using drugs or antibodies improves responses to cancer immunotherapy. However, the selective elimination or inactivation of Tregs constitutes a major challenge because these cells share the same surface markers as activated conventional, nonsuppressive T cells. Antibody-based approaches, for example, indistinguishably target both Tregs and activated effector T lymphocytes.

[0005] The use of an anti-cancer vaccine containing CRCL (Chaperone Rich Cell Lysate) has been shown to provide immunostimulatory effects. The CRCL is generated from tumor cell lysates by an isoelectric focusing technique. CRCL-treated dendritic cells and macrophages resist Treg inhibition and retain the production of pro-inflammatory cytokines and immunostimulatory potential. However, a direct effect of CRCL on Treg seems to be unlikely since the survival of Treg, FoxP3 expression and immunosuppressive function is maintained following exposure to CRCL.

[0006] Several chemotherapeutic agents (i.e. cyclophosphomide, imatinib mesylate) have been described as the negative modulators of Treg function further improving cancer vaccine efficacy. Adoptive transfer of allogeneic T cells may also increase the efficacy of tumor immunotherapy by providing adjuvant "danger" signals to the host immune cells. This effect partly stems from cytokine production by activated T lymphocytes, which foster the development of protective type-1 immune responses. However, the effects of type I cytokines, including IFN-γ, on Treg have been inconsistent. As an essential effector cytokine for cell-mediated immunity, exogenous or autocrine IFN-γ can negatively regulate Treg generation. In parallel with this concept, other studies have found that IFN-γ enhances activation-induced cell death and that this cytokine might regulate the expansion and persistence of effector T cells by enhancing intrinsic and extrinsic pathway-dependent apoptosis.

SUMMARY

[0006a] In one aspect, there is provided the use of a composition comprising activated Th1 cells and a source of disease antigens in preparation of a drug, wherein the drug is used to suppress immune tolerance and to promote a therapeutic effect in a patient with a disease, wherein the

Th1 cells and the disease antigens are administered at the same location, the activated Th1 cells being allogeneic Th-1 cells and decreasing the immunosuppressive activity of Treg cells, wherein decreasing the activity of the Treg cells: i) reduces the immune tolerance of the disease antigens in the patient, ii) induces a therapeutic effect against the disease in the patient, or iii) reduces the immunosuppressive functions in the patient, and wherein the Treg cells are CD4+CD25+FoxP3+, and the diseases comprises hematological malignancies and cancers that generate tumors present in breast, lung, liver, stomach, skin or pancreas.

[0007] In one ~~aspect~~embodiment, the present ~~invention~~disclosure relates to a method of suppressing immune tolerance of a disease in a patient. The method includes decreasing the immunosuppressive activity of Treg cells by administering a therapeutic composition comprising allogeneic Th1 cells to a

patient, wherein decreasing and/or inhibiting the activity of the Treg cells reduces the immune tolerance of disease antigens in the patient.

[0008] In another ~~aspect~~embodiment, the present ~~invention~~disclosure relates to a method for stimulating a therapeutic immune effect in a patient. The method includes decreasing the immunosuppressive activity of Treg cells by administering a therapeutic composition comprising allogeneic Th1 cells to a patient wherein decreasing and/or inhibiting the activity of the Treg cells induces a therapeutic effect against the disease in the patient.

[0009] In a further ~~aspect~~embodiment, the present ~~invention~~disclosure relates to a method of impairing the immunosuppressive functions in a patient. The method includes decreasing the immunosuppressive activity of Treg cells by administering a therapeutic composition comprising allogeneic Th1 cells to a patient wherein decreasing and/or inhibiting the activity of the Treg cells reduces the immunosuppressive functions in the patient.

[0010] In yet another ~~aspect~~embodiment, the present ~~invention~~disclosure relates to a method of suppressing immune tolerance and promoting a therapeutic effect in patients with a disease comprising administering activated Th1 cells and a source of disease antigens wherein the Th1 cells and the disease antigens are administered at the same location.

