

WHAT IS CLAIMED IS:

1. Use of an immune cell in the preparation of a medicament for treating a cancer associated with expression of a tumor antigen or target in a subject, wherein the immune cells comprise a CAR or TCR to the tumor antigen or target, and a membrane-bound IL-18, and wherein the immune cells comprise a T cell or NK cell.
2. The use of claim 1, wherein the membrane-bound IL-18 is obtained by expression of a nucleic acid comprising a nucleotide sequence encoding a polypeptide comprising a signal peptide, interleukin-18 (IL-18) and an interleukin-18 receptor (IL-18R) subunit.
3. The use of claim 2, wherein the nucleic acid comprises a nucleotide sequence selected from the group consisting of SEQ ID NOs: 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38 and 40.
4. The use of any one of claims 1-3, wherein the tumor antigen or target is selected from the group consisting of 2B4 (CD244), 4-1BB, 5T4, A33 antigen, adenocarcinoma antigen, adrenoceptor beta 3 (ADRB3), A kinase anchor protein 4 (AKAP-4), alpha- fetoprotein (AFP), anaplastic lymphoma kinase (ALK), Androgen receptor, B7H3 (CD276), β 2-integrins, BAFF, B-lymphoma cell, B cell maturation antigen (BCMA), bcr-abl (oncogene fusion protein consisting of breakpoint cluster region (BCR) and Abelson murine leukemia viral oncogene homolog 1 (Abl)), BhCG, bone marrow stromal cell antigen 2 (BST2), CCCTC-Binding Factor (Zinc Finger Protein)-Like (BORIS or Brother of the Regulator of Imprinted Sites), BST2, C242 antigen, 9-0-acetyl-CA19-9 marker, CA-125, CAEX, calreticulin, carbonic anhydrase 9 (CAIX), C-MET, CCR4, CCR5, CCR8, CD2, CD3, CD4, CD5, CD8, CD7, CD10, CD16, CD19, CD20, CD22, CD23 (IgE receptor), CD24, CD25, CD27, CD28, CD30 (TNFRSF8), CD33, CD34, CD38, CD40, CD40L, CD41, CD44, CD44V6, CD49f, CD51, CD52, CD56, CD63, CD70, CD72, CD74, CD79a, CD79b, CD80, CD84, CD96, CD97, CD100, CD123, CD125, CD133, CD137, CD138, CD150, CD152 (CTLA-4), CD160, CD171, CD179a, CD200, CD221, CD229, CD244, CD272 (BTLA), CD274 (PD-L1, B7H1), CD279 (PD-1), CD352, CD358, CD300 molecule-like family member f (CD300LF), Carcinoembryonic antigen (CEA), claudin 6 (CLDN6), C-type lectin-like molecule- 1 (CLL-1 or CLECL1), C-type lectin domain family 12 member A (CLEC12A), a cytomegalovirus (CMV) infected cell antigen, CNT0888, CRTAM (CD355), CS-1 (also referred to as CD2 subset 1, CRACC, CD319, and 19A24), CTLA-4, Cyclin B 1, chromosome X open reading frame 61 (CXORF61), Cytochrome P450 1B 1

