

METHODS AND COMPOSITIONS FOR THE TREATMENT OF MELANOMA

BACKGROUND OF THE INVENTION

[0001] Adoptive cell transfer (ACT) is a form of immunotherapy that involves the transfer of immune cells with antitumor activity into patients. ACT typically involves isolation of lymphocytes with antitumor activity from a patient, culturing the lymphocytes *in vitro* to expand the population, and then infusing the lymphocytes into the cancer-bearing host. Lymphocytes used for adoptive transfer can either be derived from the stroma of resected tumors (e.g., tumor infiltrating lymphocytes), from the lymphatics or lymph nodes, or from the blood. In some cases, the isolated lymphocytes are genetically engineered to express antitumor T cell receptors (TCRs) or chimeric antigen receptors (CARs). The lymphocytes used for infusion can be isolated from a donor (allogeneic ACT), or from the cancer-bearing host (autologous ACT).

SUMMARY

[0002] Provided herein, in certain examples, are methods for adoptive cell transfer for the treatment of melanoma. In some examples, provided are methods for the treatment of melanoma in a subject comprising administering a therapeutically effective amount of immune cells having antitumor activity to the subject, wherein the immune cells are contacted with a protein transduction domain (PTD)-MYC fusion polypeptide prior to administration to the subject. In some examples, the immune cells comprise one or more lymphocytes. In some examples, the one or more lymphocytes comprise T cells and/or B cells. In some examples, the one or more lymphocytes comprise tumor-infiltrating lymphocytes. In some examples, the melanoma is a metastatic melanoma. In some examples, the melanoma is a superficial spreading melanoma, a nodular melanoma, a lentigo maligna melanoma, or an acral melanoma. In some examples, the immune cells are obtained from a donor subject having melanoma. In some examples, donor subject and the subject receiving the immune cells are the same (i.e., autologous ACT). In some examples, donor subject and the subject receiving the immune cells are different (i.e., allogeneic ACT).

[0003] In some examples, the PTD-MYC fusion polypeptide comprises: (i) an HIV TAT protein transduction domain; and (ii) a MYC polypeptide sequence. In some examples, the PTD-MYC fusion polypeptide translocates to the nucleus of the immune cell. In some examples, the PTD-MYC fusion polypeptide exhibits a biological activity of MYC, such as the activation of MYC target genes. In some examples, the fusion peptide comprises SEQ ID NO: 1.

[0004] Described herein, in certain examples are compositions comprising (a) a MYC fusion peptide, comprising (i) a protein transduction domain; (ii) a MYC polypeptide sequence; and (b) one or more primary immune cells isolated from a donor subject that has a melanoma tumor, wherein the one or more primary immune cells are reactive against a melanoma-specific antigen. In some examples, the MYC fusion peptide translocates to the nucleus of the one or more primary immune cells. In some examples, the MYC fusion peptide exhibits a biological activity of MYC. In some examples, the MYC fusion peptide further comprises one or more molecules that link the protein transduction domain and the MYC polypeptide. In some examples, the MYC fusion peptide comprises a MYC fusion peptide with the following general structure:

[0005] protein transduction domain-X-MYC sequence,

[0006] wherein -X- is molecule that links the protein transduction domain and the MYC sequence. In some examples, the protein transduction domain sequence is a TAT protein transduction domain sequence. In some examples, the TAT protein transduction domain sequence is selected from the group consisting of TAT[48-57] and TAT[57-48]. In some examples, the MYC fusion peptide comprises SEQ ID NO: 1. In some examples, the MYC fusion peptide is acetylated. In some examples, the one or more immune cells have antitumor activity against melanoma cells. In some examples, the one or more immune cells comprises one or more lymphocytes. In some examples, the one or more lymphocytes comprises a T cell, a B cell, an NK cell, or any combination thereof. In some examples, the T cell is selected from the group consisting of naïve T cells, CD4+ T cells, CD8+ T cells, memory T cells, activated T cells, anergic T cells, tolerant T cells, chimeric T cells, and antigen-specific T cells. In some examples, the B cells are selected from the

group consisting of naïve B cells, plasma B cells, activated B cells, memory B cells, anergic B cells, tolerant B cells, chimeric B cells, and antigen-specific B cells. In some examples, the one or more lymphocytes is a tumor-infiltrating lymphocyte, T-cell receptor modified lymphocyte, or a chimeric antigen receptor modified lymphocyte. In some examples, the tumor-infiltrating lymphocyte has a CD8+CD25+ signature. In some examples, the tumor-infiltrating lymphocyte has a CD4+CD25+ signature. In some examples, the one or more immune cells comprises a detectable moiety.