[0011] In yet a further ~~aspect~~embodiment, the present ~~invention~~disclosure relates to a composition comprising a source of disease antigens and an adjuvant wherein the disease antigens are contained within chaperone proteins and the adjuvant comprises activated allogeneic Th1 cells.

BRIEF DESCRIPTION OF THE DRAWINGS

[0012] Fig. 1A is a dot plot that shows the effect on FoxP3 expression when naïve T cells are resuspended with different tumor cell lines and treated with activated emTh-1 cells

[0013] Fig. 1B is a bar graph that shows the effect on FoxP3 expression when naïve T cells are resuspended with different tumor cell lines and treated with activated emTh-1 cells.

[0014] Fig. 2A is a dot plot that shows the effect on FoxP3 expression when naïve T cells are cultured with T-cell expander beads either with or without TGF-β1, in the presence or absence of emTh-1 supernatant.

What is claimed is:

1. Use of a composition comprising activated Th1 cells and a source of disease antigens in preparation of a drug, wherein the drug is used to suppress immune tolerance and to promote a therapeutic effect in a patient with a disease,

wherein the Th1 cells and the disease antigens are administered at the same location, the activated Th1 cells being allogeneic Th-1 cells and decreasing the immunosuppressive activity of Treg cells, wherein decreasing the activity of the Treg cells: i) reduces the immune tolerance of the disease antigens in the patient, ii) induces a therapeutic effect against the disease in the patient, or iii) reduces the immunosuppressive functions in the patient, and

wherein the Treg cells are CD4+CD25+FoxP3+, and the diseases comprises hematological malignancies and cancers that generate tumors present in breast, lung, liver, stomach, skin or pancreas.

2. The use according to claim 1, wherein the suppressive activity of the Treg cells is inhibited by decreasing the conversion of naïve T cells (CD4CD25-FoxP3-) to iTreg cells.

3. The use according to claim 2, wherein the suppressive activity of the Treg cells is achieved by inhibition of nTreg cells.

4. The use according to claim 1, wherein the Th1 cells and the disease antigens are administered by intradermal injections; and/or

the activated Th1 cells are administered prior to the source of disease antigens.

5. The use according to claim 1, wherein the Th1 cells are allogeneic emTh-1 cells.

6. The use according to claim 1, wherein the source of disease antigens is chaperone rich cell lysate.

7. The use according to claim 1, wherein the Th1 cells and the source of disease antigens are administered at least 3 times and at intervals of about 3-10 days until the patient exhibits a therapeutic effect.

8. The use according to claim 1, wherein the source of disease antigens is provided in a form of lysates associated with the disease antigens.

9. The use according to claim 1, wherein the composition further comprises:

i) IFNγ;

ii) components that interact and reduce the activity of TGF-beta; or

iii) CD40L.

WHAT IS CLAIMED IS:

1. A method of suppressing immune tolerance of a disease in a patient comprising:

decreasing the immunosuppressive activity of Treg cells by administering a therapeutic composition comprising allogeneic Th1 cells to a patient wherein decreasing and/or inhibiting the activity of the Treg cells reduces the immune tolerance of disease antigens in the patient.

2. The method of claim 1 wherein the Treg cells are CD4+CD25+FoxP3+.

3. The method of claim 1 wherein the suppressive activity of the Treg cells is inhibited by decreasing the conversion of naïve T cells (CD4CD25-FoxP3-) to iTreg cells.

4. The method of claim 1 wherein the suppressive activity of the Treg cells is by inhibition of nTreg cells.

5. The method of claim 1 wherein the therapeutic composition comprises allogeneic emTh1 cells.

6. The method of claim 1 wherein the therapeutic composition further comprises disease antigens or lysates associated with the disease antigens.

7. The method of claim 6 wherein the therapeutic composition further comprises chaperone rich cell lysate of the disease antigens.

8. The method of claim 1 wherein the therapeutic composition further comprises IFNγ.

9. The method of claim 1 wherein the therapeutic composition further comprises components that interact and reduce the activity of TGF-beta.

