

CLAIMS

1. A polypeptide comprising an effector module, said effector module comprising:
i) a stimulus response element (SRE), wherein the SRE comprises a drug responsive domain (DRD), said DRD comprising human carbonic anhydrase 2 (CA2) as set forth by SEQ ID NO. 5810 or a region thereof, and further comprising one or more mutations relative to the amino acid sequence of SEQ ID NO. 5810, wherein the one or more mutations relative to the amino acid sequence of SEQ ID NO: 5810 correspond to:

a H122Y mutation in the amino acid at position 122 (H122),
a R27L mutation in the amino acid at position 27 (R27),
a T87I mutation in the amino acid at position 87 (T87),
a N252D mutation in the amino acid at position 252 (N252),
an I59N mutation in the amino acid at position 59 (I59),
a G102R mutation in the amino acid at position 102 (G102),
a L156H mutation in the amino acid at position 156 (L156),
a S56N mutation in the amino acid at position 56 (S56),
a G63D mutation in the amino acid at position 63 (G63),
an E69V mutation in the amino acid at position 69 (E69),
a N231L mutation in the amino acid at position 631 (N231),
a D71L mutation in the amino acid at position 71 (D71),
a T87N mutation in the amino acid at position 87 (T87),
a L250R mutation in the amino acid at position 250 (L250),
a D72F mutation in the amino acid at position 72 (D72),
a V241F mutation in the amino acid at position 241 (V241),
a P249L mutation in the amino acid at position 249 (P249),
a L183S mutation in the amino acid at position 183 (L183)
a L197P mutation in the amino acid at position 197 (L197),
a S172C mutation in the amino acid at position 172 (S172),
a F178Y mutation in the amino acid at position 178 (F178),
an E186D mutation in the amino acid at position 186 (E186),
or any combination thereof; and

ii) at least one payload which is operably linked to the SRE, wherein the payload comprises CD40L as set forth by SEQ ID NO. 6 or a portion thereof comprising one or more mutations relative to the amino acid sequence of SEQ ID NO. 6, wherein the one or more mutations relative to the amino acid sequence of SEQ ID NO: 6 correspond to:

a S110G mutation in the amino acid at position 110 (S110),
a F111G mutation in the amino acid at position 111 (F111),
an E112S mutation in the amino acid at position 112 (E112),
a M113G mutation in the amino acid at position 113 (M113),
a Q114G mutation in the amino acid at position 114 (Q114),
a K115S mutation in the amino acid at position 115 (K115), or
any combination thereof.

2. The polypeptide of claim 1, wherein the DRD comprises the region of human CA2 corresponding to amino acids 2 to 260 of SEQ ID NO. 5810.

3. The polypeptide of claim 1, wherein the DRD comprises the region of human CA2 corresponding to the full-length CA2 comprising amino acids 1 to 260 of SEQ ID NO. 5810.

4. The polypeptide of any one of claims 1-3, wherein the SRE is responsive to one or more stimuli.

5. The polypeptide of claim 4, wherein the stimulus is a small molecule, wherein the small molecule is selected from Acetazolamide, Celecoxib, Valdecoxib, Rofecoxib, Methazolamide, Dorzolamide, Brinzolamide, Diclofenamide, Ethoxzolamide, Zonisamide, Dansylamide, or Dichlorphenamide.

6. A composition comprising the polypeptide of any one of claims 1-5.

7. A polynucleotide encoding the polypeptide of any one of claims 1-5, wherein the polynucleotide is a DNA molecule or an RNA molecule.

8. A vector comprising the polynucleotide of claim 7.
9. A cell comprising the polypeptide of any one of claims 1-5 or the vector of claim 8.
10. The cell of claim 9, wherein:
 - (i) said cell is an immune cell for adoptive cell transfer (ACT); or
 - (ii) said cell is a CD8⁺ T cell, a CD4⁺ T cell, a helper T cell, a natural killer (NK) cell, a NKT cell, a cytotoxic T lymphocyte (CTL), a tumor infiltrating lymphocyte (TIL), a memory T cell, a regulatory T (Treg) cell, a cytokine-induced killer (CIK) cell, a dendritic cell, lymphokine activated killer (LAK) cells, a human embryonic stem cell, a mesenchymal stem cell, a hematopoietic stem cell, or a mixture thereof.
11. The cell of claim 9 or 10, wherein said cell is modified to express a chimeric antigen receptor (CAR) or an antigen-specific T cell receptor (TCR).
12. The cell of claim 11, wherein said cell is a T cell or tumor infiltrating lymphocyte.
13. A composition for use in treating a disease and/or inducing an immune response in a subject in need thereof, said composition comprising:
 - (a) a therapeutically effective amount of any of the polypeptides of claims 1-5, or the cell of any one of claims 9-12; and
 - (b) a therapeutically effective amount of a stimulus,wherein the SRE is responsive to the stimulus and wherein expression of the at least one payload is modulated in response to the stimulus to thereby treat the disease and/or induce an immune response.
14. The composition for use of claim 13, wherein the disease is cancer.
15. The composition for use according to claim 13 or 14, wherein the stimulus is selected from Acetazolamide, Celecoxib, Valdecoxib, Rofecoxib, Methazolamide, Dorzolamide, Brinzolamide, Diclofenamide, Ethoxzolamide, Zonisamide, Dansylamide, or Dichlorphenamide.