CLAIMS

What is claimed is

1. At least one recombinant polynucleotide encoding a hybrid chain synthetic antigen receptor (HC-SAR) or a functional variant thereof, the at least one HC-SAR or the functional variant comprising a heterodimer of two T-cell receptor (TCR) constant chains, the heterodimer having one or more non-TCR antigen binding domains that are operably linked to one or both TCR constant chains via optional linkers, wherein at least one TCR constant chain of the HC-SAR is a hybrid TCR constant chain, the hybrid TCR constant chain comprising at least one domain selected from the group consisting of a TCR chain constant domain (C), a TCR chain connecting peptide (ConnP), a TCR chain transmembrane (TM) domain, and a TCR chain cytoplasmic domain (CP) that is heterologous, wherein a heterologous domain is not part of a single naturally occurring polypeptide or protein and/or is not derived from a single naturally occurring polypeptide or protein, and wherein the non-TCR antigen binding domain is selected from the group consisting of

    (A) an antibody;

    (B) an antibody fragment selected from a Fv, a Fab, and a (Fab')2;

    (C) a heavy chain variable region of an antibody (vH domain) and a complementary light chain variable region of the antibody (vL domain) specific for a target antigen, such that one of said vH and vL domains is attached to a first of said two TCR constant chains of and the other of said vH and vL domains is attached to a second of said TCR constant chains;

    (D) a single chain variable fragment (scFv);

    (E) a single domain antibody (SDAB);

    (F) a camelid VHH domain;

    (G) a monomeric variable region of an antibody;

    (H) a non-immunoglobulin antigen binding scaffold;

    (I) the extracellular domain of receptor or a binding fragment thereof;

    (I) a ligand or a binding fragment thereof;

    (J) a bispecific antibody;

    (K) an autoantigen;

    (L) an HLA molecule or a fragment thereof;

(M) a β2M molecule or a fragment thereof; and

(N) an HLA/peptide complex.

2. The at least one recombinant polynucleotide of claim 1, wherein the encoded TCR constant chains of the HC-SAR are selected from the group consisting of:

i) a TCRα constant chain or a hybrid TCRα constant chain with a sequence selected from the group consisting of SEQ ID NO (PRT): 8833-8843, 8844-45, 20378, 18384-18440, 18485-18585, 21961-21986, 23294-23306, 23307-23408, 23420-23465, 23518-23520, 23558-23560, 23579-23581, 23587-89, 23595-97, 23603-05, 23611-13, 23620-22, 23631-33, 23642-44, 23653-55, 23672-73, 23679, 23681, 27936-27946, 27948-49, 27982-83, 27997, 27999, 28003, 28005, 28149-28194, 28217-28317, 28647-28672, 28686-28843, 28864-66, 29277-29286, 29888-89, 32218-32219 or a functional variant, fragment or a homolog which encodes for polypeptides with at least 70% sequence identity thereto;

ii) a TCRβ constant chain or a hybrid TCRβ constant chain with a sequence selected from the group consisting of SEQ ID NO (PRT): 8847-8867, 18259-18304, 18373-18383, 18586-18712, 23674-23675, 23680-23681, 7950-27970, 27980-81, 27984-87, 27998, 28000, 28006, 28008, 28013-28058, 28127-28137, 28318-28444, 28673-28685, 28844-46, 28854-56, 28874-76, 28884-86, 29290-29310, and 32220 or a functional variant, fragment or a homolog thereof with at least 70% sequence identity thereto;

iii) a TCRγ constant chain or a hybrid TCRγ constant chain with a sequence selected from the group consisting of SEQ ID NO (PRT): 8900-8903, 18351-18372, 18441-18462, 18474-18484, 18713-18813, 23676-77, 28105-28115, 28138-28148, 27975-76, 27977-79, 27988-93, 28002, 28010, 28012, 28195-28216, 28445-28545, 28847-51, 28857-61, 28867-28871, 28877-81, 28887-91, 29315-16 and 32222 or a functional variant, fragment or a homolog thereof with at least 70% sequence identity thereto;

iv) a TCRδ constant chain or a hybrid TCRδ with a sequence selected from the group consisting of SEQ ID NO (PRT): 8875, 18305-18350, 18362-18372,

18463-18473, 18814-18914, 23672-73, 32221 or a functional variant, fragment or a homolog thereof with at least 70% sequence identity thereto.

