or condition associated with an infection by a virus comprising administering to a subject in need thereof a pharmaceutical composition comprising:
    (i) a first recombinant polynucleotide encoding a polypeptide comprising at least two of the following (a) a sequence comprising an epitope sequence from ORF1ab, a sequence comprising an epitope sequence from membrane glycoprotein (M), and a sequence comprising an epitope sequence from nucleocapsid phosphoprotein (N); and
    (ii) a second recombinant polynucleotide encoding a 2019 SARS-CoV 2 spike protein or a variant or fragment thereof.

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75. The method of claim 71 or 74, wherein the pharmaceutical composition comprises a nanoparticle, wherein the nanoparticle comprises the first recombinant polynucleotide and the second recombinant polynucleotide.

76. The method of claim 75, wherein the nanoparticle is present in the pharmaceutical composition at a dose of from 100 ng to 500 micrograms.

77. The method of any one of claims 74-76, wherein the ratio (e.g., mass ratio) of the first recombinant polynucleotide to the second recombinant polynucleotide is from about 1:50 to 50:1.

78. A method of treating or preventing an infection by a virus or treating a respiratory disease or condition associated with an infection by a virus comprising administering to a subject in need thereof:
    (i) `a first pharmaceutical composition comprising a recombinant polynucleotide encoding a polypeptide comprising at least two of the following (a) a sequence comprising an epitope sequence from ORF1ab, a sequence comprising an epitope sequence from membrane glycoprotein (M), and a sequence comprising an epitope sequence from nucleocapsid phosphoprotein (N); and
    (ii) a second pharmaceutical composition comprising a recombinant polynucleotide encoding a 2019 SARS-CoV 2 spike protein or a variant or fragment thereof.

79. The method of claim 78, wherein the ratio (e.g., mass ratio) of the recombinant polynucleotide in (i) to the recombinant polynucleotide in (ii) is from about 1:50 to 50:1.

80. The method of claim 72 or 78, wherein the first pharmaceutical composition comprises a first nanoparticle, wherein the first nanoparticle comprises the recombinant polynucleotide encoding a polypeptide comprising at least two of the following (a) a sequence comprising an epitope sequence from ORF1ab, a sequence comprising an epitope sequence from membrane glycoprotein (M), and a sequence comprising an epitope sequence from nucleocapsid phosphoprotein (N); and wherein the second pharmaceutical composition comprises a second nanoparticle, wherein the second nanoparticle comprises the recombinant polynucleotide encoding a 2019 SARS-CoV 2 spike protein or a variant or fragment thereof.

81. The method of claim 80, wherein the first nanoparticle is present in the first pharmaceutical composition at a dose of from about 100 ng to 500 micrograms.

82. The method of claim 80, wherein the second nanoparticle is present in the second pharmaceutical composition at a dose of from about 100 ng to 500 micrograms.

83. A method of treating or preventing an infection by a virus or treating a respiratory disease or condition associated with an infection by a virus comprising administering to a subject in need thereof:
    (i) a pharmaceutical composition comprising (a) a polypeptide comprising at least two of the following (a) a sequence comprising an epitope sequence from ORF1ab, a sequence comprising an epitope sequence from membrane glycoprotein (M), and a sequence comprising an epitope

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sequence from nucleocapsid phosphoprotein (N); or (b) a polynucleotide encoding a polypeptide comprising at least two of the following (a) a sequence comprising an epitope sequence from ORF1ab, a sequence comprising an epitope sequence from membrane glycoprotein (M), and a sequence comprising an epitope sequence from nucleocapsid phosphoprotein (N); and

(ii) (a) a pharmaceutical composition comprising a polypeptide having an amino acid sequence of a 2019 SARS-CoV 2 spike protein or a variant or fragment thereof; (b) a recombinant polynucleotide encoding a 2019 SARS-CoV 2 spike protein or a variant or fragment thereof; or a 2019 SARS-CoV 2 spike protein pharmaceutical composition comprising (ii)(a) or (ii)(b);

wherein the subject receives a dose of (ii)(a) or (ii)(b) that is lower than a dose of (ii)(a) or (ii)(b) administered to a subject alone.

84. A method of treating or preventing an infection by a virus or treating a respiratory disease or condition associated with an infection by a virus comprising administering to a subject in need thereof:

(i) a pharmaceutical composition comprising (a) a polypeptide comprising at least two of the following (a) a sequence comprising an epitope sequence from ORF1ab, a sequence comprising an epitope sequence from membrane glycoprotein (M), and a sequence comprising an epitope sequence from nucleocapsid phosphoprotein (N); or (b) a polynucleotide encoding a polypeptide comprising at least two of the following (a) a sequence comprising an epitope sequence from ORF1ab, a sequence comprising an epitope sequence from membrane glycoprotein (M), and a sequence comprising an epitope sequence from nucleocapsid phosphoprotein (N); and

(ii) (a) a pharmaceutical composition comprising a polypeptide having an amino acid sequence of a 2019 SARS-CoV 2 spike protein or a variant or fragment thereof; (b) a recombinant polynucleotide encoding a 2019 SARS-CoV 2 spike protein or a variant or fragment thereof; or a 2019 SARS-CoV 2 spike protein pharmaceutical composition comprising (ii)(a) or (ii)(b);

wherein the subject receives a number of doses of (ii)(a) or (ii)(b) that is lower than a number of doses of (ii)(a) or (ii)(b) administered to a subject alone.

85. The method of claim 83, wherein the subject receives a dose of (ii)(a) or (ii)(b) that is at least 1.1, 1, 1.5, 2, 3, 4, 5, 6, 7, 8, 9, 10, 20, 30, 40, 50, 60, 70, 80, 90 or 100 times lower than a dose of (ii)(a) or (ii)(b) administered to a subject alone.

86. The method of claim 84, wherein the subject receives 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 fewer doses of (ii)(a) or (ii)(b) than the number of doses of (ii)(a) or (ii)(b) administered to a subject alone.

87. The method of claim 83 or 84, wherein the pharmaceutical composition of (i) is co-formulated with the pharmaceutical composition of (ii), wherein the pharmaceutical composition of (i) is formulated

separately from the pharmaceutical composition of (ii) or wherein the pharmaceutical composition of (i) is administered separately from the pharmaceutical composition of (ii).

88. A method of treating or preventing an infection by a virus or treating a respiratory disease or condition associated with an infection by a virus comprising administering to a subject in need thereof:

(i) a pharmaceutical composition comprising (a) a polypeptide comprising at least two of the following (a) a sequence comprising an epitope sequence from ORF1ab, a sequence comprising an epitope sequence from membrane glycoprotein (M), and a sequence comprising an epitope sequence from nucleocapsid phosphoprotein (N); or (b) a polynucleotide encoding a polypeptide comprising at least two of the following (a) a sequence comprising an epitope sequence from ORF1ab, a sequence comprising an epitope sequence from membrane glycoprotein (M), and a sequence comprising an epitope sequence from nucleocapsid phosphoprotein (N); and

(ii) a pharmaceutical composition comprising (a) a polypeptide having an amino acid sequence of a 2019 SARS-CoV 2 spike protein or a variant or fragment thereof; (b) a recombinant polynucleotide encoding a 2019 SARS-CoV 2 spike protein or a variant or fragment thereof; or a 2019 SARS-CoV 2 spike protein pharmaceutical composition comprising (ii)(a) or (ii)(b);

wherein the subject receives a dose of (i)(a) or (i)(b) that is lower than a dose of (i)(a) or (i)(b) administered to a subject alone.

89. A method of treating or preventing an infection by a virus or treating a respiratory disease or condition associated with an infection by a virus comprising administering to a subject in need thereof:

(i) a pharmaceutical composition comprising (a) a polypeptide comprising at least two of the following (a) a sequence comprising an epitope sequence from ORF1ab, a sequence comprising an epitope sequence from membrane glycoprotein (M), and a sequence comprising an epitope sequence from nucleocapsid phosphoprotein (N); or (b) a polynucleotide encoding a polypeptide comprising at least two of the following (a) a sequence comprising an epitope sequence from ORF1ab, a sequence comprising an epitope sequence from membrane glycoprotein (M), and a sequence comprising an epitope sequence from nucleocapsid phosphoprotein (N); and

(ii) a pharmaceutical composition comprising (a) a polypeptide having an amino acid sequence of a 2019 SARS-CoV 2 spike protein or a variant or fragment thereof; (b) a recombinant polynucleotide encoding a 2019 SARS-CoV 2 spike protein or a variant or fragment thereof; or a 2019 SARS-CoV 2 spike protein pharmaceutical composition comprising (ii)(a) or (ii)(b);

wherein the subject receives a number of doses of (i)(a) or (i)(b) that is lower than a number of doses of (i)(a) or (i)(b) administered to a subject alone.

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90. The method of claim 88, wherein the subject receives a dose of (i)(a) or (i)(b) that is at least 1.1, 1, 1.5, 2, 3, 4, 5, 6, 7, 8, 9, 10, 20, 30, 40, 50, 60, 70, 80, 90 or 100 times lower than a dose of (i)(a) or (i)(b) administered to a subject alone.

91. The method of claim 89, wherein the subject receives 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 fewer doses of (i)(a) or (i)(b) than the number of doses of (i)(a) or (i)(b) administered to a subject alone.

92. The method of claim 88 or 89, wherein the pharmaceutical composition of (i) is co-formulated with the pharmaceutical composition of (ii), wherein the pharmaceutical composition of (i) is formulated separately from the pharmaceutical composition of (ii) or wherein the pharmaceutical composition of (i) is administered separately from the pharmaceutical composition of (ii).

93. The method of any one of claims 28-41, 54-71, 73-77 and 83-92, wherein the pharmaceutical composition is administered at a first time point and a second time point, wherein the second time point is at least about, at most about or about 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35 or 36 days after the first time point; at least about, at most about or about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35 or 36 weeks after the first time point; or at least about, at most about or about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35 or 36 months after the first time point.

94. The method of claim 93, wherein the pharmaceutical composition is administered at a third time point, wherein the third time point is at least about, at most about or about 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35 or 36 days after the second time point; at least about, at most about or about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35 or 36 weeks after the second time point; or at least about, at most about or about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35 or 36 months after the second time point.

95. The method of claim 94, wherein the third time point is at least about, at most about or about 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49 or 50 days after the first time point; at least about, at most about or about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35 or 36 weeks after the first time point; or at least about, at most about or about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35 or 36 months after the first time point.

96. The method of any one of claims 20-27, 72, 73 and 78-82, wherein the first pharmaceutical composition is administered at a first time point and a second time point, wherein the second time point is at least about, at most about or about 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18,

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19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35 or 36 days after the first time point; at least about, at most about or about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35 or 36 weeks after the first time point; or at least about, at most about or about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35 or 36 months after the first time point.

97. The method of claim 96, wherein the first pharmaceutical composition is administered at a third time point, wherein the third time point is at least about, at most about or about 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35 or 36 days after the second time point; at least about, at most about or about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35 or 36 weeks after the second time point; or at least about, at most about or about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35 or 36 months after the second time point.

98. The method of claim 97, wherein the third time point is at least about, at most about or about 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49 or 50 days after the first time point; at least about, at most about or about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35 or 36 weeks after the first time point; or at least about, at most about or about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35 or 36 months after the first time point.

99. The method of any one of claims 96-98, wherein the second pharmaceutical composition is administered at the first time point.

100. The method of any one of claims 96-99, wherein the second pharmaceutical composition is administered at the second time point.

101. The method of any one of claims 96-100, wherein the second pharmaceutical composition is administered at the third time point.

102. The method of any one of claims 96-98, 100 or 101, wherein the second pharmaceutical composition is administered at least about, at most about or about 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35 or 36 days after the first time point; at least about, at most about or about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35 or 36 weeks after the first time point; or at least about, at most about or about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35 or 36 months after the first time point.

103. The method of any one of claims 96-98 or 101, wherein the second pharmaceutical composition is administered at least about, at most about or about 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17,

18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35 or 36 days after the second time point; at least about, at most about or about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35 or 36 weeks after the second time point; or at least about, at most about or about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35 or 36 months after the second time point.

104. A method of treating or preventing an infection by a virus or treating a respiratory disease or condition associated with an infection by a virus comprising administering to a subject in need thereof:

(i) a pharmaceutical composition comprising (a) a polypeptide comprising at least two of the following (a) a sequence comprising an epitope sequence from ORF1ab, a sequence comprising an epitope sequence from membrane glycoprotein (M), and a sequence comprising an epitope sequence from nucleocapsid phosphoprotein (N); or (b) a polynucleotide encoding a polypeptide comprising at least two of the following (a) a sequence comprising an epitope sequence from ORF1ab, a sequence comprising an epitope sequence from membrane glycoprotein (M), and a sequence comprising an epitope sequence from nucleocapsid phosphoprotein (N);

wherein the pharmaceutical composition is administered at a first time point and a second time point, wherein the second time point is at least about 2 days after the first time point.

105. The method of claim 104, wherein the pharmaceutical composition is administered at a third time point, wherein the third time point is at least about 2 days after the second time point.

106. The method of claim 104 or 105, wherein the second time point is at least about, at most about or about 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, or 35 days after the first time point, at least about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, or 35 weeks after the first time point, or at least about 1, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, or 35 months after the first time point.

107. The method of claim 105 or 106, wherein the third time point is at least about, at most about or about 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, or 35 days after the second time point, at least about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, or 35 weeks after the second time point, or at least about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, or 35 months after the second time point.

108. The method of any one of claims 105-107, wherein the third time point is at least about, at most about or about 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35 or 36 days after the first time point, at least about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11,

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12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, or 35 weeks after the first time point, or at least about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, or 35 months after the first time point.

109. The method of any one of claims 104-108, wherein the method further comprises administering to the subject: (ii) (a) a polypeptide having an amino acid sequence of a 2019 SARS-CoV 2 spike protein or a variant or fragment thereof; (b) a recombinant polynucleotide encoding a 2019 SARS-CoV 2 spike protein or a variant or fragment thereof; or a 2019 SARS-CoV 2 spike protein pharmaceutical composition comprising (ii)(a) or (ii)(b).
110. The method of any one of claims 71-109, wherein the subject has an immunodeficiency.
111. The method of any one of claims 71-110, wherein the subject has a B cell immunodeficiency.
112. A pharmaceutical composition comprising:
    (i) a recombinant polynucleotide encoding a polypeptide comprising at least two of the following (a) a sequence comprising an epitope sequence from ORF1ab, a sequence comprising an epitope sequence from membrane glycoprotein (M), and a sequence comprising an epitope sequence from nucleocapsid phosphoprotein (N); and
    (ii) a recombinant polynucleotide encoding a 2019 SARS-CoV 2 spike protein or a variant or fragment thereof.
113. The pharmaceutical composition of claim 112, wherein the ratio (e.g., mass ratio) of (i):(ii) is from 20:1 to 1:20.
114. A composition comprising:
    (i) a first pharmaceutical composition comprising a first recombinant polynucleotide encoding a polypeptide comprising at least two of the following (a) a sequence comprising an epitope sequence from ORF1ab, a sequence comprising an epitope sequence from membrane glycoprotein (M), and a sequence comprising an epitope sequence from nucleocapsid phosphoprotein (N); and
    (ii) a second pharmaceutical composition comprising a second recombinant polynucleotide encoding a 2019 SARS-CoV 2 spike protein or a variant or fragment thereof.
115. The composition of claim 114, wherein the ratio (e.g., mass ratio) of the recombinant polynucleotide in (i) to the recombinant polynucleotide in (ii) is from 1:50 to 50:1.
116. A pharmaceutical composition comprising:
    (i) a first recombinant polynucleotide encoding a polypeptide comprising at least two of the following (a) a sequence comprising an epitope sequence from ORF1ab, a sequence comprising an epitope sequence from membrane glycoprotein (M), and a sequence comprising an epitope sequence from nucleocapsid phosphoprotein (N); and

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(ii) a second recombinant polynucleotide encoding a 2019 SARS-CoV 2 spike protein or a variant or fragment thereof.

117. The pharmaceutical composition of claim 116, wherein the pharmaceutical composition comprises a nanoparticle, wherein the nanoparticle comprises the first recombinant polynucleotide and the second recombinant polynucleotide.

118. The pharmaceutical composition of claim 117, wherein the nanoparticle is present in the pharmaceutical composition at a dose of from 100 ng to 500 micrograms.

119. The pharmaceutical composition of any one of claims 116-118, wherein the ratio (e.g., mass ratio) of the first recombinant polynucleotide to the second recombinant polynucleotide is from about 1:50 to 50:1.

120. A composition comprising:

(i) a first pharmaceutical composition comprising a recombinant polynucleotide encoding a polypeptide comprising at least two of the following (a) a sequence comprising an epitope sequence from ORF1ab, a sequence comprising an epitope sequence from membrane glycoprotein (M), and a sequence comprising an epitope sequence from nucleocapsid phosphoprotein (N); and

(ii) a second pharmaceutical composition comprising a recombinant polynucleotide encoding a 2019 SARS-CoV 2 spike protein or a variant or fragment thereof.

121. The composition of claim 120, wherein the first pharmaceutical composition comprises a first nanoparticle, wherein the first nanoparticle comprises the recombinant polynucleotide encoding a polypeptide comprising at least two of the following (a) a sequence comprising an epitope sequence from ORF1ab, a sequence comprising an epitope sequence from membrane glycoprotein (M), and a sequence comprising an epitope sequence from nucleocapsid phosphoprotein (N); and wherein the second pharmaceutical composition comprises a second nanoparticle, wherein the second nanoparticle comprises the recombinant polynucleotide encoding a 2019 SARS-CoV 2 spike protein or a variant or fragment thereof.

122. The composition of claim 121, wherein the ratio (e.g., mass ratio) of the recombinant polynucleotide in (i) to the recombinant polynucleotide in (ii) is from about 1:50 to 50:1.

123. The composition of claim 121 or 122, wherein the first nanoparticle is present in the first pharmaceutical composition at a dose of from about 100 ng to 500 micrograms.

124. The composition of any one of claims 121-123, wherein the second nanoparticle is present in the second pharmaceutical composition at a dose of from about 100 ng to 500 micrograms.

125. The composition of any one of claims 121-124, wherein the recombinant polynucleotide in (i) is present in the first pharmaceutical composition at a dose of from about 50 ng to 250 micrograms

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126. The composition of any one of claims 121-125, wherein the recombinant polynucleotide in (ii) is present in the second pharmaceutical composition at a dose of from about 50 ng to 250 micrograms.
127. The composition of any one of claims 121-126 or the pharmaceutical composition of any one of claims 117-119, wherein the nanoparticle is a lipid nanoparticle.
128. The method of claim 78, wherein the ratio (e.g., mass ratio) of the first pharmaceutical composition and the second pharmaceutical composition are administered on first day and the first pharmaceutical composition and the second pharmaceutical composition are administered on a second day thereafter.
129. The method of claim 128, wherein recombinant polynucleotide in the first pharmaceutical composition administered on the first day and the recombinant polynucleotide in the second pharmaceutical composition administered on the first day are present at a ratio of about 3:1.
130. The method of claim 128 or 129, wherein recombinant polynucleotide in the first pharmaceutical composition administered on the second day and the recombinant polynucleotide in the second pharmaceutical composition administered on the second day are present at a ratio of about 3:1.
131. The method of any one of claims 78-82, wherein the second pharmaceutical composition is administered at least once before administering the first pharmaceutical composition.
132. The method of claim 128, wherein the second pharmaceutical composition is administered at least twice before administering the first pharmaceutical composition.
133. The method of claim 132, wherein the second pharmaceutical composition is administered at least 2, 3, 4, 5, or 6 months before administering the first pharmaceutical composition.
134. The method of claim 132 or 133, wherein a first administration of the second pharmaceutical composition is administered less than one month before a second administration of the second pharmaceutical composition.
135. The method of any one of claims 132-134, wherein a second administration of the second pharmaceutical composition is administered at least 2, 3, 4, 5, or 6 months before administering the first pharmaceutical composition.
136. The method of any one of claims 132-135, wherein the second pharmaceutical composition is administered at least thrice before administering the first pharmaceutical composition.
137. The method of any one of the claims 128-136 wherein the first pharmaceutical composition is administered at least 6 months after a last administration of the second pharmaceutical composition, wherein the last administration of the second pharmaceutical composition lacks the polynucleotide of the first pharmaceutical composition.
138. The method of any one of the claims 128-135 and 137, wherein the second pharmaceutical composition is administered twice before administering the first pharmaceutical composition.

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139. The method of claim 138, wherein the first pharmaceutical composition administered after the second pharmaceutical composition is administered twice further comprises a second recombinant polynucleotide encoding a 2019 SARS-CoV 2 spike protein or a variant or fragment thereof.
140. The method of claim 139, wherein the first recombinant polynucleotide in the first pharmaceutical composition and the second recombinant polynucleotide in the first pharmaceutical composition are present at a ratio of about 1:3.
141. The method of claim 138, wherein the ratio (e.g., mass ratio) of first recombinant polynucleotide in the first pharmaceutical composition to the second recombinant polynucleotide in the second pharmaceutical composition administered first is about 1:1.
142. The method of claim 138, wherein the ratio (e.g., mass ratio) of first recombinant polynucleotide in the first pharmaceutical composition to the second recombinant polynucleotide in the second pharmaceutical composition administered second is about 1:1.
143. The method of claim 138, wherein the method comprises administering the first pharmaceutical composition and the second pharmaceutical composition a third time on the same day.
144. The method of claim 143 wherein the ratio (e.g., mass ratio) of first recombinant polynucleotide in the first pharmaceutical composition to the second recombinant polynucleotide in the second pharmaceutical composition administered a third time is about 1:3.
145. The method of claim 143 wherein the ratio (e.g., mass ratio) of first recombinant polynucleotide in the first pharmaceutical composition to the second recombinant polynucleotide in the second pharmaceutical composition administered a third time is about 1:9.
146. The method any one of the method claims above, wherein the first recombinant polynucleotide is administered at a dose of about 1 microgram, 3 micrograms, 5 micrograms, 10 micrograms, 15 micrograms, or 30 micrograms.
147. The method any one of the method claims above, the total amount of the first and/or second polynucleotide administered to the subject is about 30 micrograms.
148. The method of any of the preceding claims, wherein the pharmaceutical composition is effective against a SARS-CoV-2 B1.1.529 (omicron) variant.
149. The method of any of the preceding claims, wherein the subject has SARS-CoV-2 B1.1.529 (omicron) variant.

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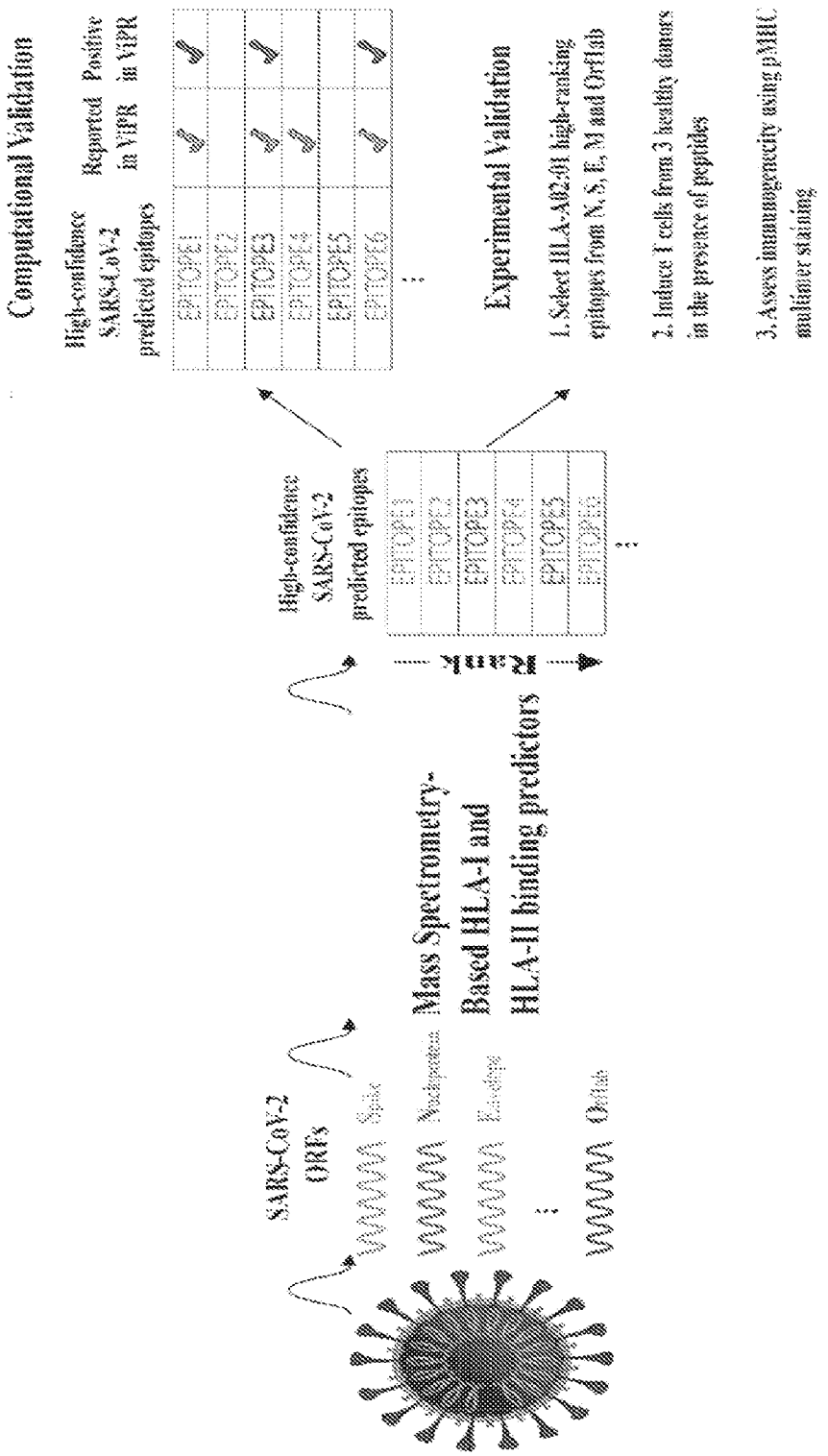
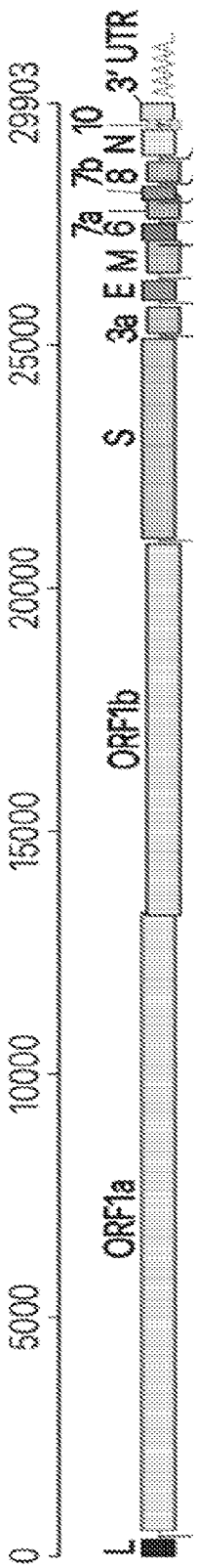
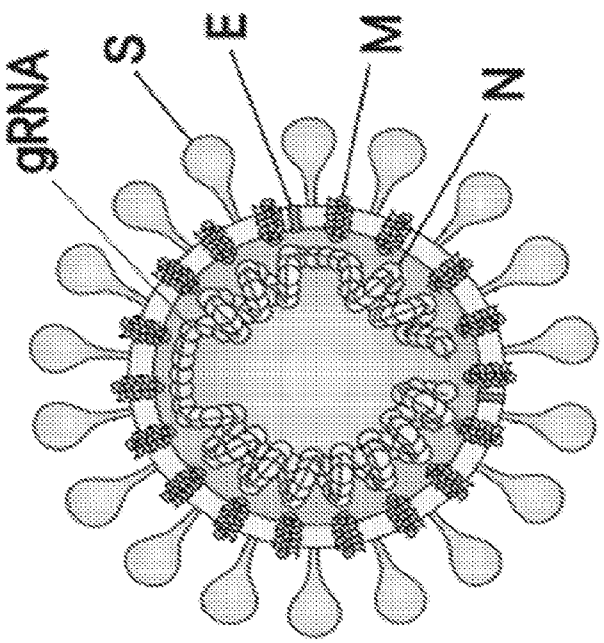

SARS-CoV-2 ORFs
Spike
Nucleocapsid
Envelope
Others
Mass Spectrometry-Based HLA-I and HLA-II binding predictors
High-confidence SARS-CoV-2 predicted epitopes
EPITOPE1
EPITOPE2
EPITOPE3
EPITOPE4
EPITOPE5
EPITOPE6
Computational Validation
High-confidence SARS-CoV-2 predicted epitopes
Reported Positive in VIPR
Experimental Validation
1. Select HLA-A02:01 high-ranking epitopes from N, S, E, M and Orf1ab
2. Induce T cells from 3 healthy donors in the presence of peptides
3. Assess immunogenecity using pMHC multimer staining

FIG. 1A





- 4 structural proteins (S, N, M, E)
- 10+ non-structural open reading frames (ORFs)
- ORF1ab proteolytically cleaved into 16 NSPs

FIG. 1B

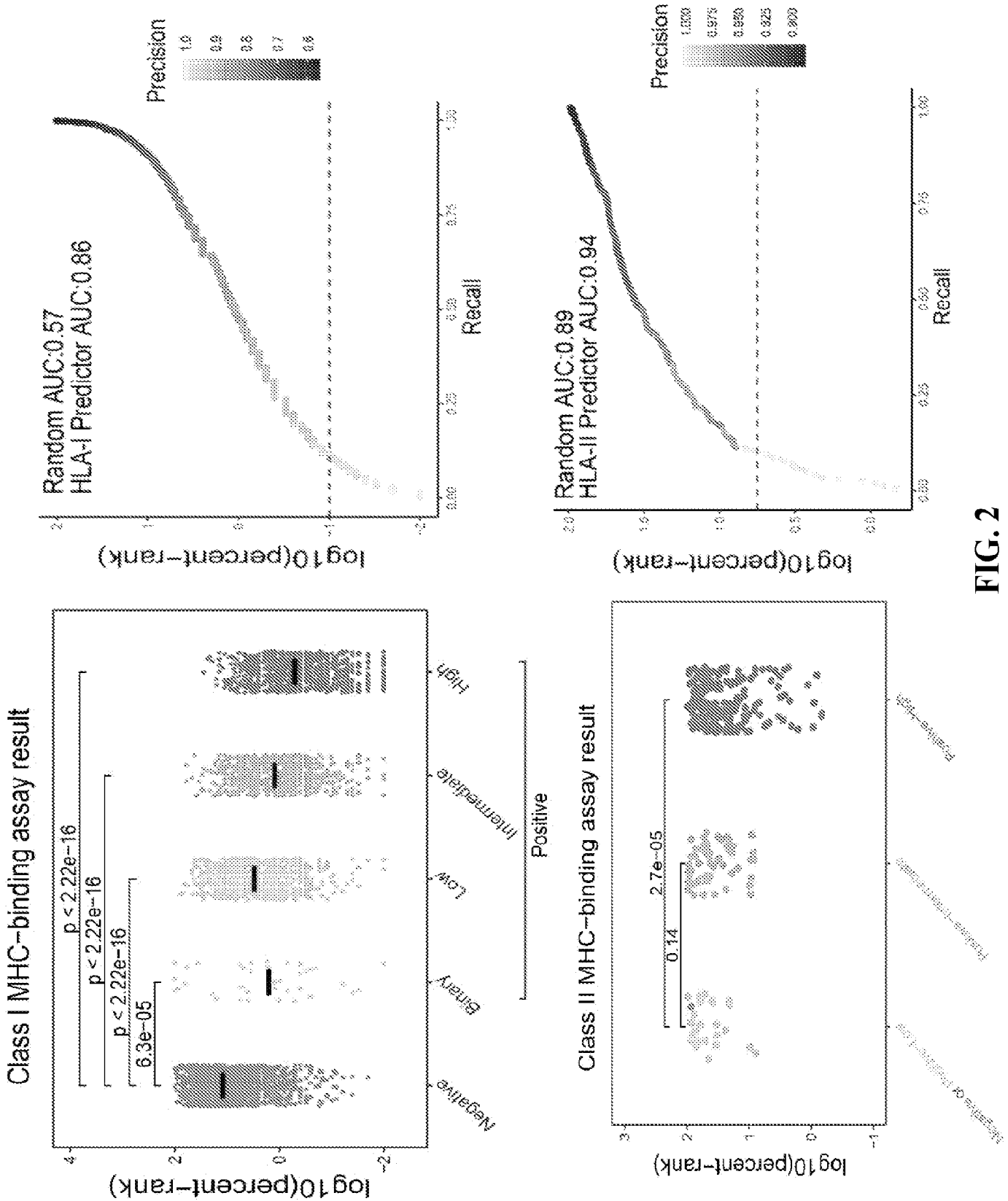

Random AUC:0.57
HLA-I Predictor AUC:0.86
Precision
log10(percent−rank)
Recall
Random AUC:0.89
HLA-II Predictor AUC:0.94
Precision
log10(percent−rank)
Recall
Class I MHC−binding assay result
p < 2.22e−16
p < 2.22e−16
p < 2.22e−16
6.3e−05
log10(percent−rank)
Negative
Binary
Low
Intermediate
High
Positive
Class II MHC−binding assay result
2.7e−05
0.14
log10(percent−rank)

FIG. 2

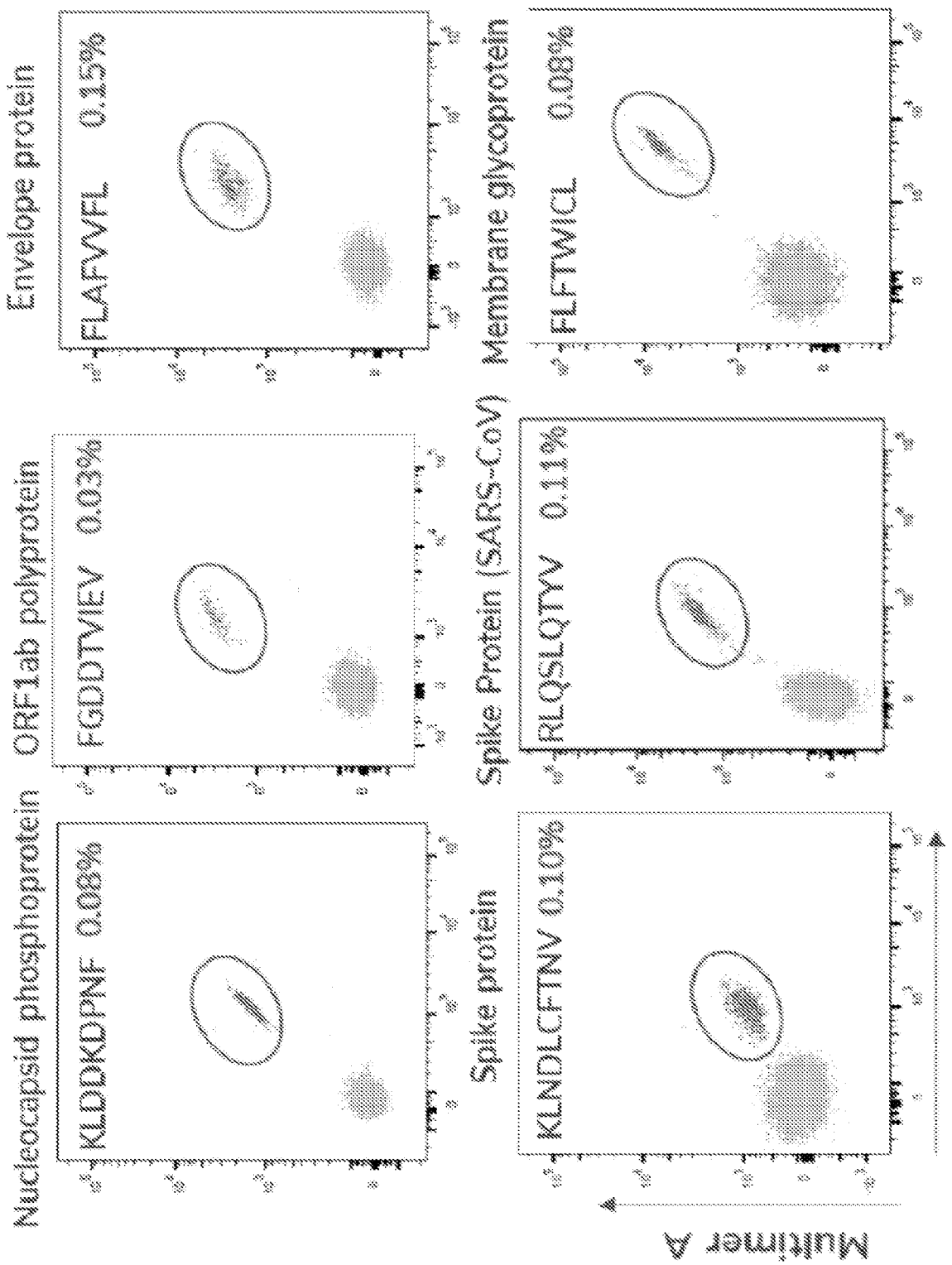

Nucleocapsid phosphoprotein
KLDDKDPNF 0.08%
ORF1ab polyprotein
FGDDTVIEV 0.03%
Envelope protein
FLAFVVFL 0.15%
Spike protein
KLNDLCFTNV 0.10%
Spike Protein (SARS-CoV)
RLQSLQTYV 0.11%
Membrane glycoprotein
FLFTWICL 0.08%
Multimer A
Multimer B

FIG. 3

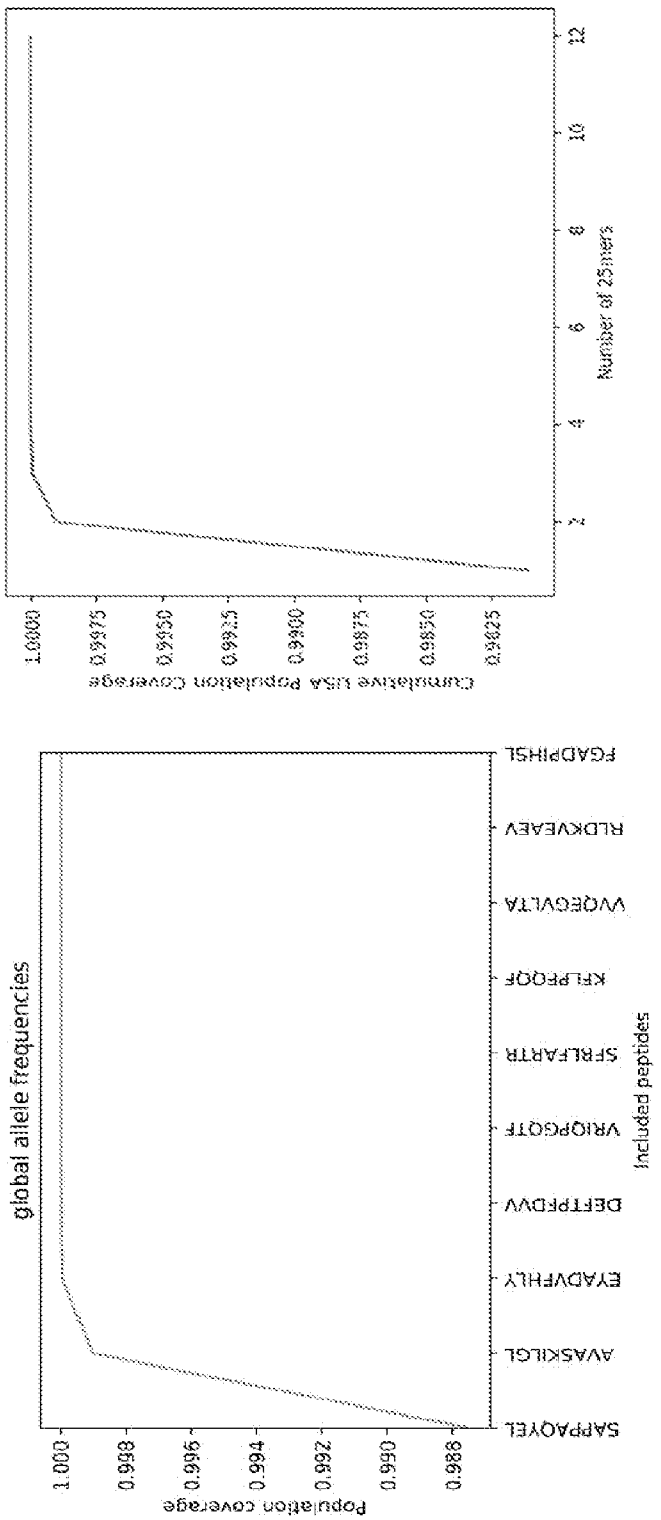

Cumulative USA Population Coverage
1.0000
0.9975
0.9950
0.9925
0.9900
0.9875
0.9850
0.9825
2
4
6
8
10
12
Number of 25mers
global allele frequencies
Population coverage
1.000
0.998
0.996
0.994
0.992
0.990
0.988
SAPPAQYEL
AVASKILGL
EYADVFHLY
DEFTPFDVV
VRIQPGQTF
SFRLFARTR
KFLPFQQF
VVQEGVLTA
RLDKVEAEV
FGADPIHSL
Included peptides

FIG. 4A

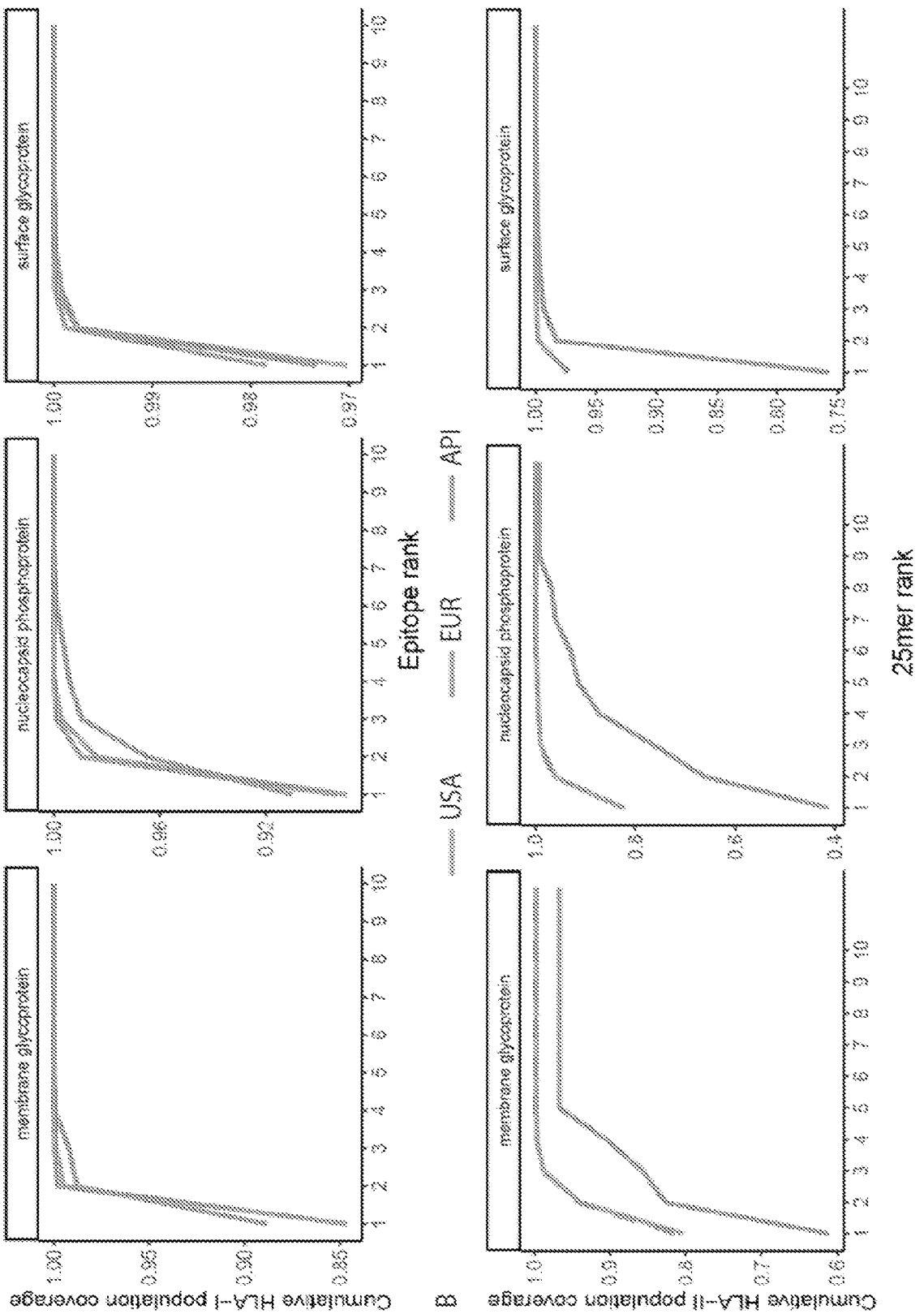

membrane glycoprotein
nucleocapsid phosphoprotein
surface glycoprotein
Cumulative HLA-I population coverage
Cumulative HLA-II population coverage
Epitope rank
25mer rank
USA
EUR
API

FIG. 4B

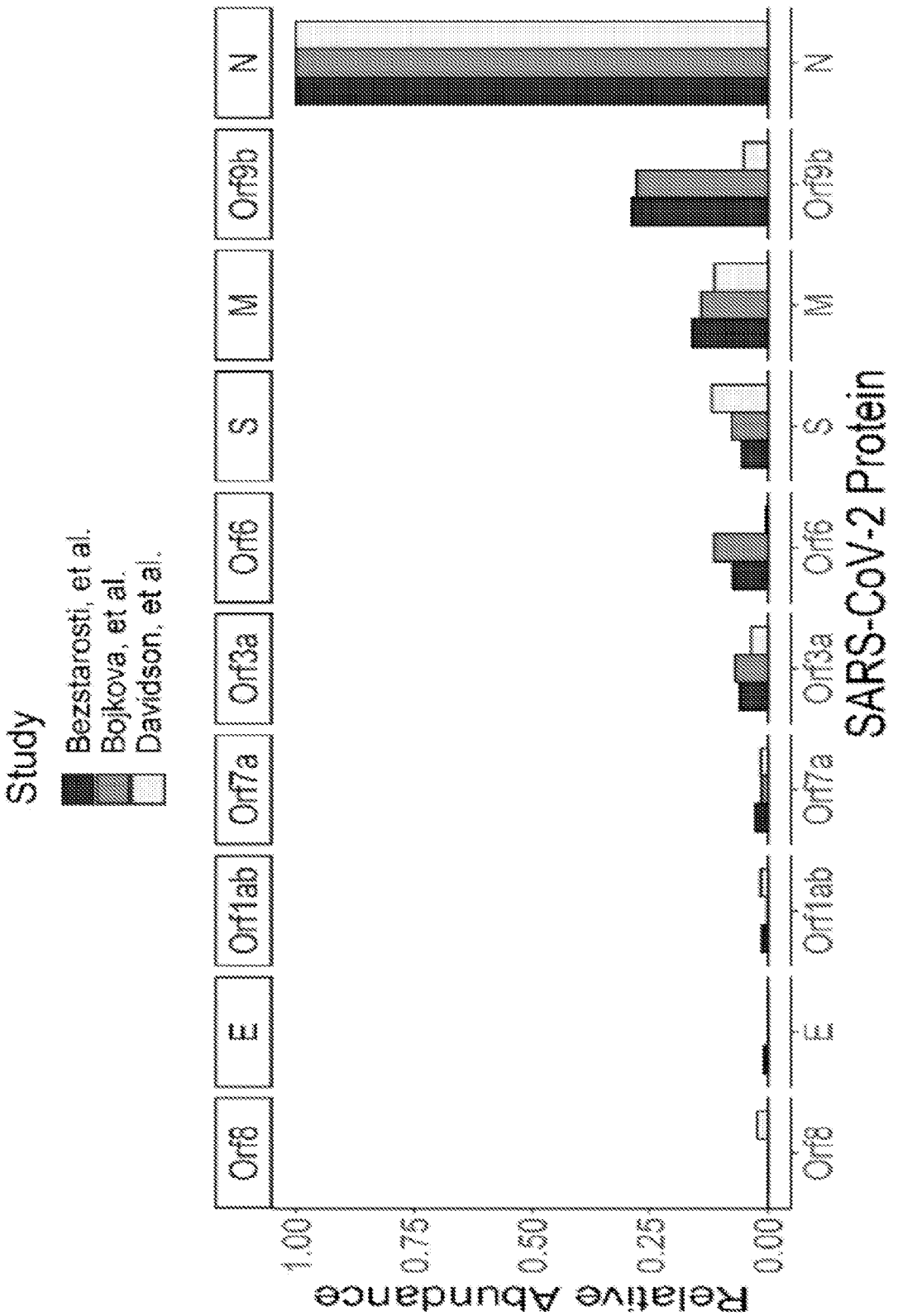

Study
Bezstarosti, et al.
Bojkova, et al.
Davidson, et al.
Orf8
E
Orf1ab
Orf7a
Orf3a
Orf6
S
M
Orf9b
N
Relative Abundance
1.00
0.75
0.50
0.25
0.00
SARS-CoV-2 Protein

FIG. 5

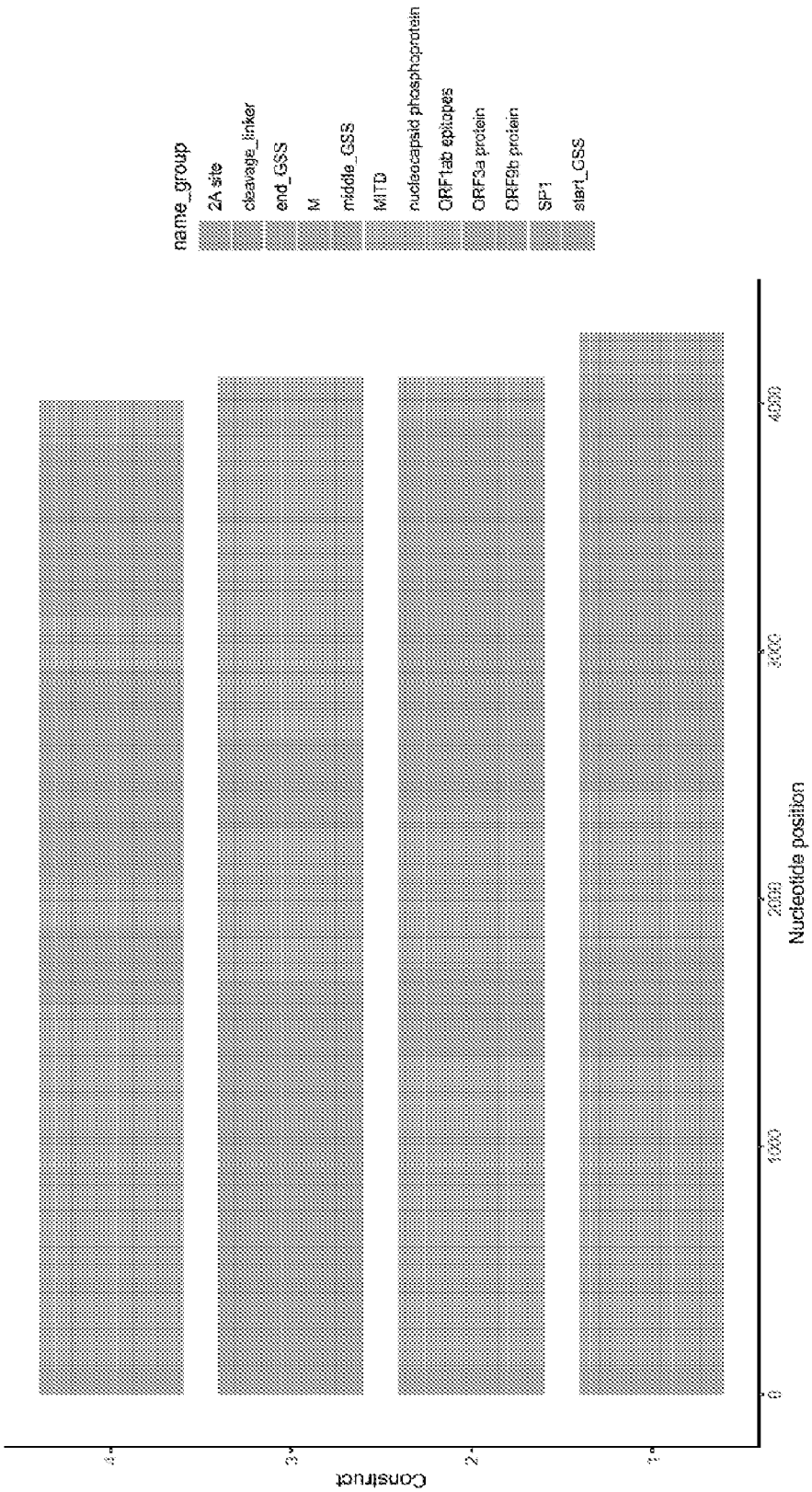

name_group
2A site
cleavage_linker
end_GSS
M
middle_GSS
MITD
nucleocapsid phosphoprotein
ORF1ab epitopes
ORF3a protein
ORF9b protein
SP1
start_GSS
Construct
4
3
2
1
0
1000
2000
3000
4000
Nucleotide position

FIG. 6A

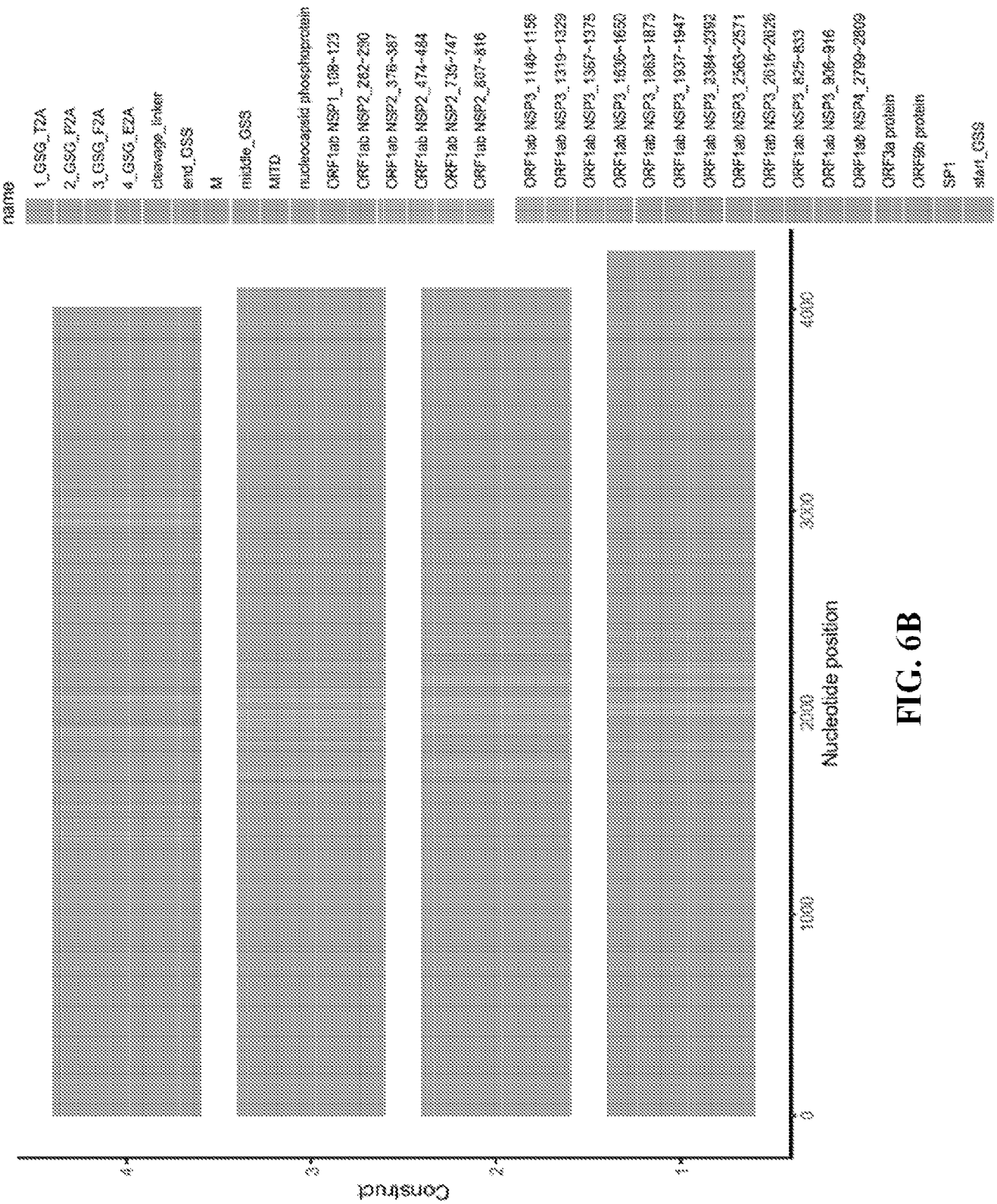

name
1_GSG_T2A
2_GSG_P2A
3_GSG_F2A
4_GSG_E2A
cleavage_linker
end_GSS
M
middle_GSS
MITD
nucleocapsid phosphoprotein
ORF1ab NSP1_ 108~123
ORF1ab NSP2_ 282~290
ORF1ab NSP2_ 376~387
ORF1ab NSP2_ 474~484
ORF1ab NSP2_ 735~747
ORF1ab NSP2_ 807~816
ORF1ab NSP3_ 1140~1156
ORF1ab NSP3_ 1319~1329
ORF1ab NSP3_ 1367~1375
ORF1ab NSP3_ 1636~1650
ORF1ab NSP3_ 1863~1873
ORF1ab NSP3_ 1937~1947
ORF1ab NSP3_ 3384~3392
ORF1ab NSP3_ 2563~2571
ORF1ab NSP3_ 2616~2626
ORF1ab NSP3_ 825~833
ORF1ab NSP3_ 806~816
ORF1ab NSP4_ 2799~2809
ORF3a protein
ORF9b protein
SP1
start_GSS
Construct
4
3
2
1
0
1000
2000
3000
4000
Nucleotide position

FIG. 6B

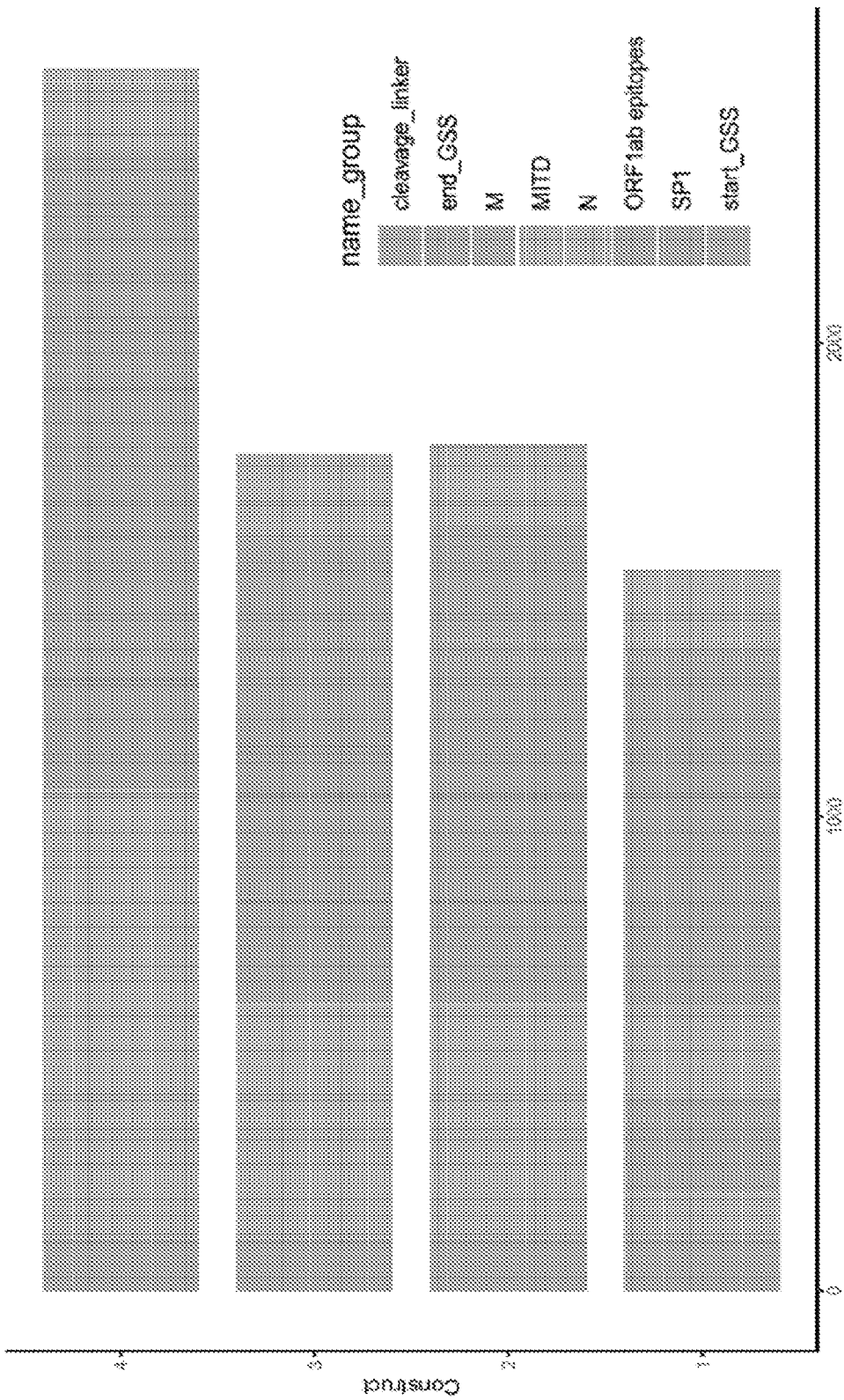

name_group
cleavage_linker
end_GSS
M
MITD
N
ORF1ab epitopes
SP1
start_GSS
Construct
4
3
2
1
0
1000
2000
Nucleotide position

FIG. 7A

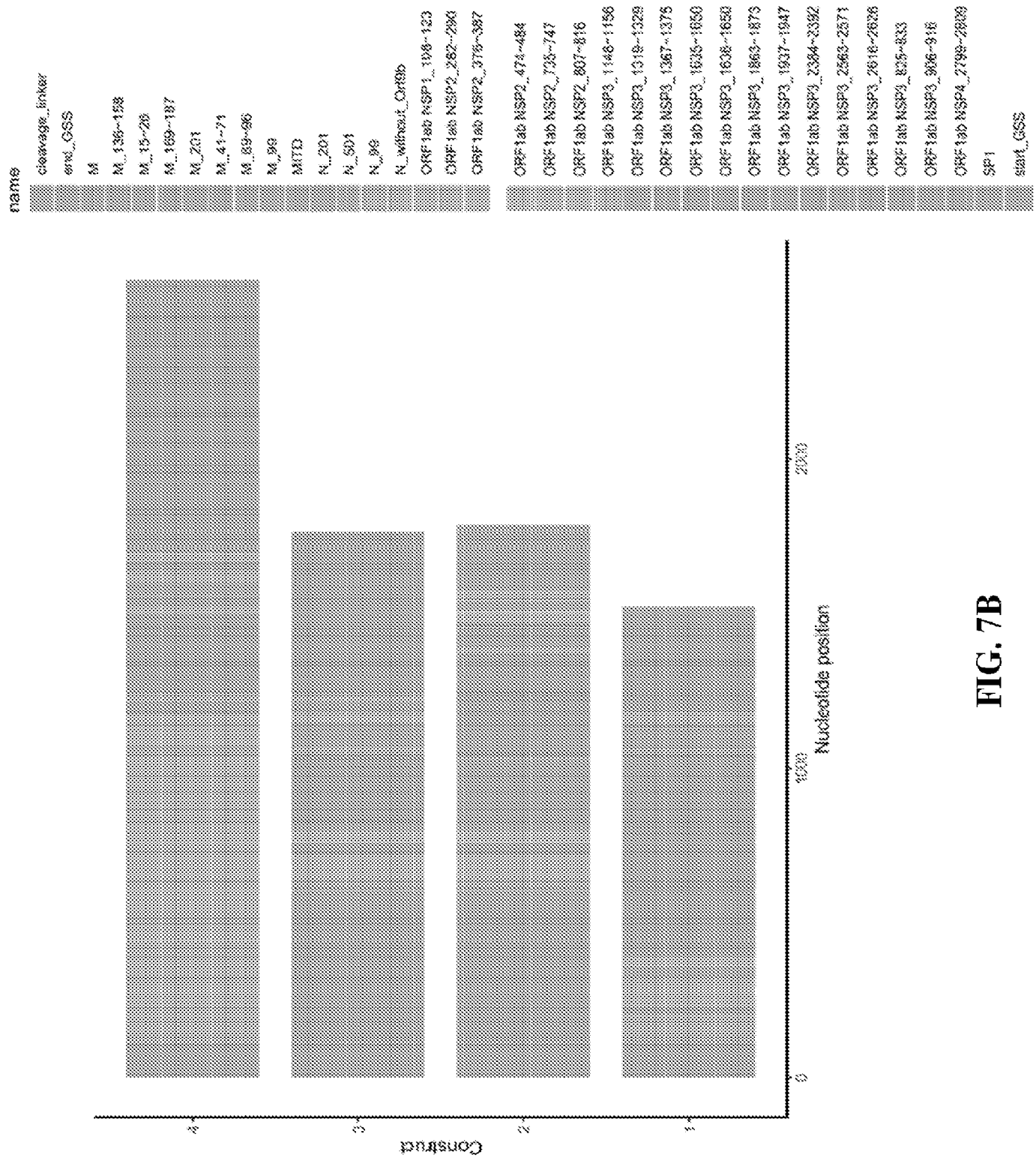

name
cleavage_linker
end_GSS
M
M_136~158
M_15~26
M_169~187
M_201
M_41~71
M_89~96
M_99
MITD
N_201
N_501
N_96
N_without_ORF9b
ORF1ab NSP1_108~123
ORF1ab NSP2_282~290
ORF1ab NSP2_376~387
ORF1ab NSP2_474~484
ORF1ab NSP2_725~747
ORF1ab NSP2_807~816
ORF1ab NSP3_1148~1156
ORF1ab NSP3_1319~1329
ORF1ab NSP3_1367~1375
ORF1ab NSP3_1635~1650
ORF1ab NSP3_1638~1650
ORF1ab NSP3_1863~1873
ORF1ab NSP3_1937~1947
ORF1ab NSP3_2384~2392
ORF1ab NSP3_2563~2571
ORF1ab NSP3_2616~2626
ORF1ab NSP3_825~833
ORF1ab NSP3_906~916
ORF1ab NSP4_2799~2809
SP1
start_GSS
Construct
4
3
2
1
0
1000
2000
Nucleotide position

