

healthy donor and then produced, and/or expanded and banked for administration to a patient with a matching (or partially matching) human leukocyte antigen (HLA) type based on a number of HLA alleles. HLA is also called the Human major histocompatibility complex (MHC). With this approach, one can extract cells from the donor of the stem cells, expand virus-specific populations *ex vivo* and, finally, infuse the T cell product into the stem cell transplant recipient to treat the viral infection in the recipient. For example, *in vitro* expanded donor-derived virus-specific T cells targeting Adv, EBV, CMV, BK, HHV6 have shown to be safe and effective when adoptively transferred to stem cell transplant patients with viral infections (Gerdesmann *et al.*, 2012). Third party donor-derived virus-specific T cells targeting such viruses have also been shown to be safe, but are only considered suitable to treat ongoing viral infections. This is because third party virus-specific T cells and other cell therapies that are generated from third party cells are recognized as non-self by the recipient immune system and are expected to be rejected.

[0006] Viral infections such as Adv, EBV, CMV, BK, HHV6, HSV-1, HSV-2, HHV8, HBV, influenza, parainfluenza, HMPV, VZV, and others are also concerns for patients who are immunocompromised for reasons other than transplantation therapy, such as age (young age or old age), immune deficiency, or treatment with immunosuppressive therapies for certain cancers or autoimmune diseases. There is a need in the art for therapies that better control or prevent the various causes of morbidity and mortality that occur in immunocompromised patients due to viral infection. This disclosure addresses this and other needs.

SUMMARY

[0007] The present disclosure includes methods for preventing or controlling a viral infection or the reactivation of a latent virus via prophylactic administration of a third-party allogeneic T cell therapy. In embodiment examples, the method comprises prophylactically administering to a patient a first antigen-specific T cell line that is a polyclonal third party T cell line, said T cell line comprising antigen specificity for one or more viral antigen. In embodiment examples, the T cell line comprises an HLA type that matches the patient's HLA type on 2 or more HLA alleles. In one aspect, the present disclosure refers to use of a first antigen-specific T cell line that is a polyclonal third-party T cell line, in the manufacture of a medicament for preventing a viral infection or the reactivation of a latent virus via a third-party allogeneic T cell therapy, said T cell line comprising antigen specificity for one or more viral antigen and said T cell line comprising an HLA type that matches the patient's HLA type on 2 or more HLA alleles, and wherein the antigen-specific T cell line is to be prophylactically administered to a patient. In one aspect, the present disclosure refers to use of a first antigen-specific T cell line that is a polyclonal third-party T cell line, in the manufacture of a medicament for controlling a viral infection or the reactivation of a latent virus via a third-party allogeneic T cell therapy, said T cell line comprising antigen specificity for one or more viral antigen and said T cell line comprising an HLA type that matches the patient's HLA type on 2 or more HLA alleles, and wherein the antigen-specific T cell line is to be prophylactically administered to a patient. In embodiment examples, the prophylactic administration is such that the patient does not show evidence of an active viral infection or of reactivation of the latent virus when the T cell line is administered. For example, in embodiment examples, the patient is administered a polyclonal third party T cell line with T cells specific for one or more viruses, wherein the patient does not have an active infection with respect to the one or

more viruses, or wherein the patient does not have any active viral infection. In embodimentexamples, the patient has no detectable viremia or viruria when the T cell line is administered.

[0008] In embodimentexamples, the patient is at a higher risk than an average person in the general population of contracting a viral infection or of having a latent virus reactivate. ~~For example, i~~In embodimentexamples, viral infection poses a greater risk to the patient's health or life than such an infection would pose to an average person in the general population. In embodimentexamples, the patient has an absolute lymphocyte count of less than about 1200, less than about 1000, less than about 900, less than about 800, less than about 700, less than about 600, or less than about 500 lymphocytes per μ L blood. In embodimentexamples, the patient lacks endogenous T cells. In embodimentexamples, the patient is seropositive for any one or more of AdV, BKV, CMV, EBV, HHV6, HHV8, RSV, influenza, parainfluenza (PIV), human metapneumovirus (hMPV), SARS-CoV-2 and HBV.