3. The at least one recombinant polynucleotide of claim 1, wherein the encoded HC-SAR comprise one or more of the following characteristics, selected from the group consisting of: **(A)** more than one domain selected from TCR constant domain (C), TCR connecting peptide (ConnP), TCR transmembrane domain (TM), and TCR cytoplasmic domain (CP) is heterologous; **(B)** the ConnP is heterologous to the TM domain, to the constant domain, or to both; **(C)** the TM domain comprises an amino acid sequence selected from SEQ ID NO: 31985–31988 or 31992; **(D)** the TM domain comprises an amino acid sequence selected from SEQ ID NO: 40606–40670 or 40737–40758, or a functional variant with 1–6 amino acid substitutions except at residue positions 7, 12, 17, and 21; **(E)** the TM domain comprises an amino acid sequence selected from SEQ ID NO: 40671–40708, or a functional variant with 1–6 substitutions except at positions 6, 12, and 16; **(F)** both of the TCR constant chains in the HC-SAR are hybrid chains; **(G)** a constant domain of at least one hybrid TCR chain is derived from an immunoglobulin (antibody); **(H)** the constant domains of both hybrid TCR chains are derived from immunoglobulins; **(I)** the at least one TCR constant chain comprises mutations that enhance dimerization of the TCR chains and reduce pairing with endogenous TCR chains (for example, cysteine substitutions forming an interchain disulfide bond); **(J)** one or both of the TCR constant chains are human codon-optimized; **(K)** one or both of the TCR constant chains are of human, mouse, or dog origin; **(L)** one or more non-TCR antigen binding domains are operably linked to the TCR constant chains via linkers; and **(M)** one or more non-scFV autonomous antigen binding domains (AABD) or fragments thereof are operationally linked to the N-terminus or proximate to the N-terminus of one or more non-TCR antigen binding domains via an optional linker, wherein the one or more autonomous antigen binding domains (AABDs) or fragments thereof are selected from the group consisting of: a single vH domain (SVH) or a fragment thereof; a single vL domain (SVL) or a fragment thereof; a vHH domain or a fragment thereof; a single domain antibody or a fragment thereof; a single variable domain of a TCR (svd-TCR) or a fragment thereof; a non-immunoglobulin antigen binding scaffold or a fragment thereof; a ligand-binding

domain of a receptor or a fragment thereof; a receptor-binding domain of a ligand; an autoantigen or a fragment thereof; an adaptor binding domain or a fragment thereof; an adaptor or a fragment thereof; an epitope or a fragment thereof; and an Fc binding domain or a fragment thereof.

4. The at least recombinant polynucleotide of claim 1, wherein the encoded HC-SAR is configured as follows:

a first hybrid chain comprises a first TCR chain transmembrane domain, a non-TCR antigen binding domain and a second TCR chain constant domain, or a functional variant or a fragment thereof, but does not comprise a first TCR chain constant domain; and

a second hybrid TCR chain comprises a second TCR chain transmembrane domain, an optional non-TCR antigen-binding domain, and a first TCR chain constant domain or a functional variant or a fragment thereof, but does not comprise a second TCR chain constant domain;

wherein the first TCR chain constant domain comprises a TCR alpha or a TCR gamma chain constant domain or a functional variant or fragment thereof, the second TCR chain constant domain comprises a TCR beta or a TCR delta chain constant domain or a functional variant or fragment thereof, and the second TCR chain transmembrane domain comprises a TCR beta or a TCR delta chain transmembrane domain or a variant thereof; or

wherein, the first TCR chain constant domain comprises a TCR alpha or a TCR delta chain constant domain or a functional variant or fragment thereof, the first TCR chain transmembrane domain comprises a TCR alpha or a TCR delta chain transmembrane domain or a functional variant thereof, the second TCR chain constant domain comprises a TCR beta or a TCR gamma chain constant domain or a functional variant thereof, and the second TCR chain transmembrane domain comprises a TCR beta or a TCR gamma chain transmembrane domain or a variant thereof.