10. The method of claim 1 wherein the therapeutic composition further comprises CD40L.

11. The method of claim 1 wherein the disease is cancer.

12. The method of claim 1 wherein the disease is an infectious disease.

13. A method for stimulating a therapeutic immune effect in a patient comprising:

decreasing the immunosuppressive activity of Treg cells by administering a therapeutic composition comprising allogeneic Th1 cells to a patient wherein decreasing and/or inhibiting the activity of the Treg cells induces a therapeutic effect against the disease in the patient.

14. The method of claim 13 wherein the Treg cells are CD4+CD25+FoxP3+.

15. The method of claim 13 wherein the suppressive activity of the Treg cells is inhibited by decreasing the conversion of naïve T cells (CD4CD25-FoxP3-) to iTreg cells.

16. The method of claim 13 wherein the suppressive activity of the Treg cells is by inhibition of nTreg cells.

17. The method of claim 13 wherein the therapeutic composition comprises allogeneic emTh-1 cells.

18. The method of claim 13 wherein the therapeutic composition further comprises disease antigens or lysates associated with the disease antigens.

19. The method of claim 18 wherein the therapeutic composition further comprises chaperone rich cell lysate of the disease antigens.

20. The method of claim 13 wherein the therapeutic composition further comprises IFNγ.

21. The method of claim 13 wherein the therapeutic composition further comprises components that interact and reduce the activity of TGF-beta.

22. The method of claim 13 wherein the therapeutic composition further comprises CD40L.

23. The method of claim 13 wherein the disease is cancer.

24. The method of claim 13 wherein the disease is an infectious disease.

25. The method of claim 13 wherein the therapeutic effect comprises promoting anti-tumor function of effector T cells and suppressing immune tolerance of the disease antigens.

26. A method of impairing the immunosuppressive functions in a patient comprising:

decreasing the immunosuppressive activity of Treg cells by administering a therapeutic composition comprising allogeneic Th1 cells to a patient wherein decreasing and/or inhibiting the activity of the Treg cells reduces the immunosuppressive functions in the patient.

27. The method of claim 26 wherein the Treg cells are CD4+CD25+FoxP3+.

28. The method of claim 26 wherein the suppressive activity of the Treg cells is inhibited by decreasing the conversion of naïve T cells (CD4CD25-FoxP3-) to iTreg cells.

29. The method of claim 26 wherein the suppressive activity of the Treg cells is by inhibition of nTreg cells.

30. The method of claim 26 wherein the therapeutic composition comprises allogeneic emTh-1 cells.

31. The method of claim 26 wherein the therapeutic composition further comprises disease antigens or lysates associated with the disease antigens.

32. The method of claim 31 wherein the therapeutic composition further comprises chaperone rich cell lysate of the disease antigens.

33. The method of claim 26 wherein the therapeutic composition further comprises IFNγ.

34. The method of claim 26 wherein the therapeutic composition further comprises components that interact and reduce the activity of TGF-beta.

35. The method of claim 26 wherein the therapeutic composition further comprises CD40L.

36. The method of claim 26 wherein the disease is cancer.

37. A method of suppressing immune tolerance and promoting a therapeutic effect in patients with a disease comprising administering activated Th1 cells and a source of disease antigens wherein the Th1 cells and the disease antigens are administered at the same location.

38. The method of claim 37 wherein the Th1 cells and the disease antigens are administered by intradermal injections.

39. The method of claim 37 wherein the activated Th1 cells are administered prior to the source of disease antigens.

40. The method of claim 37 wherein the Th1 cells are allogeneic emTh-1 cells.

41. The method of claim 37 wherein the source of disease antigens is CRCL.

42. The method of claim 37 wherein the Th1 cells and the source of disease antigens are administered at least 3 times and at intervals of about 3-10 days until the patient exhibits a therapeutic effect.

43. A composition comprising a source of disease antigens and an adjuvant wherein the disease antigens are contained within chaperone proteins and the adjuvant comprises activated allogeneic Th1 cells.