(CYP1B1), DNAM-1 (CD226), desmoglein 4, DR3, DR5, E-cadherin neoepitope, epidermal growth factor receptor (EGFR), EGF1R, epidermal growth factor receptor variant III (EGFRvIII), epithelial glycoprotein-2 (EGP-2), epithelial glycoprotein-40 (EGP-40), EGF-like module-containing mucin-like hormone receptor-like 2 (EMR2), elongation factor 2 mutated (ELF2M), endosialin, Epithelial cell adhesion molecule (EPCAM), ephrin type-A receptor 2 (EphA2), Ephrin B2, receptor tyrosine-protein kinases erb-B2,3,4 (erb-B2,3,4), ERBB, ERBB2 (Her2/neu), ERG (transmembrane protease, serine 2 (TMPRSS2) ETS fusion gene), ETA, ETS translocation-variant gene 6, located on chromosome 12p (ETV6-AML), Fc fragment of IgA receptor (FCAR or CD89), fibroblast activation protein alpha (FAP), FBP, Fc receptor-like 5 (FcRL5), fetal acetylcholine receptor (AChR), fibronectin extra domain-B, Fms-Like Tyrosine Kinase 3 (FLT3), folate-binding protein (FBP), folate receptor 1, folate receptor α , Folate receptor β , Fos-related antigen 1, Fucosyl, Fucosyl GM1; GM2, ganglioside G2 (GD2), ganglioside GD3 (aNeu5Ac(2-8)aNeu5Ac(2-3)bDGalp(1-4)bDGlc(1-3)Cer), o-acetyl-GD2 ganglioside (OAcGD2), GATR (TNFRSF 18), GM1, ganglioside GM3, hexasaccharide portion of globoH glycosphingolipid (GloboH), glycoprotein 75, Glypican-3 (GPC3), glycoprotein 100 (gp100), GPNMB, G protein-coupled receptor 20 (GPR20), G protein-coupled receptor class C group 5, member D (GPRC5D), Hepatitis A virus cellular receptor 1 (HAVCR1), human Epidermal Growth Factor Receptor 2 (HER-2), HER2/neu, HER3, HER4, HGF, high molecular weight-melanoma-associated antigen (HMWMAA), human papilloma virus E6 (HPV E6), human papilloma virus E7 (HPV E7), heat shock protein 70-2 mutated (mut hsp70-2), human scatter factor receptor kinase, human Telomerase reverse transcriptase (hTERT), HVEM, ICOS, insulin-like growth factor receptor 1 (IGF-1 receptor), IGF-I, IgG1, immunoglobulin lambda-like polypeptide 1 (IGLL1), IL-6, Interleukin 11 receptor alpha (IL-11R α), IL-13, Interleukin-13 receptor subunit alpha-2 (IL-13R α 2 or CD213A2), insulin-like growth factor I receptor (IGF1-R), integrin α 5 β 1, integrin α v β 3, intestinal carboxyl esterase, κ -light chain, KCS1, kinase insert domain receptor (KDR), KIR, KIR2DL1, KIR2DL2, KIR2DL3, KIR3DL2, KIR-L, KG2D ligands, KIT (CD117), KLRG1, LAGE-1a, LAG3, lymphocyte-specific protein tyrosine kinase (LCK), Leukocyte immunoglobulin-like receptor subfamily A member 2 (LILRA2), legumain, Leukocyte-associated immunoglobulin-like receptor 1 (LAIR1), Lewis(Y) antigen, LeY, LG, LI cell adhesion molecule (LI-CAM), LIGHT, LMP2, lymphocyte antigen 6 complex, LTBR, locus K 9 (LY6K), Ly-6, lymphocyte antigen 75 (LY75), melanoma cancer testis antigen-1 (MAD-CT-1); melanoma cancer testis antigen-2 (MAD-CT-2), MAGE, Melanoma-associated antigen 1 (MAGE-A1), MAGE-A3 melanoma antigen recognized by T cells 1 (MelanA or MART1), MelanA/MART1, Mesothelin, MAGE A3, melanoma inhibitor of apoptosis (ML-IAP),