5. The at least one recombinant polynucleotide of claim 1, wherein the encoded HC-SAR comprises two polypeptide chains configured in one of the following ways:

a) a first polypeptide chain comprising a first antigen-binding domain having a vH antibody domain, a TCR constant domain or a functional variant or fragment thereof, and a first T cell receptor domain (TCRD) having a first transmembrane domain of a first TCR subunit; and
a second polypeptide chain comprising a second antigen-binding domain having a vL antibody domain, a TCR constant domain or a functional variant or fragment thereof, and a second TCRD comprising a second transmembrane domain of a second TCR subunit,

wherein the vH antibody domain of the first antigen-binding domain and the vL antibody domain of the second antigen-binding domain form an antigen-binding module that specifically binds to a target antigen; or

b) a first polypeptide chain comprising a first antigen-binding domain having a vL antibody domain, a TCR constant domain or a functional variant or fragment thereof of a first TCR subunit, and a T cell receptor domain (TCRD) comprising a first transmembrane domain of a second TCR subunit; and
a second polypeptide chain comprising a second antigen-binding domain having a vH antibody domain, a TCR constant domain or a functional variant or fragment thereof of the second TCR subunit, and a second TCRD comprising a second transmembrane domain of the first TCR subunit,

wherein the vH antibody domain of the first antigen-binding domain and the vL antibody domain of the second antigen-binding domain form an antigen-binding module that specifically binds to a target antigen;

wherein (i) the first TCR subunit is a TCR γ chain and the second TCR subunit is a TCR δ or TCR α chain; or (ii) the first TCR subunit is a TCR δ chain and the second TCR subunit is a TCR γ or TCR β chain; or (iii) the first TCR subunit is a TCR α chain and the second TCR subunit is a TCR β or TCRγ chain; or (iv) the first TCR subunit is a TCR β chain, and the second TCR subunit is a TCR α or TCR δ chain; and

wherein optionally the first polypeptide chain further comprises a TCR connecting peptide or a functional variant or fragment thereof, and the second polypeptide chain further comprise a TCR connecting peptide or a functional variant or

fragment thereof, wherein the TCR connecting peptides or functional variants or fragments are located N-terminal to the transmembrane domain; and

wherein optionally one or both connecting peptides are heterologous to the transmembrane domain, to the constant domain, or both; or

c) a first polypeptide chain comprising a first antigen-binding domain having a vH antibody domain, a constant antibody domain, or a functional variant or fragment thereof, and a first T cell receptor domain (TCRD) comprising a first transmembrane domain of a first TCR subunit; and

a second polypeptide chain comprising a second antigen-binding domain having a vL antibody domain, a TCR constant domain or a functional variant or fragment thereof, and a second TCRD comprising a second transmembrane domain of a second TCR subunit,

wherein the vH antibody domain of the first antigen-binding domain and the vL antibody domain of the second antigen-binding domain form an antigen-binding module that specifically binds to a target antigen; or

d) a first polypeptide chain comprising a first antigen-binding domain having a vL antibody domain, a constant antibody domain or a functional variant or fragment thereof, and a T cell receptor domain (TCRD) comprising a first transmembrane domain of a first TCR subunit; and

a second polypeptide chain comprising a second antigen-binding domain having a vH antibody domain, a TCR constant domain or a functional variant or fragment thereof, and a second TCRD comprising a second transmembrane domain of a second TCR subunit,

wherein the vH antibody domain of the first antigen-binding domain and the vL antibody domain of the second antigen-binding domain form an antigen-binding module that specifically binds to a target antigen;

wherein (i) the first TCR subunit is a TCR γ chain and the second TCR subunit is a TCR δ or TCR α chain, or (ii) the first TCR subunit is a TCR δ chain and the second TCR subunit is a TCR γ or TCR β chain, or (iii) the first TCR subunit is a TCRα chain and the second TCR subunit is a TCRβ or TCR γ

chain, or (iv) the first TCR subunit is a TCRβ chain and the second TCR subunit is a TCRα or TCR δ chain; and

