

CLAIMS:

1. A T cell, comprising a modified DNAM-1 polypeptide, wherein:
the modified DNAM-1 polypeptide exhibits increased retention on the surface of the cell compared to a wild-type DNAM-1 polypeptide; and
the T cell is a human T cell.
2. The T cell 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, preferably wherein the tyrosine is substituted with a phenylalanine.
3. The T cell of claim 1 or claim 2, 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.
4. The T cell of any one of claims 1-3, wherein the DNAM-1 polypeptide:
 - lacks all or a portion of the cytoplasmic domain;
 - comprises all or a portion of the extracellular domain;
 - comprises the IgG1 domain; and/or
 - comprises the IgG2 domain.
5. The T cell 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 T cell 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 T cell of any one of claims 1 to 7, comprising a recombinant TCR and/or a chimeric antigen receptor (CAR).
8. A pharmaceutical composition, comprising the T cell of any one of claims 1-7 and a pharmaceutically acceptable carrier, and optionally a chemotherapeutic agent (for example, an immune checkpoint inhibitor) or an anti-infective agent.

9. 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. A method of increasing immune function or treating cancer in a subject, comprising administering to the subject 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.
11. The method of claim 10, further comprising administering a chemotherapeutic agent (e.g., an immune checkpoint inhibitor) to the subject.
12. The method of claim 11, wherein the immune checkpoint inhibitor is selected from among a CTLA-4, PD-1, and PD-L1 inhibitor.
13. The method of any one of claims 10 to 12, 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.
14. The method of any one of claims 10 to 13, wherein the T cell is autologous or allogeneic.
15. Use of 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, for the preparation of a medicament for treating cancer or an infection.
16. Use of 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, for the preparation of a medicament for enhancing immune function in a subject.
17. A method for predicting the likelihood that a subject with cancer will respond to therapy with an immune checkpoint inhibitor, comprising detecting the number or percentage of DNAM-1+ CD8+ T cells in a sample (e.g., a tumour sample) from the subject, and comparing the number or percentage of DNAM-1+ CD8+ cells in the sample from the subject to a reference level or amount.
18. 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.
19. The modified DNAM-1 polypeptide of claim 18, having increased surface retention when expressed in T cell compared to a wild-type DNAM-1 polypeptide when expressed in a T cell.
20. The modified DNAM-1 polypeptide of claim 18 or claim 19, 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 wild-type DNAM-1 polypeptide.