CLAIMS

What is claimed:

1. A method for allogenic hematopoietic stem cell transplantation (HSCT) comprising the steps of:
   i. administering to a subject on day 0 a minimally manipulated haploidentical hematopoietic stem cell graft infusion comprising peripheral blood stem cells (PBSC);
   ii. administering to the subject an agent which provides *in vivo* T cell depletion;
   iii. optionally expanding a population of γδ T cells *ex vivo*; and
   iv. administering to the subject a second graft infusion comprising T cells enriched in γδ T cells and depleted in αβ T cells.
2. The method of claim 1, wherein the second graft is administered about +7 to about +25 days post PBSC infusion.
3. The method of claim 2, wherein the second graft is administered about +7 to about +9 days post PBSC infusion.
4. The method of claim 1, further comprising administration prior to day 0 any preparative chemotherapy regimen known in the art.
5. The method of claim 4, wherein the preparative chemotherapy regimen is selected from Fludarabine/Busulfan/total body irradiation for myeloid diseases; total body irradiation/cyclophosphamide (TBI/CY) for acute lymphoblastic leukemia (ALL) or aggressive Non-Hodgkin lymphoma (NHL) or Hodgkin lymphoma (HL) in patients ≤ 40 years of age with no major comorbidities; and Fludarabine/total body irradiation for ALL or lymphoma in patients who are older than 40 years, or at any age with major comorbidities that portends high non-relapse mortality (NRM) with high intensity TBI/CY.
6. The method of claim 1, wherein *in vivo* T cell depletion begins after day 0 and comprises the use of any *in vivo* T cell protocol known in the art.
7. The method of claim 6, wherein the *in vivo* T cell depletion protocol is selected from cyclophosphamide treatment between days +1 and +10 relative to administering to a subject on day 0 a minimally manipulated haploidentical hematopoietic stem cell graft infusion comprising PBSC; cyclophosphamide treatment at between 30 mg/kg and 70 mg/kg, or 50 mg/kg; and cyclophosphamide treatment at between 30 mg/kg and 70 mg/kg, or 50 mg/kg at days +3 and +4.

8. The method of claim 1, further comprising administering a Graft vs. Host Disease (GvHD) prophylaxis regimen after day 0, wherein the GvHD regimen is any known in the art.

9. The method of claim 8, wherein the GvHD prophylaxis regimen is selected from providing a decreased number of immunosuppressive agents and/or a reduced concentration of one or more of said agents to be used; oral administration of CELLCEPT® (mycophenolate mofetil) at 15 mg/kg three times per day (maximum daily dose of 3 gm) starting on day +5 to day +35 relative to PBSC administration on day 0, wherein administration of an intravenous formulation of CELLCEPT® may be used until reliable oral intake is established, further comprising intravenous infusion of tacrolimus at a dosage of about 0.03 mg/kg/day, said dosage adjusted for drug interactions with concurrent medications, beginning on day +5 and converted to oral tacrolimus when oral intake is tolerated, wherein the tacrolimus will be continued until day +100 and then may be tapered to none by day +180 if there is no evidence of active GvHD; intravenous infusion of tacrolimus at a dosage of about 0.03 mg/kg/day, said dosage adjusted for drug interactions with concurrent medications, beginning on day +5 and converted to oral tacrolimus when oral intake is tolerated, wherein the tacrolimus will be continued until day +100 and then may be tapered to none by day +180 if there is no evidence of active GvHD; and intravenous infusion of tacrolimus at a dosage of about 0.03 mg/kg/day, said dosage adjusted for drug interactions with concurrent medications, beginning on day +5 and converted to oral tacrolimus when oral intake is tolerated, wherein the tacrolimus will be continued until day +50 and then may be tapered to none by day +100 if there is no evidence of active GvHD.

10. The method of claim 1, further comprising administering a growth factor after day 0, wherein the growth factor treatment regimen is any known in the art.

11. The method of claim 10, wherein the growth factor is granulocyte-colony stimulating factor (G-CSF), the administration of which is selected from day +5 to about day +20; and day +5 to about day +15.

12. The method of claim 11, wherein the G-CSF is administered at about 5 μg/kg on day +5 after transplant until neutrophil engraftment.