wherein optionally the first polypeptide chain further comprises a TCR connecting peptide or a functional variant or fragment thereof and the second polypeptide chain further comprise a TCR connecting peptide or a functional variant or fragment thereof and wherein the TCR connecting peptides or functional variants or fragments are located N-terminal to the transmembrane domain; and

wherein optionally one or both connecting peptides are heterologous to the transmembrane domain, to the constant domain or to both; or

e) a first polypeptide chain comprising a first antigen-binding domain having a vH antibody domain, a first constant antibody domain or a functional variant or fragment thereof, and a first T cell receptor domain (TCRD) comprising a first ConnP, a TM and a CP domain of a first TCR subunit; and

a second polypeptide chain comprising a second antigen-binding domain having a vL antibody domain, a second constant antibody domain or a functional variant or fragment thereof and a second TCRD comprising a second ConnP, TM and CP domains of a second TCR subunit, wherein the vH antibody domain of the first antigen-binding domain and the vL antibody domain of the second antigen-binding domain form an antigen-binding module that specifically binds to a target antigen; or

f) a first polypeptide chain comprising a first antigen-binding domain having a vL antibody domain, a first constant antibody domain or a functional variant or fragment thereof, and a first T cell receptor domain (TCRD) comprising a first ConnP, a TM and a CP domain of a first TCR subunit; and

a second polypeptide chain comprising a second antigen-binding domain comprising a vH antibody domain, a second constant antibody domain or a functional variant or fragment thereof and a second TCRD comprising a second ConnP, TM and CP domains of a second TCR subunit, wherein the vH antibody domain of the first antigen-binding domain and the vL antibody

domain of the second antigen-binding domain form an antigen-binding module that specifically binds to a target antigen; and

wherein optionally i) the ConnP, the TM and the CP domains of the at least one TCR subunits are heterologous; b) the ConnP and the TM of at least one of the TCR subunits are heterologous; c) the ConnP, the TM, and the CP of both TCR subunits are heterologous; d) the ConnP and the TM domains of both of the TCR subunits are heterologous.

6. The at least one recombinant polynucleotide of claim 1, wherein

the first TCR subunit comprises the ConnP of TCRβ and TM of TCRγ and the second TCR subunit is TCRα or TCRδ; or

the first TCR subunit comprises the ConnP of TCRγ and TM of TCRβ and the second TCR subunit is TCRα or TCRδ; or

the first TCR subunit comprises the ConnP of TCRα and TM of TCRδ and the second TCR subunit is TCRβ or TCRγ; or

the first TCR subunit comprises the ConnP of TCRδ and TM of TCRα and the second TCR subunit is TCRβ or TCRγ; or

the first TCR subunit comprises the ConnP of TCRβ and TM of TCRγ and the second TCR subunit comprises the ConnP of TCRα and TM of TCRδ or the ConnP of TCRδ and TM of TCRα; or

the first TCR subunit comprises the ConnP of TCRγ and TM of TCRβ and the second TCR subunit comprises ConnP of TCRα and TM of TCRδ or the ConnP of TCRδ and TM of TCRα; or

the first TCR subunit comprises the ConnP of TCRα and TM of TCRδ and the second TCR subunit comprises ConnP of TCRβ and TM of TCRγ or ConnP of TCRγ and TM of TCRβ; or

the first TCR subunit comprises the ConnP of TCRδ and TM of TCRα and the second TCR subunit comprises ConnP of TCRβ and TM of TCRγ or ConnP of TCRγ and TM of TCRβ.

