

CLAIMS

1. A composition comprising an effector module, said effector module comprising a stimulus response element (SRE) operably linked to a payload, wherein said payload comprises a mutant CD40L comprising a deletion of S110-G116 relative to SEQ ID NO:3820 or one or more mutations selected from Y170G, Y172G, H224G, G226F, G226H, G226W, or G227F relative to SEQ ID NO: 3820.
2. The composition of claim 1, wherein said SRE comprises, in whole or in part, a drug responsive domain (DRD) selected from an estrogen receptor (ER_γ), an *E. coli* dihydrofolate reductase ecDHFR, a FK506 binding protein (FKBP_γ), a Phosphodiesterase 5 (PDE5) protein, or a human dihydrofolate reductase (hDHFR) protein, wherein the DRD comprises one or more mutations.
3. The composition of claim 2, wherein the DRD is derived from an ER protein and wherein the DRD has an amino acid sequence comprising SEQ ID NO: 633, 637, 641, 642, 644, 646, 648, 650, 652, 654, 656, 658, 660, 662, 664, 666, 668, 670, 672, 674, 676, 678, 680, 682, 684, 686, 688, 690, 692, 694, 696, 698, 700, 702, 704, 706, 708, 710, 712, 714, 716, 718, 720, 722, 724, or 726.
4. The composition of claim 2, wherein the DRD is derived from an ecDHFR protein, and wherein the DRD has an amino acid sequence comprising SEQ ID NO: 253, 255, 264, 267, 269, 6554, 6556, 6558, 6560, 6562, 6564, 6566, 6568, 6570, 6572, 6574, 6576, 6578, 6580, 6582, 6584, 6586, 6588, or 6590.
5. The composition of claim 2, wherein the DRD is derived from a FKBP protein, and wherein the DRD has an amino acid sequence comprising SEQ ID NO: 270, 271, 272, 274, 277, 285 or 286.
6. The composition of claim 2, wherein the DRD is derived from a PDE5 protein, and wherein the DRD has an amino acid sequence comprising SEQ ID NO: 294, 296, 298, 300, 302, 306, 308,

313, 315, 317, 318, 319, 320, 321, 322, 323, 324, 325, 326, 327, 328, 329, 330, 331, 332, 333, 335, 336, 337, 338, 339, 340, 341, 342, 343, 344, 345, 346, 347, 348, 349, 350, 351, 352, 353, 354, 355, 356, 357, 358, 359, 360, 361, 362, 363, 364, 365, 366, 367, 368, 369, 370, 371, 372, 375, 378, 381, 384, 387, 389, 391, 394, 397, 400, 403, 406, 409, 412, 415, 417, 420, 422, 424, 426, 428, 430, 432, 434, 436, 438, 440, 442, 444, 446, 448, 450, 452, 454, 456, 458, 460, 462, 464, 466, 468, 470, 472, 474, 476, 478, 480, 482, 484, 486, 488, 490, 492, 494, 496, 498, 500, 502, 504, 506, 508, 510, 512, 514, 516, 518, 520, 522, 524, 526, 528, 530, 532, 534, 536, 538, 540, 542, 544, 546, 548, 550, 552, 554, 556, 558, 560, 563, 565, 567, 569, 571, 573, 575, 577, 579, 581, 583, 585, 587, 589, 591, 593, 595, 597, 599, 601, 603, 605, 607, 609, 611, 613, 615, 617, 619, 621, 623, 625, 627, 629, 631, 6406, 6408, 6410, 6412, 6414, 6416, 6418, 6420, 6422, 6424, 6426, 6428, 6430, 6432, 6434, 6436, 6438, 6440, 6442, 6444, 6446, 6448, 6450, 6452, 6454, 6456, 6458, 6460, 6462, 6464, 6466, 6468, 6470, 6472, 6474, 6476, 6478, 6480, 6482, 6484, 6486, 6488, 6490, 6492, 6494, 6496, 6498, 6500, 6502, 6504, 6506, 6508, 6510, 6512, 6514, 6516, 6518, 6520, 6522, 6524, 6526, 6528, or 6530.

7. The composition of claim 2, wherein the DRD is derived from an hDHFR protein, and wherein the DRD has an amino acid sequence comprising SEQ ID NO: 78, 80, 82, 84, 86, 88, 90, 92, 94, 96, 98, 100, 102, 104, 106, 108, 110, 112, 114, 116, 118, 119, 121, 123, 125, 127, 129, 131, 133, 135, 137, 139, 141, 143, 145, 149, 151, 153, 155, 157, 159, 161, 163, 165, 166, 168, 170, 172, 174, 176, 179, 181, 183, 187, 189, 191, 193, 195, 197, 201, 203, 205, 207, 209, 210, 212, 214, 216, 218, 221, 223, 225, 227, 229, 231, 233, 235, 237, 239, 241, 243, 245, 247, 249, 251, or 6552.

8. The composition of claim 1, wherein the DRD is responsive to or interacts with at least one stimulus.

9. The composition of claim 8, wherein the stimulus is a small molecule.

10. An effector module, said effector module comprising a drug responsive element (DRD) operably linked to a payload, wherein said DRD comprises, in whole or in part, an ER, an ecDHFR,

a FKBP, a PDE5, or an hDHFR protein comprising one or more mutations and wherein said payload comprises in whole or in part a human CD40L comprising one or more mutations.