FIG. 7B

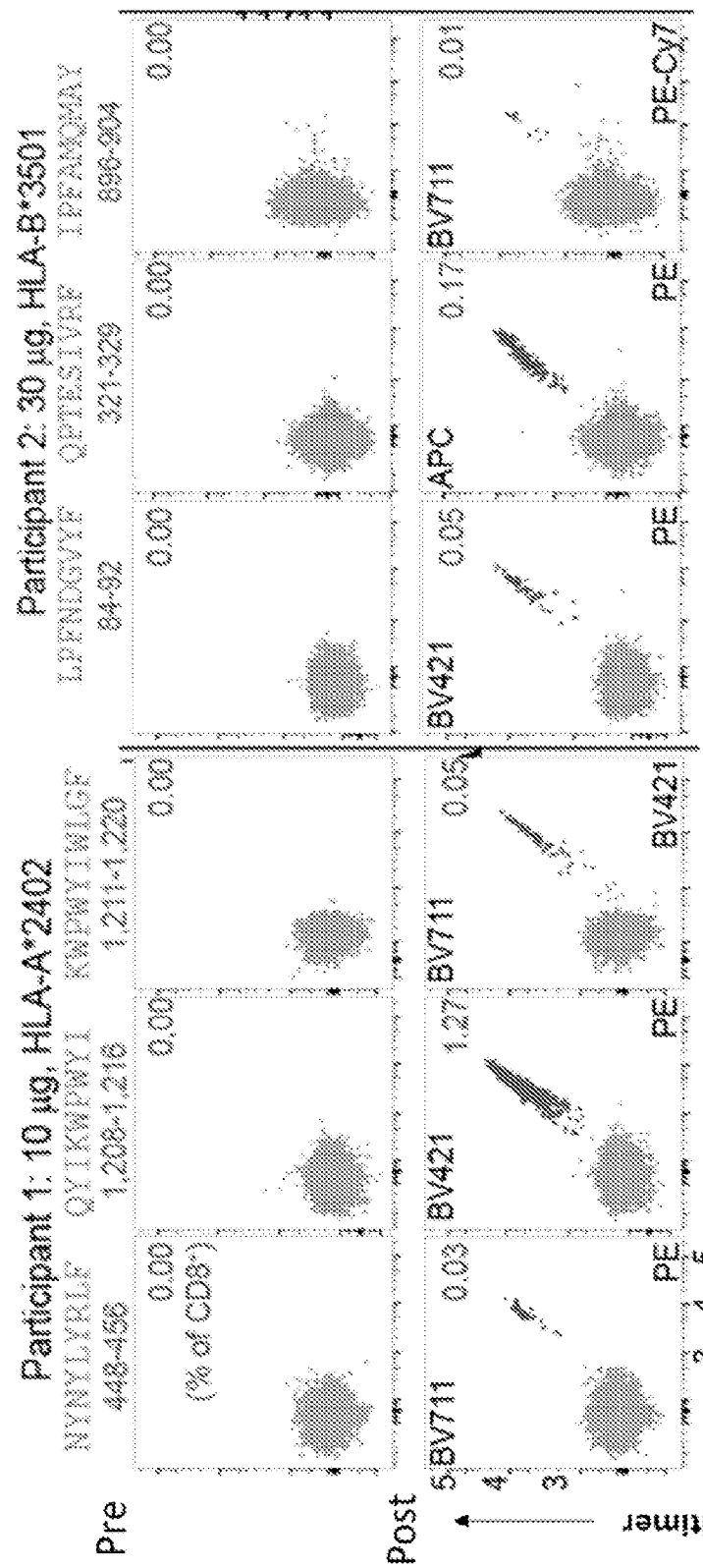

Participant 1: 10 µg, HLA-A*2402
NYNYLYRLF
448-456
QYIKWPWYI
1208-1216
KWPWYIWLGF
1211-1220
Participant 2: 30 µg, HLA-B*3501
LPRNDGVYF
84-92
QPTESIVRF
321-329
IPFAMQMAY
696-704
Pre
Post
(% of CD8+)
0.00
0.03
1.27
0.05
0.17
0.01
BV711
BV421
PE
PE-Cy7
Multimer
3
4
5

FIG. 8Ai

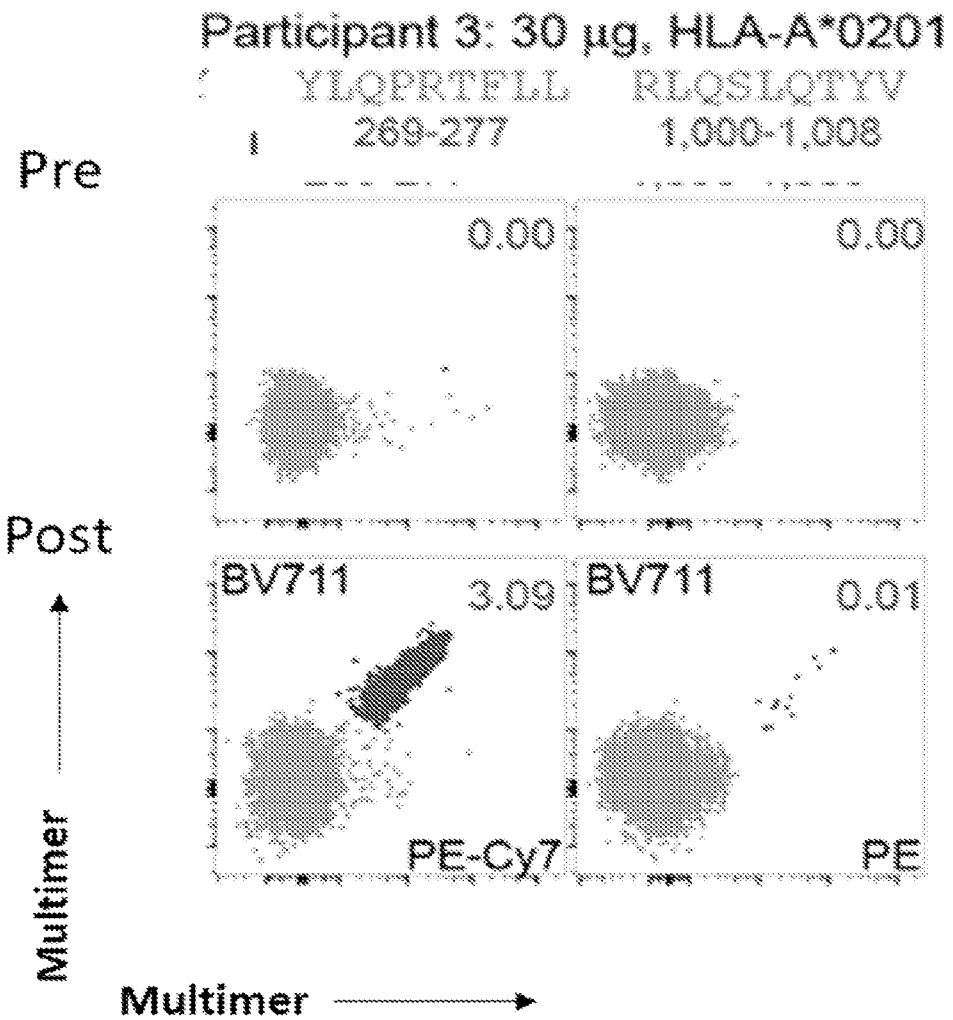

Participant 3: 30 µg, HLA-A*0201
YLQPRTFLL
269-277
RLQSLQTYV
1,000-1,008
Pre
Post
0.00
0.00
BV711
3.09
PE-Cy7
BV711
0.01
PE
Multimer
Multimer

FIG. 8Aii

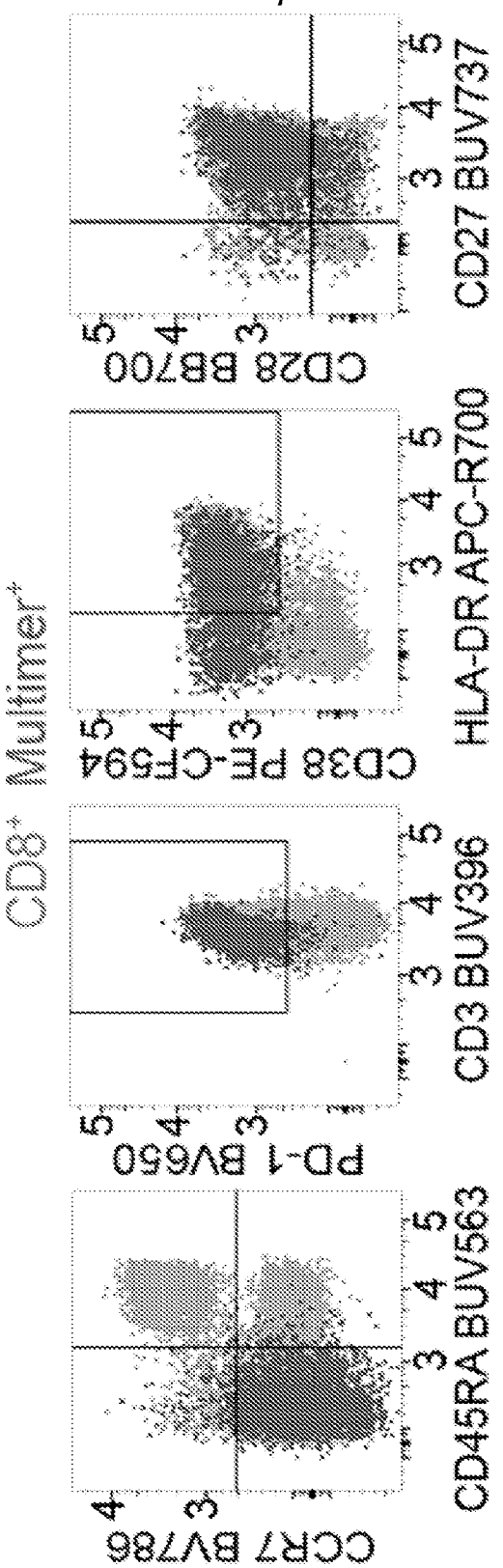

CD8+ Multimer+
PD-1 BV650
CD3 BUV396
CD38 PE-CF594
HLA-DR APC-R700
CD28 BB700
CD27 BUV737
CCR7 BV786
CD45RA BUV563

FIG. 8B

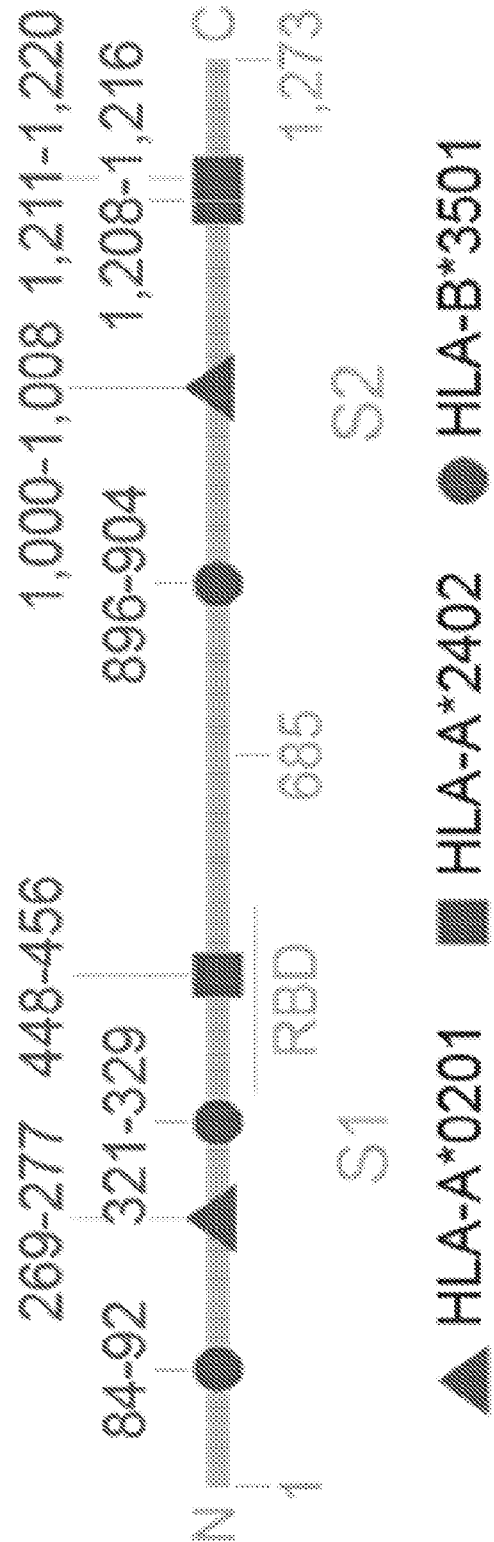

N
1
84-92
269-277
321-329
448-456
RBD
685
S1
S2
896-904
1,000-1,008
1,208-1,216
1,211-1,220
C
1,273
HLA-A*0201
HLA-A*2402
HLA-B*3501

FIG. 8C

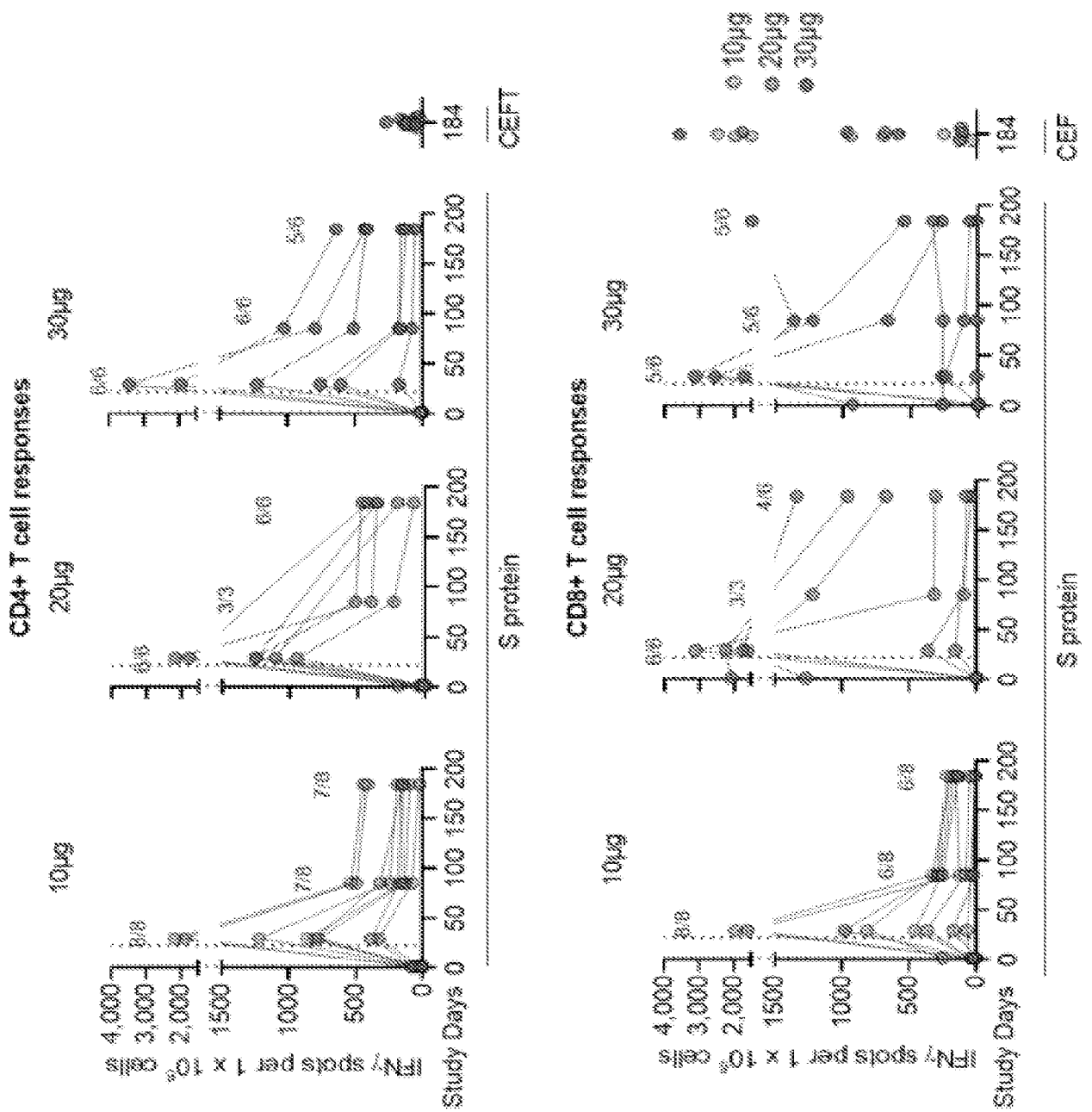

CD4+ T cell responses
CD8+ T cell responses
10µg
20µg
30µg
IFNγ spots per 1 x 10^6 cells
Study Days
S protein
CEF
CEFT
10µg
20µg
30µg

FIG. 8D

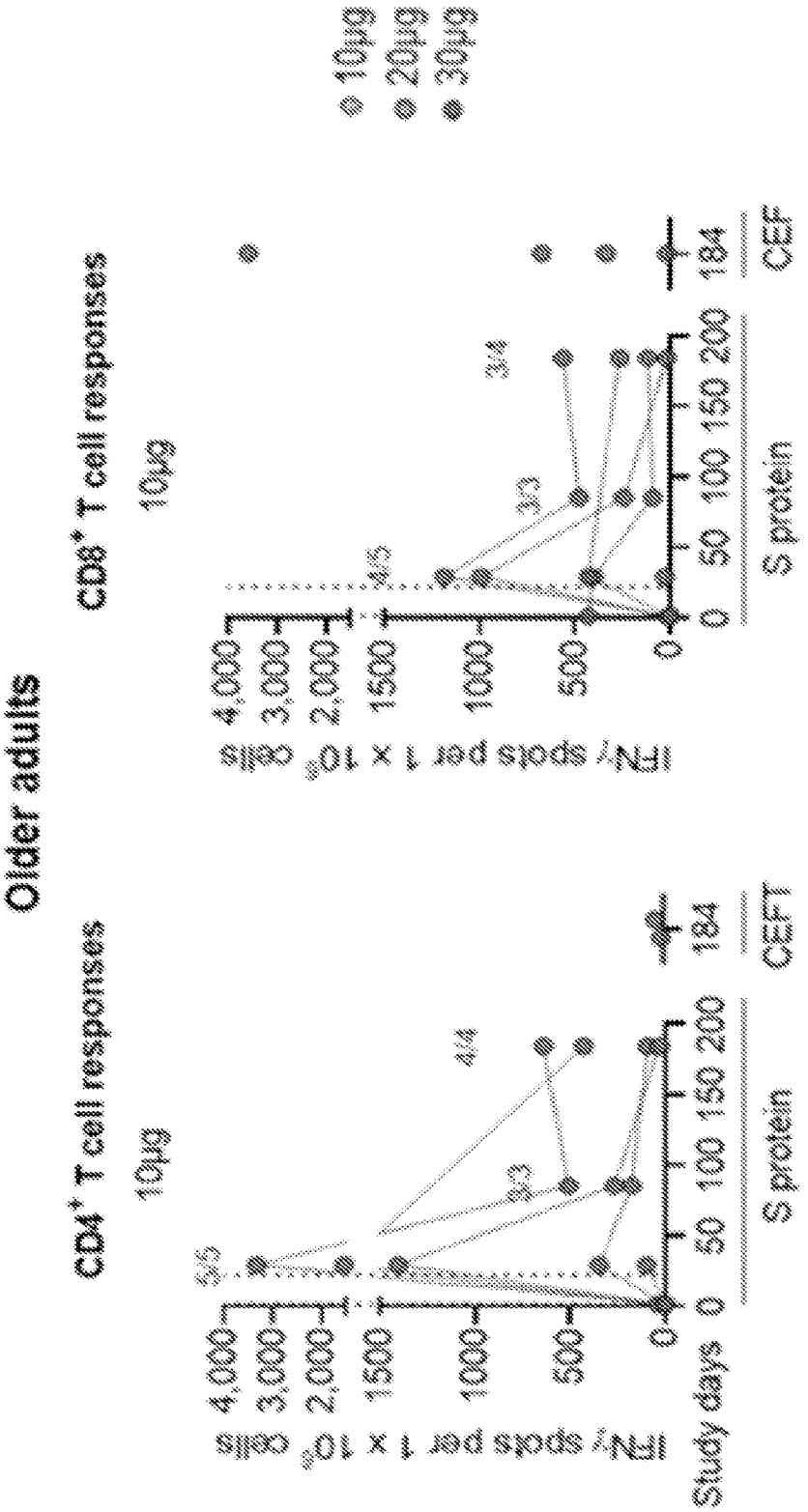

Older adults
CD4+ T cell responses
CD8+ T cell responses
10μg
10μg
20μg
30μg
IFNγ spots per 1 x 10^6 cells
4,000
3,000
2,000
1500
1000
500
0
5/5
4/4
3/3
3/4
4/5
Study days
0
50
100
150
200
184
S protein
CEF
CEFT

FIG. 8E

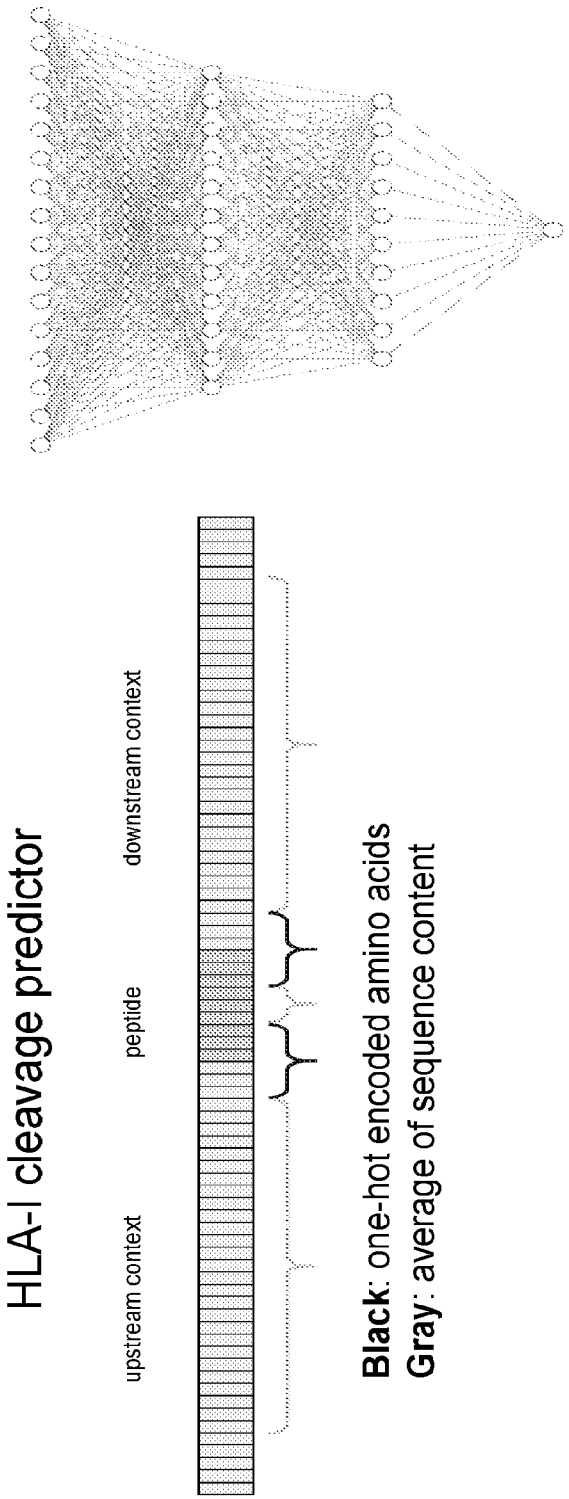
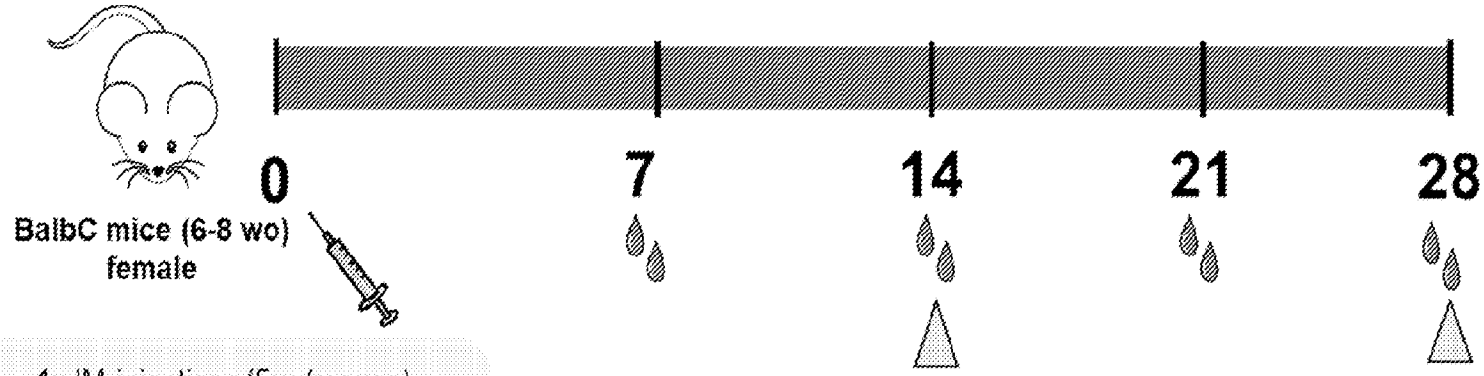

HLA-I cleavage predictor
upstream context
peptide
downstream context
Black: one-hot encoded amino acids
Gray: average of sequence content

FIG. 9



- 1x IM injections (5ug/mouse)
- Vector Backbone: modified
- All 4 strings
- viral sec and TM

Assay readouts:

1. ELISPOT (d14/d28 splenoyctes) (Tiled 15mer with 11 aa overlap)
2. Recalled cytokine responses (d28 splenocytes)
3. T cell subsets present in circulation after vaccination (d7, d14, d21, d28)

5 groups (16 animals/8-10 take down at d14/8-10 at d28)

Viral secretory domain (aa1-19) and viral TM domain (cytoplasmic tail)

Key

Low volume blood draw

Animal harvest (spleen, dLN)

FIG. 10A

0
7
14
21
28
HLA-A2.tg mice (6-8 wo) female
1x IM injections (5ug/mouse)
Vector Backbone: modified
All 4 CorVac 2.0 strings
viral sec and TM
5 groups (16 animals/8-10 take down at d14/8-10 at d28)
Viral secretory domain (aa1-19) and viral TM domain (cytoplasmic tail)
Assay readouts:
1. ELISPOT (d28 splenoyctes) (Tiled 15mer with 11 aa overlap)
2. Serum antibody responses against nucleocapsid
3. T cell subsets present in circulation after vaccination (d7, d14, d21, d28)
Key
Low volume blood draw
Animal harvest (spleen, dLN)

FIG. 10B

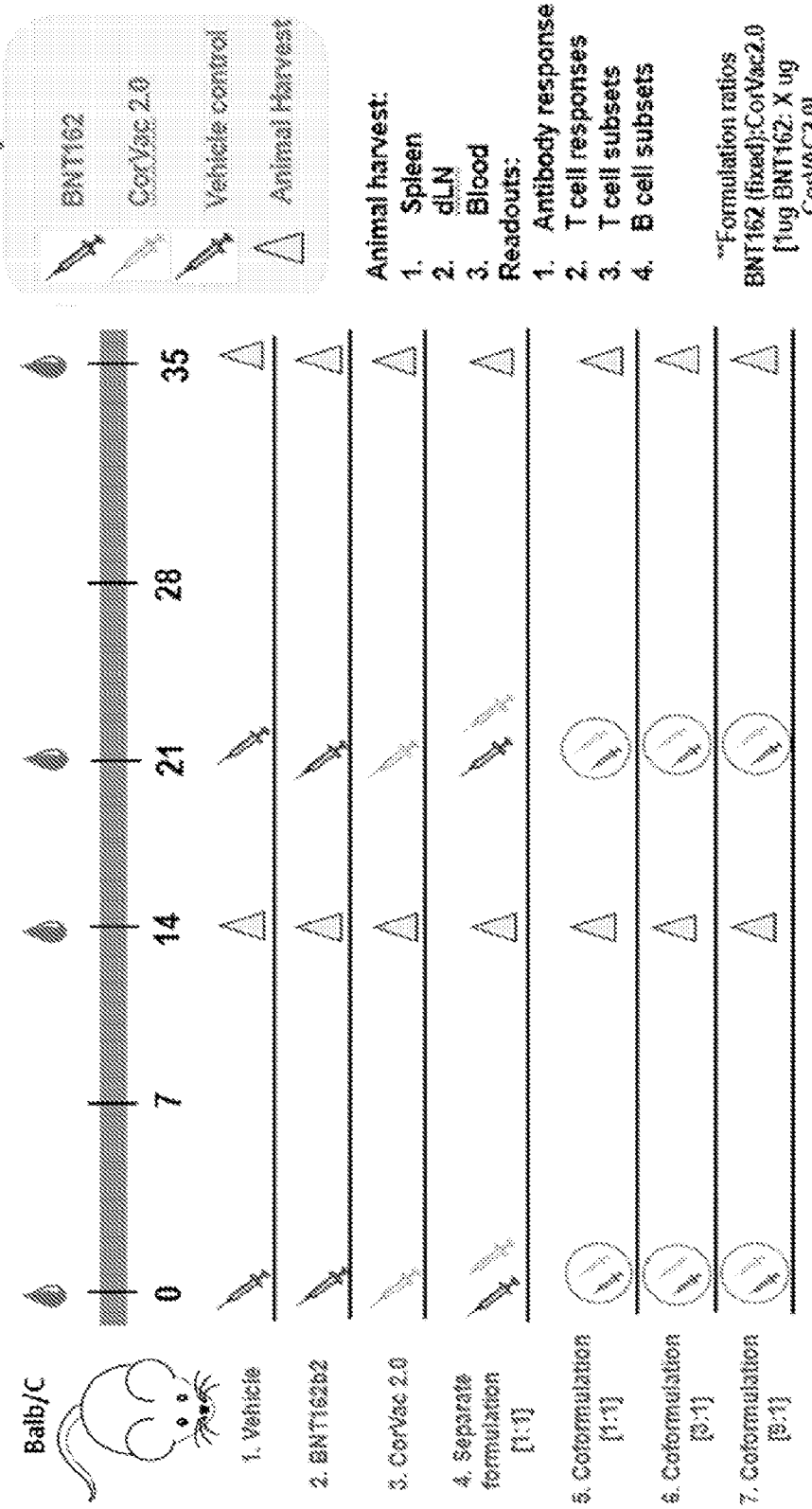

Key
BNT162
CorVac 2.0
Vehicle control
Animal Harvest
Animal harvest:
1. Spleen
2. dLN
3. Blood
Readouts:
1. Antibody response
2. T cell responses
3. T cell subsets
4. B cell subsets
**Formulation ratios
BNT162 (fixed):CorVac2.0
[1ug BNT162: X ug CorVAC2.0]
Balb/C
0
7
14
21
28
35
1. Vehicle
2. BNT162b2
3. CorVac 2.0
4. Separate formulation [1:1]
5. Coformulation [1:1]
6. Coformulation [5:1]
7. Coformulation [9:1]

FIG. 11A

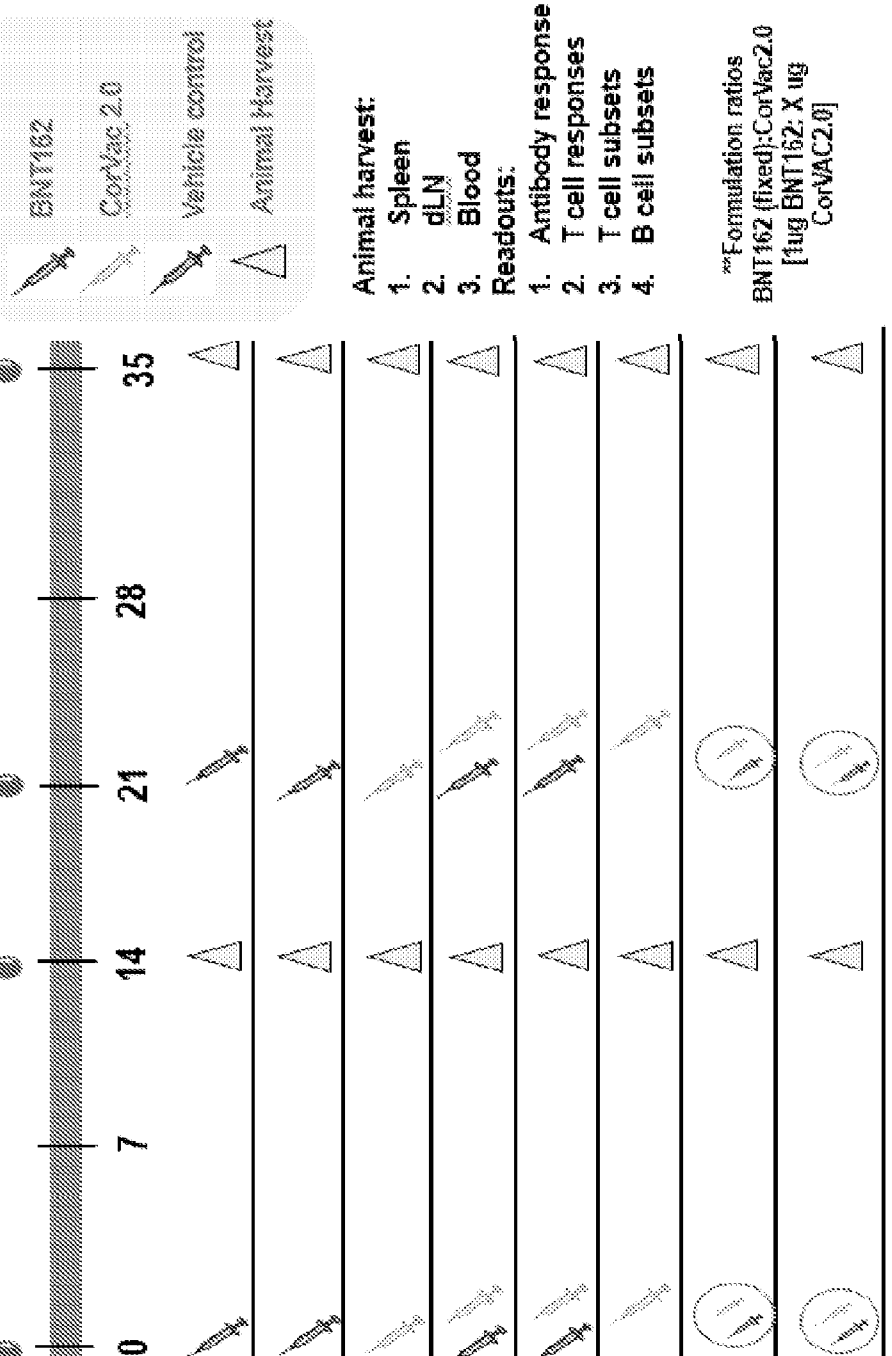

Key
BNT162
CorVac 2.0
Vehicle control
Animal Harvest
Animal harvest:
1. Spleen
2. dLN
3. Blood
Readouts:
1. Antibody response
2. T cell responses
3. T cell subsets
4. B cell subsets
**Formulation ratios
BNT162 (fixed):CorVac2.0
[1ug BNT162: X ug
CorVAC2.0]
HLA.A2Tg
0
7
14
21
28
35
1. Vehicle
2. BNT162b2
3. CorVac 2.0 1ug
4. Separate [3:1]
5. Separate [1:1]
6. CorVac 2.0
0.3ug
7. Coformulation
[3:1]
8. Coformulation
[1:1]

FIG. 11B

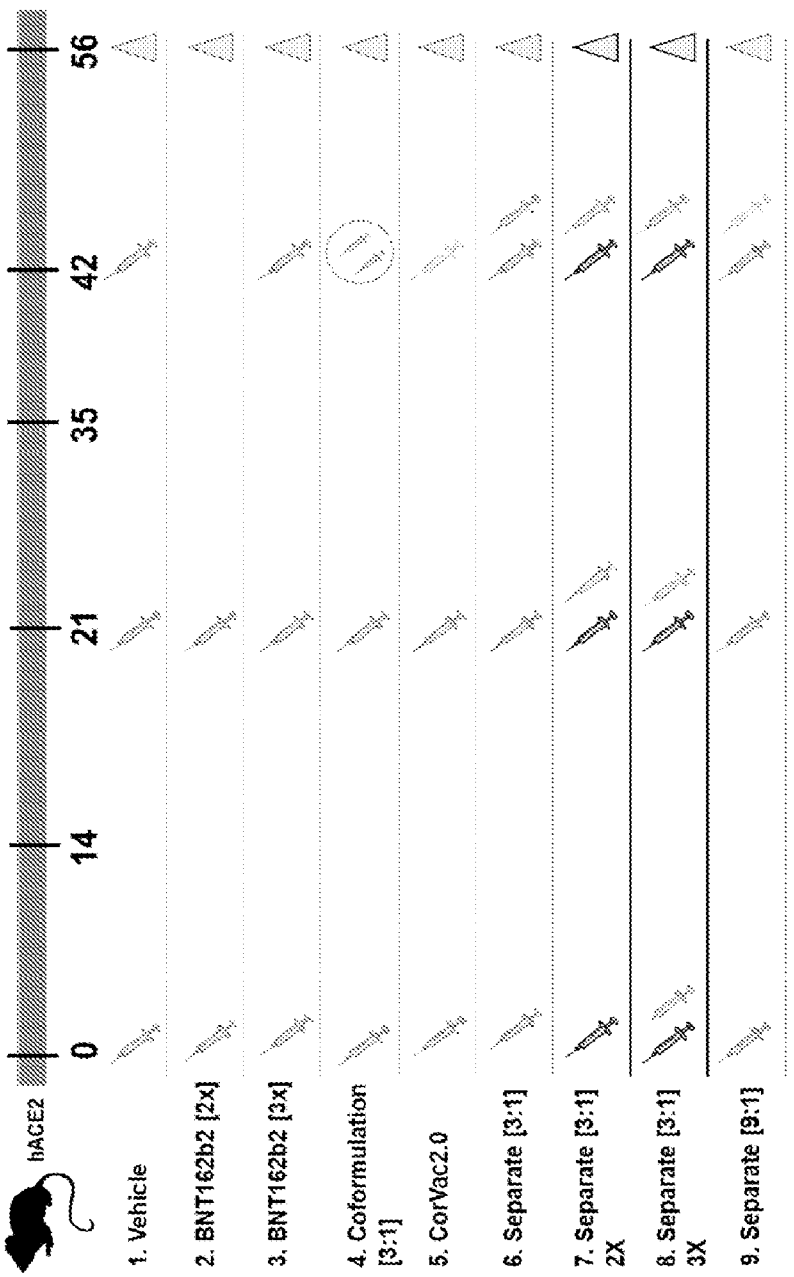

Key
BNT162
CorVac 2.0
Vehicle control
Animal Harvest
Animal harvest:
1. Spleen
2. diLN
3. Blood
Readouts:
1. Antibody response
2. T cell responses
3. T cell subsets
4. B cell subsets
**Formulation ratios
BNT162 (fixed):CorVac2.0
[1ug BNT162: X ug CorVAC2.0]
hACE2
0
14
21
35
42
56
1. Vehicle
2. BNT162b2 [2x]
3. BNT162b2 [3x]
4. Coformulation [3:1]
5. CorVac2.0
6. Separate [3:1]
7. Separate [3:1] 2X
8. Separate [3:1] 3X
9. Separate [9:1]

FIG. 11C

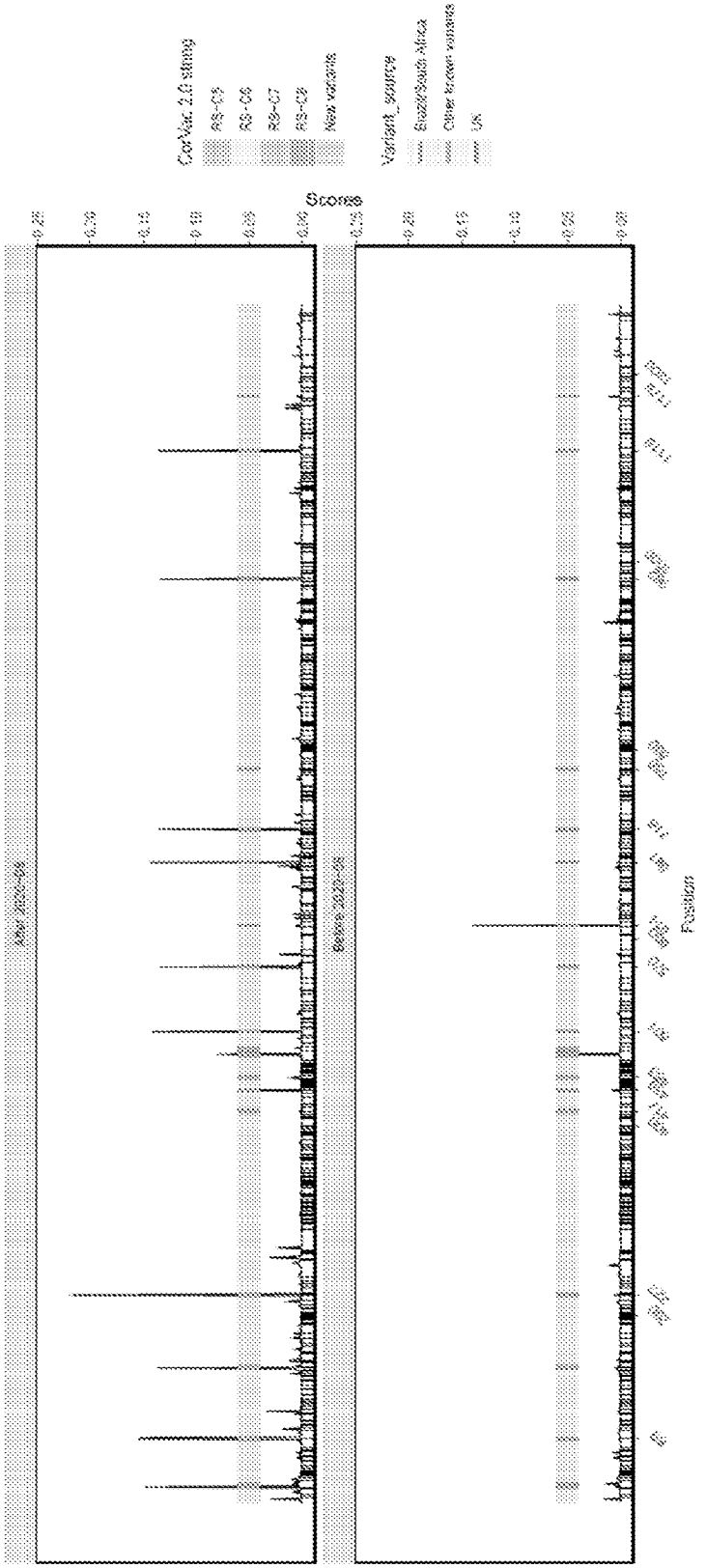

CoVac 2.0 string
RS-03
RS-06
RS-07
RS-09
New variants
Variant_source
Brazil/South Africa
Other known variants
UK
Score
Position
Alpha 2020-09
Beta 2020-09

FIG. 12A

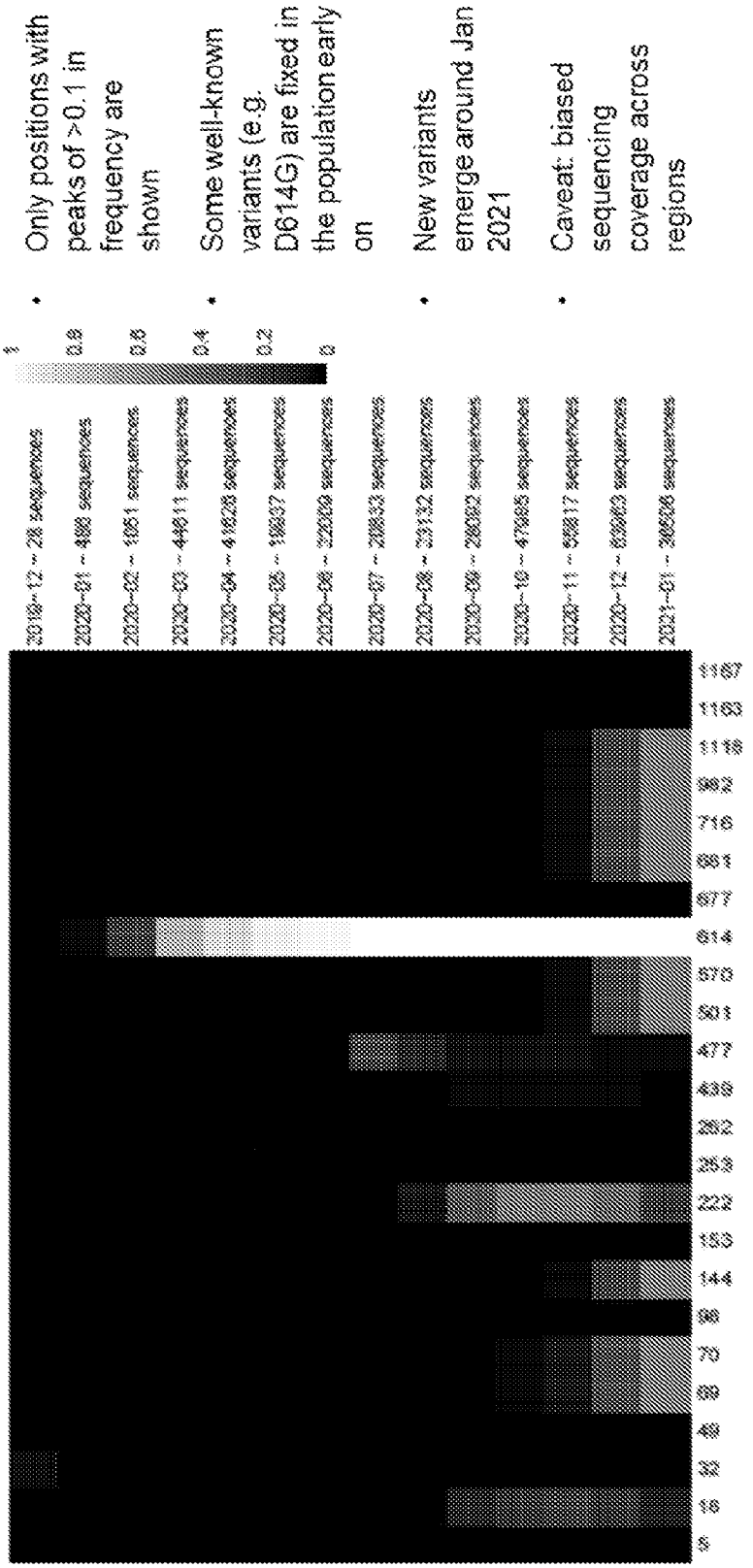

Only positions with peaks of >0.1 in frequency are shown
Some well-known variants (e.g. D614G) are fixed in the population early on
New variants emerge around Jan 2021
Caveat: biased sequencing coverage across regions
f
0.8
0.6
0.4
0.2
0
2019-12 -- 28 sequences
2020-01 -- 488 sequences
2020-02 -- 1051 sequences
2020-03 -- 44611 sequences
2020-04 -- 415628 sequences
2020-05 -- 198837 sequences
2020-06 -- 322066 sequences
2020-07 -- 208433 sequences
2020-08 -- 331132 sequences
2020-09 -- 286002 sequences
2020-10 -- 470485 sequences
2020-11 -- 558417 sequences
2020-12 -- 693463 sequences
2021-01 -- 366026 sequences
5
16
42
49
69
72
96
144
153
222
253
262
439
477
501
570
614
677
681
716
982
1116
1163
1187

FIG. 12B

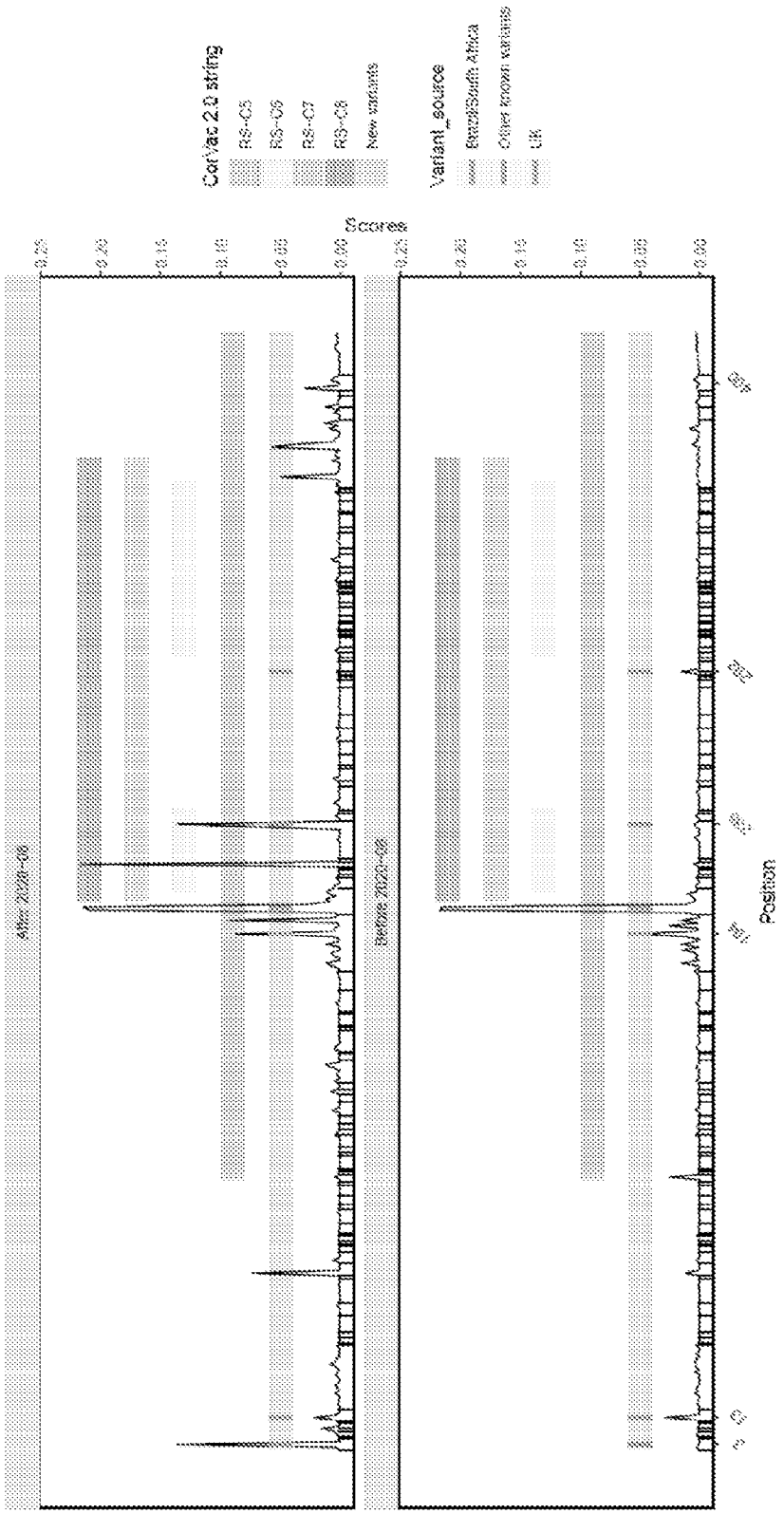

CoVac2.0 string
RS-05
RS-06
RS-07
RS-08
New variants
Variant_source
Brazil/South Africa
Other known variants
UK
Scores
After 2020-06
Before 2020-06
Position

FIG. 13A

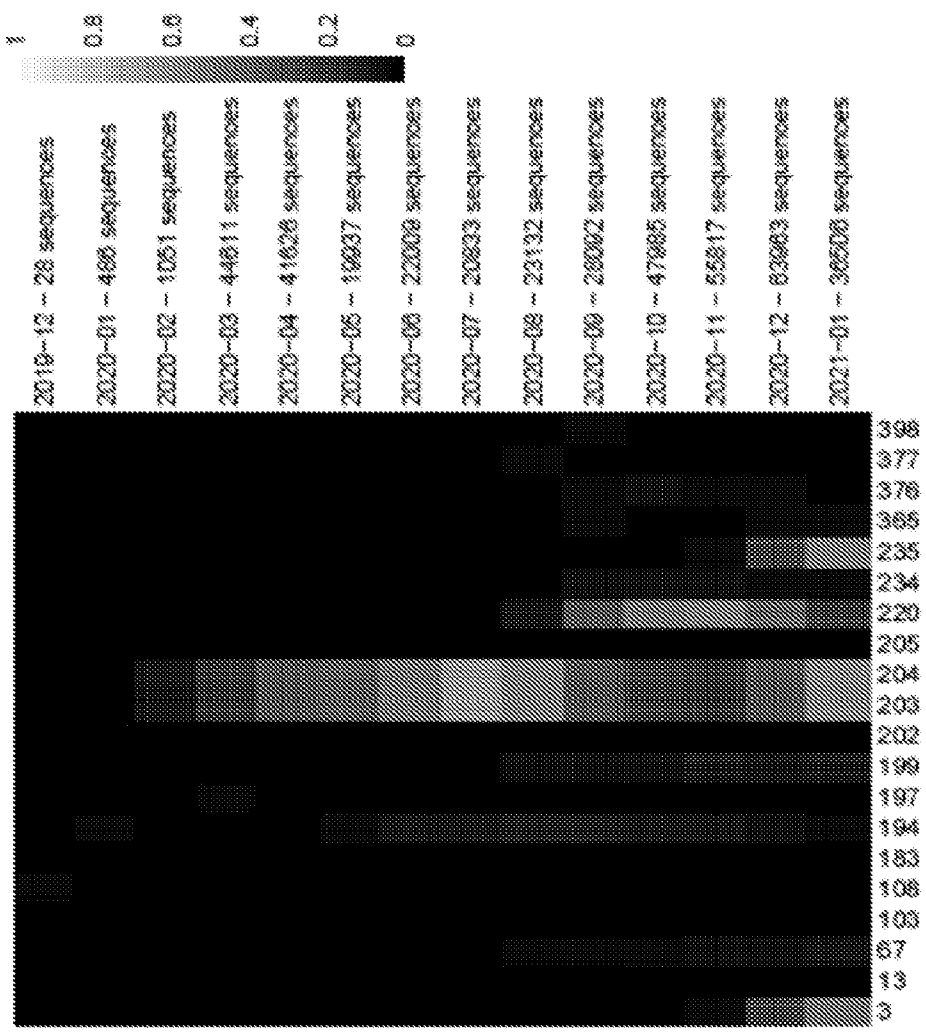

Only positions with peaks of >0.1 in frequency are shown
Early variants (e.g. 203-204 deletion) can be outcompeted by other variants (e.g. at position 220) but co-mutations (e.g. S235F, D3L) may have added competitive advantage
Caveat: biased sequencing coverage across regions
1
0.8
0.6
0.4
0.2
0
2019-12 ~ 28 sequences
2020-01 ~ 466 sequences
2020-02 ~ 1051 sequences
2020-03 ~ 44811 sequences
2020-04 ~ 414626 sequences
2020-05 ~ 196837 sequences
2020-06 ~ 220009 sequences
2020-07 ~ 202833 sequences
2020-08 ~ 231132 sequences
2020-09 ~ 280062 sequences
2020-10 ~ 479885 sequences
2020-11 ~ 558217 sequences
2020-12 ~ 639803 sequences
2021-01 ~ 365508 sequences
3
13
67
188
196
197
198
202
203
204
205
220
234
235
236
377
378

FIG. 13B

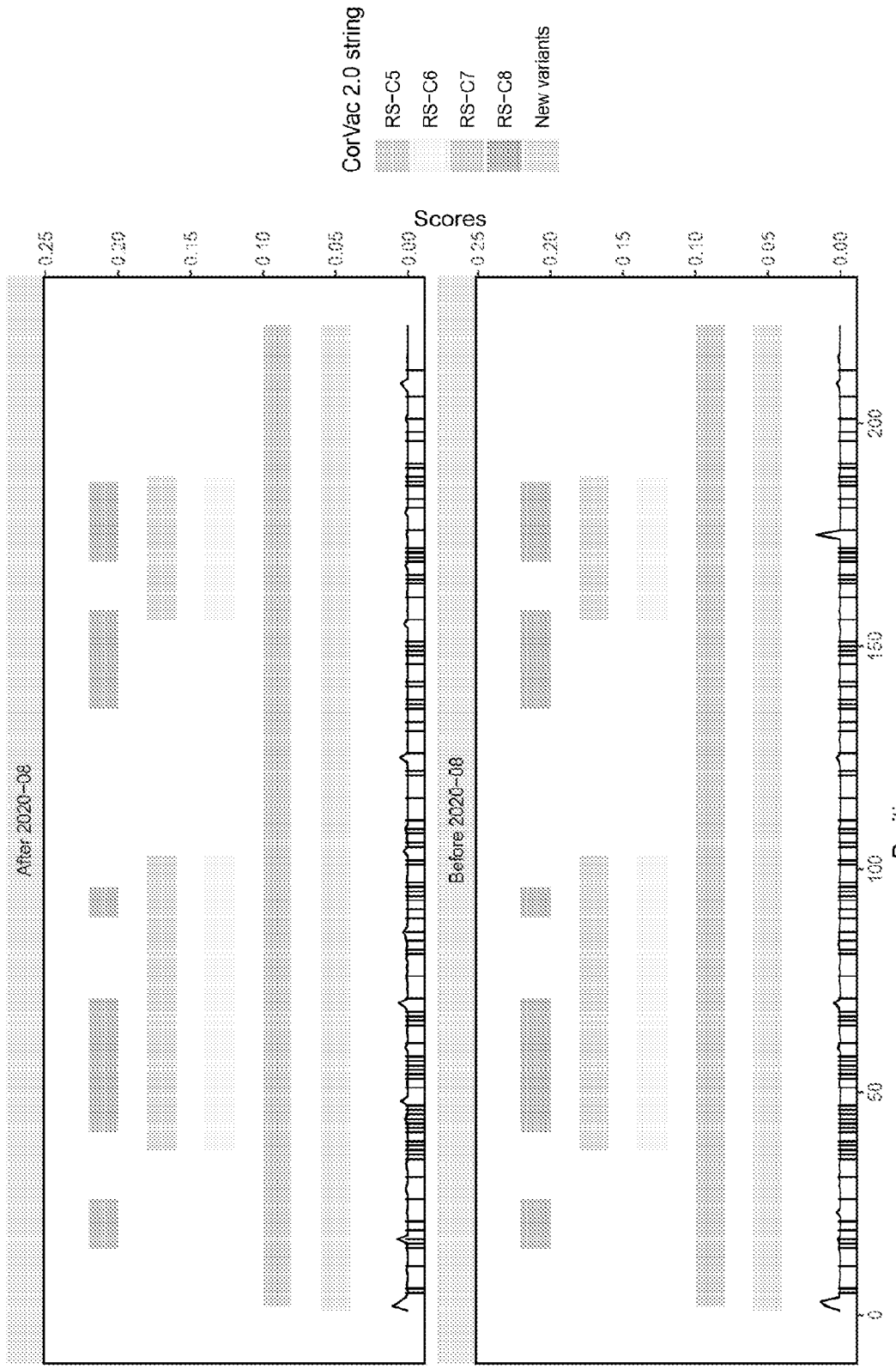

CorVac 2.0 string
RS-C5
RS-C6
RS-C7
RS-C8
New variants
Scores
After 2020-08
Before 2020-08
0.25
0.20
0.15
0.10
0.05
0.00
0
50
100
150
200
Position

FIG. 14

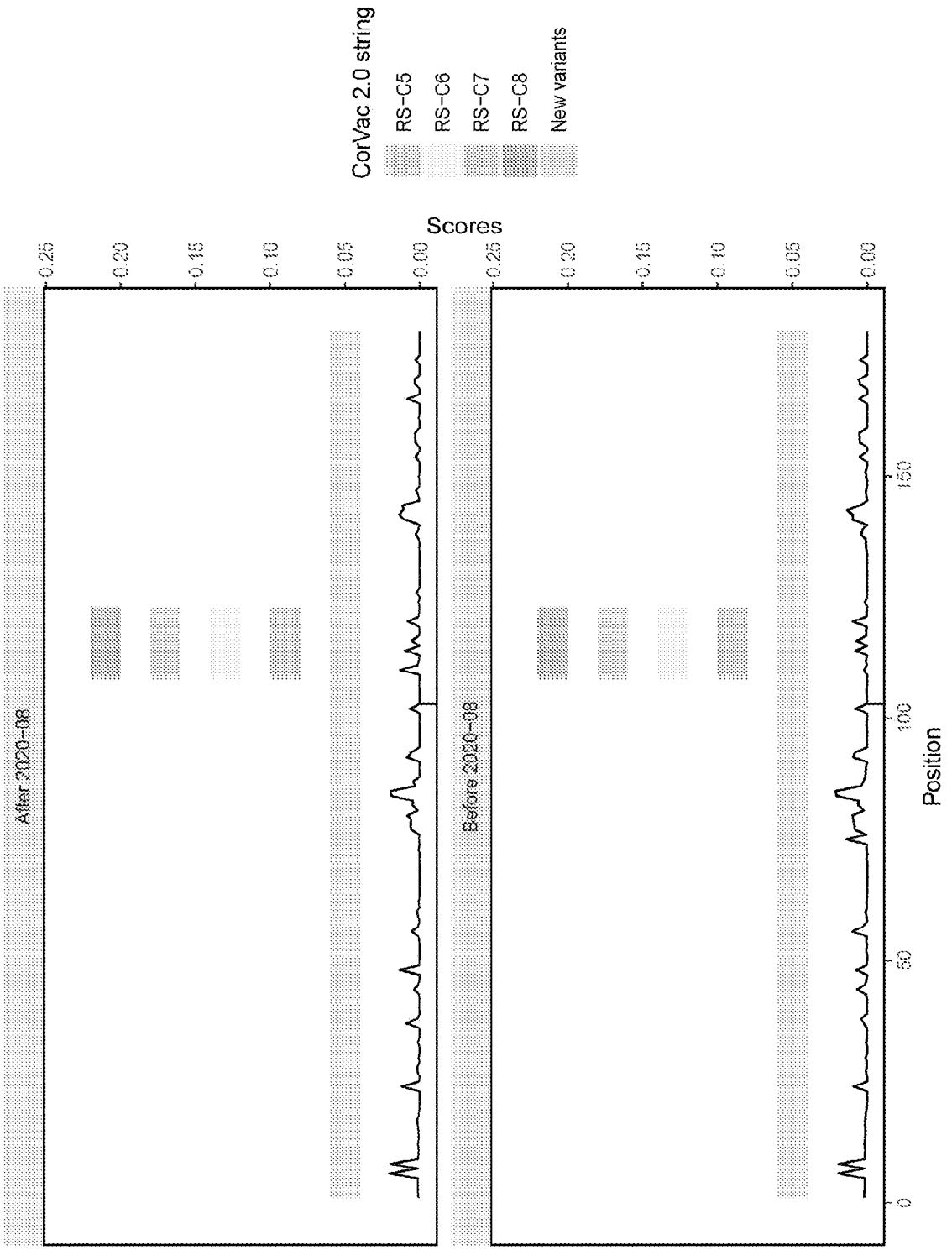

CorVac 2.0 string
RS-C5
RS-C6
RS-C7
RS-C8
New variants
Scores
0.25
0.20
0.15
0.10
0.05
0.00
After 2020-08
Before 2020-08
0
50
100
150
Position