[0007] Described herein, in certain examples are methods for treating a melanoma in a subject, comprising administering one or more modified immune cells to the subject in need thereof, wherein the one or more modified immune cells comprise a MYC fusion peptide comprising (i) a protein transduction domain; (ii) a MYC polypeptide sequence and are reactive to a tumor-specific antigen. In some examples, the one or more modified immune cells are derived from primary immune cells isolated from the subject. In some examples, the one or more modified immune cells are derived from primary immune cells isolated from a separate donor subject having the same type of melanoma. In some examples, the one or more modified immune cells are prepared by contacting the primary immune cells *in vitro* with the MYC fusion peptide following isolation. In some examples, the methods further comprise expanding the primary immune cells *in vitro* prior to contacting with the MYC fusion peptide. In some examples, the methods further comprise expanding the primary immune cells following contacting with the MYC fusion peptide. In some examples, the cells are expanded using an anti-CD3 antibody. In some examples, the cells are expanded using an irradiated allogenic feeder cells. In some examples, the cells are expanded in the presence of an exogenous cytokine. In some examples, the cytokine is interleukin-2. In some examples, the MYC fusion peptide translocates to the nucleus of the immune cell. In some examples, the MYC fusion peptide exhibits a biological activity of MYC. In some examples, the MYC fusion peptide further comprises one or more molecules that link the protein transduction domain and the MYC polypeptide. In some examples, the MYC fusion peptide comprises a MYC fusion peptide with the following general structure:

[0008] protein transduction domain-X-MYC sequence,

[0009] wherein -X- is molecule that links the protein transduction domain and the MYC sequence. In some examples, the protein transduction domain sequence is a TAT protein transduction domain sequence. In some examples, the TAT protein transduction domain sequence is selected from the group consisting of TAT[48-57] and TAT[57-48]. In some examples, the MYC fusion peptide comprises SEQ ID NO: 1. In some examples, the MYC fusion peptide is acetylated. In some examples, the one or more modified immune cells have antitumor activity against melanoma cells in the subject. In some examples, the one or more modified immune cells have antitumor activity against melanoma cells in the subject. In some examples, the one or more modified immune cells comprise one or more anergic immune cells. In some examples, the one or more immune cells comprises one or more lymphocytes. In some examples, the one or more lymphocytes comprises a T cell, a B cell, an NK, or any combination thereof. In some examples, the T cell is selected from the group consisting of naïve T cells, CD4+ T cells, CD8+ T cells, memory T cells, activated T cells, anergic T cells, tolerant T cells, chimeric T cells, and antigen-specific T cells. In some examples, the B cells are selected from the group consisting of naïve B cells, plasma B cells, activated B cells, memory B cells, anergic B cells, tolerant B cells, chimeric B cells, and antigen-specific B cells. In some examples, the one or more lymphocytes is a tumor-infiltrating lymphocyte, T-cell receptor modified lymphocyte, or a chimeric antigen receptor modified lymphocyte. In some examples, the lymphocyte has a CD8+CD28-CD152- signature. In some examples, the lymphocyte has a CD8+CD25+ signature. In some examples, the lymphocyte has a CD4+CD25+ signature. In some examples, the methods further comprise isolating the primary immune cells from the donor subject. In some examples, the donor subject has melanoma. In some examples, the one or more modified immune cells are administered intravenously, intraperitoneally, subcutaneously, intramuscularly, or intratumorally. In some examples, the methods further comprise lymphodepleting the subject prior to administration of the one or more modified immune cells. In some examples, the methods further comprise administering a cytokine to the subject. In some examples, the cytokine is administered prior to, during, or subsequent to administration of the one or more modified immune cells. In some examples, the cytokine is selected from a group consisting of interferon α , interferon β , interferon γ , complement C5a, IL-2, TNF α , CD40L, IL12, IL-23, IL15, IL17, CCL1, CCL11, CCL12,

