CLAIMS

1. A method for preparing a composition of T cells from stem or progenitor cells, the method comprising culturing a three-dimensional (3D) cell aggregate comprising:

a) a selected population of stromal cells that express a Notch ligand;

b) a selected population of stem or progenitor cells;

wherein:

(A) the 3D cell aggregate is cultured in a serum-free medium comprising insulin, biotin, transferrin, and albumin for a time period sufficient for the *in vitro* differentiation of the stem or progenitor cells to T cells; or.

(B) the 3D cell aggregate is cultured in a serum-free medium comprising insulin for a time period sufficient for the *in vitro* differentiation of the stem or progenitor cells to T cells.

2. The method of claim 1(B), wherein:

(a) the Notch ligand is an exogenous Notch ligand; and/or

(b) the method further comprises centrifugation of the stem or progenitor cells and the stromal cells to form a 3D cell aggregate; and/or

(c) the medium further comprises externally added ascorbic acid; and/or

(d) the medium further comprises externally added FLT3 ligand (FLT3L), interleukin 7 (IL-7), stem cell factor (SCF), thrombopoietin (TPO), stem cell factor (SCF), thrombopoietin (TPO), IL-2, IL-4, IL-6, IL-15, IL-21, TNF-alpha, TGF-beta, interferon-gamma, interferon-lambda, TSLP, thymopentin, pleotrophin, midkine, or combinations thereof; and/or

(e) the medium further comprises vitamins, wherein optionally the vitamins comprise biotin, DL alpha tocopherol acetate, DL alpha-tocopherol, vitamin A, choline chloride, calcium pantothenate, pantothenic acid, folic acid nicotinamide, pyridoxine, riboflavin, thiamine, inositol, vitamin B12, or combinations thereof or salts thereof, optionally wherein the vitamins comprise biotin, DL alpha tocopherol acetate, DL alpha-tocopherol, vitamin A, or combinations or salts thereof; and/or

(f) the medium further comprises proteins, wherein optionally the proteins comprise albumin or bovine serum albumin, a fraction of BSA, catalase, insulin, transferrin, superoxide dismutase, or combinations thereof; and/or

(g) the medium further comprises corticosterone, D-Galactose, ethanolamine, glutathione, L-carnitine, linoleic acid, linolenic acid, progesterone, putrescine, sodium selenite, or triodo-I-thyronine, or combinations thereof; and/or

(h) the medium comprises a B-27® supplement, xeno-free B-27® supplement, GS21™ supplement, or combinations thereof; and/or

(i) the medium comprises or futher comprises amino acids, monosaccharides, inorganic ions, optionally wherein: (A) the amino acids comprise arginine, cystine, isoleucine, leucine, lysine, methionine, glutamine, phenylalanine, threonine, tryptophan, histidine, tyrosine, or valine, or combinations thereof, or (B) the inorganic ions comprise sodium, potassium, calcium, magnesium, nitrogen, or phosphorus, or combinations or salts thereof; and/or the medium further comprises molybdenum, vanadium, iron, zinc, selenium, copper, or manganese, or combinations thereof; and/or

(j) the 3D cell aggregate: (A) comprises a defined exogenous extracellular matrix; or (B) does not comprise an exogenous matrix or a scaffold; and/or

(k) the stromal cells have an exogenous nucleotide sequence encoding a Notch ligand; and/or

(l) the Notch ligand is intact, partial, or modified DLL4, DLL1, JAG1, JAG2, or a combination thereof; and/or

(m) the stem or progenitor cells are selected from embryonic stem cells (ESCs), induced pluripotent stem cells (iPSC), human embryonic mesodermal progenitor cells, hematopoietic stem or progenitor cells, cells isolated from bone marrow, cells isolated from cord blood, cells isolated from peripheral blood, cells isolated from thymus, or cells that have been differentiated from ESC or iPSC *in vitro*; and/or

(n) the ratio between stromal cells and stem or progenitors cells is about 1:5 to 1:20; and/or

(o) the stroma cells are: (A) a murine stromal cell line, a human stromal cell line, a selected population of primary stromal cells, a selected population of stromal cells differentiated from pluripotent stem cells *in vitro*, or a combination thereof; or(B) a selected population of stromal cells differentiated from hematopoietic stem or progenitor cells *in vitro*; and/or