FIG. 15

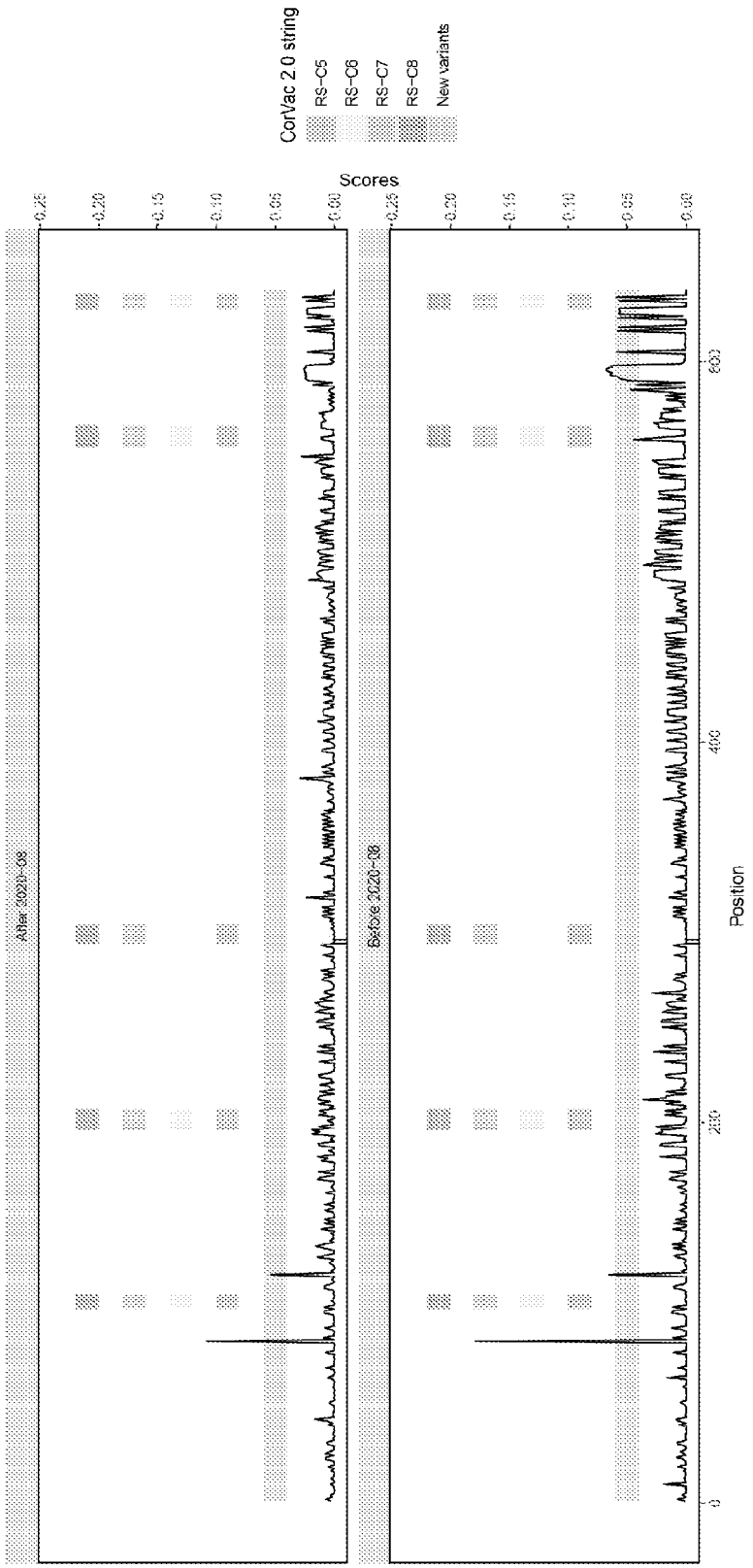

CorVac 2.0 string
RS-C5
RS-C6
RS-C7
RS-C8
New variants
Scores
After 2020-08
Before 2020-08
Position

FIG. 16

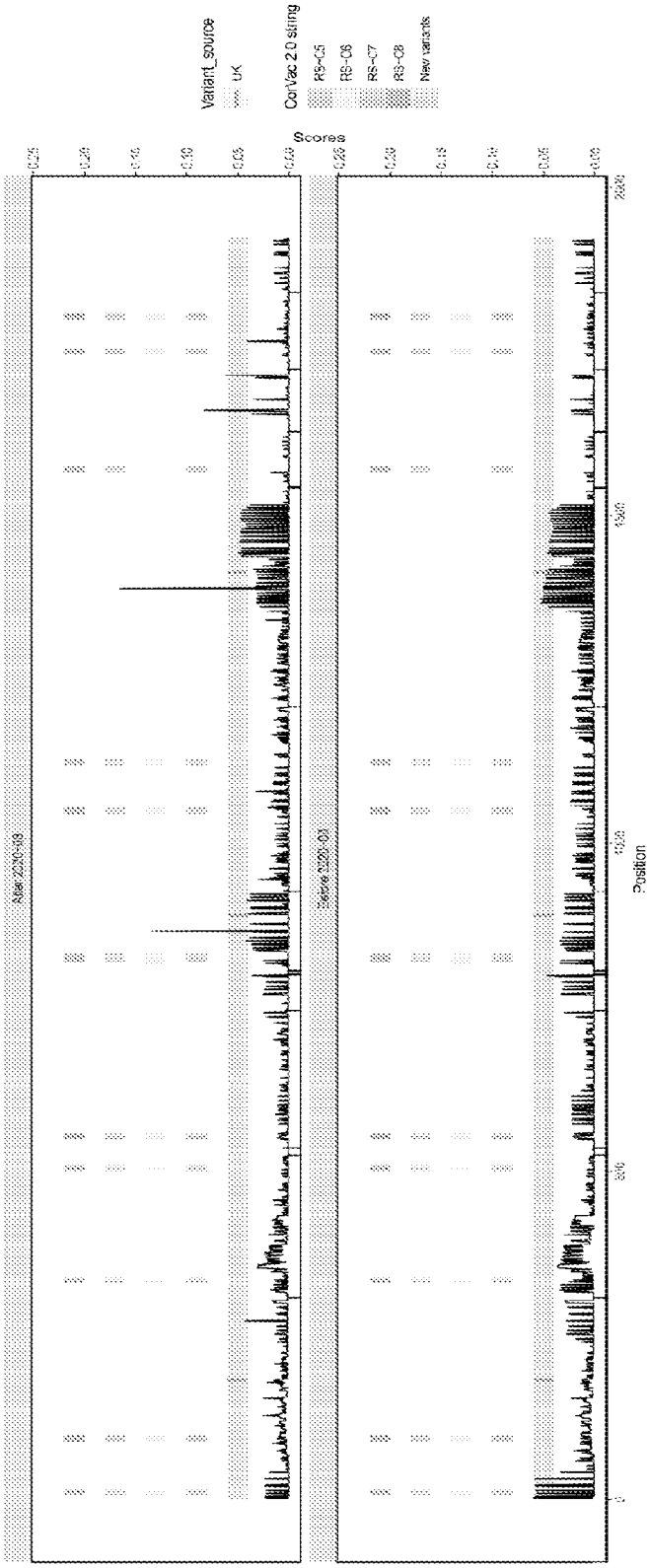

Variant_source
UK
ConVac 2.0 string
RS-C5
RS-C6
RS-C7
RS-C8
New variants
Scores
Alter 2020-09
Beta 2020-05
Position

FIG. 17

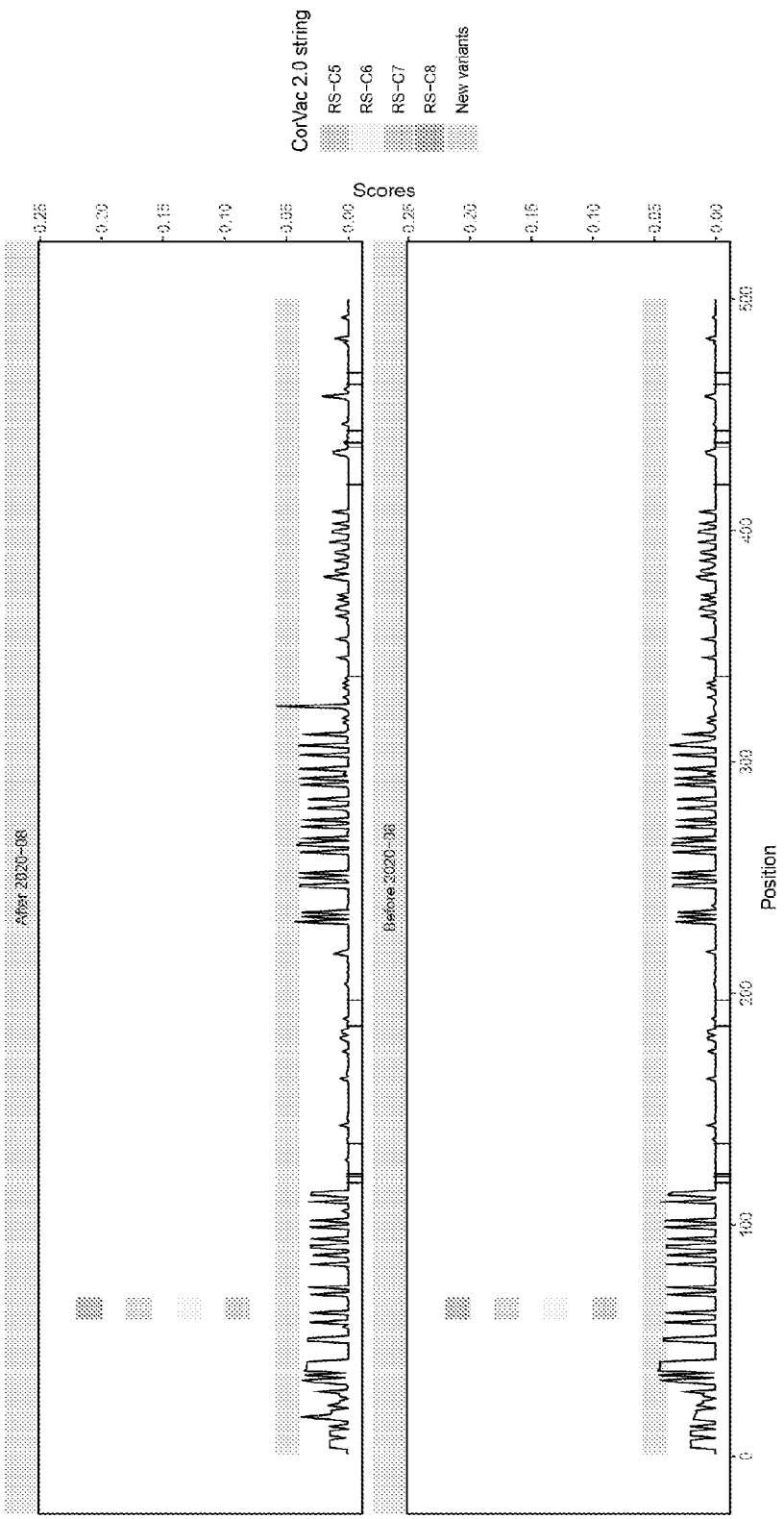

CorVac 2.0 string
RS-C5
RS-C6
RS-C7
RS-C8
New variants
Scores
After 2020-08
Before 2020-08
Position

FIG. 18

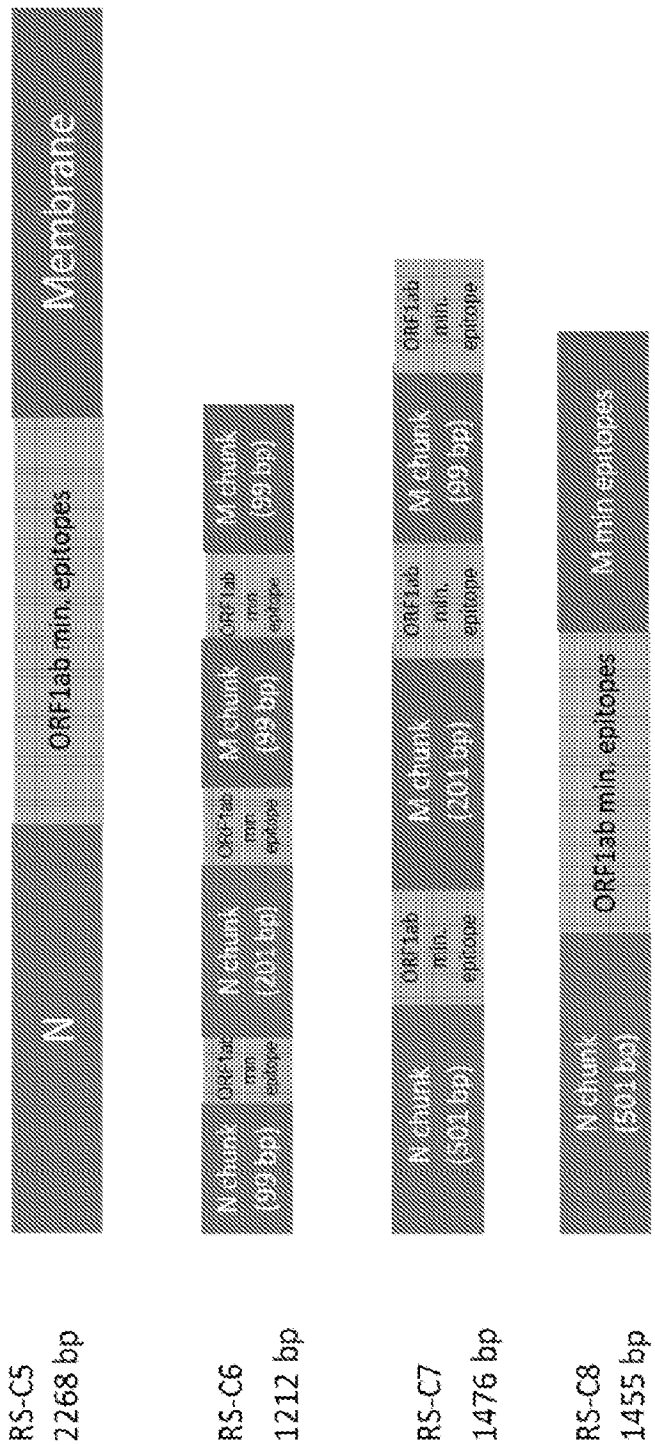

RS-C5
2268 bp
N
ORFLab min. epitopes
Membrane
RS-C6
1212 bp
N short (99 bp)
ORFLab min. epitope
M short (69 bp)
ORFLab min. epitope
M short (69 bp)
RS-C7
1476 bp
N short (201 bp)
ORFLab min. epitope
M short (201 bp)
ORFLab min. epitope
M short (99 bp)
ORFLab min. epitope
RS-C8
1455 bp
N short (501 bp)
ORFLab min. epitopes
Matrix epitopes

FIG. 19A

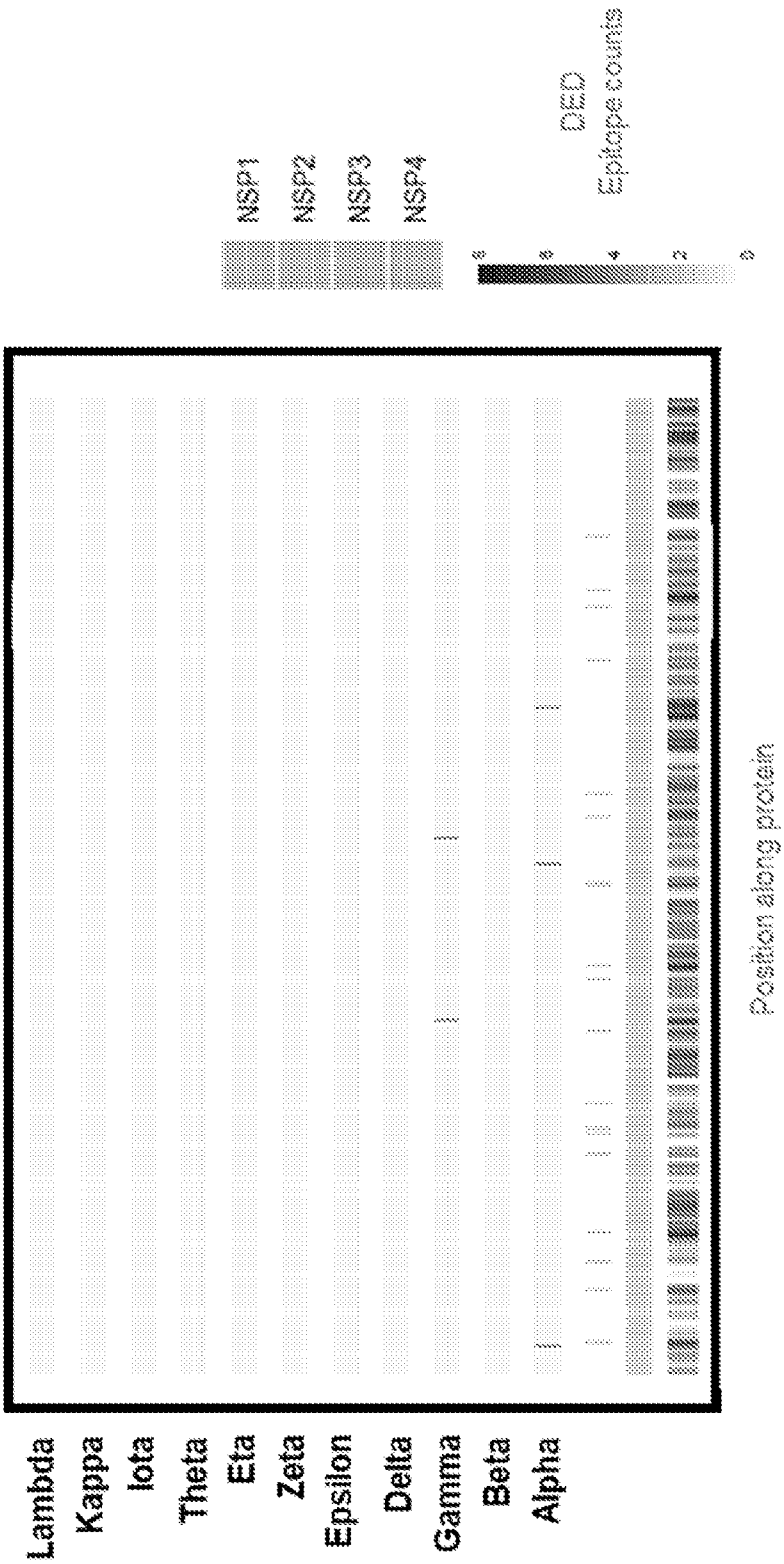

ORF1ab (NSP1-4)
Lambda
Kappa
Iota
Theta
Eta
Zeta
Epsilon
Delta
Gamma
Beta
Alpha
Position along protein
NSP1
NSP2
NSP3
NSP4
DED
Epitope counts

FIG. 19B

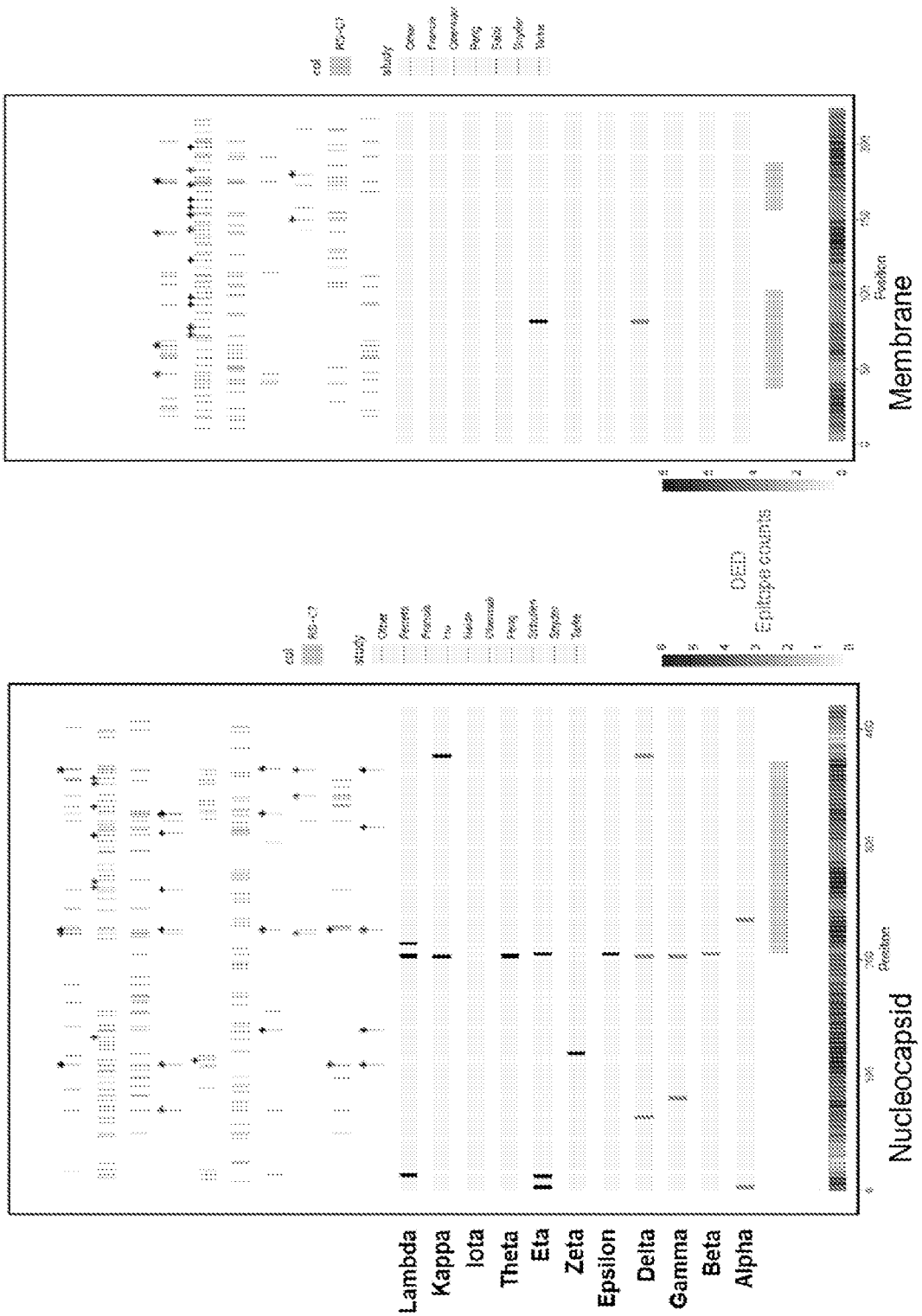

Lambda
Kappa
Iota
Theta
Eta
Zeta
Epsilon
Delta
Gamma
Beta
Alpha
Nucleocapsid
Membrane
Position
OED
Epitope counts
cell
study

FIG. 19C

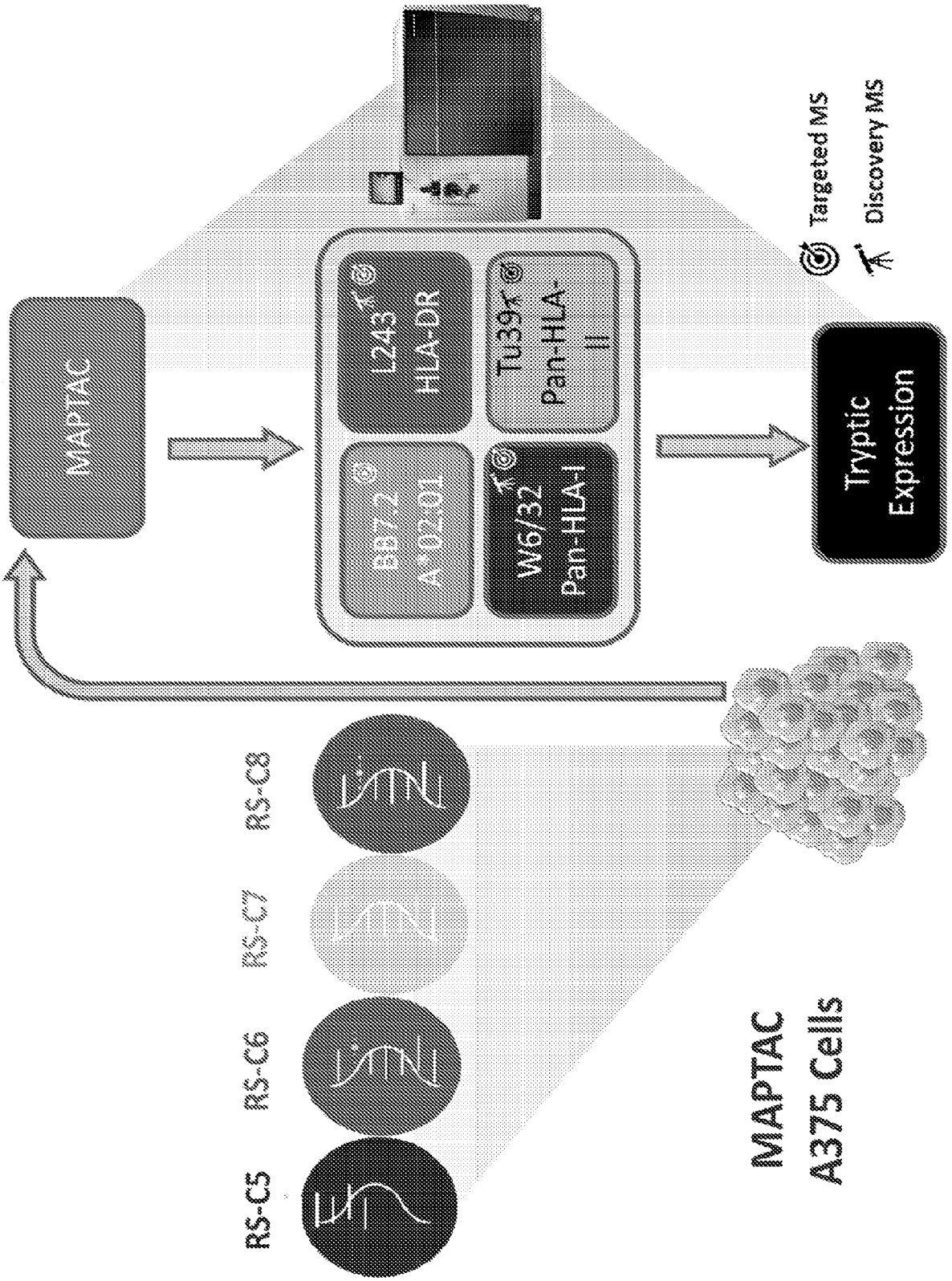

MAPTAC
B2M
A*02:01
L243
HLA-DR
W6/32
Pan-HLA-I
Tu39
Pan-HLA-II
Tryptic Expression
Targeted MS
Discovery MS
MAPTAC
A375 Cells
RS-C5
RS-C6
RS-C7
RS-C8

FIG. 20

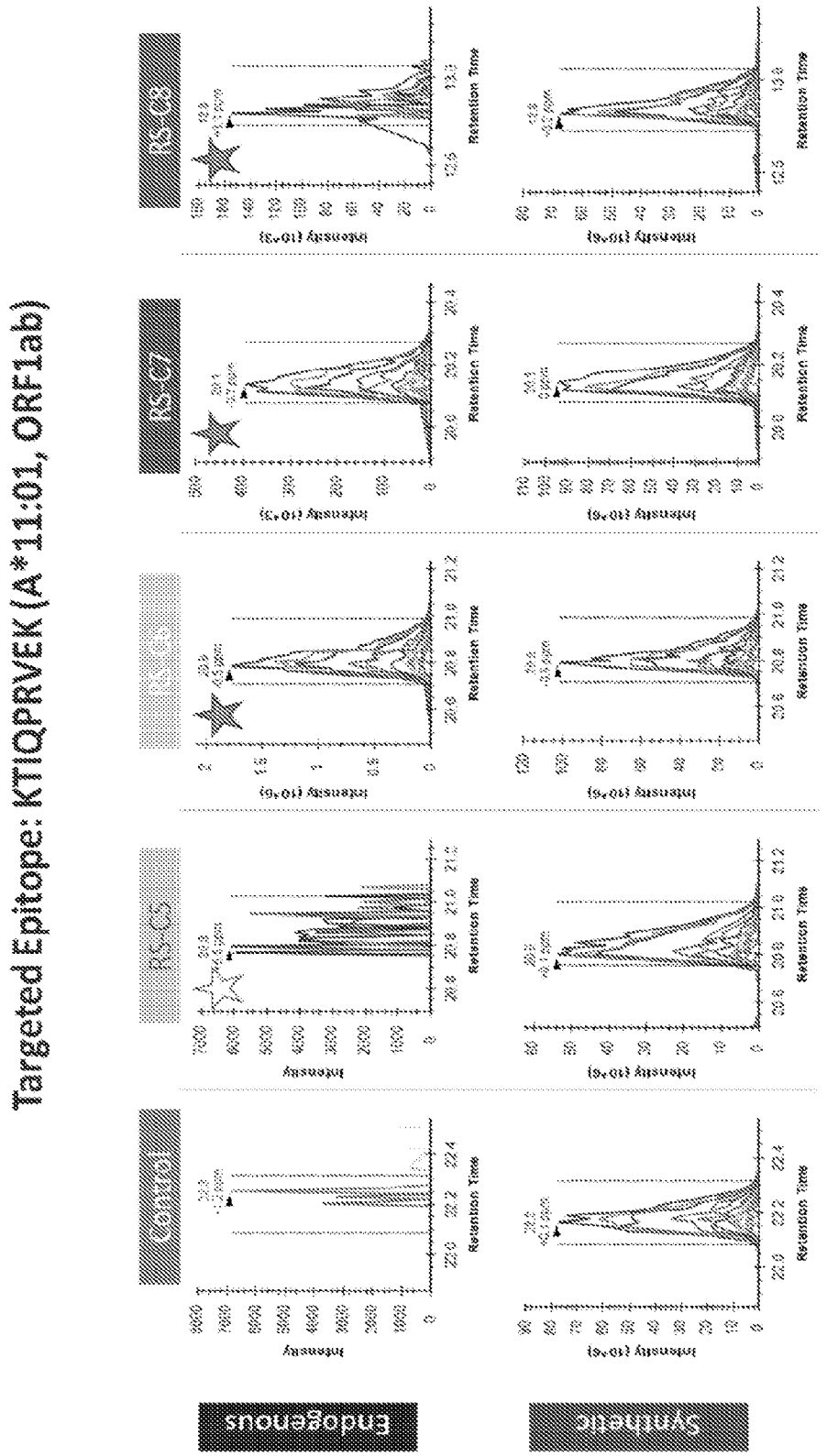

Targeted Epitope: KTIQPRVEK (A*11:01, ORF1ab)
Control
R5-C5
R5-C6
R5-C7
R5-C8
Endogenous
Synthetic
High Confidence
Moderate Confidence
Intensity
Intensity (10^6)
Intensity (10^3)
Retention Time

FIG. 21

Bold = "Immunodominant"

ORF1ab: 18 epitopes

Nucleocapsid: 6 epitopes

Membrane: 2 epitopes

Y MS Detected Epitope

Not Observed

Not Encoded

Not Assayed

Epitope	ORF	Allele	RS-C5	RS-C6	RS-C7	RS-C8
AEAELAKNV	1ab	B44:03*		Y	Y	Y
AEAELAKNVS	1ab	B08:01		Y	Y	
FGDDTVIEV	1ab	A02:01	Y		Y	Y
HVGEIPVAY	1ab	A03:01		Y	Y	Y
KTIQPRVEK	1ab	A11:01, A03:01		Y	Y	Y
PTDNYITTY	1ab	**A01:01**	Y	Y	Y	Y
QLMCCPSL	1ab	A02:01		Y		Y
SEVGPEHSLAEY	1ab	B44:03*	Y	Y		
SEVGPEHSL	1ab	B44:03*	Y	Y	Y	
TTDPSFLG	1ab	A01:01*		Y	Y	
TTDPSFLGR	1ab	A01:01*		Y	Y	
TTDPSFLGRY	1ab	**A01:01**	Y	Y	Y	Y
TTDPSFLGRYM	1ab	A01:01		Y		
PSFLGRY	1ab	A01:01*	Y	Y	Y	Y
VTNNTFTLK	1ab	**A11:01**		Y	Y	Y
YLFDESGEF	1ab	A02:01		Y	Y	Y
YLFDESGEFKL	1ab	**A02:01**		Y	Y	Y
ATSRTLSYYK	M	**A11:01**		Y	Y	Y
VATSRTLSY	M	C16:01*		Y	Y	Y
QQQQQQTVTK	N	A11:01			Y	Y
KTFPPTEPK	N	**A11:01, A03:01**		Y	Y	Y
KTFPPTEPKK	N	A11:01		Y	Y	Y
LLLDRLNQL	N	**A02:01**		Y	Y	Y
MEKQQVIL	N	B08:01		Y	Y	
QQQQQTVTK	N	A11:01			Y	Y

*Hit from W632 pulldown of endogenous alleles; binding allele inferred from RECOM

†Not compatible with RECOM predictions because of 7mer, but observed repeatedly

FIG. 22

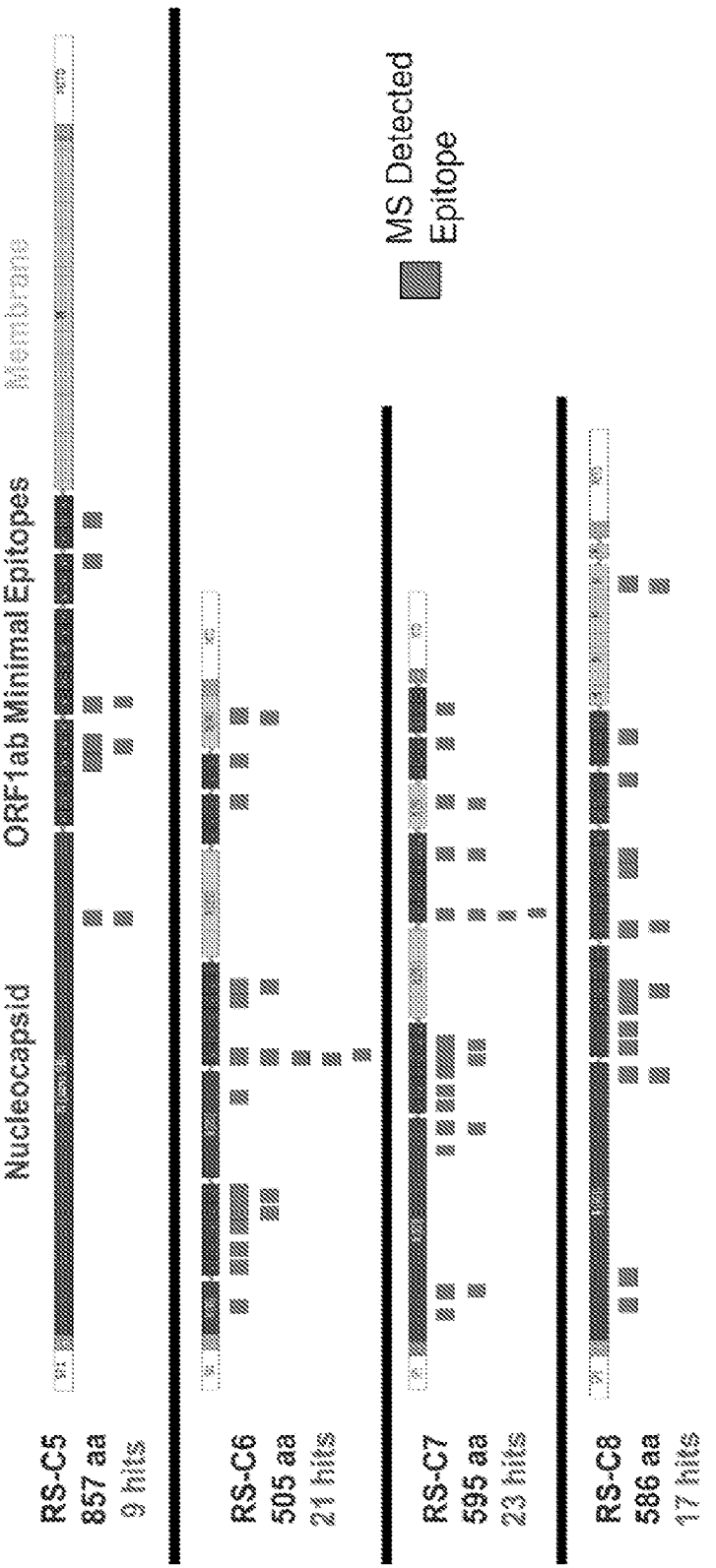

Nucleocapsid
ORF1ab Minimal Epitopes
Membrane
MS Detected Epitope
RS-C5
857 aa
9 hits
RS-C6
505 aa
21 hits
RS-C7
595 aa
23 hits
RS-C8
586 aa
17 hits

FIG. 23

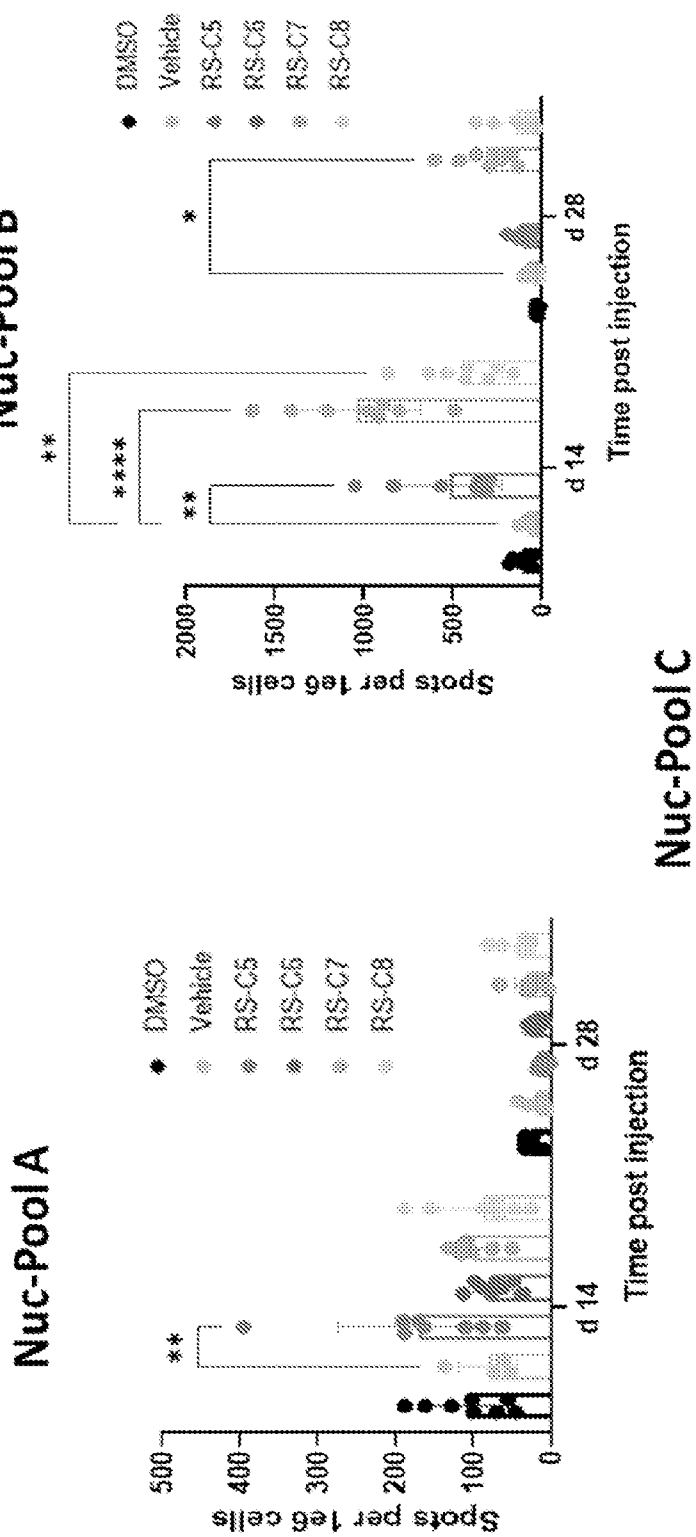

Nuc-Pool A
Spots per 1e6 cells
500
400
300
200
100
0
**
d 14
d 28
Time post injection
DMSO
Vehicle
RS-C5
RS-C6
RS-C7
RS-C8
Nuc-Pool B
Spots per 1e6 cells
2000
1500
1000
500
0
**
****
**
*
d 14
d 28
Time post injection
DMSO
Vehicle
RS-C5
RS-C6
RS-C7
RS-C8
Nuc-Pool C
Spots per 1e6 cells
600
400
200
0
****
*
d 14
d 28
Time post injection
DMSO
Vehicle
RS-C5
RS-C6
RS-C7
RS-C8

FIG. 24

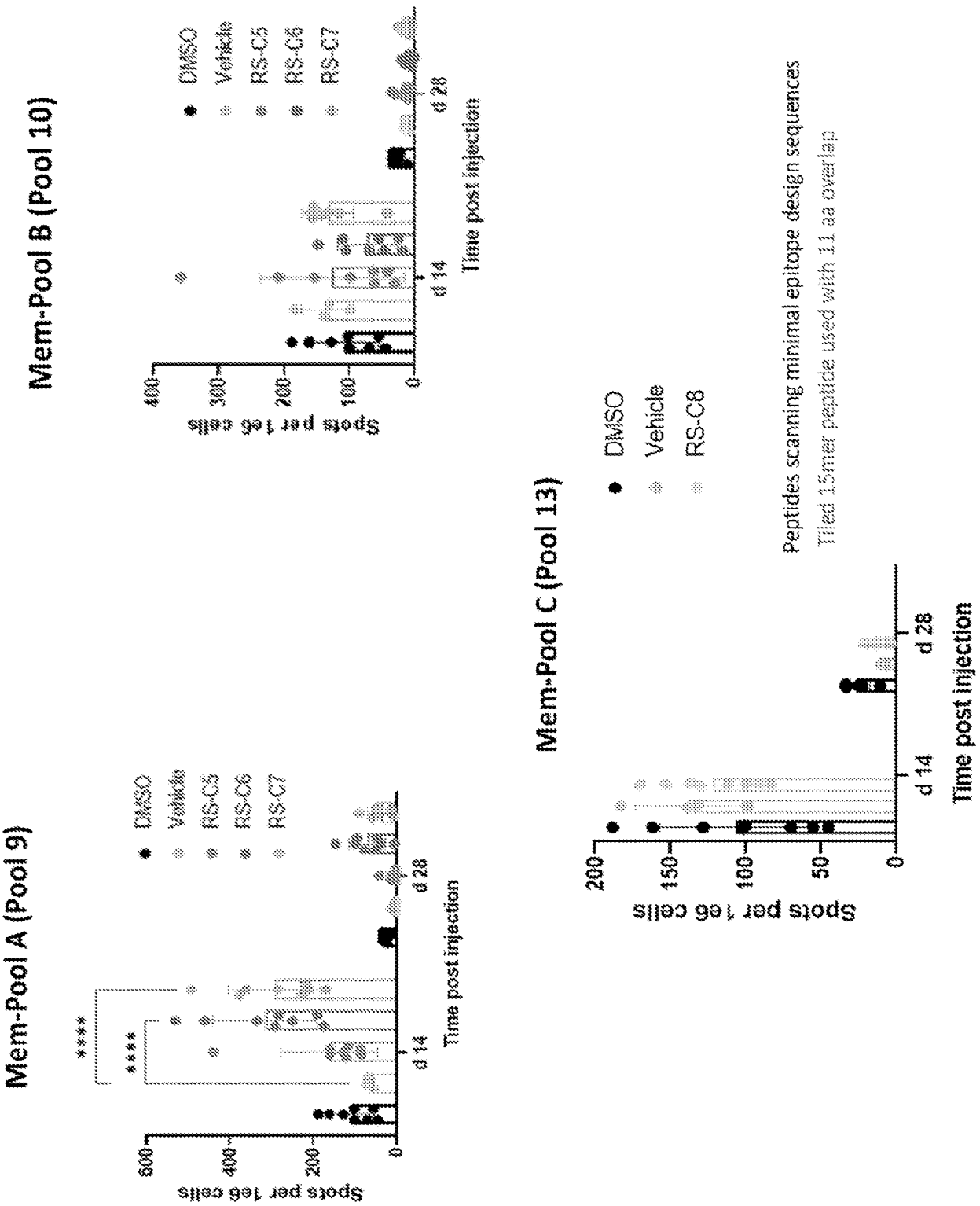

Mem-Pool A (Pool 9)
Mem-Pool B (Pool 10)
Mem-Pool C (Pool 13)
DMSO
Vehicle
RS-C5
RS-C6
RS-C7
RS-C8
****
****
Spots per 1e6 cells
Time post injection
d 14
d 28
Peptides scanning minimal epitope design sequences
Tiled 15mer peptide used with 11 aa overlap

FIG. 25

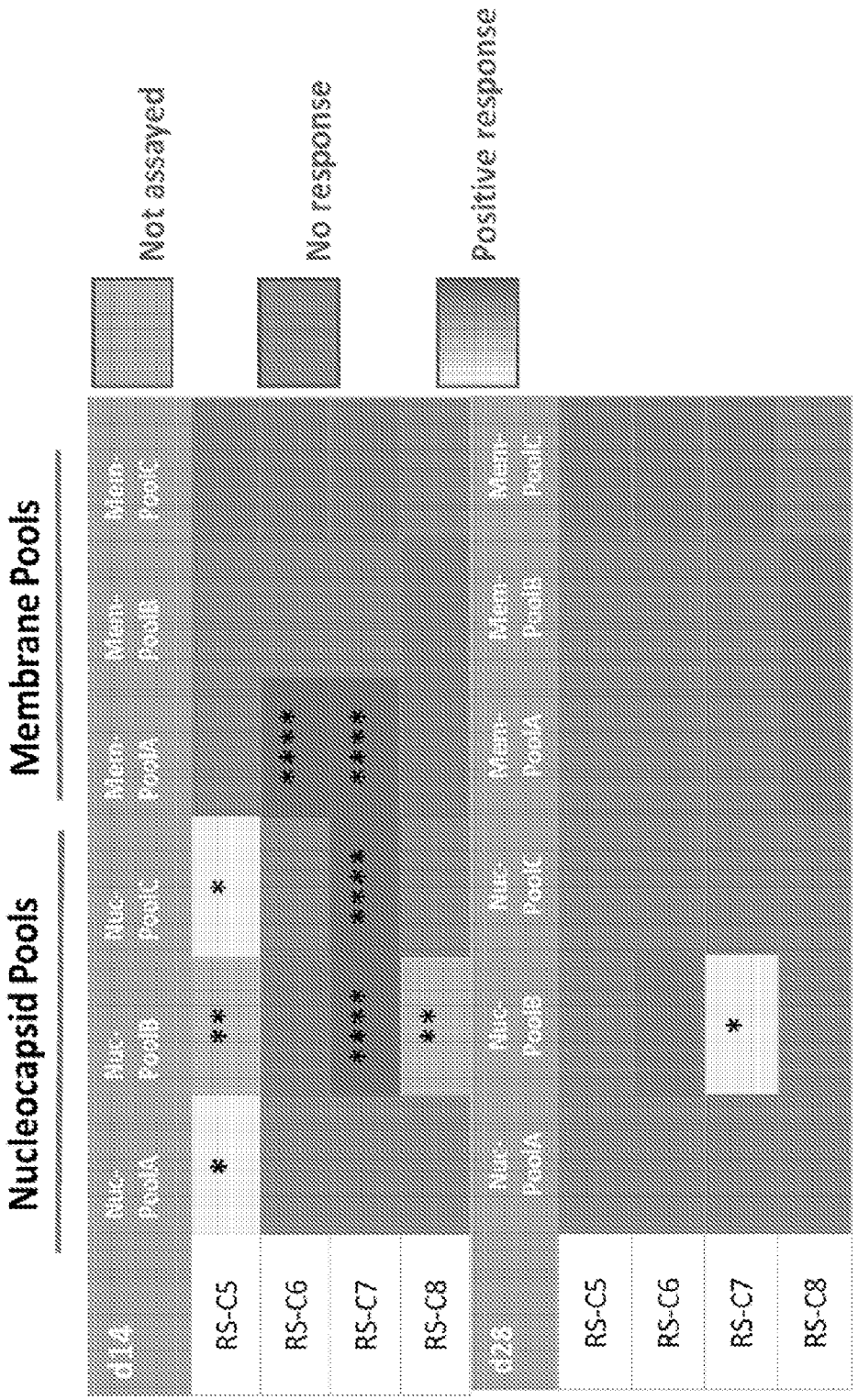

Not assayed
No response
Positive response
Nucleocapsid Pools
Membrane Pools
d14
d28
RS-C5
RS-C6
RS-C7
RS-C8
Nuc. PoolA
Nuc. PoolB
Nuc. PoolC
Mem. PoolA
Mem. PoolB
Mem. PoolC
Mem. Pools
*
**
****

FIG. 26

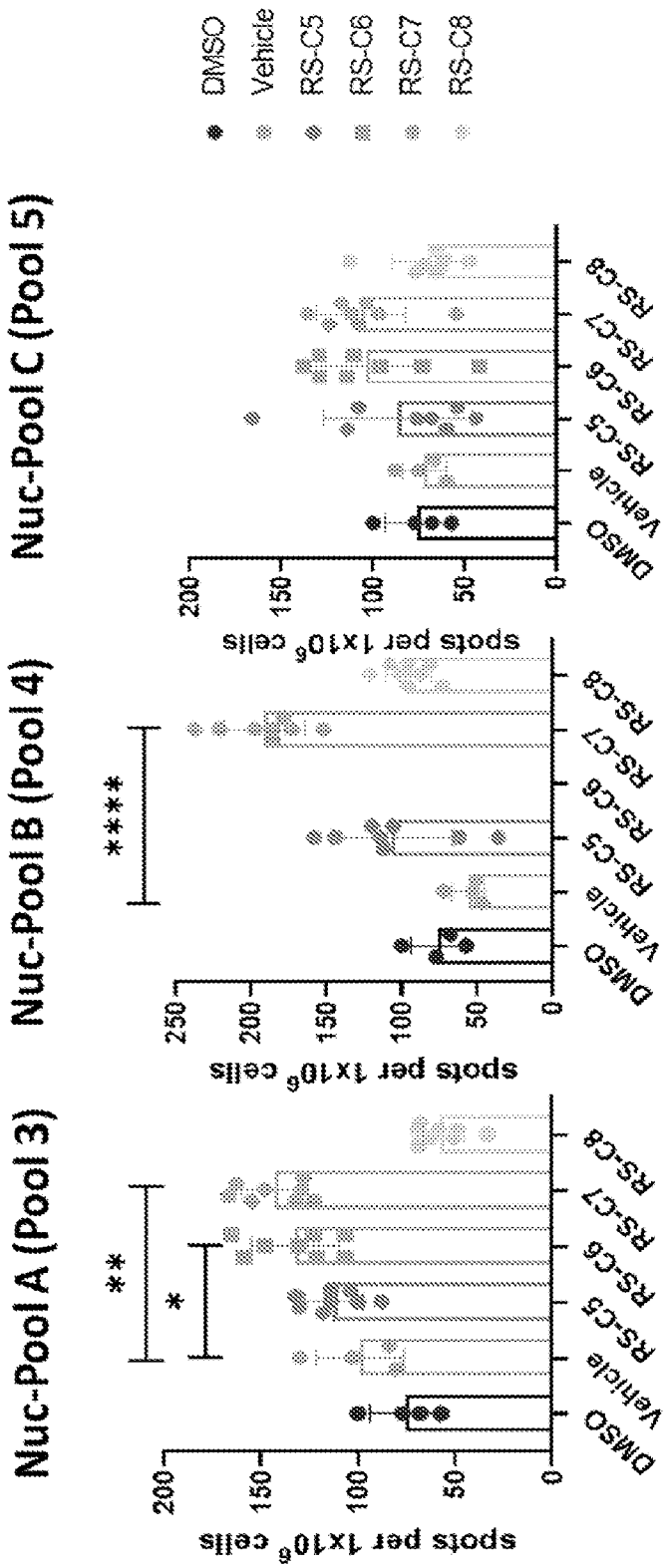

Nuc-Pool A (Pool 3)
Nuc-Pool B (Pool 4)
Nuc-Pool C (Pool 5)
DMSO
Vehicle
RS-C5
RS-C6
RS-C7
RS-C8
spots per 1x10^6 cells
**
*
****

FIG. 27

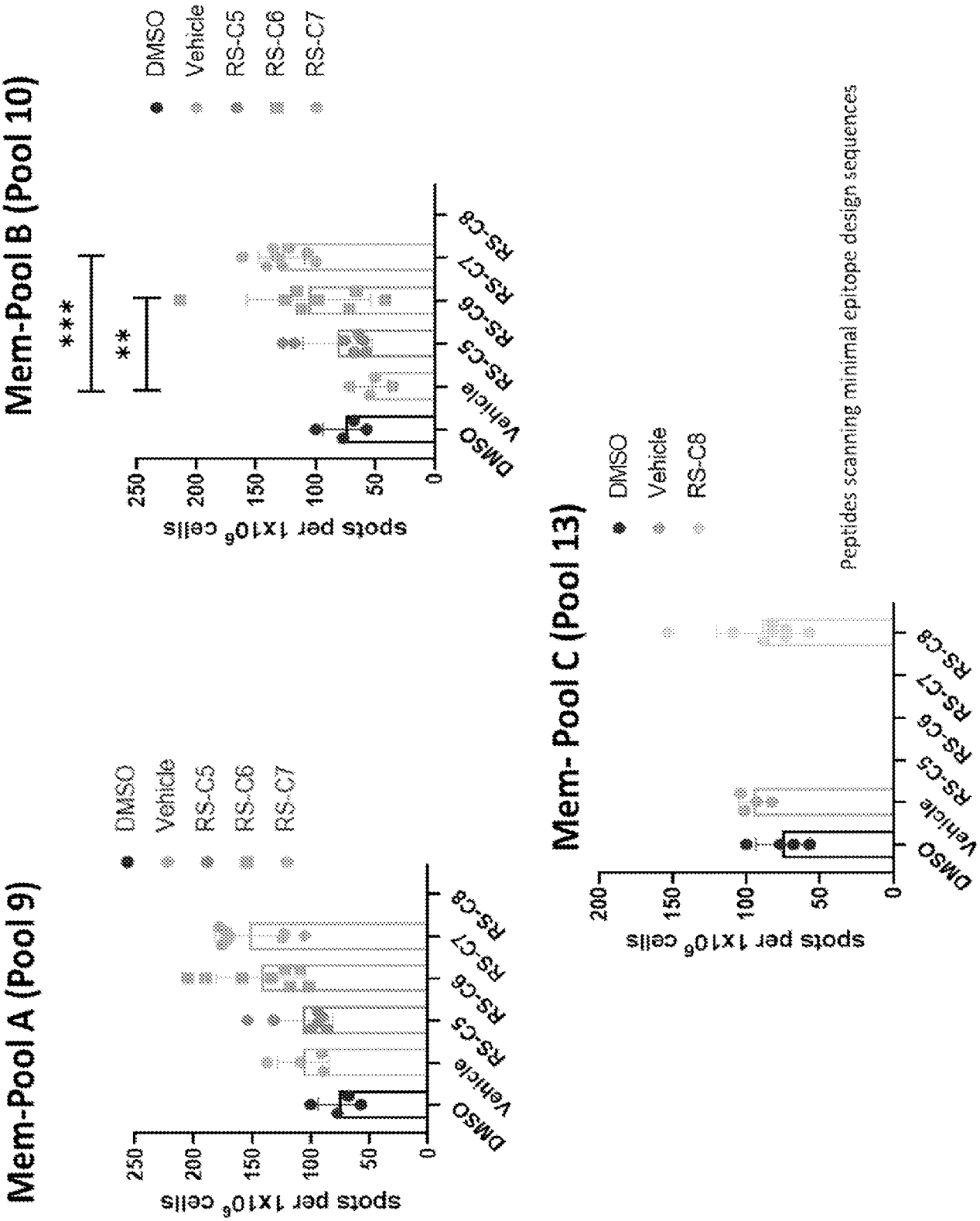

Mem-Pool A (Pool 9)
DMSO
Vehicle
RS-C5
RS-C6
RS-C7
spots per 1x10^6 cells
250
200
150
100
50
0
DMSO
Vehicle
RS-C5
RS-C6
RS-C7
RS-C8
Mem-Pool B (Pool 10)
***
**
DMSO
Vehicle
RS-C5
RS-C6
RS-C7
spots per 1x10^6 cells
250
200
150
100
50
0
DMSO
Vehicle
RS-C5
RS-C6
RS-C7
RS-C8
Mem- Pool C (Pool 13)
DMSO
Vehicle
RS-C8
spots per 1x10^6 cells
200
150
100
50
0
DMSO
Vehicle
RS-C5
RS-C6
RS-C7
RS-C8
Peptides scanning minimal epitope design sequences

FIG. 28

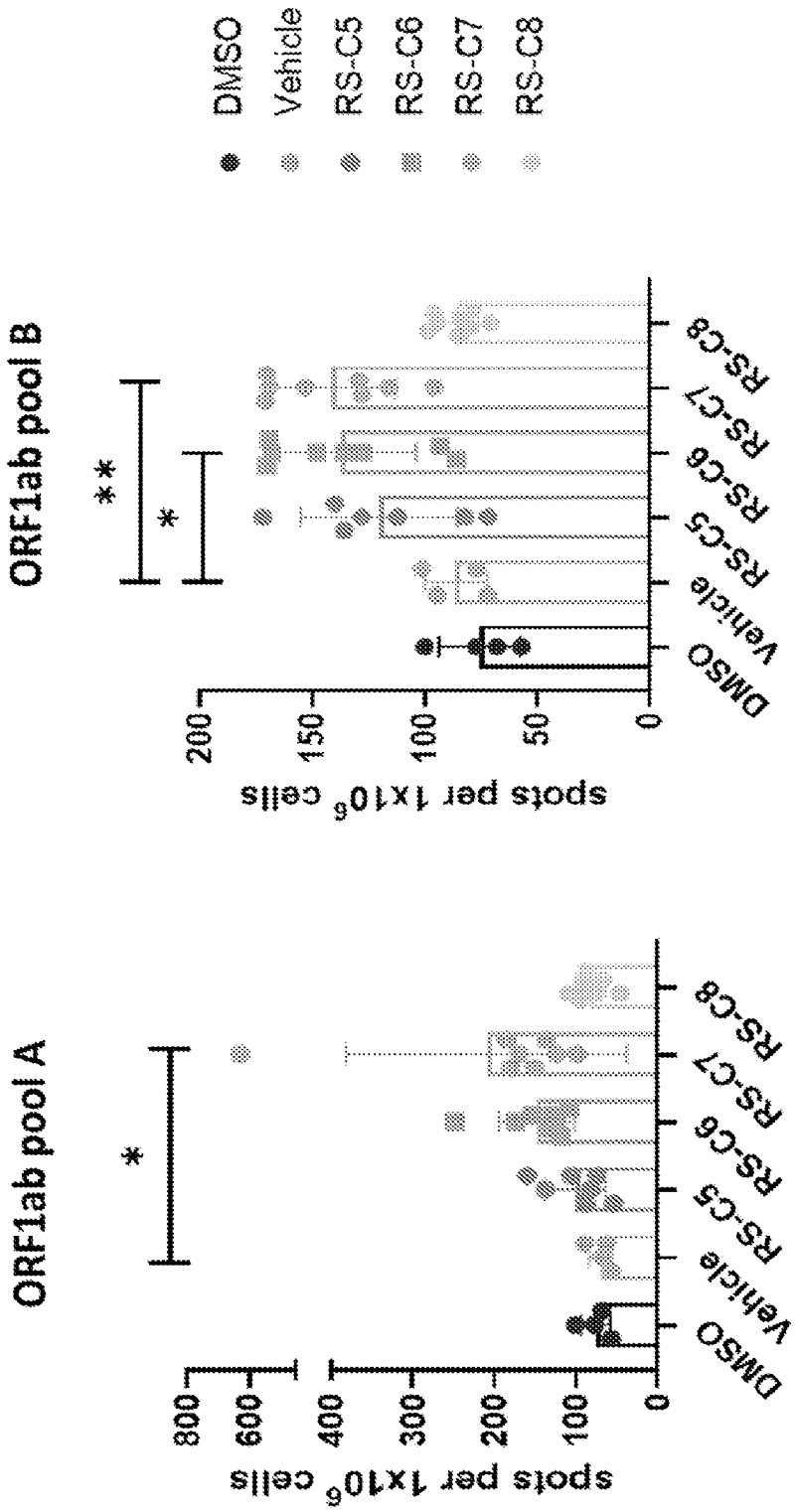

DMSO
Vehicle
RS-C5
RS-C6
RS-C7
RS-C8
ORF1ab pool A
ORF1ab pool B
spots per 1x10^6 cells
0
100
200
300
400
600
800
50
150
*
**
DMSO
Vehicle
RS-C5
RS-C6
RS-C7
RS-C8

FIG. 29

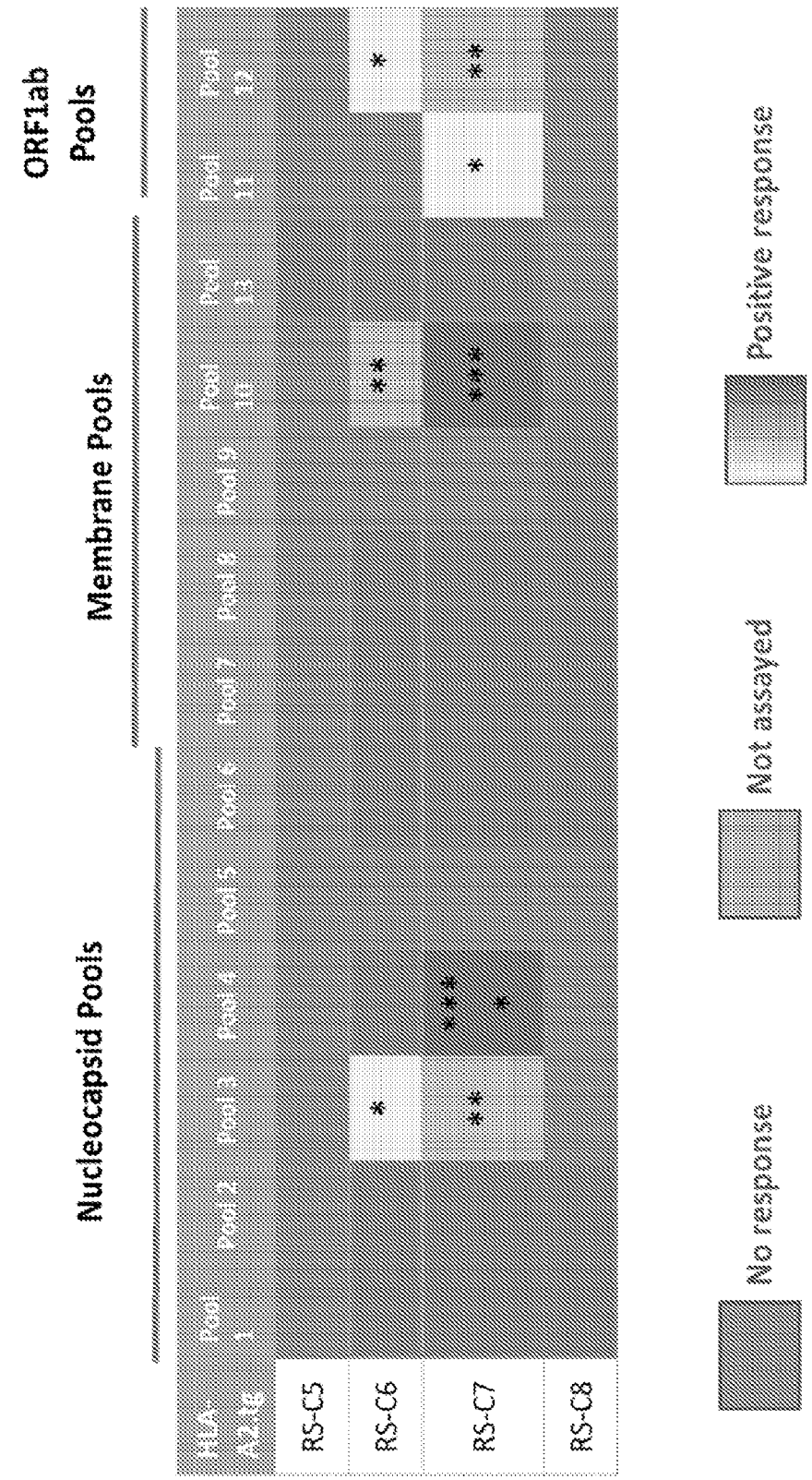

Nucleocapsid Pools
Membrane Pools
ORF1ab Pools
HLA-A*11
Pool 1
Pool 2
Pool 3
Pool 4
Pool 5
Pool 6
Pool 7
Pool 8
Pool 9
Pool 10
Pool 11
Pool 12
Pool 13
RS-C5
RS-C6
RS-C7
RS-C8
No response
Not assayed
Positive response

FIG. 30

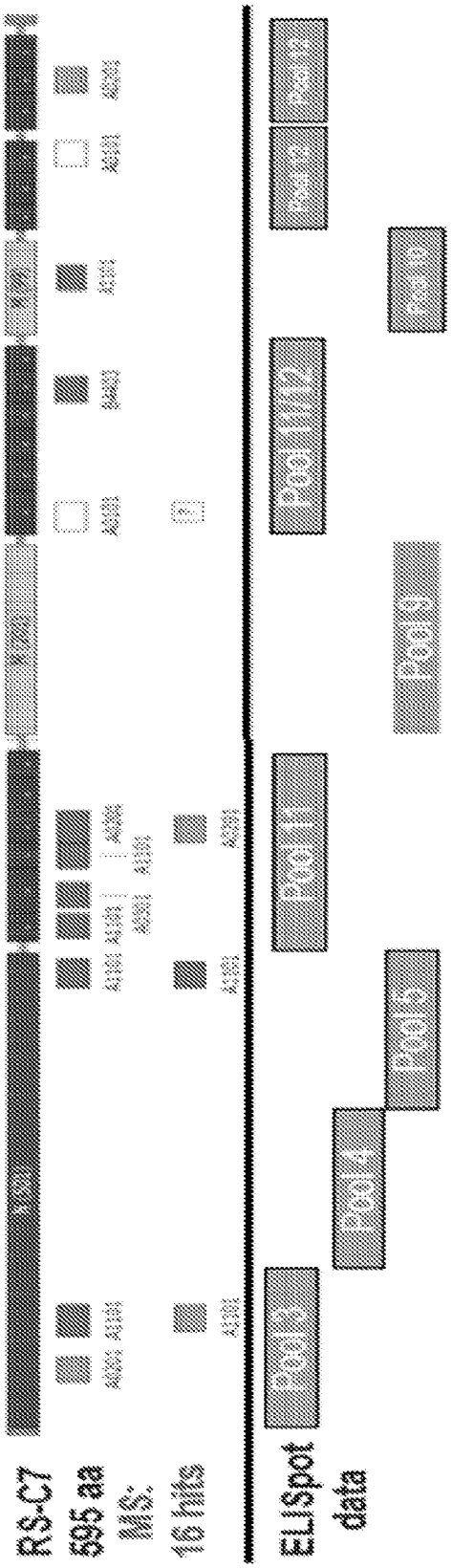

RS-C7
595 aa
MS:
16 hits
ELISpot
data
Pool 3
Pool 4
Pool 5
Pool 11
Pool 10
Pool 1/2
Pool 8
Pool 6
Pool 7
Pool 9

