[0007] Graft-versus-host disease (GVHD) is an inflammatory disease that is unique to allogeneic transplantation. It is an attack by transplanted or reconstituting leukocytes against the recipient's tissues. This can occur even if the donor and recipient are HLA-identical because the immune system can still recognize other differences between cells/tissues. Acute GVHD typically occurs in the first 3 months after transplantation and may involve the skin, intestine, or the liver. Corticosteroids such as prednisone are a standard treatment.

[0008] Chronic GVHD may also develop after allogeneic transplant and is the major source of late complications. In addition to inflammation, chronic GVHD may lead to the development of fibrosis, or scar tissue, similar to scleroderma, or other autoimmune diseases and may cause functional disability and the need for prolonged immunosuppressive therapy. GVHD is usually mediated by T cells when they react to foreign peptides presented on the MHC of the host. Thus, the use of adoptive T-cell therapies is often limited by barriers imposed by MHC disparity. This disclosure provides solutions to these barriers.

SUMMARY

[0009] The present disclosure includes methods for developing donor minibanks comprising cell therapy products such as antigen-specific T cell lines. The present disclosure includes methods for identifying one or more suitable donors from at least one donor pool that have various HLA (Human Leukocyte Antigen) allele types compatible with the majority of prospective patients. In some examples, the prospective patients have undergone allogeneic hematopoietic stem cell transplantation (HSCT). In some examples, the prospective patients have suppressed immunity or are immunocompromised. In various examples, methods in the present disclosure concern the restoration of T cell immunity of patients who are immunocompromised.

[0010] In one aspect, the present disclosure provides a method of identifying suitable donors for use in constructing a first donor minibank of antigen-specific T cell lines comprising:

(a) comparing an HLA type of each of a first plurality of potential donors from a first donor pool with each of a first plurality of prospective patients from a first prospective patient population;

(b) determining, based on the comparison in step (a), a first greatest matched donor, defined as the donor from the first donor pool that has 2 or more HLA allele matches with the greatest number of patients in the first plurality of prospective patients;

(c) selecting the first greatest matched donor for inclusion in the first donor minibank;

(d) removing from the first donor pool the first greatest matched donor thereby generating a second donor pool consisting of each of the first plurality of potential donors from the first donor pool except for the first greatest matched donor;

(e) removing from the first plurality of prospective patients each prospective patient that has 2 or more allele matches with the first greatest matched donor, thereby generating a second plurality of prospective patients consisting of each of the first plurality of prospective patients except for each prospective patient that has 2 or more allele matches with the first greatest matched donor; and

(f) repeating steps (a) through (e) one or more additional times with all donors and prospective patients that have not already been removed in accordance with steps (d) and (e), wherein each time an additional greatest matched donor is selected in accordance with step (c) that additional greatest matched donor is removed from their respective donor pool in accordance with step (d); and each time a subsequent greatest matched donor is removed from their respective donor pool, each prospective patient that has 2 or more allele matches with that subsequent greatest matched donor is removed from their respective plurality of prospective patients in accordance with step (e); thereby sequentially increasing the number of selected greatest matched donors in the first donor minibank by 1 following each cycle of the method and thereby depleting the number of the plurality of prospective patients in the patient population following each cycle of the method in accordance with their HLA matching to the selected greatest matched donors; wherein steps (a) through (e) are repeated until a desired percentage of the first prospective patient population remains in the plurality of prospective patients or until no donors remain in the donor pool, optionally, wherein

for each round of the method, steps (a) through (e) are cycled in accordance with step (f) until 5% or less of the first prospective patient population remains in the plurality of prospective patients, and optionally,

wherein the 2 or more alleles from steps (b) and (e) comprise 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 some examples, the identification of one or more suitable donors in methods of the disclosure concern the construction of a first donor minibank containing a plurality of cell therapy products. In some examples, the first donor minibank contains antigen-specific T cell lines. In some examples, methods in the present disclosure include a donor selection method. In some examples, the donor selection method comprises (a) comparing an HLA type of each of a first plurality of potential donors from a first donor pool with each of a first plurality of prospective patients from a first prospective patient population; (b) determining, based on the comparison in the above-mentioned step (a), a first greatest matched donor, wherein the first

greatest matched donor can be defined as the donor from the first donor pool that has 2 or more HLA allele matches with the greatest number of patients in the first plurality of prospective patients; (c) selecting the first greatest matched donor for inclusion in the first donor minibank; (d), removing from the first donor pool the first greatest matched donor; wherein the above-mentioned step (d) can generate a second donor pool consisting of each of the first plurality of potential donors from the first donor pool except for the first greatest matched donor; (e) removing from the first plurality of prospective patients each prospective patient that has 2 or more allele matches with the first greatest matched donor, wherein the above-mentioned step (e) comprises generating a second plurality of prospective patients consisting of each of the first plurality of prospective patients except for each prospective patient that has 2 or more allele matches with the first greatest matched donor; and (f) repeating the foregoing steps (a) through (e) one or more additional times with all donors and prospective patients that have not already been removed in accordance with the foregoing steps (d) and (e). In some examples, each time an additional greatest matched donor is selected in accordance with the foregoing step (c) that additional greatest matched donor is removed from their respective donor pool in accordance with the foregoing step (d). In some examples, each time a subsequent greatest matched donor is removed from their respective donor pool, each prospective patient that has 2 or more allele matches with that subsequent greatest matched donor is removed from their respective plurality of prospective patients in accordance with the foregoing step (e). In some examples, methods as described herein can sequentially increase the number of selected greatest matched donors in the first donor minibank by 1 following each cycle of the method. In some examples, methods as described herein can deplete the number of the plurality of prospective patients in the patient population following each cycle of the method in accordance with their HLA matching to the selected greatest matched donors. In other examples, the foregoing steps (a) through (e) can be repeated until a desired percentage of the first prospective patient population remains in the plurality of prospective patients. In other examples, the foregoing steps (a) through (e) can be repeated until no donors remain in the donor pool.

[0011] The present disclosure provides that the foregoing steps (a) – (e) of methods as described herein can be cycled in accordance with the foregoing step (f) until 5% or less of the first prospective patient population remains in the plurality of prospective patients. In some examples, the first donor minibank as described herein can comprise antigen-specific T cell lines derived from 10 or less donors. In some examples, the first donor minibank as

described herein can comprise antigen-specific T cell lines derived from 10, 9, 8, 7, 6, 5, 4, 3, or 2 donors. In some examples, the first donor minibank as described herein can comprise enough HLA variability to provide >95% of the first prospective patient population with one or more antigen-specific T cell line that is matched to the patient's HLA type on at least 2 HLA alleles. In other examples, the first donor minibank as described herein can comprise antigen-specific T cell lines derived from 5 or less donors. In some examples, the first donor minibank as described herein can provide enough HLA variability to provide >95% of the first prospective patient population with one or more antigen-specific T cell line that is matched to the patient's HLA type on at least 2 HLA alleles. In some examples, the 2 or more alleles from the foregoing steps (b) and (e) can comprise at least 2 HLA Class I alleles. In some examples, the 2 or more alleles from the foregoing steps (b) and (e) can comprise at least 2 HLA Class II alleles. In some examples, the 2 or more alleles from the foregoing steps (b) and (e) can comprise at least 1 HLA Class I allele and at least 1 HLA Class II allele. In some examples, the 2 or more alleles from the foregoing steps (b) and (e) can comprise the HLA alleles HLA A, HLA B, DRB1, and DQB1.

[0012] In some examples, the first donor pool used in the present disclosure can comprise at least 10 donors. In some examples, the first prospective patient population provided in the present disclosure can comprise at least 100 patients. In some examples, the first prospective patient population can comprise the entire worldwide allogeneic HSCT population. In some examples, the first prospective patient population can comprise the entire US allogeneic HSCT population. In some examples, the first prospective patient population can comprise all patients included in the National Marrow Donor Program (NMDP) database, available at the worldwide web address bioinformatics.bethematchclinical.org. In some examples, the first prospective patient population can comprise all patients included in the European Society for Blood and Marrow Transplantation (EBMT) database, available at the worldwide web address: ebmt.org/ebmt-patient-registry. In some examples, the entire worldwide allogeneic HSCT population can include children ages ≤ 16 years. In some examples, the entire US allogeneic HSCT population can include children ages ≤ 16 years. In some examples, the entire worldwide allogeneic HSCT population can include individuals ages ≥ 65. In some examples, the entire US allogeneic HSCT population can include individuals ages ≥ 65. In some examples, the entire worldwide allogeneic HSCT population can include children ages

≤ 5 years. In some examples, the entire US allogeneic HSCT population can include children ages ≤ 5 years.

[0013] The present disclosure provides methods of identifying suitable donors for use in constructing a donor bank made up of a plurality of minibanks of antigen-specific T cell lines. In one aspect, the present disclosure provides a method of identifying suitable donors for use in constructing a donor bank made up of a plurality of minibanks of antigen-specific T cell lines comprising,

A) performing all of the steps set forth in the method disclosed herein, thereby constructing a first minibank; and

B) repeating steps (a) through (f), as set forth in the method disclosed herein, one or more second rounds to construct one or more second minibanks, wherein, prior to starting each second round of the method, the method comprises

(i) generating a new donor pool, said new donor pool comprising:

ia. the first donor pool, less any greatest matched donors removed in accordance with each prior cycle of step (d) from the first and any prior second rounds of the method;

ib. an entirely new population of potential donors not included in the first donor pool; or

ic. a combination of ia. and ib.; and

(ii) reconstituting the first plurality of prospective patients from the first prospective patient population by returning all prospective patients that had been previously removed in accordance with each prior cycle of step (e) from the first and any prior second rounds of the method. In some examples, constructing a donor bank can comprise first developing a first minibank as described herein. In some examples, developing a first minibank can include performing all of the foregoing steps (a) – (f). In some examples, developing a first minibank for a donor bank as described herein can comprise repeating the foregoing steps (a) through (f) that involves one or more second rounds to construct one or more second minibanks.

[0014] In some examples, prior to starting each second round for constructing a bank can comprise generating a new donor pool. In some examples, the new donor pool as described herein can comprise the first donor pool, less any greatest matched donors removed in accordance with each prior cycle of the forgoing step (d) from the first and any prior second rounds. In some examples, the new donor pool as described herein can comprise an entirely new population of potential donors not included in the first donor pool. In some examples, the new donor pool as described herein can comprise a combination of the first donor pool, less any greatest matched donors removed in accordance with each prior cycle of the forgoing step (d) from the first and any prior second rounds and an entirely new population of potential donors not included in the first donor pool. In some examples, constructing a bank as described in the present method can comprise reconstituting the first plurality of prospective patients from the first prospective patient population by returning all prospective patients that had been previously removed in accordance with each prior cycle of the foregoing step (e) from the first and any prior second rounds of the method.

[0015] In some examples, each round for constructing one or more minibanks as described herein can include cycling the above-identified steps (a) through (e) in accordance with the above-identified step (f) until 5% or less of the first prospective patient population remains in the plurality of prospective patients. In some examples, each donor minibank can comprise enough HLA variability amongst the one or more greatest matched donors to provide >95% of the first prospective patient population with at least one antigen-specific T cell line that is matched to the patient's HLA type on at least 2 HLA alleles. In some examples, each resulting donor minibank can comprise antigen-specific T cell lines derived from 10 or less

donors. In some examples, each resulting donor minibank can comprise antigen-specific T cell lines derived from 5 or less donors. In some examples, the 2 or more alleles from the foregoing steps (b) and (e) can comprise at least 2 HLA Class II alleles. In other examples, the 2 or more alleles from the foregoing steps (b) and (e) can comprise at least 1 HLA Class I allele and at least 1 HLA Class II allele.

[0016] In some examples, the first donor pool used for constructing a donor bank can comprise at least 10 donors. In some examples, the first prospective patient population used for constructing a donor bank can comprise at least 100 patients. In some examples, the first prospective patient population can comprise the entire worldwide allogeneic HSCT population In some examples, the first prospective patient population can comprise the entire US allogeneic HSCT population. In some examples, the first prospective patient population can comprise all patients included in the National Marrow Donor Program (NMDP) database, available at the worldwide web address bioinformatics.bethematchclinical.org. In some examples, the first prospective patient population can comprise all patients included in the European Society for Blood and Marrow Transplantation (EBMT) database, available at the worldwide web address: ebmt.org/ebmt-patient-registry. In some examples, the entire worldwide allogeneic HSCT population can include children ages ≤ 16 years. In some examples, the entire US allogeneic HSCT population can include children ages ≤ 16 years. In some examples, the entire worldwide allogeneic HSCT population can include individuals ages ≥ 65. In some examples, the entire US allogeneic HSCT population can include individuals ages ≥ 65. In some examples, the entire worldwide allogeneic HSCT population can include children ages ≤ 5 years. In some examples, the entire US allogeneic HSCT population can include children ages ≤ 5 years.

[0017] In some examples, methods as described herein can comprise harvesting blood from each donor included in the donor bank. In other examples, methods as described herein can comprise having blood harvested from each donor included in the donor bank. In some examples, methods as described herein can comprise harvesting mononuclear cells (MNCs) from each donor included in the donor bank. In some examples, methods as described herein can comprise having MNCs harvested from each donor included in the donor bank. In some examples, harvesting MNCs from each donor can comprise isolating the MNCs or having the MNCs isolated. In one example, the MNCs comprise peripheral blood mononuclear cells

(e.g., PBMCs). In one example, the MNCs comprise blood apheresis mononuclear cells. In some examples, harvesting MNCs from each donor can comprise isolating the PBMCs or having the PBMCs isolated. In some examples, isolating MNCs can be conducted by ficoll gradient. In some examples, isolating MNCs can be conducted by density gradient. In other examples, harvesting MNCs as disclosed herein can comprise culturing the cells. In other examples, harvesting MNCs as disclosed herein can comprise cryopreserving the cells.

[0018] In some examples, the cultured MNCs or the cryopreserved MNCs can comprise contacting the cells in culture with one or more antigens under suitable culture conditions to stimulate and expand antigen-specific T cells. In other examples, the one or more antigen contacted with the cells can comprise one or more viral antigens. In other examples, the one or more antigen contacted with the cells can comprise one or more tumor associated antigens. In some examples, the one or more antigen contacted with the cells can comprise a combination of one or more viral antigen and one or more tumor associated antigen.

[0019] The present disclosure provides methods of constructing a first donor minibank of antigen-specific T cell lines. In one aspect, the present disclosure provides a method of constructing a first donor minibank of antigen-specific T cell lines comprising:

(a) comparing the HLA type of each of the first plurality of potential donors with each of the first plurality of prospective patients;

(b) determining, based on the comparison in step (a), a first greatest matched donor, defined as the donor from the first donor pool that has 2 or more allele matches with the greatest number of patients in the first plurality of prospective patients;

(c) selecting the first greatest matched donor for inclusion in the first donor minibank;

(d) removing from the first donor pool the first greatest matched donor thereby generating a second donor pool consisting of each of the first plurality of potential donors from the first donor pool except for the first greatest matched donor;

(e) removing from the first plurality of prospective patients each prospective patient that has 2 or more allele matches with the first greatest matched donor, thereby generating a second plurality of prospective patients consisting of each of the first plurality of prospective patients except for each prospective patient that has 2 or more allele matches with the first greatest matched donor;

(f) repeating steps (a) through (e) one or more additional times with all donors and prospective patients that have not already been removed in accordance with steps (d) and (e), wherein each time an additional greatest matched donor is selected in accordance with step (c) that greatest matched donor is removed from their respective donor pool in accordance with step (d); and each time a subsequent greatest matched donor is removed from their respective donor pool, each prospective patient that has 2 or more allele matches with that subsequent greatest matched donor is removed from their respective plurality of prospective patients in accordance with step (e); thereby sequentially increasing the number of selected greatest matched donors in the donor minibank by 1 following each cycle of the method and thereby depleting the number of the plurality of prospective patients in the patient population following each cycle of the method in accordance with their HLA matching to the selected greatest matched donors; wherein steps (a) through (e) are repeated until a desired percentage of the first prospective patient population remains in the plurality of prospective patients or until no donors remain in the donor pool;

(g) isolating MNCs, or having MNCs, isolated, from blood obtained from each respective donor included in the donor minibank;

(h) culturing the MNCs;

(i) contacting the MNCs in culture with one or more antigen, or one or more epitope from one or more antigen, optionally wherein the one or more antigen is selected from

(i) a tumor associated antigen;

(ii) a viral antigen; or,

(iii) at least one antigen is a viral antigen and at least one antigen is a tumor associated antigen,

wherein contacting is under suitable culture conditions to stimulate and expand a polyclonal population of antigen-specific T cells from each of the respective donor's MNCs; thereby producing a plurality of antigen-specific T cell lines, each of which comprises a polyclonal population of antigen-specific T cells derived from each respective donor's MNCs, wherein the MNCs of steps (g) through (i) are optionally PBMCs; and

(j) optionally, cryopreserving the plurality of antigen-specific T cell lines, optionally

wherein the 2 or more alleles from steps (b) and (e) comprise 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, and optionally, wherein

for each round of the method, steps (a) through (e) are cycled in accordance with step (f) until 5% or less of the first prospective patient population remains in the plurality of prospective patients and, thus, each donor minibank comprises enough HLA variability amongst the one or more greatest matched donors to provide >95% of the first prospective patient population with at least one allogeneic antigen-specific T cell line that is matched to the patient's HLA type on at least 2 HLA alleles. In some examples, the methods can include step (a) of comparing the HLA type of each of the first plurality of potential donors with each of the first plurality of prospective patients. In some examples, the methods can include step (b) of determining, based on the comparison in step (a) of the methods described in this paragraph, a first greatest matched donor. In some examples, first greatest matched donor can be defined as the donor from the first donor pool that has 2 or more allele matches with the greatest number of patients in the first plurality of prospective patients. In some examples, the methods can comprise step (c) of selecting the first greatest matched donor for inclusion in the first donor minibank. In some examples, the methods can comprise step (d) of removing from the first donor pool the first greatest matched donor. In some examples, step (d) of the methods as described herein can comprise generating a second donor pool consisting of each of the first plurality of potential donors from the first donor pool except for the first greatest matched donor.