13. The method of any of claims 1-12, wherein the method further comprises a combination of any two, three, or four of:

i. administering a preparative chemotherapy regimen prior to day 0;

ii. administering a T cell depletion protocol after day 0;

iii. administering a GvHD prophylaxis regimen after day 0; and

iv. administering a growth factor after day 0.

14. The method of claim 1, wherein the number of infused γδ T cells in the second graft infusion is less than about 5 x 10^8 γδ T cells/kg, about 1 x 10^7 γδ T cells/kg, or about 5 x 10^6 γδ T cells/kg.

15. The method of claim 1, wherein the second graft infusion comprises ≥ 60% γδ T cells; ≥ 60% γδ T cells and ≤ 5% αβ T cells; or ≥ 60% γδ T cells, ≤ 5% αβ T cells, and ≤ 25% NK cells.

16. The method of claim 1, wherein the HSCT is used in conjunction with any condition for which HSCT is used.

17. The method of claim 16, wherein the condition is selected from neoplastic hematological disorders with indication of allogenic transplant; acute lymphoblastic leukemia (ALL) with high-risk features; relapsed ALL; Hodgkin lymphoma (HL); Non-Hodgkin lymphoma (NHL); relapsed HL or NHL wherein remission duration is less than one year; relapsed HL or NHL after previous autologous transplant; HL or NHL with failure to achieve complete response (CR) with chemotherapy; myeloid malignancy; acute myeloid leukemia (AML) with intermediate/high-risk features; relapsed AML; chronic myeloid leukemia (CML) in hematological remission or chronic phase; myeloid disorder; myelodysplastic syndrome (MDS) with intermediate/high-risk features; refractory MDS; MDS with myeloproliferative disorder; primary or secondary MDS with high-risk features; refractory MDS; astrocytoma; ATRT (Atypical Teratoid Rhaboid Tumor); brain stem glioma; choroid plexus tumors, carcinoma and papilloma; craniopharyngioma; desmoplastic infantile astrocytoma; germ cell tumor; medulloblastoma; neurofibromatosis; oligodendroglioma; optic glioma; neuroblastoma; Ewing's Sarcoma; and PNET (Primitive Neuroectodermal Tumor).

18. A method for allogenic hematopoietic stem cell transplantation (HSCT) comprising the steps of:

v. administering to a subject on day 0 a haploidentical hematopoietic stem cell graft infusion comprising peripheral blood stem cells (PBSC);

vi. administering to the subject an agent which provides *in vivo* T cell depletion;

vii. optionally expanding a population of γδ T cells *ex vivo*; and

viii. administering to the subject a second graft infusion comprising T cells enriched in γδ T cells and depleted in αβ T cells.

19. The method of claim 18, wherein the second graft is administered about +7 to about +25 days post PBSC infusion.

20. The method of claim 19, wherein the second graft is administered about +7 to about +9 days post PBSC infusion.

21. The method of claim 18, further comprising administration prior to day 0 any preparative chemotherapy regimen known in the art.

22. The method of claim 21, wherein the preparative chemotherapy regimen is selected from Fludarabine/Busulfan/total body irradiation for myeloid diseases; total body irradiation/cyclophosphamide (TBI/CY) for acute lymphoblastic leukemia (ALL) or aggressive Non-Hodgkin lymphoma (NHL) or Hodgkin lymphoma (HL) in patients ≤ 40 years of age with no major comorbidities; and Fludarabine/total body irradiation for ALL or lymphoma in patients who are older than 40 years, or at any age with major comorbidities that portends high non-relapse mortality (NRM) with high intensity TBI/CY.

23. The method of claim 18, wherein *in vivo* T cell depletion begins after day 0 and comprises the use of any *in vivo* T cell protocol known in the art.

24. The method of claim 23, wherein the *in vivo* T cell depletion protocol is selected from cyclophosphamide treatment between days +1 and +10 relative to administering to a subject on day 0 a minimally manipulated haploidentical hematopoietic stem cell graft infusion comprising PBSC; cyclophosphamide treatment at between 30 mg/kg and 70 mg/kg, or 50 mg/kg; and cyclophosphamide treatment at between 30 mg/kg and 70 mg/kg, or 50 mg/kg at days +3 and +4.