FIG. 31

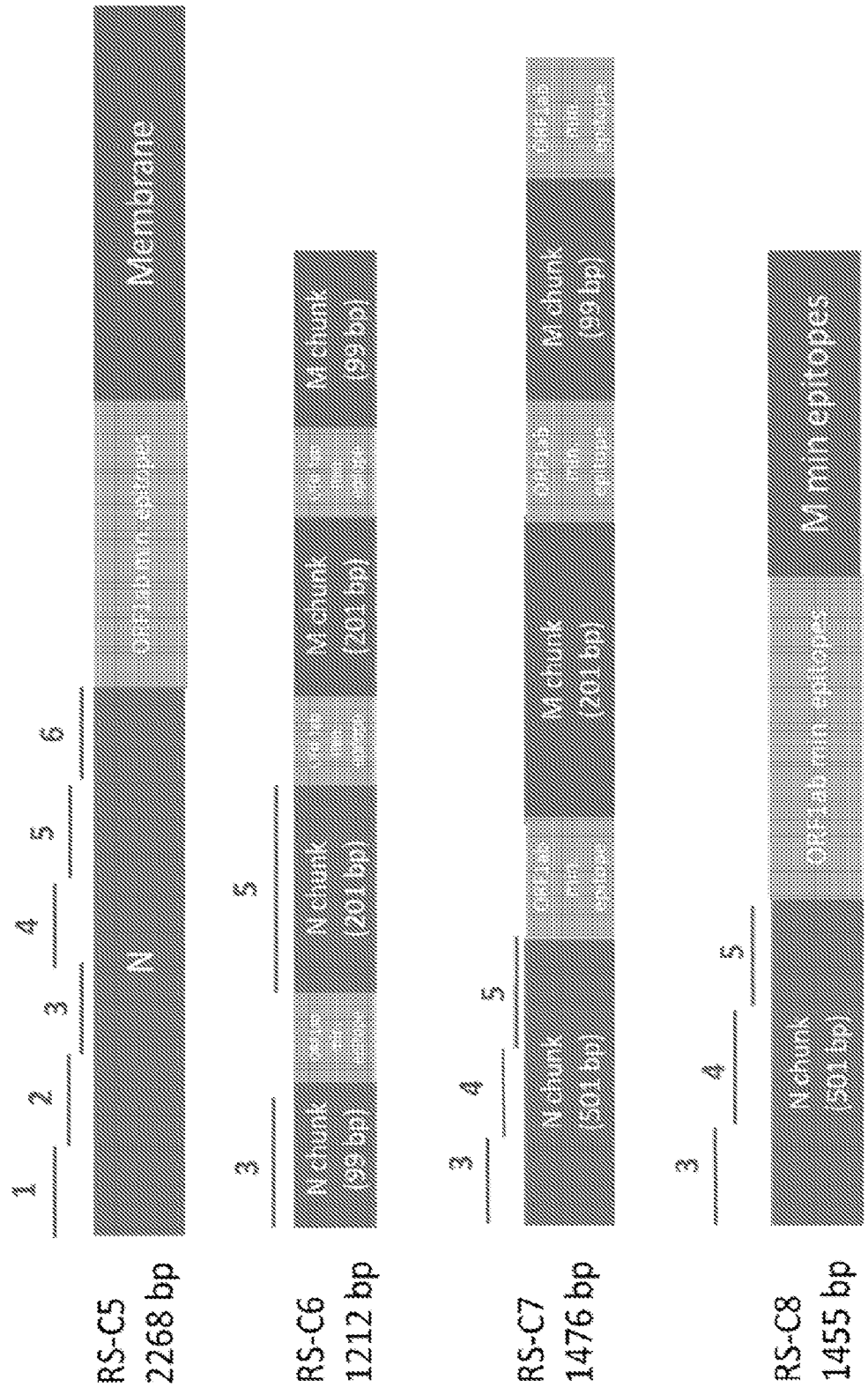

RS-C5
2268 bp
1
2
3
4
5
6
N
Membrane
RS-C6
1212 bp
3
5
M chunk
(201 bp)
M chunk
(99 bp)
RS-C7
1476 bp
3
4
5
M chunk
(201 bp)
M chunk
(99 bp)
RS-C8
1455 bp
3
4
5
M chunk
(201 bp)
M ectodomain
M transmembrane
M cytoplasmic tail
M multi epitopes

FIG. 32A

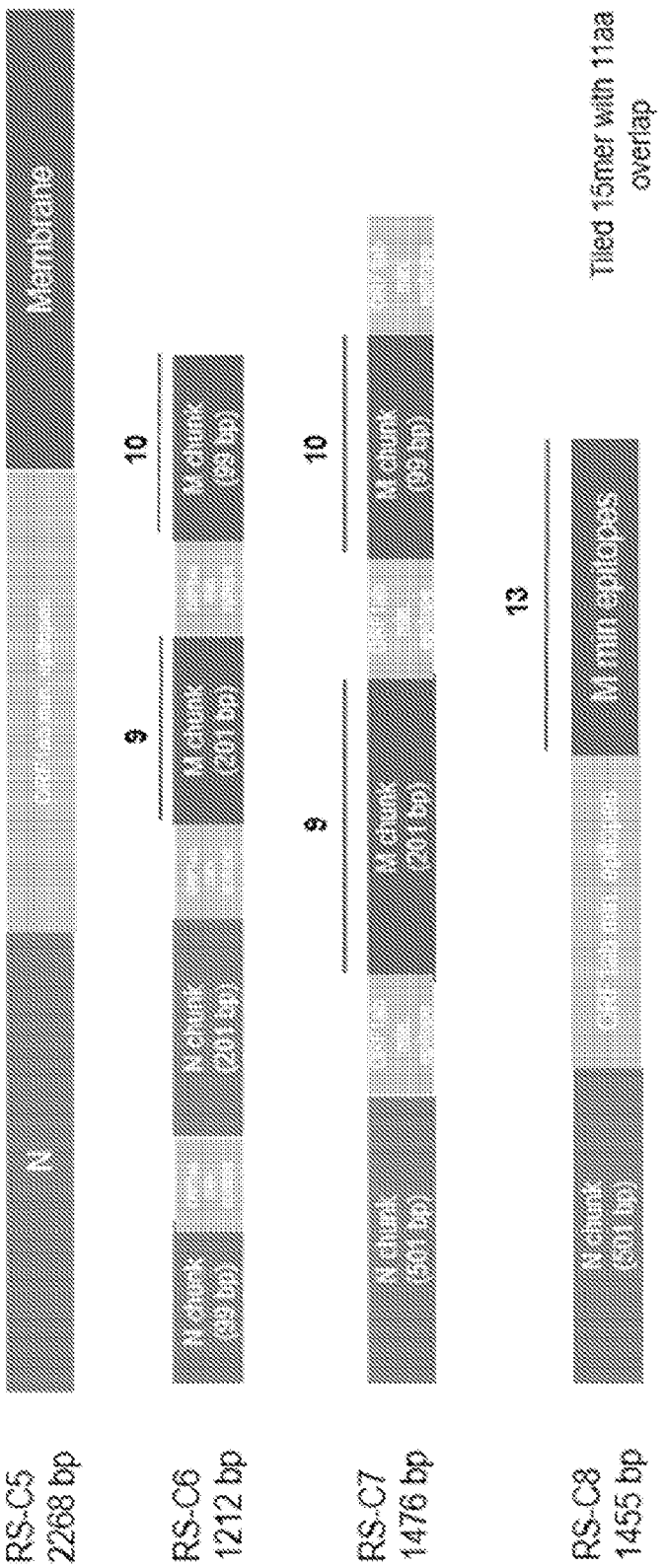

RS-C5
2268 bp
N
Membrane
7
8
9
10
RS-C6
1212 bp
N (part)
M (part)
(93 bp)
N (part)
(201 bp)
M (part)
(201 bp)
9
10
RS-C7
1476 bp
N (part)
(93 bp)
N (part)
(201 bp)
M (part)
(201 bp)
M (part)
(93 bp)
9
10
RS-C8
1455 bp
N (part)
(201 bp)
M transcripts
13
Tiled 15mer with 11aa
overlap

FIG. 32B

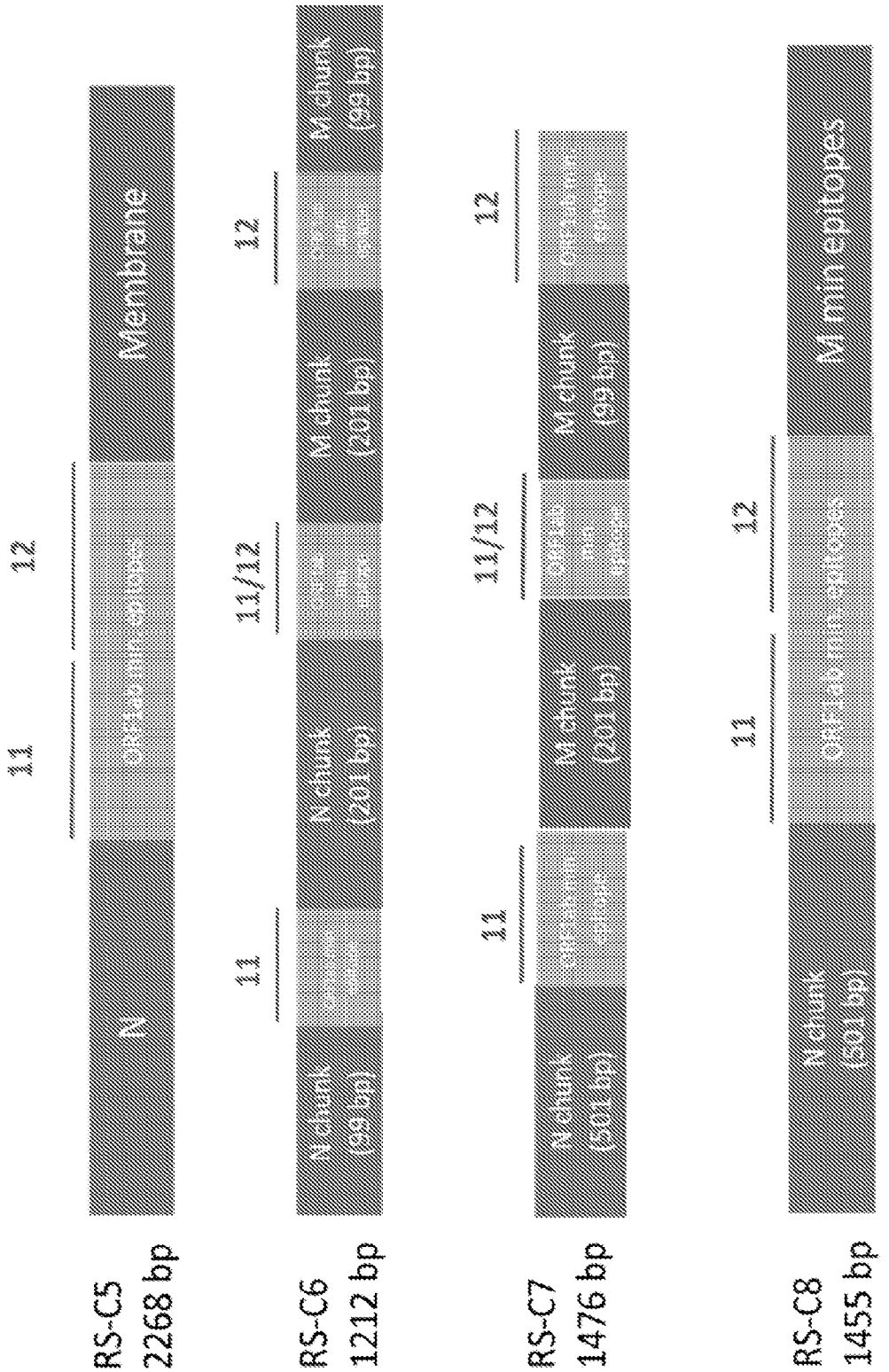

11
12
N
Membrane
RS-C5
2268 bp
11
11/12
12
M.thun
(99 bp)
M.thun
(201 bp)
M.thun
(99 bp)
RS-C6
1212 bp
11
11/12
12
M.thun
(201 bp)
M.thun
(201 bp)
M.thun
(99 bp)
RS-C7
1476 bp
11
12
M. thun epitopes
M.thun
(201 bp)
RS-C8
1455 bp

FIG. 32C

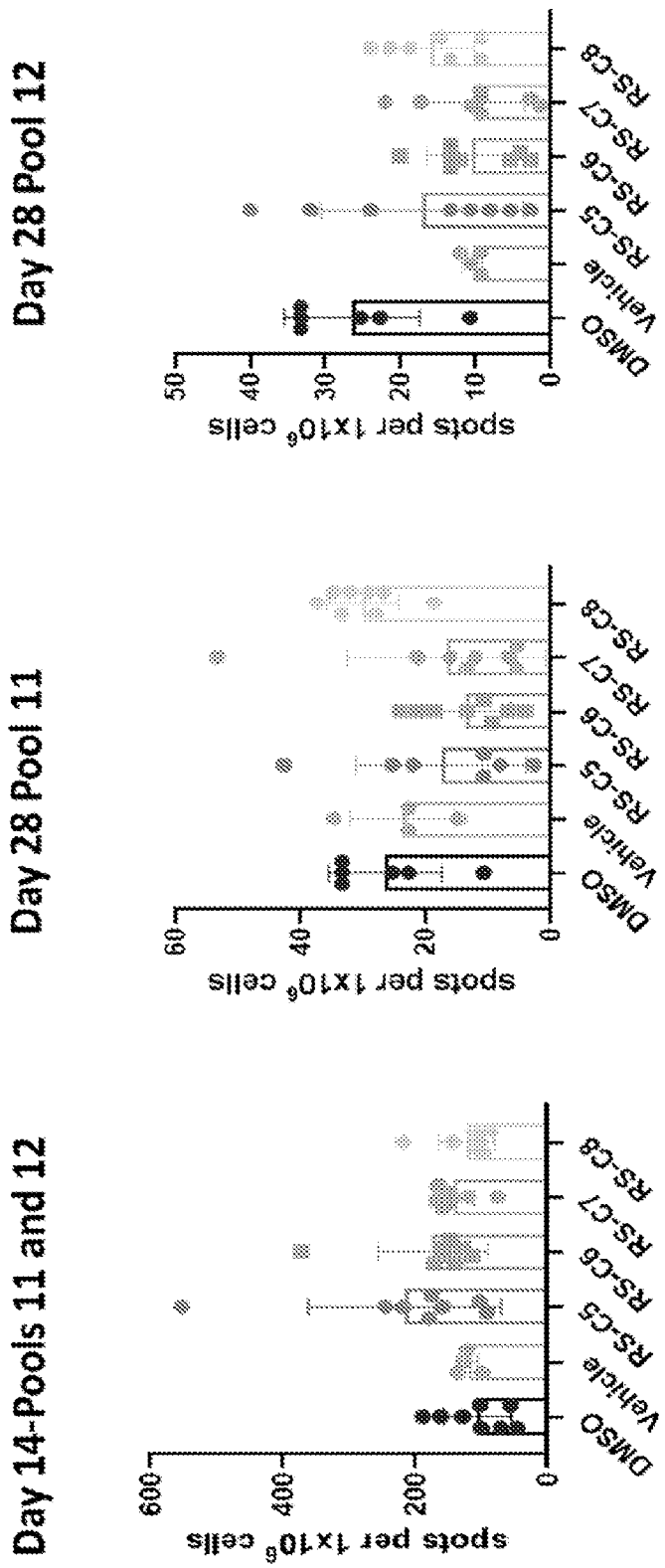

Day 14-Pools 11 and 12
Day 28 Pool 11
Day 28 Pool 12
spots per 1x10^6 cells
DMSO
Vehicle
RS-C3
RS-C6
RS-C7
RS-C8

FIG. 32D

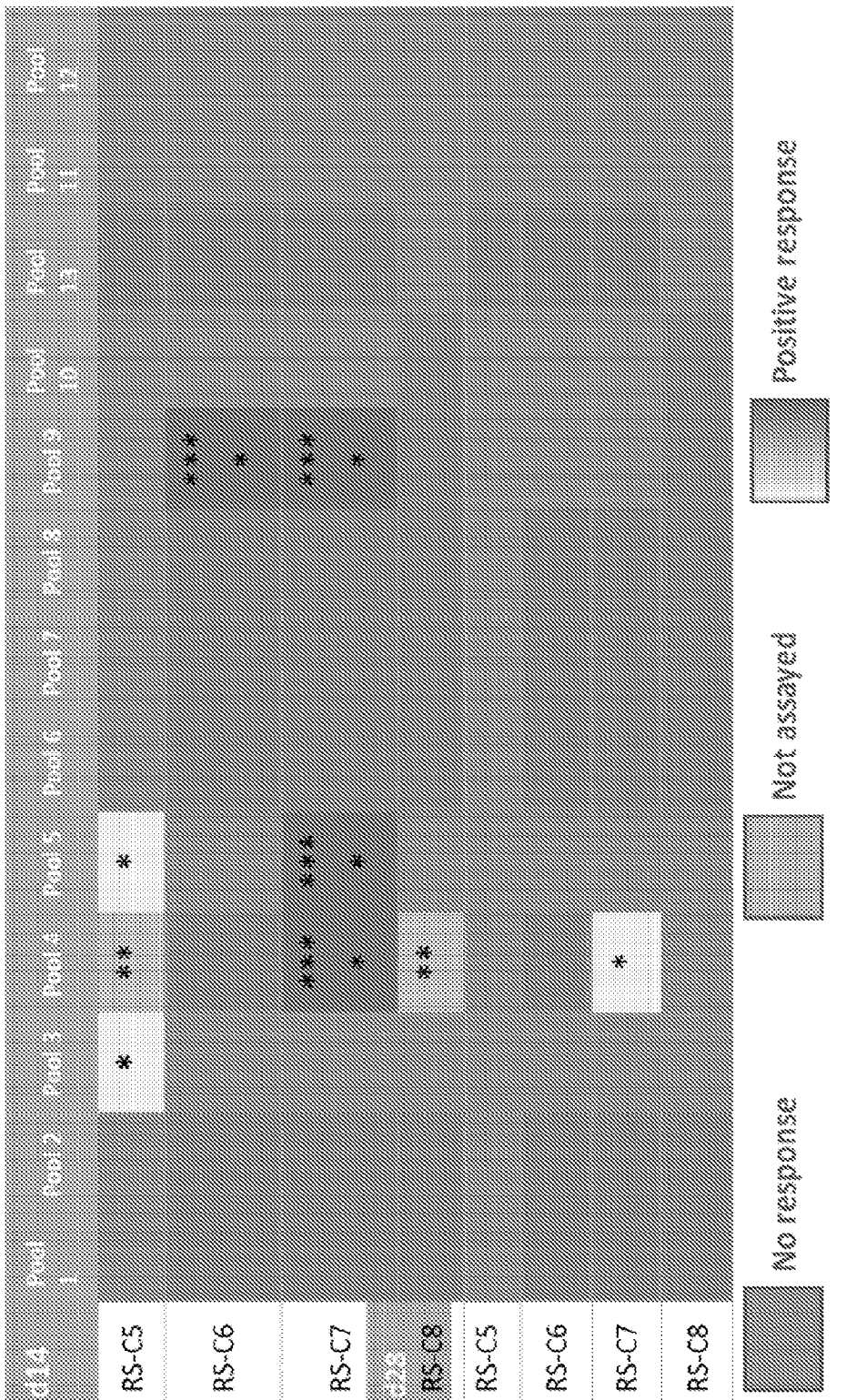

Nucleocapsid Pools
Membrane Pools
ORF1ab Pools
d14
d28
RS-C5
RS-C6
RS-C7
RS-C8
Pool 1
Pool 2
Pool 3
Pool 4
Pool 5
Pool 6
Pool 7
Pool 8
Pool 9
Pool 10
Pool 11
Pool 12
No response
Not assayed
Positive response

FIG. 32E

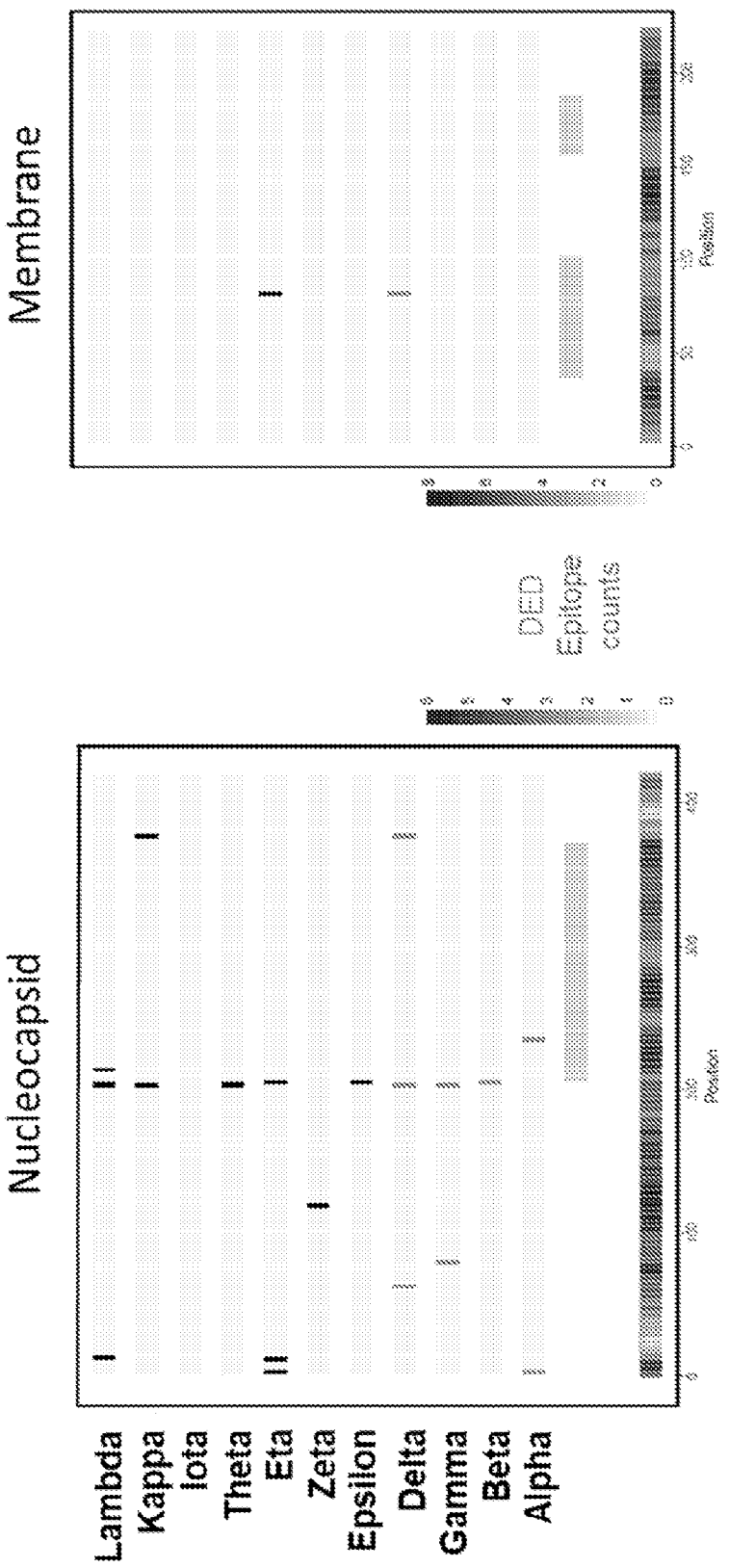

Membrane
Nucleocapsid
DED Epitope counts
Position
Lambda
Kappa
Iota
Theta
Eta
Zeta
Epsilon
Delta
Gamma
Beta
Alpha

FIG. 33

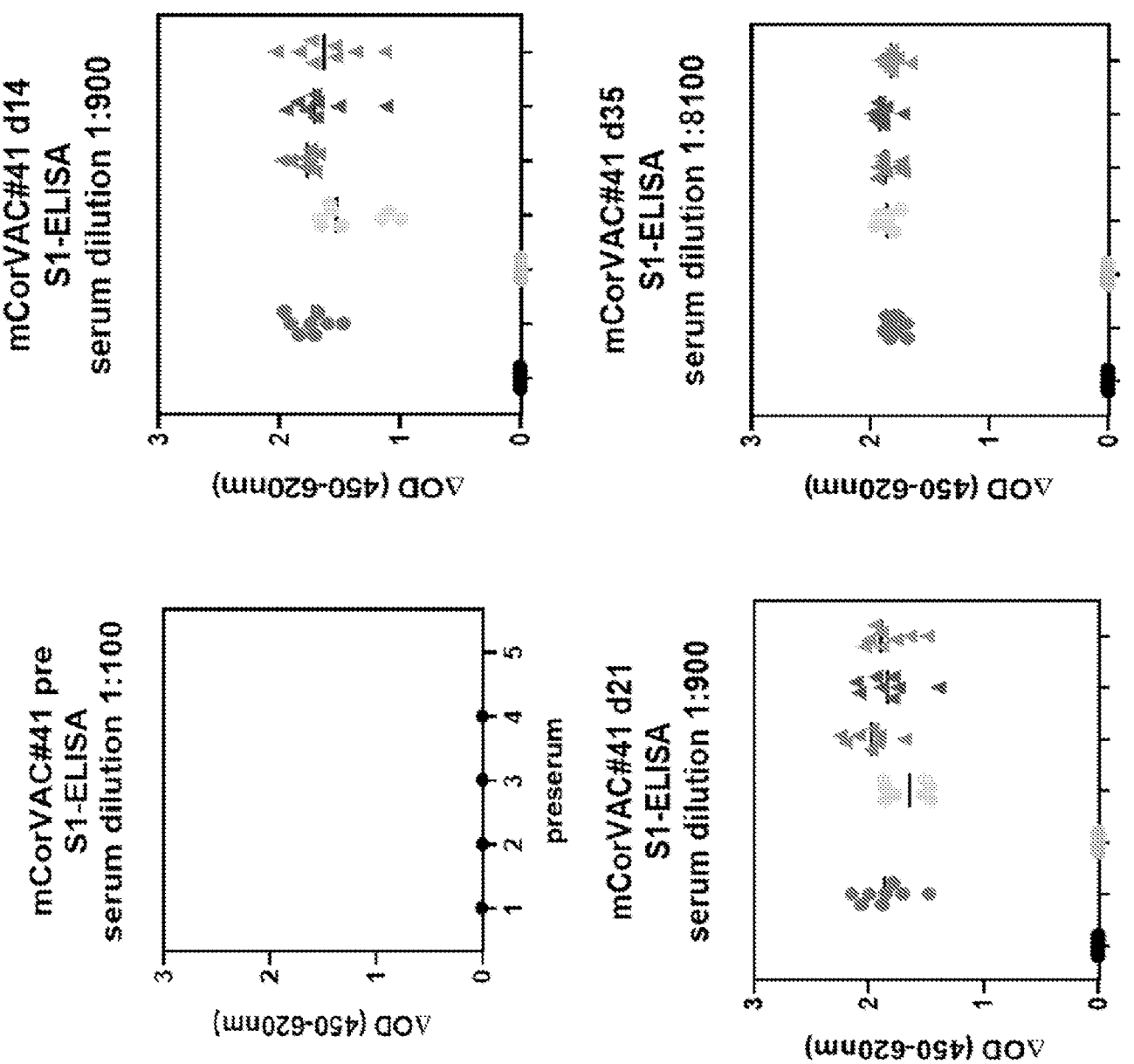

mCorVAC#41 pre
S1-ELISA
serum dilution 1:100
ΔOD (450-620nm)
preserum
mCorVAC#41 d14
S1-ELISA
serum dilution 1:900
mCorVAC#41 d21
S1-ELISA
serum dilution 1:900
mCorVAC#41 d35
S1-ELISA
serum dilution 1:8100
0.9% NaCl
BNT162b2
String C7
BNT162b2: String 1:1 (1µg+1µg)
BNT162b2: String C7 1:1 (1µg+1µg)
BNT162b2: String C7 3:1 (1µg+0.33µg)
BNT162b2: String C7 9:1 (1µg+0.1µg)
combined regimen

FIG. 34A

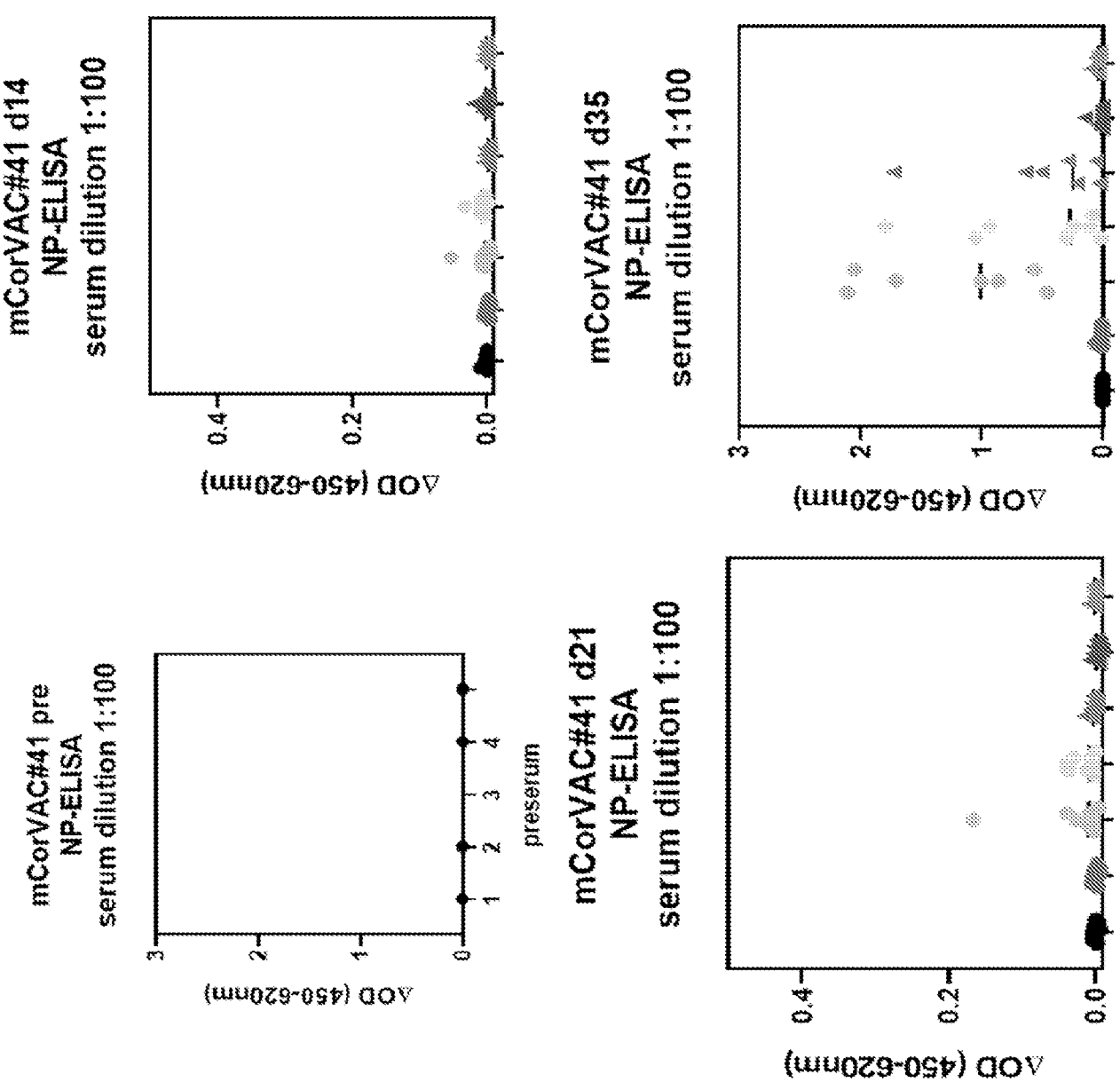

mCorVAC#41 pre
NP-ELISA
serum dilution 1:100
ΔOD (450-620nm)
preserum
mCorVAC#41 d14
NP-ELISA
serum dilution 1:100
mCorVAC#41 d21
NP-ELISA
serum dilution 1:100
mCorVAC#41 d35
NP-ELISA
serum dilution 1:100
0.9% NaCl
BNT162b2
String C7
BNT162b2:String 1:1 [1µg+1µg]
BNT162b2:String C7 1:1 [1µg+1µg]
BNT162b2:String C7 3:1 [1µg+0.33µg]
BNT162b2:String C7 9:1 [1µg+0.1µg]
formulated together

FIG. 34B

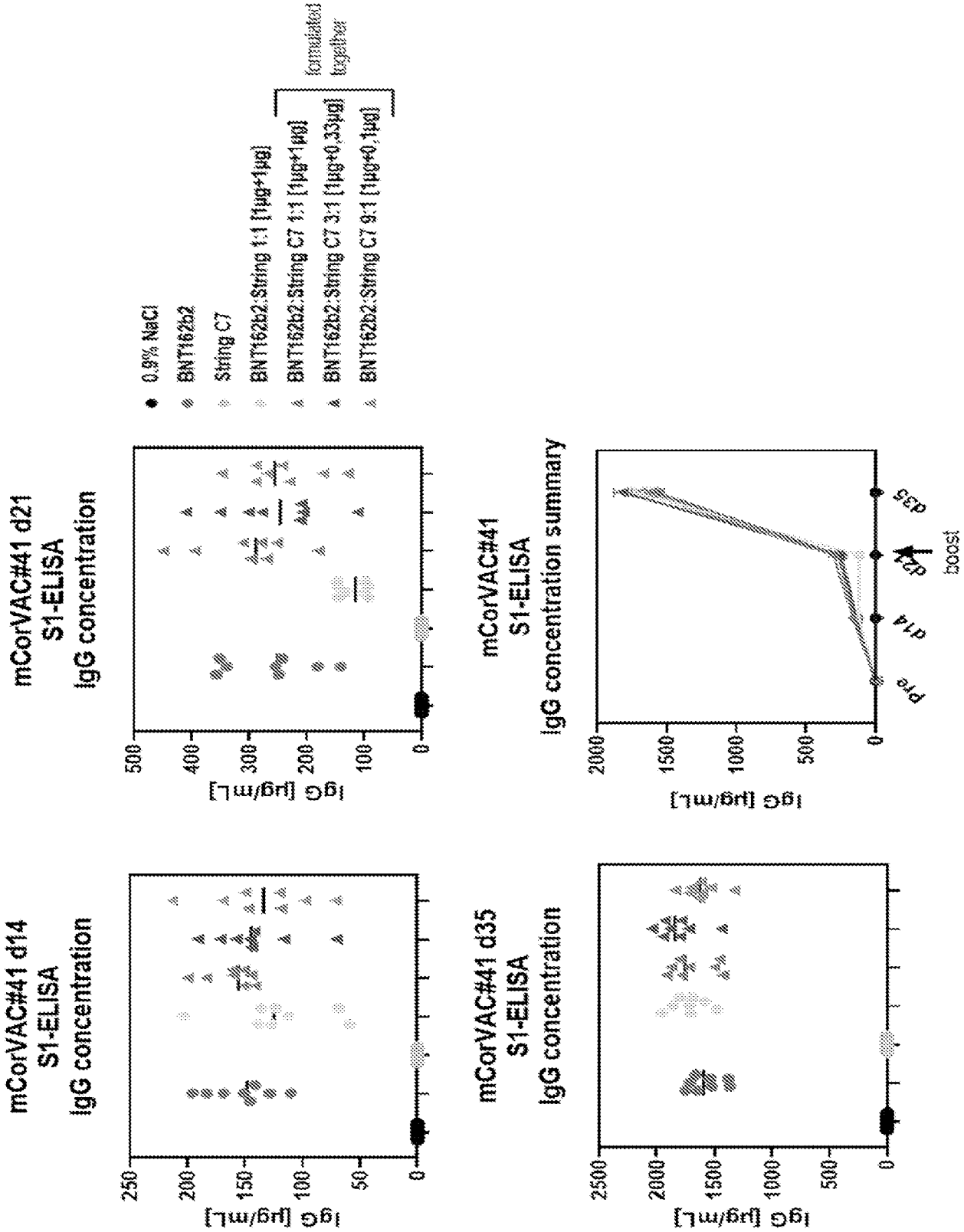

mCorVAC#41 d14
S1-ELISA
IgG concentration
IgG [µg/mL]
mCorVAC#41 d21
S1-ELISA
IgG concentration
IgG [µg/mL]
mCorVAC#41 d35
S1-ELISA
IgG concentration
IgG [µg/mL]
mCorVAC#41
S1-ELISA
IgG concentration summary
IgG [µg/mL]
d1a
d21
d35
boost
0.9% NaCl
BNT162b2
String C7
BNT162b2:String 1:1 [1µg+1µg]
BNT162b2:String C7 1:1 [1µg+1µg]
BNT162b2:String C7 3:1 [1µg+0,33µg]
BNT162b2:String C7 9:1 [1µg+0,1µg]
formulated together

FIG. 35

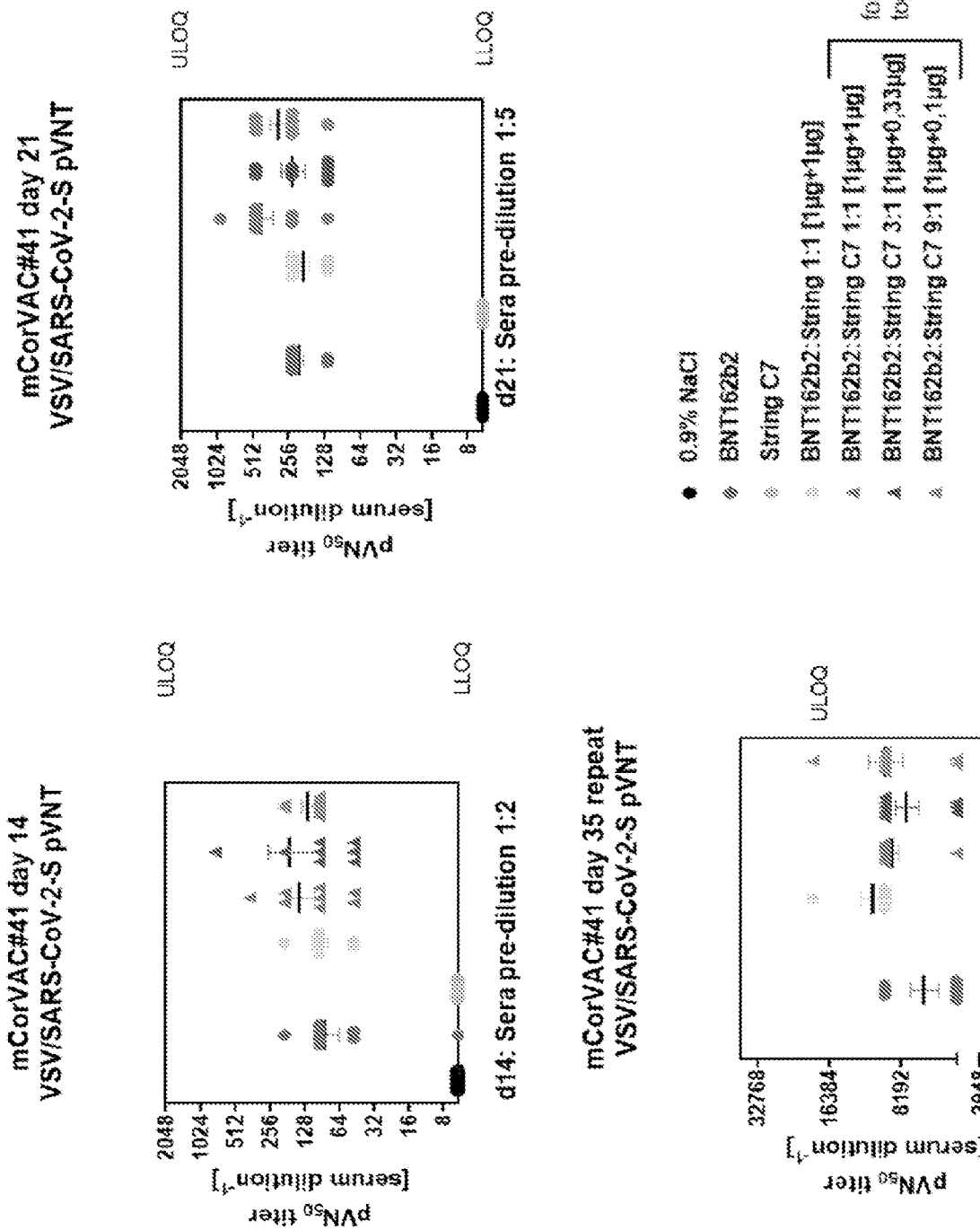

mCorVAC#41 day 14
VSV/SARS-CoV-2-S pVNT
pVN50 titer
[serum dilution²]
2048
1024
512
256
128
64
32
16
8
ULOQ
LLOQ
d14: Sera pre-dilution 1:2
mCorVAC#41 day 21
VSV/SARS-CoV-2-S pVNT
d21: Sera pre-dilution 1:5
mCorVAC#41 day 35 repeat
VSV/SARS-CoV-2-S pVNT
32768
16384
8192
d35: Sera pre-dilution 1:50
0.9% NaCl
BNT162b2
String C7
BNT162b2:String 1:1 [1µg+1µg]
BNT162b2:String C7 1:1 [1µg+1µg]
BNT162b2:String C7 3:1 [1µg+0,33µg]
BNT162b2:String C7 9:1 [1µg+0,1µg]
formulated together

FIG. 36

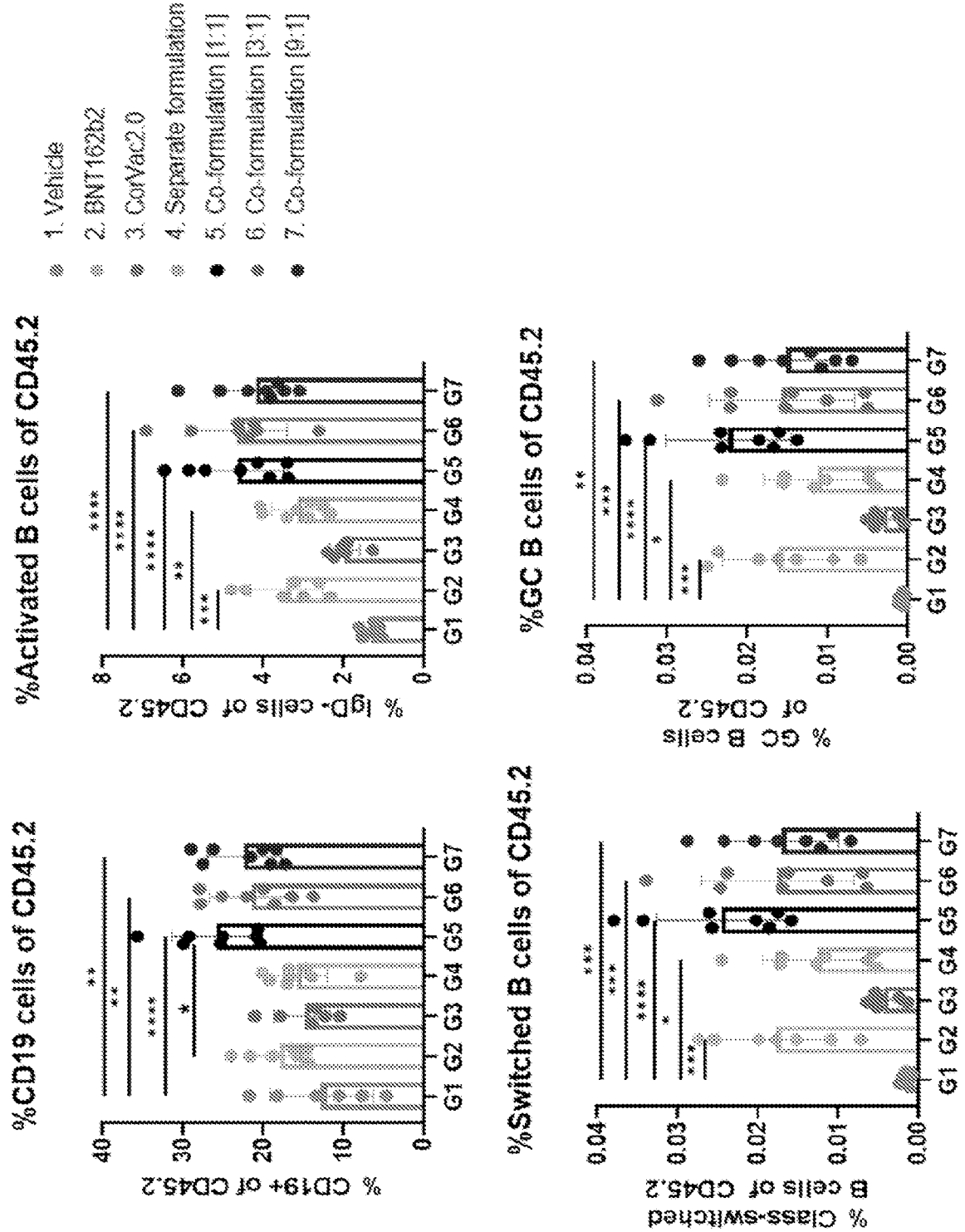

1. Vehicle
2. BNT162b2
3. CoVac2.0
4. Separate formulation
5. Co-formulation [1:1]
6. Co-formulation [3:1]
7. Co-formulation [9:1]
%CD19 cells of CD45.2
% CD19+ of CD45.2
%Activated B cells of CD45.2
% IgD- cells of CD45.2
%GC B cells of CD45.2
% GC B cells of CD45.2
%Switched B cells of CD45.2
% Class-switched B cells of CD45.2
G1 G2 G3 G4 G5 G6 G7

FIG. 37A

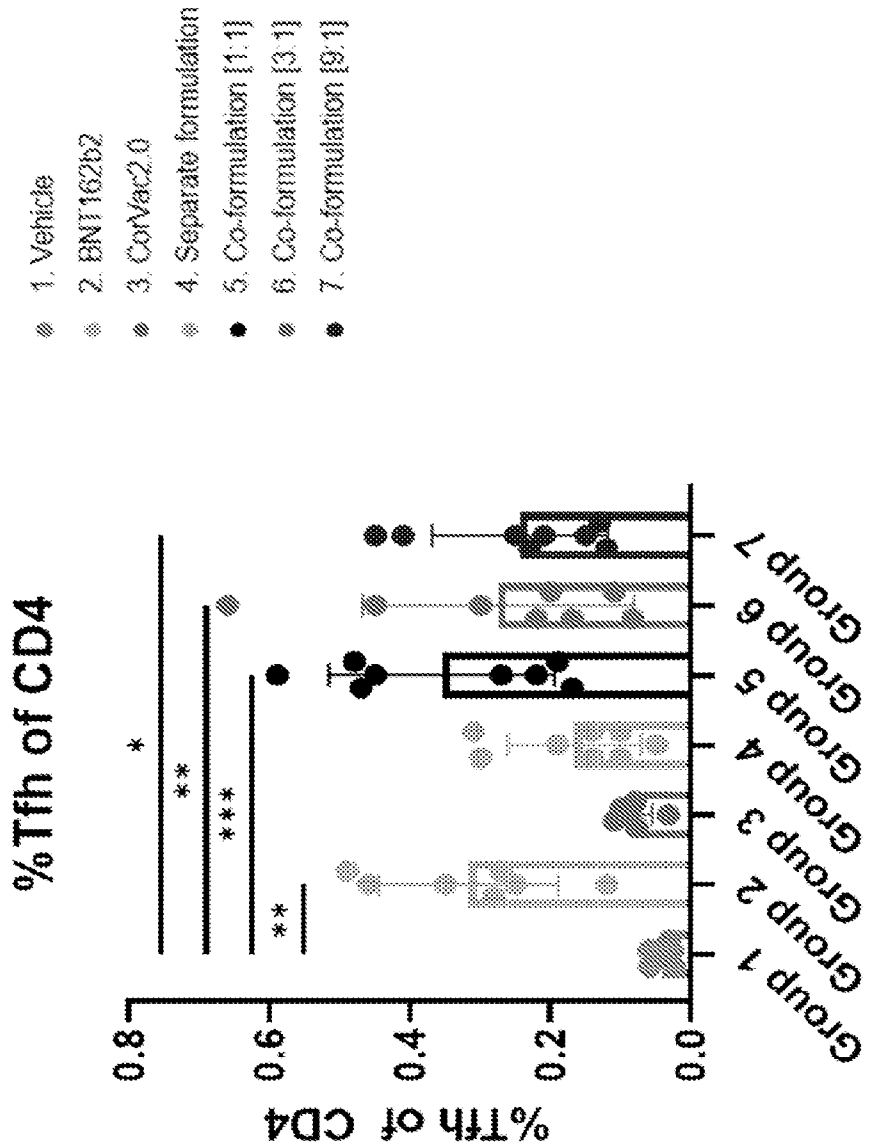

1. Vehicle
2. BNT162b2
3. CoVac2.0
4. Separate formulation
5. Co-formulation [1:1]
6. Co-formulation [3:1]
7. Co-formulation [9:1]
%Tfh of CD4
%Tfh of CD4
0.0
0.2
0.4
0.6
0.8
Group 1
Group 2
Group 3
Group 4
Group 5
Group 6
Group 7
*
**
***
**

FIG. 37B

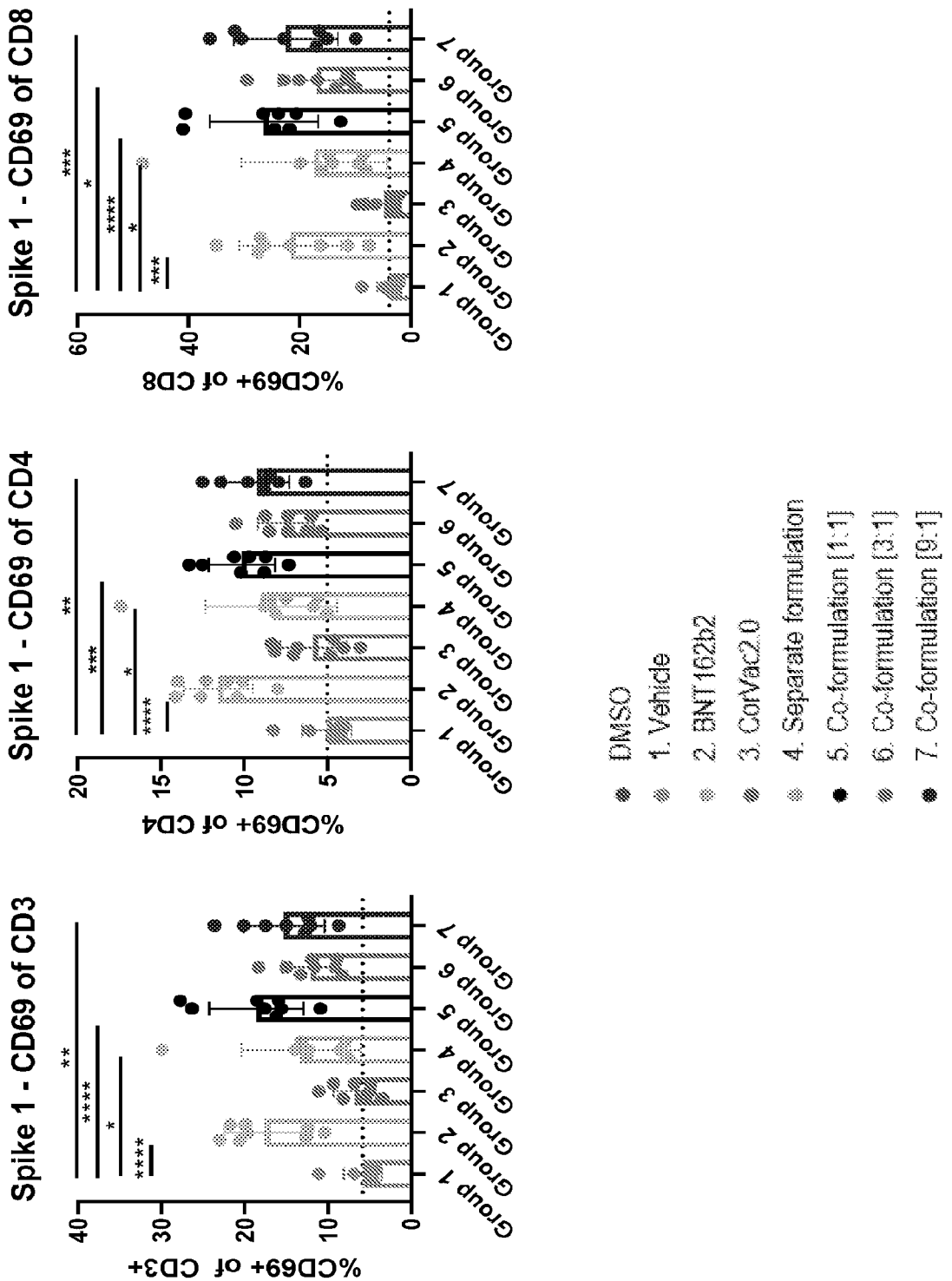

Spike 1 - CD69 of CD3
%CD69+ of CD3+
Spike 1 - CD69 of CD4
%CD69+ of CD4
Spike 1 - CD69 of CD8
%CD69+ of CD8
Group 1
Group 2
Group 3
Group 4
Group 5
Group 6
Group 7
DMSO
1. Vehicle
2. BNT162b2
3. CorVac2.0
4. Separate formulation
5. Co-formulation [1:1]
6. Co-formulation [3:1]
7. Co-formulation [9:1]

FIG. 38

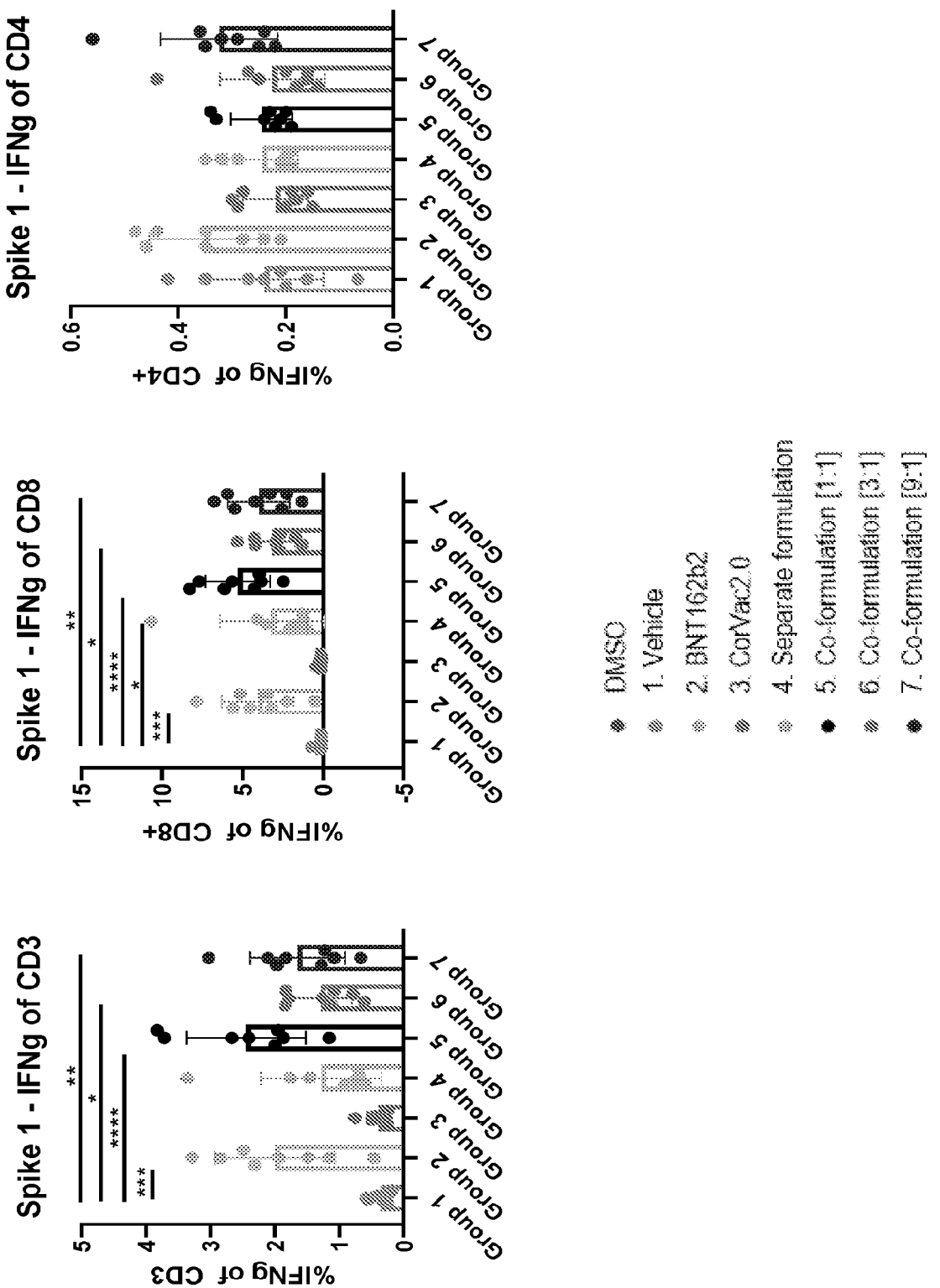

Spike 1 - IFNg of CD3
%IFNg of CD3+
Spike 1 - IFNg of CD8
%IFNg of CD8+
Spike 1 - IFNg of CD4
%IFNg of CD4+
Group 1
Group 2
Group 3
Group 4
Group 5
Group 6
Group 7
DMSO
1. Vehicle
2. BNT162b2
3. CorVac2.0
4. Separate formulation
5. Co-formulation [1:1]
6. Co-formulation [3:1]
7. Co-formulation [9:1]

FIG. 39

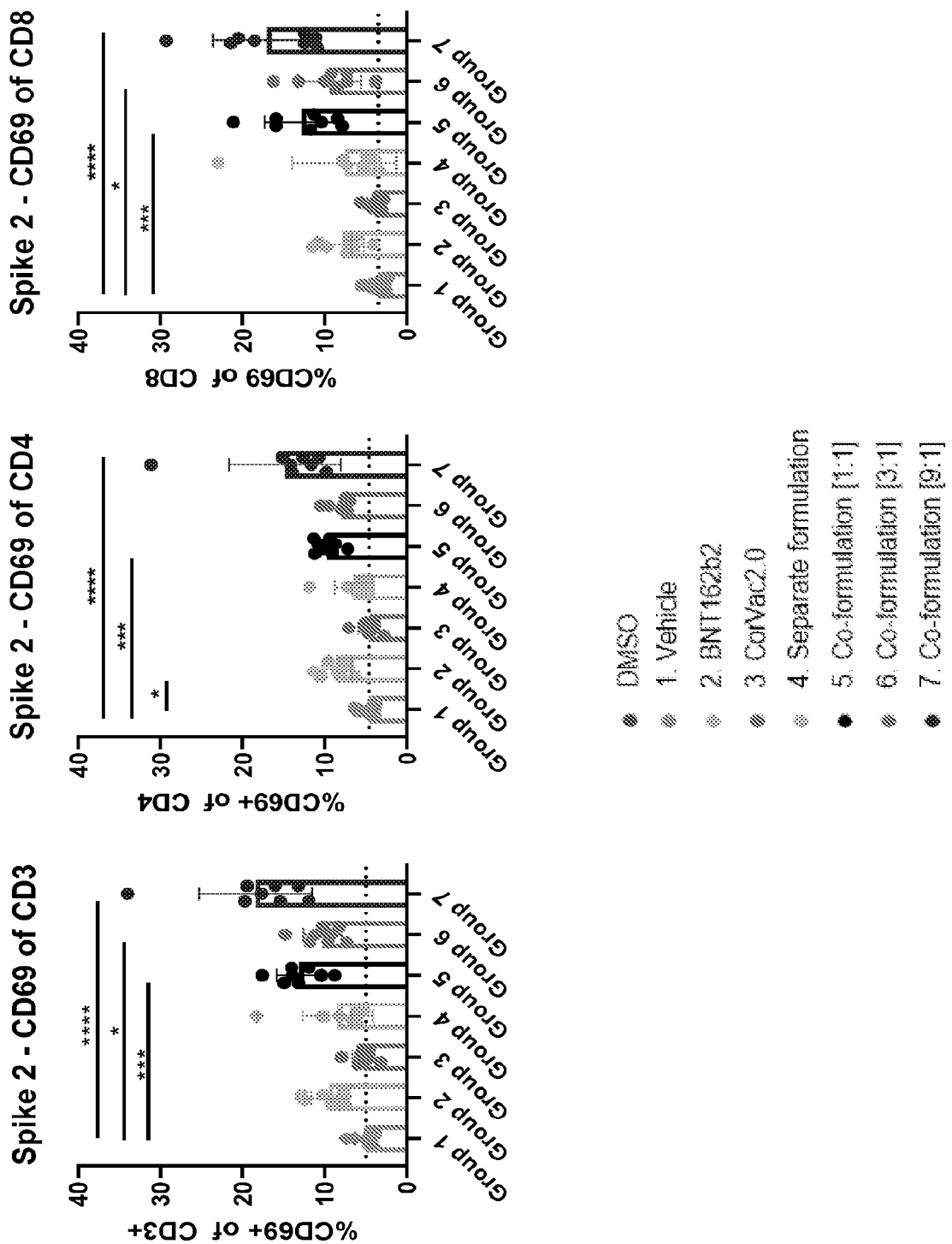

Spike 2 - CD69 of CD3
%CD69+ of CD3+
Spike 2 - CD69 of CD4
%CD69+ of CD4
Spike 2 - CD69 of CD8
%CD69 of CD8
0
10
20
30
40
*
***
****
Group 1
Group 2
Group 3
Group 4
Group 5
Group 6
Group 7
DMSO
1. Vehicle
2. BNT162b2
3. CoVac2.0
4. Separate formulation
5. Co-formulation [1:1]
6. Co-formulation [3:1]
7. Co-formulation [9:1]

FIG. 40

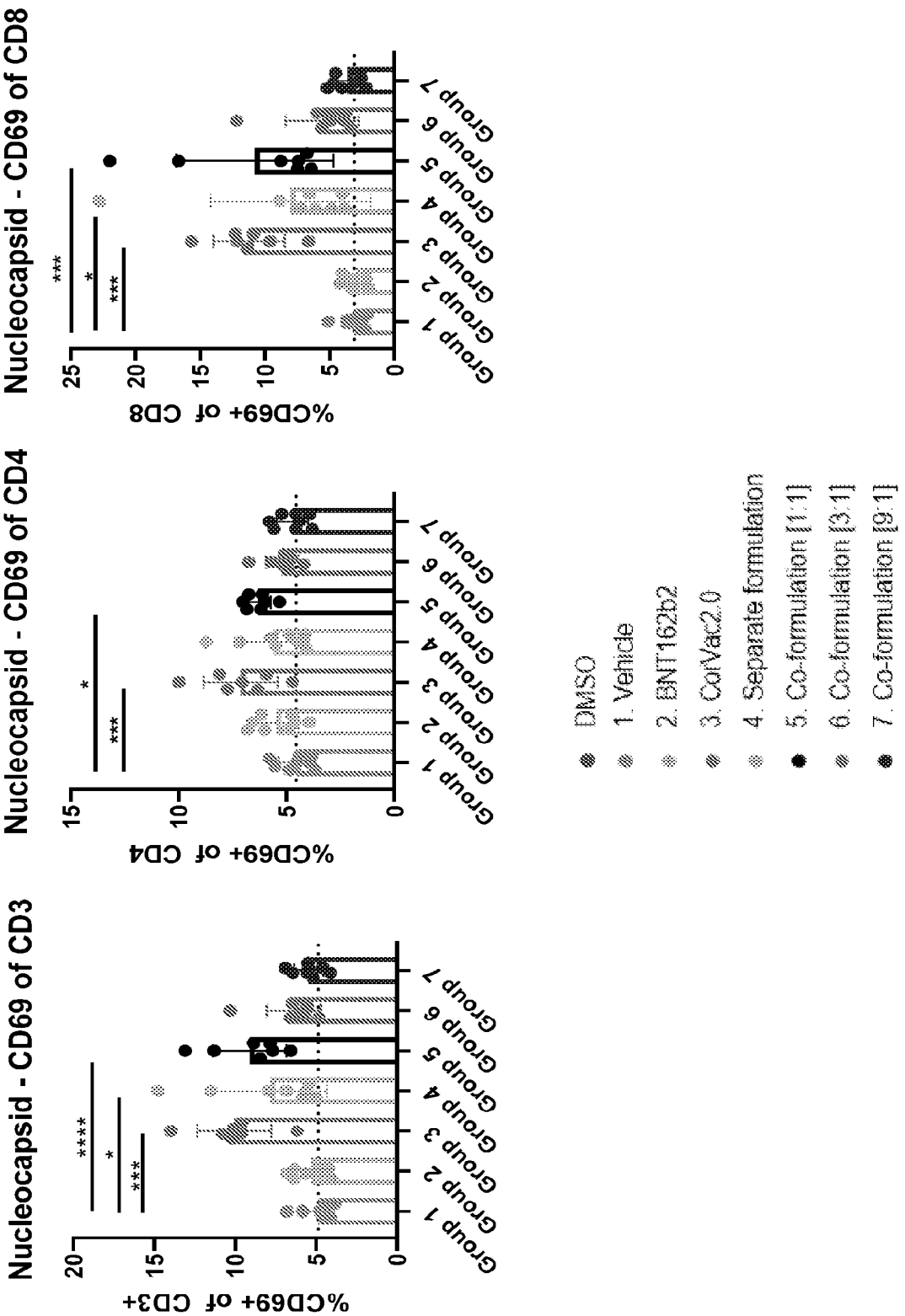

Nucleocapsid - CD69 of CD3
%CD69+ of CD3+
Nucleocapsid - CD69 of CD4
%CD69+ of CD4
Nucleocapsid - CD69 of CD8
%CD69+ of CD8
Group 1
Group 2
Group 3
Group 4
Group 5
Group 6
Group 7
DMSO
1. Vehicle
2. BNT162b2
3. CoVac2.0
4. Separate formulation
5. Co-formulation [1:1]
6. Co-formulation [3:1]
7. Co-formulation [9:1]