[0020] In some examples, the methods can comprise step (e) of removing from the first plurality of prospective patients each prospective patient that has 2 or more allele matches with the first greatest matched donor. In some examples, step (e) as described in this paragraph can generate a second plurality of prospective patients consisting of each of the first plurality of

prospective patients except for each prospective patient that has 2 or more allele matches with the first greatest matched donor.

[0021] In some examples, the methods of constructing a first donor minibank of antigen-specific T cell lines can comprise repeating steps (a) through (e) as disclosed herein one or more additional times with all donors and prospective patients that have not already been removed in accordance with steps (d) and (e) as disclosed herein. In some examples, each time an additional greatest matched donor is selected in accordance with step (c) that greatest matched donor is removed from their respective donor pool in accordance with step (d). In some examples, each time a subsequent greatest matched donor is removed from their respective donor pool, each prospective patient that has 2 or more allele matches with that subsequent greatest matched donor is removed from their respective plurality of prospective patients in accordance with step (e). In some examples, the methods as described herein can sequentially increase the number of selected greatest matched donors in the donor minibank by 1 following each cycle of the method. In some examples, the methods as described herein can deplete the number of the plurality of prospective patients in the patient population following each cycle of the method in accordance with their HLA matching to the selected greatest matched donors. In some examples, steps (a) through (e) for constructing a first donor minibank of antigen-specific T cell lines can be repeated until a desired percentage of the first prospective patient population remains in the plurality of prospective patients. In some examples, steps (a) through (e) for constructing a first donor minibank of antigen-specific T cell lines can be repeated until no donors remain in the donor pool.

[0022] In some examples, methods as described herein comprise step (g) isolating MNCs, or having MNCs, isolated, from blood obtained from each respective donor included in the donor minibank. In some examples, step (h) of the methods as described herein comprise culturing the MNCs obtained from each respective donor. In some examples, methods as described herein comprise step (i) of contacting the MNCs in culture with one or more antigen under suitable culture conditions to stimulate and expand a polyclonal population of antigen-specific T cells from each of the respective donor's MNCs. In some examples, methods as described herein comprise step (i) of contacting the MNCs in culture with one or more epitope from one or more antigen, under suitable culture conditions to stimulate and expand a polyclonal population of antigen-specific T cells from each of the respective donor's MNCs. In some examples,

methods as described herein comprise producing a plurality of antigen-specific T cell lines. In some examples, each of antigen-specific T cell lines can comprise a polyclonal population of antigen-specific T cells derived from each respective donor's MNCs. In some examples, the MNCs of steps (g) through (i) as described herein can be PBMCs. In some examples, step (j) of the methods can comprise cryopreserving the plurality of antigen-specific T cell lines.

[0023] In some examples, methods of constructing a first donor minibank of antigen-specific T cell lines as described herein can include cycling steps (a) through (e) in accordance with step (f) until 5% or less of the first prospective patient population remains in the plurality of prospective patients. In some examples, each donor minibank can comprise enough HLA variability amongst the one or more greatest matched donors to provide >95% of the first prospective patient population with at least one antigen-specific T cell line that is matched to the patient's HLA type on at least 2 HLA alleles. In some examples, each resulting donor minibank can comprise antigen-specific T cell lines derived from 10 or less donors. In some examples, each resulting donor minibank can comprise antigen-specific T cell lines derived from 5 or less donors. In some examples, the 2 or more alleles from steps (b) and (e) can comprise at least 2 HLA Class II alleles. In other examples, the 2 or more alleles from steps (b) and (e) can comprise at least 1 HLA Class I allele and at least 1 HLA Class II allele.

[0024] In some examples, the first donor pool used in the methods of constructing a first donor minibank of antigen-specific T cell lines as described herein can comprise at least 10 donors. In some examples, the first donor pool used in the methods of constructing a first donor minibank of antigen-specific T cell lines as described herein can comprise at least 100 donors. In some examples, the first prospective patient population can comprise the entire worldwide allogeneic HSCT population. In some examples, the first prospective patient population used in the methods can comprise the entire US allogeneic HSCT population. In some examples, the first prospective patient population can comprise all patients included in the National Marrow Donor Program (NMDP) database, available at the worldwide web address bioinformatics.bethematchclinical.org. In some examples, the first prospective patient population can comprise all patients included in the European Society for Blood and Marrow Transplantation (EBMT) database, available at the worldwide web address: ebmt.org/ebmt-patient-registry. In some examples, the entire worldwide allogeneic HSCT population can include children ages ≤ 16 years. In some examples, the entire US allogeneic HSCT

population can include children ages ≤ 16 years. In some examples, the entire worldwide allogeneic HSCT population can include individuals ages ≥ 65. In some examples, the entire US allogeneic HSCT population can include individuals ages ≥ 65. In some examples, the entire worldwide allogeneic HSCT population can include children ages ≤ 5 years. In some examples, the entire US allogeneic HSCT population can include children ages ≤ 5 years.

[0025] In some examples, the culturing of MNCs can be in a vessel comprising a gas permeable culture surface. In one example, the vessel can be an infusion bag with a gas permeable portion. In one example, the vessel can be a rigid vessel. In one example, the vessel can be a GRex bioreactor. In some examples, culturing the PBMCs for constructing a first donor minibank of antigen-specific T cell lines as described herein can be conducted in the presence of one or more cytokine. In one example, the cytokine can include IL4. In one example, the cytokine can include IL7. In one example, the cytokine can include IL4 and IL7. In one example, the cytokine can include IL4 and IL7, but not IL2.

[0026] Methods of constructing a first donor minibank of antigen-specific T cell lines can comprise culturing the MNCs in the presence of one or more antigen. In one example, the MNCs can be PBMCs. In some examples, the one or more antigen can be in the form of a whole protein. In some examples, the one or more antigen can be in the form of a pepmix comprising a series of overlapping peptides spanning part of or the entire sequence of each antigen. In some examples, the one or more antigen can be in the form of a combination of the form of a whole protein and the form of a pepmix comprising a series of overlapping peptides spanning part of or the entire sequence of each antigen.

[0027] Methods of constructing a first donor minibank of antigen-specific T cell lines can comprise culturing the MNCs in the presence of a plurality of pepmixes. In one example, the MNCs can be PBMCs. In some examples, each pepmix from the plurality of pepmixes can comprise a series of overlapping peptides spanning part of or the entire sequence of each antigen.

[0028] In some examples, each antigen for constructing a first donor minibank of antigen-specific T cell lines can be a tumor associated antigen. In some examples, each antigen can be a viral antigen. In some examples, at least one antigen for constructing a first donor minibank of antigen-specific T cell lines can be a viral antigen and at least one antigen can be a tumor associated antigen.

[0029] In some examples, methods as described herein for constructing donor minibanks of antigen specific T cell lines can comprise culturing MNCs from the selected donors in the presence of at least 2 different pepmixes. In some examples, methods as described herein can comprise culturing MNCs in the presence of at least 3 different pepmixes. In some examples, methods as described herein can comprise culturing MNCs in the presence of at least 4 different pepmixes. In some examples, methods as described herein can comprise culturing MNCs in the presence of at least 5 different pepmixes. In some examples, methods as described herein can comprise culturing MNCs in the presence of at least 6 different pepmixes. In some examples, methods as described herein can comprise culturing MNCs in the presence of at least 7 different pepmixes. In some examples, methods as described herein can comprise culturing MNCs in the presence of at least 8 different pepmixes. In some examples, methods as described herein can comprise culturing MNCs in the presence of at least 9 different pepmixes. In some examples, methods as described herein can comprise culturing MNCs in the presence of at least 10 different pepmixes. In some examples, methods as described herein can comprise culturing MNCs in the presence of at least 11 different pepmixes. In some examples, methods as described herein can comprise culturing MNCs in the presence of at least 12 different pepmixes. In some examples, methods as described herein can comprise culturing MNCs in the presence of at least 13 different pepmixes. In some examples, methods as described herein can comprise culturing MNCs in the presence of at least 14 different pepmixes. In some examples, methods as described herein can comprise culturing MNCs in the presence of at least 15 different pepmixes. In some examples, methods as described herein can comprise culturing MNCs in the presence of at least 16 different pepmixes. In some examples, methods as described herein can comprise culturing MNCs in the presence of at least 17 different pepmixes. In some examples, methods as described herein can comprise culturing MNCs in the presence of at least 18 different pepmixes. In some examples, methods as described herein can comprise culturing MNCs in the presence of at least 19 different pepmixes. In some examples, methods as described herein can comprise culturing MNCs in the presence of at least 20 different pepmixes. In some examples, methods as described herein can comprise culturing MNCs in the presence of at least more than 20 different pepmixes. In some examples, the MNCs can be PBMCs. In some examples, each pepmix can comprise a series of overlapping peptides spanning part of an antigen. In some examples,

each pepmix can comprise a series of overlapping peptides spanning the entire sequence of an antigen.

[0030] In some examples, methods as described herein for constructing donor minibanks of antigen specific T cell lines can comprise culturing MNCs from the selected donors in the presence of a plurality of pepmixes. In some examples, each pepmix can cover at least one antigen that is different than the antigen covered by each of the other pepmixes in the plurality of pepmixes. In some examples, 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 different antigens can be covered by the plurality of pepmixes. In some examples, at least more than 20 different antigens can be covered by the plurality of pepmixes. In some examples, at least one antigen from at least 2 different viruses can be covered by the plurality of pepmixes.

[0031] In some examples, the antigens used in methods for constructing donor minibanks of antigen specific T cell lines as described herein can be from the EBV (Epstein–Barr virus). In some examples, the antigens used in methods as described herein can be from CMV (Cytomegalovirus). In some examples, the antigens used in methods as described herein can be from Adenovirus. In some examples, the antigens used in methods as described herein can be from BK virus. In some examples, the antigens used in methods as described herein can be from JC (John Cunningham virus) virus. In some examples, the antigens used in methods as described herein can be from HHV6 (Herpesviruses 6). In some examples, the antigens used in methods as described herein can be from HHV8 (Herpesviruses 8). In some examples, the antigens used in methods as described herein can be from HBV (Hepatitis B virus). In some examples, the antigens used in methods as described herein can be from RSV (Human respiratory syncytial virus). In some examples, the antigens used in methods as described herein can be from Influenza. In some examples, the antigens used in methods as described herein can be from Parainfluenza. In some examples, the antigens used in methods as described herein can be from Bocavirus. In some examples, the antigens used in methods as described herein can be from Coronavirus. In some examples, the antigens used in methods as described herein can be from LCMV (Lymphocytic choriomeningitis virus). In some examples, the antigens used in methods as described herein can be from Mumps. In some examples, the antigens used in methods as described herein can be from Measles. In some

examples, the antigens used in methods as described herein can be from human Metapneumovirus. In some examples, the antigens used in methods as described herein can be from Parvovirus B. In some examples, the antigens used in methods as described herein can be from Rotavirus. In some examples, the antigens used in methods as described herein can be from Merkel cell virus. In some examples, the antigens used in methods as described herein can be from herpes simplex virus. In some examples, the antigens used in methods as described herein can be from HPV (Human Papillomavirus). In some examples, the antigens used in methods as described herein can be from HIV (human immunodeficiency virus). In some examples, the antigens used in methods as described herein can be from HTLV1 (Human T- cell leukemia virus, type 1). In some examples, the antigens used in methods as described herein can be from West Nile Virus. In some examples, the antigens used in methods as described herein can be from Zika virus. In some examples, the antigens used in methods as described herein can be from Ebola. In some examples, at least one pepmix can cover an antigen from each of RSV, Influenza, Parainfluenza, and HMPV (Human meta-pneumovirus). In some examples, the Influenza antigens used in the pepmixes as described herein can be influenza A antigens NP1. In some examples, the Influenza antigens used in the pepmixes as described herein can be influenza A MP1. In some examples, the Influenza antigens used in the pepmixes as described herein can be influenza A antigens NP1 and MP1. In some examples, the RSV antigens used in the pepmixes as described herein can be RSV N proteins. In some examples, the RSV antigens used in the pepmixes as described herein can be RSV F proteins. In some examples, the RSV antigens used in the pepmixes as described herein can be RSV N proteins and RSV F proteins. In some examples, the hMPV antigens used in the pepmixes as described herein can be hMPV F proteins. In some examples, the hMPV antigens used in the pepmixes as described herein can be hMPV N proteins. In some examples, the hMPV antigens used in the pepmixes as described herein can be hMPV M2-1 proteins. In some examples, the hMPV antigens used in the pepmixes as described herein can be hMPV M proteins. In some examples, the hMPV antigens used in the pepmixes as described herein can be a combination of hMPV F proteins, hMPV N proteins, hMPV M2-1, and hMPV M proteins. In some examples, the PIV antigens used in the pepmixes as described herein can be PIV M proteins. In some examples, the PIV antigens used in the pepmixes as described herein can be PIV HN proteins. In some examples, the PIV antigens used in the pepmixes as described herein can be PIV N proteins. In some examples, the PIV antigens

used in the pepmixes as described herein can be PIV F proteins. In some examples, the PIV antigens used in the pepmixes as described herein can be a combination of PIV M proteins, PIV HN proteins, PIV N proteins, and PIV F proteins.

[0032] In some examples, methods as described herein for constructing donor minibanks of antigen specific T cell lines can comprise culturing PBMCs from the selected donors in the presence of pepmixes spanning Influenza A antigen NP1 and Influenza A antigen MP1. In some examples, methods as described herein can comprise culturing PBMCs in the presence of pepmixes spanning RSV antigen N and RSV antigen F. In some examples, methods as described herein can comprise culturing PBMCs in the presence of pepmixes spanning hMPV antigen F. In some examples, methods as described herein can comprise culturing PBMCs in the presence of pepmixes spanning hMPV antigen N. In some examples, methods as described herein can comprise culturing PBMCs in the presence of pepmixes spanning hMPV antigen M2-1. In some examples, methods as described herein can comprise culturing PBMCs in the presence of pepmixes spanning hMPV antigen M. In some examples, methods as described herein can comprise culturing PBMCs in the presence of pepmixes spanning PIV antigen M. In some examples, methods as described herein can comprise culturing PBMCs in the presence of pepmixes spanning PIV antigen HN. In some examples, methods as described herein can comprise culturing PBMCs in the presence of pepmixes spanning PIV antigen N. In some examples, methods as described herein can comprise culturing PBMCs in the presence of pepmixes spanning PIV antigen F.