melanoma-specific chondroitin-sulfate proteoglycan (MCSCP), MORAb-009, MS4A1, Mucin 1 (MUC1), MUC2, MUC3, MUC4, MUC5AC, MUC5b, MUC7, MUC16, mucin CanAg, Mullerian inhibitory substance (MIS) receptor type II, v-myc avian myelocytomatosis viral oncogene neuroblastoma derived homolog (MYCN), N-glycolylneuraminic acid, N-Acetyl glucosaminyl-transferase V (NA17), neural cell adhesion molecule (NCAM), NKG2A, NKG2C, NKG2D, NKG2E ligands, NKR-P 1A, NPC-1C, NTB-A, mammary gland differentiation antigen (NY-BR-1), NY-ESO-1, oncofetal antigen (h5T4), Olfactory receptor 51E2 (OR51E2), OX40, plasma cell antigen, poly SA, proacrosin binding protein sp32 (OY-TES 1), p53, p53 mutant, pannexin 3 (PANX3), prostatic acid phosphatase (PAP), paired box protein Pax-3 (PAX3), Paired box protein Pax-5 (PAX5), prostate carcinoma tumor antigen- 1 (PCTA-1 or Galectin 8), PD-1H, Platelet-derived growth factor receptor alpha (PDGFR-alpha), PDGFR-beta, PDL192, PEN-5, phosphatidylserine, placenta- specific 1 (PLAC1), Polysialic acid, Prostase, prostatic carcinoma cells, prostein, Protease Serine 21 (Testisin or PRSS21), Proteinase3 (PR1), prostate stem cell antigen (PSCA), prostate-specific membrane antigen (PSMA), Proteasome (Prosome, Macropain) Subunit, Beta Type, Receptor for Advanced Glycation Endproducts (RAGE-1), RANKL, Ras mutant, Ras Homolog Family Member C (RhoC), RON, Receptor tyrosine kinase-like orphan receptor 1 (ROR1), renal ubiquitous 1 (RU1), renal ubiquitous 2 (RU2), sarcoma translocation breakpoints, Squamous Cell Carcinoma Antigen Recognized By T Cells 3 (SART3), SAS, SDC1, SLAMF7, sialyl Lewis adhesion molecule (sLe), Siglec-3, Siglec-7, Siglec-9, sonic hedgehog (SHH), sperm protein 17 (SPA17), Stage-specific embryonic antigen-4 (SSEA-4), STEAP, sTn antigen, synovial sarcoma X breakpoint 2 (SSX2), Survivin, Tumor-associated glycoprotein 72 (TAG72), TCR5 γ , TCR α , TCR β , TCR γ Alternate Reading Frame Protein (TARP), telomerase, TIGIT, TNF- α precursor, tumor endothelial marker 1 (TEM1/CD248), tumor endothelial marker 7-related (TEM7R), tenascin C, TGF- β 1, TGF- β 2, transglutaminase 5 (TGS5), angiopoietin-binding cell surface receptor 2 (Tie 2), TIM1, TIM2, TIM3, Tn Ag, TRAIL-R1, TRAIL-R2, Tyrosinase-related protein 2 (TRP-2), thyroid stimulating hormone receptor (TSHR), tumor antigen CTAA16.88, Tyrosinase, uroplakin 2 (UPK2), VEGF-A, VEGFR-1, vascular endothelial growth factor receptor 2 (VEGFR2), and vimentin, Wilms tumor protein (WT1), or X Antigen Family Member 1A (XAGE1).

5. A nucleic acid comprising a nucleotide sequence encoding a polypeptide comprising interleukin-18 (IL-18) and an interleukin-18 receptor (IL-18R) subunit.

6. The nucleic acid of claim 5, wherein the IL-18R subunit sequence comprises an amino acid sequence that is at least 80% identical to amino acid residues 21 to 540 of SEQ ID NO: 6 or amino acid residues 20 to 599 of SEQ ID NO: 8.
7. The nucleic acid of any one of claims 5-6, wherein the polypeptide comprises an amino acid linker connecting IL-18 and the IL-18R subunit.
8. The nucleic acid of claim 7, wherein the amino acid linker comprises a Myc linker sequence, a Whitlow linker sequence, (GGGGS)_n (SEQ ID NO: 9) wherein n is 1-6, or any combination thereof.
9. The nucleic acid of claim 5, wherein the polypeptide comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39 and 41.
10. The nucleic acid of any one of claims 5-9, wherein the polypeptide further comprises an immunoreceptor tyrosine-based activation motif (ITAM).
11. An expression vector comprising the nucleic acid of any one of claims 5-10.
12. A polypeptide encoded by the nucleic acid of any one of claims 5-10.
13. An immune cell comprising a nucleic acid of any one of claims 5-10, an expression vector of claim 11, or a polypeptide of claim 12.
14. The immune cell of claim 13, further comprising a nucleic acid sequence encoding a chimeric antigen receptor (CAR), or a T-cell receptor (TCR) that specifically binds to a tumor antigen.
15. The immune cell of claim 14 comprising a T cell or NK cell.