(p) the stromal cells express an exogenous human major histocompatibility complex (MHC); and/or

(q) the stromal cells express an exogenous antigen-specific costimulatory molecule or cytokine; and/or

(r) the stromal cells express an exogenous antigen; and/or

(s) the stem or progenitor cells have: (A) previously been frozen or (B) never been frozen; and/or

(t) the stem or progenitor cells express: (A) an exogenous T cell receptor (TCR) or a chimeric antigen receptor (CAR), or both; or (B) an endogenous T cell receptor (TCR) or a chimeric antigen receptor (CAR), or both; and/or

(u) the stem or progenitor cells express an exogenous invariant natural killer T cell (iNKT)-associated TCR; and/or

(v) the stem or progenitor cells express an exogenous antigen-specific TCR, a selection or screening marker, an *in vivo* tracking marker or an *in vivo* imaging marker, or have an exogenous genetic modification of HLA loci, Natural killer cell receptor or ligand; and/or

(w) the number of stem or progenitor cells is from 1,000 to 200,000; and/or

(x) the culturing is for a period of about two to ten weeks; and/or

(y) the culturing does not involve cell passaging; and/or

(z) the method further comprises detecting the number of $CD4^+CD8^-$ T cells, $CD4^-CD8^+$ T cells, $CD34^+$ $CD7^+$ $CD1a^+$ cells, CD3+ TCRab+ cells, CD3+ TCRgd+ cells, CD3+ TCRab+ CD4+ CD8- cells, CD3+ TCRab+ CD8+ CD4- cells, CD3+ TCRab+ CD4+ CD8- CD45RO- CD45RA+ cells, CD3+ TCRab+ CD8+ CD4- CD45RO- CD45RA+ cells, CD3+ TCRab+ CD4+ CD8- CD45RO- CD45RA+ CCR7+ cells, CD3+ TCRab+ CD8+ CD4- CD45RO- CD45RA+ CCR7+ cells, CD3+ TCRab+ CD4+ CD8- CD45RO- CD45RA+ CD27+ cells, CD3+ TCRab+ CD8+ CD4- CD45RO- CD45RA+ CD27+ cells, $CD34^+$ $CD7^+$ $CD1a^+$ cells, CD34+CD5+CD7+ cells, CD34+CD5+CD7- cells, natural killer T cells, regulatory T cells, intraepithelial lymphocytes (IELs), antigen-specific T cells using tetramer or anti-TCR antibodies, CAR T cells using modified antigens, transduced T cells using fluorescent markers, or a combination thereof; and/or

(aa) the method further comprises selecting for $CD4^+CD8^-$ T cells, $CD4^-CD8^+$ T cells, $CD34^+$ $CD7^+$ $CD1a^+$ cells, CD3+ TCRab+ cells, CD3+ TCRgd+ cells, CD3+ TCRab+ CD4+ CD8- cells, CD3+ TCRab+ CD8+ CD4- cells, CD3+ TCRab+ CD4+ CD8- CD45RO- CD45RA+ cells, CD3+ TCRab+ CD8+ CD4- CD45RO- CD45RA+ cells, CD3+ TCRab+ CD4+ CD8- CD45RO- CD45RA+ CCR7+ cells, CD3+ TCRab+ CD8+ CD4- CD45RO- CD45RA+ CCR7+ cells, CD3+ TCRab+ CD4+ CD8- CD45RO- CD45RA+ CD27+ cells, CD3+ TCRab+ CD8+ CD4- CD45RO- CD45RA+ CD27+ cells, $CD34^+$ $CD7^+$ $CD1a^+$ cells, CD34+CD5+CD7+ cells, CD34+CD5+CD7- cells, natural killer T cells, regulatory T cells,

intraepithelial lymphocytes (IELs), antigen-specific T cells using tetramer or anti-TCR antibodies, CAR T cells using modified antigens, transduced T cells using fluorescent markers, or a combination thereof; and/or