[0033] In some examples, methods as described herein for constructing donor minibanks of antigen specific T cell lines can comprise culturing PBMCs from the selected donors in the presence of pepmixes that cover an antigen from each EBV, CMV, adenovirus, BK, and HHV6. In some examples, at least one pepmix can cover an antigen from EBV, at least one pepmix can cover an antigen from CMV, at least one pepmix can cover an antigen from adenovirus, at least one pepmix can cover an antigen from BK, and at least one pepmix can cover an antigen from HHV6. In some examples, the EBV antigens can be LMP2. In some examples, the EBV antigens can be EBNA1. In some examples, the EBV antigens can be BZLF1. In some examples, the EBV antigens can be a combination of the CMV antigens. In some examples, the CMV antigens can be from IE1. In some examples, the CMV antigens can be from pp65. In some examples, the CMV antigens can be from a combination of IE1and

pp65. In some examples, the adenovirus antigens can be from Hexon. In some examples, the adenovirus antigens can be from Penton. In some examples, the adenovirus antigens can be from a combination of Hexon and Penton. In some examples, the BK virus antigens can be from VP1. In some examples, the BK virus antigens can be from large T. In some examples, the BK virus antigens can be from a combination of VP1 and large T. In some examples, the HHV6 antigens can be from U90. In some examples, the HHV6 antigens can be from U11. In some examples, the HHV6 antigens can be from U14. In some examples, the HHV6 antigens can be from a combination of U90, U11, and U14.

[0034] In some examples, methods as described herein for constructing donor minibanks of antigen specific T cell lines can comprise culturing PBMCs in the presence of pepmixes spanning EBV antigen LMP2. In some examples, methods as described herein can comprise culturing PBMCs in the presence of pepmixes spanning EBV antigen EBNA1. In some examples, methods as described herein can comprise culturing PBMCs in the presence of pepmixes spanning EBV antigen BZLF1. In some examples, methods as described herein can comprise culturing PBMCs in the presence of pepmixes spanning CMV antigen IE1. In some examples, methods as described herein can comprise culturing PBMCs in the presence of pepmixes spanning CMV antigen pp65. In some examples, methods as described herein can comprise culturing PBMCs in the presence of pepmixes spanning adenovirus antigens Hexon. In some examples, methods as described herein can comprise culturing PBMCs in the presence of pepmixes spanning Penton. In some examples, methods as described herein can comprise culturing PBMCs in the presence of pepmixes spanning BK virus antigen VP1. In some examples, methods as described herein can comprise culturing PBMCs in the presence of pepmixes spanning BK virus antigen large T. In some examples, methods as described herein can comprise culturing PBMCs in the presence of pepmixes spanning HHV6 antigen U90. In some examples, methods as described herein can comprise culturing PBMCs in the presence of pepmixes spanning HHV6 antigen U11. In some examples, methods as described herein can comprise culturing PBMCs in the presence of pepmixes spanning HHV6 antigen U14.

[0035] In some examples, methods as described herein for constructing donor minibanks of antigen specific T cell lines can comprise culturing PBMCs from the selected donors in the presence of pepmixes that cover an antigen from a coronavirus. In some examples, the coronavirus is a β-coronavirus (β-CoV). In some examples, the coronavirus is an α-

coronavirus (α-CoV). In some the β-CoV is selected from SARS-CoV, MERS-CoV, HCoVHKUl, and HCoV-OC43. In some examples, the α-CoV selected from HCoV-E229 and HCoV-NL63. In some examples, methods as described herein for constructing donor minibanks of antigen specific T cell lines can comprise culturing PBMCs with a plurality of pepmix libraries, each pepmix library containing a plurality of overlapping peptides spanning all or a portion of a SARS-CoV2 antigen or an antigen from the one or more additional viruses. In some examples, the VSTs are generated by contacting T cells with APCs such as DCs primed with a plurality of pepmix libraries, each pepmix library containing a plurality of overlapping peptides spanning all or a portion of a viral antigen, wherein at least one of the plurality of pepmix libraries spans a first antigen from SARS-CoV2 and wherein at least one (or a portion of one) additional pepmix library of the plurality of pepmix libraiies spans each second antigen. In some examples, the VSTs are generated by contacting T cells with APCs such as DCs nucleofected with at least one DNA plasmid encoding at least one SARS-CoV2 antigen, or a portion thereof, and at least one DNA plasmid encoding each second antigen, or a portion thereof. In some examples, the plasmid encodes at least one SARS-CoV2 antigen, or a portion thereof, and at least one of the additional antigens, or a portion thereof. In some examples, the VSTs comp1ise CD4+ T lymphocytes and CD8+ T-lymphocytes. In some examples, the VSTs express αβ T cell receptors. In some examples, the VSTs are MHC-restricted. In some examples, the SARS-CoV2 antigen comprises one or more antigens selected from the group consisting of nsp 1; nsp3; nsp4; nsp5; nsp6; nsp7a, nsp8, nsp10; nsp12; nsp13; nsp14; nsp15; and nsp16. In some examples, the SARS-CoV2 antigen comprises one or more antigen selected from the group consisting of Spike (S); Envelope protein (E); Matrix protein (M); and Nucleocapsid protein (N). In some examples, the SARS-CoV2 antigen comprises one or more antigen selected from the group consisting of SARS-CoV-2 (AP3A); SARS-CoV-2 (NSS); SARS-CoV-2 (ORFlO); SARS-CoV-2 (ORF9B); and SARS-CoV-2 (Yl4). In some examples, methods as described herein for constructing donor minibanks of antigen specific T cell lines can comprise culturing PBMCs from the selected donors in the presence of pepmixes that cover one or more SARS-CoV2 antigens and one or more additional antigen selected from the group consisting of PIV antigen M, PIV antigen HN, PIV antigen N, PIV antigen F, influenza antigen NPl, influenza antigen MPl, RSV antigen N, RSV antigen F, hMPV antigen M, hMPV antigen M2-1, hMPV antigen F, hMPV antigen N, and AdV antigen Hexon, AdV antigen Penton and combinations thereof. In some examples, the additional antigen

comprises PIV antigen M, PIV antigen HN, PIV antigen N, PIV antigen F, influenza antigen NPl, influenza antigen MPl, RSV antigen N, RSV antigen F, hMPV antigen M, hMPV antigen M2-1, hMPV antigen F, hMPV antigen N, AdV antigen Hex on, AdV antigen Penton and combinations thereof.

[0036] In some examples, methods as described herein for constructing donor minibanks of antigen specific T cell lines can comprise culturing PBMCs from the selected donors in the presence of pepmixes that cover an antigen from a hepatitis B virus (HBV). In some examples, the HBV antigen is selected from HBV Core antigen, HBV Surface Antigen, and each of HBV Core antigen and HBV Surface Antigen.

[0037] In some examples, methods as described herein for constructing donor minibanks of antigen specific T cell lines can comprise culturing PBMCs from the selected donors in the presence of pepmixes that cover an antigen from a Human Herpesvirus-8 (HHV-8). In some examples, the HHV-8 antigen comprises a latent antigen. In some examples the HHV-8 antigen comprises a lytic antigen. In some examples, the HHV-8 antigen is 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.

[0038] In some examples, the methods as described herein for constructing donor minibanks of antigen specific T cell lines (e.g., VSTs) comprise culturing antigen specific T cell lines ex vivo in the presence of both IL-7 and IL-4. In some examples, the VSTs have expanded sufficiently within 9-18 days of culture such that they are ready for administration to a patient. In some examples, the pepmix as described herein can comprise 15 mer peptides. In one example, peptides in the pepmix that span the antigen can overlap in sequence by 11 amino acids. In some examples, constructing a first donor minibank of antigen-specific T cell lines can comprise expanding the antigen-specific T cells. In some examples, constructing a first donor minibank of antigen-specific T cell lines can comprise testing the antigen specific T cells for antigen-specific cytotoxicity. In one aspect, the present disclosure provides a minibank of antigen-specific T cell lines produced via the method disclosed herein, optionally, a minibank of antigen-specific T cell lines derived from a plurality of donors selected via the method disclosed herein. In another aspect, the present disclosure provides a bank of antigen-specific T cell lines comprising a plurality of minibanks derived from a plurality of donors selected via the method disclosed herein. In some examples, minibanks of antigen-specific T cell lines can be produced via the methods of constructing a first donor minibank of antigen-specific T cell lines as disclosed herein. In some examples, minibanks of antigen-specific T cell lines can be derived from a plurality of donors selected via methods as described herein. In some

examples, banks of antigen-specific T cell lines can comprise a plurality of minibanks derived from a plurality of donors selected via methods as described herein.

[0039] The present disclosure provides methods of treating a disease or condition by administering to a patient one or more suitable antigen-specific T cell lines from the minibank as described herein. In one aspect, the present disclosure provides one or more suitable antigen-specific T cell lines from the minibank disclosed herein for use in treating a disease or condition in a patient, optionally wherein the sole criteria for administration of the antigen-specific T cell line to the patient is that the patient shares at least two HLA alleles with the donor from whom the MNCs, optionally PBMCs, used in the manufacture of the antigen-specific T cell line were isolated, and optionally wherein the disease or condition is a viral infection, cancer, immune deficiency, primary immune deficiency, or the patient is in need of a transplant. In some examples, the sole criterion for choosing an antigen-specific T cell line for administration to a patient is that the patient shares at least two HLA alleles with the donor from whom the MNCs used in the manufacture of the antigen-specific T cell line were isolated. In one example, the MNCs can be PBMCs. In some examples, the disease treated can be a viral infection or virus-associated disease. In some examples, the disease treated can be a cancer.

[0040] In some examples, patients being treated by one or more suitable antigen-specific T cell lines from the minibank as described herein can be immunocompromised. In some examples, the patients are immunocompromised due to a treatment the patients received to treat the disease or condition or another disease or condition. In some examples, the patients are immunocompromised due to age. In one example, patients are immunocompromised due to young age. In one example, patients are immunocompromised due to old age. In some examples, the condition treated can be an immune deficiency. In one example, the immune deficiency is primary immune deficiency. In some examples, the patients are in need of a transplant therapy.

[0041] The present disclosure comprises methods of selecting a first antigen-specific T cell line from the minibanks as described herein for administration to a subject. The present disclosure comprises methods of selecting a first antigen-specific T cell line from a minibank comprised in the bank as described herein. In one aspect, the present disclosure provides a method of selecting a first antigen-specific T cell line from the minibank disclosed herein or from a minibank comprised in the bank disclosed herein, for administration in an allogeneic T cell therapy to a patient who has received transplanted material from a transplant donor in a transplant procedure, optionally wherein the transplanted material comprises stem cells, a solid organ, and/or bone marrow, the method comprising:

(a) comparing HLA types of the patient and the transplant donor or donors to identify a first set of shared HLA alleles that are common to the patient and the transplant donor(s);

(b) comparing the first set of shared HLA alleles with the HLA types of each of the donors from whom the antigen-specific T cell lines in the minibank disclosed herein were derived or from whom the antigen-specific T cell lines in the minibank comprised in the bank disclosed herein were derived to identify T cell lines that share one or more HLA alleles with the first set of shared HLA alleles;

(c) assigning a primary numerical score based on the number of HLA alleles identified in step (b), wherein a perfect match of 8 shared alleles is assigned an arbitrary numerical score of X; 7 shared alleles is assigned a numerical score X1 that is 7/8 of X; 6 shared alleles is assigned a numerical score X2 that is 6/8 of X, and so on;

(d) comparing HLA types of the patient and each of the respective donors from whom the antigen-specific T cells in the minibank disclosed herein were derived or from whom the antigen-specific T cells in the minibank comprised in the bank disclosed herein were derived to identify one or more additional sets of shared HLA alleles common to the patient and each respective T cell line donor;

(e) assigning a secondary numerical score to each respective T cell line based on the number of shared HLA alleles identified in step (d) that are common between that T cell line and the patient, wherein a perfect match of 8 shared alleles is assigned a numerical score that is 50% of X, as defined in step (c) disclosed herein (i.e., 4, if X=8); 7 shared alleles is assigned a score of 50% of X1, as defined in step (c) disclosed herein (i.e., 3.5, if X=8); 6 shared alleles is assigned a numerical score that is 50% of X2, as defined in step (c) disclosed herein (i.e., 3, if X=8) and so on;

(f) adding together the primary score and the secondary score for each antigen-specific T cell line within the minibank disclosed herein or within the minibank comprised in the bank disclosed herein; and

(g) selecting the antigen-specific T cell line with the highest score from step (f) for administration to the patient, optionally wherein the administration is for treatment of a viral infection, a tumor, or primary immune deficiency prior to transplant, optionally wherein the first antigen specific T cell line selected in step (g) is to be administered to the patient. In some examples, selecting a first antigen-specific T cell line can be for administering an allogeneic T cell therapy to a patient who has received transplanted material (e.g. stem cells) from a transplant donor in a transplant procedure. In some examples, methods of selecting a first antigen-specific T cell line can comprise (a) comparing HLA types of the patient and the transplant donor or donors (e.g., in the case of a double cord blood transplant) to identify a first set of shared HLA alleles that are common to the patient and the transplant donor(s); (b) comparing the first set of shared HLA alleles with the HLA types of each of the donors from whom the antigen-specific T cell lines in the minibanks as described herein were derived or from whom the antigen-specific T cell lines in the minibank

comprised in the bank as described herein were derived to identify T cell lines that share one or more HLA alleles with the first set of shared HLA alleles; (c) assigning a primary numerical score based on the number of HLA alleles identified in step (b); (d) comparing HLA types of the patient and each of the respective donors from whom the antigen-specific T cells in the minibank as described herein were derived or from whom the antigen-specific T cells in the minibank comprised in the bank as described herein were derived to identify one or more additional sets of shared HLA alleles common to the patient and each respective T cell line donor; (e) assigning a secondary numerical score to each respective T cell line based on the number of shared HLA alleles identified in step (d) that are common between that T cell line and the patient; and (f) adding together the primary score and the secondary score for each antigen-specific T cell line within the minibank as described herein. In some examples, the methods can comprise step (g) selecting the antigen-specific T cell line with the highest score from step (f) of this paragraph for administration to the patient.

[0042] In some examples, a perfect match of 8 shared alleles can be assigned an arbitrary numerical score of X in the primary score. In some examples, 7 shared alleles can be assigned a numerical score X1 that is 7/8 of X. In some examples, 6 shared alleles can be assigned a numerical score X2 that is 6/8 of X. In some examples, 5 shared alleles can be assigned a numerical score X3 that is 5/8 of X. In some examples, 4 shared alleles can be assigned a numerical score X4 that is 4/8 of X. In some examples, 3 shared alleles can be assigned a numerical score X5 that is 3/8 of X. In some examples, 2 shared alleles can be assigned a numerical score X6 that is 2/8 of X. In one example, an arbitrary numerical score of X equals to 8.

[0043] In some examples, a perfect match of 8 shared alleles in the secondary score can be assigned a numerical score that is weighted 50% of the primary score. So, if the primary score X, as defined in step (c) of the immediately preceding paragraph is 8, (i.e., 4, if X=8). In some examples, 7 shared alleles can be assigned a score of 50% of X1, as defined in step (c) of the immediately preceding paragraph (i.e., 3.5, if X=8). In some examples, 6 shared alleles can be assigned a numerical score that is 50% of X2, as defined in step (c) of the immediately preceding paragraph (i.e., 3, if X=8). In some examples, any numbers of shared alleles that are 2 or more can be assigned a score by following step (e) as described in this paragraph.

[0044] In some examples, the transplanted material received by the patients as described herein can comprise stem cells. In some examples, the transplanted material received by the patients as described herein can comprise a solid organ. In some examples, the solid organ is a kidney. In some examples, the transplanted material received by the patients as described herein can comprise bone marrow. In some examples, the transplanted material received by the patients as described herein can comprise stem cells, a solid organ, and bone marrow. In some examples, the methods comprise administering the first antigen-specific T cell line selected in step (g) as described in the immediately preceding paragraph to the patient.

[0045] In some examples, the administration to the patients can be for treatment of a viral infection. In some examples, the administration to the patients can be for treatment of a tumor. In some examples, the administration to the patients can be for primary immune deficiency prior to transplant. In some examples, methods as described herein can comprise administering a second antigen-specific T cell line to the patient. In some examples, the second antigen-specific T cell line can be selected from the same minibank as the first antigen specific T cell line. In some examples, the antigen-specific T cell line can be selected from a different minibank than the minibank from which the first antigen specific T cell line was obtained. In some examples, the second antigen specific T cell line can be selected by repeating the method of selecting a first antigen-specific T cell line from a minibank or from a minibank comprised in the bank as described herein with all remaining antigen-specific T cell lines in the donor bank other than the first antigen specific T cell line.