7. The at least one recombinant polynucleotide of claim 1, wherein the HC-SAR binds to one or more of disease-associated antigens selected from the group consisting of: CD19, CD5, CD123, CD22, CD30, CD171, a CS-1 (CRACC, SLAMF7, CD319, and 19A24), CD45, a C-type lectin-like molecule-1 (CLL-1 or CLECL1), CD33, epidermal growth factor receptor variant III (EGFRviii), ganglioside G2 (GD2), ganglioside GD3, TNF receptor family member B cell maturation (BCMA), Tn antigen ((Tn Ag), prostate-specific membrane antigen (PSMA), Receptor tyrosine kinase-like orphan receptor 1 (ROR1), Fms Like Tyrosine Kinase 3 (FLT3), Tumor-associated glycoprotein 72 (TAG72), CD38, CD44v6, a glycosylated CD43 epitope expressed on acute leukemia or lymphoma but not on hematopoietic progenitors, a glycosylated CD43 epitope expressed on non-hematopoietic cancers, Carcinoembryonic antigen (CEA), Epithelial cell adhesion molecule (EPCAM), B7H3/CD276, KIT (CD117), Interleukin-13 receptor subunit alpha-2 (IL-13Ra2 or CD213A2), Mesothelin, Interleukin 11 receptor alpha (IL-11Ra), prostate stem cell antigen (PSCA), vascular endothelial growth factor receptor 2 (VEGFR2), Lewis(Y) antigen, CD24, Platelet-derived growth factor receptor beta (PDGFR-beta), Stage-specific embryonic antigen-4 (SSEA-4), CD20, Folate receptor alpha, Receptor tyrosine-protein kinase ERBB2 (Her2/neu), Mucin 1, cell surface associated (MUC1), epidermal growth factor receptor (EGFR), neural cell adhesion molecule (NCAM), carbonic anhydrase IX (CA1X), tyrosinase, Fucosyl GM1, sialyl Lewis adhesion molecule (sLe), ganglioside GM3, transglutaminase 5 (TGS5), high molecular weight-melanoma associated antigen (HMWMAA), claudin 6 (CLDN6), thyroid stimulating hormone receptor (TSHR), G protein coupled receptor class C group 5 member D (GPRC5D), chromosome X open reading frame 61 (CXORF61), CD97; CD179a, anaplastic lymphoma kinase (ALK), mammary gland differentiation antigen (NY-BR-1), Wilms tumor protein (WT1), Cancer/testis antigen 1 (NY-ESO-1), Melanoma-associated antigen 1 (MAGE-A1), melanoma antigen recognized by T cells 1 (MelanA or MARTI), Rat sarcoma (Ras) mutant, human Telomerase reverse transcriptase (hTERT), human papilloma virus E6 (HPV E6), human papilloma virus E7 (HPV E7), CD79a, CD79b, CD72, Leukocyte-associated immunoglobulin-like receptor 1 (LAIRl), C-type lectin domain family 12 member A (CLEC12A), EGF-like module-containing mucin-like hormone receptor-like 2 (EMR2), lymphocyte antigen 75 (LY75), Glypican-3 (GPC3), Fc receptor-like 5 (FCRL5), immunoglobulin lambda-like polypeptide 1 (IGLLl), Biotin, c-MYC epitope

Tag, CD34, LAMP1 TROP2, GFRalpha4, CDH17, CDH6, CDH19, CD200R, Slea (CA19.9, Sialyl Lewis Antigen), PTK7, CDH1-CD324, DLL3, IL11Ra, IL13Ra2, CD179b-IGLl1, TCR-gamma-delta, NKG2D, CD32 (FCGR2A), CSPG4-HMW-MAA, Tim1-/HVCR1, CSF2RA (GM-CSFR-alpha), TGFbetaR2, VEGFR2/KDR, Lewis Ag, TCR-alpha chain, TCR-beta1 chain, TCR-beta2 chain, TCR-gamma chain, TCR-delta chain, FITC, Luteinizing hormone receptor (LHR), Follicle stimulating hormone receptor (FSHR), Chorionic Gonadotropin Hormone receptor (CGHR), CCR4, GD3, SLAMF6, SLAMF4, HIV1 envelope glycoprotein, HTLV1-Tax, CMV pp65, EBV-EBNA3c, influenza A hemagglutinin (HA), GAD, PDL1, Guanylyl cyclase C (GCC), KSHV-K8.1 protein, KSHV-gH protein, auto antibody to desmoglein 3 (Dsg3), autoantibody to desmoglein 1 (Dsg1), HLA-A2, HLA-A2:01, HLA-B; HLA-C; HLA-DP, HLA-DM, HLA-DOA, HLA-DOB, HLA-DQ, HLA-DR; HLA-G, IGE, CD99, Lym1, Lym2, RAS G12V, Tissue Factor 1 (TF1), AFP, GPRC5D, claudin18.2 (CLD18A2 or CLDN18A.2), STEAP1, STEAP2, LIV1, NECTIN-4, CRIPTO, GPA33, BST1/CD157, low conductance chloride channel, TAJ/TNFRSF19, MPL (TPO-R), KIR3DL2, CD32b, CD229, Toso, BAFF-R, OR2H1, p95-Her2, huTAG2, immunoglobulin kappa light chain, immunoglobulin gamma light chain, SARS-cov2 spike glycoprotein, SARS-cov2 Receptor binding domain, CSF1R, mutant p53, p53-R175H mutant, p53-R248Q mutant, NPM1c, PRAME1, Melanoma-associated antigen 4 (MAGE-A4), gp100, IL23R, MYCN, and Myelin Oligodendrocyte Glycoprotein (MOG).