CCL13, CCL14-1, CCL14-2, CCL14-3, CCL15-1, CCL15-2, CCL16, CCL17, CCL18, CCL19, CCL19, CCL2, CCL20, CCL21, CCL22, CCL23-1, CCL23-2, CCL24, CCL25-1, CCL25-2, CCL26, CCL27, CCL28, CCL3, CCL3L1, CCL4, CCL4L1, CCL5, CCL6, CCL7, CCL8, CCL9, CCR10, CCR2, CCR5, CCR6, CCR7, CCR8, CCRL1, CCRL2, CX3CL1, CX3CR, CXCL1, CXCL10, CXCL11, CXCL12, CXCL13, CXCL14, CXCL15, CXCL16, CXCL2, CXCL3, CXCL4, CXCL5, CXCL6, CXCL7, CXCL8, CXCL9, CXCL9, CXCR1, CXCR2, CXCR4, CXCR5, CXCR6, CXCR7 and XCL2. In some examples, the melanoma is metastatic. In some examples, the subject is a human or an animal. In some examples, the methods further comprise administering an additional cancer therapy. In some examples, the additional cancer therapy is selected from among chemotherapy, radiation therapy, immunotherapy, monoclonal antibodies, anti-cancer nucleic acids or proteins, anti-cancer viruses or microorganisms, and any combinations thereof. In some examples, the one or more modified immune cells comprises a detectable moiety.

[0010] In one aspect, the present disclosure refers to a method for preparing modified immune cells for adoptive cell therapy for melanoma in a recipient subject, comprising contacting one or more immune cells in vitro with a MYC fusion polypeptide, wherein the immune cells are from a donor that has been exposed to one or more tumor antigens and wherein the MYC fusion peptide comprises (i) a protein transduction domain; and (ii) a MYC polypeptide sequence and are reactive to a tumor-specific antigen, wherein the one or more modified immune cells have antitumor activity against melanoma cells in the subject. Also described herein, in certain examples are methods for preparing modified immune cells for melanoma therapy, comprising contacting one or more immune cells in vitro with a MYC fusion polypeptide, wherein the immune cells are from a donor that has been exposed to one or more tumor antigens and wherein the MYC fusion peptide comprises (i) a protein transduction domain; (ii) a MYC polypeptide sequence and are reactive to a tumor-specific antigen. In some examples, the one or more modified immune cells are derived from primary immune cells isolated from a subject having melanoma. In some examples, the methods further comprise expanding the primary immune cells in vitro prior to contacting with the MYC fusion peptide. In some examples, the methods further comprise expanding the primary immune cells following contacting with the MYC fusion peptide. In some examples, the cells are expanded using an anti-CD3 antibody. In some examples, the cells are expanded using an irradiated allogenic feeder cells. In some examples, the cells are expanded in the presence of an exogenous cytokine. In some examples, the cytokine is interleukin-2. In some examples, the MYC fusion peptide translocates to the nucleus of the immune cell. In some examples, the MYC fusion peptide exhibits a biological activity of MYC. In some examples, the MYC fusion peptide further comprises one or more molecules that link the protein transduction domain

and the MYC polypeptide. In some examples, the MYC fusion peptide comprises a MYC fusion peptide with the following general structure:

[0011] protein transduction domain-X-MYC sequence,

[0012] wherein -X- is molecule that links the protein transduction domain and the MYC sequence. In some examples, the protein transduction domain sequence is a TAT protein transduction domain sequence. In some examples, the TAT protein transduction domain sequence is selected from the group consisting of TAT[48-57] and TAT[57-48]. In some examples, the MYC fusion peptide comprises SEQ ID NO: 1. In some examples, the MYC fusion peptide is acetylated. In some examples, the one or more modified immune cells have antitumor activity. In some examples, the one or more modified immune cells have antitumor activity against melanoma cells in the subject. In some examples, the one or more modified immune cells comprise one or more anergic immune cells. In some examples, the one or more immune cells comprises one or more lymphocytes. In some examples, the one or more lymphocytes comprises a T cell, a B cell, an NK, or any combination thereof. In some examples, the T cell is selected from the group consisting of naïve T cells, CD4+ T cells, CD8+ T cells, memory T cells, activated T cells, anergic T cells, tolerant T cells, chimeric T cells, and antigen-specific T cells. In some examples, the B cells are selected from the group consisting of naïve B cells, plasma B cells, activated B cells, memory B cells, anergic B cells, tolerant B cells, chimeric B cells, and antigen-specific B cells. In some examples, the one or more lymphocytes is a tumor-infiltrating lymphocyte, T-cell receptor modified lymphocyte, or a chimeric antigen receptor modified lymphocyte. In some examples, the lymphocyte has a CD8+CD28-CD152- signature. In some examples, the lymphocyte has a CD8+CD25+ signature. In some examples, the lymphocyte has a CD4+CD25+ signature.