[0046] The present disclosure provides methods of constructing a donor bank made up of a plurality of minibanks of antigen specific T cell lines. In one aspect, the present disclosure provides a method of constructing a donor bank made up of a plurality of minibanks of antigen specific T cell lines comprising

A) performing steps (a) through (j) set forth in the method disclosed herein, thereby constructing a first minibank;

B) repeating steps (a) through (j), as set forth in the method disclosed herein, one or more second rounds to construct one or more second minibanks, wherein, prior to starting each second round of the method, the method comprises

(1) generating a new donor pool, said new donor pool comprising:

a. the first donor pool, less any greatest matched donors removed in accordance with each prior cycle of step (d) from the first and any prior second rounds of the method;

b. an entirely new population of potential donors not included in the first donor pool; or

c. a combination of a. and b.; and

(2) reconstituting the first plurality of prospective patients from the first prospective patient population by returning all prospective patients that had been previously removed in accordance with each prior cycle of step (e) from the first and any prior second rounds of the method;

C) wherein steps (g) through (j) may optionally be performed following each round of the method or they may be performed at any time after step A) of the method. In some examples, the methods can comprise step A) performing steps (a) through (j) set forth in the method of constructing a first donor minibank of antigen-specific T cell lines as described herein. In some examples, a first minibank is constructed. In some examples, the methods can comprise step B) repeating steps (a) through (j) set forth in the method of constructing a first donor minibank of antigen-specific T cell lines as described herein. In some examples, one or more second rounds can be conducted to construct one or more second minibanks. In some examples, prior to starting each second round of the method as described herein, a new donor pool can be generated. In some examples, the new donor pool can comprise the first donor pool, less any greatest matched donors removed in accordance with each prior cycle of step (d) from the first and any

prior second rounds of the method of constructing a first donor minibank of antigen-specific T cell lines as described herein. In some examples, the new donor pool can comprise an entirely new population of potential donors not included in the first donor pool. In some examples, the new donor pool can comprise a combination of the new donor pool comprising the first donor pool, less any greatest matched donors removed in accordance with each prior cycle of step (d) from the first and any prior second rounds of the method of constructing a first donor minibank of antigen-specific T cell lines as described herein and an entirely new population of potential donors not included in the first donor pool.

[0047] In some examples, the methods can comprise reconstituting the first plurality of prospective patients from the first prospective patient population by returning all prospective patients that had been previously removed in accordance with each prior cycle of step (e) set forth in the method of constructing a first donor minibank of antigen-specific T cell lines as described herein from the first and any prior second rounds. In some examples, steps (g) through (j) set forth in the method of constructing a first donor minibank of antigen-specific T cell lines as described herein may optionally be performed following each round of the method or they may be performed at any time after step A) as described in the immediately preceding paragraph.

[0048] In some examples, the culturing of MNCs can be in a vessel comprising a gas permeable culture surface. In one example, the vessel can be an infusion bag with a gas permeable portion. In one example, the vessel can be a rigid vessel. In one example, the vessel can be a GRex bioreactor (Wilson Wolf, St Paul, MN). In some examples, culturing the MNCs for constructing a first donor minibank of antigen-specific T cell lines as described herein can be conducted in the presence of one or more cytokine. In one example, the MNCs can be PMBCs. In one example, the cytokine can include IL4. In one example, the cytokine can include IL7. In one example, the cytokine can include IL4 and IL7. In one example, the cytokine can include IL4 and IL7, but not IL2.

[0049] In some examples, the one or more antigen can be in the form of a whole protein. In some examples, the one or more antigen can be in the form of a pepmix comprising a series of overlapping peptides spanning part of or the entire sequence of each antigen. In some examples, the one or more antigen can be in the form of a combination of the form of a whole protein and the form of a pepmix comprising a series of overlapping peptides spanning

part of or the entire sequence of each antigen. In some examples, methods for constructing a donor bank made up of a plurality of minibanks of antigen specific T cell lines can comprise culturing the MNCs in the presence of a plurality of pepmixes. In one example, the MNCs can be PBMCs. In some examples, each pepmix from the plurality of pepmixes can comprise a series of overlapping peptides spanning part of or the entire sequence of each antigen. The antigen may be presented on a dendritic cell. The antigen may be directly contacted with the MNCs (e.g., PBMCs) from the donor selected via the method disclosed herein.

[0050] In other examples, each antigen contacted with the cells can comprise a tumor associated antigen. In other examples, each antigen can be a viral antigen. In some examples, at least one antigen contacted with the cells can be a viral antigen and at least one antigen contacted with the cells can be a tumor associated antigen.

[0051] In some examples, methods of constructing a donor bank made up of a plurality of minibanks of antigen specific T cell lines as described herein can comprise culturing MNCs in the presence of at least 2 different pepmixes. In some examples, methods as described herein can comprise culturing MNCs in the presence of at least 3 different pepmixes. In some examples, methods as described herein can comprise culturing MNCs in the presence of at least 4 different pepmixes. In some examples, methods as described herein can comprise culturing MNCs in the presence of at least 5 different pepmixes. In some examples, methods as described herein can comprise culturing MNCs in the presence of at least 6 different pepmixes. In some examples, methods as described herein can comprise culturing MNCs in the presence of at least 7 different pepmixes. In some examples, methods as described herein can comprise culturing MNCs in the presence of at least 8 different pepmixes. In some examples, methods as described herein can comprise culturing MNCs in the presence of at least 9 different pepmixes. In some examples, methods as described herein can comprise culturing MNCs in the presence of at least 10 different pepmixes. In some examples, methods as described herein can comprise culturing MNCs in the presence of at least 11 different pepmixes. In some examples, methods as described herein can comprise culturing MNCs in the presence of at least 12 different pepmixes. In some examples, methods as described herein can comprise culturing MNCs in the presence of at least 13 different pepmixes. In some examples, methods as described herein can comprise culturing MNCs in the presence of at least 14 different pepmixes. In some examples, methods as described herein can comprise

culturing MNCs in the presence of at least 15 different pepmixes. In some examples, methods as described herein can comprise culturing MNCs in the presence of at least 16 different pepmixes. In some examples, methods as described herein can comprise culturing MNCs in the presence of at least 17 different pepmixes. In some examples, methods as described herein can comprise culturing MNCs in the presence of at least 18 different pepmixes. In some examples, methods as described herein can comprise culturing MNCs in the presence of at least 19 different pepmixes. In some examples, methods as described herein can comprise culturing MNCs in the presence of at least 20 different pepmixes. In some examples, methods as described herein can comprise culturing MNCs in the presence of at least more than 20 different pepmixes. In some examples, the MNCs can be PBMCs. In some examples, each pepmix can comprise a series of overlapping peptides spanning part of an antigen. In some examples, each pepmix can comprise a series of overlapping peptides spanning the entire sequence of an antigen

[0052] In some examples, methods as described herein can comprise culturing MNCs in the presence of a plurality of pepmixes. In some examples, each pepmix can cover at least one antigen that is different than the antigen covered by each of the other pepmixes in the plurality of pepmixes. In some examples, 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 different antigens can be covered by the plurality of pepmixes. In some examples, at least more than 20 different antigens can be covered by the plurality of pepmixes. In some examples, at least one antigen from at least 2 different viruses can be covered by the plurality of pepmixes.

[0053] In some examples, the antigens used in methods as described herein can be from EBV (Epstein–Barr virus). In some examples, the antigens used in methods as described herein can be from CMV (Cytomegalovirus). In some examples, the antigens used in methods as described herein can be from Adenovirus. In some examples, the antigens used in methods as described herein can be from BK virus. In some examples, the antigens used in methods as described herein can be from JC virus (John Cunningham virus). In some examples, the antigens used in methods as described herein can be from HHV6 (Herpesviruses 6). In some examples, the antigens used in methods as described herein can be from RSV (Human respiratory syncytial virus). In some examples, the antigens used in

methods as described herein can be from Influenza. In some examples, the antigens used in methods as described herein can be from Parainfluenza. In some examples, the antigens used in methods as described herein can be from Bocavirus. In some examples, the antigens used in methods as described herein can be from Coronavirus. In some examples, the antigens used in methods as described herein can be from SARS-CoV2. In some examples, the antigens used in methods as described herein can be from LCMV (Lymphocytic choriomeningitis virus). In some examples, the antigens used in methods as described herein can be from Mumps. In some examples, the antigens used in methods as described herein can be from Measles. In some examples, the antigens used in methods as described herein can be from human Metapneumovirus. In some examples, the antigens used in methods as described herein can be from Parvovirus B. In some examples, the antigens used in methods as described herein can be from Rotavirus. In some examples, the antigens used in methods as described herein can be from Merkel cell virus. In some examples, the antigens used in methods as described herein can be from herpes simplex virus. In some examples, the antigens used in methods as described herein can be from HPV (Human Papillomavirus). In some examples, the antigens used in methods as described herein can be from HIV (human immunodeficiency virus). In some examples, the antigens used in methods as described herein can be from HTLV1 (Human T- cell leukemia virus , type 1). In some examples, the antigens used in methods as described herein can be from HHV8 (Herpesviruses 8). In some examples, the antigens used in methods as described herein can be from hepatitis B virus (HBV). In some examples, the antigens used in methods as described herein can be from West Nile Virus. In some examples, the antigens used in methods as described herein can be from Zika virus. In some examples, the antigens used in methods as described herein can be from Ebola.

[0054] In some examples, at least one pepmix can cover an antigen from each of RSV, Influenza, Parainfluenza, and HMPV (Human meta-pneumovirus). In some examples, the Influenza antigens used in the pepmixes as described herein can be influenza A antigens NP1. In some examples, the Influenza antigens used in the pepmixes as described herein can be influenza A MP1. In some examples, the Influenza antigens used in the pepmixes as described herein can be influenza A influenza A antigens NP1 and influenza A MP1. In some examples, the RSV antigens used in the pepmixes as described herein can be RSV N proteins. In some examples, the RSV antigens used in the pepmixes as described herein can

be RSV F proteins. In some examples, the RSV antigens used in the pepmixes as described herein can be RSV N proteins and RSV F proteins. In some examples, the hMPV antigens used in the pepmixes as described herein can be hMPV F proteins. In some examples, the hMPV antigens used in the pepmixes as described herein can be hMPV N proteins. In some examples, the hMPV antigens used in the pepmixes as described herein can be hMPV M2-1 proteins. In some examples, the hMPV antigens used in the pepmixes as described herein can be hMPV M proteins. In some examples, the hMPV antigens used in the pepmixes as described herein can be a combination of hMPV F proteins, hMPV N proteins, hMPV M2-1, and hMPV M proteins. In some examples, the PIV antigens used in the pepmixes as described herein can be PIV M proteins. In some examples, the PIV antigens used in the pepmixes as described herein can be PIV HN proteins. In some examples, the PIV antigens used in the pepmixes as described herein can be PIV N proteins. In some examples, the PIV antigens used in the pepmixes as described herein can be PIV F proteins. In some examples, the PIV antigens used in the pepmixes as described herein can be a combination of PIV M proteins, PIV HN proteins, PIV N proteins, and PIV F proteins.

[0055] In some examples, methods as described herein can comprise culturing MNCs or PBMCs in the presence of pepmixes spanning Influenza A antigen NP1 and Influenza A antigen MP1. In some examples, methods as described herein can comprise culturing in the presence of pepmixes spanning RSV antigen N and RSV antigen F. In some examples, methods as described herein can comprise culturing in the presence of pepmixes spanning hMPV antigen F. In some examples, methods as described herein can comprise culturing in the presence of pepmixes spanning hMPV antigen N. In some examples, methods as described herein can comprise culturing in the presence of pepmixes spanning hMPV antigen M2-1. In some examples, methods as described herein can comprise culturing in the presence of pepmixes spanning hMPV antigen M. In some examples, methods as described herein can comprise culturing in the presence of pepmixes spanning PIV antigen M. In some examples, methods as described herein can comprise culturing in the presence of pepmixes spanning PIV antigen HN. In some examples, methods as described herein can comprise culturing in the presence of pepmixes spanning PIV antigen N. In some examples, methods as described herein can comprise culturing in the presence of pepmixes spanning PIV antigen F.

[0056] In some examples, methods as described herein can comprise culturing MNCs or PBMCs in the presence of pepmixes spanning Influenza A antigen NP1 and Influenza A antigen MP1. In some examples, methods as described herein can comprise culturing in the presence of pepmixes spanning RSV antigen N and RSV antigen F. In some examples, methods as described herein can comprise culturing in the presence of pepmixes spanning hMPV antigen F. In some examples, methods as described herein can comprise culturing in the presence of pepmixes spanning hMPV antigen N. In some examples, methods as described herein can comprise culturing in the presence of pepmixes spanning hMPV antigen M2-1. In some examples, methods as described herein can comprise culturing in the presence of pepmixes spanning hMPV antigen M. In some examples, methods as described herein can comprise culturing in the presence of pepmixes spanning PIV antigen M. In some examples, methods as described herein can comprise culturing in the presence of pepmixes spanning PIV antigen HN. In some examples, methods as described herein can comprise culturing in the presence of pepmixes spanning PIV antigen N. In some examples, methods as described herein can comprise culturing in the presence of pepmixes spanning PIV antigen F.

[0057] In some examples, at least one pepmix as described herein can cover an antigen from EBV, CMV, adenovirus, BK, and HHV6. In some examples, the EBV antigen can be LMP2. In some examples, the EBV antigen can be EBNA1. In some examples, the EBV antigen can be BZLF1. In some examples, the EBV antigen can be LMP2, EBNA1, and BZLF1. In some examples, the CMV antigen can be IE1. In some examples, the CMV antigen can be pp65. In some examples, the CMV antigen can be IE1 and pp65.

[0058] In some examples, the adenovirus antigens can be Hexon. In some examples, the adenovirus antigens can be Penton. In some examples, the adenovirus antigens can be Hexon and Penton. In some examples, the BK virus antigen can be VP1. In some examples, the BK virus antigen can be large T. In some examples, the BK virus antigen can be VP1 and large T. In some examples, the HHV6 antigen can be U90. In some examples, the HHV6 antigen can be U11. In some examples, the HHV6 antigen can be U14. In some examples, the HHV6 antigen can be U90, U11, and U14.

[0059] In some examples, methods as described herein can comprise culturing MNCs or PBMCs in the presence of pepmixes spanning EBV antigen LMP2, EBV antigen EBNA1, and EBV antigen BZLF1. In some examples, methods as described herein can comprise culturing

in the presence of pepmixes spanning CMV antigen IE1 and CMV antigen pp65. In some examples, methods as described herein can comprise culturing in the presence of pepmixes spanning adenovirus antigens Hexon and adenovirus antigens Penton. In some examples, methods as described herein can comprise culturing in the presence of pepmixes spanning BK virus antigen VP1 and large T. In some examples, methods as described herein can comprise culturing in the presence of pepmixes spanning HHV6 antigen U90, HHV6 antigen U11, and HHV6 antigen U14.

[0060] In some examples, methods as described herein can comprise culturing MNCs or PBMCs in the presence of pepmixes spanning HBV Core antigen, HBV Surface Antigen, and each of HBV Core antigen and HBV Surface Antigen.

[0061] In some examples, methods as described herein can comprise culturing MNCs or PBMCs in the presence of pepmixes spanning an HHV-8 antigen 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.

[0062] In some examples, the pepmix as described herein can comprise 15 mer peptides. In one example, peptides in the pepmix that span the antigen can overlap in sequence by 11 amino acids. In some examples, constructing a first donor minibank of antigen-specific T cell lines can comprise expanding the antigen-specific T cells. In some examples, constructing a first donor minibank of antigen-specific T cell lines can comprise testing the antigen specific T cells for antigen-specific cytotoxicity.

[0063] The present disclosure provides donor banks that can comprise a plurality of minibanks of antigen-specific T cell lines. In one aspect, the present disclosure provides a donor bank comprising a plurality of minibanks of antigen-specific T cell lines, wherein the donor bank is produced via the method disclosed herein. In some examples, the donor bank can be produced via the method of constructing a donor bank made up of a plurality of minibanks of antigen specific T cell lines. The present disclosure provides methods of treating a disease or condition comprising administering to a patient one or more suitable antigen-specific T cell lines from the donor bank as described herein.

[0064] The present disclosure provides methods of treating a disease or condition by administering to a patient one or more suitable antigen-specific T cell lines from the donor bank as described herein. In one aspect, the present disclosure provides one or more suitable antigen-specific T cell lines from the donor bank disclosed herein for use in treating a disease or condition in a patient, wherein the disease or condition is a viral infection, cancer, an immune deficiency, primary immune deficiency, or the patient is in need of transplant therapy, and wherein the sole criteria for administration of the antigen-specific T cell line to the patient is that the patient shares at least two HLA alleles with the donor from whom the MNCs, optionally PBMCs, used in the manufacture of the T cell line were isolated. In some examples, the sole criteria for administration of the antigen-specific T cell line to the patient is that the patient shares at least two HLA alleles with the donor

from whom the MNCs used in the manufacture of the antigen-specific T cell line were isolated. In one example, the MNCs can be PBMCs. In some examples, the disease treated can be a viral infection. In some examples, the disease treated can be a cancer.