8. The at least one recombinant polynucleotide encoding a HC-SAR of claim 1 or 3, wherein the one or more non-TCR antigen binding domain(s) and/or AABD are selected from the group consisting of

   a) a variable light (vL) domain comprising a sequence of any one of SEQ ID Nos: 8719-8734, 20386-20396, 40759-41029, a sequence with at least 85% identity thereto in the framework region, or a sequence having up to 10 conservative amino acid substitutions in the framework region and containing the CDRs of any of the forgoing polypeptides and a complementary variable heavy (vH) domain comprising a sequence of any one of SEQ ID Nos: 8743-8758, 20405-20415, 41030-41300 or a sequence with at least 85% identity thereto in the framework region or a sequence having up to 10 conservative amino acid substitutions in the framework region and containing the CDRs of any of the forgoing polypeptides;

b) a single domain antibody, a vHH domain, a SVH, and/or FHVH domain comprising a sequence as set forth in any one of SEQ ID NOs 8792-8806, 41572-41590, 43217-43318, a sequence with at least 85% identity thereto in the framework region, or a sequence having up to 10 conservative amino acid substitutions in the framework regions and containing the CDRs of any of the forgoing polypeptides;

c) a non-immunoglobulin antigen binding domains having a sequence as set forth in any of SEQ ID Nos 43364-43375, 43406-43410, a sequence with at least 85% identity thereto, or a sequence having up to 10 conservative amino acid substitutions;

d) an scFv domains comprising light chain complementary determining regions 1-3 (LC-CDR1-3) for a selected target antigen as set forth in any of SEQ ID Nos. 20989-21015, 41591-41861; 21024-21050, 41862-42132, 21059-21085, 42133-42403, and complementary heavy chain variable region (vH) that comprises one or more of heavy chain complementary determining regions 1-3 (HC-CDR1-3) for a selected target antigen as set forth in any of SEQ ID Nos. 21094-21120 and 42404-42674; 21129-21155, 42675-42945, and 21164-21190, 42946-43216;

e) an scFv fragment having a sequence selected from the group consisting of SEQ ID Nos. 8767-8782, 20424-20434, 41301- 41571, a sequence with at least 85% identity thereto in the framework region, or a sequence each having up to 10 conservative amino acid substitutions in the framework regions and containing the CDRs of any of the forgoing polypeptides;

f) one or more receptors comprising of amino acid sequences of any of SEQ ID Nos. 43377-43392 a sequence with at least 85% identity thereto, or sequence having up to 10 conservative amino acid substitutions;

g) one or more ligands comprising a sequence of any of SEQ ID Nos. 43394-43404, a sequence with at least 85% identity thereto, or sequence having up to 10 conservative amino acid substitutions;

h) an extracellular domain of CD16A, NKG2D, CD4, PD1, or desmoglein 3 (Dsg3);

i) an extracellular domain of one or more of hTPO, mTPO, CGHα chain, CGHβ chain, FHβ chain, LHβ chain, TSHβ chain, APRIL, or any combination thereof;

j) a light chain variable region (vL) comprising one or more of light chain complementary determining regions 1-3 (LC-CDR1-3) for a selected target antigen as set forth in any of

SEQ ID Nos. 20989-21015, 41591-41861, 21024-21050, 41862-42132, 21059-21085, 42133-42403, and a complementary heavy chain variable region (vH) comprising one or more of heavy chain complementary determining regions 1-3 (HC-CDR1-3) for a selected target antigen as set forth in any of SEQ ID Nos. 21094-21120, 42404-42674, 21129-21155, 42675-42945, 21164-21190, 42946-43216; and

k) any combination thereof.