[0013] Also described herein, in certain examples, are compositions comprising: (a) one or more isolated primary immune cells that have been exposed to a melanoma cell line; and (b) a MYC fusion peptide, comprising (i) a protein transduction domain; (ii) a MYC polypeptide sequence; wherein the one or more primary immune cells are reactive against a melanoma-specific antigen.

[0014] Also described herein, in certain examples, are any of the aforementioned compositions for use in treating a melanoma. Also described herein, in certain examples, are any of the aforementioned compositions for use in the manufacture of a medicament for use in treating a melanoma.

[0015] Also described herein, in certain examples, are methods for increasing the efficacy of adoptive cell therapy or T-cell therapy in a subject comprising administering any of the aforementioned compositions.

[0015a] In one aspect, the present disclosure refers to use of a composition in the manufacture of a medicament for use in adoptive cell therapy for treating a melanoma in a recipient subject, wherein the composition comprises:

(a) a MYC fusion peptide, comprising (i) a protein transduction domain; and (ii) a MYC polypeptide sequence; and

(b) one or more primary immune cells isolated from a donor subject that has a melanoma tumor, wherein the one or more primary immune cells are reactive against a melanoma-specific antigen.

[0015b] In another aspect, the present disclosure refers to use of a composition in the manufacture of a medicament for use in adoptive cell therapy for treating a melanoma in a recipient subject, wherein the composition comprises:

(a) one or more isolated primary immune cells that have been exposed to a melanoma cell line; and

(b) a MYC fusion peptide, comprising (i) a protein transduction domain; and (ii) a MYC polypeptide sequence;

wherein the one or more primary immune cells are reactive against a melanoma-specific antigen.

[0016] Also described herein, in certain examples, are modified tumor-infiltrating lymphocytes comprising a MYC fusion peptide, comprising (i) a protein transduction domain; (ii) a MYC polypeptide sequence. In some examples, the tumor-infiltrating lymphocytes are derived from primary tumor-infiltrating lymphocytes isolated from a subject that has cancer (e.g., melanoma).

[0017] Also described herein, in certain examples, are lymphocytes comprising a chimeric antigen receptor and a MYC fusion peptide, comprising (i) a protein transduction domain; (ii) a MYC polypeptide sequence. In some examples, the lymphocytes are derived from primary lymphocytes isolated from a subject that has cancer (e.g., melanoma).

[0018] Also described herein, in certain examples, are methods for preparing a composition for adoptive cell therapy comprising contacting one or more primary immune cells with MYC fusion peptide, comprising (i) a protein transduction domain; (ii) a MYC polypeptide sequence, wherein one or more primary immune cells are isolated from a patient having melanoma, and wherein one or more primary immune cells are reactive to a melanoma-specific antigen. In one aspect, the present disclosure refers to a method for preparing a composition for adoptive cell therapy for use in treating a melanoma in a recipient subject, the method comprising contacting one or more primary immune cells in vitro with MYC fusion peptide, comprising (i) a protein transduction domain; and (ii) a MYC polypeptide sequence, wherein one or more primary immune cells are isolated from a patient having melanoma, and wherein one or more primary immune cells are reactive to a melanoma-specific antigen.