[0065] In some examples, patients being treated by one or more suitable antigen-specific T cell lines from the donor bank as described herein can be immunocompromised. In some examples, the patients are immunocompromised due to a treatment the patients received to treat the disease or condition or another disease or condition. In some examples, the patients are immunocompromised due to age. In one example, patients are immunocompromised due to young age. In one example, patients are immunocompromised due to old age. In some examples, the condition treated can be an immune deficiency. In one example, the immune deficiency is primary immune deficiency. In some examples, the patients are in need of a transplant therapy

[0066] The present disclosure provides methods of selecting a first antigen-specific T cell line from the donor bank as described herein for administering an allogeneic T cell therapy to a patient who has received transplanted material from a transplant donor in a transplant procedure. In one aspect, the present disclosure provides a method of selecting a first antigen-specific T cell line from the donor bank disclosed herein, for administration in an allogeneic T cell therapy to a patient who has received transplanted material from a transplant donor in a transplant procedure, optionally wherein the transplanted material comprises stem cells, a solid organ, and/or bone marrow, and wherein the administration is for treatment of a viral infection, a tumor, or for primary immune deficiency prior to transplant, the method comprising:

(a) comparing HLA types of the patient and the transplant donor to identify a first set of shared HLA alleles that are common to the patient and the transplant donor;

(b) comparing the first set of shared HLA alleles with the HLA types of each of the donors from whom the antigen-specific T cell lines in the donor bank disclosed herein were derived to identify T cell lines that share one or more HLA alleles with the first set of shared HLA alleles;

(c) assigning a primary numerical score based on the number of HLA alleles identified in step (b), wherein a perfect match of 8 shared alleles is assigned a score of 8, 7 shared alleles is assigned a score of 7, and so on;

(d) comparing HLA types of the patient and each of the respective donors from whom the antigen-specific T cells in the donor bank disclosed herein were derived to identify one or more additional sets of shared HLA alleles common to the patient and each respective T cell line donor;

(e) assigning a secondary numerical score to each respective T cell line based on the number of shared HLA alleles identified in step (d) that are common between that T cell line and the patient, wherein a perfect match of 8 shared alleles is assigned a score of 50% of 8, i.e., 4; 7 shared alleles is assigned a score of 50% of 7, i.e., 3.5, and so on;

(f) adding together the primary score and the secondary score for each antigen-specific T cell line within the bank disclosed herein; and

(g) selecting the first antigen-specific T cell line with the highest score from step (f) for administration to the patient, optionally wherein the first antigen-specific T cell line selected in step (g) is to be administered to the patient, wherein the administration does not result in GVHD. In some examples, the methods can comprise step (a) comparing HLA types of the patient and the transplant donor to identify a first set of shared HLA alleles that are common to the patient and the transplant donor. In some examples, the methods can comprise step (b) comparing the first set of shared HLA alleles with the HLA types of each of the donors from whom the antigen-specific T cell lines in the donor bank as described herein were derived to identify T cell lines that share one or more HLA alleles with the first set of shared HLA alleles.

[0067] In some examples, the methods can comprise step (c) assigning a primary numerical score based on the number of HLA alleles identified in step (b). In some examples, a perfect match of 8 shared alleles can be assigned a score of 8. In some examples, 7 shared alleles can be assigned a score of 7. In some examples, 6 shared alleles can be assigned a score of 6. In some examples, 5 shared alleles can be assigned a score of 5. In some examples, 5 shared alleles can be assigned a score of 5. In some examples, 3 shared alleles can be assigned a score of 3. In some examples, 2 shared alleles can be assigned a score of 2. In some examples, the methods can comprise step (d) comparing HLA types of the patient and each of the respective donors from whom the antigen-specific T cells in the donor bank as described herein were derived to identify one or more additional sets of shared HLA alleles

common to the patient and each respective T cell line donor. In some examples, the methods comprise step (e) assigning a secondary numerical score to each respective T cell line based on the number of shared HLA alleles identified in step (d) that are common between that T cell line and the patient.

[0068] In some examples, a perfect match of 8 shared alleles can be assigned a numerical score that is 50% of X identified in step (d) (i.e., 4, if X=8). In some examples, 7 shared alleles can be assigned a score of 50% of X1 identified in step (d) (i.e., 3.5, if X=8). In some examples, 6 shared alleles can be assigned a numerical score that is 50% of X2 identified in step (d) (i.e., 3, if X=8). In some examples, any numbers of shared alleles that are 2 or more can be assigned a score in accordance with0 step (d). In some examples, the methods can comprise step (f) adding together the primary score and the secondary score for each antigen-specific T cell line within the bank as described herein. In some examples, the methods can comprise step (g) selecting the first antigen-specific T cell line with the highest score from step (f) for administration to the patient.

[0069] In some examples, the transplanted material received by the patients as described herein can comprise stem cells. In some examples, the transplanted material received by the patients as described herein can comprise a solid organ. In some examples, the solid organ is a kidney. In some examples, the transplanted material received by the patients as described herein can comprise bone marrow. In some examples, the transplanted material received by the patients as described herein can comprise stem cells, a solid organ, and bone marrow. In some examples, the methods comprise administering the first antigen-specific T cell line selected in step (g) of methods of selecting a first antigen-specific T cell line from the donor bank to the patient.

[0070] In some examples, administering the first antigen-specific T cell line does not result in Graft versus host disease (GVHD). In some examples, administering the first antigen-specific T cell line can be for treatment of a viral infection. In some examples, administering the first antigen-specific T cell line can be for treatment of a tumor. In some examples, administering the first antigen-specific T cell line can be for primary immune deficiency prior to transplant. In some examples, the methods can comprise administering a second antigen-specific T cell line to the patient. In some examples, the second antigen-specific T cell line can be selected from the same donor bank as the first antigen specific T cell line. In some

examples, the second antigen-specific T cell line can be selected from a different donor minibank than the first antigen specific T cell line. In some examples, the second antigen specific T cell line can be selected by repeating the method of selecting a first antigen-specific T cell line from the donor bank as described herein with all remaining T cell lines in the donor bank other than the first antigen specific T cell line. In some examples, the second antigen specific T cell line can be administered to the patient after the first antigen specific T cell line has demonstrated treatment efficacy. In some examples, the second antigen specific T cell line can be administered to the patient after the first antigen specific T cell line has demonstrated lack of treatment efficacy. In some examples, the treatment efficacy can be against a viral infection.

[0071] In some examples, the treatment efficacy can be measured based on viremic resolution of infection from the patient. In some examples, the treatment efficacy can be measured based on viruric resolution of infection from the patient. In some examples, the treatment efficacy can be measured based on resolution of viral load in a sample from the patient. In some examples, the treatment efficacy can be measured based on viremic resolution of infection, viruric resolution of infection, and resolution of viral load in a sample from the patient. In some examples, the treatment efficacy can be measured post-administration of the antigen specific T cell line.

[0072] In some examples, the sample can be selected from a tissue sample from the patient. In some examples, the sample can be selected from a fluid sample from the patient. In some examples, the sample can be selected from cerebral spinal fluid (CSF) from the patient. In some examples, the sample can be selected from Bronchoalveolar lavage (BAL) from the patient. In some examples, the sample can be selected from stool from the patient. In some examples, the sample can be selected from a tissue sample, a fluid sample, CSF, BAL, and stool from the patient.

[0073] In some examples, the treatment efficacy can be measured by monitoring viral load detectable in the peripheral blood of the patient. In some examples, the treatment efficacy can comprise resolution of macroscopic hematuria. In some examples, the treatment efficacy can comprise reduction of hemorrhagic cystitis symptoms as measured by the CTCAE-PRO or similar assessment tool that examines patient and/or clinician-reported outcomes. In some examples, the treatment efficacy is against a cancer. In some examples, the treatment

efficacy can be measured based on tumor size reduction post-administration of the antigen specific T cell line. In some examples, the treatment efficacy can be measured by monitoring markers of disease burden. In some examples, the treatment efficacy can be measured by monitoring tumor lysis detectable in the peripheral blood/serum of the patient. In some examples, the treatment efficacy can be measured by monitoring markers of disease burden and tumor lysis detectable in the peripheral blood/serum of the patient. In some examples, the treatment efficacy can be measured by monitoring tumor status via imaging studies. In other examples, the treatment efficacy can be measured by monitoring a combination of markers of disease burden, tumor lysis detectable in the peripheral blood/serum of the patient, and tumor status via imaging studies.

[0074] In some examples, the second antigen specific T cell line can be administered to the patient after the first antigen specific T cell line has resulted in an adverse clinical response. In some examples, the adverse clinical response can comprise graft versus host disease (GVHD). In some examples, the adverse clinical response can comprise an inflammatory response. In one example, an inflammatory response can include cytokine release syndrome.

[0075] In some examples, the inflammatory response can be detected by observing one or more symptom or sign. In some examples, the one or more symptom or sign can include constitutional symptoms. In some examples, the constitutional symptoms can be fever, rigors, headache, malaise, fatigue, nausea, vomiting, or arthralgia. In some examples, the one or more symptom or sign can include vascular symptoms including hypotension. In some examples, the one or more symptom or sign can include cardiac symptoms. In one example, cardiac symptoms is arrhythmia. In some examples, the one or more symptom or sign can include respiratory compromise. In some examples, the one or more symptom or sign can include renal symptoms. In one example, the renal symptom is kidney failure. In one example, the renal symptom is uremia. In some examples, the one or more symptom or sign can include laboratory symptoms. In one example, the laboratory symptoms can be coagulopathy and a hemophagocytic lymphohistiocytosis-like syndrome.

[0076] The present disclosure provides methods of identifying suitable donors for use in constructing a first donor minibank of antigen-specific T cells. The present disclosure provides methods of constructing a first donor minibank of antigen-specific T cell lines. In one aspect, the present disclosure provides a method of identifying suitable donors for use in constructing a first donor minibank of antigen-specific T cells comprising:

(a) determining or having determined the HLA type of each of a first plurality of potential donors from a first donor pool;

(b) determining or having determined the HLA type of each of a first plurality of prospective patients from a first prospective patient population;

(c) comparing the HLA type of each of a first plurality of potential donors from a first donor pool with each of a first plurality of prospective patients from a first prospective patient population;

(d) determining, based on the comparison in step (c), a first greatest matched donor, defined as the donor from the first donor pool that has 2 or more allele matches with the greatest number of patients in the first plurality of prospective patients;

(e) selecting the first greatest matched donor for inclusion in a first donor minibank;

(f) removing from the first donor pool the first greatest matched donor thereby generating a second donor pool consisting of each of the first plurality of potential donors from the first donor pool except for the first greatest matched donor;

(g) removing from the first plurality of prospective patients each prospective patient that has 2 or more allele matches with the first greatest matched donor, thereby generating a second plurality of prospective patients consisting of each of the first plurality of prospective patients except for each prospective patient that has 2 or more allele matches with the first greatest matched donor; and

(h) repeating steps (c) through (g) one or more additional times with all donors and prospective patients that have not already been removed in accordance with steps (f) and (g), wherein each time an additional greatest matched donor is selected in accordance with step (e) that additional greatest matched donor is removed from their respective donor pool in accordance with step (f); and each time a subsequent greatest matched donor is removed from their respective donor pool, each prospective patient that has 2 or more allele matches with that subsequent greatest matched donor is removed from their respective plurality of prospective patients in accordance with step (g); thereby sequentially increasing the number of selected greatest matched donors in the first donor minibank by 1 following each cycle of the method and thereby depleting the number of the plurality of prospective patients in the patient population following each cycle of the method in accordance with their HLA matching to the selected greatest matched donors; wherein steps (c) through (g) are repeated until a desired percentage of the first prospective patient population remains in the plurality of prospective patients or until no donors remain in the donor pool. In another aspect, the present disclosure provides a method of constructing a first donor minibank of antigen-specific T cell lines comprising:

(a) determining or having determined the HLA type of each of a first plurality of potential donors from a first donor pool;

(b) determining or having determined the HLA type of each of a first plurality of prospective patients from a first prospective patient population;

(c) comparing the HLA type of each of the first plurality of potential donors with each of the first plurality of prospective patients;

(d) determining, based on the comparison in step (c), a first greatest matched donor, defined as the donor from the first donor pool that has 2 or more allele matches with the greatest number of patients in the first plurality of prospective patients;

(e) selecting the first greatest matched donor for inclusion in the first donor minibank;

(f) removing from the first donor pool the first greatest matched donor thereby generating a second donor pool consisting of each of the first plurality of potential donors from the first donor pool except for the first greatest matched donor;

(g) removing from the first plurality of prospective patients each prospective patient that has 2 or more allele matches with the first greatest matched donor, thereby generating a second plurality of prospective patients consisting of each of the first plurality of prospective patients except for each prospective patient that has 2 or more allele matches with the first greatest matched donor;

(h) repeating steps (c) through (g) one or more additional times with all donors and prospective patients that have not already been removed in accordance with steps (f) and (g), wherein each time an additional greatest matched donor is selected in accordance with step (e) that greatest matched donor is removed from their respective donor pool in accordance with step (f); and each time a subsequent greatest matched donor is removed from their respective donor pool, each prospective patient that has 2 or more allele matches with that subsequent greatest matched donor is removed from their respective plurality of prospective patients in accordance with step (g); thereby sequentially increasing the number of selected greatest matched donors in the donor minibank by 1 following each cycle of the method and thereby depleting the number of the plurality of prospective patients in the patient population following each cycle of the method in accordance with their HLA matching to the selected greatest matched donors; wherein steps (C) through (g) are repeated until a desired percentage of the first prospective patient population remains in the plurality of prospective patients or until no donors remain in the donor pool;

(i) isolating MNCs, or having MNCs, isolated, from blood obtained from each respective donor included in the donor minibank;

(j) culturing the MNCs;

(k) contacting the MNCs in culture with one or more antigen, or one or more epitope from one or more antigen, under suitable culture conditions to stimulate and expand a polyclonal population of antigen-specific T cells from each of the respective donor's MNCs; thereby producing a plurality of antigen-specific T cell lines, each of which comprises a polyclonal population of antigen-specific T cells derived from each respective donor's MNCs, wherein the MNCs of steps (i) through (k) are optionally PBMCs; and

(l) optionally, cryopreserving the plurality of antigen-specific T cell lines. In some examples, the methods can comprise step (a) determining or having determined the HLA

type of each of a first plurality of potential donors from a first donor pool. In some examples, the methods can comprise step (b) determining or having determined the HLA type of each of a first plurality of prospective patients from a first prospective patient population. In some examples, the methods can comprise step (c) comparing the HLA type of each of a first plurality of potential donors from a first donor pool with each of a first plurality of prospective patients from a first prospective patient population. In some examples, the methods can comprise step (d) determining, based on the comparison in step (d) as described in this paragraph, a first greatest matched donor, defined as the donor from the first donor pool that has 2 or more allele matches with the greatest number of patients in the first plurality of prospective patients.

[0077] In some examples, the methods can comprise step (e) selecting the first greatest matched donor for inclusion in a first donor minibank. In some examples, the methods can comprise step (f) removing from the first donor pool the first greatest matched donor thereby generating a second donor pool consisting of each of the first plurality of potential donors from the first donor pool except for the first greatest matched donor. In some examples, the methods can comprise step (g) removing from the first plurality of prospective patients each prospective patient that has 2 or more allele matches with the first greatest matched donor. In some examples, step (g) can comprise generating a second plurality of prospective patients consisting of each of the first plurality of prospective patients except for each prospective patient that has 2 or more allele matches with the first greatest matched donor.

[0078] In some examples, the methods can comprise step (h) repeating steps (c) through (g) one or more additional times with all donors and prospective patients that have not already been removed in accordance with steps (f) and (g). In some examples, each time an additional greatest matched donor is selected in accordance with step (e) that additional greatest matched donor is removed from their respective donor pool in accordance with step (f). In some examples, each time a subsequent greatest matched donor is removed from their respective donor pool, each prospective patient that has 2 or more allele matches with that subsequent greatest matched donor is removed from their respective plurality of prospective patients in accordance with step (g). In some examples, step (h) sequentially increases the number of selected greatest matched donors in the first donor minibank by 1 following each cycle of the method. In some examples, step (h) can comprise depleting the number of the plurality of

prospective patients in the patient population following each cycle of the method in accordance with their HLA matching to the selected greatest matched donors. In some examples, steps (c) through (g) can be repeated until a desired percentage of the first prospective patient population remains in the plurality of prospective patients. In some examples, steps (c) through (g) can be repeated until no donors remain in the donor pool.