FIG. 41A

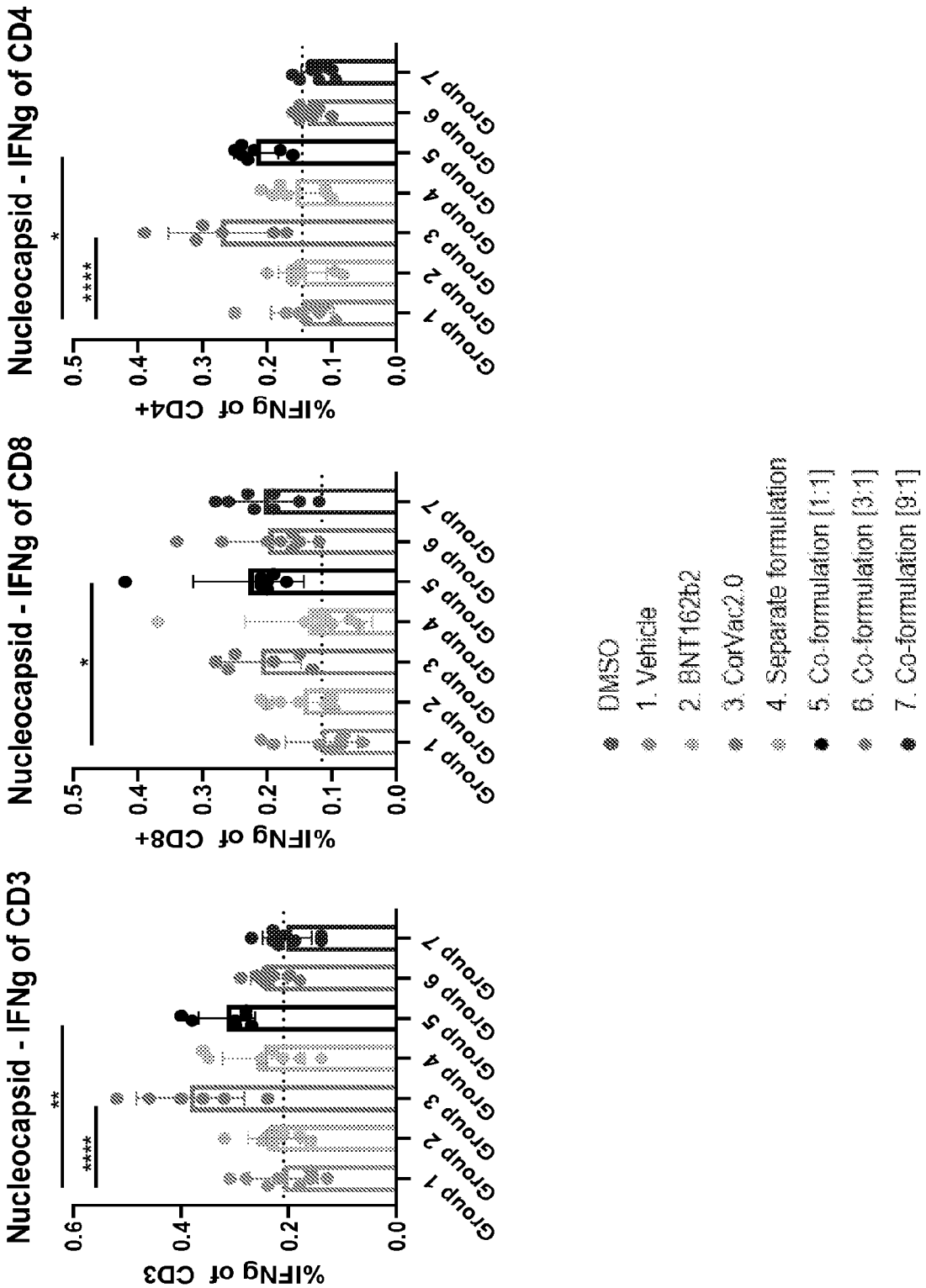

Nucleocapsid - IFNg of CD3
%IFNg of CD3
0.0
0.2
0.4
0.6
****
**
Group 1
Group 2
Group 3
Group 4
Group 5
Group 6
Group 7
Nucleocapsid - IFNg of CD8
%IFNg of CD8+
0.0
0.1
0.2
0.3
0.4
0.5
*
Group 1
Group 2
Group 3
Group 4
Group 5
Group 6
Group 7
Nucleocapsid - IFNg of CD4
%IFNg of CD4+
0.0
0.1
0.2
0.3
0.4
0.5
****
*
Group 1
Group 2
Group 3
Group 4
Group 5
Group 6
Group 7
DMSO
1. Vehicle
2. BNT162b2
3. CoVac2.0
4. Separate formulation
5. Co-formulation [1:1]
6. Co-formulation [3:1]
7. Co-formulation [9:1]

FIG. 41B

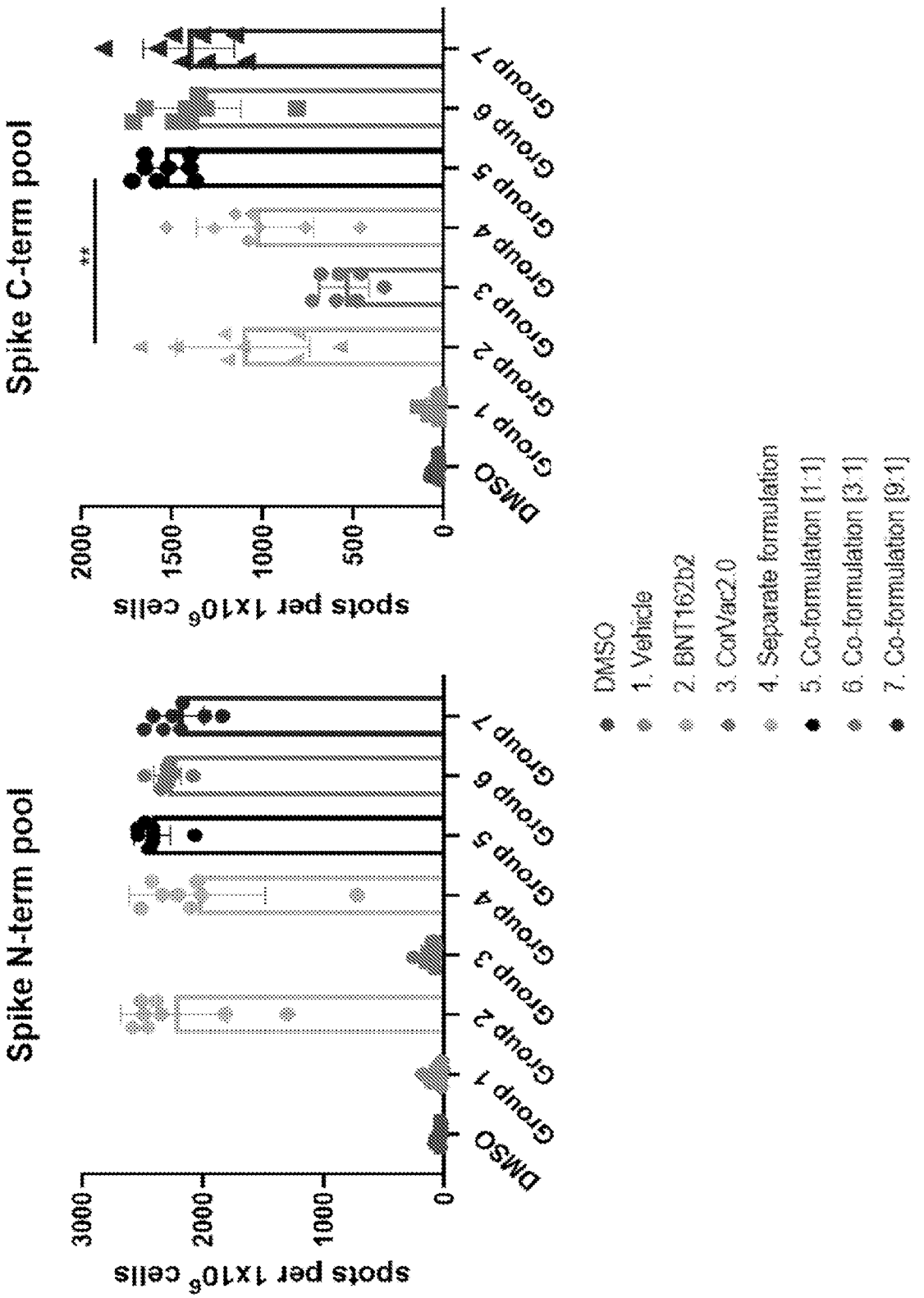

Spike C-term pool
Spike N-term pool
spots per 1x10^6 cells
DMSO
Group 1
Group 2
Group 3
Group 4
Group 5
Group 6
Group 7
**
0
500
1000
1500
2000
0
1000
2000
3000
DMSO
1. Vehicle
2. BNT162b2
3. CoVac2.0
4. Separate formulation
5. Co-formulation (1:1)
6. Co-formulation (3:1)
7. Co-formulation (9:1)

FIG. 42

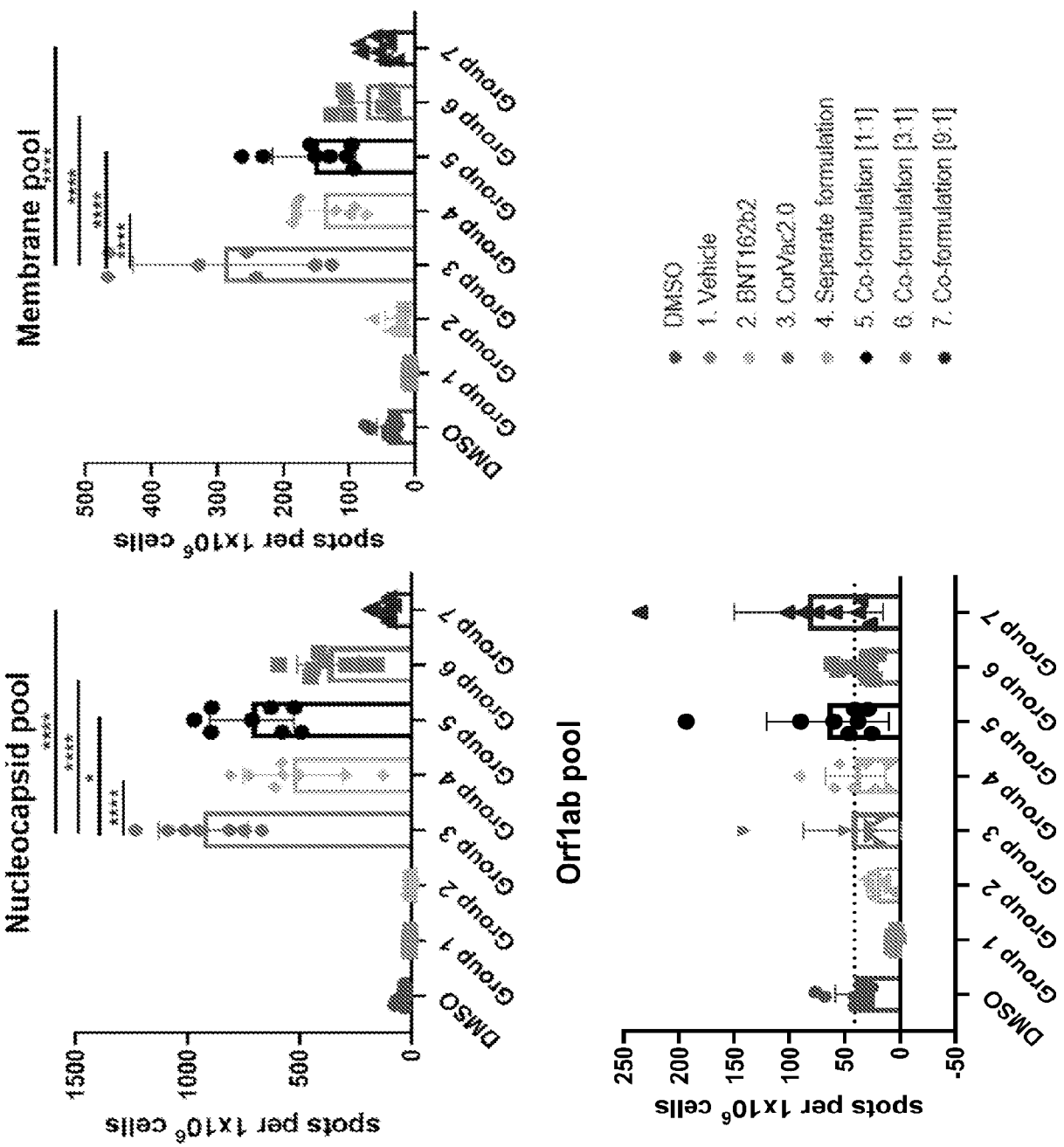

Membrane pool
spots per 1x10^6 cells
500
400
300
200
100
0
DMSO
Group 1
Group 2
Group 3
Group 4
Group 5
Group 6
Group 7
Nucleocapsid pool
spots per 1x10^6 cells
1500
1000
500
0
DMSO
Group 1
Group 2
Group 3
Group 4
Group 5
Group 6
Group 7
Orf1ab pool
spots per 1x10^6 cells
250
200
150
100
50
0
-50
DMSO
Group 1
Group 2
Group 3
Group 4
Group 5
Group 6
Group 7
DMSO
1. Vehicle
2. BNT162b2
3. CoVac2.0
4. Separate formulation
5. Co-formulation [1:1]
6. Co-formulation [3:1]
7. Co-formulation [9:1]

FIG. 43

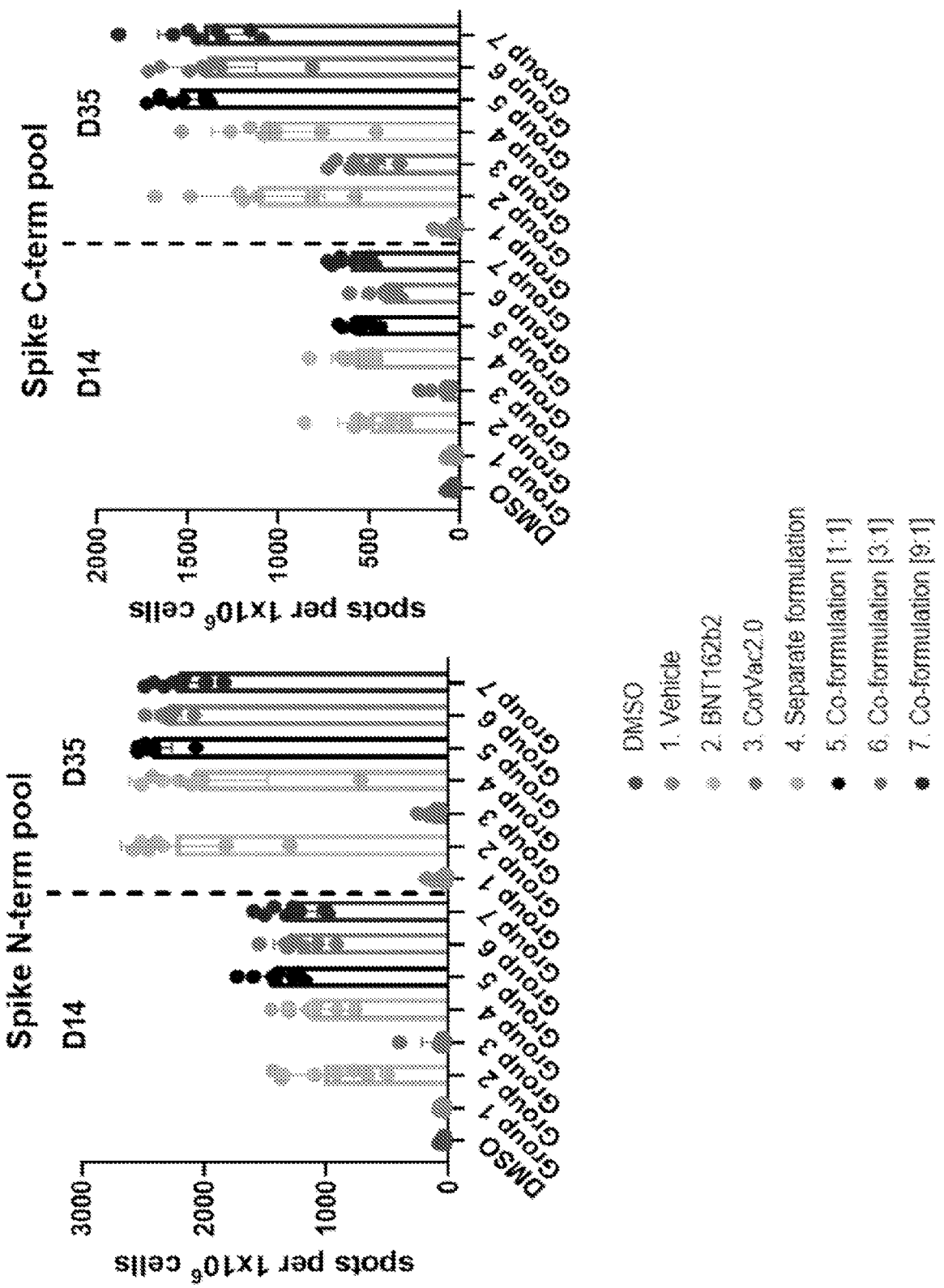

Spike N-term pool
D14
D35
spots per 1x10^6 cells
3000
2000
1000
0
DMSO
Group 1
Group 2
Group 3
Group 4
Group 5
Group 6
Group 7
Spike C-term pool
D14
D35
spots per 1x10^6 cells
2000
1500
1000
500
0
DMSO
Group 1
Group 2
Group 3
Group 4
Group 5
Group 6
Group 7
DMSO
1. Vehicle
2. BNT162b2
3. CoVac2.0
4. Separate formulation
5. Co-formulation [1:1]
6. Co-formulation [3:1]
7. Co-formulation [9:1]

FIG. 44

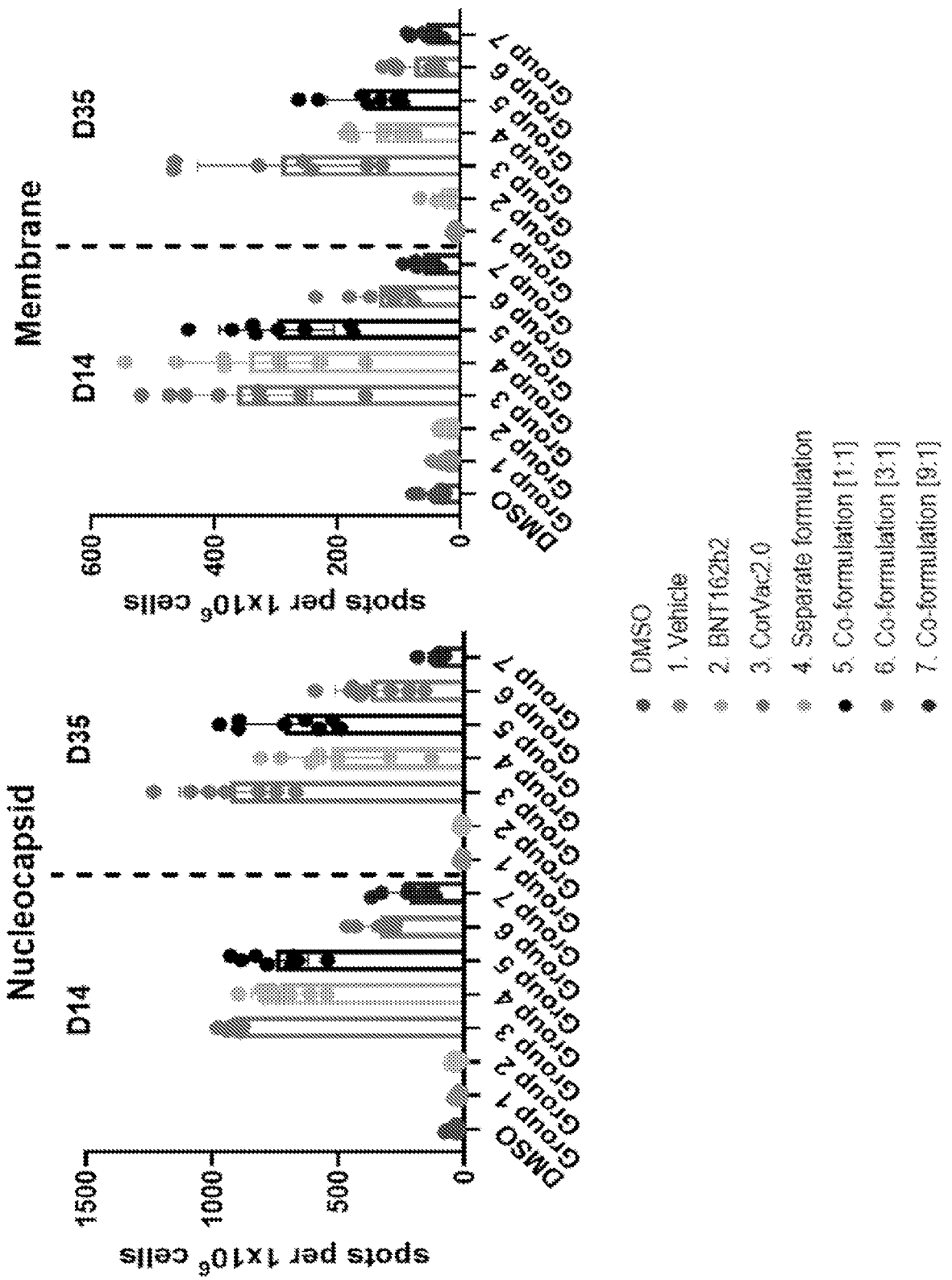

Membrane
D14
D35
spots per 1x10^6 cells
600
400
200
0
DMSO
Group 1
Group 2
Group 3
Group 4
Group 5
Group 6
Group 7
Nucleocapsid
1500
1000
500
DMSO
1. Vehicle
2. BNT162b2
3. CoVac2.0
4. Separate formulation
5. Co-formulation [1:1]
6. Co-formulation [3:1]
7. Co-formulation [9:1]

FIG. 45

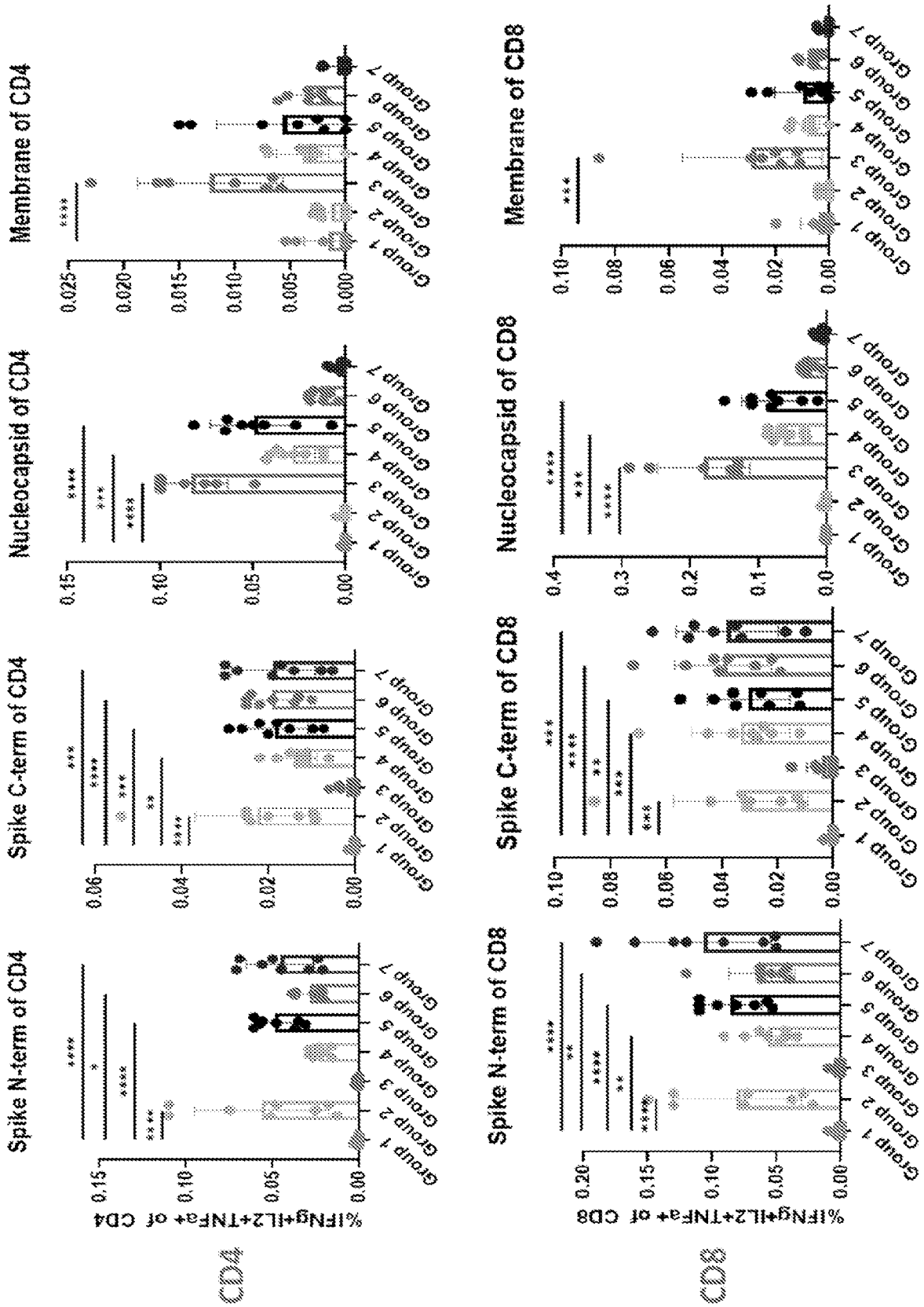

CD4
CD8
Spike N-term of CD4
Spike C-term of CD4
Nucleocapsid of CD4
Membrane of CD4
Spike N-term of CD8
Spike C-term of CD8
Nucleocapsid of CD8
Membrane of CD8
%IFNg+IL2+TNFa+ of CD4
%IFNg+IL2+TNFa+ of CD8
Group 1
Group 2
Group 3
Group 4
Group 5
Group 6
Group 7

FIG. 46

Spike N

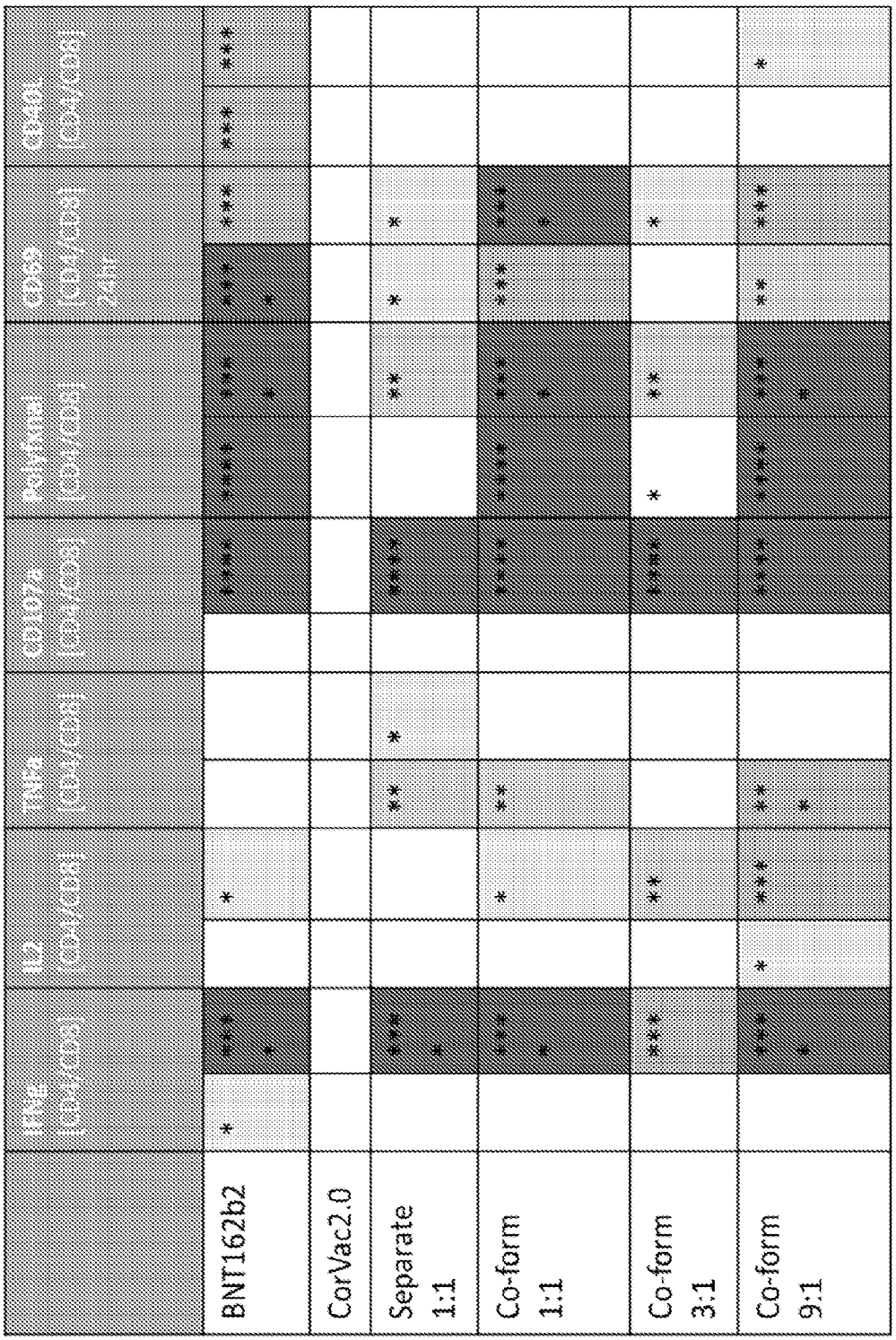


FIG. 47

Spike C

	IFNγ (pg/mL)		IL2 (pg/mL)		TNFα (pg/mL)		CD107a (pg/mL)		Polyfunct (pg/mL)		CD69 (pg/mL) 24hr		CD40L (pg/mL)	
BNT162b2	**		***	*	*				****	***	*			
CorVac2.0	**		*											
Separate 1:1	**		*		***	***			**	***				
Co-form 1:1	***		***	*	***	*	*		***	**	***	***		
Co-form 3:1	*		*		*				****	****		*		
Co-form 9:1	****	****	**		***	*			***	***	***	*	***	*

FIG. 48

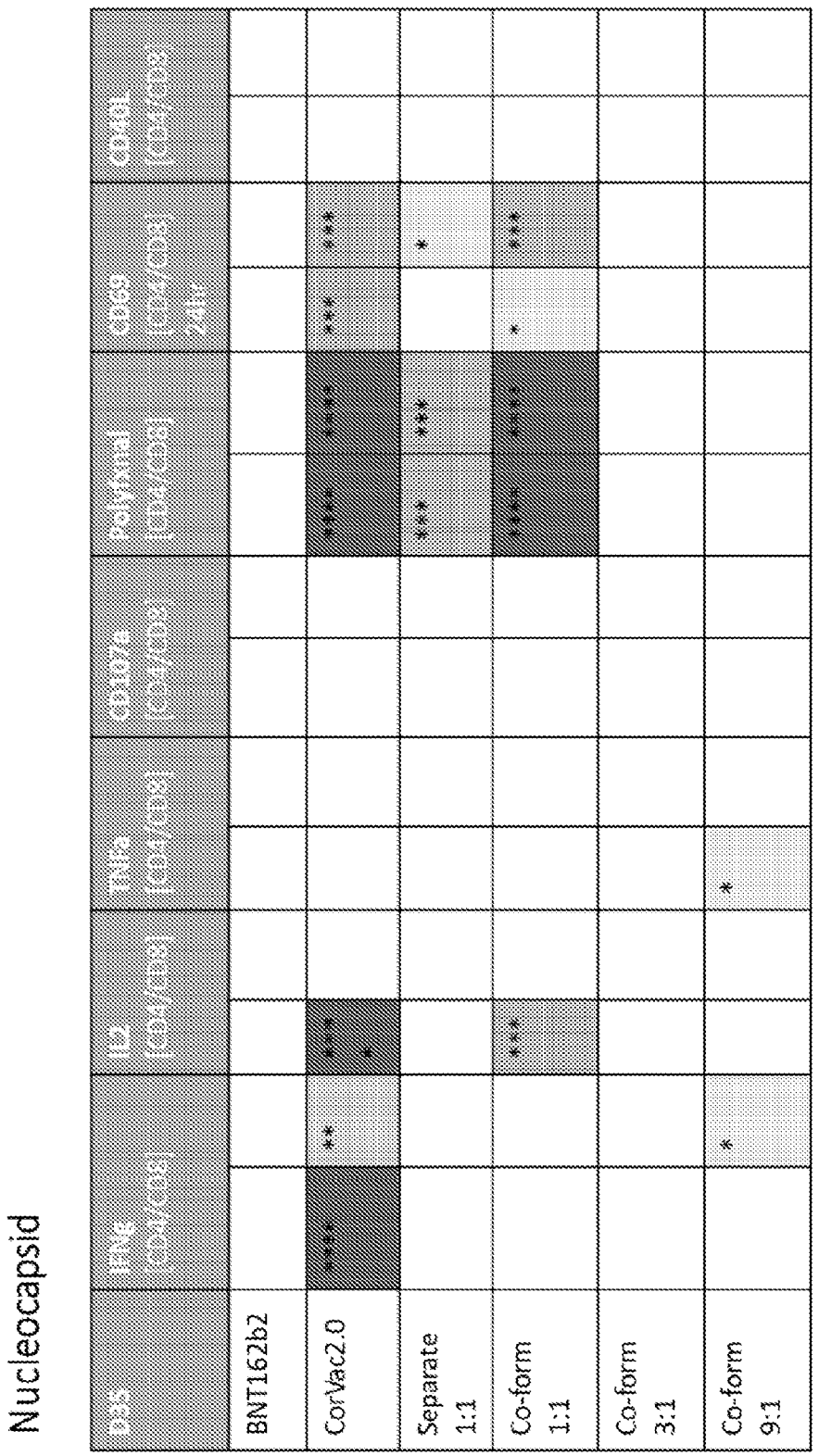

Nucleocapsid
BNT162b2
CorVac2.0
Separate 1:1
Co-form 1:1
Co-form 3:1
Co-form 9:1
BNT162b2 (30µg/100µl)
IL2 (10µg/100µl)
BNT162b2 (30µg/100µl)
CorVac2.0 (5µg/100µl)
BNT162b2 (30µg/100µl) + CorVac2.0 (5µg/100µl)
BNT162b2 (30µg/100µl) + CorVac2.0 (5µg/100µl) + IL2 (10µg/100µl)
PBS

FIG. 49

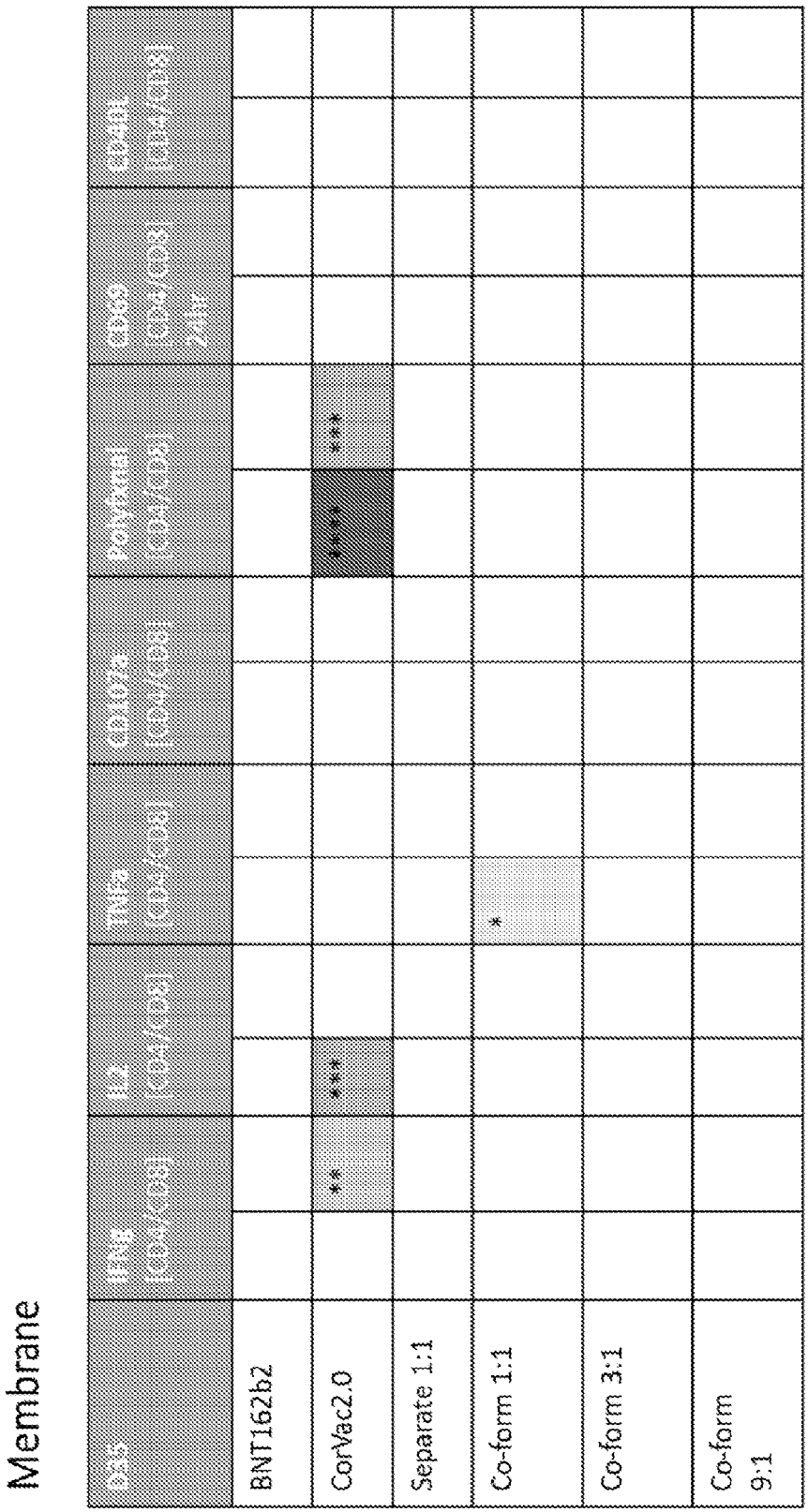

Membrane
DAS
BNT162b2
CorVac2.0
Separate 1:1
Co-form 1:1
Co-form 3:1
Co-form 9:1
IFNg (cDAY1/D8)
IL2 (cDAY1/D8)
TNFa (cDAY1/D8)
CD107a (cDAY1/D8)
Polyfunct (cDAY1/D8)
CD69 (cDAY1/D8 24hr
CD69 (mDAY1/D8)
**
***
*
****
***

FIG. 50

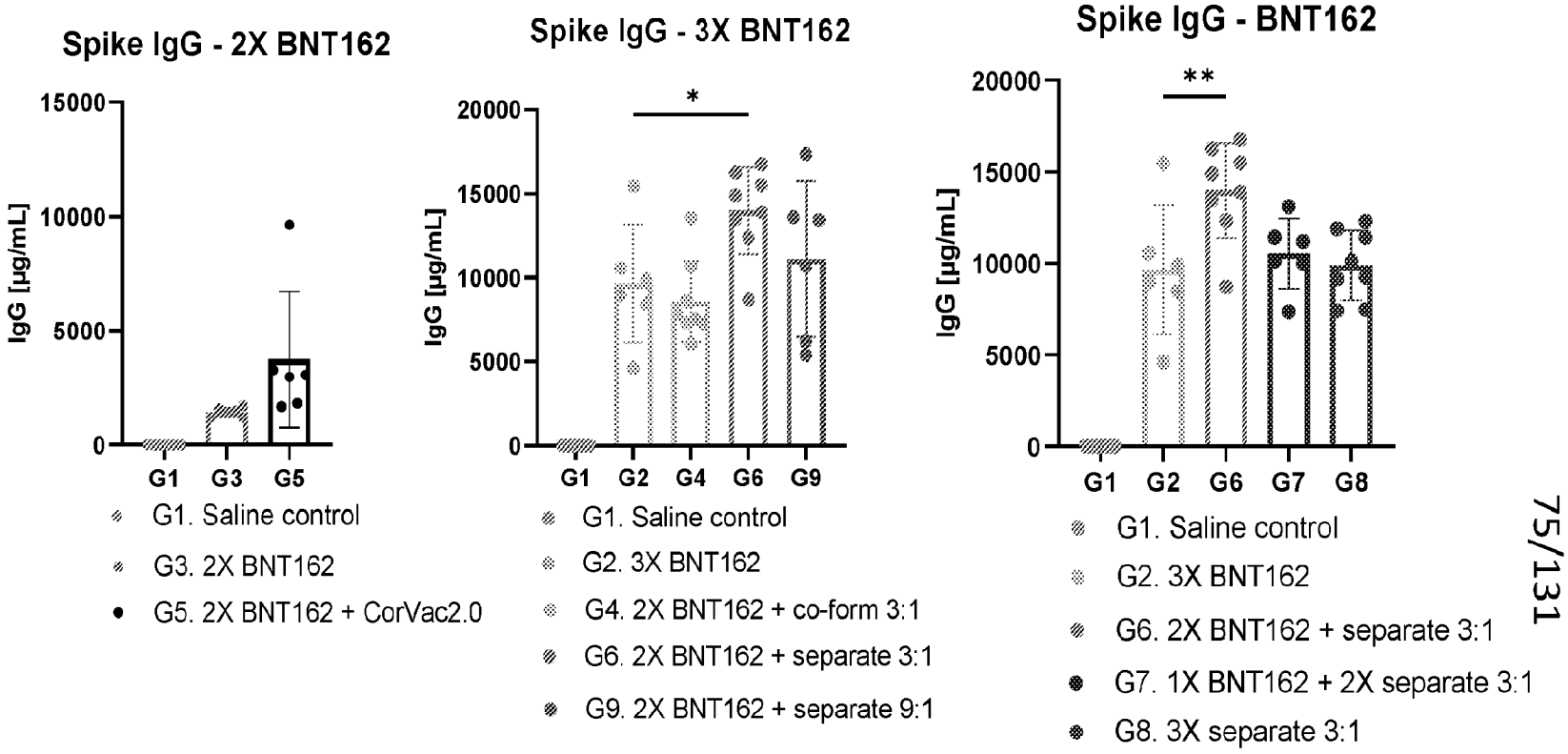
size (n=X)	group	Description			Dose [µg] BNT162b2/CorVac 2.0	Day													
		prime	boost	boost		-x	0		14		21			35		42			56
6	1	0.9% NaCl	0.9% NaCl	0.9% NaCl	-														
6	2	BNT162b2	BNT162b2	BNT162b2	1 ug														
6	3	BNT162b2	BNT162b2	0.9% NaCl	1 ug														
8	4	BNT162b2	BNT162b2	coformulation BNT162b2:String C7	1ug/0.3 ug														
6	5	BNT162b2	BNT162b2	String C7	1ug/0.3ug														
8	6	BNT162b2	BNT162b2	Separately BNT162b2:String C7	1ug/0.3ug														
6	7	BNT162b2	Separately BNT162b2:String C7 1ug/0.3ug	Separately BNT162b2: String C7 1ug/0.3ug	1ug/0.3ug														
8	8	Separately BNT162b2: String C7 1ug/0.3ug	Separately BNT162b2: String C7 1ug/0.3ug	Separately BNT162b2: String C7 1ug/0.3ug	1ug/0.3ug														
6	9	BNT162b2	BNT162b2	Separately BNT162b2:String C7 1ug/0.11ug	1ug/ 0.11ug														

Application (i.m.): 20µL in one leg

Blood collection r.b./ Serum generation (Aliquots)

Final blood collection/ Serum generation / Spleen for Splenocyte preparation/ lymph nodes

FIG. 51



CorVac2.0 alone slightly boosts Spike IgG production

Separately formulated 3:1 boosts Spike IgG production

Inclusion of multiple doses of separately formulated CorVac2.0 does not negatively impact Spike IgG responses

FIG. 52

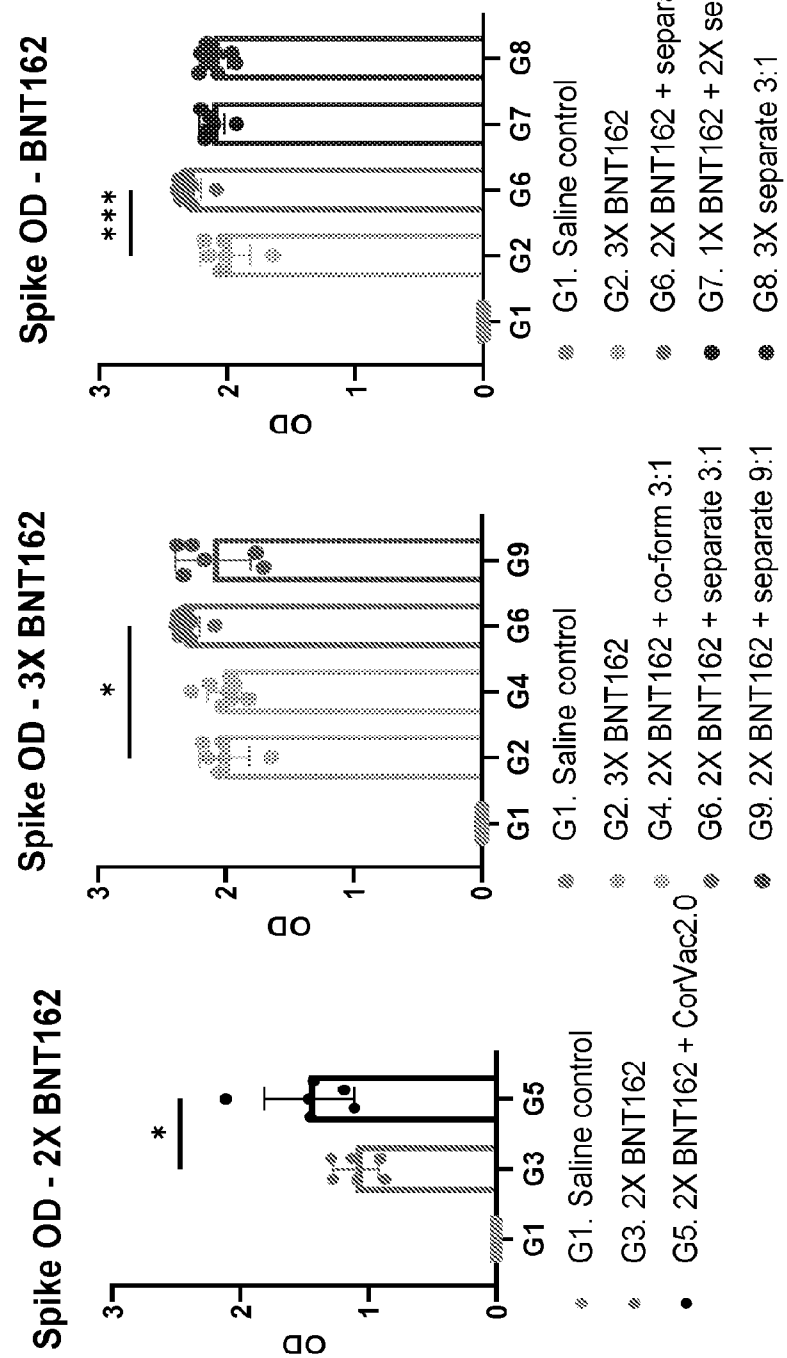

Spike OD - 2X BNT162
Spike OD - 3X BNT162
Spike OD - BNT162
OD
0
1
2
3
*
***
G1
G2
G3
G4
G5
G6
G7
G8
G9
G1. Saline control
G2. 3X BNT162
G3. 2X BNT162
G4. 2X BNT162 + co-form 3:1
G5. 2X BNT162 + CorVac2.0
G6. 2X BNT162 + separate 3:1
G7. 1X BNT162 + 2X separate 3:1
G8. 3X separate 3:1
G9. 2X BNT162 + separate 9:1

FIG. 53

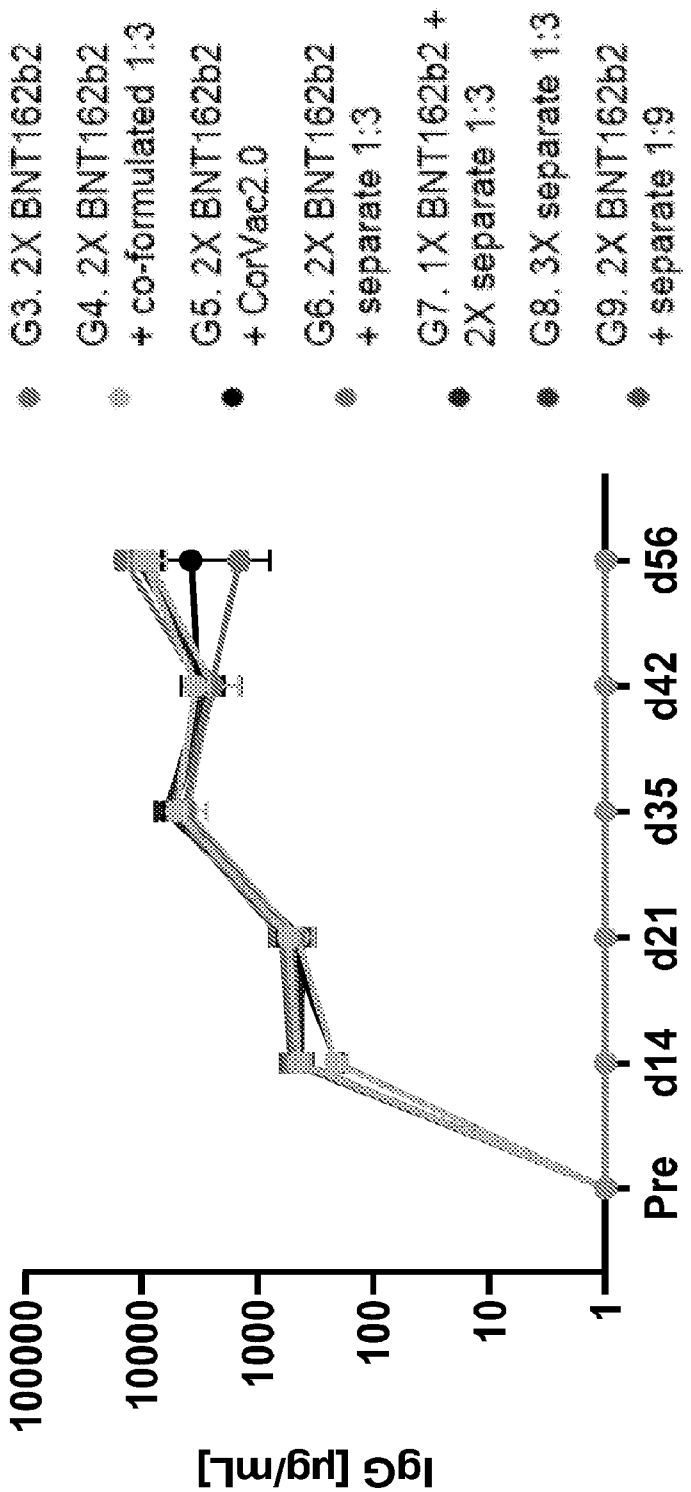

Spike IgG - kinetics
IgG [µg/mL]
100000
10000
1000
100
10
1
Pre
d14
d21
d35
d42
d56
DMSO
G1. Saline control
G2. 3X BNT162b2
G3. 2X BNT162b2
G4. 2X BNT162b2 + co-formulated 1:3
G5. 2X BNT162b2 + CoVac2.0
G6. 2X BNT162b2 + separate 1:3
G7. 1X BNT162b2 + 2X separate 1:3
G8. 3X separate 1:3
G9. 2X BNT162b2 + separate 1:9

FIG. 54

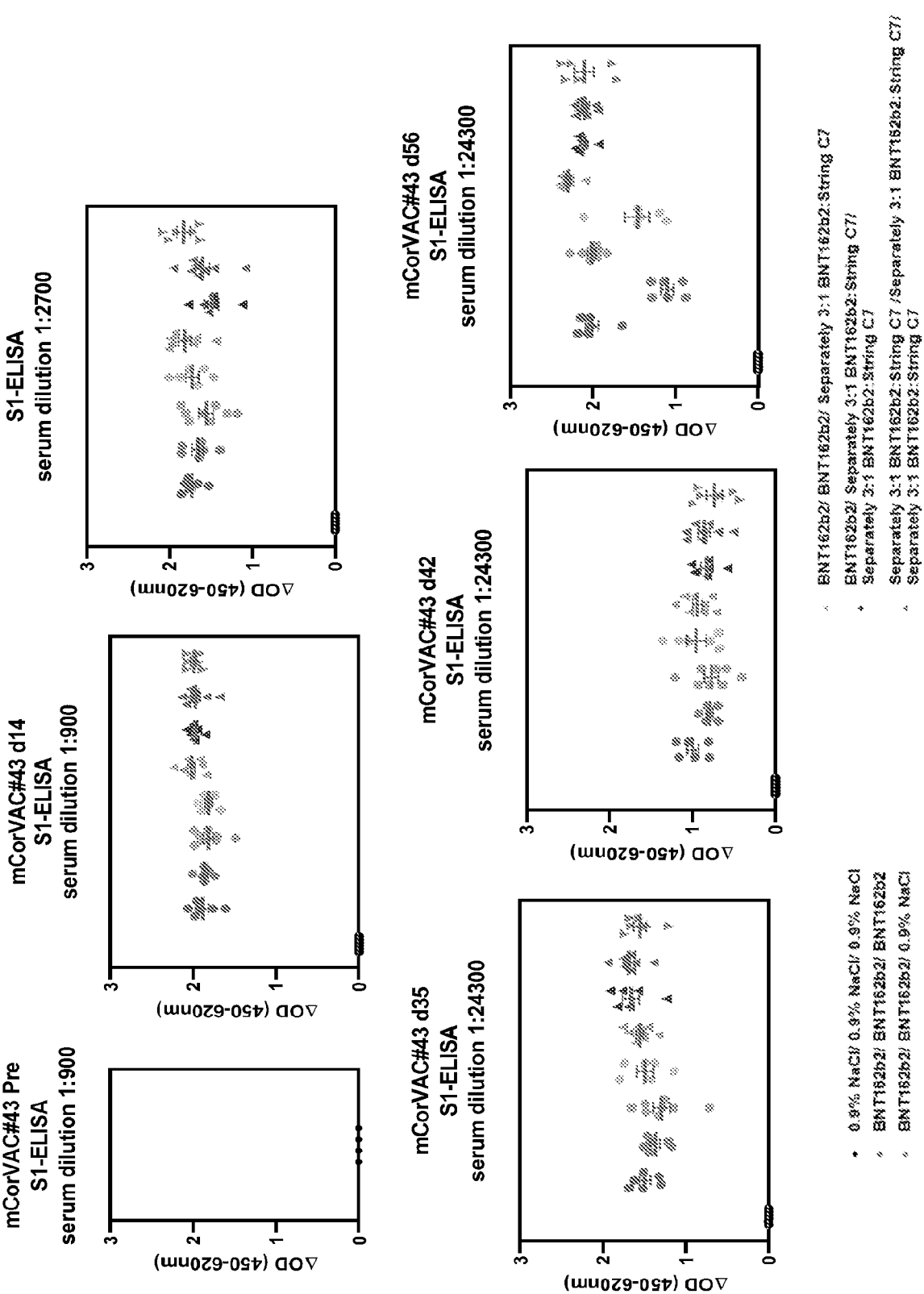

mCorVAC#43 Pre
S1-ELISA
serum dilution 1:900
mCorVAC#43 d14
S1-ELISA
serum dilution 1:900
mCorVAC#43 d21
S1-ELISA
serum dilution 1:2700
mCorVAC#43 d35
S1-ELISA
serum dilution 1:24300
mCorVAC#43 d42
S1-ELISA
serum dilution 1:24300
mCorVAC#43 d56
S1-ELISA
serum dilution 1:24300
ΔOD (450-620nm)
0
1
2
3
0.9% NaCl/ 0.9% NaCl/ 0.9% NaCl
BNT162b2/ BNT162b2/ BNT162b2
BNT162b2/ BNT162b2/ 0.9% NaCl
BNT162b2/ BNT162b2: String C7
BNT162b2/ BNT162b2/ String C7
BNT162b2/ BNT162b2/ Separately 3:1 BNT162b2: String C7
BNT162b2/ Separately 3:1 BNT162b2: String C7/
Separately 3:1 BNT162b2: String C7 /Separately 3:1 BNT162b2: String C7/
Separately 3:1 BNT162b2: String C7
BNT162b2/ BNT162b2/ Separately 9:1 BNT162b2: String C7

FIG. 55

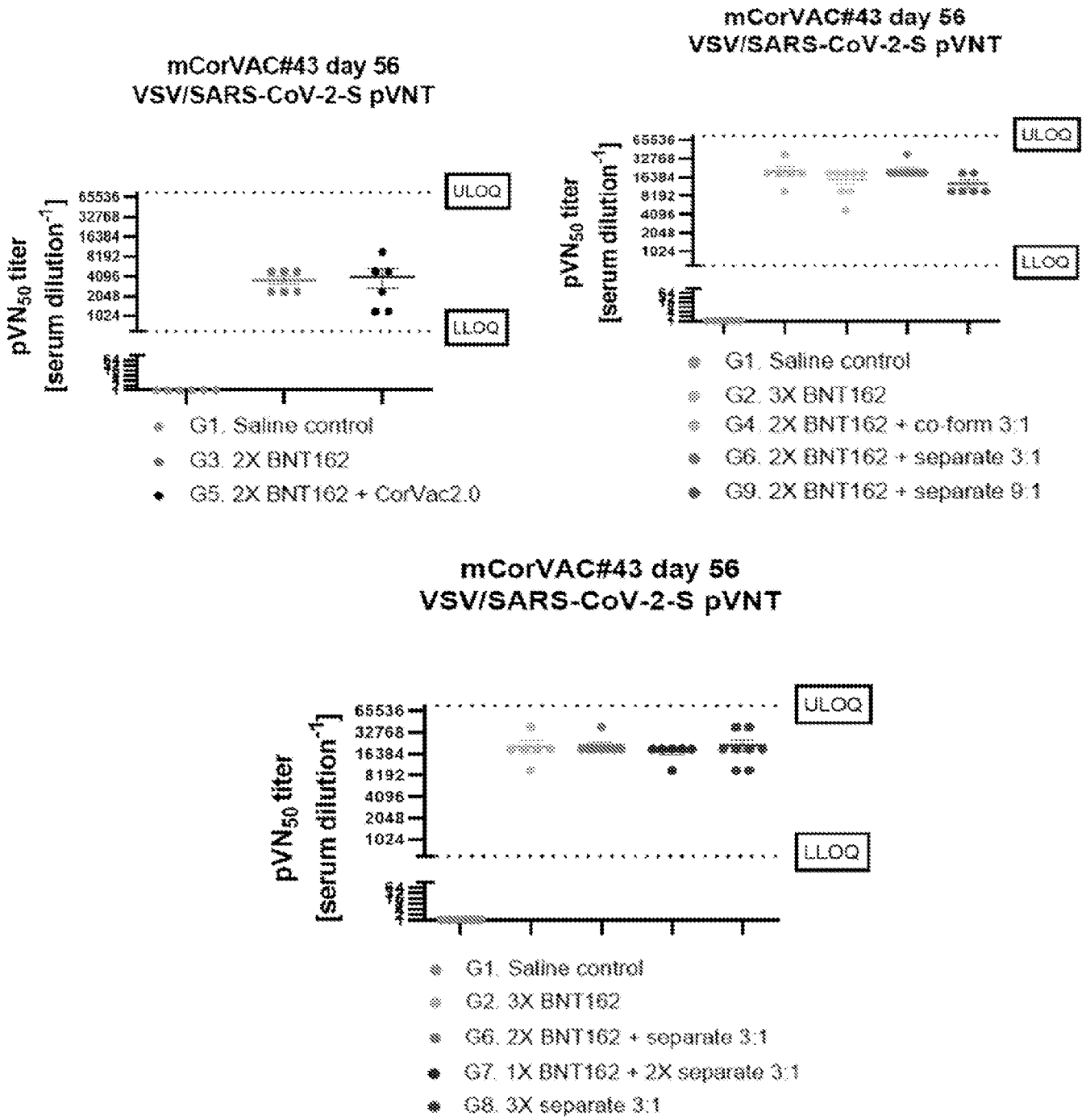

mCorVAC#43 day 56
VSV/SARS-CoV-2-S pVNT
pVN50 titer
[serum dilution-1]
65536
32768
16384
8192
4096
2048
1024
ULOQ
LLOQ
G1. Saline control
G3. 2X BNT162
G5. 2X BNT162 + CorVac2.0
mCorVAC#43 day 56
VSV/SARS-CoV-2-S pVNT
pVN50 titer
[serum dilution-1]
ULOQ
LLOQ
G1. Saline control
G2. 3X BNT162
G4. 2X BNT162 + co-form 3:1
G6. 2X BNT162 + separate 3:1
G9. 2X BNT162 + separate 9:1
mCorVAC#43 day 56
VSV/SARS-CoV-2-S pVNT
pVN50 titer
[serum dilution-1]
65536
32768
16384
8192
4096
2048
1024
ULOQ
LLOQ
G1. Saline control
G2. 3X BNT162
G6. 2X BNT162 + separate 3:1
G7. 1X BNT162 + 2X separate 3:1
G8. 3X separate 3:1

FIG. 56

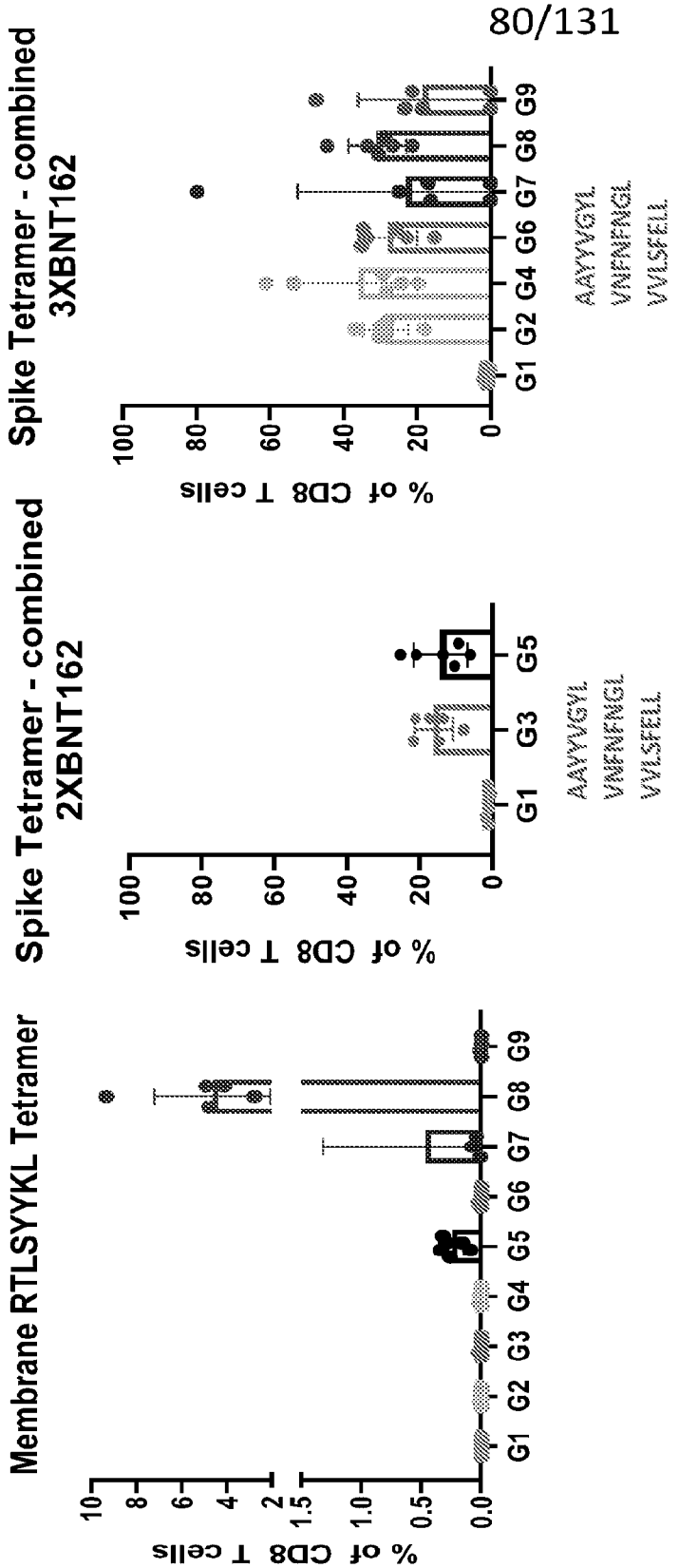

Membrane RTLSYYKL Tetramer
% of CD8 T cells
G1 G2 G3 G4 G5 G6 G7 G8 G9
Spike Tetramer - combined 2XBNT162
% of CD8 T cells
G1 G3 G5
AAYYVGYL
VNFNFNGL
VVLSFELL
Spike Tetramer - combined 3XBNT162
% of CD8 T cells
G1 G2 G4 G6 G7 G8 G9
AAYYVGYL
VNFNFNGL
VVLSFELL
G1. Saline control
G2. 3X BNT162b2
G3. 2X BNT162b2
G4. 2X BNT162b2 + co-formulated 1:3
G5. 2X BNT162b2 + CorVac2.0
G6. 2X BNT162b2 + separate 1:3
G7. 1X BNT162b2 + 2X separate 1:3
G8. 3X separate 1:3
G9. 2X BNT162b2 + separate 1:9