(bb) the method further comprises increasing the number of $CD4^+CD8^-$ T cells, $CD4^-$ $CD8^+$ T cells, $CD34^+$ $CD7^+$ $CD1a^+$ cells, CD3+ TCRab+ cells, CD3+ TCRgd+ cells, CD3+ TCRab+ CD4+ CD8- cells, CD3+ TCRab+ CD8+ CD4- cells, CD3+ TCRab+ CD4+ CD8- CD45RO- CD45RA+ cells, CD3+ TCRab+ CD8+ CD4- CD45RO- CD45RA+ cells, CD3+ TCRab+ CD4+ CD8- CD45RO- CD45RA+ CCR7+ cells, CD3+ TCRab+ CD8+ CD4- CD45RO- CD45RA+ CCR7+ cells, CD3+ TCRab+ CD4+ CD8- CD45RO- CD45RA+ CD27+ cells, CD3+ TCRab+ CD8+ CD4- CD45RO- CD45RA+ CD27+ cells, $CD34^+$ $CD7^+$ $CD1a^+$ cells, CD34+CD5+CD7+ cells, CD34+CD5+CD7- cells, natural killer T cells, regulatory T cells, intraepithelial lymphocytes (IELs), antigen-specific T cells using tetramer or anti-TCR antibodies, CAR T cells using modified antigens, transduced T cells using fluorescent markers, or a combination thereof; and/or

(cc) the method further comprises: (A) administering the T cells from the 3D cell aggregate to a subject in need thereof; or (B) differentiating the T cells from the 3D cell aggregate; and/or

(dd) the T cells from the 3D cell aggregate do not express an endogenous TCR through allelic exclusion; and/or

(ee) the T cells from the 3D cell aggregate express an exogenous TCR or CAR; and/or

(ff) the time period is 2-16 weeks; and/or

(gg) the T cells undergo positive selection; and/or

(hh) the cell aggregate further comprises tumor cells or tumor antigen; and/or

(ii) the method further comprises isolating endogenously-expressed TCRs from the T cells, wherein optionally the method further comprises priming the T cells, and optionally the T cells are primed with antigen presenting cells, and optionally the antigen presenting cells present tumor antigens.

3. A cell culture composition, comprising:

(A)

a) a three-dimensional (3D) cell aggregate, comprising:

i) a selected population of stromal cells that express Notch ligand;

ii) a selected population of stem or progenitor cells; and

b) a serum-free medium comprising insulin, wherein optionally:

(B) (a) the Notch ligand is an exogenous Notch ligand; and/or

(b) the medium further comprise externally added ascorbic acidand/or

(c) the medium further comprise externally added FLT3 ligand (FLT3L), interleukin 7 (IL-7), stem cell factor (SCF), thrombopoietin (TPO), IL-2, IL-4, IL-6, IL-15, IL-21, TNF-alpha, TGF-beta, interferon-gamma, interferon-lambda, TSLP, thymopentin, pleotrophin, midkine, or a combination thereof; and/or

(d) the medium further comprises vitamins, wherein optionally the vitamins comprise: (A) biotin, DL alpha tocopherol acetate, DL alpha-tocopherol, vitamin A, choline chloride, calcium pantothenate, pantothenic acid, folic acid nicotinamide, pyridoxine, riboflavin, thiamine, inositol, vitamin B12, or combinations thereof or salts thereof; or (B) biotin, DL alpha tocopherol acetate, DL alpha-tocopherol, vitamin A, or combinations or salts thereof; and/or

(e) the medium further comprises proteins; and optionally the proteins comprise albumin or bovine serum albumin, a fraction of BSA, catalase, insulin, transferrin, superoxide dismutase, or combinations thereof; and/or

(f) the medium further comprises corticosterone, D-Galactose, ethanolamine, glutathione, L-carnitine, linoleic acid, linolenic acid, progesterone, putrescine, sodium selenite, or triodo-I-thyronine, or combinations thereof; and/or

(g) the medium comprises a B-27® supplement, xeno-free B-27® supplement, GS21™ supplement, or combinations thereof; and/or

(h) the medium comprises or futher comprises amino acids, monosaccharides, or inorganic ions, or combinations thereof, wherein optionally: (A) the amino acids comprise arginine, cystine, isoleucine, leucine, lysine, methionine, glutamine, phenylalanine, threonine, tryptophan, histidine, tyrosine, or valine, or combinations thereof; or (B) the inorganic ions comprise sodium, potassium, calcium, magnesium, nitrogen, or phosphorus, or combinations or salts thereof; and/or