[0079] In some examples, the present disclosure provides administering to a patient one or more suitable antigen-specific T cell lines from the donor minibank or the donor bank made of a plurality of the donor minibanks that comprise a plurality of viral antigens including at least one first antigen from parainfluenza virus type 3 (PIV-3) and at least one second antigen from one or more second virus. In some examples, the at least one second antigen is respiratory syncytial virus (RSV). In some examples, the at least one second antigen is influenza. In some examples, the at least one second antigen is human metapneumovirus (hMPV).

[0079a] In one aspect, the present disclosure provides a method of selecting a first antigen-specific T cell line from a donor minibank, for administration in an allogeneic T cell therapy to a patient who has received a solid organ transplant material from a transplant donor in a transplant procedure, the method comprising:

(a) comparing HLA types of the transplant donor and each of the respective donors from whom the antigen-specific T cells in the donor bank were derived to identify T cell lines that share one or more HLA alleles with the transplant donor;

(b) assigning a primary numerical score based on the number of shared HLA alleles identified in step (a), wherein a perfect match of 8 shared alleles is assigned an arbitrary numerical score of X; 7 shared alleles is assigned a numerical score X1 that is 7/8 of X; 6 shared alleles is assigned a numerical score X2 that is 6/8 of X, 5 shared alleles is assigned a numerical score X3 that is 5/8 of X, 4 shared alleles is assigned a numerical score X4 that is 4/8 of X, 3 shared alleles is assigned a numerical score X5 that is 3/8 of X, 2 shared alleles is assigned a numerical score X6 that is 2/8 of X, 1 shared allele is assigned a numerical score X7 that is 1/8 of X;

(c) comparing HLA types of the patient and each of the respective donors from whom the antigen-specific T cells in the donor bank were derived to identify T cell lines that share one or more HLA alleles with the patient;

(d) assigning a secondary numerical score based on the number of shared HLA alleles identified in step (c), wherein a perfect match of 8 shared alleles is assigned an arbitrary numerical score of X; 7 shared alleles is assigned a numerical score X1 that is 7/8 of X; 6 shared alleles is assigned a numerical score X2 that is 6/8 of X, 5 shared alleles is assigned a numerical score X3 that is 5/8 of X, 4 shared alleles is assigned a numerical score X4 that is 4/8 of X, 3 shared alleles is assigned a numerical score X5 that is 3/8 of X, 2 shared alleles is assigned a numerical score X6 that is 2/8 of X, 1 shared allele is assigned a numerical score X7 that is 1/8 of X; and wherein the secondary numerical score is optionally weighted lower than the primary score, optionally, wherein the solid organ is a kidney, and the secondary numerical score is weighted 25% of the primary numerical score.

[0079b] In another aspect, the present disclosure provides a method of selecting a first antigen-specific T cell line from the minibank disclosed herein or from a minibank comprised in the bank disclosed herein, for administration in an allogeneic T cell therapy to a patient who has received a bone marrow transplant from a transplant donor in a transplant procedure, the method comprising:

(a) comparing HLA types of the patient and the transplant donor or donors to identify a first set of shared HLA alleles that are common to the patient and the transplant donor(s);

(b) comparing the first set of shared HLA alleles with the HLA types of each of the donors from whom the antigen-specific T cell lines in the minibank disclosed herein were derived or from whom the antigen-specific T cell lines in the minibank comprised in the bank disclosed herein were derived to identify T cell lines that share one or more HLA alleles with the first set of shared HLA alleles;

(c) assigning a primary numerical score based on the number of HLA alleles identified in step (b), wherein a perfect match of 8 shared alleles is assigned an arbitrary numerical score of X; 7 shared alleles is assigned a numerical score X1 that is 7/8 of X; 6 shared alleles is assigned a numerical score X2 that is 6/8 of X, and so on;

(d) comparing HLA types of the patient and each of the respective donors from whom the antigen-specific T cells in the minibank disclosed herein were derived or from whom the antigen-specific T cells in the minibank comprised in the bank disclosed herein were derived to identify one or more additional sets of shared HLA alleles common to the patient and each respective T cell line donor;

(e) assigning a secondary numerical score to each respective T cell line based on the number of shared HLA alleles identified in step (d) that are common between that T cell line and the patient, wherein a perfect match of 8 shared alleles is assigned an arbitrary numerical score of X; 7 shared alleles is assigned a numerical score X1 that is 7/8 of X; 6 shared alleles is assigned a numerical score X2 that is 6/8 of X, 5 shared alleles is assigned a numerical score X3 that is 5/8 of X, 4 shared alleles is assigned a numerical score X4 that is 4/8 of X, 3 shared alleles is assigned a numerical score X5 that is 3/8 of X, 2 shared alleles is assigned a numerical score X6 that is 2/8 of X, 1 shared allele is assigned a numerical score X7 that is 1/8 of X; and wherein the secondary numerical score is weighted lower than the primary score

(f) adding together the primary score and the secondary score for each antigen-specific T cell line within the minibank disclosed herein or within the minibank comprised in the bank disclosed herein; and

(g) selecting the antigen-specific T cell line with the highest score from step (f) for administration to the patient, optionally, wherein the secondary numerical score is weighted 50% of the primary numerical score.

[0079c] In yet another aspect, the present disclosure provides a minibank comprising a plurality of antigen-specific T cell lines derived from a plurality of different donors, optionally from (i) 30 or less different donors, (ii) from 4 to 30 different donors or (iii) from 4, 5, 6, 7, 8, 9, or 10 different donors, optionally wherein the donors collectively match on at least 2 alleles with at least 95% of the prospective patient population; wherein the HLA type of each donor differs on at least one HLA allele, and wherein the HLA type of each donor is selected to ensure that the plurality of different donors collectively match on at least 2 alleles with the greatest possible number of patients in a prospective patient population, optionally wherein each antigen specific T cell line includes CD4+ T-lymphocytes and CD8+ T- lymphocytes, T cells expressing αβ T cell receptors, MHC-restricted T- lymphocytes, or any combination thereof.

[0079d] In one aspect, the present disclosure provides a universal antigen specific T cell therapy product comprising a plurality of antigen-specific T cell lines derived from a plurality of different donors; wherein the HLA type of each donor differs on at least one HLA allele, and wherein the HLA type of each donor is selected to ensure that the plurality of different donors collectively match on at least 2 alleles with the greatest possible number of patients in a prospective patient population, optionally comprising a pool of the plurality of antigen-specific T cell lines, each of which were produced separately as individual cell lines, optionally wherein the plurality of antigen-specific T cell lines comprise sufficient HLA diversity with respect to one another that they collectively provide at least one antigen specific T cell line that is matched on at least 2 HLA alleles with >95% of the prospective patient population, optionally wherein each cell line in the plurality of antigen-specific T cell lines comprise 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, optionally, comprising 10 or less antigen-specific T cell lines, optionally wherein the first prospective patient population comprises at least 100 patients, optionally, wherein the first prospective patient population comprises the entire worldwide or the entire US allogeneic HSCT population; the entire worldwide or the entire US allogeneic HSCT population of children ages ≤ 16 years; the entire worldwide or the entire US allogeneic HSCT population of individuals ages ≥ 65; and/or the entire worldwide or the entire US allogeneic HSCT population of children ages ≤ 5 years.

[0079e] In another aspect, the present disclosure provides a universal antigen specific T cell therapy product comprising a pool of all the antigen specific T cell lines included in the minibank disclosed herein.

BRIEF DESCRIPTION OF THE DRAWINGS

[0080] FIG. 1 represents the general overview of the selection process of donor banks for use in a patient with a refractory viral infection. Abbreviations: HLA: The human leukocyte antigen. HSCT: Hematopoietic stem cell transplant.

[0081] FIG. 2 represents part of the donor selection process. Each donor is compared with patient population to identify the donor who accommodates the majority of patients with a antigen-specific T cell lines based on HLA matching, with a 2-allele minimum threshold.

[0082] FIG. 3 represents part of the donor selection process. The donor who accommodates the majority of patients is (i) shortlisted for antigen-specific T cell lines production; (ii) removed from the general donor pool; and (iii) all patients accommodated by this donor are removed from the patient population.

[0083] FIG. 4 represents part of the donor selection process. The same step as described in FIG. 2 is repeated identifying the donor who best covers the remaining patients and, then remove both the donor and accommodated patients from further consideration.

CLAIMS

1. A method of identifying suitable donors for use in constructing a first donor minibank of antigen-specific T cell lines comprising:

(a) comparing an HLA type of each of a first plurality of potential donors from a first donor pool with each of a first plurality of prospective patients from a first prospective patient population;

(b) determining, based on the comparison in step (a), a first greatest matched donor, defined as the donor from the first donor pool that has 2 or more HLA allele matches with the greatest number of patients in the first plurality of prospective patients;

(c) selecting the first greatest matched donor for inclusion in the first donor minibank;

(d) removing from the first donor pool the first greatest matched donor thereby generating a second donor pool consisting of each of the first plurality of potential donors from the first donor pool except for the first greatest matched donor;

(e) removing from the first plurality of prospective patients each prospective patient that has 2 or more allele matches with the first greatest matched donor, thereby generating a second plurality of prospective patients consisting of each of the first plurality of prospective patients except for each prospective patient that has 2 or more allele matches with the first greatest matched donor; and

(f) repeating steps (a) through (e) one or more additional times with all donors and prospective patients that have not already been removed in accordance with steps (d) and (e), wherein each time an additional greatest matched donor is selected in accordance with step (c) that additional greatest matched donor is removed from their respective donor pool in accordance with step (d); and each time a subsequent greatest matched donor is removed from their respective donor pool, each prospective patient that has 2 or more allele matches with that subsequent greatest matched donor is removed from their respective plurality of prospective patients in accordance with step (e); thereby sequentially increasing the number of selected greatest matched donors in the first donor minibank by 1 following each cycle of the method and thereby depleting the number of the plurality of prospective patients in the patient population following each cycle of the method in accordance with their HLA matching to the selected greatest matched donors; wherein steps (a) through (e) are repeated until a desired percentage of the first prospective patient population remains in the plurality of prospective patients or until no donors remain in the donor pool, optionally, wherein

for each round of the method, steps (a) through (e) are cycled in accordance with step (f) until 5% or less of the first prospective patient population remains in the plurality of prospective patients, and optionally,

wherein the 2 or more alleles from steps (b) and (e) comprise 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.

2. The method of claim 1, wherein the first donor minibank comprises antigen-specific T cell lines derived from 10 or less donors, optionally from 5 or less donors, and comprises enough HLA variability to provide >95% of the first prospective patient population with one or more antigen-specific T cell line that is matched to the patient's HLA type on at least 2 HLA alleles.

3. The method of claim 1, wherein the first donor pool comprises at least 10 donors, optionally wherein the first prospective patient population comprises at least 100 patients.

4. The method of any one of claims 1-3, wherein the first prospective patient population comprises the entire worldwide or the entire US allogeneic HSCT population; the entire worldwide or the entire US allogeneic HSCT population of children ages ≤ 16 years; the entire worldwide or the entire US allogeneic HSCT population of individuals ages ≥ 65; and/or the entire worldwide or the entire US allogeneic HSCT population of children ages ≤ 5 years.

5. A method of identifying suitable donors for use in constructing a donor bank made up of a plurality of minibanks of antigen-specific T cell lines comprising,

A) performing all of the steps set forth in the method of any one of claims 1-4, thereby constructing a first minibank; and

B) repeating steps (a) through (f), as set forth in the method of claim 1, one or more second rounds to construct one or more second minibanks, wherein, prior to starting each second round of the method, the method comprises

(i) generating a new donor pool, said new donor pool comprising:

ia. the first donor pool, less any greatest matched donors removed in accordance with each prior cycle of step (d) from the first and any prior second rounds of the method;

ib. an entirely new population of potential donors not included in the first donor pool; or

ic. a combination of ia. and ib.; and

(ii) reconstituting the first plurality of prospective patients from the first prospective patient population by returning all prospective patients that had been previously removed in accordance with each prior cycle of step (e) from the first and any prior second rounds of the method.

6. The method of any one of claims 1-5, further comprising

(i) harvesting blood from each donor included in the donor bank, or having blood harvested from each donor included in the donor bank, optionally harvesting mononuclear cells (MNCs) from each donor included in the donor bank, or having MNCs harvested from each donor included in the donor bank, optionally wherein the MNCs comprise peripheral blood

mononuclear cells (PBMCs), optionally wherein the MNCs and PBMCs are isolated by ficoll gradient or by density gradient, and optionally the method further comprising,

(ii) culturing or cryopreserving the cells, and optionally,

(iii) contacting the cells in culture with one or more antigens under suitable culture conditions to stimulate and expand antigen-specific T cells; wherein optionally, the one or more antigen comprises (a) one or more viral antigen, (b) one or more tumor associated antigen; or (c) a combination of (a) and (b).

7. A method of constructing a first donor minibank of antigen-specific T cell lines comprising:

(a) comparing the HLA type of each of the first plurality of potential donors with each of the first plurality of prospective patients;

(b) determining, based on the comparison in step (a), a first greatest matched donor, defined as the donor from the first donor pool that has 2 or more allele matches with the greatest number of patients in the first plurality of prospective patients;

(c) selecting the first greatest matched donor for inclusion in the first donor minibank;

(d) removing from the first donor pool the first greatest matched donor thereby generating a second donor pool consisting of each of the first plurality of potential donors from the first donor pool except for the first greatest matched donor;

(e) removing from the first plurality of prospective patients each prospective patient that has 2 or more allele matches with the first greatest matched donor, thereby generating a second plurality of prospective patients consisting of each of the first plurality of prospective patients except for each prospective patient that has 2 or more allele matches with the first greatest matched donor;

(f) repeating steps (a) through (e) one or more additional times with all donors and prospective patients that have not already been removed in accordance with steps (d) and (e), wherein each time an additional greatest matched donor is selected in accordance with step (c) that greatest matched donor is removed from their respective donor pool in accordance with step (d); and each time a subsequent greatest matched donor is removed from their respective donor pool, each prospective patient that has 2 or more allele matches with that subsequent greatest matched donor is removed from their respective plurality of prospective patients in accordance with step (e); thereby sequentially increasing the number of selected greatest matched donors in the donor minibank by 1 following each cycle of the method and thereby depleting the number of the plurality of prospective patients in the patient population following each cycle of the method in accordance with their HLA matching to the selected greatest matched donors; wherein steps (a) through (e) are repeated until a desired percentage of the first prospective patient population remains in the plurality of prospective patients or until no donors remain in the donor pool;

(g) isolating MNCs, or having MNCs, isolated, from blood obtained from each respective donor included in the donor minibank;

(h) culturing the MNCs;

(i) contacting the MNCs in culture with one or more antigen, or one or more epitope from one or more antigen, optionally wherein the one or more antigen is selected from

(i) a tumor associated antigen;

(ii) a viral antigen; or,

(iii) at least one antigen is a viral antigen and at least one antigen is a tumor associated antigen,

wherein contacting is under suitable culture conditions to stimulate and expand a polyclonal population of antigen-specific T cells from each of the respective donor's MNCs; thereby producing a plurality of antigen-specific T cell lines, each of which comprises a polyclonal population of antigen-specific T cells derived from each respective donor's MNCs, wherein the MNCs of steps (g) through (i) are optionally PBMCs; and

(j) optionally, cryopreserving the plurality of antigen-specific T cell lines, optionally wherein the 2 or more alleles from steps (b) and (e) comprise 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, and optionally, wherein

for each round of the method, steps (a) through (e) are cycled in accordance with step (f) until 5% or less of the first prospective patient population remains in the plurality of prospective patients and, thus, each donor minibank comprises enough HLA variability amongst the one or more greatest matched donors to provide >95% of the first prospective patient population with at least one allogeneic antigen-specific T cell line that is matched to the patient's HLA type on at least 2 HLA alleles.

8. The method of claim 7, wherein the donor minibank comprises antigen-specific T cell lines derived from 10 or less donors, optionally from 5 or less donors and comprises enough HLA variability amongst the antigen-specific T cell lines to provide >95% of the first prospective patient population with one or more allogeneic antigen-specific T cell line that is matched to the patient's HLA type on at least 2 HLA alleles.