[0009] In embodimentexamples, the patient is immunocompromised. In embodimentexamples, the patient is immunocompromised due to a disease or condition, due to a treatment the patient received to treat a disease or condition, or due to age. In embodimentexamples, the patient is scheduled to undergo or has undergone a hematopoietic stem cell transplant (HSCT), solid organ transplant, or tissue transplant. In embodimentexamples, the subject is in need of HSCT therapy, a solid organ transplant, or a tissue transplant. ~~For example, i~~In embodimentexamples, the patient is in need of or has had a kidney, liver, heart, heart valve, lung, pancreas, intestine, cornea, musculoskeletal, connective tissue, skin, hand, or face transplant. In embodimentexamples, the patient is receiving immunosuppressive therapy to prevent rejection of the transplant. In embodimentexamples, the subject has cancer, e.g., a leukemia, myeloma, or lymphoma. In embodimentexamples, the subject has a cancer and is in need of HSCT. In embodimentexamples, the subject has one or more nonmalignant diseases and is in need of HSCT. ~~For example, i~~In embodimentexamples, the subject has aplastic anemia, a myelodysplastic syndrome, or an immunodeficiency syndrome. In embodimentexamples, the subject is receiving immunosuppressive or chemotherapeutic therapy as a cancer treatment.

[0010] In embodimentexamples, the treatment the patient received to treat a disease or condition is selected from the group consisting of reduced intensity conditioning, myeloablative conditioning, non-myeloablative conditioning, chemotherapy, and immunosuppressive drugs.

[0011] In embodimentexamples, the patient is immunocompromised due to age, e.g., due to young or old age. In embodimentexamples, the patient is less than 1 year of age, less than 9 months of age, less

than 6 months of age, less than 3 months of age, or less than 1 month of age. In embodimentexamples, the patient is more than 65 years of age, more than 70 years of age, more than 75 years of age, or more than 80 years of age.

[0012] In embodimentexamples, the patient has an immune deficiency condition. ~~For example,~~ ~~i~~In embodimentexamples, the subject has a primary immune deficiency, e.g., a primary immune deficiency disease (PIDD). In embodimentexamples, the patient has an acquired immune deficiency condition. In embodimentexamples, the subject has a human immunodeficiency virus (HIV) infection, and/or the subject has acquired immune deficiency syndrome (AIDS).

[0013] In embodimentexamples, the uses or methods provided herein for preventing or controlling a viral infection or the reactivation of a latent virus via prophylactic administration of a third-party allogeneic T cell therapy comprise prophylactically administering a first polyclonal third party antigen-specific T cell, wherein the T cell line is administered to the patient a plurality of times (e.g., 2, 3, 4, 5, 6, or more times). ~~For example,~~ ~~i~~In embodimentexamples, the first antigen-specific T cell line is administered to the patient in a second administration 4-12 weeks after a first administration. In embodimentexamples, the first antigen-specific T cell line is administered to the patient in a second administration about 4-12 weeks after a first administration. In embodimentexamples, the first antigen-specific T cell line is administered to the patient every 4-12 weeks, e.g., every 4 weeks, every 5 weeks, every 6 weeks, every 7 weeks, every 8 weeks, every 9 weeks, every 10 weeks, every 11 weeks, or every 12 weeks. In embodimentexamples, the first antigen-specific T cell line is administered to the patient about every 4-12 weeks, e.g., about every 4 weeks, about every 5 weeks, about every 6 weeks, about every 7 weeks, about every 8 weeks, about every 9 weeks, about every 10 weeks, about every 11 weeks, or about every 12 weeks. In embodimentexamples, the time between administrations of the first antigen-specific T cell line varies. ~~For example,~~ ~~i~~In embodimentexamples, after the first administration of the first antigen-specific T cell line, the patient is monitored for the persistence of the T cell line and/or is monitored for viremia and/or viruria, and the first antigen-specific T cell line is administered in subsequent administrations accordingly. In embodimentexamples, the first antigen-specific T cell line is administered to the subject repeatedly for the duration of time that the subject is at risk and/or at high risk of a viral infection or reactivation of latent virus, and/or until the patient is no longer immunocompromised.

[0014] In embodimentexamples, as an alternative to or in addition to multiple administrations of the first antigen-specific T cell line, the patient is administered a composition comprising

a peptide or whole antigen that corresponds to an antigen for which the first antigen-specific T cell line is specific. In [embodimentexamples](#), the composition is administered after the first antigen-specific T cell line. In [embodimentexamples](#), the composition comprising the peptide or whole antigen is administered to the subject 4 to 12 weeks after administration of the first antigen-specific T cell line. In [embodimentexamples](#), the composition comprising the peptide or whole antigen is administered to the subject about 4 to about 12 weeks after administration of the first antigen-specific T cell line. In [embodimentexamples](#), the composition is administered multiple times after the first antigen-specific T cell line. ~~For example, i~~In [embodimentexamples](#), the composition comprising the peptide or whole antigen is administered to the subject every 4 weeks, every 5 weeks, every 6 weeks, every 7 weeks, every 8 weeks, every 9 weeks, every 10 weeks, every 11 weeks, or every 12 weeks after administration of the first antigen-specific T cell line. In [embodimentexamples](#), the composition comprising the peptide or whole antigen is administered to the subject about every 4 weeks, about every 5 weeks, about every 6 weeks, about every 7 weeks, about every 8 weeks, about every 9 weeks, about every 10 weeks, about every 11 weeks, or about every 12 weeks after administration of the first antigen-specific T cell line. In [embodimentexamples](#), the composition comprising the peptide or whole antigen is administered 2, 3, 4, 5, 6, or more times. In [embodimentexamples](#), the composition comprising the peptide or whole antigen is administered after the first antigen-specific T cell line is administered to the subject, and is repeatedly administered for the duration of time that the subject is at risk and/or at high risk of a viral infection or reactivation of latent virus, and/or until the patient is no longer immunocompromised. In [embodimentexamples](#), the composition comprising the peptide or whole antigen further comprises an adjuvant.