~~11. The effector module of claim 10, wherein the effector module comprises an amino acid sequence selected from: SEQ ID NO: 6546, or SEQ ID NO: 6550, or SEQ ID NO: 6620, or SEQ ID NO: 6622, or SEQ ID NO: 6624, or SEQ ID NO: 6626, or SEQ ID NO: 6628, or SEQ ID NO: 6630, or SEQ ID NO: 6632, or SEQ ID NO: 6634, or SEQ ID NO: 6636, or SEQ ID NO: 6638, or SEQ ID NO: 6640, or SEQ ID NO: 6642, or SEQ ID NO: 6644, or SEQ ID NO: 6646, or SEQ ID NO: 6648, or SEQ ID NO: 6650, or SEQ ID NO: 6652, or SEQ ID NO: 6654, or SEQ ID NO: 6656, or SEQ ID NO: 6658, or SEQ ID NO: 6660, or SEQ ID NO: 6662, or SEQ ID NO: 6664, or SEQ ID NO: 6666, or SEQ ID NO: 6668, or SEQ ID NO: 6670, or SEQ ID NO: 6672~~ The effector module of claim 10, wherein the effector module comprises.

12. The effector module of claim 10, wherein the DRD comprises an amino acid sequence of SEQ ID NO: 253, 255, 264, 267, 269, 6554, 6556, 6558, 6560, 6562, 6564, 6566, 6568, 6570, 6572, 6574, 6576, 6578, 6580, 6582, 6584, 6586, 6588, or 6590.

13. The effector module of claim 10, wherein the DRD comprises an amino acid sequence of SEQ ID NO: 633, 637, 641, 642, 644, 646, 648, 650, 652, 654, 656, 658, 660, 662, 664, 666, 668, 670, 672, 674, 676, 678, 680, 682, 684, 686, 688, 690, 692, 694, 696, 698, 700, 702, 704, 706, 708, 710, 712, 714, 716, 718, 720, 722, 724, or 726.

14. The effector module of claim 10, wherein the DRD comprises an amino acid sequence of SEQ ID NO: 270, 271, 272, 274, 277, 285 or 286.

15. The effector module of claim 10, wherein the DRD comprises an amino acid sequence of SEQ ID NO: 294, 296, 298, 300, 302, 306, 308, 313, 315, 317, 318, 319, 320, 321, 322, 323, 324, 325, 326, 327, 328, 329, 330, 331, 332, 333, 335, 336, 337, 338, 339, 340, 341, 342, 343, 344, 345, 346, 347, 348, 349, 350, 351, 352, 353, 354, 355, 356, 357, 358, 359, 360, 361, 362, 363, 364, 365, 366, 367, 368, 369, 370, 371, 372, 375, 378, 381, 384, 387, 389, 391, 394, 397, 400, 403, 406, 409, 412, 415, 417, 420, 422, 424, 426, 428, 430, 432, 434, 436, 438, 440, 442, 444,

446, 448, 450, 452, 454, 456, 458, 460, 462, 464, 466, 468, 470, 472, 474, 476, 478, 480, 482, 484, 486, 488, 490, 492, 494, 496, 498, 500, 502, 504, 506, 508, 510, 512, 514, 516, 518, 520, 522, 524, 526, 528, 530, 532, 534, 536, 538, 540, 542, 544, 546, 548, 550, 552, 554, 556, 558, 560, 563, 565, 567, 569, 571, 573, 575, 577, 579, 581, 583, 585, 587, 589, 591, 593, 595, 597, 599, 601, 603, 605, 607, 609, 611, 613, 615, 617, 619, 621, 623, 625, 627, 629, 631, 6406, 6408, 6410, 6412, 6414, 6416, 6418, 6420, 6422, 6424, 6426, 6428, 6430, 6432, 6434, 6436, 6438, 6440, 6442, 6444, 6446, 6448, 6450, 6452, 6454, 6456, 6458, 6460, 6462, 6464, 6466, 6468, 6470, 6472, 6474, 6476, 6478, 6480, 6482, 6484, 6486, 6488, 6490, 6492, 6494, 6496, 6498, 6500, 6502, 6504, 6506, 6508, 6510, 6512, 6514, 6516, 6518, 6520, 6522, 6524, 6526, 6528, or 6530.

16. The effector module of claim 10, wherein the DRD comprises an amino acid sequence of SEQ ID NO: 78, 80, 82, 84, 86, 88, 90, 92, 94, 96, 98, 100, 102, 104, 106, 108, 110, 112, 114, 116, 118, 119, 121, 123, 125, 127, 129, 131, 133, 135, 137, 139, 141, 143, 145, 149, 151, 153, 155, 157, 159, 161, 163, 165, 166, 168, 170, 172, 174, 176, 179, 181, 183, 187, 189, 191, 193, 195, 197, 201, 203, 205, 207, 209, 210, 212, 214, 216, 218, 221, 223, 225, 227, 229, 231, 233, 235, 237, 239, 241, 243, 245, 247, 249, 251, or 6552.

17. The effector module of ~~claim 10~~ claim 10, wherein the DRD is responsive to or interacts with at least one stimulus.

18. The effector module of claim ~~16~~ 17, wherein the stimulus is a small molecule, and said molecule is Trimethoprim (TMP) or Methotrexate (MTX-).

19. The effector module of claim ~~15~~ 17, wherein the stimulus is a small molecule, and said small molecule is Vardenafil, Tadalafil or Sildenafil.

20. The effector module of claim ~~13~~ 17, wherein the stimulus is a small molecule, and said small molecule is Bazedoxifene, Raloxifene, or Shield-1.