FIG. 57

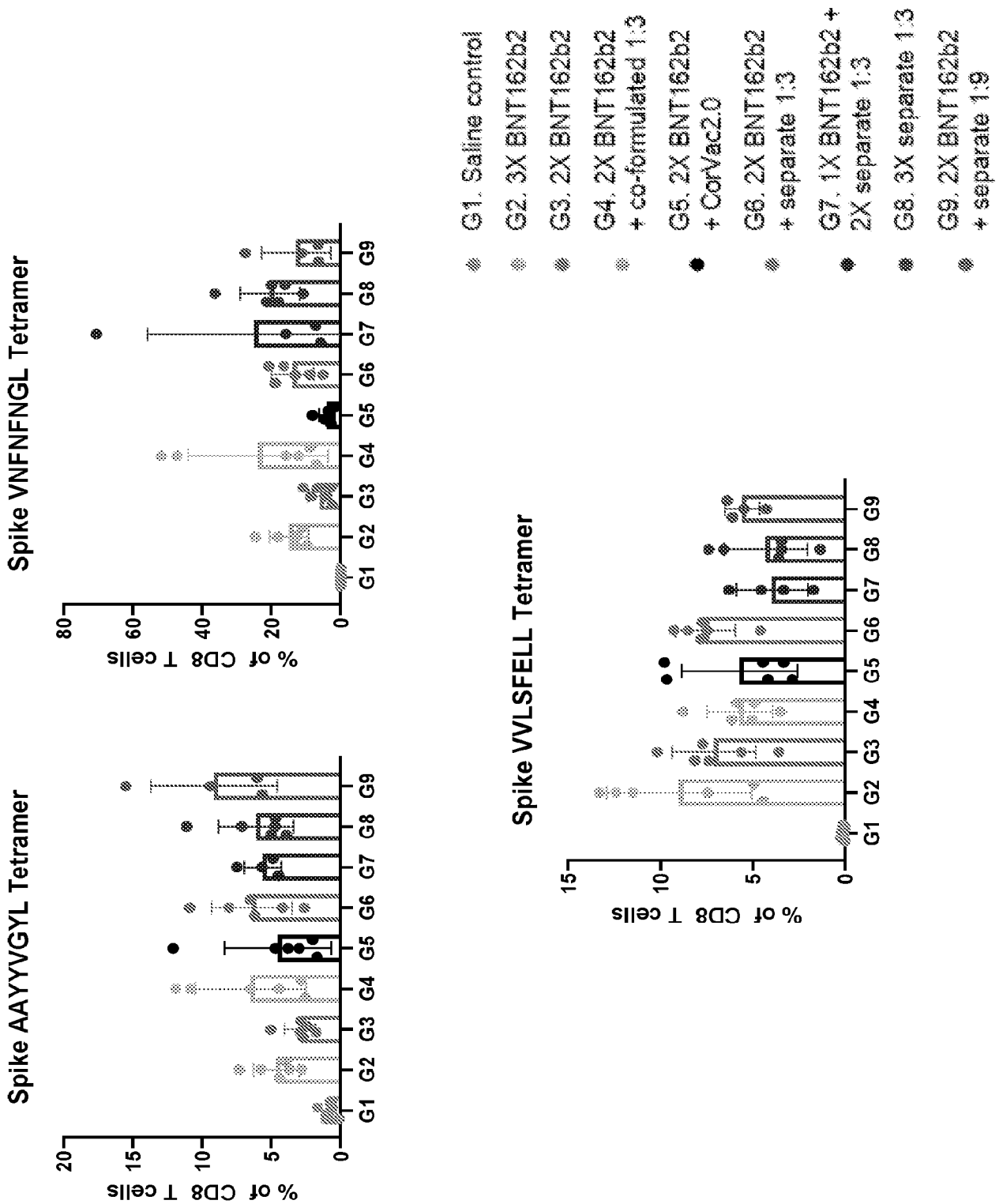

Spike AAYYVGYL Tetramer
% of CD8 T cells
0
5
10
15
20
G1 G2 G3 G4 G5 G6 G7 G8 G9
Spike VNFNFNGL Tetramer
% of CD8 T cells
0
20
40
60
80
G1 G2 G3 G4 G5 G6 G7 G8 G9
G1. Saline control
G2. 3X BNT162b2
G3. 2X BNT162b2
G4. 2X BNT162b2 + co-formulated 1:3
G5. 2X BNT162b2 + CorVac2.0
G6. 2X BNT162b2 + separate 1:3
G7. 1X BNT162b2 + 2X separate 1:3
G8. 3X separate 1:3
G9. 2X BNT162b2 + separate 1:9
Spike VVLSFELL Tetramer
% of CD8 T cells
0
5
10
15
G1 G2 G3 G4 G5 G6 G7 G8 G9

FIG. 58

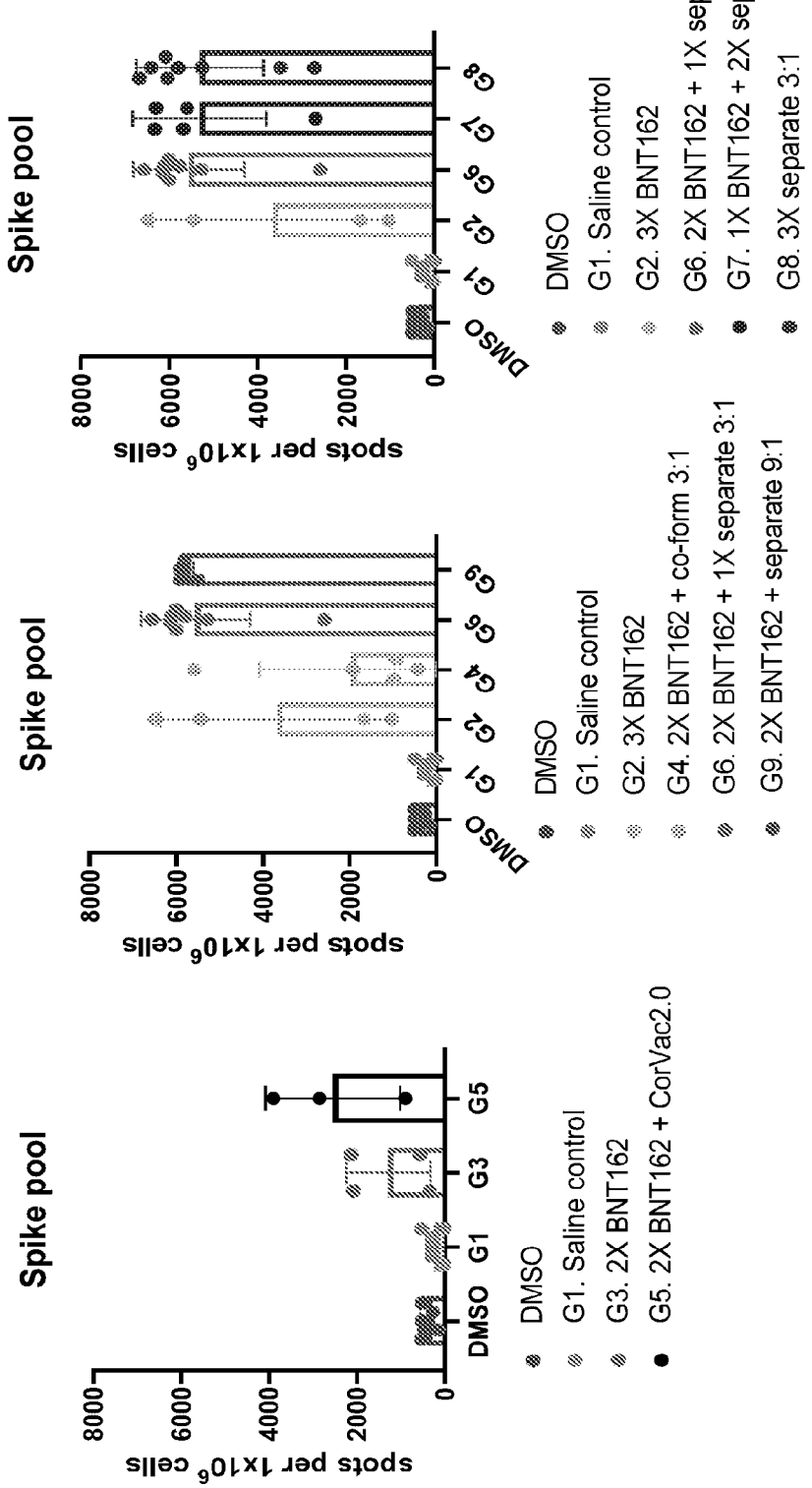

Spike pool
spots per 1x10^6 cells
8000
6000
4000
2000
0
DMSO
G1
G3
G5
DMSO
G1. Saline control
G3. 2X BNT162
G5. 2X BNT162 + CorVac2.0
Spike pool
spots per 1x10^6 cells
DMSO
G1
G2
G4
G6
G9
DMSO
G1. Saline control
G2. 3X BNT162
G4. 2X BNT162 + co-form 3:1
G6. 2X BNT162 + 1X separate 3:1
G9. 2X BNT162 + separate 9:1
Spike pool
spots per 1x10^6 cells
DMSO
G1
G2
G6
G7
G8
DMSO
G1. Saline control
G2. 3X BNT162
G6. 2X BNT162 + 1X separate 3:1
G7. 1X BNT162 + 2X separate 3:1
G8. 3X separate 3:1

FIG. 59

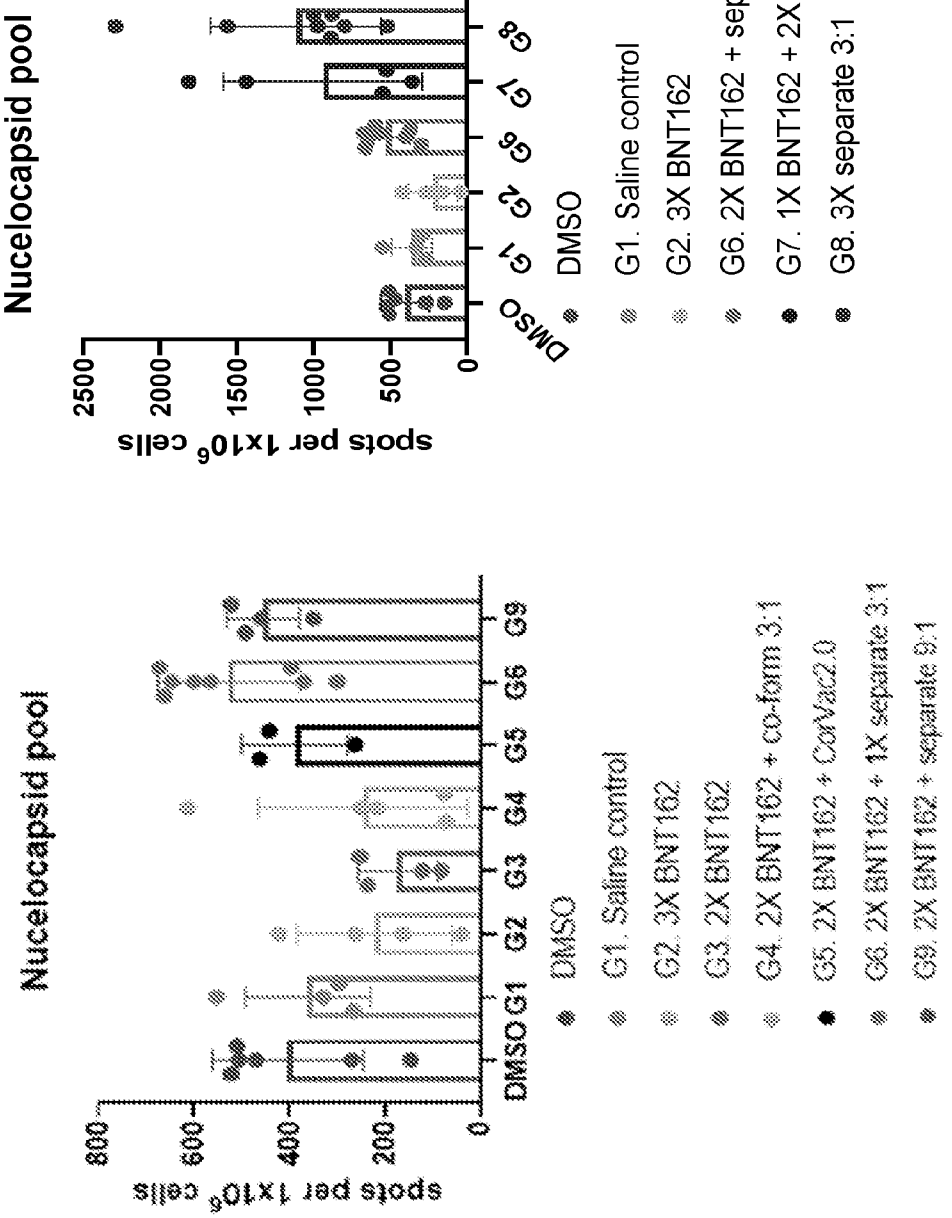

Nucelocapsid pool
spots per 1x10^6 cells
800
600
400
200
0
DMSO G1 G2 G3 G4 G5 G6 G9
DMSO
G1. Saline control
G2. 3X BNT162
G3. 2X BNT162
G4. 2X BNT162 + co-form 3:1
G5. 2X BNT162 + CoVax2.0
G6. 2X BNT162 + 1X separate 3:1
G9. 2X BNT162 + separate 9:1
Nucelocapsid pool
spots per 1x10^6 cells
2500
2000
1500
1000
500
0
DMSO G1 G2 G3 G6 G7 G8
DMSO
G1. Saline control
G2. 3X BNT162
G6. 2X BNT162 + separate 3:1
G7. 1X BNT162 + 2X separate 3:1
G8. 3X separate 3:1

FIG. 60

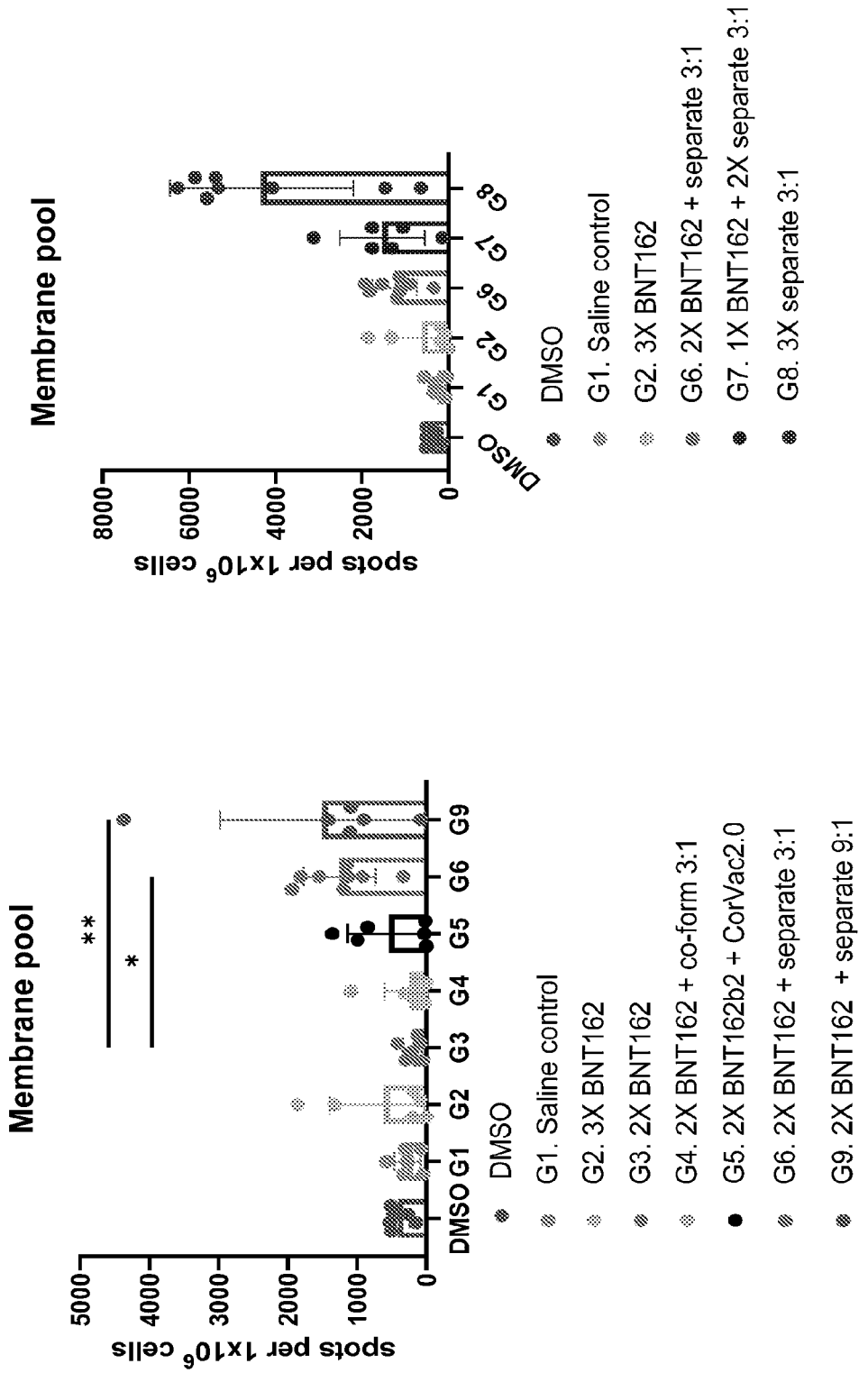

Membrane pool
spots per 1x10^6 cells
5000
4000
3000
2000
1000
0
**
*
DMSO G1 G2 G3 G4 G5 G6 G9
DMSO
G1. Saline control
G2. 3X BNT162
G3. 2X BNT162
G4. 2X BNT162 + co-form 3:1
G5. 2X BNT162b2 + CorVac2.0
G6. 2X BNT162 + separate 3:1
G9. 2X BNT162 + separate 9:1
Membrane pool
spots per 1x10^6 cells
8000
6000
4000
2000
0
DMSO G1 G2 G3 G6 G7 G8
DMSO
G1. Saline control
G2. 3X BNT162
G6. 2X BNT162 + separate 3:1
G7. 1X BNT162 + 2X separate 3:1
G8. 3X separate 3:1

FIG. 61

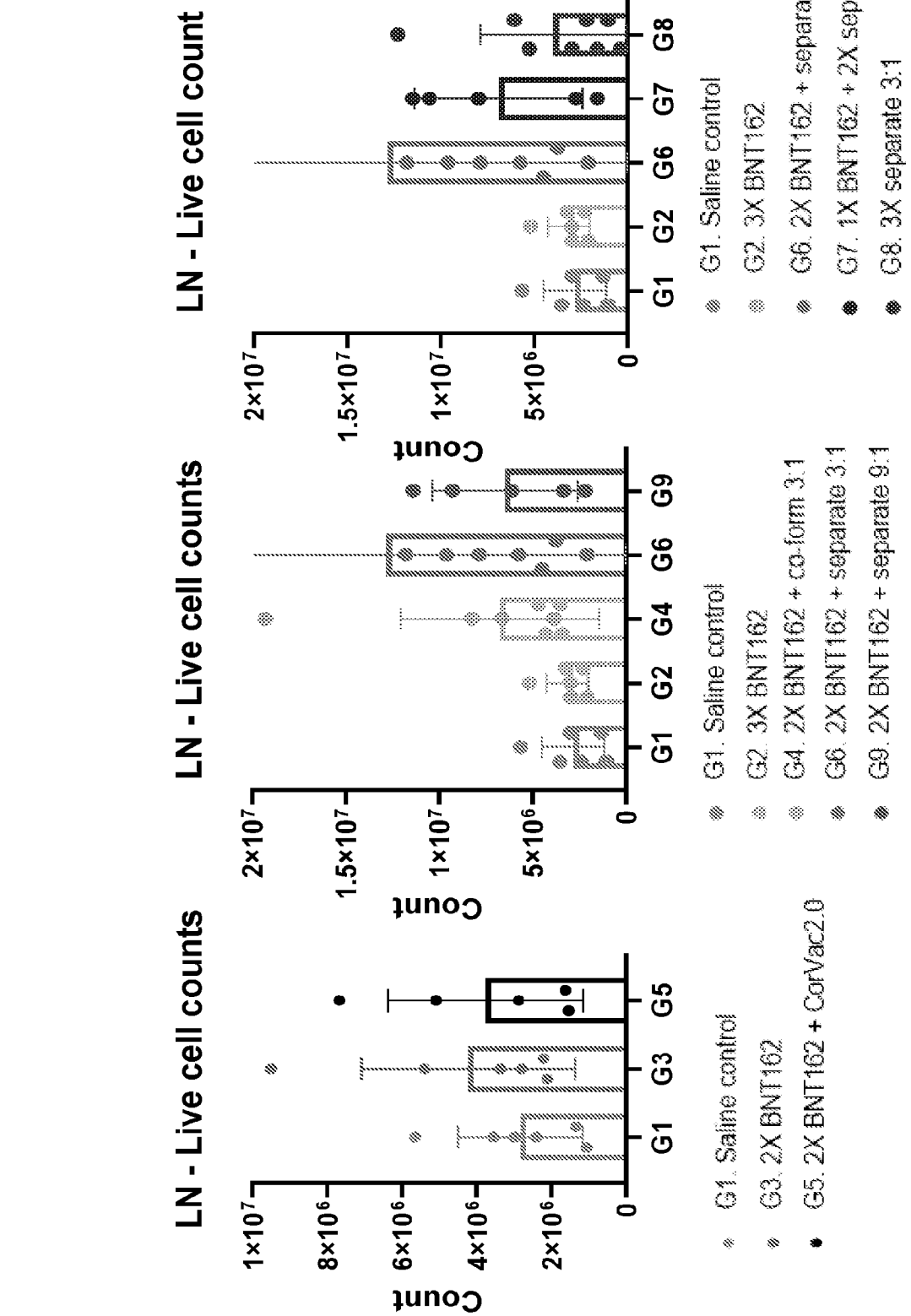

LN - Live cell counts
Count
1×10^7
8×10^6
6×10^6
4×10^6
2×10^6
0
G1 G3 G5
G1. Saline control
G3. 2X BNT162
G5. 2X BNT162 + CorVac2.0
LN - Live cell counts
Count
2×10^7
1.5×10^7
1×10^7
5×10^6
0
G1 G2 G4 G6 G9
G1. Saline control
G2. 3X BNT162
G4. 2X BNT162 + co-form 3:1
G6. 2X BNT162 + separate 3:1
G9. 2X BNT162 + separate 9:1
LN - Live cell count
Count
2×10^7
1.5×10^7
1×10^7
5×10^6
0
G1 G2 G6 G7 G8
G1. Saline control
G2. 3X BNT162
G6. 2X BNT162 + separate 3:1
G7. 1X BNT162 + 2X separate 3:1
G8. 3X separate 3:1

FIG. 62

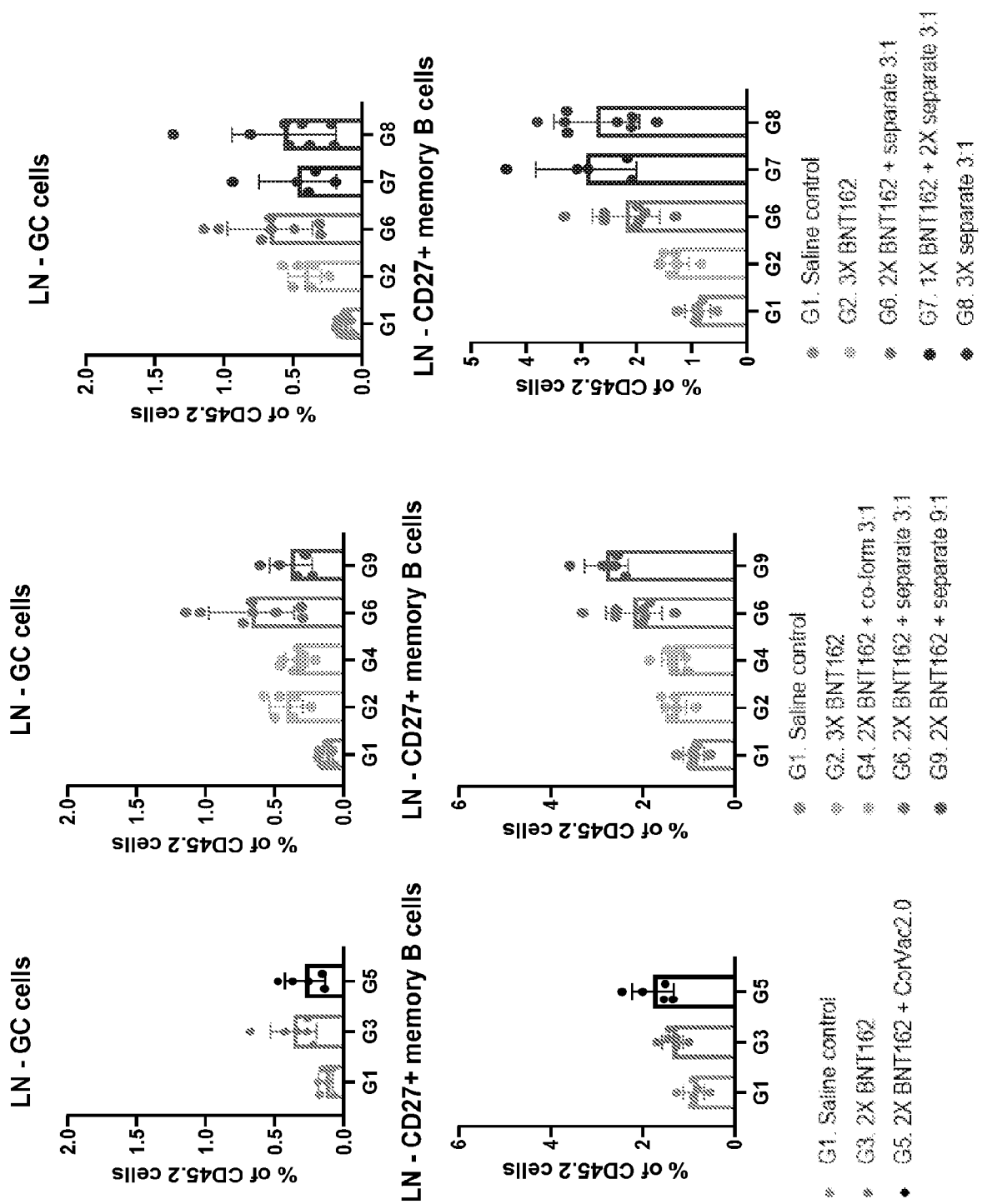

LN - GC cells
% of CD45.2 cells
G1 G3 G5
LN - CD27+ memory B cells
% of CD45.2 cells
G1 G2 G4 G6 G9
LN - GC cells
% of CD45.2 cells
G1 G2 G6 G7 G8
LN - CD27+ memory B cells
% of CD45.2 cells
G1 G2 G6 G7 G8
G1. Saline control
G3. 2X BNT162
G5. 2X BNT162 + CorVac2.0
G1. Saline control
G2. 3X BNT162
G4. 2X BNT162 + co-form 3:1
G6. 2X BNT162 + separate 3:1
G9. 2X BNT162 + separate 9:1
G1. Saline control
G2. 3X BNT162
G6. 2X BNT162 + separate 3:1
G7. 1X BNT162 + 2X separate 3:1
G8. 3X separate 3:1

FIG. 63

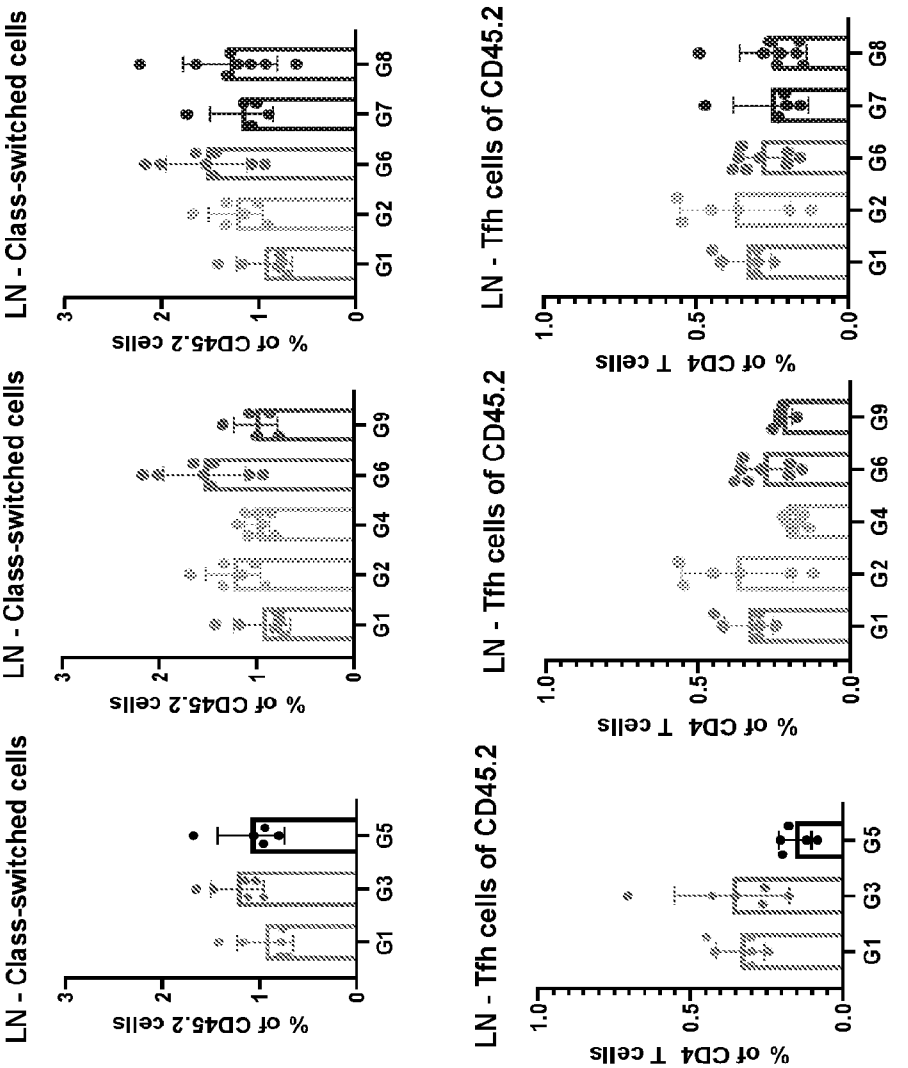

% of CD45.2
LN - Class-switched cells
% of CD45.2 cells
G1
G3
G5
LN - Class-switched cells
% of CD45.2 cells
G1
G2
G4
G6
G9
LN - Class-switched cells
% of CD45.2 cells
G1
G2
G6
G7
G8
LN - Tfh cells of CD45.2
% of CD4 T cells
G1
G3
G5
LN - Tfh cells of CD45.2
% of CD4 T cells
G1
G2
G4
G6
G9
LN - Tfh cells of CD45.2
% of CD4 T cells
G1
G2
G6
G7
G8

FIG. 64A

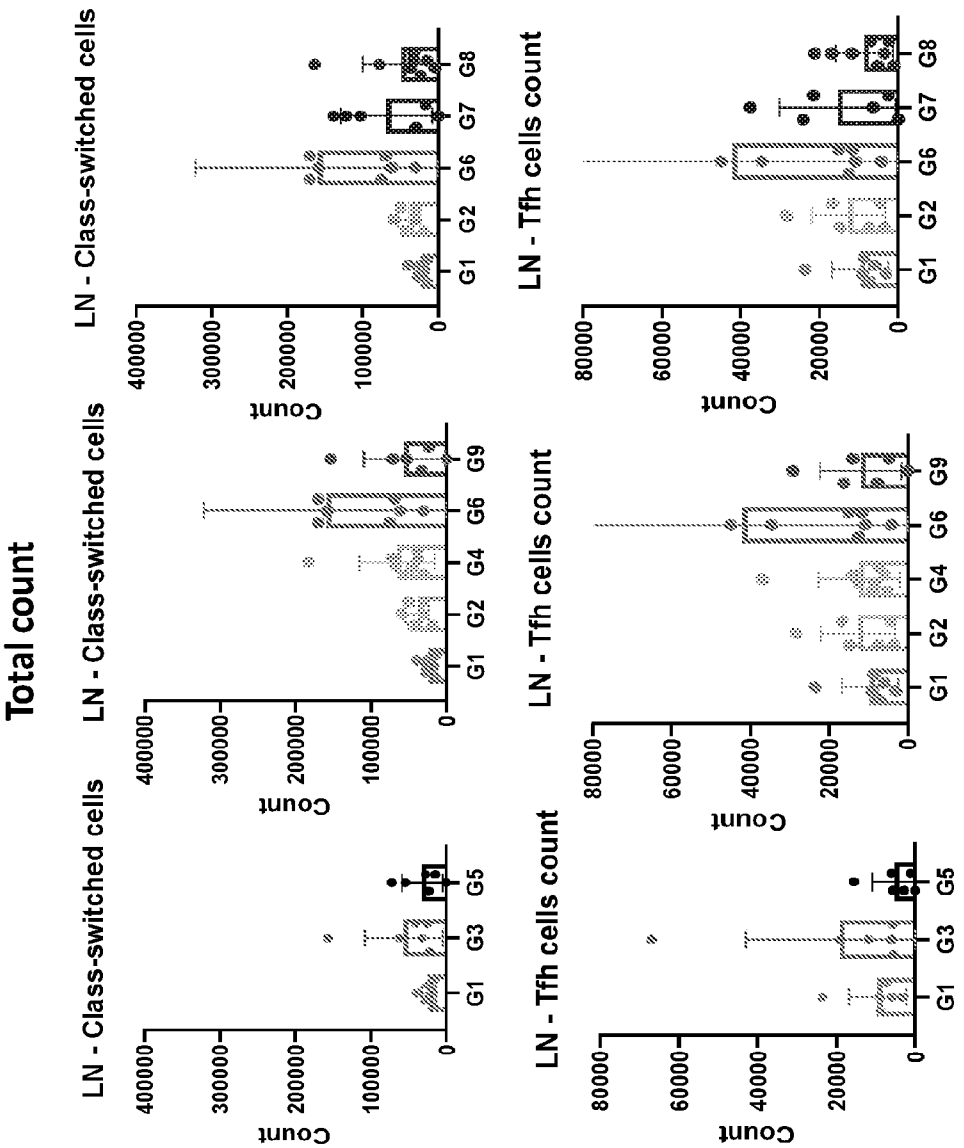

Total count
LN - Class-switched cells
LN - Class-switched cells
LN - Class-switched cells
LN - Tfh cells count
LN - Tfh cells count
LN - Tfh cells count
Count
400000
300000
200000
100000
0
80000
60000
40000
20000
G1
G2
G3
G4
G5
G6
G7
G8
G9

FIG. 64B

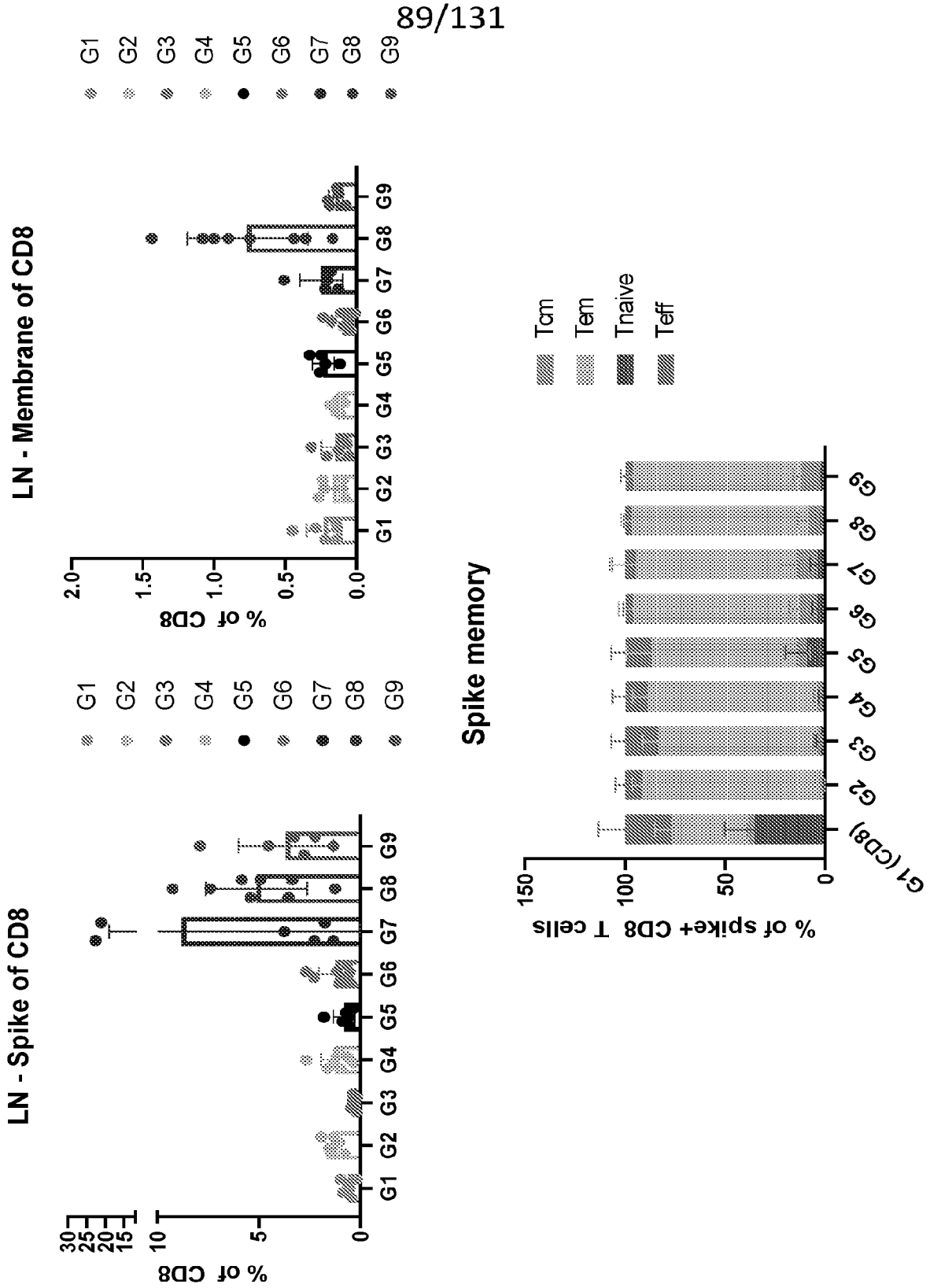

LN - Spike of CD8
% of CD8
30
25
20
15
10
5
0
G1 G2 G3 G4 G5 G6 G7 G8 G9
G1
G2
G3
G4
G5
G6
G7
G8
G9
LN - Membrane of CD8
% of CD8
2.0
1.5
1.0
0.5
0.0
G1 G2 G3 G4 G5 G6 G7 G8 G9
G1
G2
G3
G4
G5
G6
G7
G8
G9
Spike memory
Tcm
Tem
Tnaive
Teff
% of spike+ CD8 T cells
150
100
50
0
G1 (CD8)
G2
G3
G4
G5
G6
G7
G8
G9

FIG. 65

size (n= X)	group	Description		Dose [µg] BNT162b2/ CorVac 2.0	Day													
		prime	boost		-x	0			14			21			35			42				56
8	1	0.9% NaCl	0.9% NaCl	-	-1	0			14			21			35			42				
14	2	String C7	String C7	1	-1	0			14			21			35			42				
14	3	String C7	String C7	0.3	-1	0			14			21			35			42				
14	4	String C7	String C7	0.1	-1	0			14			21			35			42				
12	5	BNT162b2	BNT162b2	1	-1	0			14			21			35			42				
14	6	Separately BNT162b2:String C7	Separately BNT162b2:String C7	1/0.3	-1	0			14			21			35			42				

FIG. 66

size (n=X)	group	Description			Dose [µg] BNT162b2/ CorVac 2.0	Day -x	Day 0		Day 14		Day 21		Day 35		Day 42		Day 56
		prime	boost														
4	7	0.9% NaCl	0.9% NaCl	0.9% NaCl	-												
8	8	BNT162b2	BNT162b2	0.9% NaCl	1 ug												
8	9	BNT162b2	BNT162b2	BNT162b2	1 ug												
8	10	BNT162b2	BNT162b2	coformulation BNT162b2:String C7	1ug/0.3 ug												
8	11	BNT162b2	BNT162b2	String C7	1ug/1ug												
8	12	BNT162b2	BNT162b2	Separately BNT162b2:String C7	1ug/0.3ug												
8	13	BNT162b2	BNT162b2	Separately BNT162b2:String C7 1ug/0.11ug	1ug/0.11 ug												

Application (i.m.): 20µL in one leg

Blood collection r.b./ Serum generation (Aliquots)

Final blood collection/ Serum generation / Spleen for Splenocyte preparation/ lymph nodes

FIG. 66 (continued)

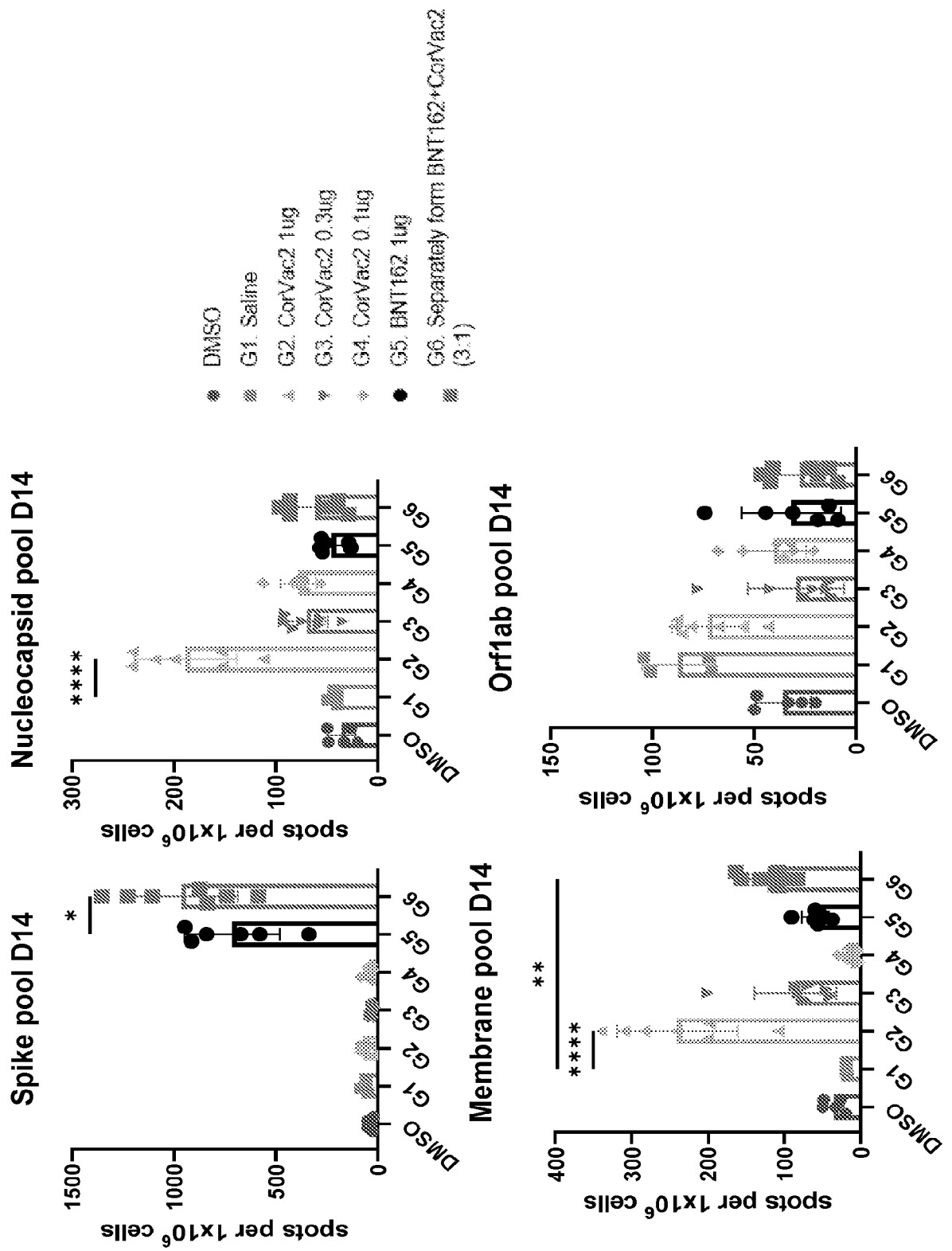

Nucleocapsid pool D14
Spike pool D14
Orf1ab pool D14
Membrane pool D14
spots per 1x10^6 cells
DMSO
G1. Saline
G2. CorVac2 1ug
G3. CorVac2 0.3ug
G4. CorVac2 0.1ug
G5. BNT162 1ug
G6. Separately form BNT162+CorVac2 (3:1)
DMSO G1 G2 G3 G4 G5 G6
****
*
**

FIG. 67A

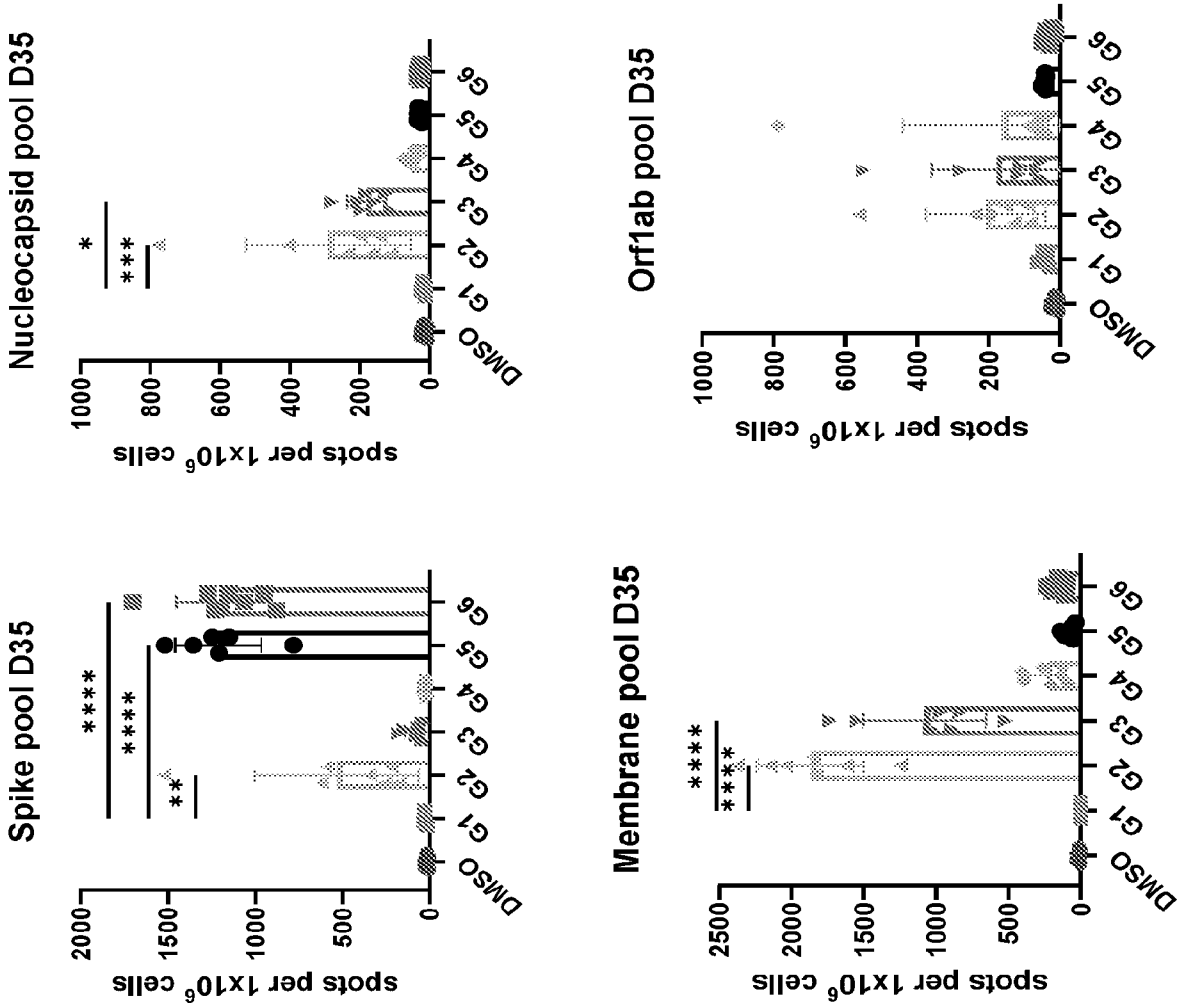

DMSO
G1. Saline
G2. CorVac2 1ug
G3. CorVac2 0.3ug
G4. CorVac2 0.1ug
G5. BNT162 1ug
G6. Separately form BNT162+CorVac2 (3:1)
Nucleocapsid pool D35
Orf1ab pool D35
Spike pool D35
Membrane pool D35
spots per 1x10^6 cells
DMSO G1 G2 G3 G4 G5 G6
*
***
**
****

FIG. 67B

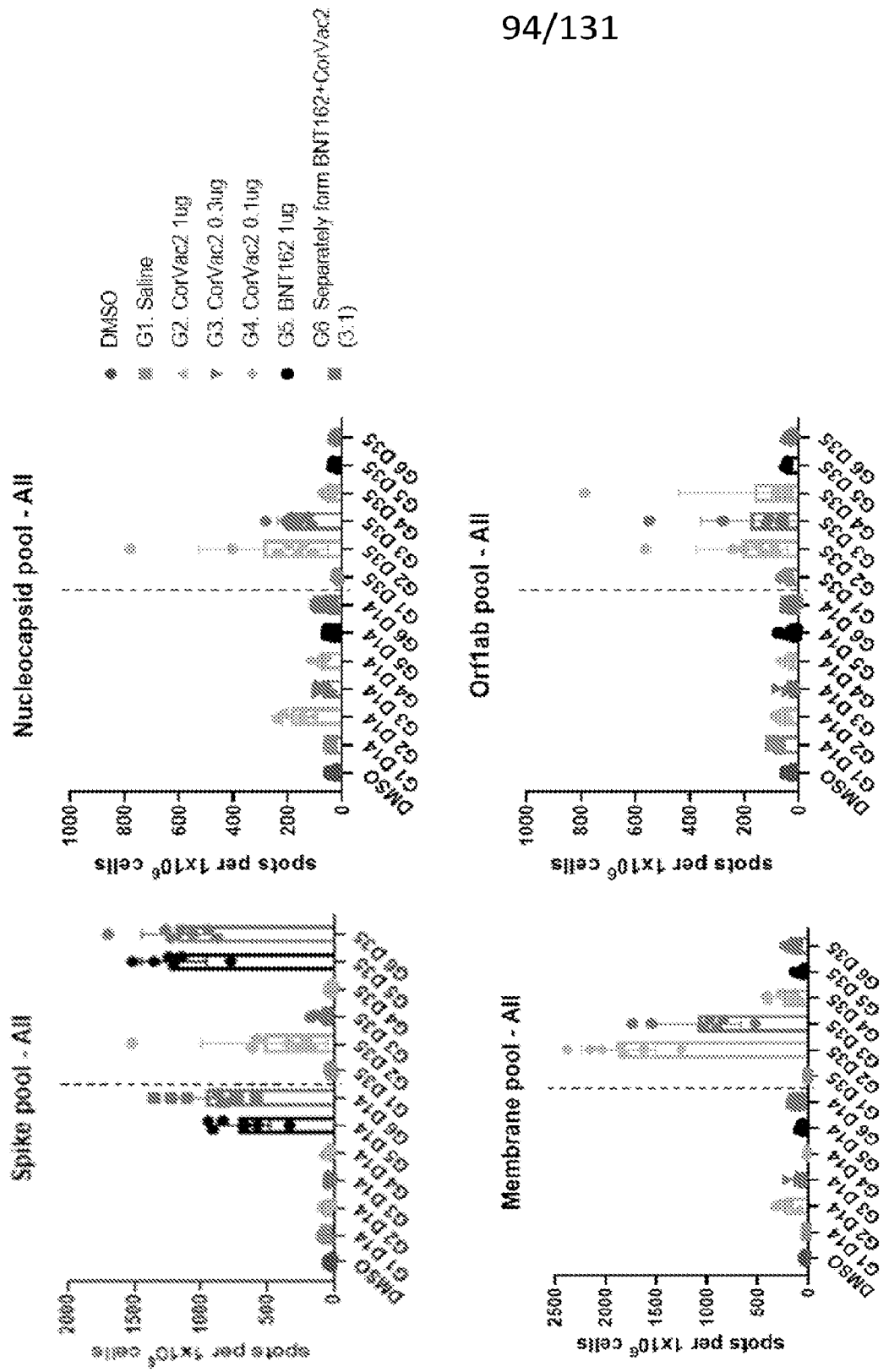

DMSO
G1. Saline
G2. CorVac2 1ug
G3. CorVac2 0.3ug
G4. CorVac2 0.1ug
G5. BNT162 1ug
G6 Separately form BNT162+CorVac2 (3:1)
Nucleocapsid pool - All
Orf1ab pool - All
Spike pool - All
Membrane pool - All
spots per 1x10^6 cells

FIG. 67C

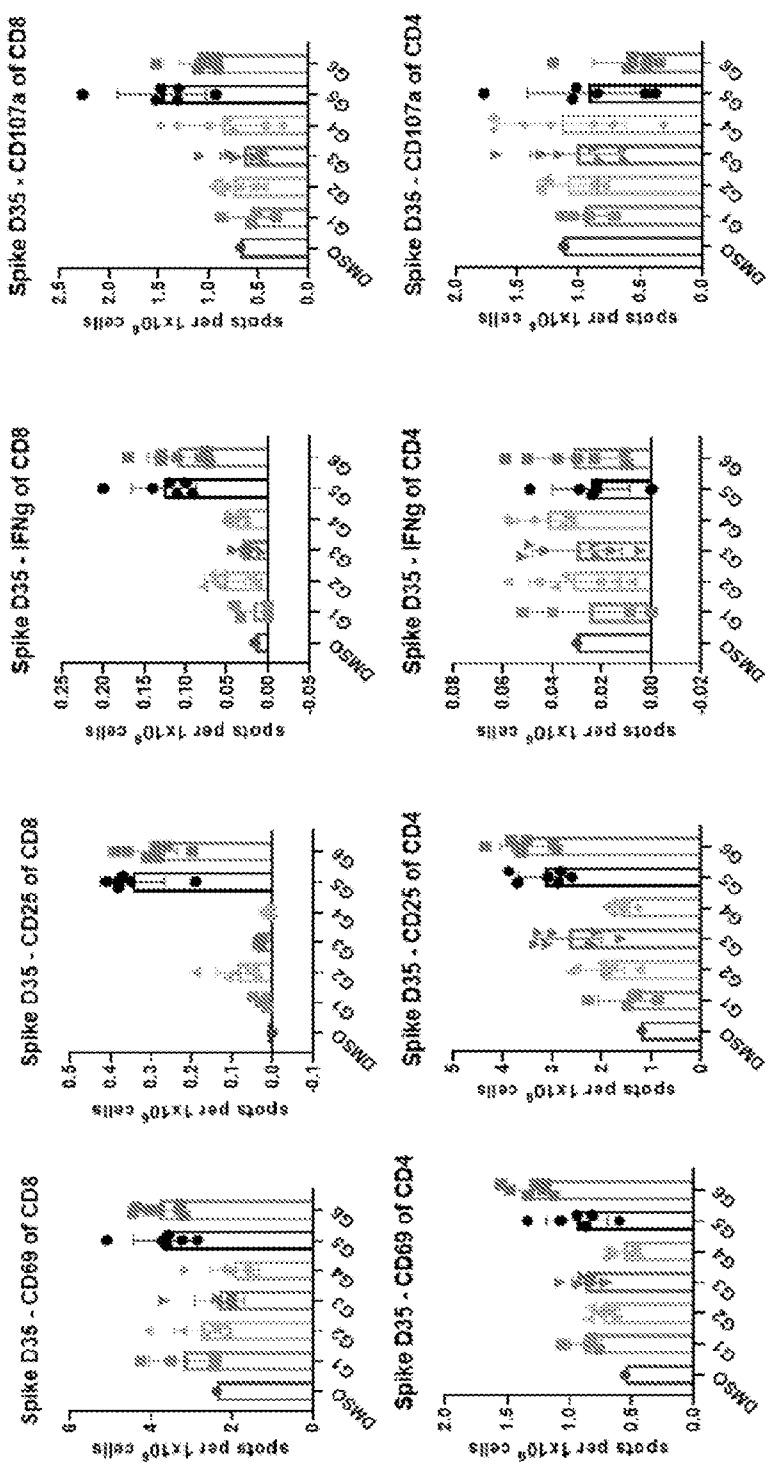

CD8
CD4
Spike D35 - CD69 of CD8
Spike D35 - CD25 of CD8
Spike D35 - IFNg of CD8
Spike D35 - CD107a of CD8
Spike D35 - CD69 of CD4
Spike D35 - CD25 of CD4
Spike D35 - IFNg of CD4
Spike D35 - CD107a of CD4
spots per 1x10^5 cells
DMSO
G1. Saline
G2. CorVac2 1ug
G3. CorVac2 0.3ug
G4. CorVac2 0.1ug
G5. BNT162 1ug
G6. Separately form BNT162+CorVac2 (3:1)

FIG. 67D

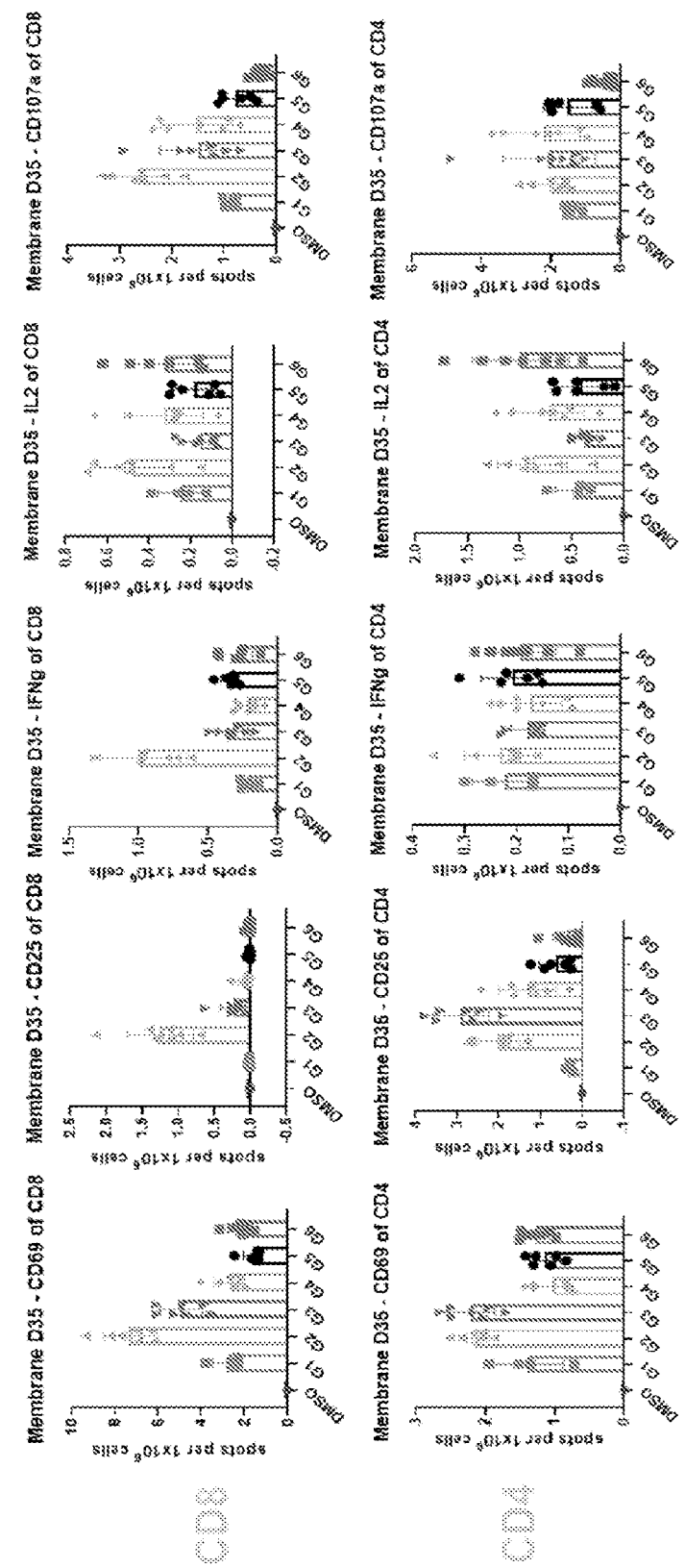

CD8
CD4
Membrane D35 - CD69 of CD8
Membrane D35 - CD25 of CD8
Membrane D35 - IFNg of CD8
Membrane D35 - IL2 of CD8
Membrane D35 - CD107a of CD8
Membrane D36 - CD69 of CD4
Membrane D36 - CD25 of CD4
Membrane D35 - IFNg of CD4
Membrane D35 - IL2 of CD4
Membrane D35 - CD107a of CD4
spots per 1x10^5 cells
DMSO
G1
G2
G3
G4
G5
G6
UnStim
G1: Saline
G2: ConVac2 1ug
G3: ConVac2 0.3ug
G4: ConVac2 0.1ug
G5: BNT162 1ug
G6: Separately form BNT162+ConVac2 (0.1)

FIG. 67E

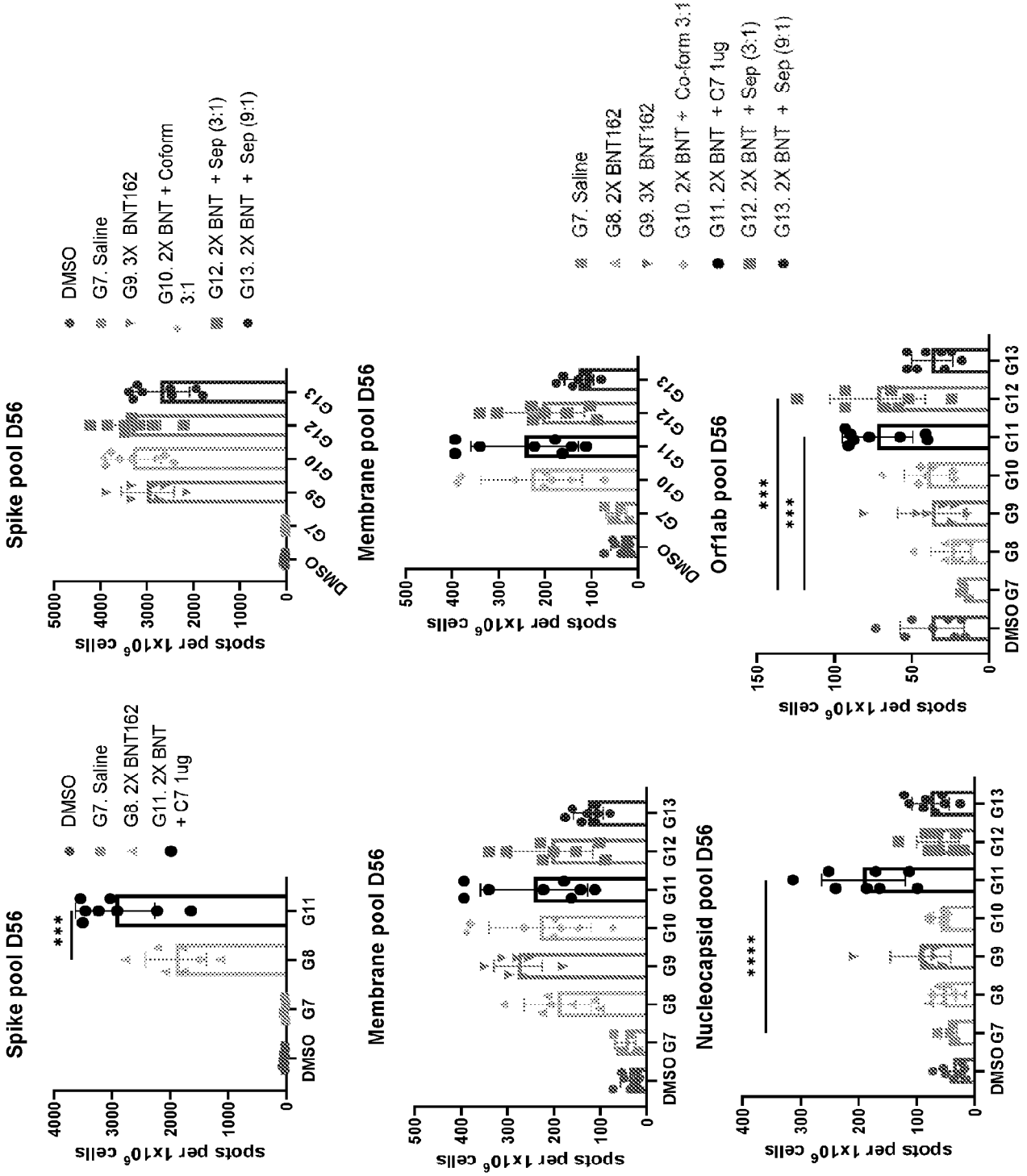

Spike pool D56
spots per 1x10^6 cells
DMSO
G7. Saline
G8. 2X BNT162
G11. 2X BNT + C7 1ug
***
DMSO G7 G8 G11
Spike pool D56
spots per 1x10^6 cells
DMSO
G7. Saline
G9. 3X BNT162
G10. 2X BNT + Coform 3:1
G12. 2X BNT + Sep (3:1)
G13. 2X BNT + Sep (9:1)
DMSO G7 G9 G10 G12 G13
Membrane pool D56
spots per 1x10^6 cells
DMSO G7 G8 G9 G10 G11 G12 G13
Membrane pool D56
spots per 1x10^6 cells
G7. Saline
G8. 2X BNT162
G9. 3X BNT162
G10. 2X BNT + Co-form 3:1
G11. 2X BNT + C7 1ug
G12. 2X BNT + Sep (3:1)
G13. 2X BNT + Sep (9:1)
DMSO G7 G10 G11 G12 G13
Nucleocapsid pool D56
spots per 1x10^6 cells
****
DMSO G7 G8 G9 G10 G11 G12 G13
Orf1ab pool D56
spots per 1x10^6 cells
***
***
DMSO G7 G8 G9 G10 G11 G12 G13