[0015] In [embodimentexamples](#), the [uses or](#) methods provided herein further comprise administering to the patient one or more second antigen-specific T cell lines; or administering to the patient 2, 3, 4, 5, 6, 7, 8, 9, or 10 more second antigen-specific T cell lines. In [embodimentexamples](#), the first and the second antigen-specific T cell lines are administered to the patient concurrently or sequentially. In [embodimentexamples](#), the one or more second antigen-specific T cell lines are administered to the patient a plurality of times. ~~For example, i~~In [embodimentexamples](#), the one or more second antigen-specific T cell lines are administered to the patient every 4-12 weeks, e.g., every 4 weeks, every 5 weeks, every 6 weeks, every 7 weeks, every 8 weeks, every 9 weeks, every 10 weeks, every 11 weeks, or every 12 weeks. In [embodimentexamples](#), the one or more second antigen-specific T cell lines are administered to the patient about every 4-12 weeks, e.g., about every 4 weeks, about every 5 weeks, about every 6 weeks, about every

7 weeks, about every 8 weeks, about every 9 weeks, about every 10 weeks, about every 11 weeks, or about every 12 weeks. In [embodimentexamples](#), the one or more second antigen-specific T cell line is administered until the patient is no longer immunocompromised. In [embodimentexamples](#), the second antigen-specific T cell line comprises the same antigen specificity as the first antigen-specific T cell line, but is generated from a different donor. In [embodimentexamples](#), the second antigen-specific T cell line comprises some of the same antigen specificity as the first antigen specific T cell line. In [embodimentexamples](#), the second antigen-specific T cell line comprises different antigen specificity than the first antigen-specific T cell line. In [embodimentexamples](#), the 2 or more HLA alleles that are matched between the patient and the first antigen-specific T cell line and/or any second antigen-specific T cell line comprises at least 2 HLA Class I alleles; at least 2 HLA Class II alleles; or at least 1 HLA Class I allele and at least 1 HLA Class II allele. In [embodimentexample](#), the HLA types are HLA-A, HLA-B, HLA- DR, and/or HLA-DQ.

[0016] In [embodimentexamples](#), the third party VSTs have not been genetically modified. In [embodimentexamples](#), the third party VSTs have not been modified to reduce recognition and rejection by host immune cells. ~~For example, i~~In [embodimentexamples](#), the third party VSTs have not been modified to remove HLA and/or TCR molecules from the VST cell surface.

[0017] In [embodimentexamples](#), the present disclosure provides [uses or](#) methods [for](#) preventing or controlling a viral infection or the reactivation of a latent virus via prophylactic administration of a third-party allogeneic T cell therapy comprising prophylactically administering a first polyclonal third party antigen-specific T cell, wherein the viral infection is from a virus selected from EBV, CMV, Adenovirus, BK, JC virus, HHV6, RSV, Influenza, Parainfluenza, Bocavirus, Coronavirus (e.g., SARS-CoV-2), LCMV, Mumps, Measles, human Metapneumovirus, Parvovirus B, Rotavirus, merkel cell virus, herpes simplex virus, HPV, HIV, HTLV1, HHV8 and West Nile Virus, zika virus, ebola. In [embodimentexamples](#), the first and/or second antigen-specific T cell line comprises antigen specificity for at least one antigen or a portion thereof from a single virus. In [embodimentexamples](#), the single virus is selected from EBV, CMV, Adenovirus, BK, JC virus, HHV6, RSV, Influenza, Parainfluenza, Bocavirus, Coronavirus, LCMV, Mumps, Measles, human Metapneumovirus, Parvovirus B, Rotavirus, merkel cell virus, herpes simplex virus, HPV, HIV, HTLV1, HHV8 and West Nile Virus, zika virus, ebola. In particular [embodimentexamples](#), the single virus is HBV or HHV8. In [embodimentexample](#), the first antigen-specific T cell line comprises specificity for two or more antigens or a portion thereof from the single virus.

