

CLAIMS

1. A stimulus response element (SRE) comprising at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% identity to a human carbonic anhydrase 2 (CA2; SEQ ID NO: 11717)~~in whole or in part,~~ wherein the CA2 ~~further~~ comprises one or more mutations selected from L156H, I59N, G102R, S56N, G63D, D71L, E186D, W208S, E69V, N231I, R27L, T87I, H122Y, N252D, D72F, V241F, P249L, T87N, L250R, L183S, S172C, F178Y, L197P, or any combination thereof.
2. The SRE of claim 1, wherein the SRE is CA2 (aa 2-260 of WT, L156H)(SEQ ID NO: 210600), CA2 (L156H)(SEQ ID NO: 210602), CA2 (aa 2-260 of WT, I59N, G102R)(SEQ ID NO: 210598), CA2 (aa 2-260 of WT, S56N)(SEQ ID NO: 210498), CA2 (aa 2-260 of WT, G63D, E69V, N231I)(SEQ ID NO: 210748), CA2 (aa 2-260 of WT, R27L, T87I, H122Y, N252D)(SEQ ID NO: 210702), CA2 (aa 2-260 of WT, D72F, V241F, P249L)(SEQ ID NO: 210503), CA2 (aa 2-260 of WT, D71L, T87N, L250R)(SEQ ID NO: 210510), CA2 (aa 2-260 of WT, L183S)(SEQ ID NO: 210512), CA2 (aa 2-260 of WT, L156H, S172C, F178Y, E186D)(SEQ ID NO: 210756), CA2 (aa 2-260 of WT, L197P)(SEQ ID NO: 210760), or CA2 (aa 2-260 of WT, W208S)(SEQ ID NO: 210494).
3. The SRE of claim 2, wherein the SRE is CA2 (aa 2-260 of WT, L156H), said SRE comprising SEQ ID NO: 210600.
4. The SRE of claim 2, wherein the SRE is CA2 (L156H), said SRE comprising SEQ ID NO: 210602.
5. The SRE of claim 2, wherein the SRE is CA2 (aa 2-260 of WT, S56N), said SRE comprising SEQ ID NO: 210498.
6. The SRE of claim 1, wherein the mutation is S56N.
7. The SRE of claim 1, wherein the SRE is responsive to one or more stimuli.

8. The SRE of claim 7, wherein the stimulus is a small molecule and wherein the small molecule is Acetazolamide or Celecoxib.
9. A CA2 biocircuit system comprising at least one effector module, said at least one effector module comprising:
- (a) a stimulus response element (SRE) comprising at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% identity to a human carbonic anhydrase 2 (CA2; SEQ ID NO: 11717)~~in whole or in part,~~ wherein the CA2 ~~further~~ comprises one or more mutations selected from L156H, I59N, G102R, S56N, G63D, D71L, E186D, W208S, E69V, N231I, R27L, T87I, H122Y, N252D, D72F, V241F, P249L, T87N, L250R, L183S, S172C, F178Y, L197P, or any combination thereof; and
 - (b) at least one payload, wherein the at least one payload is attached, appended or associated with said SRE.
10. The CA2 biocircuit system of claim 9, wherein the SRE is CA2 (aa 2-260 of WT, L156H)(SEQ ID NO: 210600), CA2 (L156H)(SEQ ID NO: 210602), CA2 (aa 2-260 of WT, I59N, G102R)(SEQ ID NO: 210598), CA2 (aa 2-260 of WT, S56N)(SEQ ID NO: 210498), CA2 (aa 2-260 of WT, G63D, E69V, N231I)(SEQ ID NO: 210748), CA2 (aa 2-260 of WT, R27L, T87I, H122Y, N252D)(SEQ ID NO: 210702), CA2 (aa 2-260 of WT, D72F, V241F, P249L)(SEQ ID NO: 210503), CA2 (aa 2-260 of WT, D71L, T87N, L250R)(SEQ ID NO: 210510), CA2 (aa 2-260 of WT, L183S)(SEQ ID NO: 210512), CA2 (aa 2-260 of WT, L156H, S172C, F178Y, E186D)(SEQ ID NO: 210756), CA2 (aa 2-260 of WT, L197P)(SEQ ID NO: 210760), or CA2 (aa 2-260 of WT, W208S)(SEQ ID NO: 210494).
11. The CA2 biocircuit system of claim 10, wherein the SRE is CA2 (aa 2-260 of WT, L156H), said SRE comprising SEQ ID NO: 210600.

12. The CA2 biocircuit system of claim 10, wherein the SRE is CA2 (L156H), said SRE comprising SEQ ID NO: 210602.
13. The CA2 biocircuit system of claim 10, wherein the SRE is CA2 (aa 2-260 of WT, S56N), said SRE comprising SEQ ID NO: 210498.
14. The CA2 biocircuit system of claim 9, wherein the mutation is S56N.
15. The CA2 biocircuit system of claim 9, wherein the payload is a cytokine or a CAR.
16. The CA2 biocircuit system of claim 9, wherein the payload is IL-12, CD40L, or CD19 CAR.
17. The CA2 biocircuit system of claim 16, wherein the IL-12 is membrane bound IL-12.
18. The CA2 ~~biocircuit~~biocircuit system of claim 9, wherein the effector molecule comprises the amino acid sequence of SEQ ID NO: 210927, 210935, 210939, 210933, 210937, 210929, 210931, 210941, 210943, 210945, or 210947.
19. The CA2 biocircuit system of claim 9, wherein the effector molecule comprises the amino acid sequence of SEQ ID NO: 210692, 210694, or 210955.
20. The CA2 biocircuit system of claim 9, wherein the SRE is responsive to one or more stimuli, wherein the one or more stimuli comprise a small molecule and wherein the small molecule is Acetazolamide or Celecoxib.