(i) the medium further comprises molybdenum, vanadium, iron, zinc, selenium, copper, or manganese, or combinations thereof; and/or

(j) the 3D cell aggregate comprises a defined exogenous extracellular matrix and/or

(k) the 3D cell aggregate does not comprise an exogenous matrix or a scaffold and/or

(l) the stromal cells have an exogenous nucleotide sequence encoding a Notch ligand; and/or

(m) the Notch ligand is intact, partial, or modified DLL4, DLL1, JAG1, JAG2, or a combination thereof; and/or

(n) the stem or progenitor cells are selected from ESCs, iPSCs, human embryonic mesodermal progenitor cells, hematopoietic stem or progenitor cells, cells isolated from bone marrow, cells isolated from cord blood, cells isolated from peripheral blood, cells isolated from thymus, or cells that have been differentiated from ESCs or iPSC *in vitro*; and/or

(o) the ratio between stromal cells and stem or progenitors cells is about 1:5 to 1:20; and/or

(p) the stroma cells are a murine stromal cell line, a human stromal cell line, a selected population of primary stromal cells, a selected population of stromal cells differentiated from pluripotent stem cells *in vitro*, or a combination thereof; and/or

(q) the stroma cells are a selected population of stromal cells differentiated from hematopoietic stem or progenitor cells *in vitro*; and/or

(r) the stem or progenitor cells have: (A) previously been frozen, or (B) never been frozen; and/or

(s) the stromal cells express: (A) an exogenous human major histocompatibility complex (MHC); or (B) an exogenous antigen-specific costimulatory molecule, cytokine, antigen, or extracellular matrix protein, or any other bioactive molecule or genes that modulate T cell differentiation, proliferation, or function; and/or

(t) the stem or progenitor cells express an exogenous T cell receptor (TCR) or a chimeric antigen receptor (CAR), or both; and/or

(u) the stem or progenitor cells express an exogenous invariant natural killer T cell (iNKT) associated TCR; and/or

(v) the stem or progenitor cells express an exogenous antigen-specific TCR or have an exogenous genetic modification of genes that modulate T cell differentiation, expansion or function; and/or

(w) the number of stem or progenitor cells is from 1 to 200,000.

4. A method for producing T cells, comprising culturing the cell culture composition of claim 3, thereby producing T cells, wherein optionally:

(a) the method is further defined as a method for producing antigen-specific T cells, wherein the progenitor cells express an exogenous antigen-specific TCR or CAR; and/or

(b) the method further comprises detecting the number of $CD4^+CD8^-$ T cells, $CD4^-$ $CD8^+$ T cells, $CD34^+$ $CD7^+$ $CD1a^+$ cells, CD3+ TCRab+ cells, CD3+ TCRgd+ cells, CD3+ TCRab+ CD4+ CD8- cells, CD3+ TCRab+ CD8+ CD4- cells, CD3+ TCRab+ CD4+ CD8- CD45RO- CD45RA+ cells, CD3+ TCRab+ CD8+ CD4- CD45RO- CD45RA+ cells, CD3+

TCRab+ CD4+ CD8- CD45RO- CD45RA+ CCR7+ cells, CD3+ TCRab+ CD8+ CD4- CD45RO- CD45RA+ CCR7+ cells, CD3+ TCRab+ CD4+ CD8- CD45RO- CD45RA+ CD27+ cells, CD3+ TCRab+ CD8+ CD4- CD45RO- CD45RA+ CD27+ cells, $CD34^+$ $CD7^+$ $CD1a^+$ cells, CD34+CD5+CD7+ cells, CD34+CD5+CD7- cells, natural killer T cells, regulatory T cells, intraepithelial lymphocytes (IELs), antigen-specific T cells using tetramer or anti-TCR antibodies, CAR T cells using modified antigens, transduced T cells using fluorescent markers, or a combination thereof; and/or