[0018] In [embodimentexamples](#), the present disclosure provides [uses or](#) methods [for](#) preventing or controlling a viral infection or the reactivation of a latent virus via prophylactic administration of a third-party allogeneic T cell therapy comprising prophylactically administering a first polyclonal third party antigen-specific T cell, wherein the first antigen-specific T cell line comprises antigen specificity for at least one antigen or a portion thereof, from 1-10 different viruses. In [embodimentexamples](#), the first antigen-specific T cell line comprises antigen specificity for 2-5 antigens from each of at least two different viruses or at least a portion of 2-5 antigens from each of at least two different viruses. In [embodimentexamples](#), the second antigen-specific T cell line comprises antigen specificity for at least one antigen or a portion thereof, from 1-10 different viruses. In [embodimentexamples](#), the second antigen-specific T cell line comprises antigen specificity for 2-5 antigens from each of at least two different viruses or at least a portion of 2-5 antigens from each of at least two different viruses.

[0019] In [embodimentexamples](#), the antigen is a viral antigen from a virus selected from EBV, CMV, Adenovirus, BK, JC virus, HHV6, RSV, Influenza, Parainfluenza, Bocavirus, Coronavirus, LCMV, Mumps, Measles, human Metapneumovirus (HMPV), Parvovirus B, Rotavirus, merkel cell virus, herpes simplex virus, HPV, HIV, HTLV1, HHV8, West Nile Virus, zika virus, and ebola. In [embodimentexamples](#), the first and/or the second antigen-specific T cell comprises specificity for at least one antigen from each of the following viruses: RSV, Influenza, Parainfluenza, and HMPV. In [embodimentexamples](#), the Influenza antigens are selected from influenza A antigens NP1, MP1, and a combination thereof; the RSV antigens are selected from N, F, and a combination thereof; the hMPV antigens are selected from F, N, M2-1, M, and a combination thereof; and the PIV antigens are selected from M, HN, N, F, and a combination thereof.

[0020] In [embodimentexample](#), the first and/or the second antigen-specific T cell comprises specificity for at least one antigen from each of the following viruses: EBV, CMV, adenovirus, BK, HHV6. In [embodimentexamples](#), EBV antigens are selected from LMP2, EBNA1, BZLF1, and a combination thereof; the CMV antigens are selected from IE1, pp65, and a combination thereof; the adenovirus antigens are selected from Hexon, Penton, and a combination thereof; the BK virus antigens are selected from VP1, large T, and a combination thereof; and the HHV6 antigens are selected from U90, U11, U14, and a combination thereof.

[0021] In [embodimentexamples](#), the first and/or the second antigen-specific T cell comprises specificity for at least one antigen from HBV. In [embodimentexamples](#), the antigens from HHV8 are selected from

LANA-1 (ORF3); LANA-2 (vIRF3, K10.5); vCYC (ORF72); RTA (ORF50); vFLIP (ORF71); Kaposin (ORF12, K12); gB (ORF8); MIR1 (K3); SSB (ORF6); TS (ORF70), and a combination thereof.

[0022] In [embodimentexamples](#), first and/or the second antigen-specific T cell comprises specificity for at least one antigen from HHV8. In [embodimentexamples](#), the antigens from HBV are selected from HBV core antigen, HBV Surface Antigen, and a combination of HBV core antigen and HBV Surface Antigen.

[0023] In [embodimentexamples](#), the antigen-specific T cells provided herein for use in the methods provided herein are produced by culturing, in the presence of the antigens or a portion thereof, mononuclear cells from a suitable donor having an HLA type that matches the patient's HLA type on 2 or more HLA alleles. In [embodimentexamples](#), the antigen-specific T cells are produced by culturing, in the presence of pepmixes spanning the antigens, or a portion thereof, mononuclear cells from a suitable donor having an HLA type that matches the patient's HLA type on 2 or more HLA alleles. In [embodimentexamples](#), the culturing is in the presence of IL4 and IL7. In [embodimentexamples](#), the pepmix comprises 15 mer peptides. In [embodimentexamples](#), the peptides in the pepmix that span the antigen overlap in sequence by 11 amino acids. In [embodimentexamples](#), the antigen-specific T cells provided herein for use in the methods provided herein are produced by culturing, in the presence of the antigens or a portion thereof, peripheral blood mononuclear cells (PBMCs) from a suitable donor having an HLA type that matches the patient's HLA type on 2 or more HLA alleles. In [embodimentexamples](#), the antigen-specific T cells are produced by culturing, in the presence of pepmixes spanning the antigens, or a portion thereof, PBMCs from a suitable donor having an HLA type that matches the patient's HLA type on 2 or more HLA alleles. In [embodimentexamples](#), the culturing is in the presence of IL4 and IL7. In [embodimentexamples](#), the pepmix comprises 15 mer peptides. In [embodimentexamples](#), the peptides in the pepmix that span the antigen overlap in sequence by 11 amino acids. In [embodimentexamples](#), the present disclosure provides [uses or](#) methods [for](#) preventing or controlling a viral infection or the reactivation of a latent virus via prophylactic administration of a third-party allogeneic T cell therapy comprising prophylactically administering a first polyclonal third party antigen-specific T cell and optionally one or more second polyclonal third party antigen-specific T cell line, wherein the first and /or one or more of each second T cell lines persist in vivo for at least about 4 weeks, at least about 6 weeks, at least about 8 weeks, at least about 10 weeks, or at least about 12 weeks. In [embodimentexamples](#), the first and/or one or more of each second T cell lines persist in vivo for at least about 4 weeks, at least about 6 weeks, at least about 8 weeks, at least about 10