9. The method of claim 7, wherein the first donor pool comprises at least 10 donors, optionally wherein the first prospective patient population comprises at least 100 patients.

10. The method of any one of claims 7-9, wherein the first prospective patient population comprises the entire worldwide or the entire US allogeneic HSCT population; the entire worldwide or the entire US allogeneic HSCT population of children ages ≤ 16 years; the entire worldwide or the entire US allogeneic HSCT population of individuals ages ≥ 65; and/or the entire worldwide or the entire US allogeneic HSCT population of children ages ≤ 5 years.

11. The method of claim 7, wherein the culturing is

in a vessel comprising a gas permeable culture surface, optionally wherein the vessel is an infusion bag with a gas permeable portion, rigid vessel, or GRex bioreactor, and optionally wherein the method further comprises

culturing the PBMCs in the presence of one or more cytokine, optionally wherein the cytokine comprises

(a) IL4,

(b) IL7,

(c) IL4 and IL7, or

(d) IL4 and IL7, but not IL2.

12. The method of any one of claims 7-11, wherein the MNCs, optionally PBMCs, are cultured in the presence of one or more antigen in the form of (i) a whole protein, (ii) a pepmix comprising a series of overlapping peptides spanning part of or the entire sequence of each antigen, (iii) a plurality of pepmixes, or (iv) a combination of (i) and (ii), optionally wherein each pepmix comprises a series of overlapping peptides spanning part of or the entire sequence of each antigen, optionally wherein each pepmix comprises 15 mer peptides, and wherein the peptides that span the antigen overlap in sequence by 11 amino acids, optionally wherein (a) each antigen is a tumor associated antigen; (b) at least one antigen is a viral antigen and at least one antigen is a tumor-associated antigen; or (c) each antigen is a viral antigen.

13. The method of any one of claims 7-12, comprising culturing the MNCs, optionally, PBMCs in the presence of at least 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, or more different pepmixes, each pepmix

(i) comprises a series of overlapping peptides spanning part of or the entire sequence of an antigen, and optionally

(ii) covers at least one antigen that is different than the antigen covered by each of the other pepmixes in the plurality of pepmixes, and wherein at least 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20 or more different antigens are covered by the plurality of pepmixes, optionally, wherein at least one antigen from at least 2 different viruses are covered by the plurality of pepmixes, optionally, wherein the viral antigen 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, HBV, HCV, HPV, HIV, HTLV1, HHV8 and West Nile Virus, zika virus, ebola, optionally wherein

(i) the EBV antigens are selected from LMP2, EBNA1, BZLF1, and a combination thereof;

(ii) the CMV antigens are selected from IE1, pp65, and a combination thereof;

(iii) the adenovirus antigens are selected from Hexon, Penton, and a combination thereof;

(iv) the BK virus antigens are selected from VP1, large T, and a combination thereof;

(v) the HHV6 antigens are selected from U90, U11, U14, and a combination thereof;

(vi) the Influenza antigens are selected from influenza A antigens NP1, MP1, and a combination thereof;

(vii) the RSV antigens are selected from N, F, and a combination thereof;

(viii) the hMPV antigens are selected from F, N, M2-1, M, and a combination thereof;

(ix) the PIV antigens are selected from M, HN, N, F, and a combination thereof;

(x) the HBV antigen is HBV core antigen, HBV Surface Antigen, or HBV core antigen and HBV Surface Antigen;

(xi) the HHV8 antigen is 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; and,

(xii) the coronavirus is a α-coronavirus (α-CoV) or a β-coronavirus (β-CoV), optionally wherein the β-CoV is selected from SARS-CoV, SARS-CoV2, MERS-CoV, HCoV-HKU1, and HCoV-OC43, and optionally wherein the SARS-CoV2 antigen comprises

(a) one or more antigen selected from the group consisting of nsp1; nsp3; nsp4; nsp5; nsp6; nsp7a, nsp8, nsp10; nsp12; nsp13; nsp14; nsp15; and nsp16;

(b) one or more antigen selected from the group consisting of Spike (S); Envelope protein (E); Matrix protein (M); and Nucleocapsid protein (N); and/or,

(c) one or more antigen selected from the group consisting of SARS-CoV-2 (AP3A); SARS-CoV-2 (NS7); SARS-CoV-2 (NS8); SARS-CoV-2 (ORF10); SARS-CoV-2 (ORF9B); and SARS-CoV-2 (Y14).

14. The method of any one of claims 12-13, wherein at least one pepmix covers an antigen from each of the following viruses:

(a) RSV, Influenza, Parainfluenza, Human meta-pneumovirus (HMPV);

(b) EBV, CMV, adenovirus, BK, HHV6;

(c) HBV; and/or,

(d) HHV8.

15. A minibank of antigen-specific T cell lines produced via the method of any one of claims 7-14, optionally, a minibank of antigen-specific T cell lines derived from a plurality of donors selected via the method of any one of claims 1-6.

16. One or more suitable antigen-specific T cell lines from the minibank of claim 15 for use in treating a disease or condition in a patient, optionally wherein the sole criteria for administration of the antigen-specific T cell line to the patient is that the patient shares at least two HLA alleles with the donor from whom the MNCs, optionally PBMCs, used in the manufacture of the antigen-specific T cell line were isolated, and optionally wherein the disease or condition is a viral infection, cancer, immune deficiency, primary immune deficiency, or the patient is in need of a transplant.

17. The one or more suitable antigen-specific T cell lines for use according to claim 16, wherein the patient is immunocompromised, and optionally, wherein (i) the patient is immunocompromised due to a treatment the patient received to treat the disease or condition, due to another disease or condition, due to young age, or due to old age, or (ii) the patient has an immune deficiency, optionally, wherein the immune deficiency is primary immune deficiency, optionally, wherein the patient is in need of a transplant.

18. A bank of antigen-specific T cell lines comprising a plurality of minibanks derived from a plurality of donors selected via the method of any one of claims 1-6.

19. A method of selecting a first antigen-specific T cell line from the minibank of claim 15 or from a minibank comprised in the bank of claim 18, for administration in an allogeneic T cell therapy to a patient who has received transplanted material from a transplant donor in a transplant procedure, optionally wherein the transplanted material comprises stem cells, a solid organ, and/or bone marrow, the method comprising:

(a) comparing HLA types of the patient and the transplant donor or donors to identify a first set of shared HLA alleles that are common to the patient and the transplant donor(s);

(b) comparing the first set of shared HLA alleles with the HLA types of each of the donors from whom the antigen-specific T cell lines in the minibank of claim 15 were derived or from whom the antigen-specific T cell lines in the minibank comprised in the bank of claim 16 were derived to identify T cell lines that share one or more HLA alleles with the first set of shared HLA alleles;

(c) assigning a primary numerical score based on the number of HLA alleles identified in step (b), wherein a perfect match of 8 shared alleles is assigned an arbitrary numerical score of X; 7 shared alleles is assigned a numerical score X1 that is 7/8 of X; 6 shared alleles is assigned a numerical score X2 that is 6/8 of X, and so on;

(d) comparing HLA types of the patient and each of the respective donors from whom the antigen-specific T cells in the minibank of claim 15 were derived or from whom the antigen-specific T cells in the minibank comprised in the bank of claim 18 were derived to identify one or more additional sets of shared HLA alleles common to the patient and each respective T cell line donor;

(e) assigning a secondary numerical score to each respective T cell line based on the number of shared HLA alleles identified in step (d) that are common between that T cell line and the patient, wherein a perfect match of 8 shared alleles is assigned a numerical score that is 50% of X, as defined in step (c) of this claim (i.e., 4, if X=8); 7 shared alleles is assigned a score of 50% of X1, as defined in step (c) of this claim (i.e., 3.5, if X=8); 6 shared alleles is assigned a numerical score that is 50% of X2, as defined in step (c) of this claim (i.e., 3, if X=8) and so on;

(f) adding together the primary score and the secondary score for each antigen-specific T cell line within the minibank of claim 15 or within the minibank comprised in the bank of claim 18; and

(g) selecting the antigen-specific T cell line with the highest score from step (f) for administration to the patient, optionally wherein the administration is for treatment of a viral infection, a tumor, or primary immune deficiency prior to transplant, optionally wherein the first antigen specific T cell line selected in step (g) is to be administered to the patient.

20. The method of claim 19, wherein X=8.

21. The method of any one of claims 19-20, wherein a second antigen-specific T cell line is to be administered to the patient, optionally wherein the second antigen-specific T cell line is selected from

(a) the same minibank as the first antigen-specific T cell line, or

(b) a different minibank from which the first antigen specific T cell line was obtained, optionally, wherein the second antigen specific T cell line is selected by repeating the method of claim 19 with all remaining antigen-specific T cell lines in the donor bank other than the first antigen specific T cell line.

22. A method of constructing a donor bank made up of a plurality of minibanks of antigen specific T cell lines comprising

A) performing steps (a) through (j) set forth in the method of claim 7, thereby constructing a first minibank;

B) repeating steps (a) through (j), as set forth in the method of claim 7, one or more second rounds to construct one or more second minibanks, wherein, prior to starting each second round of the method, the method comprises

(1) generating a new donor pool, said new donor pool comprising:

a. the first donor pool, less any greatest matched donors removed in accordance with each prior cycle of step (d) from the first and any prior second rounds of the method;

b. an entirely new population of potential donors not included in the first donor pool; or

c. a combination of a. and b.; and

(2) reconstituting the first plurality of prospective patients from the first prospective patient population by returning all prospective patients that had been previously removed in accordance with each prior cycle of step (e) from the first and any prior second rounds of the method;

C) wherein steps (g) through (j) may optionally be performed following each round of the method or they may be performed at any time after step A) of the method.

23. The method of claim 22, wherein the culturing is
in a vessel comprising a gas permeable culture surface, optionally and wherein the vessel is an infusion bag with a gas permeable portion, rigid vessel, or GRex bioreactor, optionally wherein the method further comprises culturing the PBMCs in the presence of one or more cytokine, optionally wherein the cytokine comprises
(a) IL4,
(b) IL7,
(c) IL4 and IL7, or
(d) IL4 and IL7, but not IL2.

24. The method of any one of claims 22-23, wherein the MNCs, optionally PBMCs, are cultured in the presence of one or more antigen in the form of (i) a whole protein, (ii) a pepmix comprising a series of overlapping peptides spanning part of or the entire sequence of each antigen, (iii) a plurality of pepmixes, or (iv) a combination of (i) and (ii), optionally wherein each pepmix comprises a series of overlapping peptides spanning part of or the entire sequence of each antigen, optionally wherein each pepmix comprises 15 mer peptides, and wherein the peptides that span the antigen overlap in sequence by 11 amino acids, optionally wherein (a)

each antigen is a tumor associated antigen; (b) at least one antigen is a viral antigen and at least one antigen is a tumor-associated antigen; or (c) each antigen is a viral antigen.

25. The method of any one of claims 22-24, comprising culturing the MNCs, optionally PBMCs, in the presence of at least 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, or more different pepmixes, each pepmix

(i) comprises a series of overlapping peptides spanning part of or the entire sequence of an antigen, and optionally

(ii) covers at least one antigen that is different than the antigen covered by each of the other pepmixes in the plurality of pepmixes, and wherein the at least 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20 or more different antigens are covered by the plurality of pepmixes, optionally wherein at least one antigen from at least 2 different viruses are covered by the plurality of pepmixes, optionally wherein the viral antigen 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, HBV, HCV, HPV, HIV, HTLV1, HHV8, zika virus, ebola, and West Nile Virus, optionally wherein

(i) the EBV antigens are selected from LMP2, EBNA1, BZLF1, and a combination thereof;

(ii) the CMV antigens are selected from IE1, pp65, and a combination thereof;

(iii) the adenovirus antigens are selected from Hexon, Penton, and a combination thereof;

(iv) the BK virus antigens are selected from VP1, large T, and a combination thereof;

(v) the HHV6 antigens are selected from U90, U11, U14, and a combination thereof;

(vi) the Influenza antigens are selected from influenza A antigens NP1, MP1, and a combination thereof;

(vii) the RSV antigens are selected from N, F, and a combination thereof;

(viii) the hMPV antigens are selected from F, N, M2-1, M, and a combination thereof;

(ix) the PIV antigens are selected from M, HN, N, F, and a combination thereof;

(x) the HBV antigen is HBV Core antigen; HBV Surface Antigen, or each of HBV Core antigen and HBV Surface Antigen;

(xi) the HHV8 antigen is 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; and,

(xii) the coronavirus is a α-coronavirus (α-CoV) or β-coronavirus (β-CoV), optionally wherein the β-CoV is selected from SARS-CoV, SARS-CoV2, MERS-CoV, HCoV-HKU1, and HCoV-OC43, and optionally wherein the SARS-CoV2 antigen comprises

(a) one or more antigen selected from the group consisting of nsp1; nsp3; nsp4; nsp5; nsp6; nsp7a, nsp8, nsp10; nsp12; nsp13; nsp14; nsp15; and nsp16;

(b) one or more antigen selected from the group consisting of Spike (S); Envelope protein (E); Matrix protein (M); and Nucleocapsid protein (N); and/or,

(c) one or more antigen selected from the group consisting of SARS-CoV-2 (AP3A); SARS-CoV-2 (NS7); SARS-CoV-2 (NS8); SARS-CoV-2 (ORF10); SARS-CoV-2 (ORF9B); and SARS-CoV-2 (Y14).

26. The method of any one of claims 24-25, wherein at least one pepmix covers an antigen from each of the following viruses:

(a) RSV, Influenza, Parainfluenza, Human metapneumovirus (HMPV);
(b) EBV, CMV, adenovirus, BK, HHV6;
(c) HBV; and/or,
(d) HHV8.

27. A donor bank comprising a plurality of minibanks of antigen-specific T cell lines, wherein the donor bank is produced via the method of any one of claims 22-26.

28. One or more suitable antigen-specific T cell lines from the donor bank of claim 27 for use in treating a disease or condition in a patient, wherein the disease or condition is a viral infection, cancer, an immune deficiency, primary immune deficiency, or the patient is in need of transplant therapy, and

wherein the sole criteria for administration of the antigen-specific T cell line to the patient is that the patient shares at least two HLA alleles with the donor from whom the MNCs, optionally PBMCs, used in the manufacture of the T cell line were isolated.

29. The one or more suitable antigen-specific T cell lines for use according to claim 28, wherein the patient is immunocompromised, and wherein the patient is immunocompromised due to a treatment the patient received to treat the disease or condition, due to another disease or condition, due to young age, or due to old age.

30. A method of selecting a first antigen-specific T cell line from the donor bank of claim 27, for administration in an allogeneic T cell therapy to a patient who has received transplanted material from a transplant donor in a transplant procedure, optionally wherein the transplanted material comprises stem cells, a solid organ, and/or bone marrow, and wherein the administration is for treatment of a viral infection, a tumor, or for primary immune deficiency prior to transplant, the method comprising:

(a) comparing HLA types of the patient and the transplant donor to identify a first set of shared HLA alleles that are common to the patient and the transplant donor;

(b) comparing the first set of shared HLA alleles with the HLA types of each of the donors from whom the antigen-specific T cell lines in the donor bank of claim 27 were derived to identify T cell lines that share one or more HLA alleles with the first set of shared HLA alleles;

(c) assigning a primary numerical score based on the number of HLA alleles identified in step (b), wherein a perfect match of 8 shared alleles is assigned a score of 8, 7 shared alleles is assigned a score of 7, and so on;

(d) comparing HLA types of the patient and each of the respective donors from whom the antigen-specific T cells in the donor bank of claim 27 were derived to identify one or more additional sets of shared HLA alleles common to the patient and each respective T cell line donor;

(e) assigning a secondary numerical score to each respective T cell line based on the number of shared HLA alleles identified in step (d) that are common between that T cell line and

the patient, wherein a perfect match of 8 shared alleles is assigned a score of 50% of 8, i.e., 4; 7 shared alleles is assigned a score of 50% of 7, i.e., 3.5, and so on;

(f) adding together the primary score and the secondary score for each antigen-specific T cell line within the bank of claim 27; and

(g) selecting the first antigen-specific T cell line with the highest score from step (f) for administration to the patient, optionally wherein the first antigen-specific T cell line selected in step (g) is to be administered to the patient, wherein the administration does not result in GVHD.