[0019] Also provided are kits comprising the MYC-fusion polypeptides and/or MYC-fusion polypeptide-modified immune cells provided herein for use in treating a melanoma. In some examples, the kit comprises one or more reagents for the detection of the administered MYC-fusion polypeptides and/or MYC-fusion polypeptide-modified immune cells. In some examples, the kit comprises cells for treatment with a MYC-fusion polypeptide provided herein, for example, hematopoietic stem cells, donor leukocytes, T

cells, or NK cells. In some examples, the kit comprises associated instructions for using the MYC-fusion polypeptides and/or MYC-fusion polypeptide-modified immune cells.

BRIEF DESCRIPTION OF THE DRAWINGS

[0020] FIG. 1 illustrates results for survival of melanoma tumor-bearing mice following infusion of lymphocytes from tumor -bearing donor mice treated with TAT-MYC for 1 hour. Mice were treated with TAT-MYC lymphocytes, lymph cells treated with a control protein or left untreated. Day of death recorded with day of treatment as Day 0.

[0021] FIG. 2 illustrates results for survival of melanoma tumor-bearing mice following infusion of lymphocytes from tumor -bearing donor mice treated with TAT-MYC (repeat of experiment shown in Fig. 1). Mice were treated with TAT-MYC lymphocytes, lymph cells treated with a control protein or left untreated. Day of death recorded with day of treatment as Day 0.

[0022] FIG. 3 illustrates results for survival of melanoma tumor-bearing mice following infusion of different amounts of lymphocytes from tumor-bearing donor mice treated with TAT-MYC. Mice were treated with TAT-MYC lymphocytes, lymph cells treated with a control protein or left untreated. Day of death recorded with day of treatment as Day 0.

[0023] FIG. 4 illustrates results for survival of melanoma tumor-bearing mice following infusion of different amounts of lymphocytes from tumor-bearing donor mice treated with TAT-MYC. Mice were treated with TAT-MYC lymphocytes, lymph cells treated with a control protein or left untreated. Day of death recorded with day of treatment as Day 0.

DETAILED DESCRIPTION OF THE INVENTION

[0024] The present disclosure is not to be limited in terms of the particular embodiments described in this application, which are intended as single illustrations of individual aspects of the disclosure. All the various embodiments of the present disclosure will not be described herein. Many modifications and variations of the disclosure can be made without departing from its spirit and scope, as will be apparent to those skilled in the art. Functionally equivalent methods and apparatuses within the scope of the disclosure, in addition to those

WHAT IS CLAIMED IS:

1. Use of a composition in the manufacture of a medicament for use in adoptive cell therapy for treating a melanoma in a recipient subject, wherein the composition comprises:
 - (a) a MYC fusion peptide, comprising (i) a protein transduction domain; and (ii) a MYC polypeptide sequence; and
 - (b) one or more primary immune cells isolated from a donor subject that has a melanoma tumor, wherein the one or more primary immune cells are reactive against a melanoma-specific antigen.
2. The use of claim 1, wherein the MYC fusion peptide translocates to the nucleus of the one or more primary immune cells.
3. The use of any one of claims 1-2, wherein the MYC fusion peptide exhibits a biological activity of MYC.
4. The use of any one of claims 1-3, wherein the MYC fusion peptide further comprises one or more molecules that link the protein transduction domain and the MYC polypeptide.
5. The use of any one of claims 1-4, wherein the MYC fusion peptide comprises a MYC fusion peptide with the following general structure:

protein transduction domain-X-MYC sequence,
wherein -X- is molecule that links the protein transduction domain and the MYC sequence.
6. The use of any one of claims 1-5, wherein the protein transduction domain sequence is a TAT protein transduction domain sequence.
7. The use of claim 6, wherein the TAT protein transduction domain sequence is selected from the group consisting of TAT[48-57] and TAT[57-48].