(c) the method further comprises increasing the number of $CD4^+CD8^-$ T cells, $CD4^-$ $CD8^+$ T cells, $CD34^+$ $CD7^+$ $CD1a^+$ cells, $CD34^+$ $CD7^+$ $CD1a^+$ cells, CD3+ TCRab+ cells, CD3+ TCRgd+ cells, CD3+ TCRab+ CD4+ CD8-, CD3+ TCRab+ CD8+ CD4- cells, CD3+ TCRab+ CD4+ CD8- CD45RO- CD45RA+ cells, CD3+ TCRab+ CD8+ CD4- CD45RO- CD45RA+ cells, CD3+ TCRab+ CD4+ CD8- CD45RO- CD45RA+ CCR7+ cells, CD3+ TCRab+ CD8+ CD4- CD45RO- CD45RA+ CCR7+ cells, CD3+ TCRab+ CD4+ CD8- CD45RO- CD45RA+ CD27+ cells, CD3+ TCRab+ CD8+ CD4- CD45RO- CD45RA+ CD27+ cells, $CD34^+$ $CD7^+$ $CD1a^+$ cells, CD34+CD5+CD7+ cells, CD34+CD5+CD7- cells, natural killer T cells, regulatory T cells, intraepithelial lymphocytes (IELs), antigen-specific T cells using tetramer or anti-TCR antibodies, CAR T cells using modified antigens, transduced T cells using fluorescent markers, or a combination thereof.

5. An isolated T cell or population of T cells comprising a chimeric antigen receptor (CAR), wherein the T cells have an intraepithelial lymphocyte phenotype, wherein optionally:

(a) the T cells are TCR-; and/or

(b) the T cells are CD4- CD8+, CD4+ CD8-, CD4+ CD8+, CD4- CD8-, TCRab+, TCRgd+, CD5+CD7+, CD5+CD7+CD3-CD4-CD8-, CD5+CD7+CD3-CD4-CD8aa, or combinations thereof, wherein optionally the T cells are CD5+CD7+CD3-CD4-CD8-, and optionally the T cells are CD5+CD7+CD3-CD4-CD8aa; and/or

(c) the CAR comprises a CD19 CAR; and/or

(d) the T cells further comprise an exogenous TCR, wherein optionally the T cells are CD3+; and/or

(e) the T cells are $CD4^+CD8^-$ T cells, $CD4^-CD8^+$ T cells, $CD34^+$ $CD7^+$ $CD1a^+$ cells, CD3+ TCRab+, CD3+ TCRgd+ cells, CD3+ TCRab+ CD4+ CD8- cells, CD3+ TCRab+ CD8+ CD4- cells, CD3+ TCRab+ CD4+ CD8- CD45RO- CD45RA+ cells, CD3+ TCRab+ CD8+ CD4- CD45RO- CD45RA+ cells, CD3+ TCRab+ CD4+ CD8- CD45RO- CD45RA+

CCR7+ cells, CD3+ TCRab+ CD8+ CD4- CD45RO- CD45RA+ CCR7+ cells, CD3+ TCRab+ CD4+ CD8- CD45RO- CD45RA+ CD27+ cells, CD3+ TCRab+ CD8+ CD4- CD45RO- CD45RA+ CD27+, $CD34^+$ $CD7^+$ $CD1a^+$ cells, CD34+CD5+CD7+ cells, CD34+CD5+CD7- cells, natural killer T cells, regulatory T cells, antigen-specific T cells, intraepithelial lymphocyte T cells, or cells that are CD45+, CD11b+, CD11b-, CD15+, CD15-, CD24+, CD24-, CD114+, CD114-, CD182+, CD182-, CD4+, CD4-, CD14+, CD14-, CD11a+, CD11a-, CD91+, CD91-, CD16+, CD16-, CD3+, CD3-, CD25+, CD25-, Foxp3+, Fox3p-, CD8+, CD8-, CD19+, CD19-, CD20+, CD20-, CD24+, CD24, CD38+, CD38-, CD22+, CD22-, CD61+, CD61-, CD16+, CD16-, CD56+, CD56-, CD31+, CD31-, CD30+, CD30-, CD38+, or CD38- or combinations thereof.