31. The method of claim 30, wherein a second antigen-specific T cell line is to be administered to the patient, optionally wherein the second antigen-specific T cell line is selected from

(a) the same donor bank as the first antigen specific T cell line, or

(b) a different donor minibank than the first antigen specific T cell line, optionally, wherein the second antigen specific T cell line is selected by repeating the method of claim 30 with all remaining T cell lines in the donor bank other than the first antigen specific T cell line, optionally, wherein the second antigen specific T cell line is to be administered to the patient after the first antigen specific T cell line has demonstrated treatment efficacy or demonstrated lack of treatment efficacy, and either

(a) the treatment efficacy is against a viral infection, wherein the treatment efficacy is measured by monitoring viral load detectable in the peripheral blood of the patient, or

(b) the treatment efficacy is against a cancer and the treatment efficacy is measured based on tumor size reduction post-administration of the antigen specific T cell line, optionally,

wherein the treatment efficacy is measured based on (i) viremic resolution of infection, (ii) viruric resolution of infection, and/or (iii) resolution of viral load in a sample from the patient, wherein the sample is optionally selected from a tissue sample from the patient, a fluid sample from the patient, cerebral spinal fluid (CSF) from the patient, BAL from the patient, stool from the patient, and a combination thereof, post-administration of the antigen specific T cell line, optionally, wherein the treatment efficacy comprises (i) resolution of macroscopic hematuria; reduction of hemorrhagic cystitis symptoms as measured by the CTCAE-PRO or similar assessment tool that examines patient and/or clinician-reported outcomes.

32. The method of any one of claims 21 and 31, wherein the second antigen specific T cell line is to be administered to the patient after the first antigen specific T cell line has resulted in an adverse clinical response, optionally wherein the adverse clinical response comprises graft versus host disease (GVHD) or an inflammatory response such as cytokine release syndrome, optionally

wherein inflammatory response is detected by observing one or more symptom or sign selected from

(i) constitutional symptoms selected from fever, rigors, headache, malaise, fatigue, nausea, vomiting, arthralgia;

(ii) vascular symptoms including hypotension;

(iii) cardiac symptoms including arrhythmia;

(iv) respiratory compromise;

(v) renal symptoms including kidney failure and uremia; and,

(vi) laboratory symptoms including coagulopathy and a hemophagocytic lymphohistiocytosis-like syndrome.

33. A method of identifying suitable donors for use in constructing a first donor minibank of antigen-specific T cells comprising:

(a) determining or having determined the HLA type of each of a first plurality of potential donors from a first donor pool;

(b) determining or having determined the HLA type of each of a first plurality of prospective patients from a first prospective patient population;

(c) comparing the HLA type of each of a first plurality of potential donors from a first donor pool with each of a first plurality of prospective patients from a first prospective patient population;

(d) determining, based on the comparison in step (c), a first greatest matched donor, defined as the donor from the first donor pool that has 2 or more allele matches with the greatest number of patients in the first plurality of prospective patients;

(e) selecting the first greatest matched donor for inclusion in a first donor minibank;

(f) removing from the first donor pool the first greatest matched donor thereby generating a second donor pool consisting of each of the first plurality of potential donors from the first donor pool except for the first greatest matched donor;

(g) removing from the first plurality of prospective patients each prospective patient that has 2 or more allele matches with the first greatest matched donor, thereby generating a second plurality of prospective patients consisting of each of the first plurality of prospective patients except for each prospective patient that has 2 or more allele matches with the first greatest matched donor; and

(h) repeating steps (c) through (g) one or more additional times with all donors and prospective patients that have not already been removed in accordance with steps (f) and (g), wherein each time an additional greatest matched donor is selected in accordance with step (e) that additional greatest matched donor is removed from their respective donor pool in accordance with step (f); and each time a subsequent greatest matched donor is removed from their respective donor pool, each prospective patient that has 2 or more allele matches with that subsequent greatest matched donor is removed from their respective plurality of prospective patients in accordance with step (g); thereby sequentially increasing the number of selected greatest matched donors in the first donor minibank by 1 following each cycle of the method and thereby depleting the number of the plurality of prospective patients in the patient population following each cycle of the method in accordance with their HLA matching to the selected greatest matched donors; wherein steps (c) through (g) are repeated until a desired percentage of

the first prospective patient population remains in the plurality of prospective patients or until no donors remain in the donor pool.

34. A method of constructing a first donor minibank of antigen-specific T cell lines comprising:

(a) determining or having determined the HLA type of each of a first plurality of potential donors from a first donor pool;

(b) determining or having determined the HLA type of each of a first plurality of prospective patients from a first prospective patient population;

(c) comparing the HLA type of each of the first plurality of potential donors with each of the first plurality of prospective patients;

(d) determining, based on the comparison in step (c), a first greatest matched donor, defined as the donor from the first donor pool that has 2 or more allele matches with the greatest number of patients in the first plurality of prospective patients;

(e) selecting the first greatest matched donor for inclusion in the first donor minibank;

(f) removing from the first donor pool the first greatest matched donor thereby generating a second donor pool consisting of each of the first plurality of potential donors from the first donor pool except for the first greatest matched donor;

(g) removing from the first plurality of prospective patients each prospective patient that has 2 or more allele matches with the first greatest matched donor, thereby generating a second plurality of prospective patients consisting of each of the first plurality of prospective patients except for each prospective patient that has 2 or more allele matches with the first greatest matched donor;

(h) repeating steps (c) through (g) one or more additional times with all donors and prospective patients that have not already been removed in accordance with steps (f) and (g), wherein each time an additional greatest matched donor is selected in accordance with step (e) that greatest matched donor is removed from their respective donor pool in accordance with step (f); and each time a subsequent greatest matched donor is removed from their respective donor pool, each prospective patient that has 2 or more allele matches with that subsequent greatest matched donor is removed from their respective plurality of prospective patients in accordance with step (g); thereby sequentially increasing the number of selected greatest matched donors in the donor minibank by 1 following each cycle of the method and thereby depleting the number of the plurality of prospective patients in the patient population following each cycle of the method in accordance with their HLA matching to the selected greatest matched donors; wherein steps (C) through (g) are repeated until a desired percentage of the first prospective patient population remains in the plurality of prospective patients or until no donors remain in the donor pool;

(i) isolating MNCs, or having MNCs, isolated, from blood obtained from each respective donor included in the donor minibank;

(j) culturing the MNCs;

(k) contacting the MNCs in culture with one or more antigen, or one or more epitope from one or more antigen, under suitable culture conditions to stimulate and expand a polyclonal population of antigen-specific T cells from each of the respective donor's MNCs; thereby producing a plurality of antigen-specific T cell lines, each of which comprises a polyclonal population of antigen-specific T cells derived from each respective donor's MNCs, wherein the MNCs of steps (i) through (k) are optionally PBMCs; and

(l) optionally, cryopreserving the plurality of antigen-specific T cell lines.

35. The method of any one of claims 19-21 and 30-32, wherein the HLA types that are compared comprise the HLA alleles HLA A, HLA B, DRB1, and DQB1.

36. The method of any one of claims 19-21, 30-32 and 35, wherein the method firstly compares each cell line in the minibank with the HLA type of the patient and then secondly compares each cell line in the minibank with the HLA type of the transplant donor and generates an overall total score used to establish a ranking hierarchy of matching cell lines.

37. The method of any one of claims 19-21, 30-32 and 35-36, wherein a cell line is deemed suitable for infusion to a patient if the cell line is matched on 2 or more HLA alleles to the patient and to the transplant donor.

38. A method of selecting a first antigen-specific T cell line from a donor minibank, for administration in an allogeneic T cell therapy to a patient who has received a solid organ transplant material from a transplant donor in a transplant procedure, the method comprising:

(a) comparing HLA types of the transplant donor and each of the respective donors from whom the antigen-specific T cells in the donor bank were derived to identify T cell lines that share one or more HLA alleles with the transplant donor;
(b) assigning a primary numerical score based on the number of shared HLA alleles identified in step (a), wherein a perfect match of 8 shared alleles is assigned an arbitrary numerical score of X; 7 shared alleles is assigned a numerical score X1 that is 7/8 of X; 6 shared alleles is assigned a numerical score X2 that is 6/8 of X, 5 shared alleles is assigned a numerical score X3 that is 5/8 of X, 4 shared alleles is assigned a numerical score X4 that is 4/8 of X, 3 shared alleles is assigned a numerical score X5 that is 3/8 of X, 2 shared alleles is assigned a numerical score X6 that is 2/8 of X, 1 shared allele is assigned a numerical score X7 that is 1/8 of X;
(c) comparing HLA types of the patient and each of the respective donors from whom the antigen-specific T cells in the donor bank were derived to identify T cell lines that share one or more HLA alleles with the patient;
(d) assigning a secondary numerical score based on the number of shared HLA alleles identified in step (c), wherein a perfect match of 8 shared alleles is assigned an arbitrary

numerical score of X; 7 shared alleles is assigned a numerical score X1 that is 7/8 of X; 6 shared alleles is assigned a numerical score X2 that is 6/8 of X, 5 shared alleles is assigned a numerical score X3 that is 5/8 of X, 4 shared alleles is assigned a numerical score X4 that is 4/8 of X, 3 shared alleles is assigned a numerical score X5 that is 3/8 of X, 2 shared alleles is assigned a numerical score X6 that is 2/8 of X, 1 shared allele is assigned a numerical score X7 that is 1/8 of X; and wherein the secondary numerical score is optionally weighted lower than the primary score, optionally, wherein the solid organ is a kidney, and the secondary numerical score is weighted 25% of the primary numerical score.

39. A method of selecting a first antigen-specific T cell line from the minibank of claim 13 or 15 or from a minibank comprised in the bank of claim 16, for administration in an allogeneic T cell therapy to a patient who has received a bone marrow transplant from a transplant donor in a transplant procedure, the method comprising:

(a) comparing HLA types of the patient and the transplant donor or donors to identify a first set of shared HLA alleles that are common to the patient and the transplant donor(s);

(b) comparing the first set of shared HLA alleles with the HLA types of each of the donors from whom the antigen-specific T cell lines in the minibank of claim 13 or 15 were derived or from whom the antigen-specific T cell lines in the minibank comprised in the bank of claim 16 were derived to identify T cell lines that share one or more HLA alleles with the first set of shared HLA alleles;

(c) assigning a primary numerical score based on the number of HLA alleles identified in step (b), wherein a perfect match of 8 shared alleles is assigned an arbitrary numerical score of X; 7 shared alleles is assigned a numerical score X1 that is 7/8 of X; 6 shared alleles is assigned a numerical score X2 that is 6/8 of X, and so on;

(d) comparing HLA types of the patient and each of the respective donors from whom the antigen-specific T cells in the minibank of claim 13 or 15 were derived or from whom the antigen-specific T cells in the minibank comprised in the bank of claim 16 were derived to identify one or more additional sets of shared HLA alleles common to the patient and each respective T cell line donor;

(e) assigning a secondary numerical score to each respective T cell line based on the number of shared HLA alleles identified in step (d) that are common between that T cell line and the patient, wherein a perfect match of 8 shared alleles is assigned an arbitrary numerical score of X; 7 shared alleles is assigned a numerical score X1 that is 7/8 of X; 6 shared alleles is assigned a numerical score X2 that is 6/8 of X, 5 shared alleles is assigned a numerical score X3 that is 5/8 of X, 4 shared alleles is assigned a numerical score X4 that is 4/8 of X, 3 shared alleles is assigned a numerical score X5 that is 3/8 of X, 2 shared alleles is assigned a numerical score X6 that is 2/8 of X, 1 shared allele is assigned a numerical score X7 that is 1/8 of X; and wherein the secondary numerical score is weighted lower than the primary score

(f) adding together the primary score and the secondary score for each antigen-specific T cell line within the minibank of claim 13 or 15 or within the minibank comprised in the bank of claim 16; and

(g) selecting the antigen-specific T cell line with the highest score from step (f) for administration to the patient, optionally, wherein the secondary numerical score is weighted 50% of the primary numerical score.

40. A minibank comprising a plurality of antigen-specific T cell lines derived from a plurality of different donors, optionally from (i) 30 or less different donors, (ii) from 4 to 30 different donors or (iii) from 4, 5, 6, 7, 8, 9, or 10 different donors, optionally wherein the donors collectively match on at least 2 alleles with at least 95% of the prospective patient population; wherein the HLA type of each donor differs on at least one HLA allele, and wherein the HLA type of each donor is selected to ensure that the plurality of different donors collectively match on at least 2 alleles with the greatest possible number of patients in a prospective patient population, optionally

wherein each antigen specific T cell line includes CD4+ T-lymphocytes and CD8+ T-lymphocytes, T cells expressing αβ T cell receptors, MHC-restricted T- lymphocytes, or any combination thereof.

41. The minibank of claim 40, wherein the 2 or more alleles comprise 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, optionally, wherein the prospective patient population comprises at least 100 patients, optionally, wherein the prospective patient population comprises the entire worldwide or the entire US allogeneic HSCT population; the entire worldwide or the entire US allogeneic HSCT population of children ages ≤ 16 years; the entire worldwide or the entire US allogeneic HSCT population of individuals ages ≥ 65; and/or the entire worldwide or the entire US allogeneic HSCT population of children ages ≤ 5 years, optionally, wherein each antigen specific T cell line is polyclonal or each antigen specific T cell line is directed to the same target antigen or antigens, optionally wherein each antigen specific T cell line includes CD4+ T-lymphocytes and CD8+ T-lymphocytes, optionally, wherein each antigen specific T cell line includes T cells expressing αβ T cell receptors, optionally, wherein each antigen specific T cell line includes MHC-restricted T-lymphocytes, optionally, wherein each antigen-specific T cell line targets

(a) at least one tumor associated antigen;

(b) at least one viral antigen; or,

(c) at least one viral antigen and at least one tumor associated antigen.

42. The minibank of any one of claims 40-41, wherein at least one antigen from at least 2 different viruses are targeted by each antigen specific T cell line.

43. The minibank of any one of claims 40-42, wherein the antigen specific T cell lines target at least one viral antigen 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, HBV, HIV, HTLV1, HHV8, zika virus, ebola, and West Nile Virus, optionally wherein

(i) the EBV antigens are selected from LMP2, EBNA1, BZLF1, and a combination thereof;

(ii) the CMV antigens are selected from IE1, pp65, and a combination thereof;

(iii) the adenovirus antigens are selected from Hexon, Penton, and a combination thereof;

(iv) the BK virus antigens are selected from VP1, large T, and a combination thereof; and,

(v) the HHV6 antigens are selected from U90, U11, U14, and a combination thereof;

(vi) the Influenza antigens are selected from influenza A antigens NP1, MP1, and a combination thereof;

(vii) the RSV antigens are selected from N, F, and a combination thereof;

(viii) the hMPV antigens are selected from F, N, M2-1, M, and a combination thereof;

(ix) the PIV antigens are selected from M, HN, N, F, and a combination thereof;

(x) the HBV antigen is HBV Core antigen; HBV Surface Antigen, or each of HBV Core antigen and HBV Surface Antigen; and,

(xi) the HHV8 antigen is 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,

optionally wherein the antigen specific T cell lines target at least two HHV8 antigen 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).

44. The minibank of any one of claims 40-43, wherein the antigen specific T cell lines target at least one viral antigen from each of the following viruses:

(a) RSV, Influenza, Parainfluenza, Human metapneumovirus (HMPV);

(b) EBV, CMV, adenovirus, BK, HHV6;

(c) HBV; and/or,

(d) HHV8.

45. A universal antigen specific T cell therapy product comprising a plurality of antigen-specific T cell lines derived from a plurality of different donors; wherein the HLA type of each donor differs on at least one HLA allele, and wherein the HLA type of each donor is selected to ensure that the plurality of different donors collectively match on at least 2 alleles with the greatest possible number of patients in a prospective patient population, optionally comprising a pool of the plurality of antigen-specific T cell lines, each of which were produced separately as individual cell lines, optionally

wherein the plurality of antigen-specific T cell lines comprise sufficient HLA diversity with respect to one another that they collectively provide at least one antigen specific T cell line that is matched on at least 2 HLA alleles with >95% of the prospective patient population, optionally

wherein each cell line in the plurality of antigen-specific T cell lines comprise 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, optionally, comprising 10 or less antigen-specific T cell lines, optionally wherein the first prospective patient population comprises at least 100 patients, optionally, wherein the first prospective patient population comprises the entire worldwide or the entire US allogeneic HSCT population; the entire worldwide or the entire US allogeneic HSCT population of children ages ≤ 16 years; the entire worldwide or the entire US allogeneic HSCT population of individuals ages ≥ 65; and/or the entire worldwide or the entire US allogeneic HSCT population of children ages ≤ 5 years.

46. A universal antigen specific T cell therapy product comprising a pool of all the antigen specific T cell lines included in the minibank of any one of claims 40-44.