8. The use of any one of claims 1-7, wherein the MYC fusion peptide comprises SEQ ID NO: 1.
9. The use of any one of claims 1-8, wherein the MYC fusion peptide is acetylated.
10. The use of any one of claims 1-9, wherein the one or more immune cells have antitumor activity against melanoma cells.
11. The use of any one of claims 1-10, wherein the one or more immune cells comprise one or more lymphocytes.
12. The use of claim 11, wherein the one or more lymphocytes comprise a T cell, a B cell, an NK cell, or any combination thereof.
13. The use of claim 12, wherein the T cell is selected from the group consisting of a naïve T cell, CD4+ T cell, CD8+ T cell, memory T cell, activated T cell, anergic T cell, tolerant T cell, chimeric T cell, and antigen-specific T cell.
14. The use of claim 12, wherein the B cell is selected from the group consisting of a naïve B cell, plasma B cell, activated B cell, memory B cell, anergic B cell, tolerant B cell, chimeric B cell, and antigen-specific B cell.
15. The use of any one of claims 11-14, wherein the one or more lymphocytes are a tumor-infiltrating lymphocyte, T-cell receptor modified lymphocyte, or a chimeric antigen receptor modified lymphocyte.
16. The use of claim 15, wherein the tumor-infiltrating lymphocyte has a CD8+CD28-CD152- signature, a CD8+CD25+ signature, or a CD4+CD25+ signature..

17. The use of any one of claims 1-16, wherein the one or more immune cells comprise a detectable moiety.
18. The use of any one of claims 11-17, wherein the one or more immune cells are derived from primary immune cells isolated from the recipient subject.
19. The use of any one of claims 1-17, wherein the one or more immune cells are derived from primary immune cells isolated from a separate donor subject having the same type of melanoma.
20. The use of any one of claims 18-19, wherein the one or more immune cells are prepared by contacting the primary immune cells in vitro with the MYC fusion peptide following isolation.
21. The use of claim 20, wherein the primary immune cells are expanded in vitro prior to contacting with the MYC fusion peptide.
22. The use of claim 20, wherein the primary immune cells are expanded following contacting with the MYC fusion peptide.
23. The use of any one of claims 21-22, wherein the cells are expanded using an anti-CD3 antibody.
24. The use of any one of claims 21-23, wherein the cells are expanded using an irradiated allogenic feeder cells.
25. The use of any one of claims 21-24, wherein the cells are expanded in the presence of an exogenous cytokine.
26. The use of claim 25, wherein the cytokine is interleukin-2.

27. The use of any one of claims 18-26, wherein the one or more immune cells are formulated to be administered intravenously, intraperitoneally, subcutaneously, intramuscularly, or intratumorally.
28. The use of any one of claims 18-27, wherein the recipient subject is lymphodepleted prior to administration of the one or more immune cells.
29. The use of any one of claims 18-28, wherein the recipient subject has been administered a cytokine prior to, during, or subsequent to administration of the one or more immune cells.
30. The use of claim 29, wherein the cytokine is selected from a group consisting of interferon α , interferon β , interferon γ , complement C5a, IL-2, TNF α , CD40L, IL12, IL-23, IL15, IL17, CCL1, CCL11, CCL12, CCL13, CCL14-1, CCL14-2, CCL14-3, CCL15-1, CCL15-2, CCL16, CCL17, CCL18, CCL19, CCL19, CCL2, CCL20, CCL21, CCL22, CCL23-1, CCL23-2, CCL24, CCL25-1, CCL25-2, CCL26, CCL27, CCL28, CCL3, CCL3L1, CCL4, CCL4L1, CCL5, CCL6, CCL7, CCL8, CCL9, CCR10, CCR2, CCR5, CCR6, CCR7, CCR8, CCRL1, CCRL2, CX3CL1, CX3CR, CXCL1, CXCL10, CXCL11, CXCL12, CXCL13, CXCL14, CXCL15, CXCL16, CXCL2, CXCL3, CXCL4, CXCL5, CXCL6, CXCL7, CXCL8, CXCL9, CXCL9, CXCR1, CXCR2, CXCR4, CXCR5, CXCR6, CXCR7 and XCL2.
31. The use of any one of claims 18-30, wherein the melanoma is metastatic.
32. The use of any one of claims 18-31, wherein the recipient subject is a human or a non-human animal.
33. The use of any one of claims 18-32, wherein the recipient subject has been administered an additional cancer therapy.

