

CLAIMS:

1. A pharmaceutical composition that comprises a T cell comprising a modified DNAM-1 polypeptide and a pharmaceutically acceptable carrier, wherein:
 - the modified DNAM-1 polypeptide exhibits increased retention on the surface of the cell compared to a wild-type DNAM-1 polypeptide;
 - wherein the DNAM-1 polypeptide comprises at least one modification selected from:
 - the AP-2 binding motif YXXF at positions corresponding to positions 325-328 of SEQ ID NO: 1, wherein the modification abolishes the AP-2 binding motif YXXF;
 - the AP-2 binding motif EXXXLF at positions corresponding to positions 282-287 of SEQ ID NO: 1, wherein the modification abolishes the AP-2 binding motif EXXXLF; and/or
 - the Cbl-B binding motif ((D/N)XpY) at positions corresponding to positions 320-322 of SEQ ID NO: 1, wherein the modification abolishes the Cbl-B binding motif; and
 - the T cell is a human T cell.
2. The pharmaceutical composition of claim 1, wherein the DNAM-1 polypeptide comprises a modification of a tyrosine at a position corresponding to position 322 of SEQ ID NO: 1.
3. The pharmaceutical composition of claim 3, wherein the tyrosine is substituted with a phenylalanine.
4. The pharmaceutical composition of any one of claims 1-3, wherein the DNAM-1 polypeptide:
 - lacks all or a portion of the cytoplasmic domain corresponding to amino acid residues 277 to 336 of SEQ ID NO: 1;
 - comprises all or a portion of the extracellular domain corresponding to amino acid residues 19 to 248 to 336 of SEQ ID NO: 1;
 - comprises an IgG1 domain; and/or
 - comprises an IgG2 domain.

5. The pharmaceutical composition of any one of claims 1 to 4, wherein the DNAM-1 polypeptide comprises a sequence of amino acids set forth in any one of SEQ ID NOs: 5-9 or 21-30, or a sequence having at least or about 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% sequence identity thereto, wherein the DNAM-1 polypeptide does not comprise the same sequence as a wild-type DNAM-1 polypeptide.
6. The pharmaceutical composition of any one of claims 1 to 5, wherein the T cell is a CD8+ T cell, a CD4+ T cell, and/or an $\alpha\beta$ T cell or a $\gamma\delta$ T cell.
7. The pharmaceutical composition of any one of claims 1 to 7, comprising a recombinant TCR and/or a chimeric antigen receptor (CAR).
8. The pharmaceutical composition of any one of claims 1-7, further comprising a chemotherapeutic agent (for example, an immune checkpoint inhibitor) or an anti-infective agent.
9. A pharmaceutical composition that comprises a T cell population produced by a method comprising: obtaining a sample of T cells from a subject; selecting DNAM+ T cells from the sample; and expanding the DNAM+ T cells to produce a T cell population for adoptive T cell therapy, and optionally further comprising engineering the DNAM+ T cells to express a CAR or a transgenic TCR.
10. The use of a T cell of any one of claims 1 to 7, the pharmaceutical composition of claim 8, or the T cell population of claim 9 in the manufacture of a medicament for increasing immune function in a subject.
11. The use of a T cell of any one of claims 1 to 7, the pharmaceutical composition of claim 8, or the T cell population of claim 9 in the manufacture of a medicament for use in treating cancer or an infection in a subject.
12. The use of claim 11, wherein the T cell of any one of claims 1 to 7, the pharmaceutical composition of claim 8, or the T cell population of claim 9 is to be administered with a chemotherapeutic agent (e.g., an immune checkpoint inhibitor) to the subject.

13. The use of claim 12, wherein the immune checkpoint inhibitor is selected from among a CTLA-4, PD-1, and PD-L1 inhibitor.
14. The use of any one of claims 11 to 13, wherein the cancer is skin cancer (e.g., melanoma), lung cancer, breast cancer, ovarian cancer, gastric cancer, bladder cancer, pancreatic cancer, endometrial cancer, colon cancer, kidney cancer, esophageal cancer, prostate cancer, colorectal cancer, glioblastoma, head and neck cancer, neuroblastoma, or hepatocellular carcinoma.
15. The method of any one of claims 10 to 14, wherein the T cell is autologous or allogeneic.
16. A modified DNAM-1 polypeptide comprising one or more of the following:
 - a modification of the AP-2 binding motif YXXF at positions corresponding to positions 325-328 of SEQ ID NO: 1, wherein the modification abolishes the AP-2 binding motif YXXF;
 - a modification of the AP-2 binding motif EXXXLF at positions corresponding to positions 282-287 of SEQ ID NO: 1, wherein the modification abolishes the AP-2 binding motif EXXXLF;
 - a modification of the Cbl-b binding motif ((D/N)XpY) at positions corresponding to positions 320-322 of SEQ ID NO: 1, wherein the modification abolishes the Cbl-B binding motif; and/or
 - a modification (e.g., an amino acid substitution or deletion) of the lysine at the position corresponding to position 295 and/or the lysine at the position corresponding to position 333 of SEQ ID NO: 1.
17. The modified DNAM-1 polypeptide of claim 16, having increased surface retention when expressed in T cell compared to a wild-type DNAM-1 polypeptide when expressed in a T cell.
18. The modified DNAM-1 polypeptide of claim 16 or claim 17, comprising a sequence of amino acids set forth in any one of SEQ ID NOs: 5-9 or 21-30, or a sequence having at least or about 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99%

sequence identity thereto, wherein the DNAM-1 polypeptide does not comprise the same sequence as a wildtype DNAM-1 polypeptide.