25. The method of claim 18, further comprising administering a Graft vs. Host Disease (GvHD) prophylaxis regimen after day 0, wherein the GvHD regimen is any known in the art.

26. The method of claim 25, wherein the GvHD prophylaxis regimen is selected from providing a decreased number of immunosuppressive agents and/or a reduced concentration of one or more of said agents to be used; oral administration of CELLCEPT® (mycophenolate mofetil) at 15 mg/kg three times per day (maximum daily dose of 3 gm) starting on day +5 to day +35 relative to PBSC administration

on day 0, wherein administration of an intravenous formulation of CELLCEPT® may be used until reliable oral intake is established, further comprising intravenous infusion of tacrolimus at a dosage of about 0.03 mg/kg/day, said dosage adjusted for drug interactions with concurrent medications, beginning on day +5 and converted to oral tacrolimus when oral intake is tolerated, wherein the tacrolimus will be continued until day +100 and then may be tapered to none by day +180 if there is no evidence of active GvHD; intravenous infusion of tacrolimus at a dosage of about 0.03 mg/kg/day, said dosage adjusted for drug interactions with concurrent medications, beginning on day +5 and converted to oral tacrolimus when oral intake is tolerated, wherein the tacrolimus will be continued until day +100 and then may be tapered to none by day +180 if there is no evidence of active GvHD; and intravenous infusion of tacrolimus at a dosage of about 0.03 mg/kg/day, said dosage adjusted for drug interactions with concurrent medications, beginning on day +5 and converted to oral tacrolimus when oral intake is tolerated, wherein the tacrolimus will be continued until day +50 and then may be tapered to none by day +100 if there is no evidence of active GvHD.

27. The method of claim 18, further comprising administering a growth factor after day 0, wherein the growth factor treatment regimen is any known in the art.

28. The method of claim 27, wherein the growth factor is granulocyte-colony stimulating factor (G-CSF), the administration of which is selected from day +5 to about day +20; and day +5 to about day +15.

29. The method of claim 28, wherein the G-CSF is administered at about 5 μg/kg on day +5 after transplant until neutrophil engraftment.

30. The method of any of claims 18-29, wherein the method further comprises a combination of any two, three, or four of:

v. administering a preparative chemotherapy regimen prior to day 0;

vi. administering a T cell depletion protocol after day 0;

vii. administering a GvHD prophylaxis regimen after day 0; and

viii. administering a growth factor after day 0.

31. The method of claim 18, wherein the number of infused γδ T cells in the second graft infusion is less than about 5 x 10^8 γδ T cells/kg, about 1 x 10^7 γδ T cells/kg, or about 5 x 10^6 γδ T cells/kg.

32. The method of claim 18, wherein the second graft infusion comprises $\geq 60\%$ γδ T cells; $\geq 60\%$ γδ T cells and $\leq 5\%$ αβ T cells; or $\geq 60\%$ γδ T cells, $\leq 5\%$ αβ T cells, and $\leq 25\%$ NK cells.

33. The method of claim 18, wherein the HSCT is used in conjunction with any condition for which HSCT is used.

34. The method of claim 33, wherein the condition is selected from neoplastic hematological disorders with indication of allogenic transplant; acute lymphoblastic leukemia (ALL) with high-risk features; relapsed ALL; Hodgkin lymphoma (HL); Non-Hodgkin lymphoma (NHL); relapsed HL or NHL wherein remission duration is less than one year; relapsed HL or NHL after previous autologous transplant; HL or NHL with failure to achieve complete response (CR) with chemotherapy; myeloid malignancy; acute myeloid leukemia (AML) with intermediate/high-risk features; relapsed AML; chronic myeloid leukemia (CML) in hematological remission or chronic phase; myeloid disorder; myelodysplastic syndrome (MDS) with intermediate/high-risk features; refractory MDS; MDS with myeloproliferative disorder; primary or secondary MDS with high-risk features; refractory MDS; astrocytoma; ATRT (Atypical Teratoid Rhaboid Tumor); brain stem glioma; choroid plexus tumors, carcinoma and papilloma; craniopharyngioma; desmoplastic infantile astrocytoma; germ cell tumor; medulloblastoma; neurofibromatosis; oligodendroglioma; optic glioma; neuroblastoma; Ewing's Sarcoma; and PNET (Primitive Neuroectodermal Tumor).