6. An isolated T cell or population of T cells, wherein the T cells express an exogenous TCR or CAR and wherein the T cells are $CD4^+CD8^-$ T cells, $CD4^-CD8^+$ T cells, $CD34^+$ $CD7^+$ $CD1a^+$ cells, CD3+ TCRab+, CD3+ TCRgd+, CD3+ TCRab+ CD4+ CD8-, CD3+ TCRab+ CD8+ CD4-, CD3+ TCRab+ CD4+ CD8- CD45RO- CD45RA+, CD3+ TCRab+ CD8+ CD4- CD45RO- CD45RA+, CD3+ TCRab+ CD4+ CD8- CD45RO- CD45RA+ CCR7+, CD3+ TCRab+ CD8+ CD4- CD45RO- CD45RA+ CCR7+, CD3+ TCRab+ CD4+ CD8- CD45RO- CD45RA+ CD27+, CD3+ TCRab+ CD8+ CD4- CD45RO- CD45RA+ CD27+, $CD34^+$ $CD7^+$ $CD1a^+$ cells, CD34+CD5+CD7+, CD34+CD5+CD7-, natural killer T cells, regulatory T cells, antigen-specific T cells, intraepithelial lymphocyte T cells, CD45+, CD11b+, CD11b-, CD15+, CD15-, CD24+, CD24-, CD114+, CD114-, CD182+, CD182-, CD4+, CD4-, CD14+, CD14-, CD11a+, CD11a-, CD91+, CD91-, CD16+, CD16-, CD3+, CD3-, CD25+, CD25-, Foxp3+, Fox3p-, CD8+, CD8-, CD19+, CD19-, CD20+, CD20-, CD24+, CD24, CD38+, CD38-, CD22+, CD22-, CD61+, CD61-, CD16+, CD16-, CD56+, CD56-, CD31+, CD31-, CD30+, CD30-, CD38+, or CD38- cells or cells with a combination thereof.

7. The T cells of claim 5 or claim 6, wherein:

(a) the T cells are a population of T cells and wherein the population of T cell comprises at least 50% of the cells are mature naïve CD8 or CD4 single positive cells; or the cells express an exogenous invariant natural killer T cell (iNKT) associated TCR; and/or

(b) the cells have been differentiated *in vitro* from stem or progenitor cells, optionally wherein the stem or progenitor cells are selected from ESCs, iPSCs, human embryonic mesodermal progenitor cells, hematopoietic stem or progenitor cells, cells isolated from bone

marrow, cells isolated from cord blood, cells isolated from peripheral blood, cells isolated from thymus, or cells that have been differentiated from ESCs or iPSC *in vitro*; and/or (c) the endogenous TCR has been suppressed through allelic exclusion.

8. An *in vitro* differentiated T cell or T cell precursor comprising an exogenous TCR for use in a method for treating a patient comprising administering to the patient the *in vitro* differentiated T cell or T cell precursor comprising an exogenous TCR, wherein optionally:

(A)

(a) the T cell comprises the exogenous TCR and an additional antigen or ligand recognition receptor, wherein optionally the additional antigen recognition receptor is not a TCR molecule, and optionally the additional antigen recognition receptor is a chimeric antigen receptor (CAR), optionally wherein the CAR is a tumor antigen-specific CAR; and/or

(b) the exogenous TCR comprises a TCR from NKTs; and/or

(c) the exogenous TCR comprises proteins expressed from a: (A) TCR-alpha and TCR-beta genes, or (B) TCR-gamma and TCR-delta genes, or (C) TCR-alpha and TCR-beta genes and the antigen recognition receptor comprises proteins expressed from the TCR-gamma and TCR-delta genes, or (D) TCR-gamma and TCR-delta genes and the antigen recognition receptor comprises proteins expressed from the TCR-alpha and TCR-beta genes; and/or

(d) the exogenous TCR is an engineered molecule that mimics TCR signaling,

wherein optionally the exogenous TCR is specific for a first antigen and the additional antigen recognition receptor is specific for a second antigen and optionally the first and second antigens are cancer cell antigens expressed by the cancer cells of the patient; and/or

(B)

(a) the exogenous TCR is a virus-specific TCR, a xeno-specific TCR, a cancer cell-specific TCR, a bacteria-specific TCR, or a cancer-testis antigen-specific TCR; and/or