weeks, or at least about 12 weeks absent any active infection in the patient. ~~For example, in~~ some ~~embodiment examples~~, the first and /or one or more of each second T cell lines persist in vivo for 4 weeks, 6 weeks, 8 weeks, 10 weeks, 12 weeks, or more than 12 weeks. In ~~embodiment examples~~, the first and/or one or more of each second T cell lines persist in vivo for 4 weeks, 6 weeks, 8 weeks 10 weeks, 12 weeks, or more than 12 weeks absent any active infection in the patient

BRIEF DESCRIPTION OF THE DRAWINGS

[0024] The following drawings form part of the present specification and are included to further demonstrate certain aspects of the present invention. The invention may be better understood by reference to one or more of these drawings in combination with the detailed description of the specification embodiments presented herein.

[0025] **FIG. 1.** is a schematic showing general manufacturing concepts of the antigen-specific T cell lines.

[0026] **FIG. 2** is a flowchart of manufacturing of the antigen-specific T cell lines.

[0027] **FIG. 3A-3D. Characteristics of generated CMVST lines and degree of matching with screened subjects (3A)** T cell expansion of CMVSTs achieved over a 20-day period based on cell counting using trypan blue exclusion. (n=8). **(3B)** Phenotype of the expanded CMVST lines on the day of cryopreservation (mean $\pm$ SEM, n=8) and **(3C)** frequency of antigen-specific T cells as determined by IFN- γ ELISpot assay after overnight stimulation of CMVSTs with IE1 and pp65 antigen-spanning pepmixes. Results are reported as spot forming cells (SFC) per 2×10^5 VSTs plated. CMVST lines with a total of $2:30 \text{ SFC}/2 \times 10^5$ were considered to be positive. (n=8). **(3D)** Number of matching HLA antigens (of 8 total) of CMVST lines identified for clinical use with recipient HLA of screened patients (n=29).

[0028] **FIG. 4. Treatment outcomes in individual patients infected with cytomegalovirus (CMV).** Depiction of plasma CMV viral loads (IU/mL) in patients 2 weeks prior to (viral load level closest to week -2), immediately before (pre) and after (post) infusion (weeks 2, 4 and 6) of CMVSTs. Arrows indicate infusion timepoints.

CLAIMS

1. ~~A method of preventing a viral infection or the reactivation of a latent virus via a third-party allogeneic T cell therapy, the method comprising prophylactically administering to a patient~~Use of a first ~~antigen-specific~~antigen-specific T cell line that is a polyclonal ~~third-party~~third-party T cell line, in the manufacture of a medicament for preventing a viral infection or the reactivation of a latent virus via a third-party allogeneic T cell therapy, said T cell line comprising antigen specificity for one or more viral antigen and said T cell line comprising an HLA type that matches the patient's HLA type on 2 or more HLA alleles, and wherein the antigen-specific T cell line is to be prophylactically administered to a patient.

2. ~~A method of controlling a viral infection or the reactivation of a latent virus via a third-party allogeneic T cell therapy, the method comprising prophylactically administering to a patient~~Use of a first ~~antigen-specific~~antigen-specific T cell line that is a polyclonal ~~third-party~~third-party T cell line, in the manufacture of a medicament for controlling a viral infection or the reactivation of a latent virus via a third-party allogeneic T cell therapy, said T cell line comprising antigen specificity for one or more viral antigen and said T cell line comprising an HLA type that matches the patient's HLA type on 2 or more HLA alleles, and wherein the antigen-specific T cell line is to be prophylactically administered to a patient.

3. The use according to~~method of~~ claim 1 or claim 2, wherein
(a) the patient is at a higher risk than an average person in the general population of contracting a viral infection or of having a latent virus reactivate; and/or
(b) the viral infection poses a greater risk to the patient's health or life than such an infection would pose to an average person in the general population.