FIG. 67F

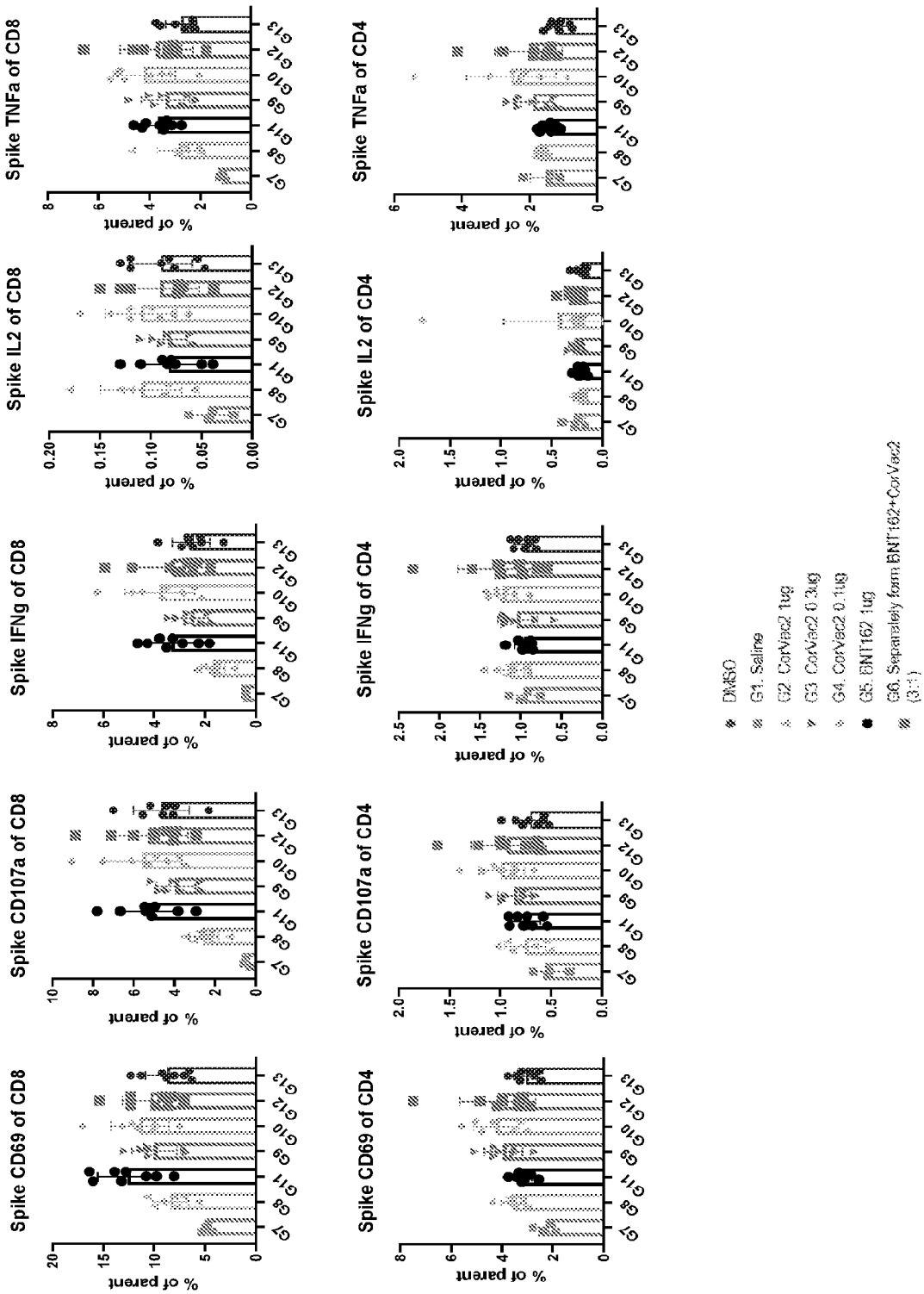

Spike CD69 of CD8
Spike CD107a of CD8
Spike IFNg of CD8
Spike IL2 of CD8
Spike TNFa of CD8
Spike CD69 of CD4
Spike CD107a of CD4
Spike IFNg of CD4
Spike IL2 of CD4
Spike TNFa of CD4
% of parent
G7 G8 G11 G9 G10 G12 G13
DMSO
G1. Saline
G2. CorVac2 1ug
G3. CorVac2 0.3ug
G4. CorVac2 0.1ug
G5. BNT162 1ug
G6. Separately form BNT162+CorVac2 (3:1)

FIG. 67G

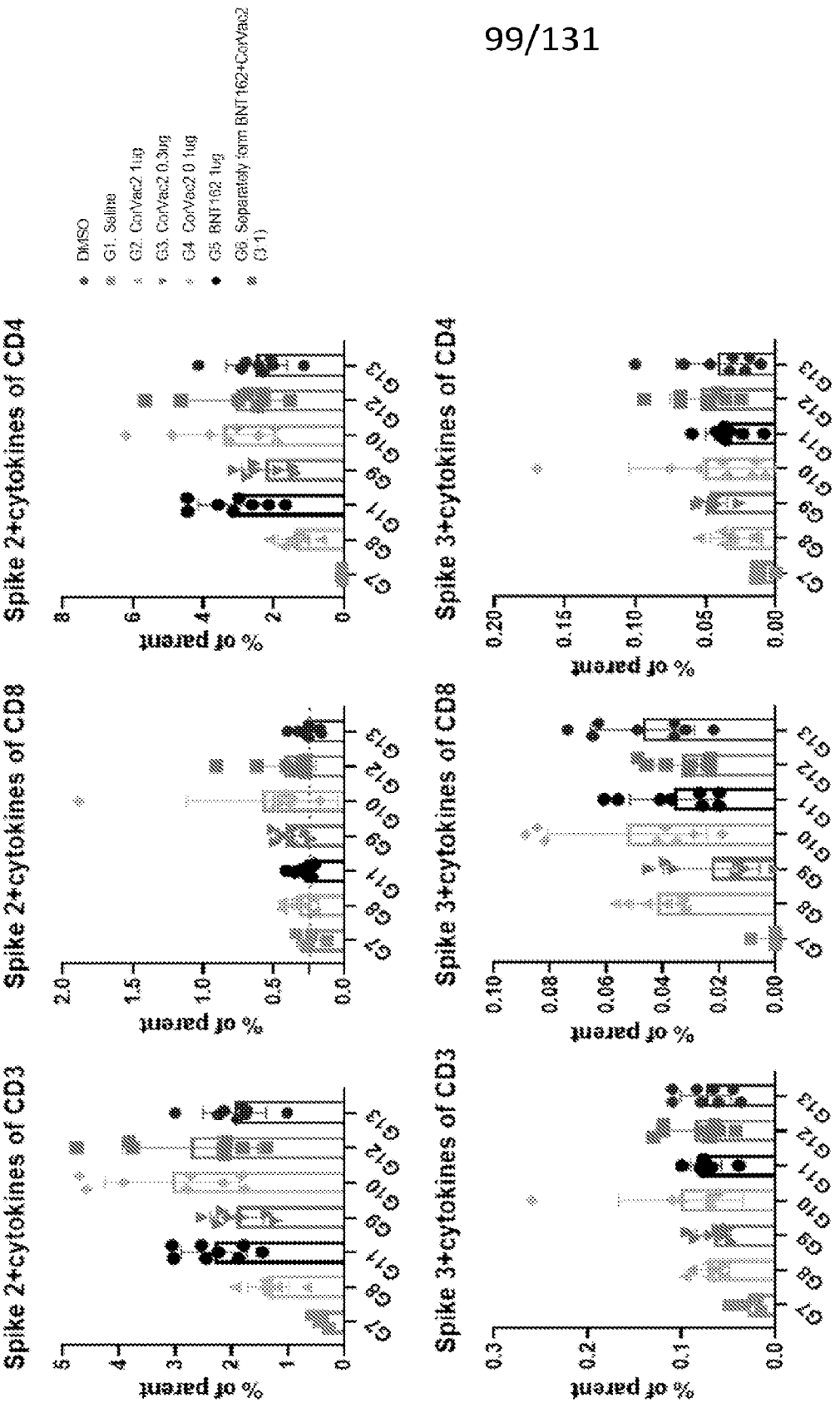

DMSO
G1. Saline
G2. CoVac2 1ug
G3. CoVac2 0.3ug
G4. CoVac2 0.1ug
G5. BNT162 1ug
G6. Separately term BNT162+CoVac2 (3:1)
Spike 2+cytokines of CD4
Spike 2+cytokines of CD8
Spike 2+cytokines of CD3
Spike 3+cytokines of CD4
Spike 3+cytokines of CD8
Spike 3+cytokines of CD3
% of parent
G7
G8
G9
G10
G11
G12
G13

FIG. 67H

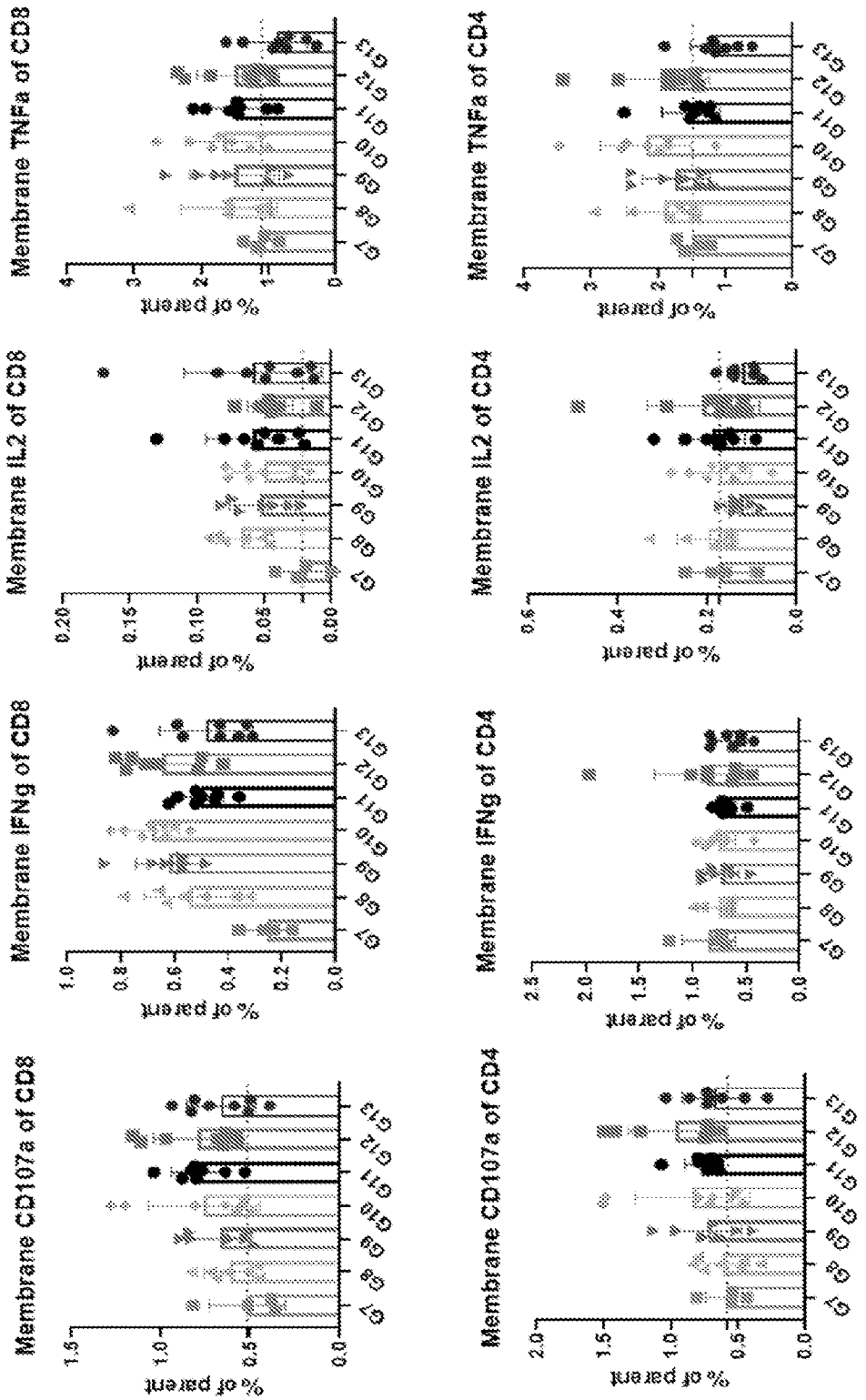

Membrane CD107a of CD8
Membrane IFNg of CD8
Membrane IL2 of CD8
Membrane TNFa of CD8
Membrane CD107a of CD4
Membrane IFNg of CD4
Membrane IL2 of CD4
Membrane TNFa of CD4
% of parent
G7
G8
G9
G10
G11
G12
G13
DMSO
G1. Saline
G2. CorVac2 1ug
G3. CorVac2 0.3ug
G4. CorVac2 0.1ug
G5. BNT162 1ug
G6. Separately form BNT162+CorVac2 (3:1)

FIG. 67I

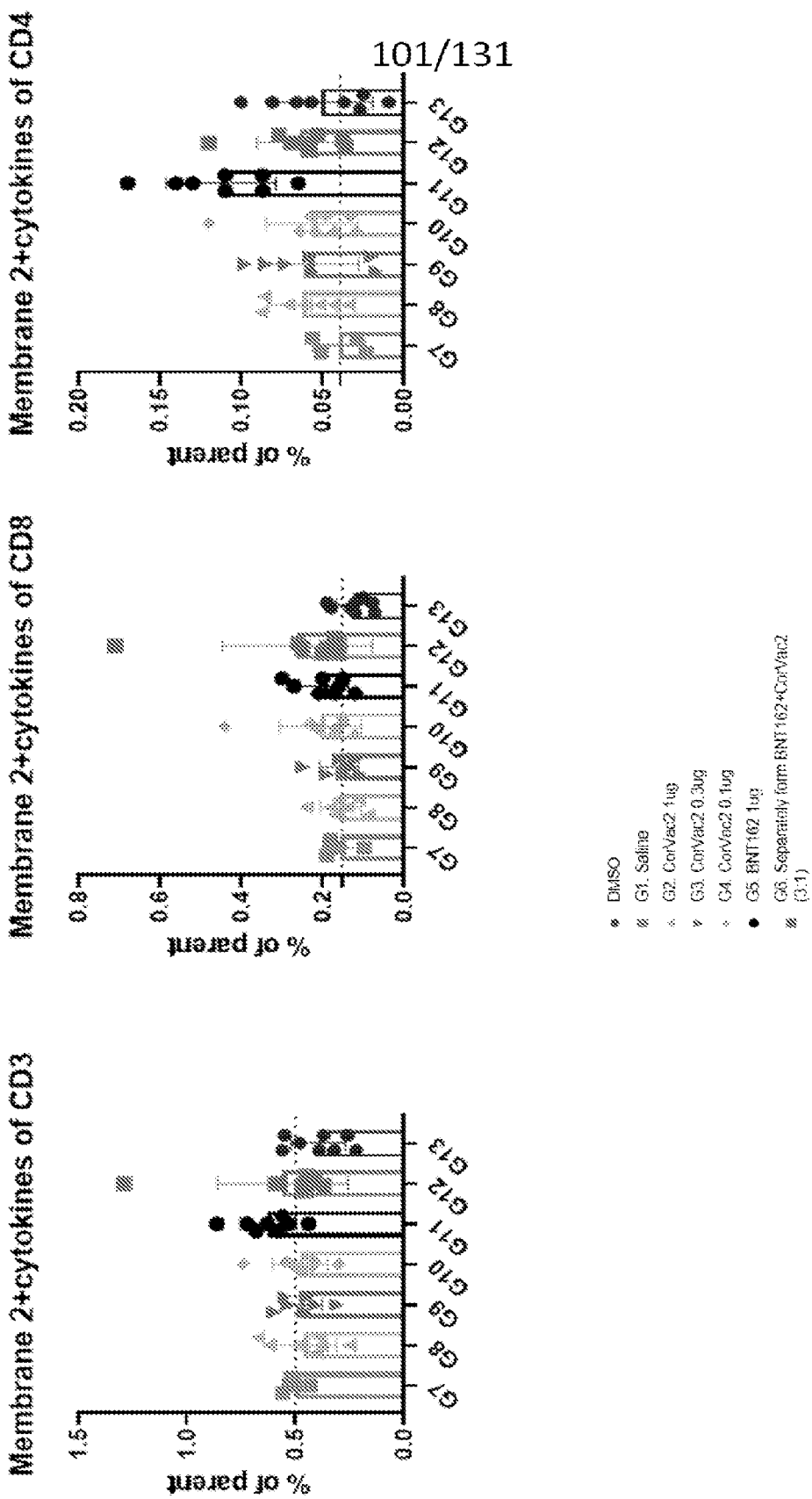

Membrane 2+cytokines of CD3
Membrane 2+cytokines of CD8
Membrane 2+cytokines of CD4
% of parent
0.0
0.5
1.0
1.5
0.2
0.4
0.6
0.8
0.00
0.05
0.10
0.15
0.20
G7
G8
G9
G10
G11
G12
G13
DMSO
G1. Saline
G2. CorVac2 1ug
G3. CorVac2 0.3ug
G4. CorVac2 0.1ug
G5 BNT162 1ug
G6. Separately form BNT162+CorVac2 (3:1)

FIG. 67J

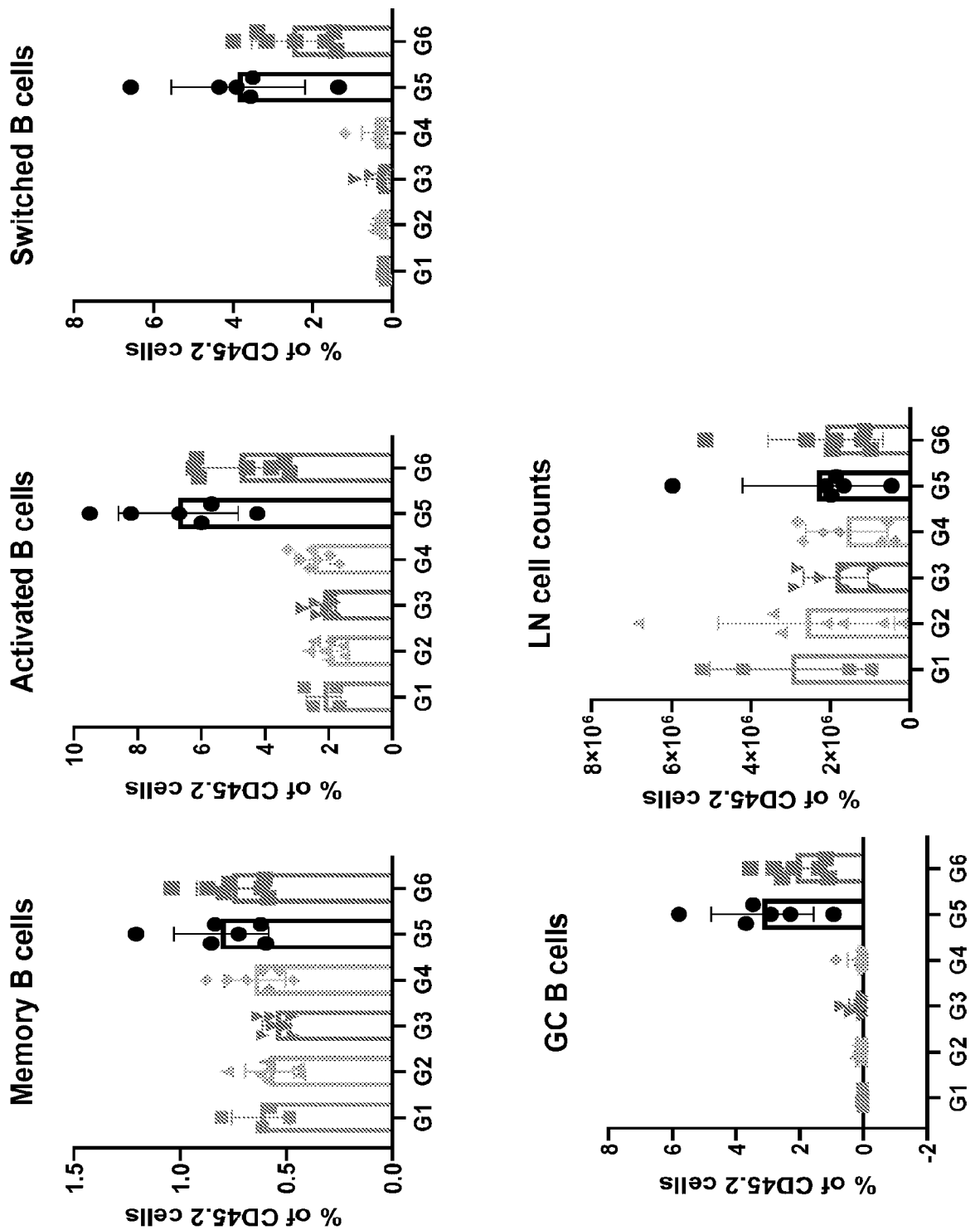

Switched B cells
% of CD45.2 cells
0
2
4
6
8
G1 G2 G3 G4 G5 G6
Activated B cells
% of CD45.2 cells
0
2
4
6
8
10
G1 G2 G3 G4 G5 G6
Memory B cells
% of CD45.2 cells
0.0
0.5
1.0
1.5
G1 G2 G3 G4 G5 G6
LN cell counts
% of CD45.2 cells
0
2×10^6
4×10^6
6×10^6
8×10^6
G1 G2 G3 G4 G5 G6
GC B cells
% of CD45.2 cells
-2
0
2
4
6
8
G1 G2 G3 G4 G5 G6

FIG. 68A

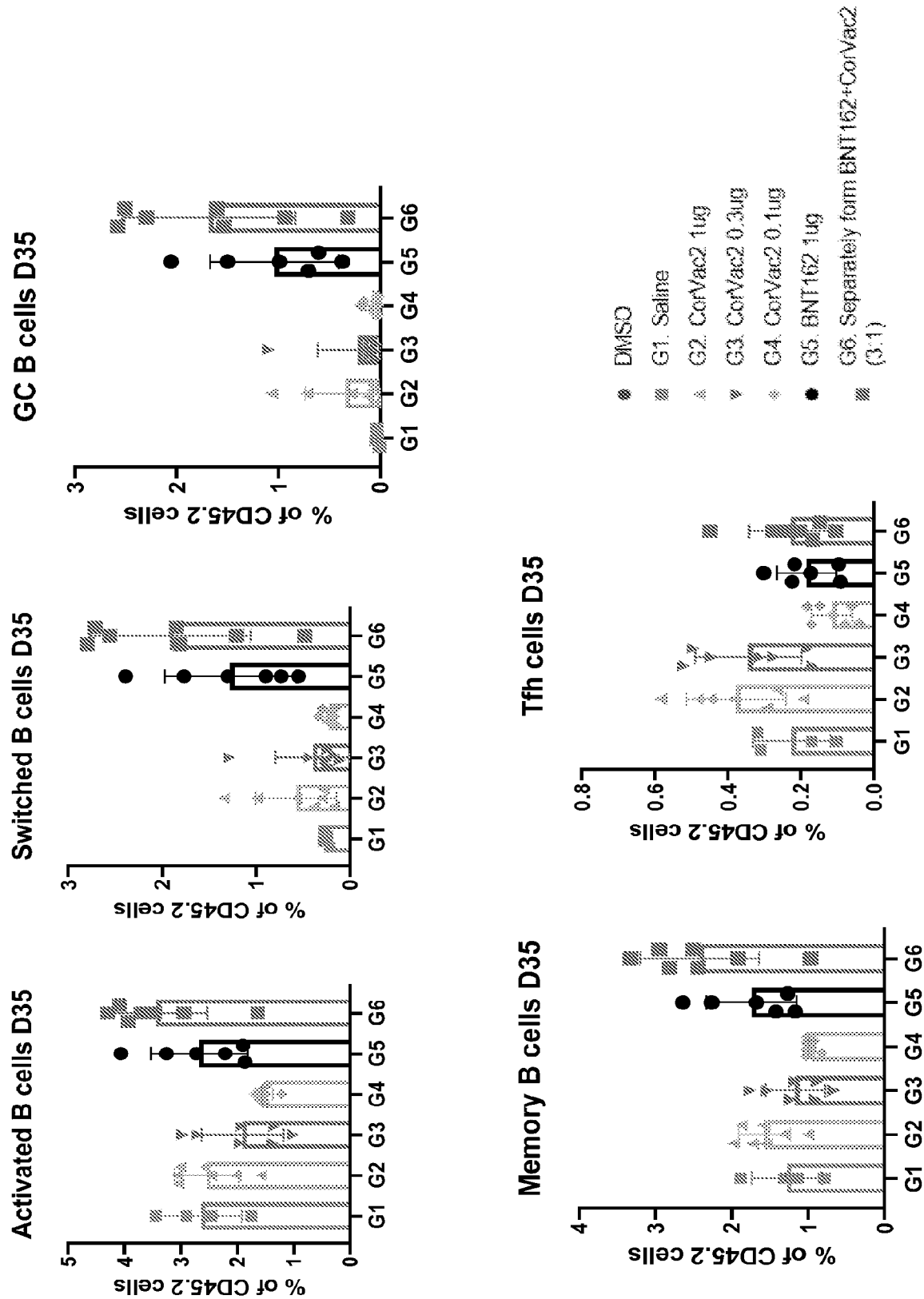

Activated B cells D35
Switched B cells D35
GC B cells D35
Memory B cells D35
Tfh cells D35
% of CD45.2 cells
G1 G2 G3 G4 G5 G6
DMSO
G1. Saline
G2. CorVac2 1ug
G3. CorVac2 0.3ug
G4. CorVac2 0.1ug
G5 BNT162 1ug
G6. Separately form BNT162+CorVac2 (3:1)

FIG. 68B

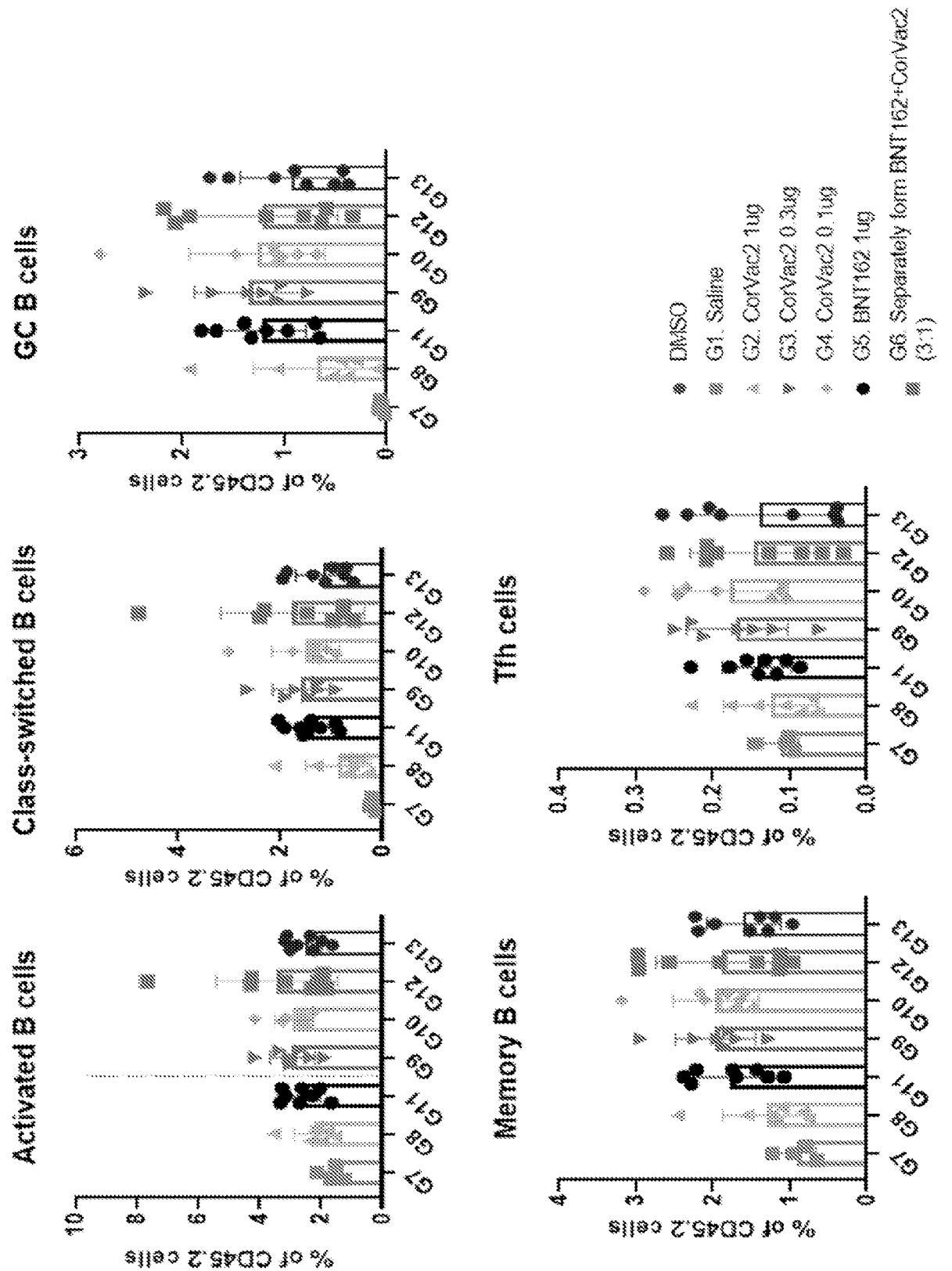

Activated B cells
Class-switched B cells
GC B cells
Memory B cells
Tfh cells
% of CD45.2 cells
G1
G8
G11
G9
G10
G12
G13
DMSO
G1. Saline
G2. CorVac2 1ug
G3. CorVac2 0.3ug
G4. CorVac2 0.1ug
G5. BNT162 1ug
G6. Separately form BNT162+CorVac2 (3:1)

FIG. 68C

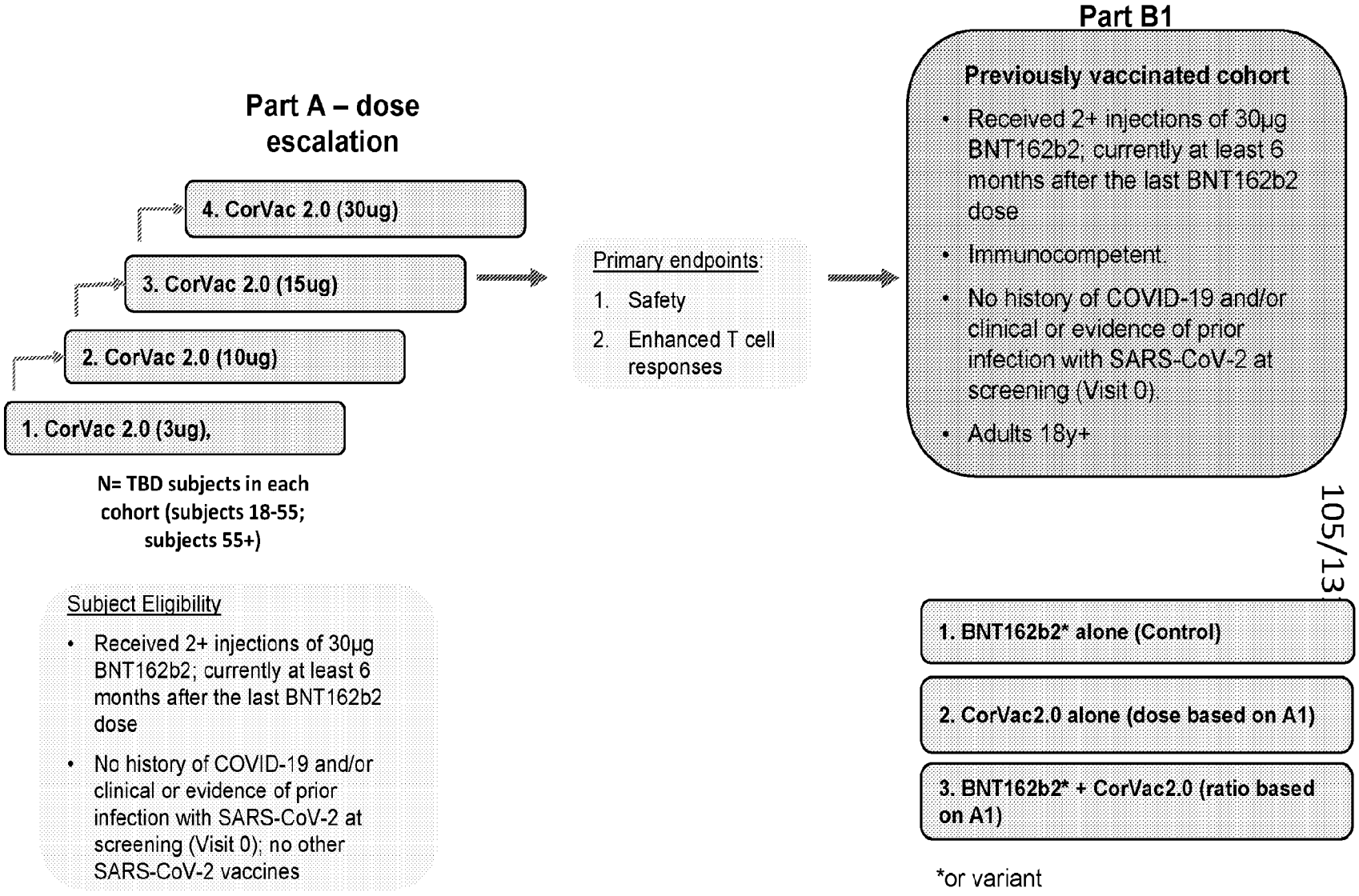

Part A – dose escalation
4. CorVac 2.0 (30ug)
3. CorVac 2.0 (15ug)
2. CorVac 2.0 (10ug)
1. CorVac 2.0 (3ug),
N= TBD subjects in each cohort (subjects 18-55; subjects 55+)
Subject Eligibility
• Received 2+ injections of 30µg BNT162b2; currently at least 6 months after the last BNT162b2 dose
• No history of COVID-19 and/or clinical or evidence of prior infection with SARS-CoV-2 at screening (Visit 0); no other SARS-CoV-2 vaccines
Primary endpoints:
1. Safety
2. Enhanced T cell responses
Part B1
Previously vaccinated cohort
• Received 2+ injections of 30µg BNT162b2; currently at least 6 months after the last BNT162b2 dose
• Immunocompetent.
• No history of COVID-19 and/or clinical or evidence of prior infection with SARS-CoV-2 at screening (Visit 0).
• Adults 18y+
1. BNT162b2* alone (Control)
2. CorVac2.0 alone (dose based on A1)
3. BNT162b2* + CorVac2.0 (ratio based on A1)
*or variant

FIG. 69

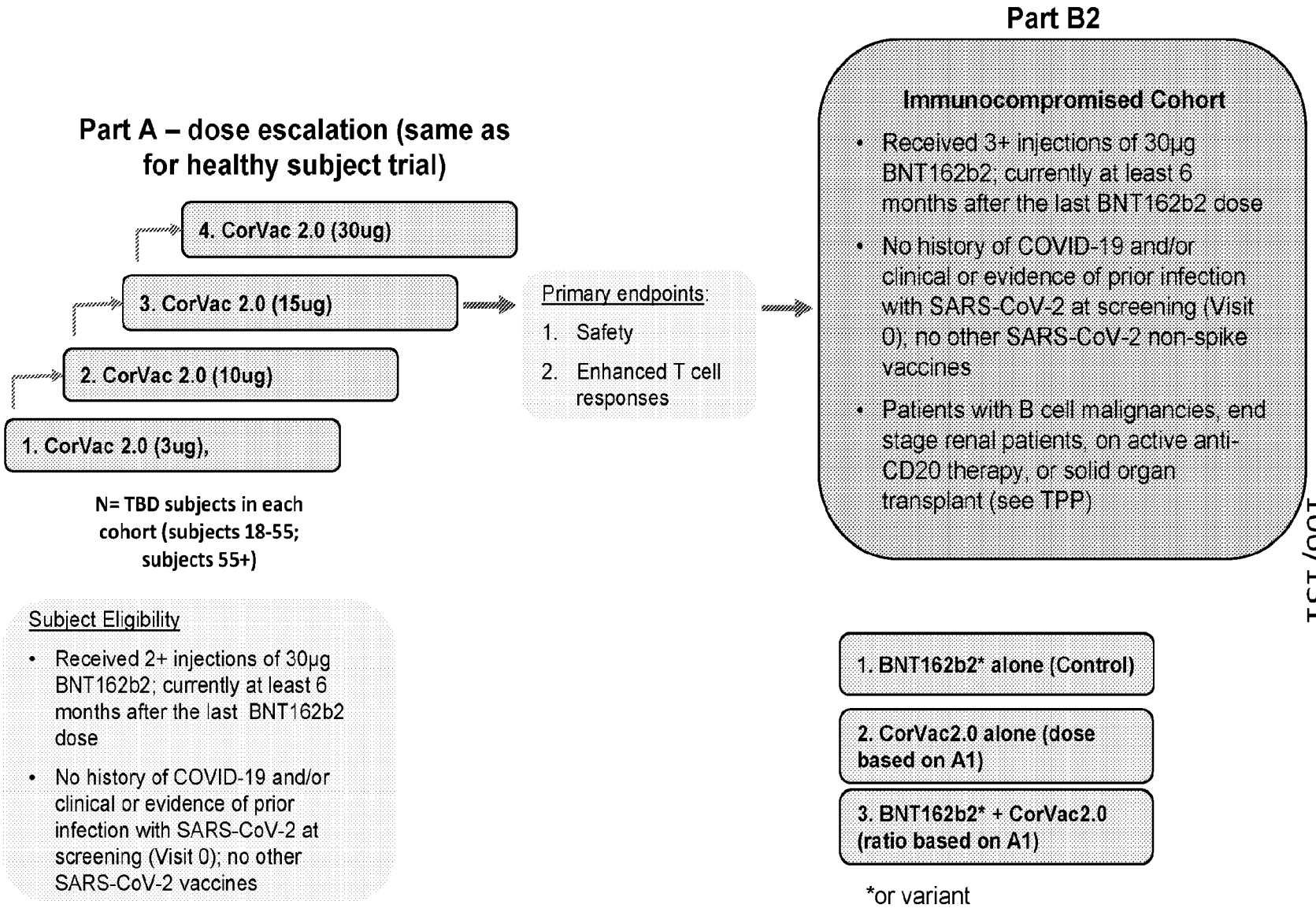

Part A – dose escalation (same as for healthy subject trial)
4. CorVac 2.0 (30ug)
3. CorVac 2.0 (15ug)
2. CorVac 2.0 (10ug)
1. CorVac 2.0 (3ug),
N= TBD subjects in each cohort (subjects 18-55; subjects 55+)
Primary endpoints:
1. Safety
2. Enhanced T cell responses
Part B2
Immunocompromised Cohort
• Received 3+ injections of 30µg BNT162b2; currently at least 6 months after the last BNT162b2 dose
• No history of COVID-19 and/or clinical or evidence of prior infection with SARS-CoV-2 at screening (Visit 0); no other SARS-CoV-2 non-spike vaccines
• Patients with B cell malignancies, end stage renal patients, on active anti-CD20 therapy, or solid organ transplant (see TPP)
Subject Eligibility
• Received 2+ injections of 30µg BNT162b2; currently at least 6 months after the last BNT162b2 dose
• No history of COVID-19 and/or clinical or evidence of prior infection with SARS-CoV-2 at screening (Visit 0); no other SARS-CoV-2 vaccines
1. BNT162b2* alone (Control)
2. CorVac2.0 alone (dose based on A1)
3. BNT162b2* + CorVac2.0 (ratio based on A1)
*or variant

FIG. 70

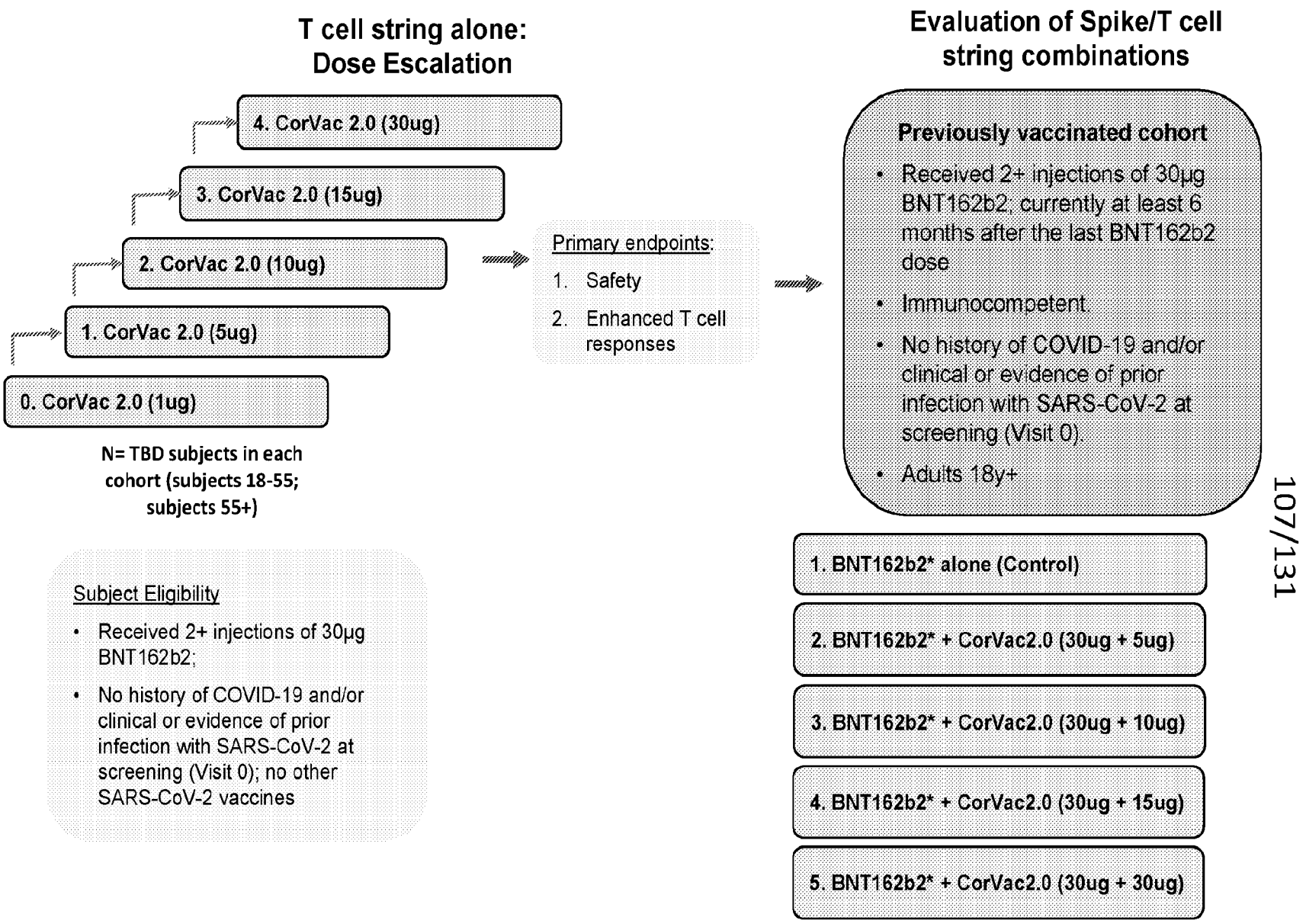

T cell string alone:
Dose Escalation
4. CorVac 2.0 (30ug)
3. CorVac 2.0 (15ug)
2. CorVac 2.0 (10ug)
1. CorVac 2.0 (5ug)
0. CorVac 2.0 (1ug)
N= TBD subjects in each cohort (subjects 18-55; subjects 55+)
Primary endpoints:
1. Safety
2. Enhanced T cell responses
Subject Eligibility
• Received 2+ injections of 30µg BNT162b2;
• No history of COVID-19 and/or clinical or evidence of prior infection with SARS-CoV-2 at screening (Visit 0); no other SARS-CoV-2 vaccines
Evaluation of Spike/T cell string combinations
Previously vaccinated cohort
• Received 2+ injections of 30µg BNT162b2; currently at least 6 months after the last BNT162b2 dose
• Immunocompetent
• No history of COVID-19 and/or clinical or evidence of prior infection with SARS-CoV-2 at screening (Visit 0)
• Adults 18y+
1. BNT162b2* alone (Control)
2. BNT162b2* + CorVac2.0 (30ug + 5ug)
3. BNT162b2* + CorVac2.0 (30ug + 10ug)
4. BNT162b2* + CorVac2.0 (30ug + 15ug)
5. BNT162b2* + CorVac2.0 (30ug + 30ug)
*or variant
BNT162b2 T cell data suggest 10ug are sufficient for T cell response

FIG. 71

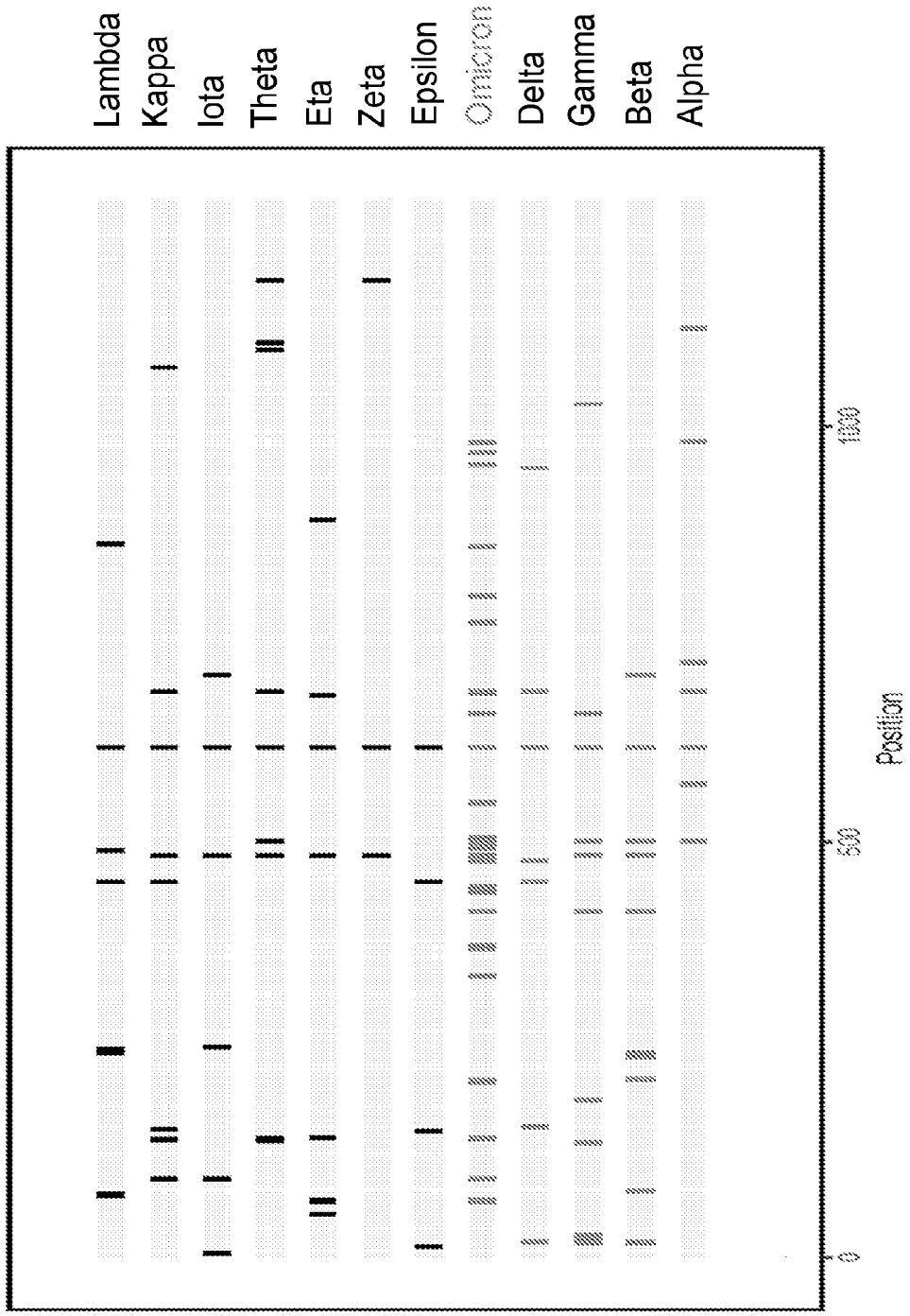

Lambda
Kappa
Iota
Theta
Eta
Zeta
Epsilon
Omicron
Delta
Gamma
Beta
Alpha
0
500
1000
Position

FIG. 72

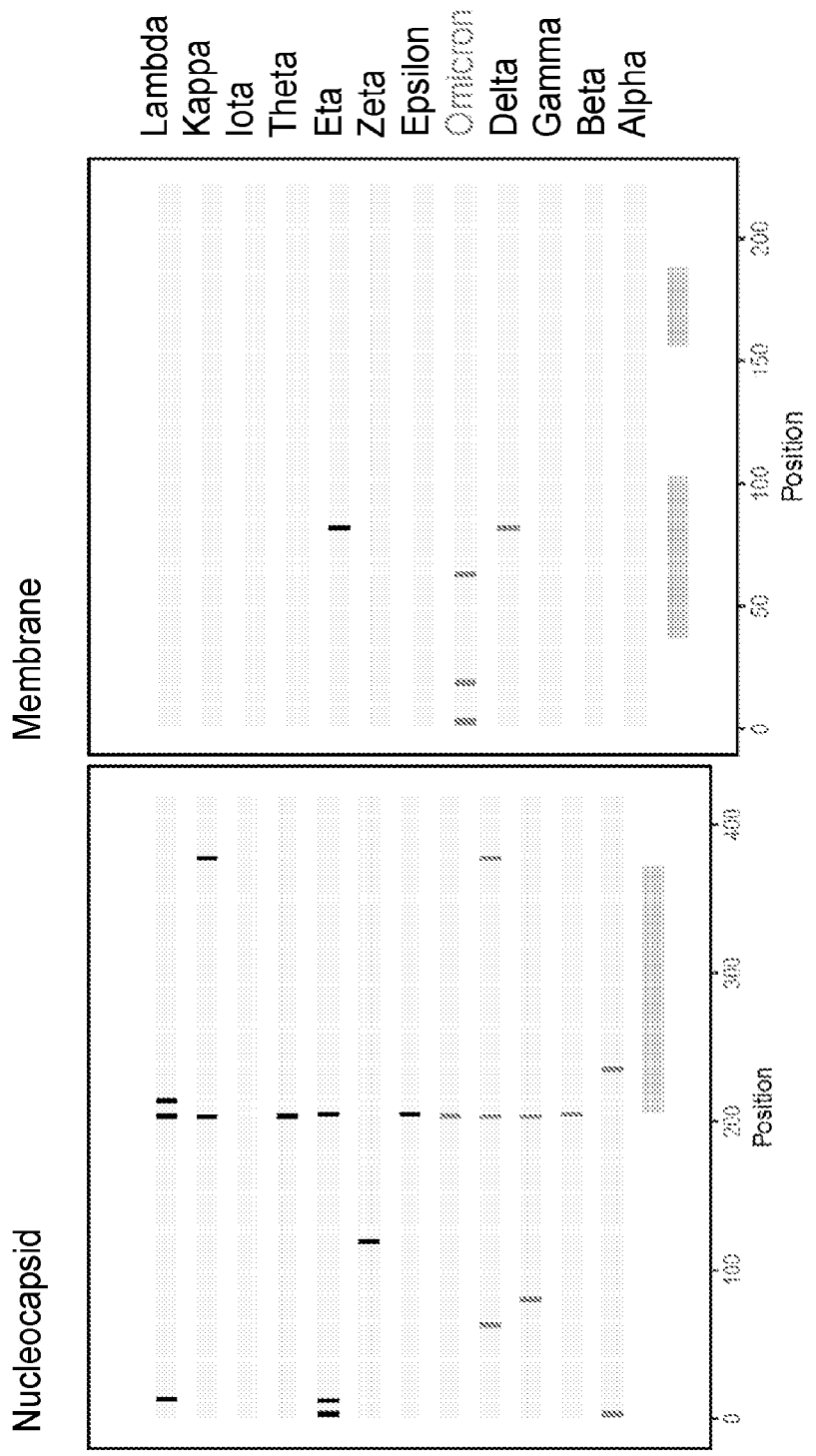

Nucleocapsid
Membrane
Lambda
Kappa
Iota
Theta
Eta
Zeta
Epsilon
Omicron
Delta
Gamma
Beta
Alpha
0
100
200
300
400
Position
0
50
100
150
200
Position
CorVac 2.0

FIG. 73

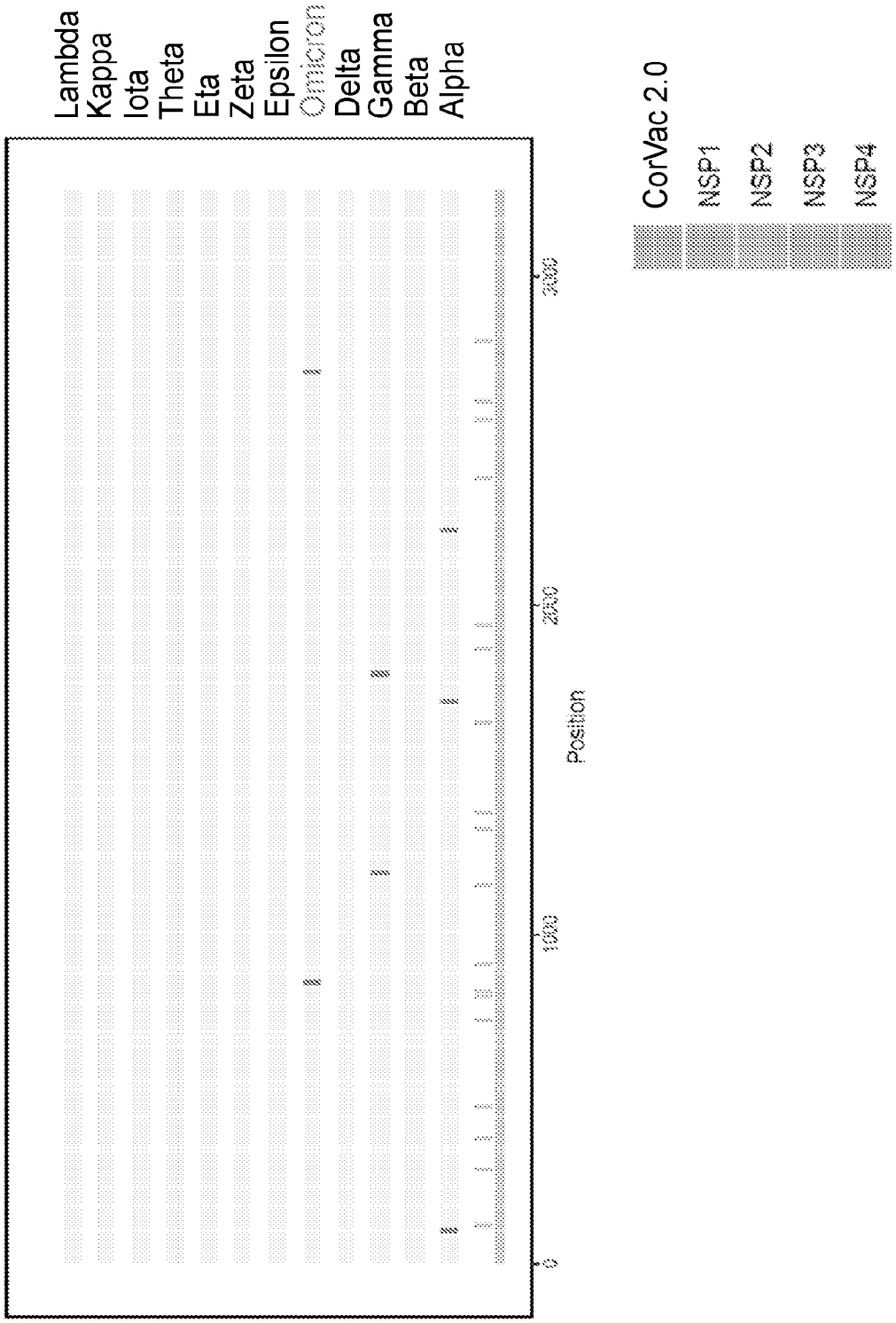

Lambda
Kappa
Iota
Theta
Eta
Zeta
Epsilon
Omicron
Delta
Gamma
Beta
Alpha
0
1000
2000
3000
Position
CorVac 2.0
NSP1
NSP2
NSP3
NSP4

FIG. 74

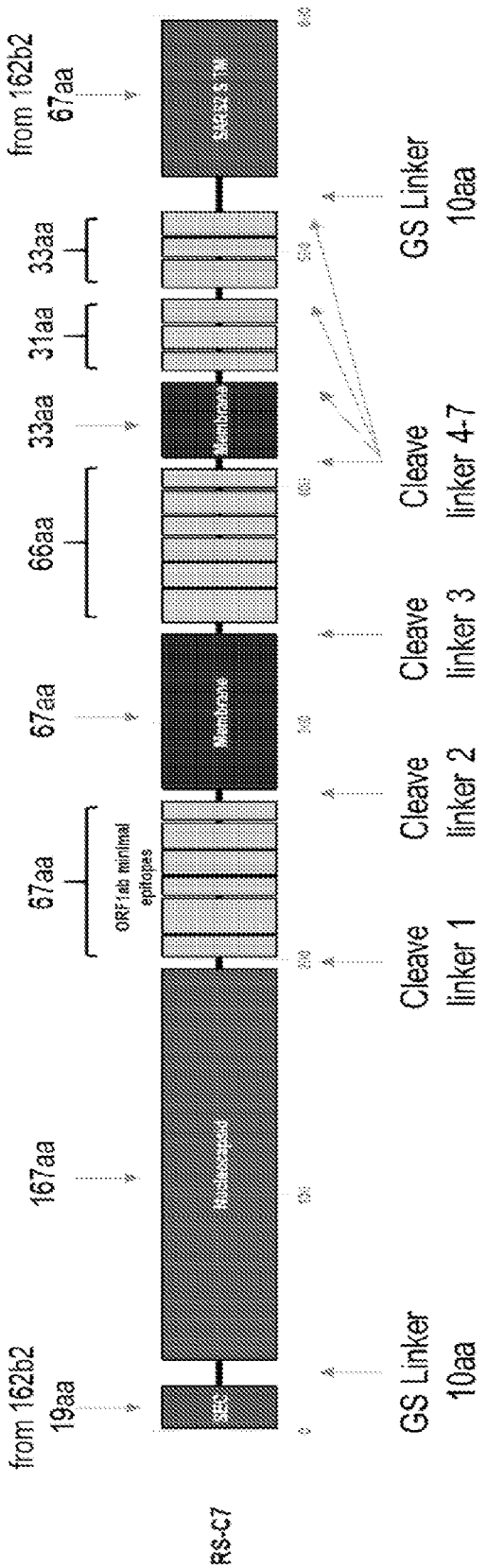

RS-C7
from 162b2
19aa
167aa
67aa
ORF1ab minimal epitopes
67aa
66aa
33aa
31aa
33aa
from 162b2
67aa
GS Linker
10aa
Cleave
linker 1
Cleave
linker 2
Cleave
linker 3
Cleave
linker 4-7
GS Linker
10aa
Membrane
Membrane
0
200
400
600
800

FIG. 75A

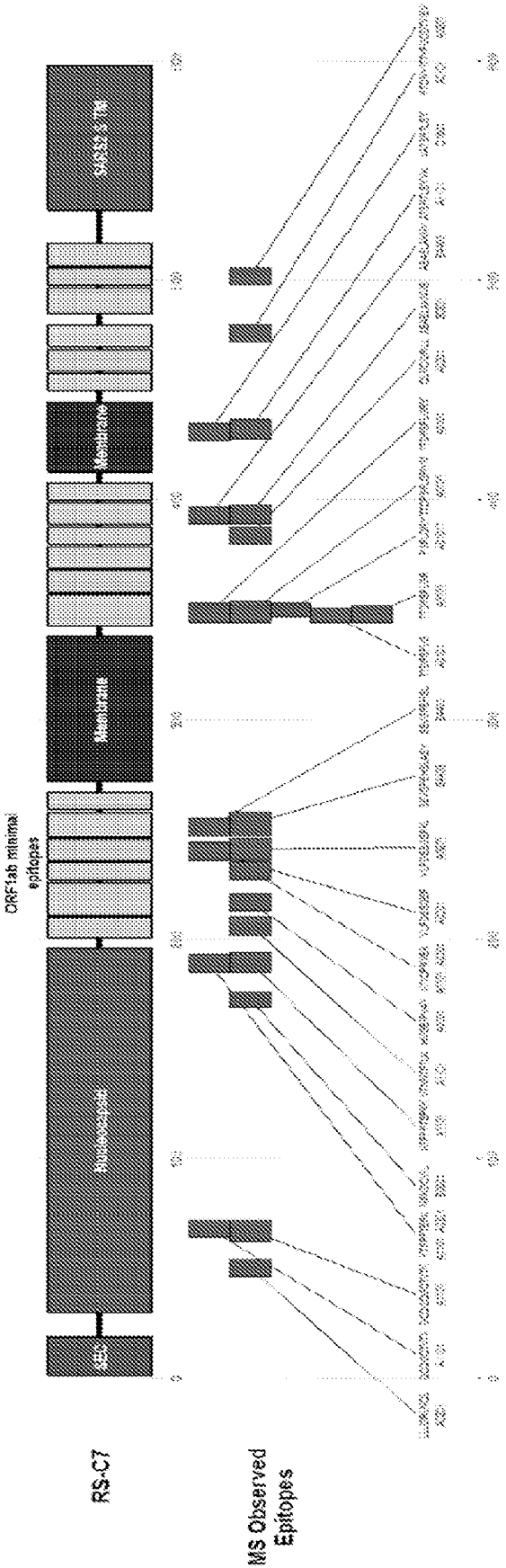

RS-C7
MS Observed Epitopes
ORF1ab minimal epitopes
3BD
Membrane
Membrane
0 50 100 150 200 250 300 350 400 450 500

FIG. 75B

peptide	start	end	length	score	seq_type
YHFF	1	4	4		Linker
HTTDPSFLGRYMSAL	5	19	15	0.376208	epitope
FADDLNQLTGY	20	30	11	2.947135	epitope
HTDFSSEIIGY	31	41	11	2.944603	epitope
QLMCQPILL	42	50	9	1.967348	epitope
AEAELAKNVSL	51	61	11	0.517577	epitope
ILGTVSWNL	62	70	9	0.596325	epitope
KRRY	71	74	4		linker
LLSAGIFGA	75	83	9	0.529516	epitope
ITDVFYKENSY	84	94	11	2.105188	epitope
KVPTDNYITTY	95	105	11	1.134409	epitope
ARMA	106	109	4		linker
APKEIIFLEGETL	110	122	13	1.175399	epitope
FGDDTVIEV	123	131	9	2.679615	epitope
AIILASFSAST	132	142	11	0.747335	epitope
RRMA	143	146	4		linker
MVTNNTFTLK	147	156	10	0.742596	epitope
VPHVGEIPVAYRKVLL	157	172	16	2.066211	epitope
KTIQPRVEK	173	181	9	2.922006	epitope
YLFDESGEFKL	182	192	11	2.269281	epitope
SEVGPEHSLAEY	193	204	12	1.662412	epitope
YIFFASFYY	205	213	9	0.210118	epitope
KRNG	214	218	4		linker