(b) the T cells are allogenic to the recipient; and/or

(c) the patient has cancer and optionally the method is for treating cancer in the subject; and optionally the cancer is selected from lung cancer, prostate cancer, ovarian cancer, testicular cancer, brain cancer, skin cancer, melanoma, colon cancer, rectal cancer, gastric cancer, esophageal cancer, tracheal cancer, head & neck cancer, pancreatic cancer, liver cancer, breast cancer, ovarian cancer, lymphoid cancers including lymphoma and multiple myeloma, leukemia, sarcomas of bone or soft tissue, cervical cancer, and vulvar cancer; and/or (d) the method further comprises administration of an antigen, wherein the

antigen is recognized by the exogenous TCR, wherein optionally the antigen is purified, conjugated to other molecules, or presented by a cell or cell-like vehicle; and/or (e) the exogenous TCR is non-alloreactive; and/or (f) the exogenous TCR is inert.

9. The method of any of claims 2-6 or the *in vitro* differentiated T cell or T cell precursor for use according to claim 8, wherein the CAR is a virus antigen-specific CAR or a bacterium antigen-specific CAR.

10. The *in vitro* differentiated T cell or T cell precursor according to claim 8 or 9 or the method according to claim 9, wherein:

the patient has or is at risk of having a microbial infection, wherein optionally: (A) the first and second antigens are virus antigens expressed by the same virus type or by cells infected with the said virus type; or (B) the first and second antigens are bacterial cell antigens expressed by the same bacterium or in cells infected with said bacterium; or

the exogenous TCR is a NY-ESO-1 specific TCR; and/or wherein:

(a) the method further comprises administration of an antigen presenting cell to the patient, wherein optionally: (A) the antigen presenting cell is a dendritic cell, or (B) an artificial antigen presenting cell,

wherein optionally the antigen presenting cell is loaded with an antigen that is recognized by the exogenous TCR or CAR; and/or

(b) the T cell further comprises expression of FOXP3, wherein optionally the T cell is engineered or selected to express FOXP3, and optionally the FOXP3 expression is constitutive,

optionally wherein the subject has or is at risk of having an autoimmune disease, graft versus host disease (GVHD), or graft rejection, and optionally the method is for treating an autoimmune disease, GVHD, or graft rejection.

11. An *in vitro* differentiated T cell or T cell precursor comprising an exogenous TCR, wherein optionally:

(a) the TCR is a virus-specific TCR, a xeno-specific TCR, a cancer cell-specific TCR, a bacteria-specific TCR, or a cancer-testis antigen-specific TCR; and/or

(b) the T cells further comprise an additional antigen recognition receptor, wherein optionally the additional antigen recognition receptor is a chimeric antigen receptor (CAR),

wherein optionally the CAR is a tumor antigen-specific CAR or the CAR is a viral antigen-specific CAR; and/or

(c) the exogenous TCR comprises proteins expressed from a: (A) TCR-alpha and TCR-beta genes, or (B) TCR-gamma and TCR-delta genes.

12. The T cell of claim 11(b), wherein:

(a) the exogenous TCR comprises proteins expressed from a TCR-alpha and TCR-beta genes and the antigen recognition receptor comprises proteins expressed from the TCR-gamma and TCR-delta genes, or

(b) the exogenous TCR comprises proteins expressed from a TCR-gamma and TCR-delta genes and the antigen recognition receptor comprises proteins expressed from the TCR-alpha and TCR-beta genes; or

(c) the additional antigen recognition receptor is not a TCR molecule, wherein optionally the additional antigen recognition receptor is a chimeric antigen receptor (CAR), wherein optionally the CAR is a tumor antigen-specific CAR or the CAR is a viral antigen-specific CAR.

13. The T cell of any one of claims 11-12, wherein the exogenous TCR is specific for a first antigen and the additional antigen recognition receptor is specific for a second antigen., wherein optionally the first and second antigens are:

(a) cancer cell antigens expressed by cells of a cancer, or

(b) viral antigens expressed by a virus or cells infected with said virus, or

(c) bacteria antigens expressed by cells of a bacterium or cells infected with said bacterium;

optionally wherein the exogenous TCR is a NY-ESO-1 specific TCR; and

optionally wherein the T cell further comprises expression of FOXP3, wherein optionally the T cell is engineered or selected to express FOXP3, and optionally the FOXP3 expression is constitutive.