4. ~~The method of any one of claims 1-3, wherein the viral infection poses a greater risk to the patient's health or life than such an infection would pose to an average person in the general population.~~

~~5.4.~~ The use according to~~method of~~ any one of claims 1-~~43~~, wherein
(a) the patient does not show evidence of an active viral infection or of reactivation of the latent virus when the T cell line is administered; and/or
(b) the patient has no detectable viremia or viruria when the T cell line is administered.

~~6.~~ The method of any one of claims 1-5, wherein the patient has no detectable viremia or viruria when the T cell line is administered.

~~7.5.~~ The use according to~~method of~~ any one of claims 1-~~64~~, wherein
(a) the patient has an absolute lymphocyte count of less than 800 lymphocytes per μ L blood; and/or
(b) the patient lacks endogenous T cells.

~~8.~~ The method of any one of claims 1-7, wherein the patient lacks endogenous T cells.

~~9.6.~~ The use according to~~method of~~ any one of claims 1-~~85~~, wherein the patient is seropositive for any one or more of AdV, BKV, CMV, EBV, HHV6, HHV8, RSV, influenza, PIV, hMPV HBV, and SARS-CoV-2.

~~10.7.~~ The use according to~~method of~~ any one of claims 1-~~96~~, wherein
(a) the first antigen-specific T cell line is to be administered to the patient a plurality of times;
(b) the first antigen-specific T cell line is to be administered to the patient in a second administration about 4-12 weeks after a first administration;
(c) the first antigen-specific T cell line is to be administered to the patient about every 4-12 weeks;

(d) the patient is immunocompromised, and wherein the first antigen- specific T cell line is to be administered to the patient about every 4-12 weeks until the patient is no longer immunocompromised; and/or

(e) the patient is to be administered a composition comprising a peptide or whole antigen that corresponds to the antigen for which the first antigen-specific T cell line is specific, and wherein the peptide or whole antigen is to be administered to the subject about 4-12 weeks after administration of the first antigen-specific T cell line.

~~11.—The method of any one of claims 1-10, wherein the first antigen-specific T cell line is administered to the patient in a second administration about 4-12 weeks after a first administration.~~

~~12.—The method of any one of claims 1-11, wherein the first antigen-specific T cell line is administered to the patient about every 4-12 weeks.~~

~~13.—The method of claim 12, wherein the patient is immunocompromised, and wherein the first antigen-specific T cell line is administered to the patient about every 4-12 weeks until the patient is no longer immunocompromised.~~

~~14.—The method of any one of claims 1-13, wherein the patient is administered a composition comprising a peptide or whole antigen that corresponds to the antigen for which the first antigen-specific T cell line is specific, and wherein the peptide or whole antigen is administered to the subject about 4-12 weeks after administration of the first antigen-specific T cell line.~~

15.8. The ~~method-use according to~~ claim 147, wherein the composition further comprises an adjuvant.

16.9. The ~~method-use according to~~ any one of claims 1-158,

- (a) ~~further comprising administering to the patient wherein~~ one or more second antigen-specific T cell lines is to be further administered to the patient; or
- (b) ~~further comprising administering to the patient wherein~~ 2, 3, 4, 5, 6, 7, 8, 9, or 10 more second ~~antigen-specific antigen-specific~~ T cell lines is to be further administered to the patient.

~~17.10.~~ The ~~method-use according to~~ claim ~~169~~, wherein the first and the second antigen-specific T cell lines are to be administered to the patient concurrently or sequentially.

~~18.~~—The method of claim ~~16~~, wherein the first and the second antigen-specific T cell lines are administered to the patient sequentially.

~~19.11.~~ The ~~method-use according to~~ any one of claims ~~16-189-10~~, wherein

(a) the one or more second antigen-specific T cell lines are to be administered to the patient a plurality of times; and/or

(b) the patient is immunocompromised, and wherein the one or more second antigen-specific T cell lines are to be administered to the patient about every 6-12 weeks until the patient is no longer immunocompromised.

~~20.~~—The method of claim ~~19~~, wherein the patient is immunocompromised, and wherein the one or more second antigen-specific T cell lines are administered to the patient about every ~~6-12 weeks until the patient is no longer immunocompromised.~~

~~21.12.~~ The ~~method-use according to~~ any one of claims ~~16-209-11~~, wherein at least one, and optionally each, second antigen-specific T cell line comprises the same antigen specificity as the first antigen-specific T cell line, but is generated from a different donor.

~~22.13.~~ The ~~method-use according to~~ any one of claims 1-~~2112~~, wherein the 2 or more HLA alleles that are matched between the patient and the first antigen-specific T cell line and/or any second antigen-specific T cell line if one was administered comprises at least 2 HLA Class I alleles; at least 2 HLA Class II alleles; or at least 1 HLA Class I allele and at least 1 HLA Class II allele.