34. The use of claim 33, wherein the additional cancer therapy is selected from among chemotherapy, radiation therapy, immunotherapy, monoclonal antibodies, anti-cancer nucleic acids or proteins, anti-cancer viruses or microorganisms, and any combinations thereof
35. A method for preparing modified immune cells for adoptive cell therapy for melanoma in a recipient subject, comprising contacting one or more immune cells in vitro with a MYC fusion polypeptide, wherein the immune cells are from a donor that has been exposed to one or more tumor antigens and wherein the MYC fusion peptide comprises (i) a protein transduction domain; and (ii) a MYC polypeptide sequence and are reactive to a tumor-specific antigen, wherein the one or more modified immune cells have antitumor activity against melanoma cells in the subject.
36. The method of claim 35, wherein the one or more modified immune cells are derived from primary immune cells isolated from a subject having melanoma.
37. The method of any one of claims 35-36, further comprising expanding the primary immune cells in vitro prior to contacting with the MYC fusion peptide.
38. The method of any one of claims 35-36, further comprising expanding the primary immune cells following contacting with the MYC fusion peptide.
39. The method of any one of claims 35-38, wherein the cells are expanded using an anti-CD3 antibody.
40. The method of any one of claims 35-39, wherein the cells are expanded using an irradiated allogenic feeder cells.
41. The method of any one of claims 35-40, wherein the cells are expanded in the presence of an exogenous cytokine.
42. The method of claim 41, wherein the cytokine is interleukin-2.

43. The method of any one of claims 35-42, wherein the MYC fusion peptide translocates to the nucleus of the immune cell.
44. The method of any one of claims 35-43, wherein the MYC fusion peptide exhibits a biological activity of MYC.
45. The method of any one of claims 35-44, wherein the MYC fusion peptide further comprises one or more molecules that link the protein transduction domain and the MYC polypeptide.
46. The method of any one of claims 35-45, wherein the MYC fusion peptide comprises a MYC fusion peptide with the following general structure:
protein transduction domain-X-MYC sequence,
wherein -X- is molecule that links the protein transduction domain and the MYC sequence.
47. The method of any one of claims 35-46, wherein the protein transduction domain sequence is a TAT protein transduction domain sequence.
48. The method of claim 47, wherein the TAT protein transduction domain sequence is selected from the group consisting of TAT[48-57] and TAT[57-48].
49. The method of any one of claims 35-48, wherein the MYC fusion peptide comprises SEQ ID NO: 1.
50. The method of any one of claims 35-49, wherein the MYC fusion peptide is acetylated.
51. The method of any one of claims 35-50, wherein the one or more modified immune cells have antitumor activity.

52. The method of any one of claims 35-51, wherein the one or more modified immune cells comprise one or more anergic immune cells.
53. The method of any one of claims 35-52, wherein the one or more immune cells comprises one or more lymphocytes.
54. The method of claim 53, wherein the one or more lymphocytes comprise a T cell, a B cell, an NK, or any combination thereof.
55. The method of claim 54, wherein the T cell is selected from the group consisting of a naïve T cell, CD4+ T cell, CD8+ T cell, memory T cell, activated T cell, anergic T cell, tolerant T cell, chimeric T cell, and antigen-specific T cell.
56. The method of claim 54, wherein the B cell is selected from the group consisting of a naïve B cell, plasma B cell, activated B cell, memory B cell, anergic B cell, tolerant B cell, chimeric B cell, and antigen-specific B cell.
57. The method of claim 53, wherein the one or more lymphocytes comprise a tumor-infiltrating lymphocyte, T-cell receptor modified lymphocyte, or a chimeric antigen receptor modified lymphocyte.
58. The method of claim 53, wherein the lymphocyte has a CD8+CD28-CD152- signature, a CD8+CD25+ signature, or a CD4+CD25+ signature.
59. A method for preparing a composition for adoptive cell therapy for use in treating a melanoma in a recipient subject, the method comprising contacting one or more primary immune cells in vitro with MYC fusion peptide, comprising (i) a protein transduction domain; and (ii) a MYC polypeptide sequence, wherein one or more primary immune cells are isolated from a patient having melanoma, and wherein one or more primary immune cells are reactive to a melanoma-specific antigen.

60. Use of a composition in the manufacture of a medicament for use in adoptive cell therapy for treating a melanoma in a recipient subject, wherein the composition comprises:

- (a) one or more isolated primary immune cells that have been exposed to a melanoma cell line; and
- (b) a MYC fusion peptide, comprising (i) a protein transduction domain; and (ii) a MYC polypeptide sequence;

wherein the one or more primary immune cells are reactive against a melanoma-specific antigen.