FIG. 76

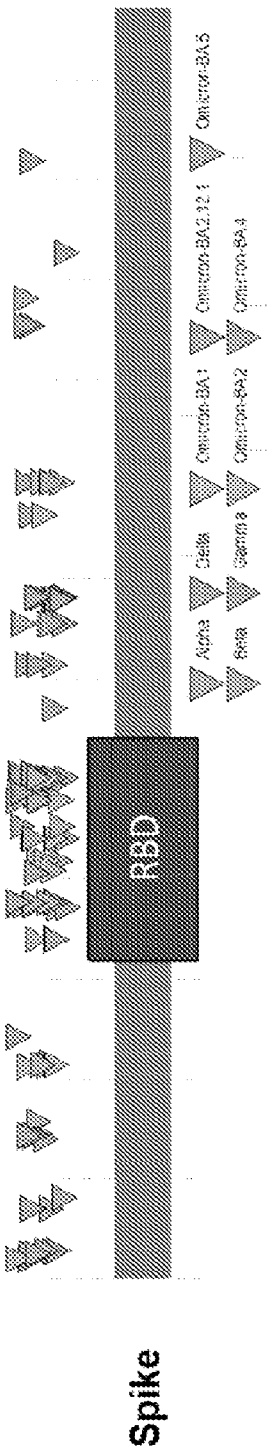
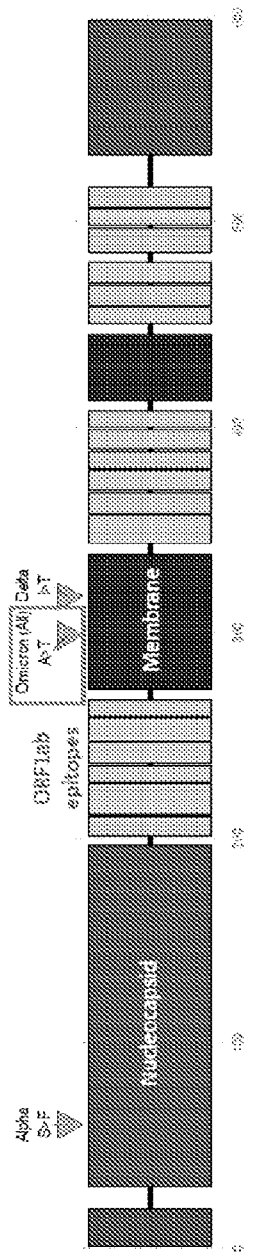

Spike
RBD
Alpha
Beta
Delta
Gamma
Omicron-BA1
Omicron-BA2
Omicron-BA.2.12.1
Omicron-BA.4
Omicron-BA.5

FIG. 77A


Alpha
S-2
Unglycosylated
C3F1ab
epitopes
Omicron (All)
Delta
Membrane

RS C7

FIG. 77B

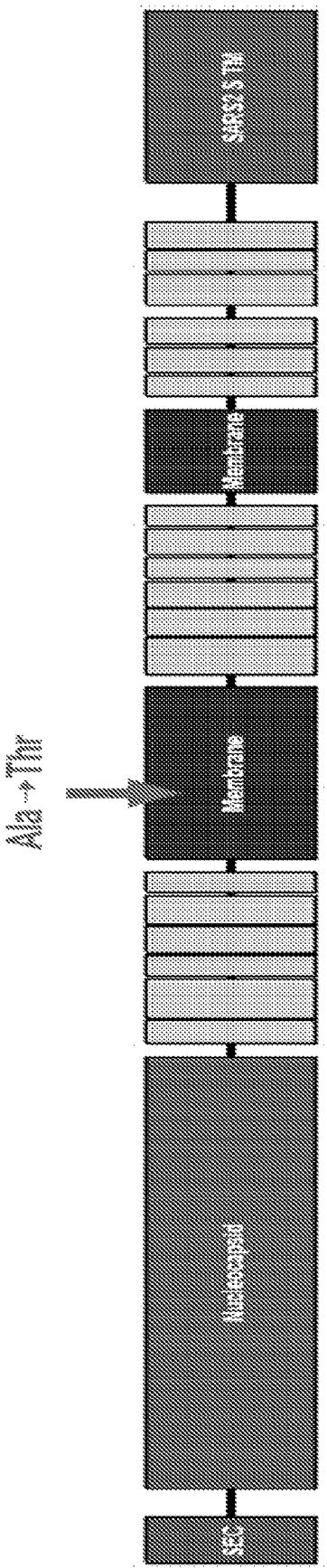


FIG. 77C

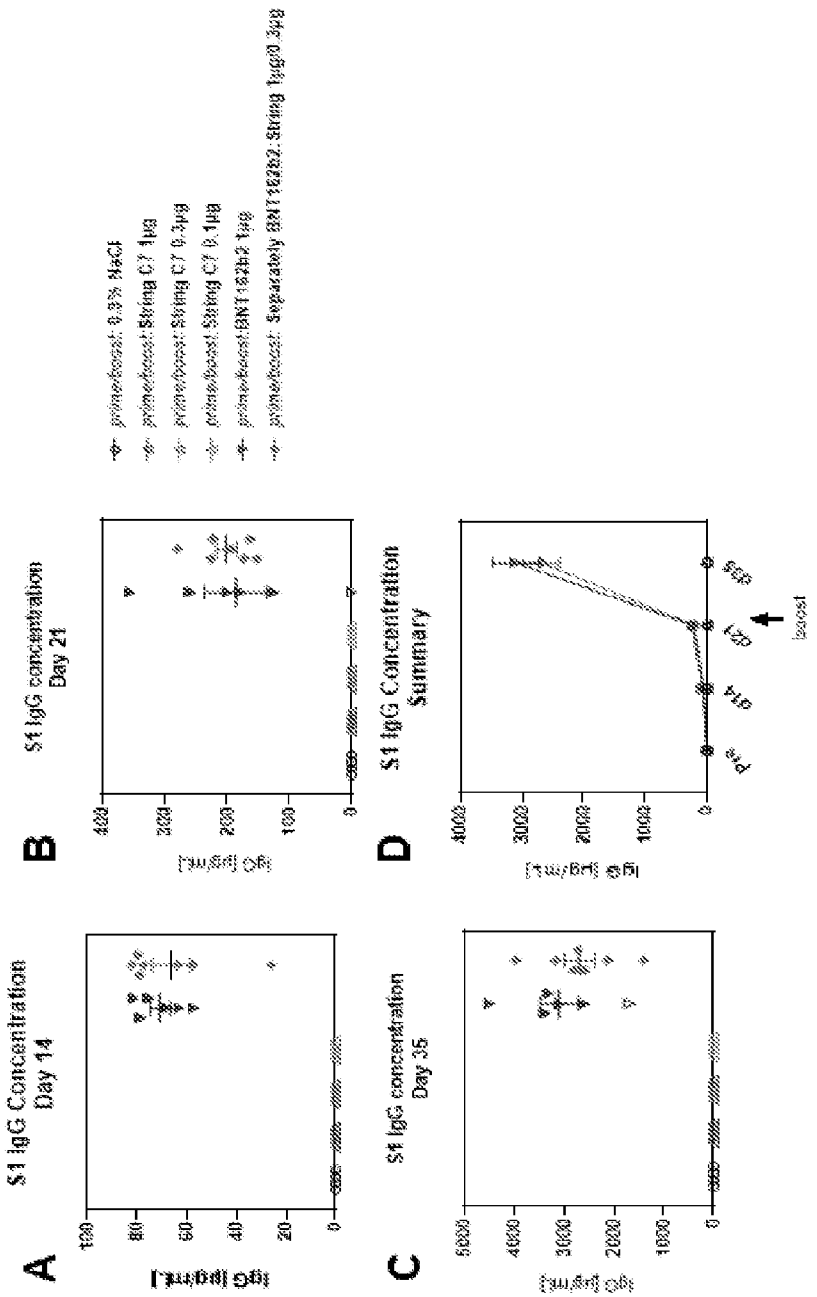

A
S1 IgG Concentration
Day 14
IgG [µg/mL]
B
S1 IgG concentration
Day 21
IgG [µg/mL]
prime/boost: 0.9% NaCl
prime/boost: String C7 1µg
prime/boost: String C7 0.3µg
prime/boost: String C7 0.1µg
prime/boost: BNT162b2 1µg
prime/boost: Separately BNT162b2: String 1µg/0.3µg
C
S1 IgG concentration
Day 35
IgG [µg/mL]
D
S1 IgG Concentration
Summary
IgG [µg/mL]
boost

FIG. 78A

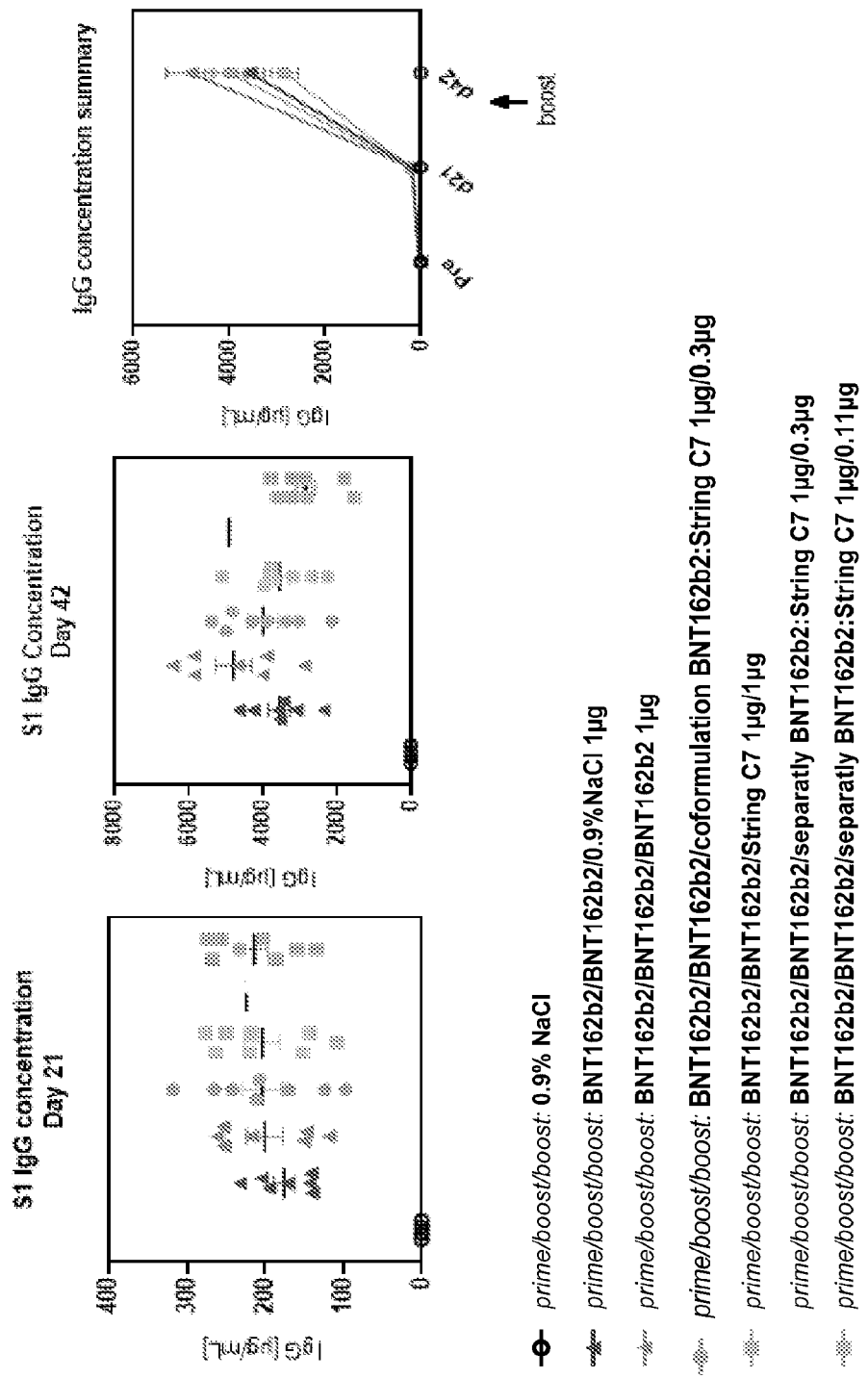

S1 IgG concentration
Day 21
IgG (µg/mL)
400
300
200
100
0
S1 IgG Concentration
Day 42
IgG (µg/mL)
8000
6000
4000
2000
0
IgG concentration summary
IgG (µg/mL)
6000
4000
2000
0
pre
d21
d42
boost
prime/boost/boost: 0.9% NaCl
prime/boost/boost: BNT162b2/BNT162b2/0.9%NaCl 1µg
prime/boost/boost: BNT162b2/BNT162b2/BNT162b2 1µg
prime/boost/boost: BNT162b2/BNT162b2/coformulation BNT162b2:String C7 1µg/0.3µg
prime/boost/boost: BNT162b2/BNT162b2/String C7 1µg/1µg
prime/boost/boost: BNT162b2/BNT162b2/separatly BNT162b2:String C7 1µg/0.3µg
prime/boost/boost: BNT162b2/BNT162b2/separatly BNT162b2:String C7 1µg/0.11µg

FIG. 78B

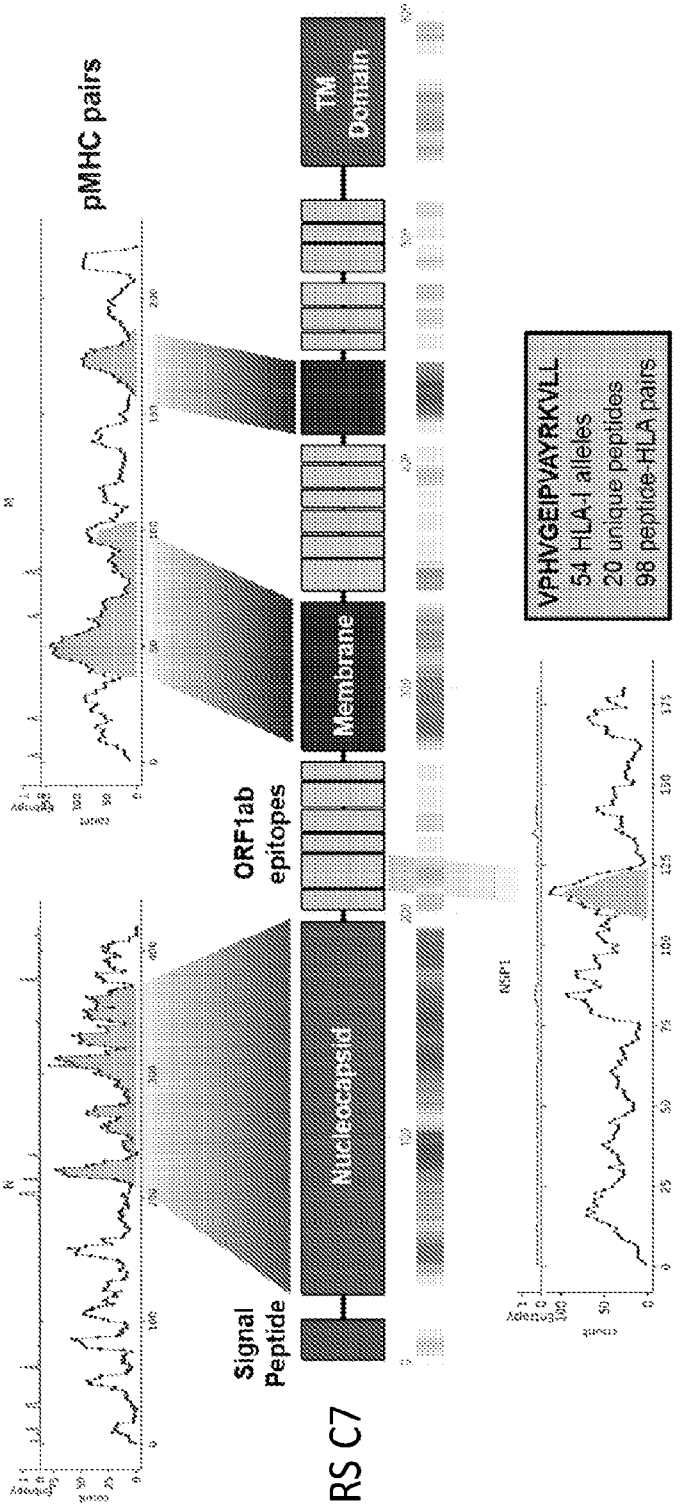

pMHC pairs
TM Domain
Membrane
ORF1ab epitopes
Nucleocapsid
Signal Peptide
RS C7
NSP1
VPHVGEIPVAYRKVLL
54 HLA I alleles
20 unique peptides
98 peptide-HLA pairs

FIG. 79

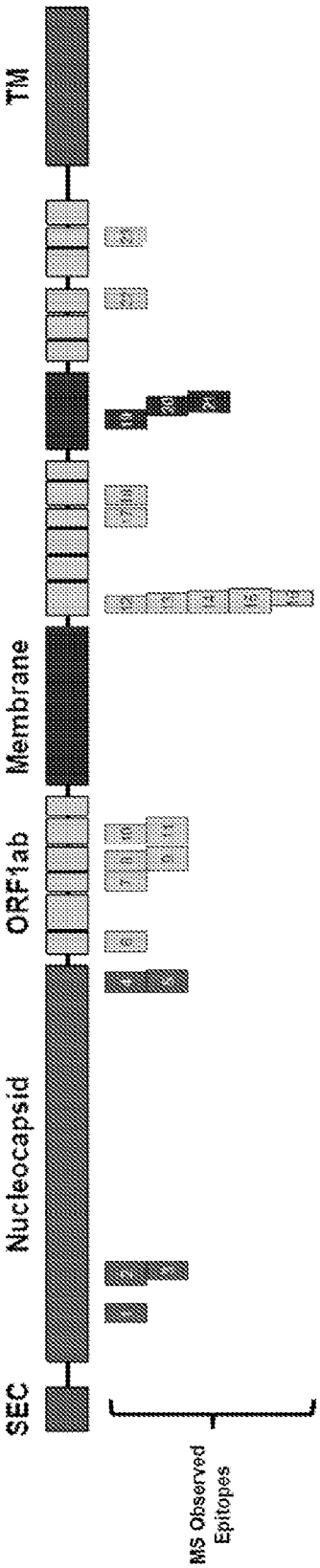


FIG. 80A

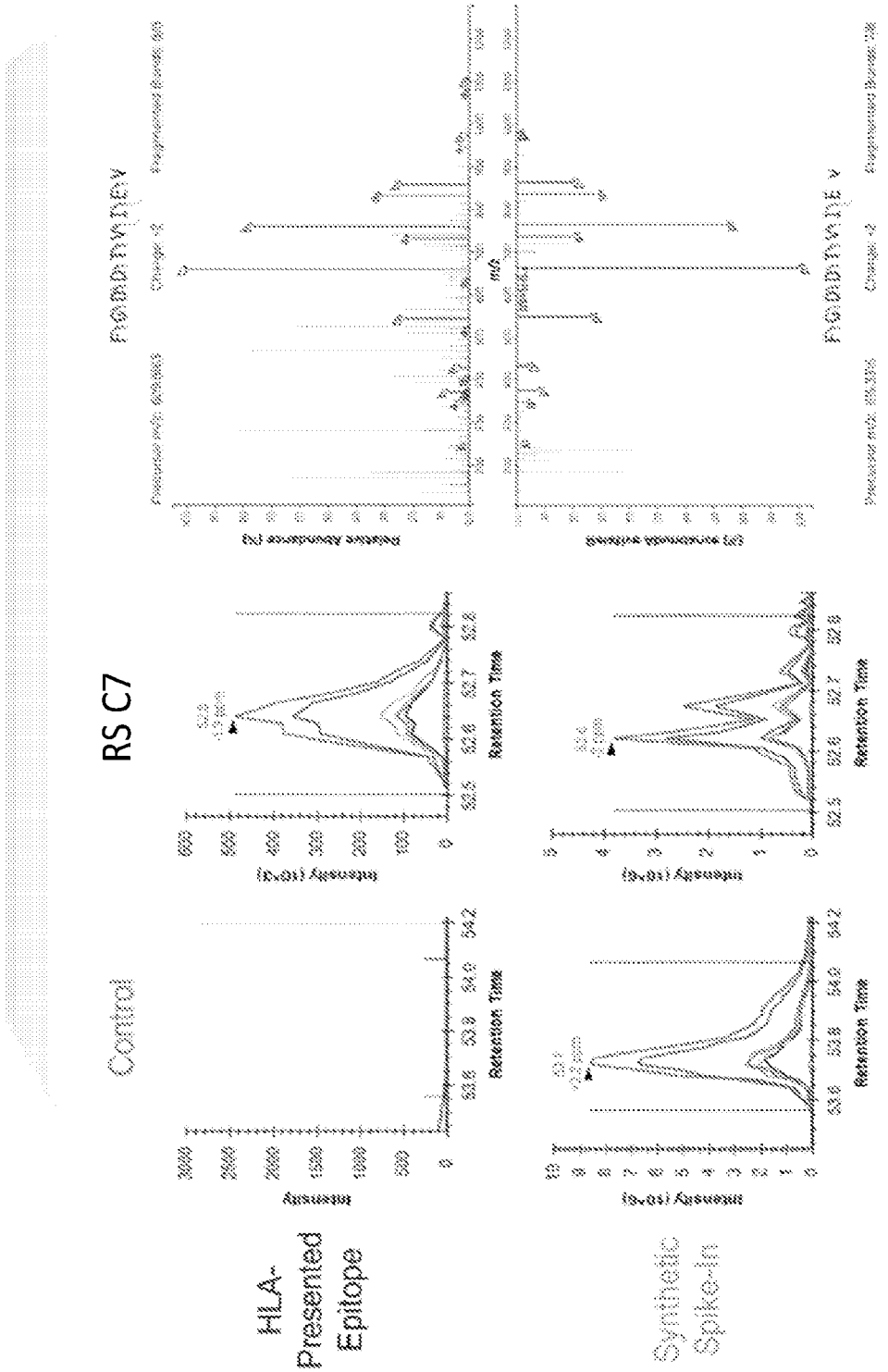
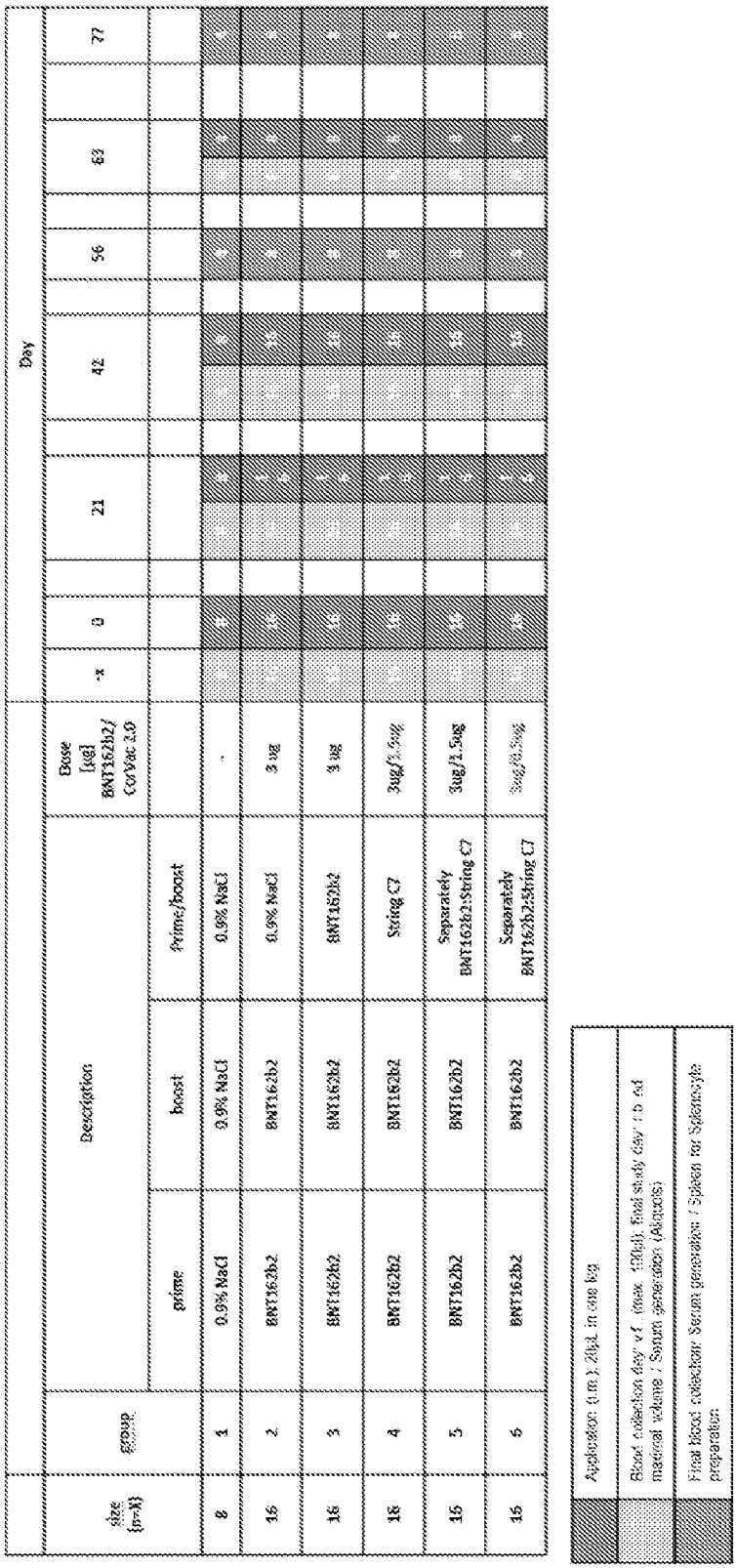

Control
RS C7
HLA-Presented Epitope
Synthetic Spike-In
Retention Time

FIG. 80B


Day
size (n=N)
group
Description
prime
boost
prime/boost
Dose [µg] BNT162b2/ CoVac 2.0
-x
0
21
42
56
63
77
8 1 0.9% NaCl 0.9% NaCl 0.9% NaCl - - -

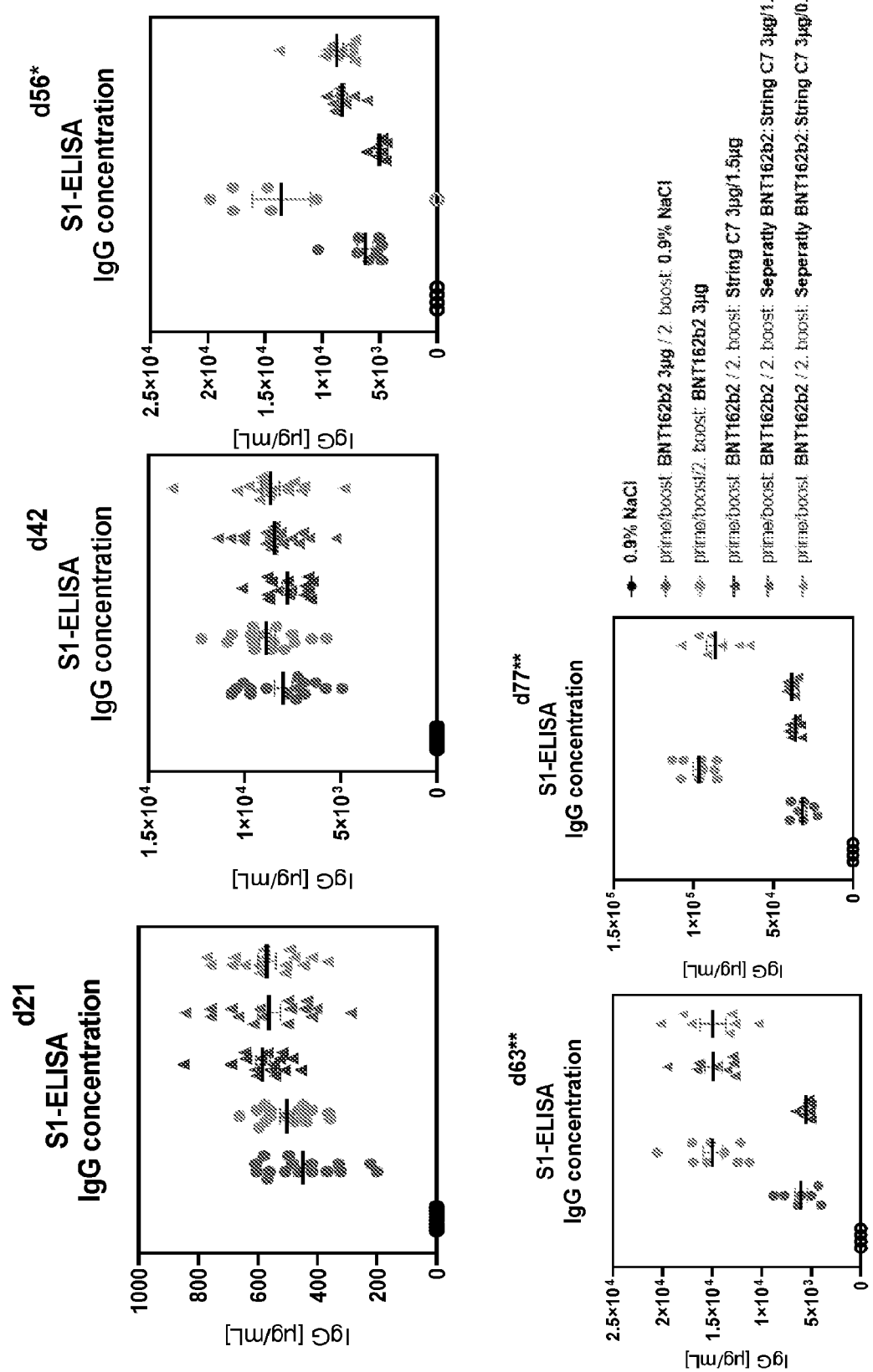

d21
S1-ELISA
IgG concentration
IgG [µg/mL]
1000
800
600
400
200
0
d42
S1-ELISA
IgG concentration
IgG [µg/mL]
1.5×10^4
1×10^4
5×10^3
0
d56*
S1-ELISA
IgG concentration
IgG [µg/mL]
2.5×10^4
2×10^4
1.5×10^4
1×10^4
5×10^3
0
d63**
S1-ELISA
IgG concentration
IgG [µg/mL]
2.5×10^4
2×10^4
1.5×10^4
1×10^4
5×10^3
0
d77**
S1-ELISA
IgG concentration
IgG [µg/mL]
1.5×10^5
1×10^5
5×10^4
0
0.9% NaCl
prime/boost: BNT162b2 3µg / 2. boost: 0.9% NaCl
prime/boost/2. boost: BNT162b2 3µg
prime/boost: BNT162b2 / 2. boost: String C7 3µg/1.5µg
prime/boost: BNT162b2 / 2. boost: Seperatly BNT162b2:String C7 3µg/1.5µg
prime/boost: BNT162b2 / 2. boost: Seperatly BNT162b2:String C7 3µg/0.5µg

FIG. 82A

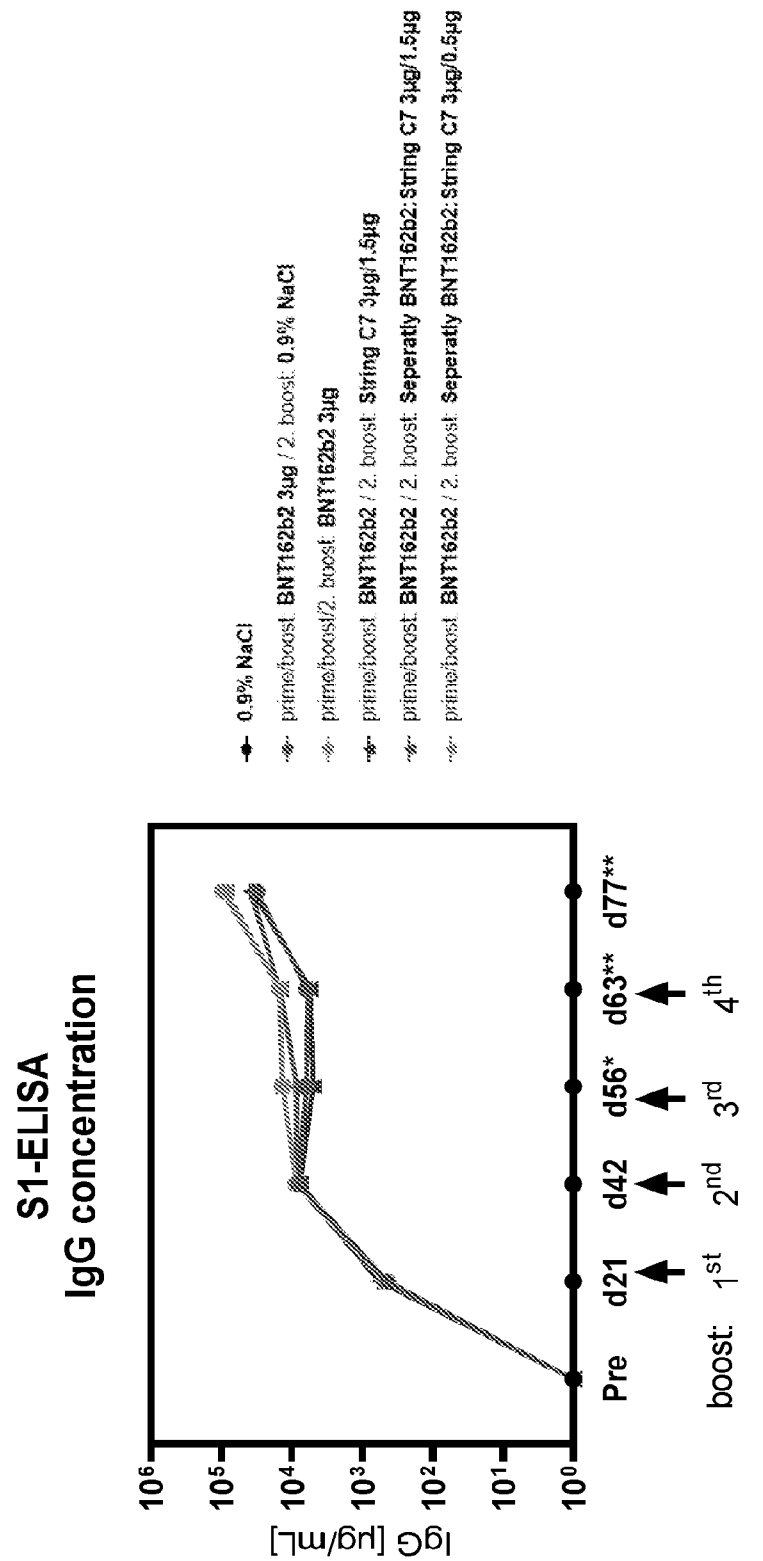

S1-ELISA
IgG concentration
IgG [µg/mL]
10^6
10^5
10^4
10^3
10^2
10^1
10^0
Pre
d21
d42
d56*
d63**
d77**
boost: 1st 2nd 3rd 4th
0.9% NaCl
prime/boost: BNT162b2 3µg / 2. boost: 0.9% NaCl
prime/boost/2. boost: BNT162b2 3µg
prime/boost: BNT162b2 / 2. boost: String C7 3µg/1.5µg
prime/boost: BNT162b2 / 2. boost: Seperatly BNT162b2:String C7 3µg/1.5µg
prime/boost: BNT162b2 / 2. boost: Seperatly BNT162b2:String C7 3µg/0.5µg

FIG. 82B

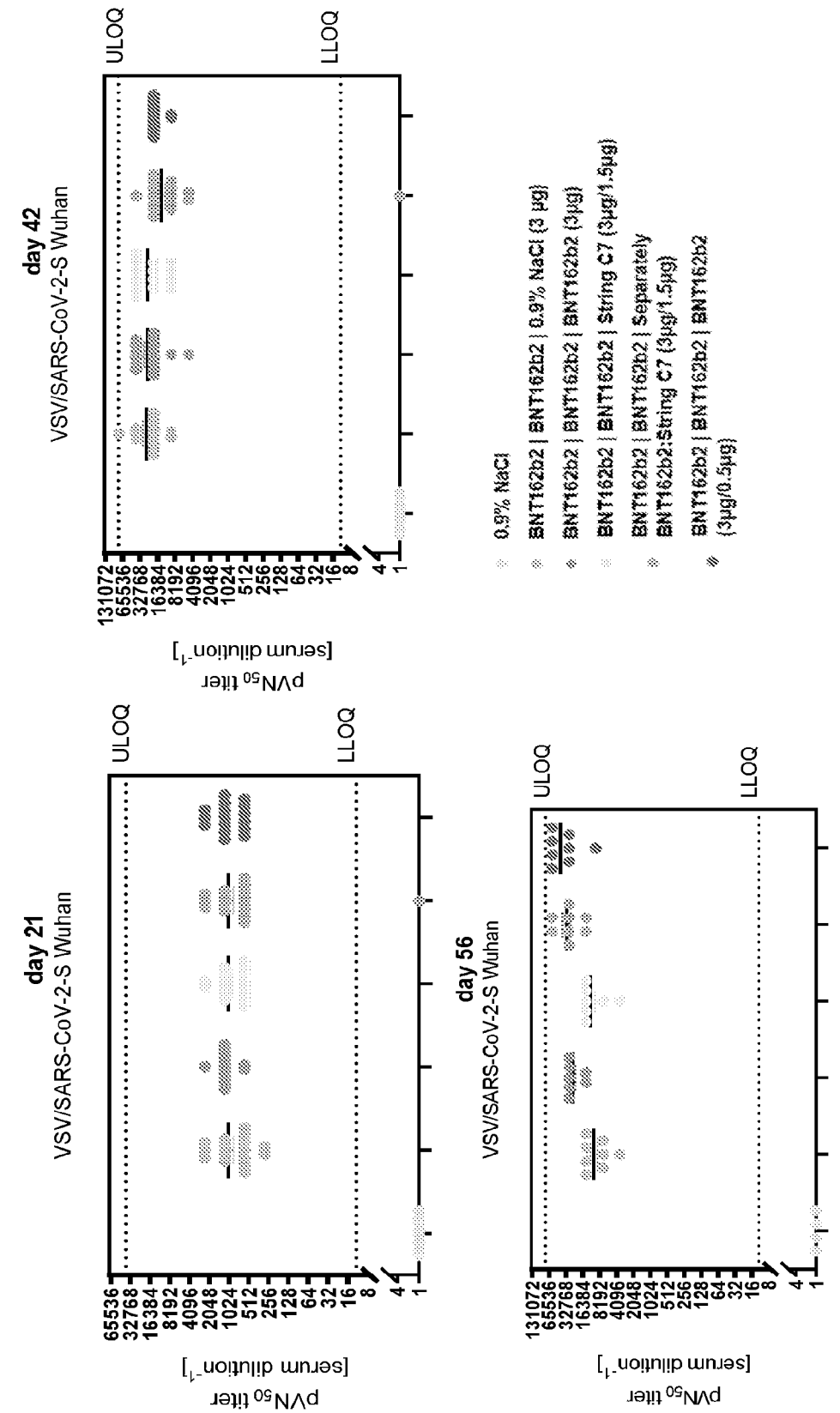

day 21
VSV/SARS-CoV-2-S Wuhan
day 42
VSV/SARS-CoV-2-S Wuhan
day 56
VSV/SARS-CoV-2-S Wuhan
ULOQ
LLOQ
pVN50 titer
[serum dilution-1]
65536
32768
16384
8192
4096
2048
1024
512
256
128
64
32
16
8
4
1
131072
0.9% NaCl
BNT162b2 | BNT162b2 | 0.9% NaCl (3 µg)
BNT162b2 | BNT162b2 | BNT162b2 (3µg)
BNT162b2 | BNT162b2 | String C7 (3µg/1.5µg)
BNT162b2 | BNT162b2 | Separately
BNT162b2:String C7 (3µg/1.5µg)
BNT162b2 | BNT162b2 | BNT162b2 (3µg/0.5µg)

FIG. 83A

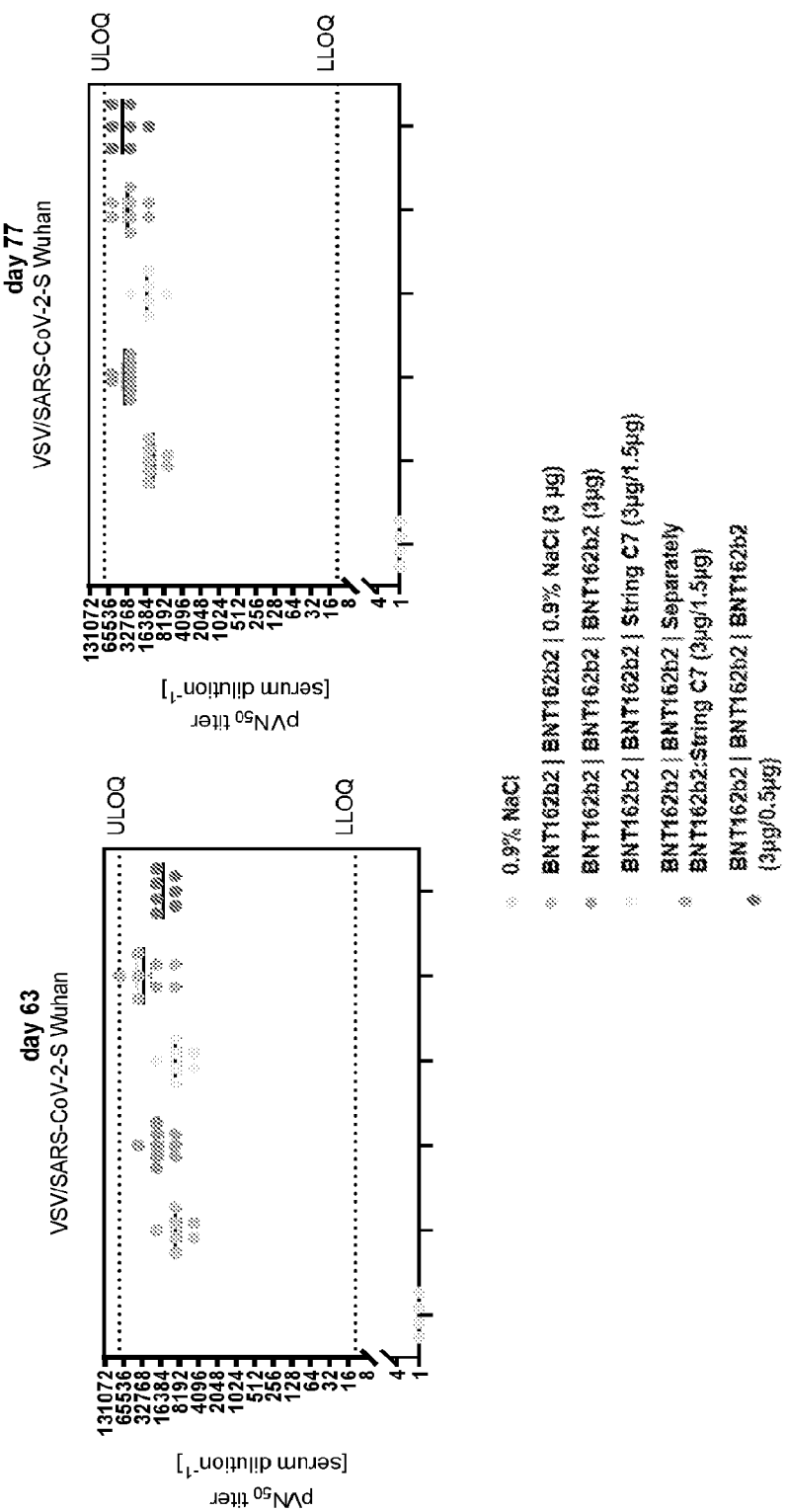

day 63
VSV/SARS-CoV-2-S Wuhan
day 77
VSV/SARS-CoV-2-S Wuhan
pVN50 titer
[serum dilution-1]
131072
65536
32768
16384
8192
4096
2048
1024
512
256
128
64
32
16
8
4
1
ULOQ
LLOQ
0.9% NaCl
BNT162b2 | BNT162b2 | 0.9% NaCl (3 µg)
BNT162b2 | BNT162b2 | BNT162b2 (3µg)
BNT162b2 | BNT162b2 | String C7 (3µg/1.5µg)
BNT162b2 | BNT162b2 | Separately
BNT162b2:String C7 (3µg/1.5µg)
BNT162b2 | BNT162b2 | BNT162b2
(3µg/0.5µg)

FIG. 83B

Efficacy in Syrian Hamsters

size (n=X)	group	Description		Dose (µg)	Day													
		prime	boost		-X	0		14		21		35		37		42		
14	1	0.9% NaCl	0.9% NaCl	-	X	X		X		X		X		X		X		
14	2	BNT162b2	BNT162b2	9	X	X		X		X		X		X		X		
14	3	String C7	String C7	9	X	X		X		X		X		X		X		
14	4	String C7	String C7	4.5	X	X		X		X		X		X		X		
14	5	Separately BNT162b2:String C7	Separately BNT162b2:String C7	9/9	X	X		X		X		X		X		X		
14	6	Separately BNT162b2:String C7	Separately BNT162b2:String C7	9/4.5	X	X		X		X		X		X		X		

prime boost Challenge harvest harvest

Monitor weight

Application (i.m.) 20µL in one leg

Blood collection (final as much as possible, 120µl for others), V. fasc (max 80µl) / Serum generation (Aliquots)

Final blood collection/ Serum generation / Spleen and Lymph node collection

Viral challenge on D35 / Weight measurement until harvest

Harvest for viral titer and pathology – For pathology, collect lung tissue; Measure viral titer in lung and nasal turbinates

FIG. 84

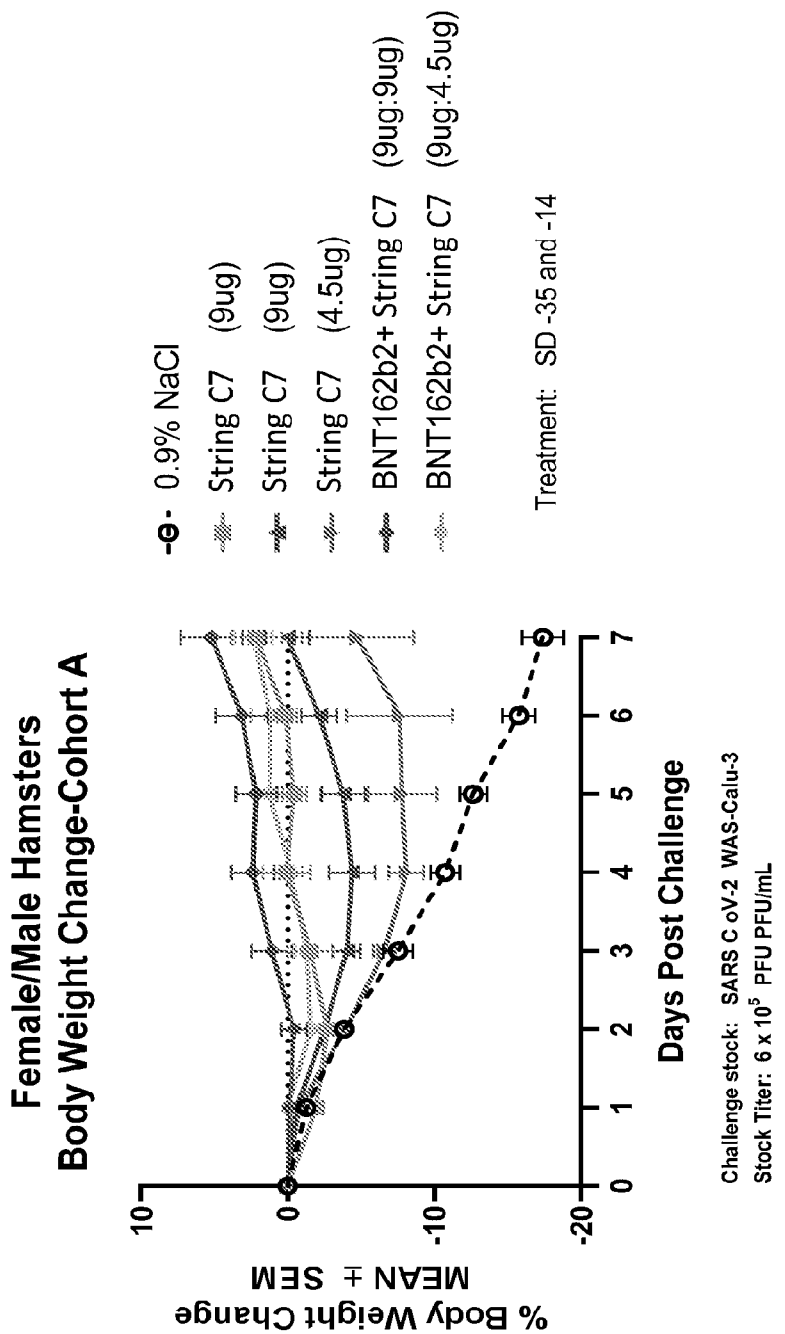

Female/Male Hamsters
Body Weight Change-Cohort A
% Body Weight Change
MEAN ± SEM
10
0
-10
-20
0 1 2 3 4 5 6 7
Days Post Challenge
Challenge stock: SARS C oV-2 WAS-Calu-3
Stock Titer: 6 x 10^5 PFU PFU/mL
0.9% NaCl
String C7 (9ug)
String C7 (9ug)
String C7 (4.5ug)
BNT162b2+ String C7 (9ug:9ug)
BNT162b2+ String C7 (9ug:4.5ug)
Treatment: SD -35 and -14

FIG. 85

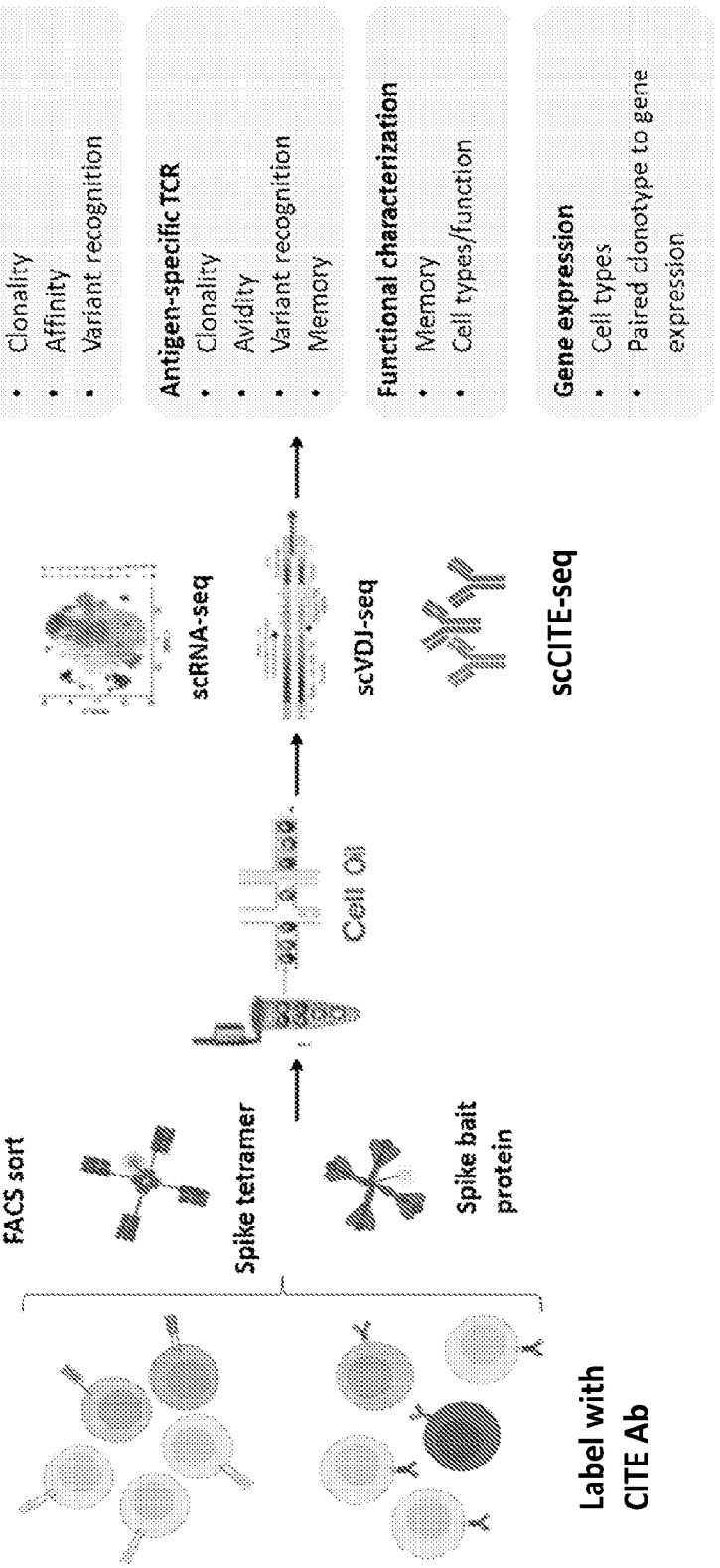

Antigen-specific antibodies
• Clonality
• Affinity
• Variant recognition
Antigen-specific TCR
• Clonality
• Avidity
• Variant recognition
• Memory
Functional characterization
• Memory
• Cell types/function
Gene expression
• Cell types
• Paired clonotype to gene expression
scRNA-seq
scVDJ-seq
scCITE-seq
Cell Ol
FACS sort
Spike tetramer
Spike bait protein
Label with CITE Ab

FIG. 86

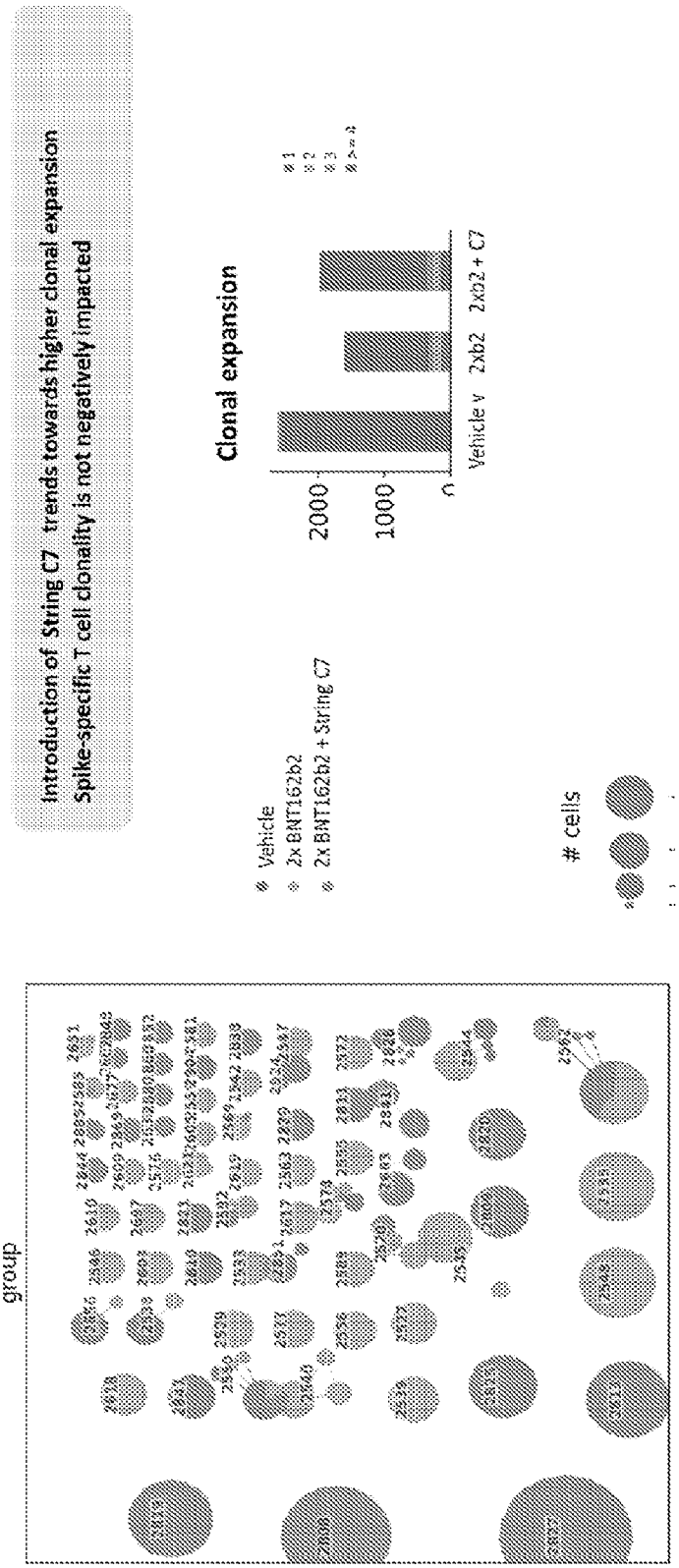

Introduction of String C7 trends towards higher clonal expansion
Spike-specific T cell clonality is not negatively impacted
Clonal expansion
Vehicle
2x BNT162b2
2x BNT162b2 + String C7
2000
1000
0
Vehicle v 2xb2 2xb2 + C7
cells
group

FIG. 87

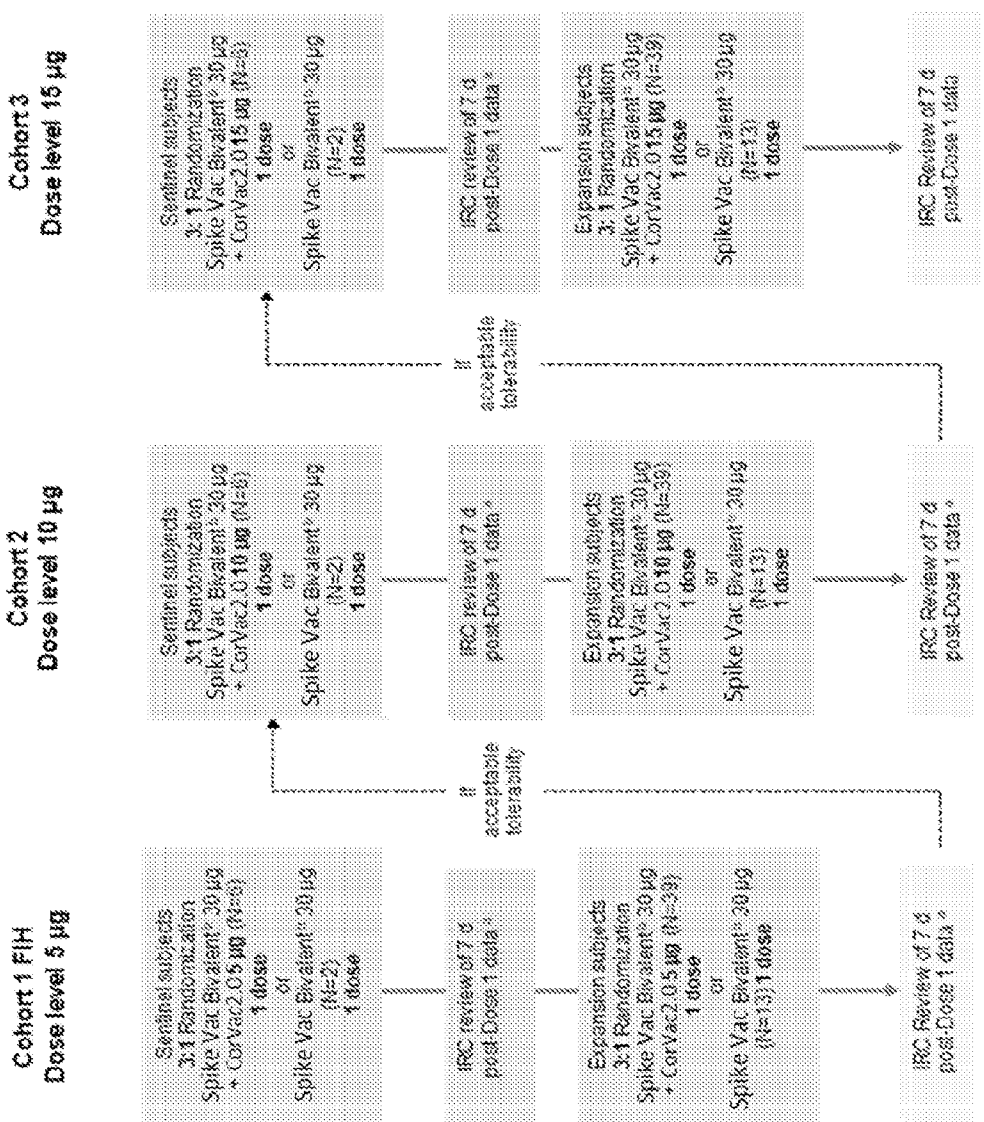

Cohort 1 FIH
Dose level 5 µg
Cohort 2
Dose level 10 µg
Cohort 3
Dose level 15 µg
Sentinel subjects
3:1 Randomization
Spike Vac Bivalent* 30 µg
+ CorVac2.0 5 µg (N=39)
1 dose
or
Spike Vac Bivalent* 30µg
(N=2)
1 dose
IRC review of 7 d
post-Dose 1 data*
Expansion subjects
3:1 Randomization
Spike Vac Bivalent* 30 µg
+ CorVac2.0 5 µg (N=39)
1 dose
or
Spike Vac Bivalent* 30µg
(N=13) 1 dose
IRC Review of 7 d
post-Dose 1 data*
If acceptable tolerability
Sentinel subjects
3:1 Randomization
Spike Vac Bivalent* 30 µg
+ CorVac2.0 10 µg (N=39)
1 dose
or
Spike Vac Bivalent* 30µg
(N=2)
1 dose
IRC review of 7 d
post-Dose 1 data*
Expansion subjects
3:1 Randomization
Spike Vac Bivalent* 30 µg
+ CorVac2.0 10 µg (N=39)
1 dose
or
Spike Vac Bivalent* 30µg
(N=13)
1 dose
IRC Review of 7 d
post-Dose 1 data*
If acceptable tolerability
Sentinel subjects
3:1 Randomization
Spike Vac Bivalent* 30 µg
+ CorVac2.0 15 µg (N=39)
1 dose
or
Spike Vac Bivalent* 30µg
(N=2)
1 dose
IRC review of 7 d
post-Dose 1 data*
Expansion subjects
3:1 Randomization
Spike Vac Bivalent* 30 µg
+ CorVac2.0 15 µg (N=39)
1 dose
or
Spike Vac Bivalent* 30µg
(N=13)
1 dose
IRC Review of 7 d
post-Dose 1 data

FIG. 88

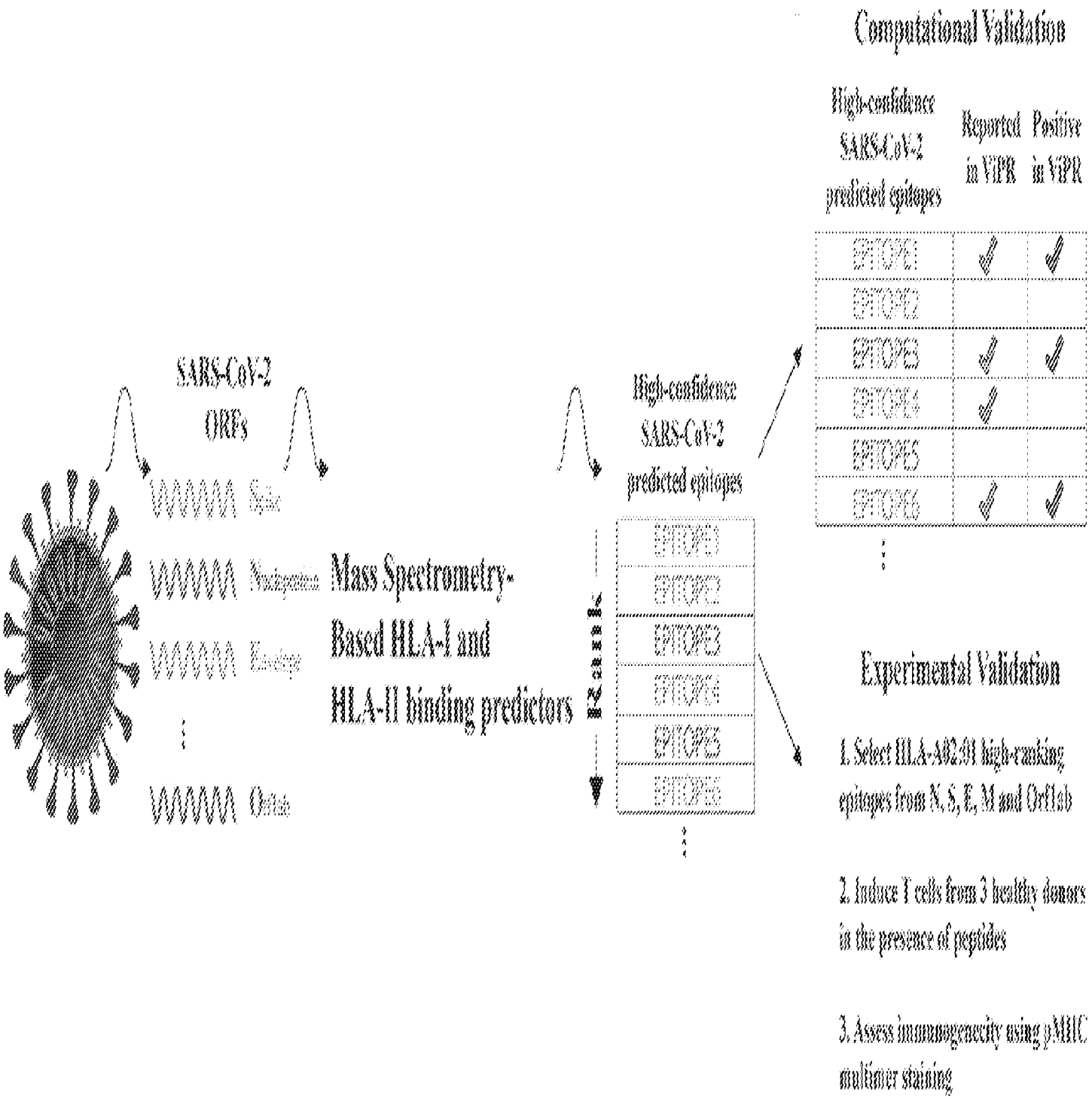

Computational Validation
High-confidence SARS-CoV-2 predicted epitopes
Reported in VIPR
Positive in VIPR
EPITOPE1
EPITOPE2
EPITOPE3
EPITOPE4
EPITOPE5
EPITOPE6
SARS-CoV-2 ORFs
S
Nucleocapsid
E
Orf1a
Mass Spectrometry-Based HLA-I and HLA-II binding predictors
High-confidence SARS-CoV-2 predicted epitopes
EPITOPE1
EPITOPE2
EPITOPE3
EPITOPE4
EPITOPE5
EPITOPE6
Experimental Validation
1. Select HLA-A02:01 high-ranking epitopes from N, S, E, M and Orf1ab
2. Induce T cells from 3 healthy donors in the presence of peptides
3. Assess immunogenecity using pMHC multimer staining

FIG. 1A