9. The at least one recombinant polynucleotide of claim 1, wherein

a) the recombinant polynucleotide comprises a nucleic sequence selected from the group consisting of SEQ ID NO:32272, 32275, 32551-32599, 33581-33672, 33737-33839, 33894-33986, 34051-34143, 34208-34301, 34365-34458, 34522-34614, 34679-34771, 34836-34928, 34993-35085, 35151-35242, 35307-35399, 35464-35556, 35621-35714, 35935-36027, 36092-36184, 36249-36341, 36406-36498, 37505-37597, 37662-37754, 37819-37911, 37976-38068, 38133-38225, 38290-38382, 38447-38539, 38604-38696, 38918-39010, 39075-39167, 39232-39324, 39389-39481, 39546- 39638, 39860-39951, 39703-39795, 40017- 40109, 40146-40434, 40484-40485, and 8076-8103, or a sequence with at least 70% sequence identity thereto; and/or

b) the encoded HC-SAR has a sequence that is at least 80% identical to a sequence encoded by a recombinant polynucleotide comprising a nucleic sequence selected from the group consisting of SEQ ID NO:32272, 32275, 32551-32599, 33581-33672, 33737-33839, 33894-33986, 34051-34143, 34208-34301, 34365-34458, 34522-34614, 34679-34771, 34836-34928, 34993-35085, 35151-35242, 35307-35399, 35464-35556, 35621-35714, 35935-36027, 36092-36184, 36249-36341, 36406-36498, 37505-37597, 37662-37754, 37819-37911, 37976-38068, 38133-38225, 38290-38382, 38447-38539, 38604-38696, 38918-39010, 39075-39167, 39232-39324, 39389-39481, 39546- 39638, 39860-39951, 39703-39795, 40017- 40109, 40146-40434, 40484-40485, and 8076-8103.

10. A hybrid chain synthetic antigen receptor (HC-SAR) polypeptide encoded by a recombinant polynucleotide of claim 1.

11. A vector comprising the recombinant polynucleotide of claim 1, wherein the vector is selected from the group consisting of: a DNA vector, an RNA vector, a plasmid, a lentivirus vector, an adenoviral vector, a retrovirus vector, a baculovirus vector, a Sleeping Beauty transposon vector, and a piggyBac transposon vector.

12. An immune effector cell or a stem cell that

    (i) expresses an HC-SAR polypeptide of claim 10; and/or

    (ii) has been transfected with the one or more recombinant polynucleotides of claim 1; and/or

    (iii) has been transduced with the one or more vectors of claim 11.

13. A composition comprising at least one recombinant polynucleotide of claim 1, and/or at least one HC-SAR polypeptide of claim 10, and/or a vector of claim 11, and/or or an immune effector cell of claim 12, together with a pharmaceutically acceptable carrier or excipient, for use in providing anti-disease immunity to a subject.

14. Use of a composition of claim 13 in the manufacture of a medicament for the treatment of a disorder in a subject, wherein the disorder is selected from the group consisting of: cancer, an infectious disease, an allergic disease, a degenerative disease, or an autoimmune disease.

15. The composition of claim 13, which further comprises – or is co-administered in combination with – a stem cell, wherein in said stem cell one or more target antigens of the HC-SAR have been deleted or mutated so as to not be recognized by the HC-SAR, and optionally wherein the one or more target antigens in the stem cell are selected from the group consisting of: CD19, CD20, CD22, CD30, CD33, CD38, CD45, CD70, CD79b, CD123, CD138, CD157, CD179b, CD200R, CD276 (B7-H3), CD324, MPL (TPOR), FLT3, Lym1, Lym2, CS1, BCMA, GPRC5D, CLL-1, CSF2RA, LAMP1, TSHR, Tn antigen, NKG2D, CXCR4, TCR-β1, TCR-β2, BST1 (CD157), IL1RAP, ALK, Folate Receptor 1, and ROR1.