23-14. The ~~method-use according to~~ any one of claims 1-~~22~~13, wherein the viral infection is from a virus selected from EBV, CMV, Adenovirus, BK, JC virus, HHV6, RSV, Influenza, Parainfluenza, Bocavirus, Coronavirus, LCMV, Mumps, Measles, human Metapneumovirus, Parvovirus B, Rotavirus, merkel cell virus, herpes simplex virus, HPV, HIV, HTLV1, HHV8, HBV, West Nile Virus, Zika virus, and Ebola virus.

24-15. The ~~method-use according to~~ any one of claims 1-~~23~~14, wherein the first and/or second antigen-specific T cell line comprises antigen specificity for at least one antigen or a portion thereof from a single virus.

25-16. The ~~method-use according to~~ claim ~~24~~15, wherein the single virus is selected from EBV, CMV, Adenovirus, BK, JC virus, HHV6, RSV, Influenza, Parainfluenza, Bocavirus, Coronavirus, LCMV, Mumps, Measles, human Metapneumo_virus, Parvovirus B, Rotavirus, merkel cell virus, herpes simplex virus, HPV, HIV, HTLV1, HHV8, HBV, West Nile Virus, Zika virus, and Ebola virus.

~~26. The method of claim 25, wherein the single virus is HBV or HHV8.~~

27-17. The ~~method-use according to~~ any one of claims ~~24-26~~15-16, wherein the first antigen-specific T cell line comprises specificity for two or more antigens or a portion thereof from the single virus.

28-18. The ~~method-use according to~~ any one of claims 1-~~23~~14, wherein
(a) the first antigen-specific T cell line comprises antigen specificity for at least one antigen or a portion thereof, from at least two different viruses;

(b) the first antigen-specific T cell line comprises antigen specificity for at least one antigen or a portion thereof, from 1-10 different viruses;

(c) the first antigen-specific T cell line comprises antigen specificity for 2-5 antigens from each of at least two different viruses or at least a portion of 2-5 antigens from each of at least two different viruses.

~~29. The method of any one of claims 1-23, wherein the first antigen-specific T cell line comprises antigen specificity for at least one antigen or a portion thereof, from 1-10 different viruses.~~

~~30. The method of any one of claims 1-23, wherein the first antigen-specific T cell line comprises antigen specificity for 2-5 antigens from each of at least two different viruses or at least a portion of 2-5 antigens from each of at least two different viruses.~~

~~31.19.~~ The ~~method-use according to~~ any one of claims ~~13-30~~18, wherein
(a) the second antigen-specific T cell line comprises antigen specificity for at least one antigen or a portion thereof, from 1-10 different viruses; or
(b) the second antigen-specific T cell line comprises antigen specificity for 2-5 antigens from each of at least two different viruses or at least a portion of 2-5 antigens from each of at least two different viruses.

~~32. The method of any one of claims 13-31, wherein the second antigen-specific T cell line comprises antigen specificity for 2-5 antigens from each of at least two different viruses or at least a portion of 2-5 antigens from each of at least two different viruses.~~

~~33.20.~~ The ~~method-use according to~~ any one of claims 1-~~32~~19, wherein the antigen is a viral antigen from a virus selected from EBV, CMV, Adenovirus, BK, JC virus, HHV6, RSV, Influenza, Parainfluenza, Bocavirus, Coronavirus, LCMV, Mumps, Measles, human Metapneumovirus (HMPV), Parvovirus B, Rotavirus, merkel cell virus, herpes simplex virus, HPV, HIV, HTLV1, HHV8, HBV, West Nile Virus, Zika virus, and Ebola virus.

~~34.21.~~ The ~~method-use according to~~ any one of claims 1-~~23~~14, wherein the first and/or the second antigen-specific T cell comprises
(a) specificity for at least one antigen from each of the following viruses: RSV, Influenza, Parainfluenza, and HMPV;

(b) specificity for at least one antigen from each of the following viruses: EBV, CMV, adenovirus, BK, HHV6;

(c) specificity for at least one antigen from HBV; or

(d) specificity for at least one antigen from HHV8.

~~35-22.~~ The ~~method-use according to~~ claim ~~3421~~, wherein

(a) the Influenza antigens are selected from influenza A antigens NP1, MP1, and a combination thereof; the RSV antigens are selected from N, F, and a combination thereof; the hMPV antigens are selected from F, N, M2-1, M, and a combination thereof; and the PIV antigens are selected from M, HN, N, F, and a combination thereof;
or

(b) the EBV antigens are selected from LMP2, EBNA1, BZLF1, and a combination thereof; the CMV antigens are selected from IE1, pp65, and a combination thereof; the adenovirus antigens are selected from Hexon, Penton, and a combination thereof; the BK virus antigens are selected from VP1, large T, and a combination thereof; and the HHV6 antigens are selected from U90, U11, U14, and a combination thereof.