14. A method for delivery of an agent to exogenous TCR-expressing T cell in a patient with said exogenous TCR-expressing T cells comprising administering to the patient an agent conjugated to an antigen, wherein the antigen is recognized by the exogenous TCR, wherein optionally:

(a) the exogenous TCR is inert; and/or

(b) the agent is an elimination agent.

15. A method for the *in vitro* selection and isolation of the T cells of any of claims 11-13 comprising contacting a composition comprising the T cells with an agent that specifically binds to the exogenous TCR to make an agent-TCR expressing cell complex and purifying the agent-TCR expressing cell complex from the composition, wherein optionally:

(a) the agent is an antibody, or a peptide-MHC multimer; and/or

(b) the agent is attached to a solid support; and/or

(c) the method further comprises administration of a secondary molecule that specifically binds to the agent, optionally wherein the secondary molecule is attached to a solid support.

16. The method of claim 15(b) or 15(c), wherein:
(a) the method further comprises separation of the solid support and bound molecules from the composition, wherein optionally (b) the method further comprises washing the solid support and associated molecules one or more times.

17. The method of any of claims 15-16(a), wherein the agent or secondary molecule is conjugated to a fluorescent molecule.

18. The method of any of claims 15-17, wherein:

(A) purifying the agent-TCR expressing cell complex comprises:

(a) flow cytometry, fluorescence activated cell sorting (FACS), beads, and/or columns; and/or

(b) a purification based on other T cell markers, wherein optionally the other T cell markers are one or more of CD4, CD8, CD45RA, CD45RO, CCR7/CD197, CD62L, CD27, CD28, and CD1a; and/or

(c) the method further comprises dissociating the agent from the agent-TCR expressing cell complex; or

(B) the method further comprises culturing the purified TCR expressing cells,

optionally wherein the method further comprises freezing the purified TCR expressing cells.

19. A method for:

(A) making the T cell of any of claim 11-13 comprising

a) transferring an exogenous TCR or TCR-derivative into a stem cell or progenitor cell; and

b) differentiating the stem or progenitor cell into a T cell or T cell precursor,

wherein optionally differentiating the stem or immune progenitor cell into a T cell comprises the method of any one of claims 2-3(A), wherein optionally:

(a) the stem or progenitor cell is contacted with cognate MHC and/or peptide molecules prior to, simultaneously, and/or after contact with a differentiating agent; and/or

(b) differentiating the stem or progenitor cell into a T cell comprises co-culturing stem or progenitor cells with stromal cells expressing a Notch ligand, and optionally the stromal cells are OP9 cells, MS5, or HS27 cells, wherein optionally the Notch ligand is Delta-like 1 (Dll1) and/or the method further comprises contacting the co-cultured stem or progenitor cells and stromal cells with Flt-3 ligand and/or IL-7, wherein optionally differentiating the stem or immune progenitor cell into a T cell comprises the method of any one of claims 2-3(A); or

(B) increasing the number of T cells in a subject or for treating a disease or condition in a subject, the method comprising administering to a subject an effective amount of T cells or antigen-specific T cells, prepared according to any of claims 2-3(A), or the T cells of any one of claims 11-13 or 5-7, wherein optionally:

(a) the subject has been determined to have or is at risk for an autoimmune disease, a cancer, an infection, an immunodeficiency, or a combination thereof; and/or (b) the T cells are regulatory T cells, optionally wherein the subject has been determined to have or is at risk for an autoimmune disease; or

(C) producing T cells that do not react with a self-antigen, comprising culturing a three-dimensional (3D) cell aggregate with a serum-free medium at a concentration effective for producing T cells from the 3D cell aggregate, wherein the 3D cell aggregate comprises: a) a selected population of stromal cells that express a Notch ligand and b) a selected population of stem or progenitor cells, wherein one or more cells of a) or b) express an exogenous self-antigen; thereby the 3D cell aggregate produce T cells that do not react with a self-antigen, wherein optionally one or more of the cells of a) or b) express an exogenous self-MHC.