~~36. The method of any one of claims 1-23, wherein the first and/or the second antigen-specific T-cell comprises specificity for at least one antigen from each of the following viruses: EBV, CMV, adenovirus, BK, HHV6.~~

~~37. The method of claim 36, wherein the EBV antigens are selected from LMP2, EBNA1, BZLF1, and a combination thereof; the CMV antigens are selected from IE1, pp65, and a combination thereof; the adenovirus antigens are selected from Hexon, Penton, and a combination thereof; the BK virus antigens are selected from VP1, large T, and a combination thereof; and the HHV6 antigens are selected from U90, U11, U14, and a combination thereof.~~

~~38. The method of any one of claims 1-33, wherein the first and/or the second antigen-specific T-cell comprises specificity for at least one antigen from HBV.~~

~~39. The method of any one of claims 1-33, wherein the first and/or the second antigen-~~

~~specific T cell comprises specificity for at least one antigen from HHV8.~~

40-23. The ~~method-use according to~~ any one of the preceding claims, wherein the antigen-specific T cells are produced by

(a) culturing, in the presence of the antigens or a portion thereof, mononuclear cells from a suitable donor having an HLA type that matches the patient's HLA type on 2 or more HLA alleles; or

(b) culturing, in the presence of pepmixes spanning the antigens, or a portion thereof, mononuclear cells from a suitable donor having an HLA type that matches the patient's HLA type on 2 or more HLA alleles.

~~41. The method of any one of the preceding claims, wherein the antigen-specific T cells are produced by culturing, in the presence of pepmixes spanning the antigens, or a portion thereof, mononuclear cells from a suitable donor having an HLA type that matches the patient's HLA type on 2 or more HLA alleles.~~

42-24. The ~~method-use according to~~ claim ~~40 or 41~~23, wherein the culturing is in the presence of IL4 and IL7.

43-25. The ~~method-use according to~~ claim ~~42~~24, wherein the pepmix comprises 15 mer peptides.

44-26. The ~~method-use according to~~ any one of claims ~~41-43~~23-25, wherein the peptides in the pepmix that span the antigen overlap in sequence by 11 amino acids.

45-27. The ~~method-use according to~~ any one of the preceding claims, wherein the patient is immunocompromised.

46-28. The ~~method-use according to~~ any one of the preceding claims, wherein the patient is immunocompromised due to a treatment the patient received to treat a disease or condition.

47-29. The ~~method-use according to~~ claim ~~46~~28, wherein the treatment is:

(a) a hematopoietic stem cell transplant, solid organ transplant, or anti-cancer agent; or

(b) reduced intensity conditioning, myeloablative conditioning, non-myeloablative conditioning, chemotherapy, and immunosuppressive drugs.

~~48.—The method of claim 46, wherein the treatment the patient received to treat a disease or condition is selected from the group consisting of reduced intensity conditioning, myeloablative conditioning, non myeloablative conditioning, chemotherapy, and immunosuppressive drugs.~~

49.30. The ~~method—use according to~~ claim ~~45~~27, wherein the patient is immunocompromised due to age.

~~50.—The method of claim 49, wherein the patient is less than 1 year of age.~~

~~51.—The method of claim 49, wherein the patient is more than 65 years of age.~~

52.31. The ~~method—use according to~~ claim ~~45~~27, wherein

(a) the subject-patient has an immune deficiency condition;

(b) the patient has an HIV infection; and/or

(c) the patient has leukemia, myeloma, or lymphoma and is in need of a hematopoietic stem cell transplant therapy.

~~53.—The method of claim 45, wherein the immune deficiency is primary immune deficiency.~~

~~54.—The method of claim 45, wherein the subject has an HIV infection.~~

55.32. The ~~method—use according to~~ any one of the preceding claims, wherein the patient is in need of a transplant therapy.

~~56.—The method of claim 45, wherein the patient has a leukemia, myeloma, or lymphoma~~

~~and is in need of a hematopoietic stem cell transplant therapy.~~

~~57.33.~~ The ~~method-use according to~~ any one of the preceding claims, wherein the first and /or one or more of each second T cell lines:

~~(a) persist in vivo for at least 12 weeks; or~~

~~(b) persists in vivo for at least 12 weeks absent any active infection in the patient.~~

~~58.—The method of any one of the preceding claims, wherein the first and /or one or more of each second T cell lines persist in vivo for at least 12 weeks absent any active infection in the patient.~~